Mechanism and Synthetic Use of Paternò-Büchi Reactions: Spin-Mapping and Photo-Aldol Reactions

Inaugural-Dissertation

zur

Erlangung des Doktorgrades

der Mathematisch-Naturwissenschaftlichen Fakultät

der Universität zu Köln

vorgelegt von

Samir Bondock

aus Mansoura

(Ägypten)

Köln 2003

Berichterstatter:	Prof. Dr. A. G. Griesbeck
	Prof. Dr. H. G. Schmalz
Tag der mündlichen Prüfung:	7. 05. 2003

Acknowledgements

I would like to thank Prof. Dr. Axel G. Griesbeck for giving me the opportunity to perform my Ph.D in his group and for his valuable help throughout this work.

I am also grateful to Prof. Dr. H. G. Schmalz and Prof. Dr. G. Meyer for the interest they have shown in this manuscript by accepting to act as referees.

I would like also to acknowledge Prof. Dr. M. S. Gudipati, University of Maryland, for his help and cooperation.

I owe special thanks to the egyptian government for the Ph.D grant.

Prof. Dr. D. Döpp, University of Duisburg is thanked for providing unpublished work during the preparation of CRC reviews.

I am indebted to all staff member of Chemistry Department, Faculty of Science, Mansoura University, Egypt.

All my thanks go to my collegues Tamer El-Idreesy, Stefan Schiffer, Claus Miara, Nesmine Maptue and Anna Bartoschek for the nice work atmosphere. Peter Cygon receives special thanks for his help and friendly cooperation.

Dr. Hans Schmickler, Ms. Ingrid Hoven and Ms. Kathrin Ermer receive a special thanks not only for NMR analyses but also for friendly reaction even when I brought ten probes every day.

The author thanks Mr. Christof Schmitz for UV, IR and elemental analyses and Dr. Mathias Schäfer for mass spectrometry. Dr. Johann Lex is thanked for the X-ray analyses.

Ms. Ingrid Vongerichten and Ms. Monika Boyo should not be forgotten here for their precious help.

A last thank go to my family, my brother Ahmed and of course to my mother for their support during theses 4 years.

List of Publications and Presentations

Publications

1. "Spin-Directed Stereoselectivity of Carbonyl-Alkene Photocycloadditions"
   Axel G. Griesbeck, Maren Fiege, Samir Bondock and Murthy S. Gudipati,
   Organic Letters **2000**, 2, 3623-3625.
2. "Paternò-Büchi reactions of Allylic Alcohols and Acetates with Aliphatic Aldehydes: Evidences for Hydrogen-Bond Activation in the Excited Singlet and Triplet States?
   Axel G. Griesbeck and Samir Bondock,
   J. Am. Chem. Soc. **2001**, 123, 6191-6192.
3. "Temperatur- und Viskositätsabhängigkeit der spingesteuerten Stereoselektivität von Carbonyl-Alken-Photocycloadditionen"
   Axel G. Griesbeck, Samir Bondock und Murthy S. Gudipati,
   Angew. Chem. **2001**, 113, 4828-4832; *Angew. Chem. Int. Ed*. **2001**, 40, 4684-4687.
4. "Spin-Imposed Stereoselection in the Photocycloaddition of cis- and trans-Cyclooctene with Aliphatic Aldehydes"
   Axel G. Griesbeck and Samir Bondock,
   Photochem. Photobiol. Sciences. **2002**, 1, 81-83.
5. "Photo Aldol Reactions with 5-Methoxyoxazoles: Highly Regio- and Diastereoselective Synthesis of α-Amino-β-Hydroxy Carboxylic Acid Derivatives"
   Axel G. Griesbeck and Samir Bondock,
   Can. J. Chem. **2003**, 81, 1-5.
6. "The excimer radiation system: a powerful tool for preparative organic photochemistry. A technical note"
   Axel, G. Griesbeck, Nesmine Maptue, Samir Bondock and Michael Oelgemöller ,
   Photochem. Photobiol. Sciences. **2003**, 2, 450-451.
7. "Photochemical Oxetane Formation: Intermolecular Reactions"
   Axel G. Griesbeck and Samir Bondock,
   in *CRC Handbook of Organic Photochemistry and Photobiology*, William M. Horspool, Phil-S. Song (Hrsg) CRC press: Boca Raton, **2003**, in press.
8. "Photochemical Oxetane Formation: Mechanism and Stereochemistry"
   Axel G. Griesbeck and Samir Bondock,
   in *CRC Handbook of Organic Photochemistry and Photobiology*, William M. Horspool, Phil-S. Song (Hrsg) CRC press: Boca Raton, **2003**, in press.

9. "Substantial ^{2}H-Magnetic Isotope Effects on the Diastereoselectivity of Triplet Photocycloaddition Reactions"
   Axel G. Griesbeck and Samir Bondock,
   J. Am. Chem. Soc. **2003**, submitted.
10. "Synthesis of quaternary α-amino β-hydroxy carboxylic acids. 1. Photo aldol reactions of 5-methoxy oxazoles with aldehydes"
   Axel G. Griesbeck , Samir Bondock and Johann Lex,
   J. Org. Chem. **2003**, in preparation.
11. "Synthesis of quaternary α-amino β-hydroxy carboxylic acids. 2. Photo aldol reactions of 5-methoxy oxazoles with α-keto esters"
   Axel G. Griesbeck , Samir Bondock and Johann Lex,
   J. Org. Chem. **2003**, in preparation.

Posters

1. "Spin-Mapping of [2+2]-Photocycloadditions: Concentration-, Solvent Viscosity- and Temperature Effects"
   Axel G. Griesbeck, Samir Bondock and Murthy S. Gudipati,
   Gordon-Research-Conference, New London, USA July **2001**
2. Spin-Mapping of [2+2]-Photocycloadditions: Concentrations, Temperature, and Solvent Viscosity Effects"
   Axel G. Griesbeck, Samir Bondock, Maren Fiege, and Murthy S. Gudipati,
   Photochirogenesis, Osaka, Japan, September **2001**
3. "Paternò-Büchi-Reaktionen von Allylalkoholen und Allylacetaten mit Aldehyden: Konzentrationsstudien und Spinselecktivität "
   Axel G. Griesbeck, Samir Bondock und Maren Fiege,
   Meeting of the German Chemical Society, Würzburg, september **2001**.
4. "Diastereoselective Photochemical Synthesis of α-Amino-β-Hydroxy Carboxylic Acid Derivatives by Photocycloaddition of Carbonyl Compounds to Oxazoles"
   Samir Bondock and Axel G. Griesbeck,
   IUPAC Conference on Photochemistry, Budapest, Hungary, July **2002**.

5. "Stereoselectivity of [2+2]-Photocycloadditions: Magnetic Isotope Effects"
   Samir Bondock and Axel G. Griesbeck,
   Meeting of the German Chemical Society, Mülheim/Ruhr, April **2003**.

This work was carried out from May 2000 to May 2003 under the supervision of Prof. Dr. Axel G. Griesbeck at the Institute of Organic Chemistry, University of Cologne.

Abbreviation

Ac	Acetyl
Bn	Benzyl
B.p	Boiling point (°C)
BR	Biradical
Bu	Butyl
Bu^i	Isobutyl
Bu^{sec}	*sec*-Butyl
Bu^t	*tert*-Butyl
cc	*cis,cis*
CIP	Contact ion pair
Cp	Centipoise
DCC	Dicyclohexylcarbodiimide
de	Diastereomeric excess
DEPT	Distortionless Enhancement by Polarization Transfer
DMAP	N,N-Dimethylaminopyridine
DMF	Dimethylformamid
dr	Diastereomeric ratio
ΔE_{ST}	Energy difference between the singlet and triplet state
EA	Ethylacetate
EIE	Equilibrium isotope effect
Et	Ethyl
F	Fluorescence intensity
F_0	Initial fluorescence intensity
h	Hour
HE	n-Hexane
HFC	Hyperfine coupling
HMBC	Heteronuclear Multiple Bond Correlation
HOMO	Highest Occupied Molecular Orbital
IC	Internal conversion

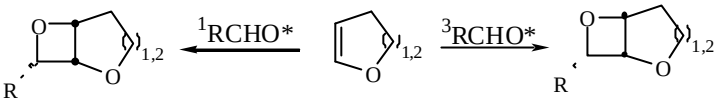
i-Bu	Isobutyl
i-Pr	Isopropyl
ISC	Intersystem Crossing
k_{diff}	Molecular diffusion rate constant
k_q	Bimolecular quenching rate constant
LUMO	Lowest Unoccupied Molecular Orbital
M	Molarity
Me	Methyl
MIE	Magnetic isotope effect
min	Minute
M.p	Melting point (°C)
Naph	Naphthyl
NOE	Nuclear Overhauser Enhancement
NOESY	Nuclear Overhauser Enhancement Spectroscopy
OAc	Acetate
o-Tol.	*ortho*-Tolualdehyde
PET	Photoinduced electron transfer
Ph	Phenyl
Pr	Propyl
Pr^i	Isopropyl
Q	Quencher
ROESY	Rotating Frame Overhauser Enhancement Spectroscopy
R_f	Retention factor
R_s	Reaction probabilty from singlet channel
R_t	Retention time
R_T	Reaction probabilty from triplet channel
RT	Room temperature
S_0	Ground state
S_1	First excited singlet state
Sbo	Samir Bondock
S-1,4-BR	Singlet 1,4-biradical
SLR	Spin-Lattice Relaxation
SOC	Spin-Orbit Coupling
SOI	Secondary Orbital Interaction

T_1	First excited triplet state
T-1,4-BR	Triplet 1,4-biradical
tc	*trans,cis*
TEA	Triethyl amine
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMEDA	Tetramethylethylenediamine
TMS	Trimethylsilyl
tt	*trans,trans*
ε	Molar extinction coefficient
ϕ_T	Relative triplet quantum yield
η	Viscosity
Δ	Reflux
Φ	Quantum yield
λ_{ex}	Excited wavelength
μ	Micro (10^{-6})
τ	Lifetime
*	Excited state
[ ]	Molar concentration

Contents

Abstract

The concentration dependence of the diastereoselectivity of the Paternò-Büchi reaction of a series of cyclic enolethers, cyclooctene, allylic alcohols and acetates, respectively, with aromatic as well as aliphatic aldehydes was studied. For most aliphatic aldehydes, a sharp transition from low to high diastereoselectivity was observed, indicating a distinct switch from singlet to triplet photocycloaddition with different selectivity controlling mechanisms.

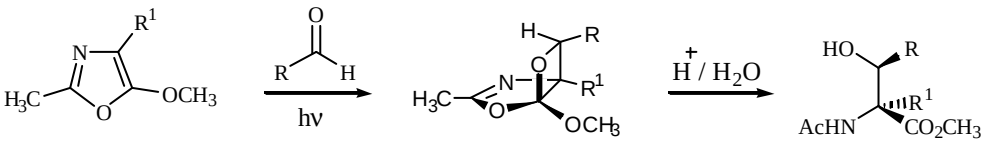


low (*endo*/*exo*) diastereoselectivity
R = Me, Et, i-Bu

high (*endo*/*exo*) diastereoselectivity
R = Me, Et, i-Bu, Ph

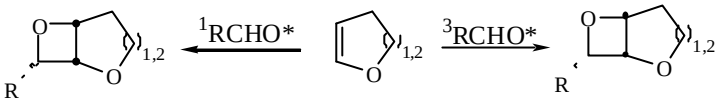
Furthermore, the effect of solvent viscosity and temperature on the spin-directed stereoselectivity of the carbonyl-ene photocycloaddition was investigated. The variation of the solvent viscosity over a large range resulted in a weak but significant increase in the *endo*-selectivity of triplet benzaldehyde cycloaddition to 2,3-dihydrofuran from 82 to 91 %. For aliphatic aldehydes, the diastereoselectivity strongly increased with increasing solvent viscosity. The temperature dependence of the *endo/exo*-selectivity with aliphatic aldehydes RCHO (R = Me, Et, i-Bu) showed characteristic non-linear behavoir with inversion points from which activation parameters for singlet as well as the triplet photocycloaddition were determined.

5-Methoxyoxazole derivatives were prepared and evaluated with respect to their use as diene components in stereoselective Paternò-Büchi reaction. These oxazoles were versatile synthetic building blocks that reacted with various photoexcited aliphatic as well as aromatic carbonyl compounds with high regioselectvity and excellent *exo*-diastereoselectvity. Hydrolysis of the primary photoadducts resulted in twofold ring-opening and provided a convenient and high yielding access to *erythro* (S*,S*) α-amino-β-hydroxy carboxylic acid derivatives.



Kurzzusammenfassung

Die Konzentrationsabhängigkeit der Diastereoselektivität von Paternò-Büchi-Reaktionen einer Reihe cyclischer Enolether, Allylalkohole und –acetate mit aromatischen bzw. aliphatischen Aldehyden wurde untersucht. Bei den meisten aliphatischen Aldehyden wurde ein relativ scharfer Übergang von niedriger zu hoher Diastereoselektivität registriert, der auf einen klar ausgeprägten Wechsel zwischen Singulett- und Triplett-Photocycloaddition mit jeweils unterschiedlichen Kontrollmechanismen hinweist.

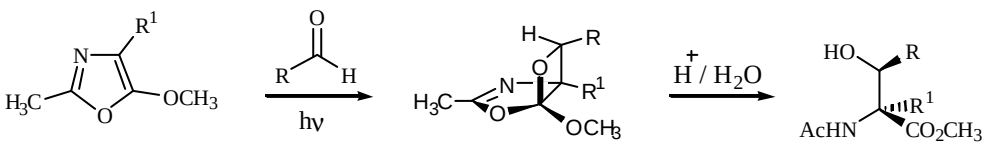


low (*endo*/*exo*)
diastereoselectivity
R = Me, Et, i-Bu

high (*endo*/*exo*)
diastereoselectivity
R = Me, Et, i-Bu, Ph

Weiterhin wurde der Effekt von Lösungsmittelviskosität sowie Reaktionstemperatur auf die spin-gesteuerte Stereoselektivtiät der Carbonyl-En-Photocycloaddition untersucht. Die Variation der Lösungsmittelviskosität über einen grossen Bereich ergab eine kleine, aber signifikante Erhöhung der *endo*-Selektivität von 82% auf 91% für die Addition von Triplett-Benzaldehyd an 2,3-Dihydrofuran. Im Falle aliphatischer Aldehyde stiegt die Diastereoselektivität stark mit zunehmender Lösungsmittelviskosität an. Die Temperaturabhängigkeit der *endo/exo*-Selektivität aliphatischer Aldehyde RCHO (R = Me, Et, i-Bu) wies ein charakteristisches nicht-lineares Verhalten mit Inversionspunkten auf, aus dem Aktivierungsparameter sowohl für die Singulett- als auch die Triplett-Photocycloaddition ermittelt wurden.

Derivate von 5-Methoxyoxazol wurden hergestellt und auf ihre Eignung als Dienkomponenten in stereoselektiven Paternò-Büchi-Reaktionen untersucht. Diese Oxazole erwiesen sich als vielseitige Bausteine, welche mit verschiedenen angeregten aliphatischen sowie aromatischen Carbonylkomponenten mit hoher Regio- und exzellenter (*exo*)-Diastereoselektivität reagierten. Die Hydrolyse der primären Cycloaddukte führte zu einer zweifachen Ringöffnung und ergab so einen bequemen und mit hohen Ausbeuten verlaufenden Zugang zu *erythro* (S*,S*) α-Amino-β-hydroxycarbonsäurederivaten.



1. Introduction

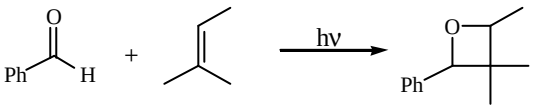
General outlook of spin chemistry

In a recent brilliant feature article[1], Ahmed H. Zewail presented a striking and impressive overview of the new frontier in modern chemistry-femtochemistry, which explores atomic motions on the potential energy surface, vibrational and rotational coherence of the wave pacets, and transition state spectra, geometry, and dynamics. Another new frontier is *spin chemistry*, which monitors the behavior of angular momentum (spin) of electrons and nuclei in chemical reactions (including coherence of spin wave pacets), spin dynamics and spin state of evolution of reactants.

Spin chemistry is based on the fundamental and universal principle of spin conservation: all chemical reactions are spin-selective, they are allowed only for those spin states of reactants whose total spin is identical to that of products. Spin chemistry is unique: it introduces in chemistry magnetic interactions. Contributing almost nothing in chemical energy, being negligibly small and traditionally ignorable, magnetic interactions are the only ones which are able to change electron spin of reactants and switch over the reaction between spin-allowed and spin-forbidden channels. Ultimately, they control chemical reactivity and write a new magnetic scenario of chemical reaction.[2]

Historical

The [2+2] photocycloaddition of a carbonyl compound with an alkene is termed Paternò-Büchi reaction. The process described in the original publication by Paternò and Chieffi in 1909 was the addition of benzaldehyde to 2-methyl-2-butene using solar irradiation.[3] Although Paternò and Chieffi suggested the correct structure for the photoproduct, it was not until 1954 that Büchi and collaborators[4] reinvestigated the reaction and confirmed unambiguously the structure proposed originally by the Italian scientists.



Scheme 1.1: Paternò-Büchi reaction of benzaldehyde with 2-methyl-2-butene.

The Paternò-Büchi reaction has become familiar to chemists interested in both the mechanistic aspects of the photochemistry and applications in modern organic synthesis. Since the first review of the Paternò-Büchi reaction in 1968[5], several reviews have been devoted to the mechanistic aspects and also to synthetic application.[6-9]

1.1 Mechanistic studies

The light-absorbing species responsible for Paternò-Büchi cycloaddition is usually the carbonyl addend. The long wavelength absorption band for alkanones and alkanals appears at 280-300 nm and corresponds to a weak transition (log ε~10-20) involving excitation of a non-bonding electron on oxygen (n,π^*) (Figure 1.1).

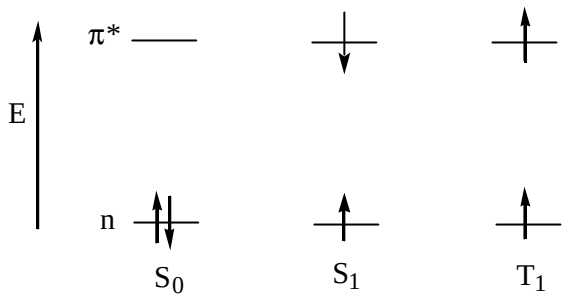


Figure 1.1: Molecular orbital diagram and electron occupation for ground (S_0), first excited singlet (S_1), and first excited triplet states (T_1) for carbonyl compounds.

Aromatic and other simple conjugated carbonyl compounds undergo a similar n,π^* transition at 320-350 nm. Quinones and 1,2-dicarbonyl compounds absorb in the 400-500 nm range. Absorption data for representative carbonyl compounds is collected in Table1.1.

Table 1.1: Absorption data and excitation energies for carbonyl compounds.

Carbonyl compound	λ max (nm)	E (S_1) (kcal/mol)	E (T_1) (kcal/mol)
Butanal	280	85	78
Acetone	280	85	78
Benzaldehyde	290	82	72
Benzophenone	330	75	68
Biacetyl	420	62	56
p-Benzoquinone	456	58	50

Excitation in the short wavelength bands of these carbonyl chromophores or at higher energy is followed by rapid non-radiative decay to the lowest vibrational level of the first excited singlet carbonyl state (S_1) (Figure 1.2). The half occupied molecular orbitals (e.g., n and π^*), generated on absorption of a photon, initially have paired electron spins (Figure 1.1). However, a more stable electronic configuration is one having unpaired or parallel spins. The

triplet excited electronic state (T_1) is not easily accessible through direct excitation due to spin forbidden excitation, but is generated through intersystem crossing (ISC) (Figure 1.2).

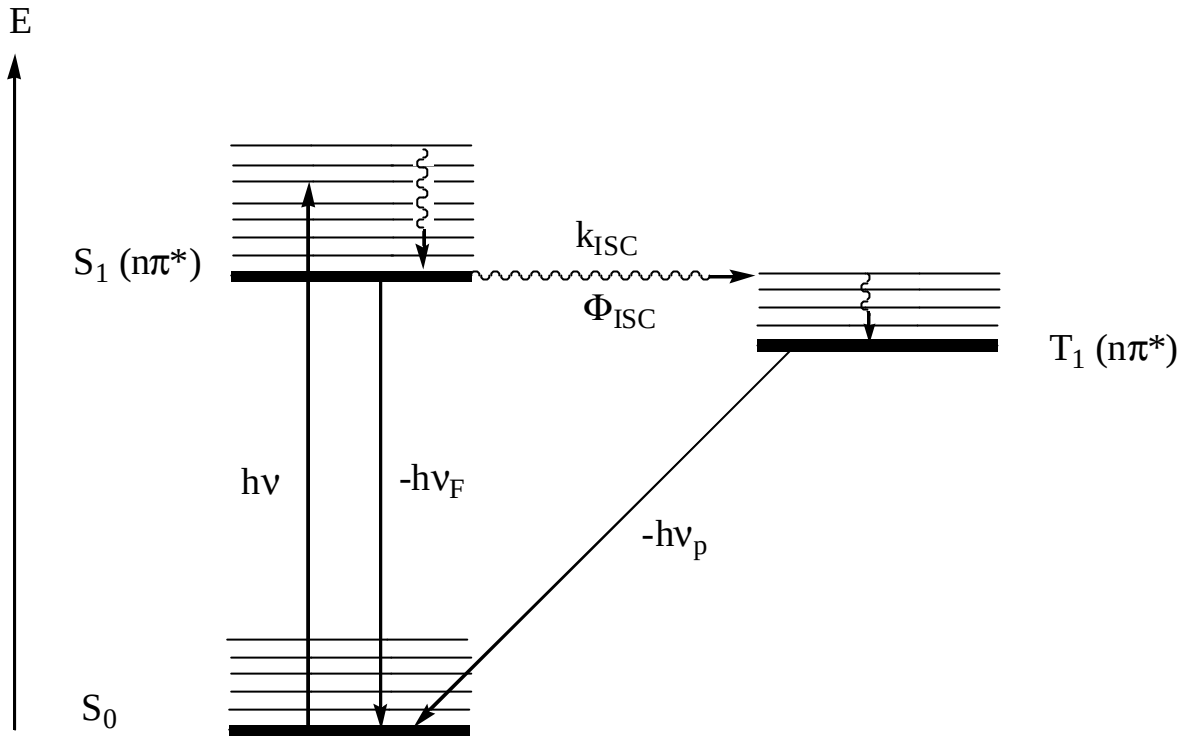
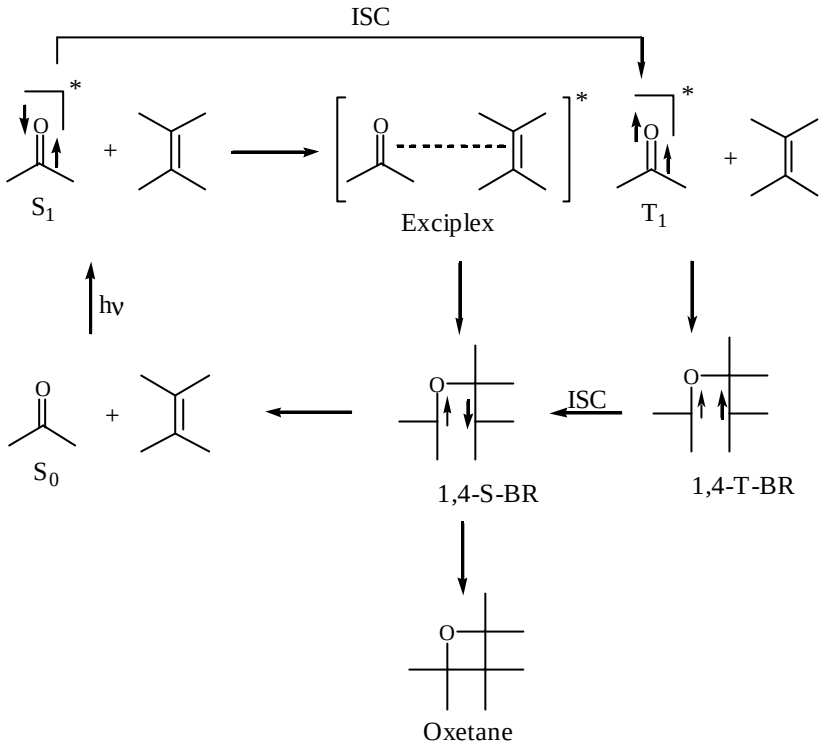


Figure 1.2: Molecular state (Jablonski) diagram for carbonyl compounds.

1.2 Mechanism of Paternò-Büchi reactions

The early step of the reaction mechanism involves the addition of the triplet excited carbonyl compound to the alkene and the formation of a triplet 1,4-biradical. The triplet 1,4-biradical must undergo ISC to form a singlet 1,4-biradical, which might cleave to give the starting material or undergo carbon-carbon bond formation to give the oxetane (see Scheme 1.2).



Scheme 1.2: Mechanism of Paternò-Büchi reactions.

It is widely accepted, that the immediate precursors of the oxetanes are biradicals[10] whose existance has been evidenced by chemical means[11] as well as by the application of picosecond spectroscopy.[12] Two mechanisms have been proposed to explain the low-energy pathways leading to the biradical intermediate.[10,13]

(1) Nucleophilic attack initiated by the half-occupied π^*-orbital of the carbonyl oxygen atom to the unoccupied π^*-orbital of an electron-deficient olefin in the plane of the molecule. This LUMO-LUMO interaction is called "parallel approach".

(2) An electrophilic attack initiated by the half occupied n-orbital of the carbonyl oxygen atom to the unoccupied π^*-orbital of an electron rich olefin in a perpendicular direction to the plane of the molecule. This HOMO-HOMO interaction is called a "perpendicular approach". Thus, the immediate precursors of these intermediates are $^3\pi\pi^*$ or $^3n\pi^*$ states. From their interaction with a suitable ground state substrate, three types of intermediates can possibly be formed:[13]

(a) an exciplex with the excitation localized on one of the two partners.

(b) a neutral "conventional" biradical.

(c) an ionic biradical or radical ion pair.

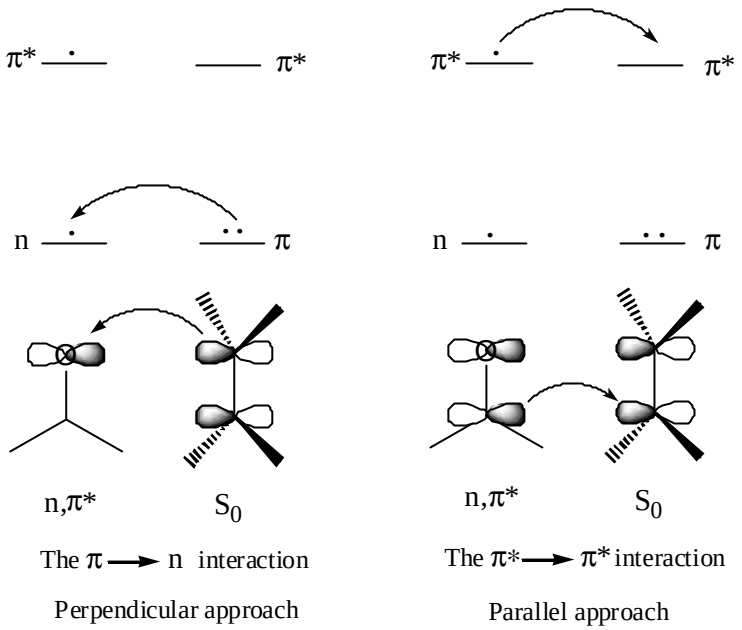


Figure 1.3: Orbital interactions for the n, π* addition of carbonyl compounds to alkenes.

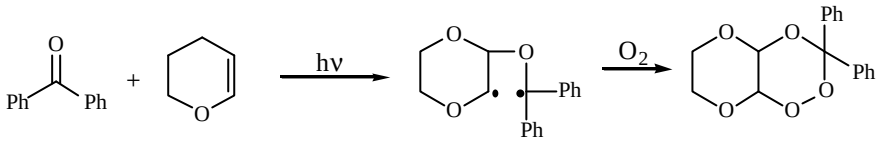
1.3 1,n-Biradicals

Biradicals have been proposed as reaction intermediates in thermal and photochemical reactions since many years, but only recently were trapping reactions and direct detection reported.[14] Berson[15] defined biradicals as "even-electron molecules that have one bond less than the number permitted by the standard rules of valence". Michl[16] and Bonacic-Koutecky defined a biradical or a biradicaloid as a molecule with an even number of electrons whose simple MO description contains two approximately nonbonding orbitals containing only two electrons in low energy electronic states. In a perfect biradical these orbitals are degenerate (of exactly the same energy) whereas in a biradicaloid they are only approximately degenerate. They represent the active space in the simple model. Wirz[17] reported that the energy difference between the singlet and the triplet state of a biradical is not more than 10 kJ/mol whereas in a biradicaloid this difference could be reach to 100 kJ/mol.

1.4 Biradical generation and trapping

Biradicals can be generated by a wide range of thermal and photochemical reactions.[18] Norrish type II[19, 20] reaction of aryl alkyl ketones is usually used for the production of 1,4-biradicals as well as Paternò-Büchi reactions. Furthermore, the photoenolization of o-alkyl-substituted aromatic ketones, Norrish type I[21] cleavage of aliphatic carbonyl compound after the elimination of carbon monoxide and photoinduced nitrogen loss from azo compounds[22] have been employed as source of generation of biradicals. 1,4-Paternò-Büchi biradicals have been proposed as intermediates in the cycloaddition of triplet ketones to olefins. The 1,4-

biradicals were trapped directly with oxygen[12,23] and sulfur dioxide.[24] Freilich and Peters have detected the 1,4-biradical from benzophenone and 1,4-dioxene which was also trapped by oxygen to give a 1,2,4-trioxane.



λ = 525 nm
τ = 1.6 ns

Scheme 1.3: Trapping of 1,4-triplet biradical with oxygen.

1.5 Lifetime of triplet 1,n-biradicals

The lifetime of triplet 1,n-biradicals is usually determined by the intersystem crossing rate ($\tau_{BR} = 1/k_{ISC}$). This means, that the biradical has to stay in the triplet manifold for a defined time, because without spin flip it can not undergo bond formation or bond cleavage. These steps would lead to triplet excited open-shell species and thus would be highly endergonic.[25] Three mechanisms operate for the interaction between singlet and triplet states of 1,n-biradicals: electron-nuclear hyperfine coupling (HFC), spin-lattice relaxation (SLR), and spin-orbit coupling (SOC).[26] HFC is an important control factor for biradicals with long carbon chains between the radical centers.[27] SOC plays the dominant role in biradicals with shorter distances between the radical centers, whereas SLR seems to contribute only marginally in general. In contrast to other mechanisms, SOC is strongly dependent on the geometry of the triplet biradical. This was first summarized in three rules stated by Salem and Rowland[28] in 1972:

(a) SOC decreases with increasing distance between the two spin-bearing atoms. Because there is also the possibility of through-bond interaction, not only is the actual distance between the two radical centers important (corresponding to a conformational dependence) but also the number of bonds (n-1).

(b) Conservation of total angular momentum could be achieved when the axes of the p orbitals at the radical centers are oriented perpendicular to each other (see Figure1.4).

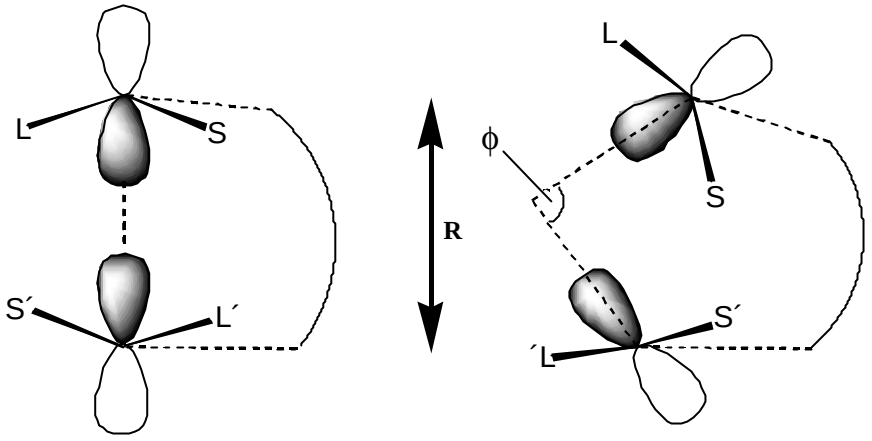


Figure 1.4: Singlet and triplet approach.

(c) SOC is proportional to the ionic character of the singlet state.

Summarizing these three rules, a pronounced conformational and structural dependence should result for the lifetime of triplet 1,n-biradical.

A numerical equation for SOC was given by Doubleday *et al*. from calculations on trimethylene :[26]

$$SOC = B(R)\ |S|\ \sin\Phi$$

where B (R) is a function of the distance R between the radical centers, Φ is the angle between the p orbitals at these positions, and $|S|$ is the overlap integral for these orbitals.

Spin-orbit coupling (SOC) controls the rate of ISC for tetramethylene, 2-oxatetramethylene or trimethylene triplet biradicals, i.e. strong SOC enhances the intersystem crossing rate and lowers the lifetime of triplet biradicals. A remarkable proof for these rules are the 1,3-biradical lifetimes for triplet 1,3-cyclopentadiyl (I, τ = ca. 100 ns) and for bicyclo [2.2.1] heptane-2,7-diyl (II, τ < 100 ps).[29]

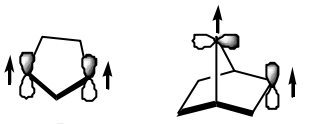
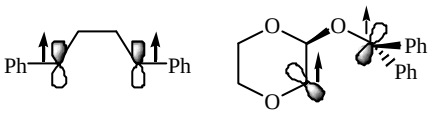


Figure 1.5: Conformation of 1,3-triplet biradicals.

In contrast to rather long-lived tetramethylenes (e.g., biradical III, with τ = 190 ns),[18a] the 2-oxatetramethylenes (preoxetane) formed during the Paternò-Büchi reaction are much shorter lived. For the triplet biradical IV from benzophenone and dioxene, a lifetime of 1.6 ns was determined by laser flash photolysis.[23]



III
τ = 190 ns

IV
τ = 1.6 ns

Figure 1.6: Conformation of 1,4-triplet biradicals.

In recent publications by Michl[30] and Adam[31] and coworkers, these rules which help to estimate the magnitude of SOC, were modified due to new experimental and theoretical results. The spatial orientation of the two singly occupied orbitals has been determined to be highly important for the biradical lifetime, whereas the through-space distance between the radical centers plays a subordinate role and the degree of ionic contribution in the corresponding singlet state often seems to be overestimated. This clearly indicates that for flexible 1,4-biradicals not only one conformational arrangement is responsible for facilitating ISC, but many. After transition from the triplet to singlet potential energy surface, immediate product formation is expected. Thus, the ISC is expected to proceed concerted with the formation of a new bond or the cleavage of the primary formed single bond. Recently, conformational dependence of spin-orbit coupling (SOC) in flexible Paternò-Büchi biradicals has been studied with high-level *ab initio* methods by A. Kutateladze[32] for the originally published model system 2,3-dihydrofuran and benzaldehyde. The relevant geometrical parameters are presented in Figure 1.7. Spin-orbit coupling was mapped out as a function of three torsional angles: α (rotation about C1-C2 bond), β (C2-O3), and γ (O3-C4), with conformations designated as (α, β, γ). The *ab initio* results revealed two distinct areas of elevated SOC values (Figure 1.7), one corresponding to the region whereby a *cisoid* conformation in the C-C-O-C fragment brings the two odd-electron orbitals closer to each other, and the other area corresponding to the partially eclipsed conformation laking direct overlap between the spin centers.

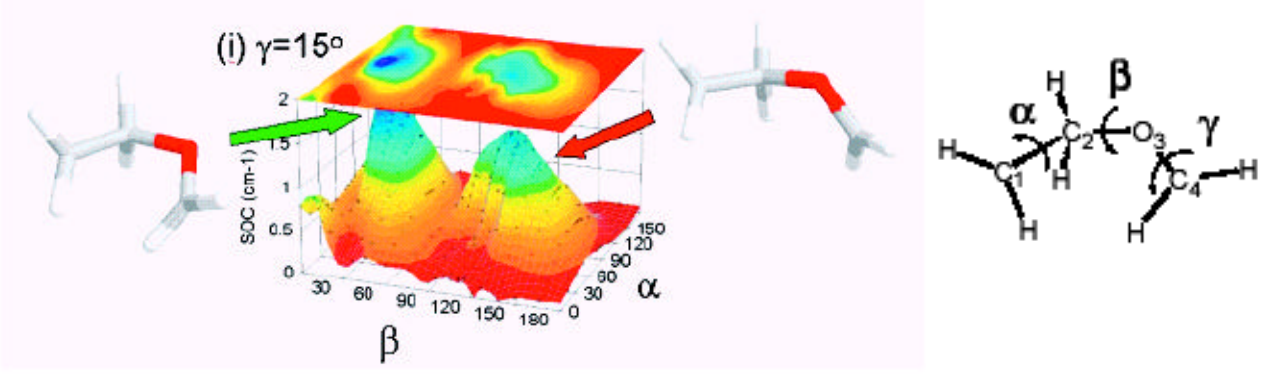
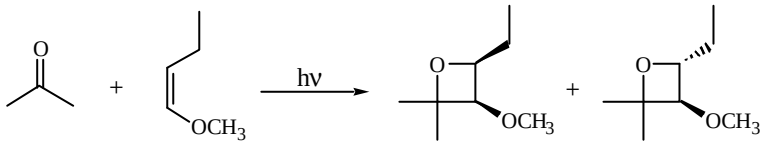


Figure 1.7: Selected 3-D sections of the four-dimensional SOC dependence in PB diradical.

The largest single-triplet energy gap, approximately 2 kcal/mol, was found for a *gauche* conformer (also a minimum SOC conformation). This accounts for the experimental results, i.e. high diastereoselectivity and moderate quantum yield as well as relatively short biradical lifetimes in comparison with the tetramethylenes. The decisive role of the oxygen in the 2-oxatetramethylene radical becomes apparent in the second important area from which lower diastereoselectivity is expected.

1.6 State Selectivity : Singlet excited carbonyl compounds

Due to rapid intersystem crossing from S_1, the aromatic carbonyl compounds used for the investigation of product stereoselectivity reflect "pure" T_1 (n,π^*) photochemistry.[33] The corresponding aliphatic carbonyl compounds have a k_{isc} about 10-fold lower and therefore they can react from S_1 as well as T_1.[34] Addition of triplet quenchers moderates the reactivity pattern. Using cyclohexene as starting material and acetaldehyde as carbonyl added in the presence and absence of a triplet quencher (1,3-pentadiene), different *endo/exo* ratios were obtained. The amount of *endo* diastereoisomer decreased with increasing amounts of triplet quencher. This indicates that the reaction *via* the triplet biradical is highly *endo* selective in contrast to analogus reaction *via* the singlet excited acetaldehyde. Turro and Wriede[35] reported that photolysis of acetone and 1-methoxy-1-butene gave two stereoisomers of the 2-methoxy oxetane. The stereoselectivity of the photoaddition was dependent on the spin state of the reacted acetone. Singlet excited acetone gave *cis* oxetane predominatly, whereas triplet excited acetone gave a mixture of *cis* and *trans* oxetanes in equal ratio.

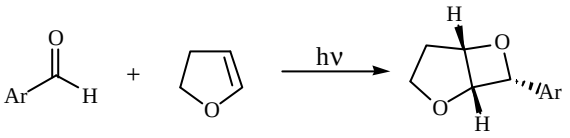


acetone T_1 1 : 1

acetone S_1 4 : 1

Scheme 1.4: Photocycloaddition of acetone with 1-methoxy-1-butene.

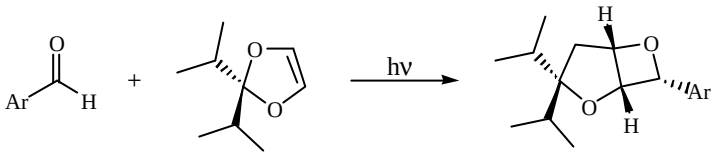
Naphthaldehydes can be used in Paternò-Büchi reactions as singlet excited carbonyl components.[36] The reaction efficiencies and chemical yields are normaly much lower compared to other aromatic ketones or aldehydes, but chemo- and regioselectivities are often identical. The Paternò-Büchi reaction of 2-naphthaldehyde with 2,3-dihydrofuran is a singlet process (as shown by triplet sensitization experiments) and gives exclusively the *exo*-diastereoisomer.



Ar =	d.r. = *endo*/*exo*
Mesityl	> 98 : 2
α-naphthyl	< 98 : 2
β-naphthyl	< 98 : 2

Scheme 1.5: Photocycloaddition of aromatic aldehydes with 2,3-dihydrofuran.

A similar example was found for the photoaddition of 2,2-bis-isopropyl-1,3-dioxolene: the *endo/exo*-ratio is inverted for oxetane formation when going from triplet excited mesitaldehyde to the singlet excited naphthaldehyde as substrate.

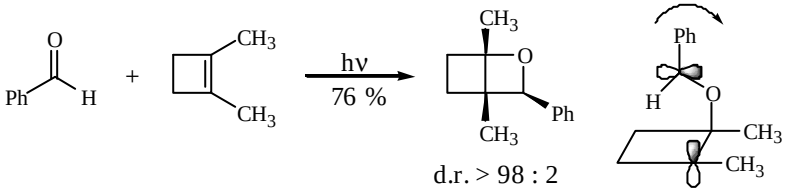


Ar =	d.r. = *endo*/*exo*
Mesityl	80 : 20
α-naphthyl	17 : 83

Scheme 1.6: Photocycloaddition of aromatic aldehyde with 2,2-bis-isopropyl-1,3-dioxene.

1.7 Substituent effects

Two structural features made the conformational analysis of the spin-inversion geometries of unsubstituted cycloalkenes straightforward: the two sites of the alkene part were well differentiated concerning the degree of substitution and steric hindrance. Methyl-substituted cycloalkenes, however, have two ISC-reactive sites and thus, the *endo/exo* ratio, drops significantly.[37] The Paternò-Büchi reaction of 1,2-dimethylcyclobutene with benzaldehyde gave solely the *exo*-diastereoisomer.

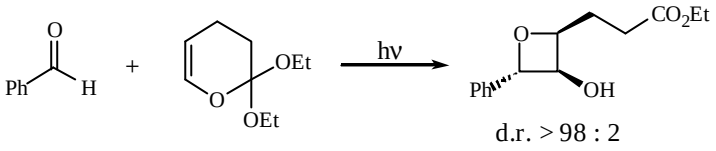


d.r. > 98 : 2

Scheme 1.7: Photocycloaddition of benzaldehyde with 1,2-dimethylcyclobutene.

This is exactly predicted by ISC-geometry model, because the *bis*-methylated site of the cycloalkene is now sterically more demanding and the biradical combination trajectory involves the approach from the less shielded cyclobutene plane.

Steric hindrance can also reach a critical value during bond formation and might favor the formation of the thermodynamically stable product. Park[38] and coworkers reported, that the photocycloaddition of benzaldehyde to 2,2-diethoxy-3,4-dihydro-2H-pyran gave preferentially the *exo*-phenyl product.

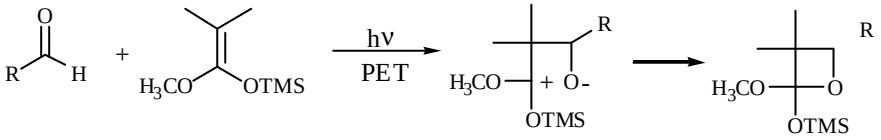


d.r. > 98 : 2

Scheme 1.8: Photocycloaddition of benzaldehyde with 2,2-diethoxy-3,4-dihydro-2H-pyran.

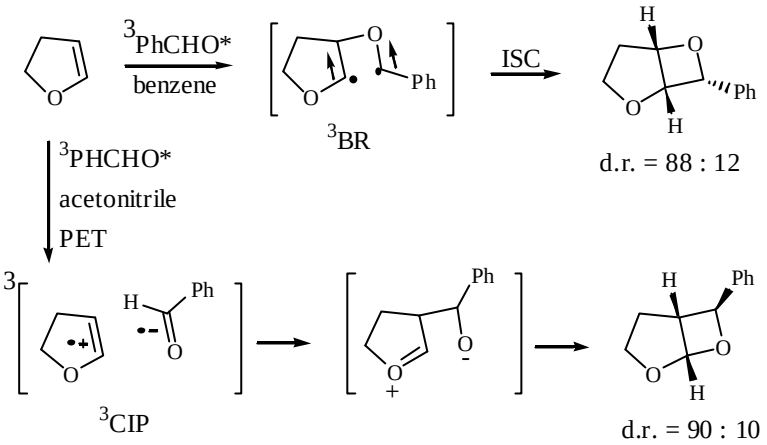
1.8 Photoinduced-electron transfer (PET) in the Paternò-Büchi reaction

Another feature which might oppose the ISC-geometry model is primary photoinduced electron transfer (PET). If this process is energetically feasible, the geometric restrictions might be circumvented, i.e. intersystem crossing can occur at the stage of the radical ion pair and a singlet 1,4-biradical or 1,4-zwitterion can be formed depending on the reaction conditions. In polar solvents, the assumption of a 1,4-zwitterion as decisive intermediate is reasonable. Both regio- and diastereoselectivity are influenced by this mechanistic scenario. The regioselectivity is now only a consequence of a maximum charge stabilization and the no longer a consequence of the primary interaction between the excited carbonyl compound and alkene. Whereas 3-alkoxyoxetanes are prefentially formed from triplet excited aldehydes and enol ethers, 2-alkoxyoxetanes result from the reaction of triplet excited ketones or aldehydes and highly electron rich ketene silylacetals.[39]



Scheme 1.9: PET control of the regioselectivity.

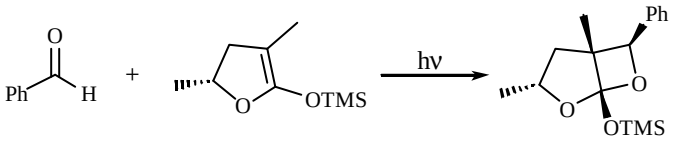
In the second case, PET which gives the carbonyl radical anion and the ketene acetal radical cation is energetically feasible.[40] PET might be followed by ISC and formation of a highly stabilized 1,4-zwitterion intermediate. By processing the photocycloaddition in a highly polar solvent which reduces the coulombic term in the Rehm-Weller equation,[41] PET becomes compatible with radical pathways. This effect was observed with 2,3-dihydrofuran as electron-rich substrate which gave the 3-alkoxyoxetane in high (88:12) *endo*-selectivity when reacted with triplet excited benzaldehyde in unpolar solvents.



Scheme 1.10: PET in Paternò-Büchi reaction.

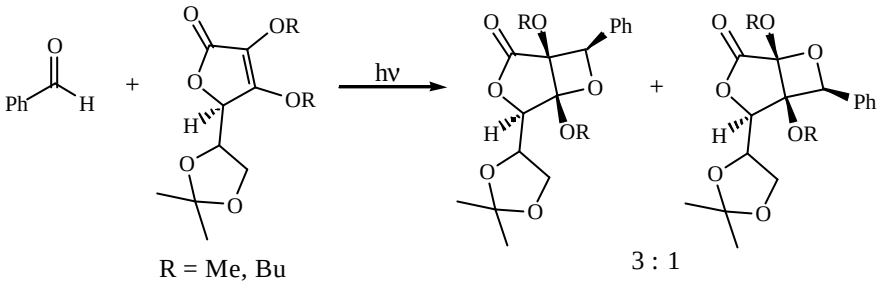
In acetonitile, however, also the corresponding 2-alkoxyoxetane was detected. The relative amount of this product correlated with solvent polarity parameters, thus indicates PET as the responsible mechanism. The major diastereoisomer obtained from the PET-cycloaddition of benzaldehyde with 2,3-dihydrofuran was the *exo*-phenyl isomer (d.r. 90 : 10).[42] Thus, a switch from 1,4-biradical to 1,4-zwitterion path leads also to an *inversion* of regio- and diastereoselectivity. A mechanism which involves a sequence of PET, formation of a contact ion pair (CIP) and charge recombination to give a triplet 1,4-biradical[43] also explains the change in regioselectivity.

Abe and coworkers[44] have also observed this stereochemical effect in the Paternò-Büchi reaction of aromatic aldehydes with cyclic ketene acetals. The addition of benzaldehyde to the 5-silyloxy-substituted 2,3-dihydrofuran resulted in the *exo*-phenyl product in low yield.



Scheme 1.11: Photocycloaddition of cyclic enolether with benzaldehyde.

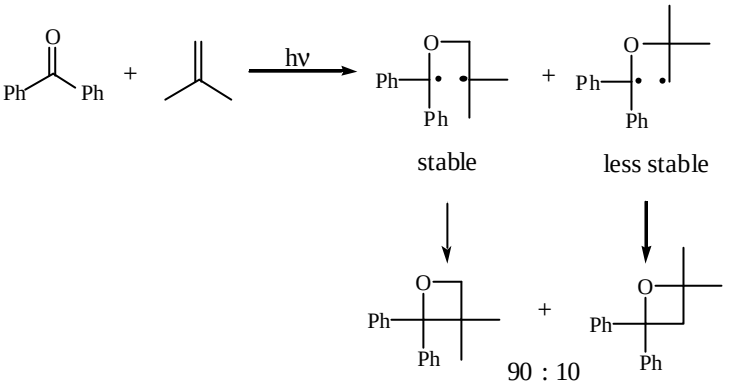
Kulkarni and coworkers reported the photocycloaddition of benzaldehyde with 2,3-dialkylated ascorbic acid acetonides result in the formation of two regioisomeric products.[45] Both oxetanes were formed exclusively with *exo*-phenyl configuration. The observed regio- and diastereoselectivity are in accord with the assumption of a PET process involving the oxidation of the ascorbic derivatives and the formation of the carbonyl radical anions. In these special cases, the 1,4-biradical and 1,4-zwitterion stabilization result in the same product regioselectivity. The relative configuration of the products favors the assumption of a PET process.



Scheme 1.12: Photocycloaddition of benzaldehyde with 2,3-dialkylated ascorbic acid acetonides.

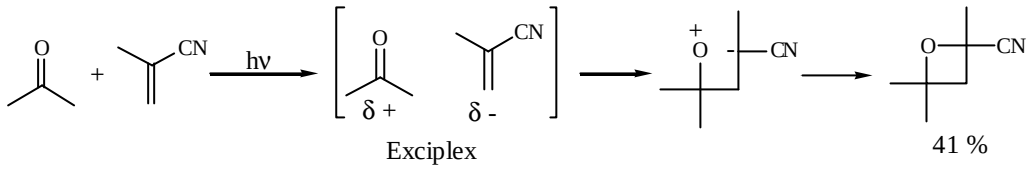
1.9 Regioselectivity of Paternò-Büchi reactions

The Paternò-Büchi reaction is a powerful synthetic tool because it can be applied to a wide of alkenes and carbonyl compounds. However, the application of the reaction is greatly limited because the normal regioselectivity does not always satisfy the synthetic requirement. In general, the regioselectivity of the Paternò-Büchi reaction is controlled by the substituents on the alkenes and the type of carbonyl compound involved. The photoaddition of benzophenone to isobutene[46] gave two regioisomer in 90 : 10 ratio with preference of the oxetane that results from the most stable biradical intermediate.



Scheme 1.13: Regioselectivity of Paternò-Büchi reaction.

This rule holds relatively weak if cycloadditions involving a pronounced degree of charge transfer are also considered (for example, photoreactions of biacetyl). In addition, photoreactions of aliphatic ketones and electron-deficient alkenes often lead to high yields of 2,4-disubstituted oxetanes. The photocycloaddition of acetone to 2-methyl propenenitrile give only one regioisomer.[47] The mechanism proposed for singlet addition of acetone to alkene involves formation of an exciplex with a certain degree of charge transfer.[48] These results were rationalized in terms of a Michael addition of the electronically excited carbonyl compound (*umpolung*) to acrylonitrile.[6]



Scheme 1.14: Regioselectivity of Paternò-Büchi reaction with electron -poor alkenes.

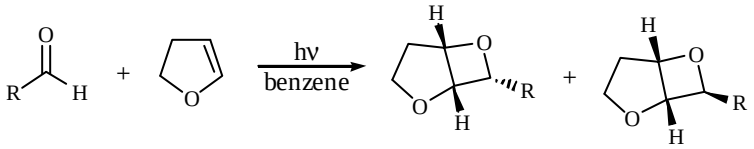
1.10 Diastereoselectivity in the Paternò-Büchi reaction

Simple (non-induced) diastereoselectivity in general describes a selection process where two stereogenic elements (or more) are generated in a chemical process without stereogenic elements present already in the starting materials, whereas induced diastereoselectivity describes a selection process where stereogenic elements are generated in a chemical process from substrates with at least one stereogenic elements already present. Thus, in case of Paternò-Büchi reactions, the combination of two prostereogenic substrate molecules leads to a photoadduct with a maximum of three new stereogenic centers.

1.10.1 Simple diastereoselectivity

1.10.1.1 Paternò-Büchi reactions with 2,3-dihydrofuran and furan

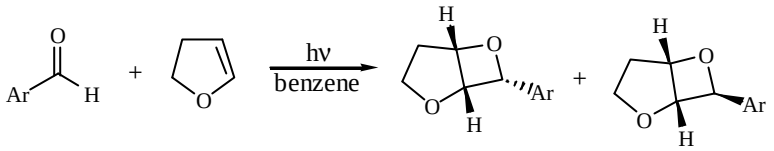
The simple diastereoselectivity of Paternò-Büchi reaction of 2,3-dihydrofuran and furan with prochiral carbonyl compounds was intensively investigated by Griesbeck and coworkers.[49] They found that the [2+2] photocycloaddition of 2,3-dihydrofuran with different aliphatic aldehydes in nonpolar solvent gave oxetanes with high regioselectivty and surprising simple diastereoselectivities. The dihydrofuran addition to acetaldehyde resulted in a 45 : 55 mixture of *endo* and *exo* diastereoisomer. With increasing size of the α-carbonyl substituted (Me-Et-Bu^{i}-Bu^{t}), the simple diastereoselectivity increased with preferential formation of the *endo* stereoisomer.



R =	d.r. = *endo*/*exo*
Me	45 : 55
Et	58 : 42
i-Bu	67 : 33
t-Bu	91 : 9

Scheme 1.15: Photocycloaddition of aliphatic aldehydes with 2,3-dihydrofuran.

The benzaldehyde addition, which was most intensively investigated gave a 88 : 12 mixture of *endo* and *exo* diastereoisomers in benzene solution. Thus, the thermodynamically less stable stereoisomers (> 1.5 kcal/mol, *ab initio* calculation) were formed preferentially. To further enlarge the phenyl substituent, *o*-tolyl and mesitaldehyde as well as 2,4-di-*tert*-butyl-6-methylbenzaldehyde were used and actually the diastereoselectivity did further increase.[50]



Ar =	d.r. = *endo*/*exo*
Ph	88 : 12
o-Tol.	92 : 8
Mes.	> 98 : 2
2,4-di-t-Bu-6-Me-Ph	> 98 : 2

Scheme 1.16: Photocycloaddition of aromatic aldehydes with 2,3-dihydrofuran.

The formation of the *endo* isomers can be rationalized on the basic of spin-orbit coupling controlled geometies of the triplet 1,4-biradical.[51] The conformer **A** and **B** are expected to be similarly populated; however, ISC from **A** results in product formation, whereas ISC from **B** leads to cleavage of the singlet biradical and formation of the starting material. Spin inversion is coupled with a torque, which in the case of conformers **A** and **C** leads to an immediate formation of the new C-C bond. Thus, the torque induced in conformer **A** rotates the large substituent (R) over the plane and results in formation of the *endo* diastereoisomer. From conformer **C**, preferentially the *exo* diastereoisomeric product is formed.

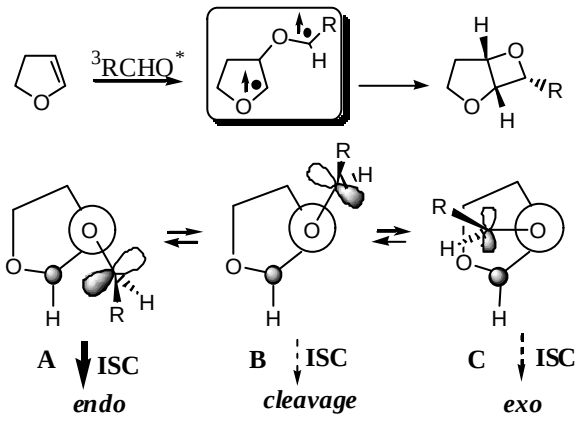
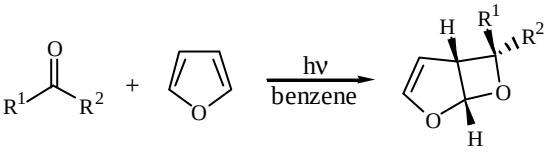


Figure 1.8: Model for *endo*-selective formation of oxetanes derived from 2,3-dihydrofuran.

The photocycloaddition of furan with aromatic and aliphatic aldehydes processed with unusual high *exo*-diastereoselectivity to give the bicyclic oxetanes in good yield. The diastereoselectivities (*exo/endo*) of the Paternò-Büchi reaction of furan with acetaldehyde,

propionaldehyde and benzaldehyde were 19 : 1, 82 : 1 and 212 : 1, respectively. Surprisingly, the exchange of the hydrogen in benzaldehyde by a methoxy group completely inverts the diastereoselectivity in the photocycloaddition with furan. Further modification of the α-substituent in the benzoyl substrates uncovered a distinct dependence of the *exo/endo* -ratio on the size of this substituent. The photocycloaddition of acetophenone with furan gave only one product, whereas a 77 : 23 mixture of diastereoisomers resulted from the addition of benzoyl cyanide. Increasing the size of the aryl group from phenyl to mesityl in aroyl cyanides led to an increase in *exo*-diastereoselectivity from 3.7 : 1 up to 16 : 1.[42]



R^1 =	R^2 =	d.r. = *exo*-R^1/*endo*-R^1
Ph	H	212 : 1
Ph	Me	> 49 : 1
Ph	CN	3.7 : 1
Ph	CO_2Me	1 : 9
Ph	OMe	1 : 19
Mes	CN	16 : 1
t-Bu	CO_2Me	< 1 : 49

Scheme 1.17: Paternò-Büchi reaction of furan.

As already described for the dihydrofuran case, ISC from conformer **A** and **C** are expected to lead to *endo* and *exo* diastereoisomer, respectively. An alternative explaination for the high *exo*-selectivity in the furan-aldehyde photocycloaddition could be an enlarged lifetime of the singlet 1,4-biradical which is formed after ISC. However, this concept predicts thermodynamic control for the formation of all cycloaddition products, whether, they are formed from triplet excited aldehydes or ketones, ester, etc. In addition to that, an interaction between the allylic and the exocyclic radical in the 1,4-biradical (as depicted in strucure **C**) must be crucial for the dominance of this biradical geometry for rapid ISC. This effect can be described as secondary orbital interaction which facilitates intersystem crossing by means of an increase in spin-orbit coupling.

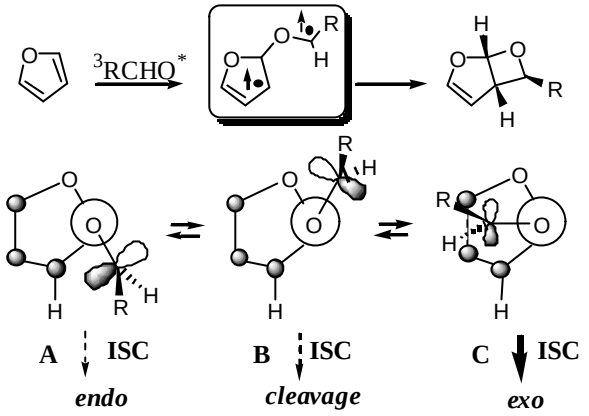
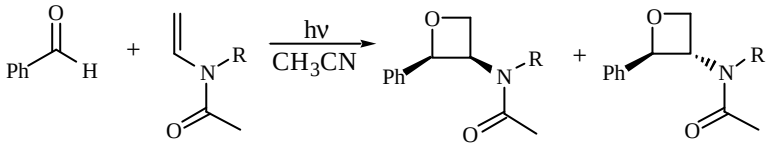


Figure 1.9: Model for *exo*- selective formation of oxetanes derived from furan.

1.10.1.2 Paternò-Büchi reactions with enamines

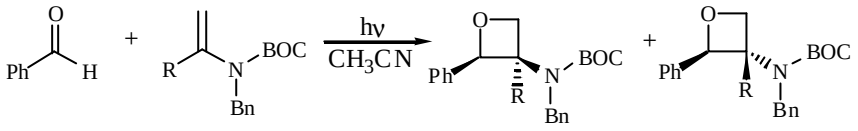
In the last decade, there were many report on the reaction of acyclic olefins with asymmetric carbonyl compounds which procceed with high simple diastereoselectivity. Bach[52] and coworkers investigated the photocycloaddition of N-acyl enamine with benzaldehyde and noticed that the reaction proceeds with excellent regioselectivity and good diastereoselectivity. Also, the thermodynamically less stable *cis* isomer prevailed similar to the *endo* selectivity in the case of 2,3-dihydrofuran.



R =	d.r. = *cis/trans*
H	79 : 21
Bn	89 : 11
Pr	> 90 : 10

Scheme 1.18: Photocycloaddition of benzaldehyde with enamide.

Recently, Bach and coworker reported, that the photocycloaddition of α-alkyl-substituted ene carbamates to benzaldehyde afforded 3-aminooxetanes in moderate to good yields (46-71%). An increase in the steric bulk of the alkyl substituent R shifted the diastereomeric ratio *cis/trans* in the direction of the thermodynamically less stable *cis*-product (29 : 71 for R = Me) up to (57 : 43 for R = cyclohexyl).[53]

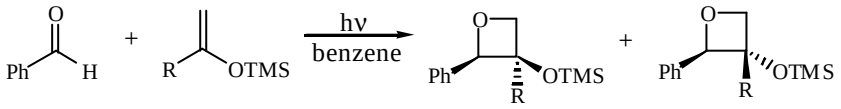


R =	d.r. = *cis/trans*
Me	29 : 71
Et	34 : 66
i-Pr	54 : 46
Ch_x	57 : 43
H	87 : 13

Scheme 1.19: Photocycloaddition of benzaldehyde with enamide.

1.10.1.3 Paternò-Büchi reactions with acyclic enol ether

Alkenes with moderate oxidation potentials were investigated by the Bach group in the last decade.[54] They have intensively studied the complex stereoselectivity of the Paternò-Büchi reaction of acyclic trialkyl silylenol ethers with aromatic aldehydes and developed an impressive set of synthetic applications.[55] A series of photocycloaddition reactions of benzaldehyde to trimethylsilyl (TMS) enol ethers showed a stereoselectivity trend which at the first sight was in contradiction to the rules described above, i.e. the thermodynamically more stable *trans* steroisomers (with respect to the C-substituent at C-2 and C-3) were formed preferentially and the *trans/cis* ratio increases with increasing size of the C-3 substituent.



R =	d.r. = *cis/trans*
Me	30 : 70
Et	17 : 83
i-Pr	12 : 88
t-Bu	9 : 91
Ph	8 : 92

Scheme 1.20: Paternò-Büchi reactions of benzaldehyde with silylenol ether.

The stereoselectivity might in these cases be attributed to a memory effect from the approach geometry between the triplet excited benzaldehyde and the alkene as depicted in Figure 1.10.

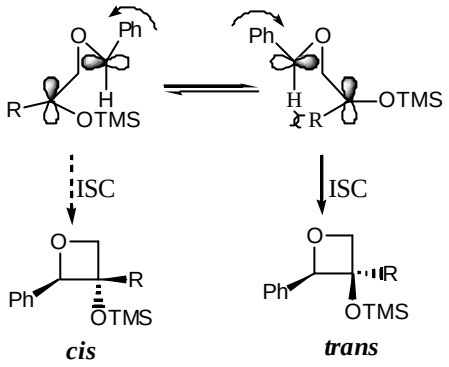
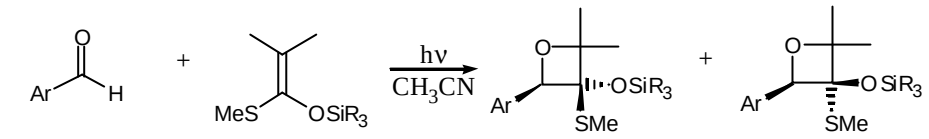


Figure 1.10: Mechanistic scenario for the formation of *cis* and *trans* oxetanes.

Abe and coworkers have also observed this stereochemical effect in the Paternò-Büchi reaction of p-cyanobenzaldehyde with thiosilylketene acetals.[56]



Ar = p-CN-C_6H_4

SiR_3 =	d.r. = *cis/trans*
$SiBu^tMe_2$	20 : 80
$SiMe_3$	18 : 82

Scheme 1.21: Photocycloaddition of ketene-O,S-acetal with p-cyanobenzaldehyde.

Abe rationalized the formation of the thermodynamically more stable *trans* isomer due to the interaction between the electronically excited carbonyl and the sulfur atom, this interaction favors the formation of conformer (**A**) than (**B**). The sulfur-derived control of *trans* isomer formation is depicted in Figure 1.11.

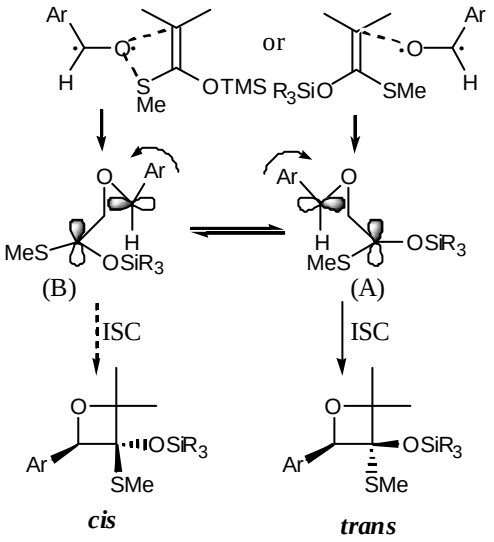
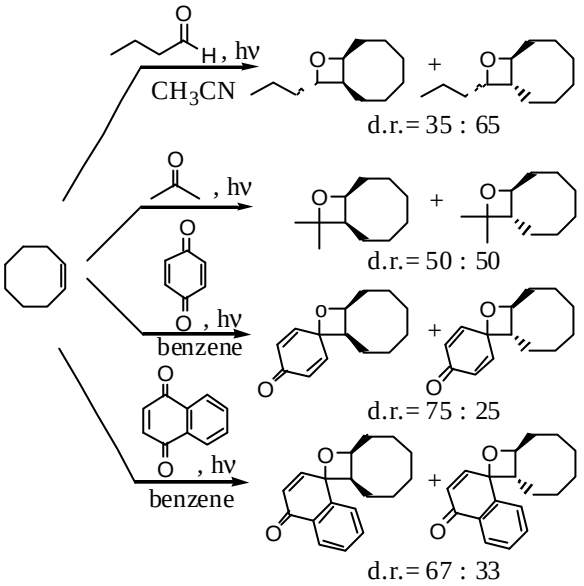


Figure 1.11: Sulfur control regio- and stereoselectivity.

1.10.1.4 Paternò-Büchi reactions with cyclooctene

Recently, cyclooctene was used as an olefinic substrate in Paternò-Büchi reaction with different carbonyl compounds. The simple diastereoselectivity was moderate. In all cases, there were two diastereoisomers (*cis* and *trans* oxetanes) with moderate diastereomeric ratio. Butanal,[57] 1,4-naphthoquinone,[58] 1,4-benzoquinone[59] and acetone[60] were applied as the carbonyl compounds with *cis*-cyclooctene. The authors rationalized the *cis/trans* selectivity on the basis of the formation of triplet 1,4-biradical which has a relatively long lifetime in order to allow rotate around C-C bond and hence led to formation of the *trans*-diastereoisomer.



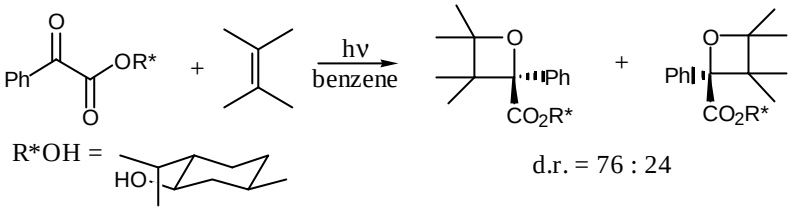
Scheme 1.22: Paternò-Büchi reactions with cyclooctene.

1.10.2 Induced diastereoselectivity

There are many reviews[7,8] in the literature on the induced-diastereoselectivity of the Paternò-Büchi reaction using chiral reaction partners. In principle, one can induce diastereoselectivity through using chiral carbonyl compounds or chiral olefins.

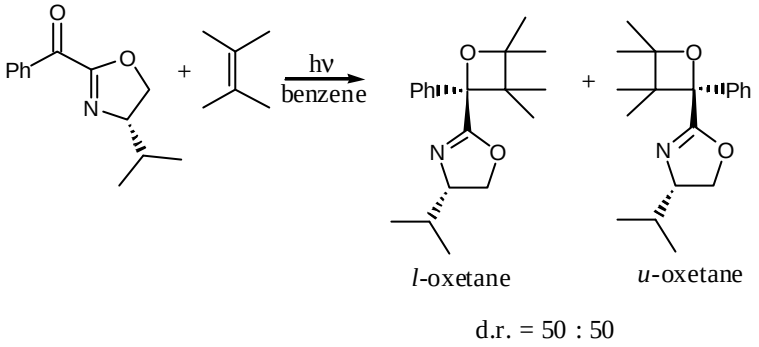
1.10.2.1 Induction by the carbonyl compound

The first report concerning an asymmetric Paternò-Büchi reaction with a chiral carbonyl component was reported in 1979 by Gotthardt and Lenz.[61] The photocycloaddition of the enantiomerically pure (-)-menthyl ester of phenylglyoxylic acid with 2,3-dimethyl-2-butene gave the oxetane with a diastereomeric excess of only 37%.



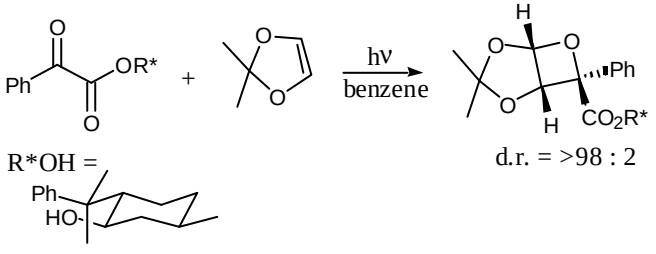
Scheme 1.23: Photocycloaddition of chiral phenylglyoxylates with tetramethylethylene.

Oppenländer and Schönholzer studied the diastereofacial differentiation in the Paternò-Büchi reaction using 4-(S-)-isopropyl-2-benzoyl-2-oxazoline (prepared from condensation of phenylglyoxylic acid with (S)-valinol) as a chiral auxiliary.[62] The [2+2] photocycloaddition gave a mixture of diastereoisomeric *l*-and *u*-oxetanes with equal amounts.



Scheme 1.24: Paternò-Büchi reaction of a benzoyloxazoline with tetramethylethylene.

The unique behavior of chiral phenyl glyoxylates was demonstrated by Scharf and coworkers.[63] Despite the fact that in all cases the stereogenic centers are localized in the alcohol part of the α-keto ester and therefore remarkably far away from the reactive triplet excited carbonyl group, the induced diastereoselectivities were exceedingly high, e.g. >98%, in the photocycloaddition of 1,3-dioxole with 8-phenylmenthol as the the chiral auxiliary.

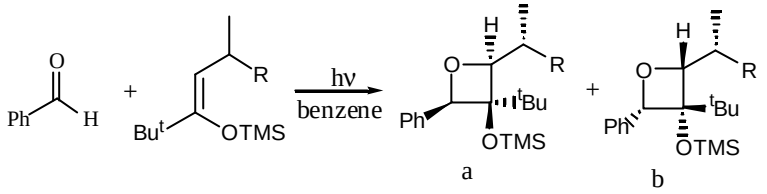


Scheme 1.25: Asymmetric induction in Paternò-Büchi reaction.

1.10.2.2 Induction by the alkene component

The induced diastereoselectivity in the Paternò- Büchi reaction using stereogenic center in the olefin was recently investigated by Bach and coworkers in the photocycloaddition for chiral silylenolethers with benzaldehyde.[64] The substituent R^L at the stereogenic center attached to

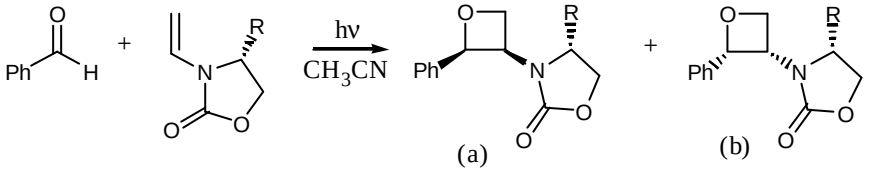
the γ-position of the silyl enolether were varied in order to evaluate the influence of steric bulk and electronic effect. In accordance with the 1,3-allylic strain model[65] the facial diastereoselectivity was best with large (R^L = t-Bu, $SiMe_2Ph$) and polar (R^L = OMe) substituents at the γ-position of the silyl enolether (d.r. up to 95 : 5).



R =	d.r. (a : b)
Et	61 : 39
i-Pr	70 : 30
Ph	71 : 29
t-Bu	95 : 5

Scheme 1.26: Photocycloaddition of benzaldehyde with silylenol ether.

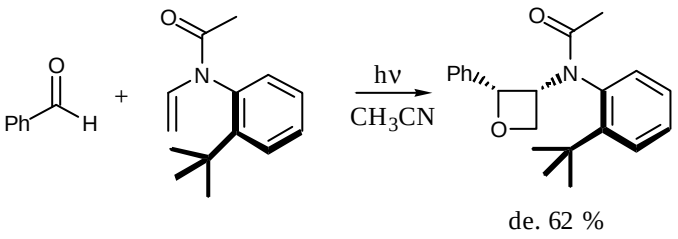
Several efforts, made by Bach and coworkers to apply chiral auxiliaries in N-acyl enamines that facilitated a facial differentiation in 1,4-biradical intermediate, failed. In all cases, they obtained a racemic mixture of oxetanes with moderate diastereoselectivity.[66]



R =	d.r. (a : b)
Ph	65 : 35
Bn	19 : 81

Scheme 1.27: Photocycloaddition of benzaldehyde with a chiral enamide.

Moreover, the photocycloaddition of axially chiral racemic N-acyl enamine with benzaldehyde yielded predominantly oxetanes with moderate diastereomeric excess.[67]

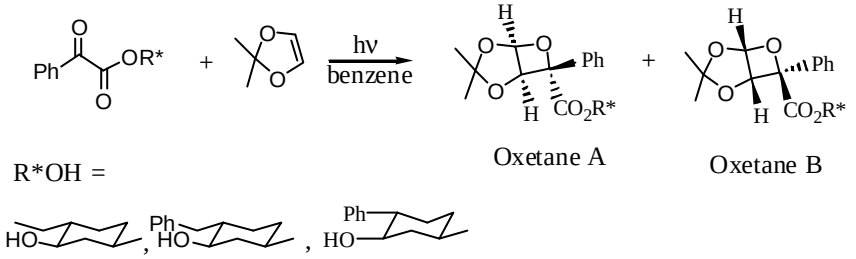


de. 62 %

Scheme 1.28: Photocycloaddition of benzaldehyde with chiral acylenamine.

1.11 Effect of temperature on the diastereoselectivity of Paternò-Büchi reactions

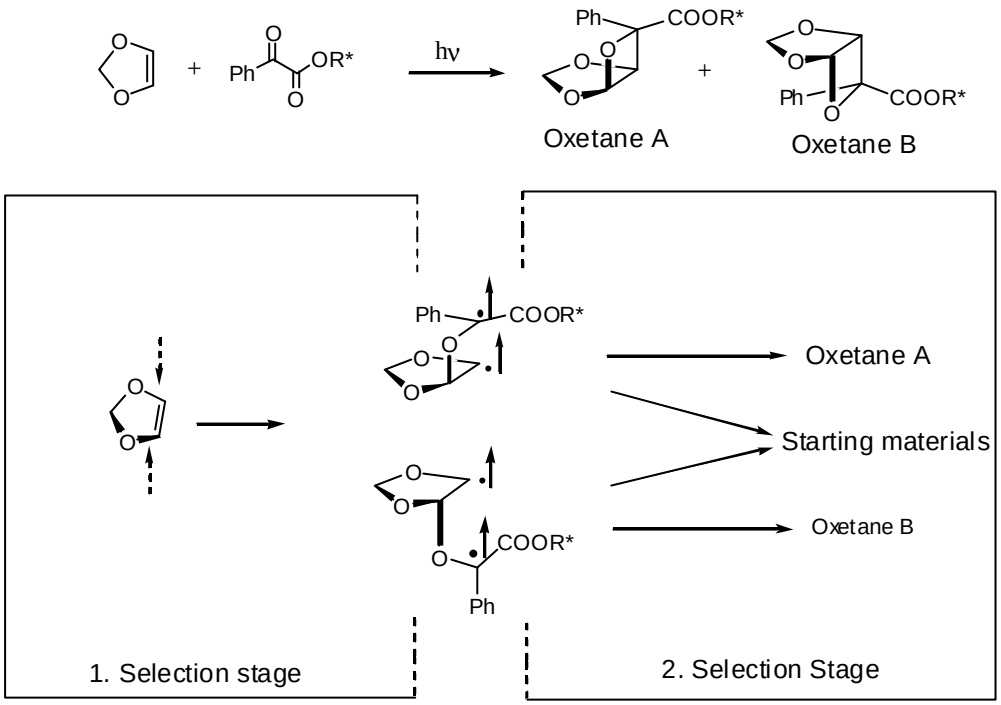
The temperature dependence of the auxiliary-induced diastereoselectivity was intensively studied by Scharf group.[68] In the Paternò-Büchi reaction of the chiral phenylglyoxylates with electron-rich cycloalkenes, the diastereomeric oxetanes are formed *endo*-phenyl selective in high chemical yields. Scharf *et al*. observed a striking temperature dependence of the facial selectivity which resembled the isoselectivity reactions investigated by Giese[69] in carbene and simple radical reactions. In addition to isoselectivity points, however, inversion temperatures were discovered at which the influence of the reaction temperature on the degree of stereoselectivity was inverted.



Scheme 1.29: Photocycloaddition of chiral phenylglyoxylates with 2,2-dimethyl-1,3-dioxole.

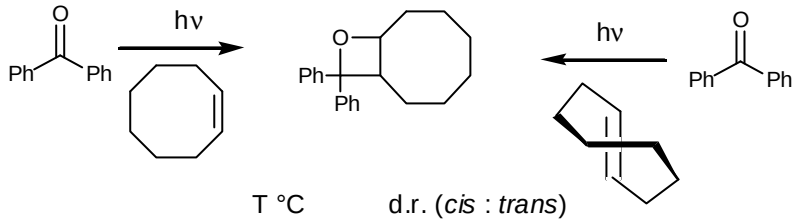
A straightforward mechanistic interpretation of this phenomenon in Paternò-Büchi reaction is the assumption of a two-stage process with one stage predominately determined by the activation entropy term and the other by the activation enthalpy. At the inversion temperature, the selectivity determining step changes from entropy to enthalpy determined and thus also the temperature/selectivity behavoir. No inversion temperatures were detected for simple diastereoselectivity. Actually, the diastereoselectivity of the second bond formation is more than 98% in all cases investigated by Scharf *et al*. This clearly results from a process at stage (2) that can not be influenced by temperature effects on stage (1). From the analysis of simple and induced diastereoselectivities, as well as from the temperature dependence of the facial diastereoselectivity, a reaction mechanism results which described the origin of product stereochemistry as a subtle combination of facial approach, biradical conformational equilibration, retrocleavage, and C-C bond formation. A simple kinetic picture for this scenario is shown in scheme 1.30. The *endo/exo* (simple) selectivity (*endo*-Ph selectivity) results from the last step in the reaction sequence, i.e., after spin-inversion from several possible biradical conformers, the *exo*- and *endo*-diastereoisomers (with already determined facial selectivity) are formed in competition with C-O bond cleavage. Whether or not singlet biradicals are involved in this process is still an open question. In any case, the lifetimes for these species are expected to be extremely short, and bond rotations cannot compete with C-C

bond formation or C-O bond cleavage. Thus, the simple diastereoselectivity maps the ISC geometry for the triplet 1,4-biradicals.



Scheme 1.30: The two-stage model for the Paternò-Büchi reaction.

Recently, Adam and coworker investigated the Paternò-Büchi reaction of *cis*-cyclooctene as well as *trans*-cyclooctene with triplet carbonyl partners.[70] They reported an unprecedent temperature-dependent diastereoselectivity in the [2+2] photocycloaddition of benzophenone with *cis* and *trans* cyclooctenes. They document the unusual case, that the lower-energy substrate diastereoisomer (*cis*-cyclooctene) affords, with increasing temperature the higher-energy product diastereoisomer (*trans*-oxetane). These unprecedented experimental facts on the [2+2] photocycloaddition of the diastereomeric cyclooctenes with benzophenone were rationalized in terms of a consistent mechanism: (i) The *cis*-cyclooctene displays a remarkable temperature dependence, in that the *trans*-oxetane is favored with increasing temperature; (ii) for *trans*-cyclooctene, the *trans* geometry is preserved in *trans*-oxetane cycloadduct over a broad temperature range of 180 °C; (iii) the extent of *trans* to *cis* isomerisation in the cycloaddition with *trans*-cyclooctene increase with temperature.

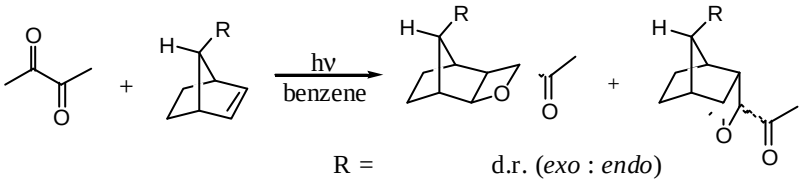


T °C	d.r. (*cis* : *trans*)
-95	98 : 2
-20	45 : 55
100	20 : 80

Scheme 1.31: Paternò-Büchi reaction of benzophenone with *cis*- and *trans*-cyclooctenes.

1.12 Effect of hydroxy groups on the stereoselectivity of Paternò-Büchi reactions

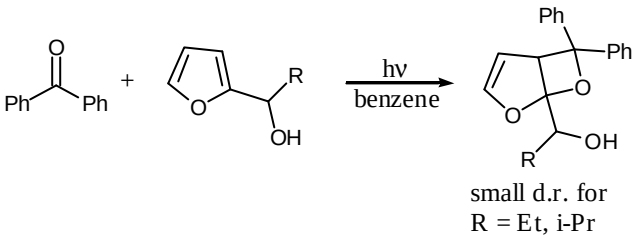
The first study of the effect of the hydroxy group on the Paternò-Büchi reaction of substituted norbornene with biacetyl was reported by Sauers and coworker.[71] The addition of biacetyl to norbornene is highly *exo* selective, whereas the *syn*-7-*tert*-butyl derivative showed inverted *exo*-selectivity. Introduction of a hydroxy group at the 7-*syn*-position of norbornene reinverts the diastereoselectivity: in this case, the *exo*-adduct is formed with de >97%. The later effect could be due to the hydrogen bonding forces between the hydroxy function and the electron-rich π* system orient the reactive species on the *exo*-face of the molecule.



R =	d.r. (*exo* : *endo*)
H	>96 : 4
t-Bu	<3 : 97
OH	>97 : 3

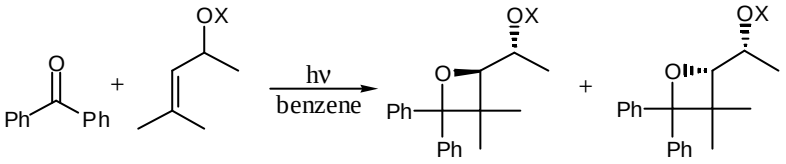
Scheme 1.32: Photocycloaddition of norbornene with biacetyl.

The Paternò-Büchi reaction between 2-furylmethanol derivatives and benzophenone was recently reported by D`Auria and coworkers.[72] They explained the regio- and stereoselectivity of the reaction by assuming a controlling function of both the substituent on the 2-furylmethanol derivatives and the hydroxy group in order to favor the approach of the carbonyl group towards a prochiral face of the furan. They have also reported that no photoadduct was obtained when the hydroxy group is protected by alkylation.



Scheme 1.33: Photocycloaddition of 2-furylmethanols with benzophenone.

More recently, Adam reported that hydrogen bonding directed regio and diastereoselectivity of the [2+2] photocycloaddition of benzophenone to chiral allylic alcohols.[73] The Paternò-Büchi reaction of electronically excited benzophenone with chiral allylic alcohols afforded only one regioisomer of the diastereomeric *threo*, *erythro*-oxetanes. Hydrogen bonding between the allylic alcohol and the incoming triplet excited benzophenone as an attractive interaction accounts for the marked regio- and the *threo*-diastereoselectivity. The diastereoselectivity was reduced in the presence of protic solvents (due to competition intermolecular hydrogen bonding) and disappeared when the hydroxy group is protected by silyl ether which can not serve as hydrogen-bonding donor.

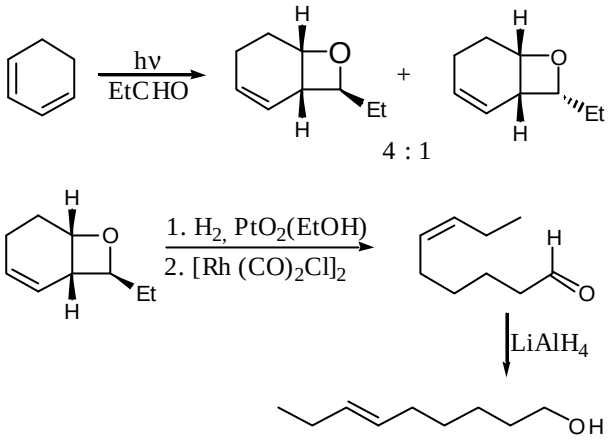


X=	Solvent	d.r. (*threo* : *erythro*)
H	C_6D_6	90 : 10
H	C_6D_6/CD_3COD (1:1)	69 : 31
$SiMe^tBu$	C_6D_6	52 : 48

Scheme 1.34: Paternò-Büchi reaction of allylic alcohols with benzophenone.

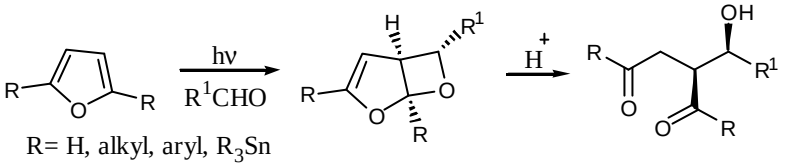
1.13 Synthetic applications of the Paternò-Büchi reaction

Kubota and coworkers found that irradiation of propanal in the presence of 1,3-cyclohexadiene produced the corresponding oxetanes in a 4:1 ratio.[74] These adduct were thought to occur *via* an attack of the first excited singlet state of propanal to the diene. The synthesis of (E)-6-nonen-1-ol, a component of the sex pheromone of the Mediterranean fruit fly, applied this process as the first step.[75] Hydrogenation and metal catalyzed [2+2] cycloreversion gave aldehyde, which then was easily converted to the target molecule by reduction.



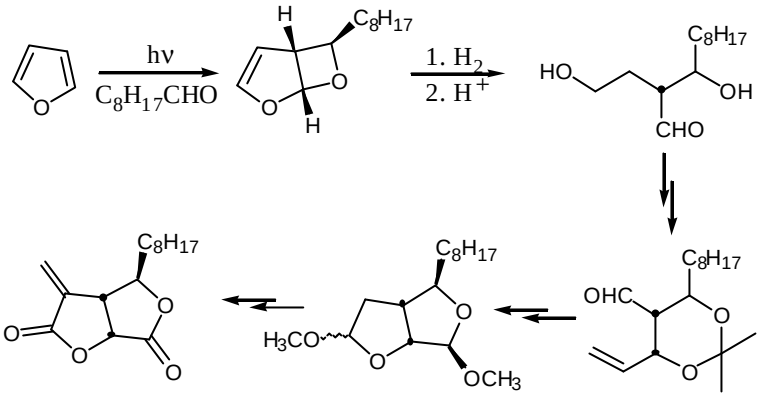
Scheme 1.35: Synthesis of (E)-6-nonen-1-ol.

Schreiber and coworkers have used the photocycloadduct of furan and carbonyl compound as the key intermediate for the synthesis of complex molecules.[76] Schreiber was the first to recognize that the bicyclic adducts formed in these reactions could be unmasked under acidic conditions to afford *threo* aldol products of 1,4-dicarbonyl compounds. This strategy has been exploited in the synthesis of a variety of novel natural products.



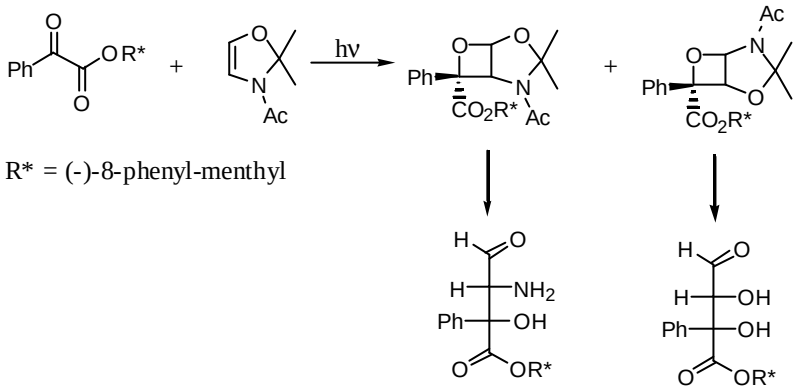
Scheme 1.36: Synthesis of *threo* β-hydroxy ketone.

An application of this strategy is the synthesis of the antifungal metabolite (±)-avenaciolide,[77] shown in Scheme 1.37. The photoadduct was hydrogenated and hydrolyzed to give the aldehyde. Reaction of the aldehyde with vinyl magnesium bromide and subsequent manipulation afforded another aldehyde, which could be transformed *via* ozonolysis, epimerization of the dialdehyde and acidification of the dialdehyde acetonide to a protected bis-lactol. Oxidation and methylenation then afforded the desired target.



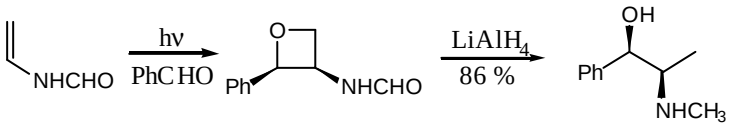
Scheme 1.37: Synthesis of (±)-avenaciolide.

Scharf and coworkers have explored the 2,3-dihydrooxazole-carbonyl photocycloaddition for asymmetric synthesis. Irradiation of chiral α-keto ester with 2,2-dimethyl-3-N-acetyl-2,3-dihydrooxazole gave two regioisomeric oxetanes which under solvolysis yield *erythro* sugars and *erythro* α-amino carbohydrates.[78]



Scheme 1.38: Synthesis of *erythro* sugars and *erythro* α-amino carbohydrates.

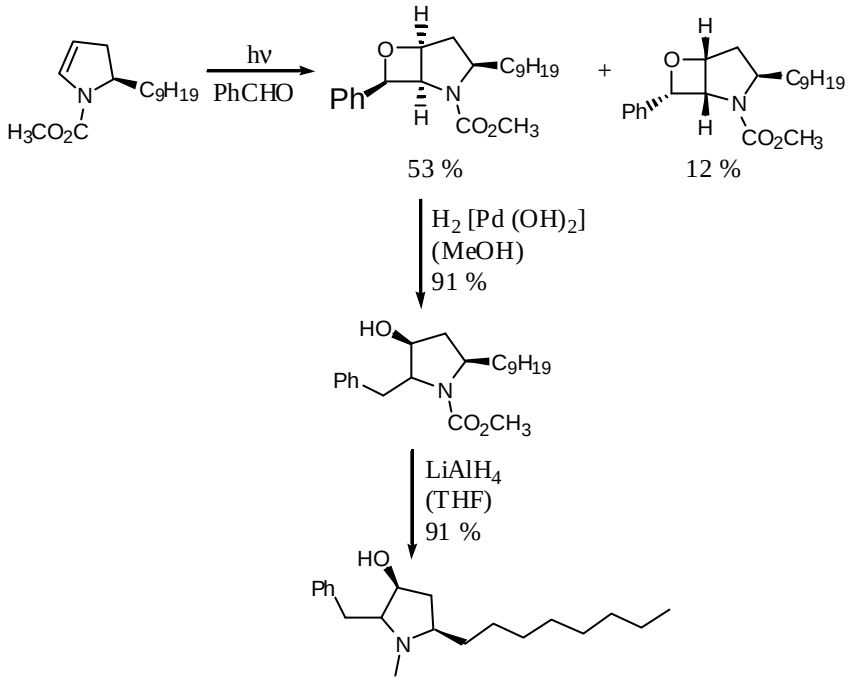
Recent investigations from the Bach group were focused on enamides as substrates. The resulting 3-aminooxetanes were used for the synthesis of chiral 1,2-aminoalcohols.[79] The photocycloaddition of N-vinyl formamide and benzaldehyde gave 3-aminooxetane, which was converted to pseudoephedrine in a single step by treatment with $LiAlH_4$.



Scheme 1.39: Synthesis of pseudoephedrine.

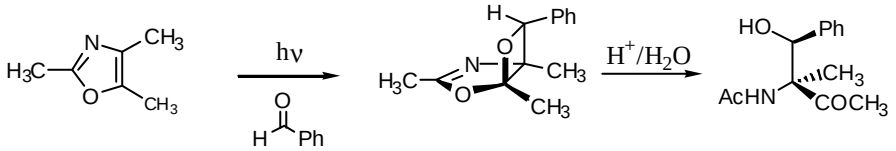
Bach and coworkers have been also developed the total synthesis of the antifungal agent (±)-preussin *via* the photocycloaddition of benzaldehyde with 2,3-dihydropyrrole. The ring

opening of the photoadduct gave a hydroxypyrrolidine which after hydrogenolysis gave the enantiomerically pure target molecule (+)-preussin.[80]



Scheme 1.40: Synthesis of (+)-preussin.

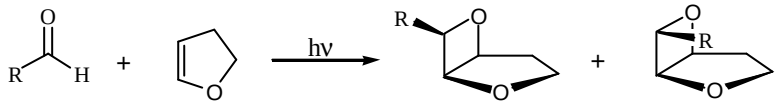
Recently, Griesbeck and Fiege published the photocycloaddition of an oxazole to carbonyl compounds as a convenient route for the synthesis of *erythro* α-amino-β-hydroxy ketones. Irradiation of 2,4,5-trimethyloxazole with benzaldehyde gave the bicyclic oxetane with highly *exo*-diastereoselectivity. The bicyclic oxetane is highly sensitive to hydrolysis and underwent twofold ring opening to give *erythro*- α-acetamido-β-hydroxy ketone.[81]



Scheme 1.41: Synthesis of *erythro* α-acetamido-β-hydroxy ketone.

2. Projected work

To the best of our knowledge, there was no detailed investigation on the connection between spin state and stereoselectivity in [2+2]-photocycloadditions. At first, I decided to study the concentration dependence of the simple diastereoselectivity of the Paternò-Büchi reaction of electron-rich cycloalkenes with aliphatic as well as aromatic aldehydes in order to evaluate the difference of stereoselectivity between singlet and triplet photoreaction. In addition, I proposed to investigate the effect of solvent polarity as well as solvent viscosity on the spin-selectivity of the photocycloaddition reaction of 2,3-dihydrofuran with aldehydes. The unusual nonlinear temperature dependence of the stereoselectivity of Paternò-Büchi photocycloadditions of electron-rich cycloalkenes with chiral phenylglyoxylates served as the basis for the development of the isoinversion principle by Scharf and coworkers.[68] The influence of the excited-state spin multiplicity was not observed in these studies because substrates with high ISC rates were used and thus exclusive bimolecular triplet reactions were expected.[82] Thus, I intended to study the effect of temperature on simple diastereoselectivity in the singlet and the triplet photocycloaddition reaction of 2,3-dihydrofuran with aldehydes.



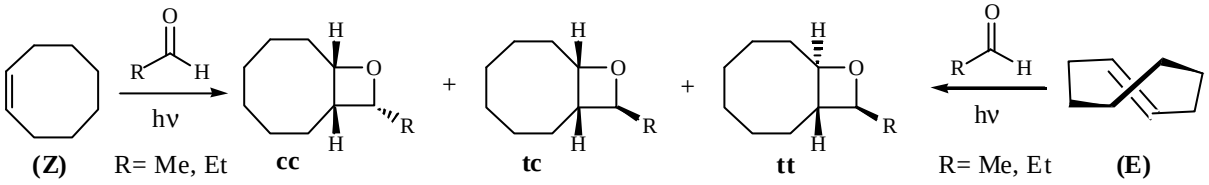
R= Ph, Me, Et, Bu^i

Effect of concentration on d.r. ?

Effect of solvent viscosity on d.r. ?

Effect of temperature on d.r. ?

In the light of recent research activities in the field of enantioselective cyclooctene photoisomerisation[83] and diastereoselective photocycloaddition,[70] I became interested in spin-directed effects on both the addition of electronically excited carbonyl compounds and the photoisomerisation process of cyclooctene. In a previous study by Jones *et al.*, it was shown that the stereoselectivity of the Paternò-Büchi reaction with *cis*-cyclooctene is indeed influenced by the substrate concentration, but no further conclusions were drawn concerning the mechanism of the spin-inversion process from the triplet 1,4-biradical.[57] Triplet excited aliphatic aldehydes with E_T in the 80 kcal/mol range are capable of *cis-trans* photoisomerisation of cyclooctenes wheras the singlets have energies that are too low for singlet-singlet energy transfer. It was thus of interest to study whether aliphatic aldehydes show spin-selectivity with respect to the *cis/trans* oxetane ratio and/or the *endo/exo*-selectivity relevant for the *cis*-photoadduct.



Effect of concentration on d.r. ?

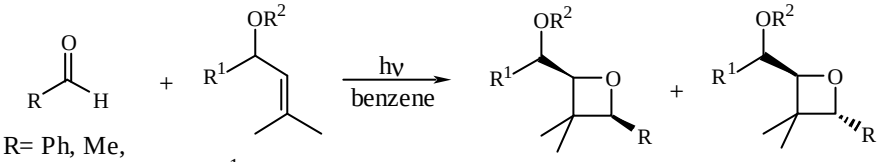
Do Z-E-isomerisation influence on d.r. ?

The concept of hydrogen-bonding as a tool for directing photochemical reactions has been reported for intermolecular [2+2] and [4+2] cycloadditions.[73,84] However, there was yet no conclusion about the effect of hydrogen bonding on the excited singlet and triplet states. I investigated the Paternò-Büchi reaction of allylic alcohols and acetates with aldehydes to test the influence of hydrogen bonding on the excited singlet and triplet state. The study addressed the following questions:

(a) is there a specific spin-directing effect connected with hydrogen bonding?,

(b) do hydrogen-bonding interactions influence induced as well as non-induced "simple" diastereoselectivity?,

(c) does hydrogen-bonding effect the rate of the Paternò-Büchi reaction?



R= Ph, Me, Et, Bu^i

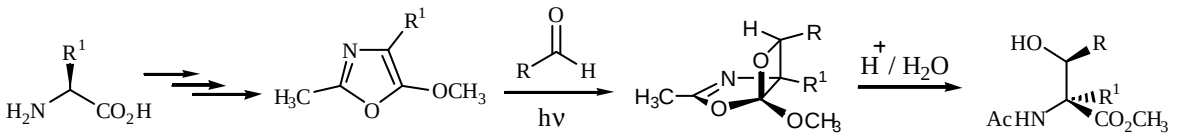
R^1= H, CH_3

R^2= H, Ac

degree of regioselectivity ?

degree of diastereoselectivity ?

In a second part, I studied synthetic applications of the Paternò-Büchi reaction of aldehydes and α-ketoesters with oxazoles, a reaction which has been developed in this research group in the last years. A series of interesting starting materials from the chiral pool of amino acids should be synthesized and transformed photochemically into bicyclic oxetanes. The selectivity of these reactions and further transformations of these highly interesting and reactive products were to be investigated in order to examplify the importance of this synthetic pathway.



R^1 = H, Me, Et, n-Pr, i-Pr, i-Bu, *sec*-Bu

Diastereoselectivity ?

Diastereoselectivity ?

3. Results and Discussion

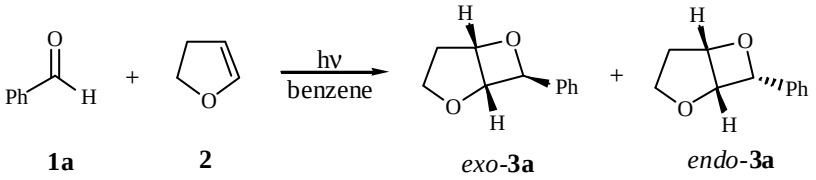
3.1 Effect of concentration on simple diastereoselectivity of Paternò-Büchi reactions

In order to evaluate the differences in simple diastereoselectivity of the Paternò-Büchi reaction in the *singlet versus* the *triplet* channel, the concentration dependence of the [2+2] photocycloaddition of aldehydes with electron-rich cycloalkenes was investigated. As alkene reagents, 2,3-dihydrofuran, 2,3-dihydropyran, cyclopentene, 5-methyl-2,3-dihydrofuran, 2,2-dimethyl-2,3-dihydrofuran and furan were used. As aliphatic aldehydes I used acetaldehyde, propionaldehyde, 3-methylbutyraldehyde, pivalaldehyde, 3-phenylpropionaldehyde and 2-methylbutyraldehyde. Benzaldehyde was applied as an aromatic aldehyde.

3.1.1 Photocycloaddition of 2,3-dihydrofuran

3.1.1.1 Reaction with benzaldehyde

It is well known that aromatic aldehydes exhibit high intersystem crossing rates and quantum yields and thus exclusively react *via* their first excited *triplet* states in intermolecular photocycloaddition.[37,49] On irradiation of a benzene solution of benzaldehyde **1a** and 2,3-dihydrofuran **2**, two cycloadducts *exo*-**3a** and *endo*-**3b** were formed in a 12 : 88 ratio with high yield.



1a **2** *exo*-**3a** *endo*-**3a**

Scheme 3.1: Photocycloaddition of benzaldehyde with 2,3-dihydrofuran.

Both substrates (**1a** and **2**) were applied in a 1:1 ratio over a broad concentration range, showing no significant effect on the simple (*endo/exo*) diastereoselectivity (see Figure 3.1)

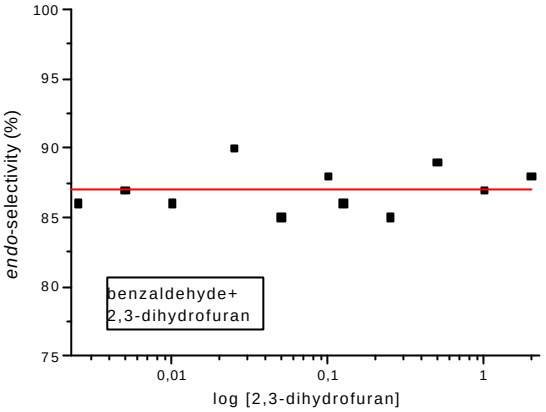
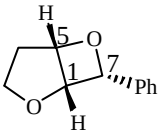


Figure 3.1: Concentration/selectivity profile of the benzaldehyde/2,3-dihydrofuran photocycloaddition.

The relative configuration of the diastereoisomers *exo*-**3a** and *endo*-**3a** were deduced from their ^{1}H-NMR spectra on the basis of the aromatic ring current effect by the phenyl group. H-5 in the *exo*-diastereoisomer absorbs at higher field (4.64 ppm) compared with the *endo*-isomer (5.05 ppm) due to the shielding effect of the benzene ring (see Table 3.1).

Table 3.1: Chemical shift (δ_{ppm}) of H-1, H-5 and H-7 for *exo*-**3a** and *endo*-**3a**.

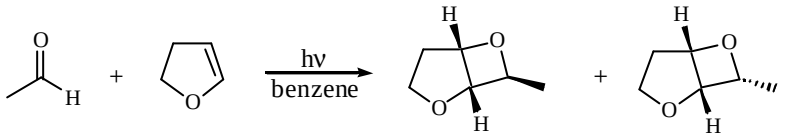


endo-**3a**

Compound	H-1	H-5	H-7
exo-**3a**	5.50	4.64	5.41
endo-**3a**	5.51	5.05	5.80

3.1.1.2 Reaction with acetaldehyde

The lifetimes of the first excited singlet state of aliphatic aldehydes are in the 1-2 ns range.[85] Thus, appropriate trapping reagents can intercept these singlets in diffusion-controlled bimolecular processes. The addition of 2,3-dihydrofuran to electronically excited acetaldehyde in benzene at a wide range of substrate concentrations afforded two diastereoisomers *exo*-**3b** and *endo*-**3b**. The diastereomeric ratios were determined by GC and NMR analyses.



1b **2** *exo*-**3b** *endo*-**3b**

Scheme 3.2: Photocycloaddition of acetaldehyde with 2,3-dihydrofuran.

Figure 3.2 shows the effect of concentration variation on the *endo/exo* diastereoselectivity of acetaldehyde/2,3-dihydrofuran photocycloaddition. At higher concentrations the selectivity switched to 42 : 58 wheras at lower concentration the selectivity reached 76 : 24 with preferential formation of the *endo* diastereoisomer.

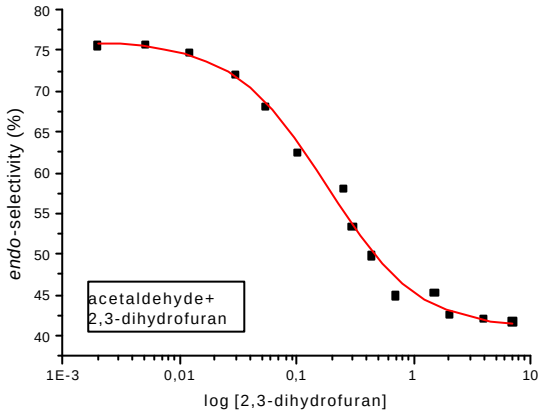
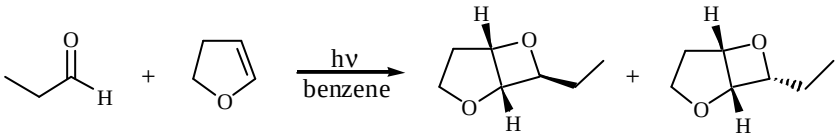


Figure 3.2: Concentration/selectivity profile of the acetaldehyde/2,3-dihydrofuran photocycloaddition.

3.1.1.3 Reaction with propionaldehyde

Photolysis of an equimolar ratio of propionaldehyde and 2,3-dihydrofuran in benzene solution gave the two diastereoisomers *exo*-**3c** and *endo*-**3c**.



1c **2** *exo*-**3c** *endo*-**3c**

Scheme 3.3: Photocycloaddition of propionaldehyde with 2,3-dihydrofuran.

The diastereomeric ratios of the photoadducts were strongly affected by the concentration of substrate. Figure 3.3 displays the effect of concentration variation on the *endo/exo* diastereoselectivity of the propionaldehyde/2,3-dihydrofuran photocycloaddition. In the low concentration region (< 0.02 M), the diastereoselectivity reached a plateau with an *endo/exo*

ratio of ca. 85 : 15. Likewise, in the high concentration region (>0.8M) the diastereoselectivity become constant with ca. 1: 1 *endo/exo* ratio. The diastereomeric ratios were determined by GC and ^{1}H-NMR analyses. Figure 3.4 shows the GC trace of the *exo*- and *endo*-diastereoisomers of the photocycloaddition of propionaldehyde with 2,3-dihydrofuran at different substrate concentrations. The *exo*-isomer has low retention time compared with the *endo*-isomer.

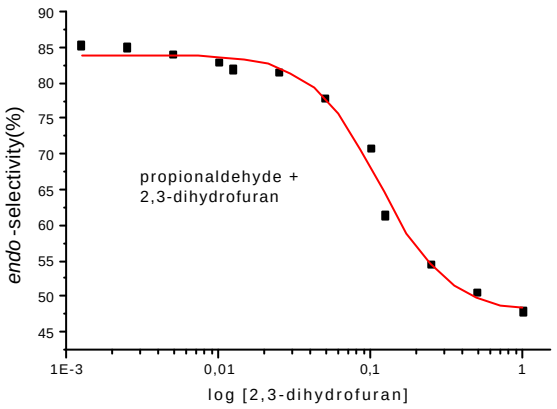


Figure 3.3: Concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran photocycloaddition.

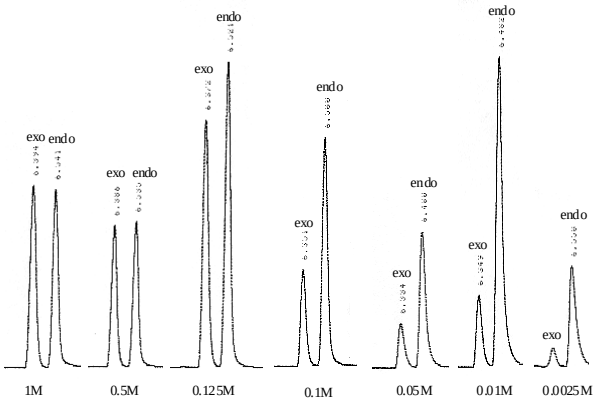


Figure 3.4: GC trace analysis of the propionaldehyde/2,3-dihydrofuran photocycloaddition.

The relative configuration of the photoadducts were established by nOe measurements. The *exo*-diastereoisomer shows strong nOe enhancements between H-1 and CH_3 group. This phenomena is illustrated in Figure 3.5, which summarizes the pertinent nOe data recorded for the diastereoisomer *exo*-**3c**. The *endo*-diastereoisomer did not show significant nOe enhancements between the CH_3 group and the proton H-1.

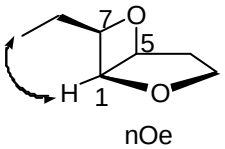


Figure 3.5: NOE interaction in bicyclic oxetane *exo*-**3c**.

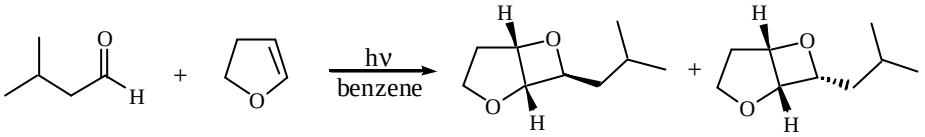
Furthermore, the chemical shift of the proton H-1 is distinctly different in either pair of bicyclic oxetane diastereoisomers *exo*-**3c** and *endo*-**3c**. It resonates at lower field in the *endo*-isomer (δ = 4.75 ppm) and at higher field in the *exo*-isomer (δ = 4.51 ppm) (see Table 3.2).

Table 3.2: Chemical shift (δ_{ppm}) of H-1, H-5 and H-7 for *exo*-**3c** and *endo*-**3c**.

Compound	H-1	H-5	H-7
exo-**3c**	4.51	5.25	4.31
endo-**3c**	4.75	5.34	4.60

3.1.1.4 Reaction with 3-methylbutyraldehyde

The [2+2] photocycloaddition of electronically excited 3-methylbutryaldehyde with 2,3-dihydrofuran in benzene afforded the two diastereoisomers *exo*-**3d** and *endo*-**3d**.



1d **2** *exo*-**3d** *endo*-**3d**

Scheme 3.4: Photocycloaddition of 3-methylbutyraldehyde with 2,3-dihydrofuran.

Analogous to acetaldehyde and propionaldehyde, the diastereomeric ratios *endo/exo* were strongly influenced by the concentration of substrates. The diastereomeric ratios were determined by using GC and ^{1}H-NMR analyses. Figure 3.6 shows the effect of concentration variation on the *endo/exo* diastereoselectivity of the 3-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition. In the low concentration region (< 0.01M) the diastereoselectivity reached a plateau with an *endo/exo* ratio of ca. 87 : 13. At high concentration the selectivity switched to 53 : 47. The structure of the photoadducts were established using ^{1}H-NMR and ^{13}C-NMR analyses.

Figure 3.7 shows the GC trace of the *exo*- and *endo*- diastereoisomers of the photocycloaddition of 3-methylbutyraldehyde with 2,3-dihydrofuran at different substrate concentrations. Analogous to propionaldehyde/2,3-dihydrofuran photoadducts, the *exo*-isomer has low retention time compared with the *endo*-isomer.

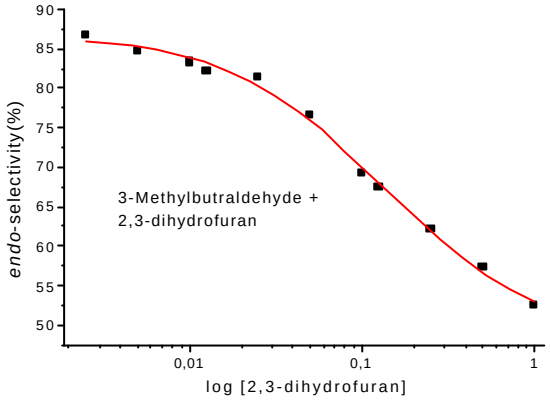


Figure 3.6: Concentration/selectivity profile of the 3-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition.

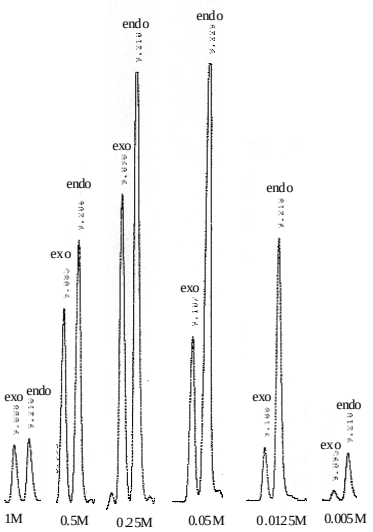
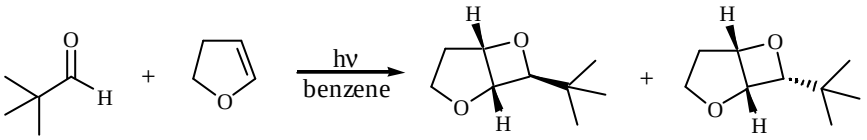


Figure 3.7: GC trace analysis of the 3-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition.

3.1.1.5 Reaction with pivalaldehyde

Pivalaldehyde, when irradiated in the presence of 2,3-dihydrofuran, delivered the diastereoisomer *exo*-**3e** and *endo*-**3e** in moderate yield.



1e **2** *exo*-**3e** *endo*-**3e**

Scheme 3.5: Photocycloaddition of pivalaldehyde with 2,3-dihydrofuran.

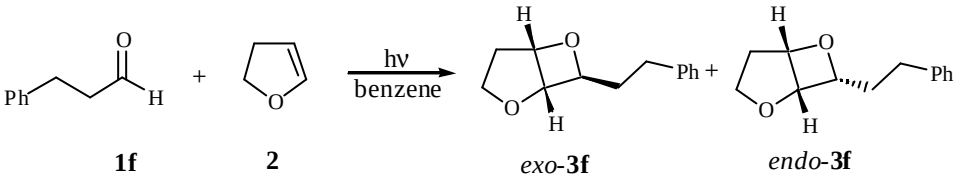
Interestingly, the diastereomeric ratios of the photoadducts were depended only little on the concentration of substrate (see Table 3.3).

Table 3.3: Concentration dependence on simple diastereoselectivity of the pivalaldehyde/2,3-dihydrofuran photocycloaddition reaction.

Conc. (M)	d.r. (*exo* : *endo*)
1	54.1 : 45.9
0.5	51.0 : 49.0
0.125	50.0 : 50.0

3.1.1.6 Reaction with 3-phenylpropionaldehyde

Irradiation of a benzene solution of equimolar amount of 2,3-dihydrofuran and 3-phenylpropionaldehyde afforded two diastereoisomers *exo*-**3f** and *endo*-**3f**.



1f **2** *exo*-**3f** *endo*-**3f**

Scheme 3.6: Photocycloaddition of 3-phenylpropionaldehyde with 2,3-dihydrofuran.

Figure 3.8 displays a linear correlation between the *endo*-selectivity and concentration, i.e. the *endo*-selectivity increases with decreasing substrate concentration. The diastereomeric ratio *endo/exo* at 1M was 50 : 50 and 70 : 30 at 0.125 M. The structure of the photoadducts were identified using ^{1}H-NMR, ^{13}C-NMR and DEPT analyses. The diastereomeric ratios were determined by using GC and ^{1}H-NMR analyses.

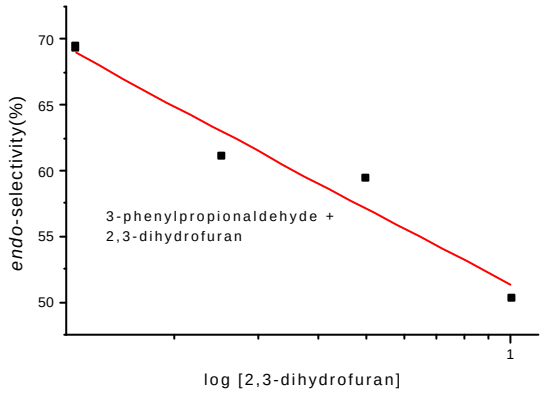
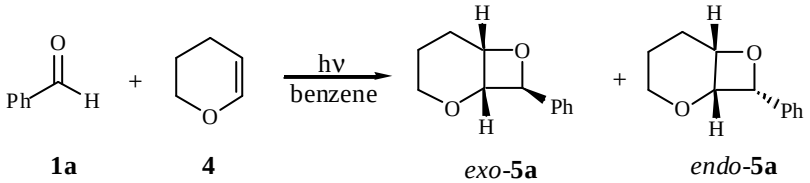


Figure 3.8: Concentration/selectivity profile of the 3-phenylpropionaldehyde/2,3-dihydrofuran photocycloaddition.

3.1.2 Photocycloaddition of 2,3-dihydropyran

3.1.2.1 Reaction with benzaldehyde

Photolysis of benzaldehyde with 2,3-dihydropyran in benzene afforded two diastereoisomers *exo*-**5a** and *endo*-**5a** in moderate yield with high regio- and stereoselectivity.



1a **4** *exo*-**5a** *endo*-**5a**

Scheme 3.7: Photocycloaddition of benzaldehyde with 2,3-dihydropyran.

The diastereomeric ratios were constant over a wide range of concentration similar to the reaction with 2,3-dihydrofuran (see Figure 3.9). The diastereomeric ratios were determined by using GC and NMR analyses. The strucure of the photoadducts were identified from ^{1}H-NMR and ^{13}C-NMR analyses.

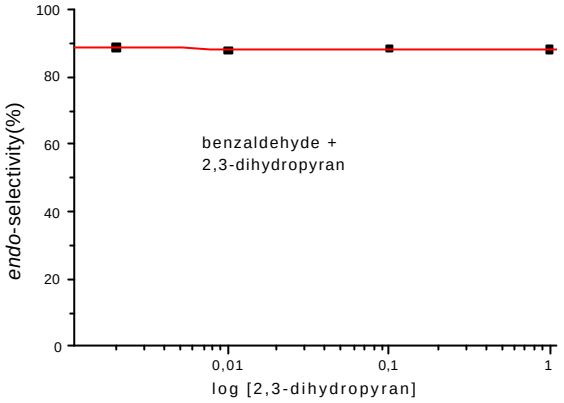
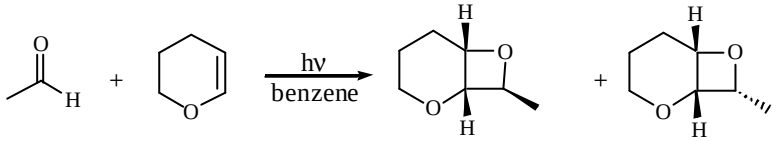


Figure 3.9: Concentration/selectivity profile of the benzaldehyde/2,3-dihydropyran photocycloaddition.

3.1.2.2 Reaction with acetaldehyde

The photoaddition of electronically excited acetaldehyde to 2,3-dihydropyran in benzene gave two diastereoisomers *exo*-**5b** and *endo*-**5b**.



1b **4** *exo*-**5b** *endo*-**5b**

Scheme 3.8: Photocycloaddition of acetaldehyde with 2,3-dihydropyran.

The diastereomeric ratios *endo/exo* were substantially dependent on the concentration of substrate. When the substrate concentration was lowered from 1 to 0.002 M, a distinct increase in the amount of *endo*-diastereoisomer was obtained. Figure 3.11 shows the GC trace of the *exo*- and *endo*-diastereoisomers of the photocycloaddition of acetaldehyde with 2,3-dihydropyran at different substrate concentrations. In contrast to 2,3-dihydrofuran photocycloaddition, the *endo*-isomer has low retention time compared with the *exo*-isomer of the 2,3-dihydropyran photocycloaddition.

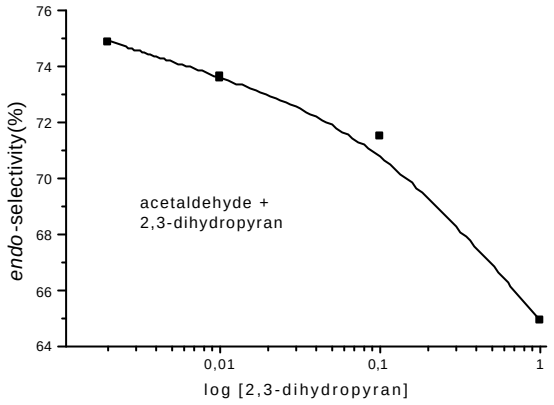


Figure 3.10: Concentration/selectivity profile of the acetaldehyde/2,3-dihydropyran photocycloaddition.

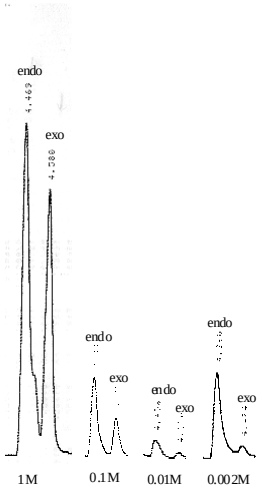
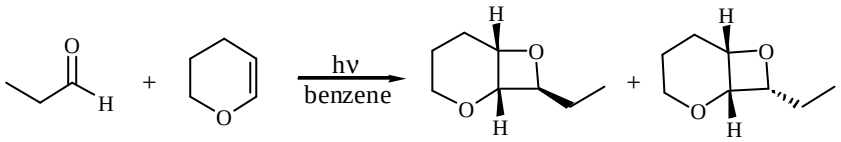


Figure 3.11: GC trace analysis of the acetaldehyde/2,3-dihydropyran photocycloaddition.

3.1.2.3 Reaction with propionaldehyde

Irradiation of propionaldehyde with 2,3-dihydropyran in benzene gave the bicyclic oxetanes *exo*-**5c** and *endo*-**5c** in concentration-dependent ratios.



1c **4** *exo*-**5c** *endo*-**5c**

Scheme 3.9: Photocycloaddition of propionaldehyde with 2,3-dihydropyran.

In contrast to the results with 2,3-dihydrofuran, the selectivity curve was much less steeper and showed a non-linear behavoir in the region between 1M and 0.01M (see Figure 3.12). The diastereomeric ratios were determined by high resolution ^{1}H-NMR measurements of the crude product mixtures and the structure of the products were elucidated by their ^{1}H-NMR and ^{13}C-NMR spectral data. Figure 3.13 shows the GC trace of the *exo*- and *endo*-diastereoisomers of the photocycloaddition of propionaldehyde with 2,3-dihydropyran at different substrate concentrations. Analogous to acetaldehyde/2,3-dihydropyran photoadducts, the *endo*-isomer has low retention time compared with the *exo*-isomer.

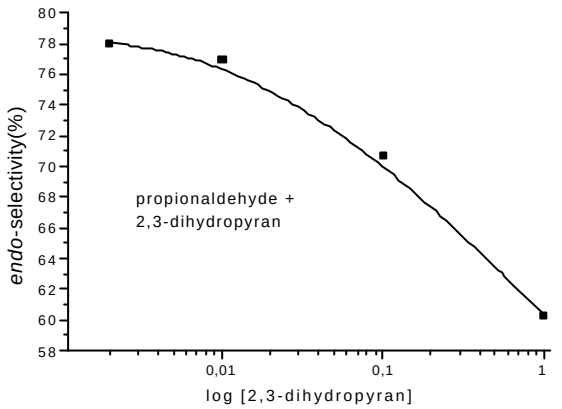


Figure 3.12: Concentration/selectivity profile of the propionaldehyde/2,3-dihydropyran photocycloaddition.

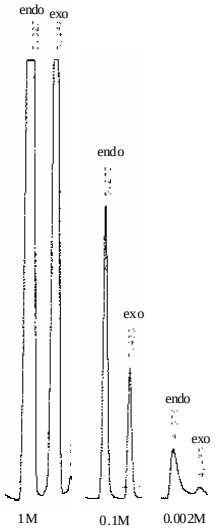
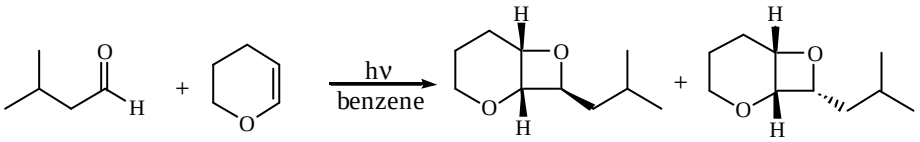


Figure 3.13: GC trace analysis of the propionaldehyde/2,3-dihydropyran photocycloaddition.

3.1.2.4 Reaction with 3-methylbutyraldehyde

The [2+2] cycloaddition of 3-methylbutyraldehyde with 2,3-dihydropyran afforded the two diastereoisomers *exo*-**5d** and *endo*-**5d** .



1d **4** *exo*-**5d** *endo*-**5d**

Scheme 3.10: Photocycloaddition of 3-methylbutyraldehyde with 2,3-dihydropyran.

Figure 3.14 displays the effect of concentration variation on the *endo/exo* diastereoselectivity of the 3-methylbutyraldehyde/2,3-dihydropyran photocycloaddition. At high concentration (1M) the diastereomeric ratio *endo/exo* was moderate (60 : 40) while at low concentration (0.002M) the *endo*-selectivity dominated (72 : 28).

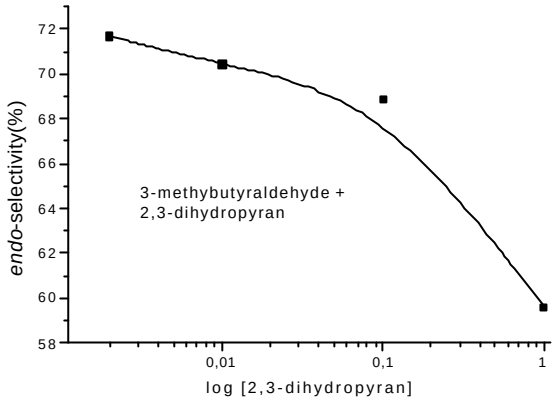
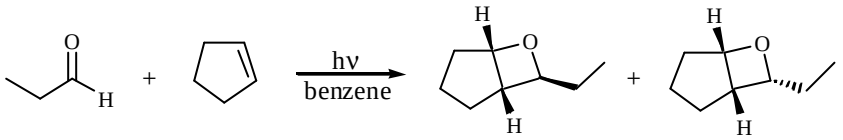


Figure 3.14: Concentration/selectivity profile of the 3-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition.

3.1.3 Photocycloaddition of cyclopentene with propionaldehyde

Cyclopentene, when irradiated with propionaldehyde in benzene, gave also two diastereoisomers *exo*-**7b** and *endo*-**7b**.



1c **6** *exo*-**7c** *endo*-**7c**

Scheme 3.11: Photocycloaddition of cyclopentene with propionaldehyde.

The diastereomeric *endo/exo* ratios were slightly depended on the substrate concentration.

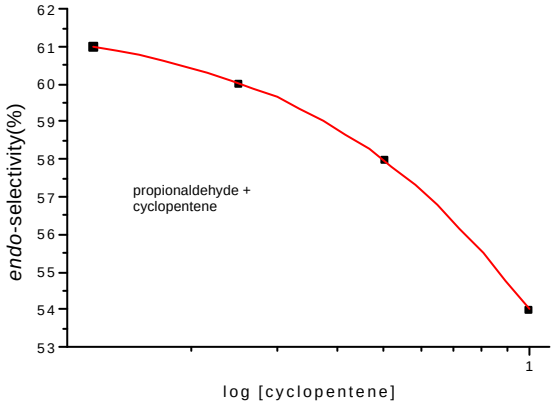


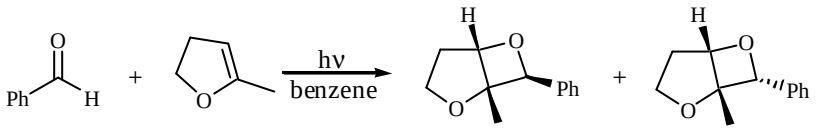
Figure 3.15: Concentration/selectivity profile of the propionaldehyde/cyclopentene photocycloaddition.

3.1.4 Photocycloaddition of 5-methyl-2,3-dihydrofuran

It was already documented that alkyl-substituted cycloalkenes react with electronically excited carbonyl compounds with moderate diastereoselectivity in comparison with unsubstituted cycloalkenes due to the additional steric hindrance by the extra alkyl group. To further understand this concept, the concentration effect on the stereoselectivity of the photoaddition of 5-methyl-2,3-dihydrofuran with aldehydes was studied.

3.1.4.1 Reaction with benzaldehyde

Irradiation of benzaldehyde with 5-methyl-2,3-dihydrofuran in benzene afforded two diastereoisomers *exo*-**9a** and *endo*-**9a**.



1a **8** *exo*-**9a** *endo*-**9a**

Scheme 3.12: Photocycloaddition of benzaldehyde with 5-methyl-2,3-dihydrofuran.

The diastereomeric ratio *endo/exo* (60 : 40) was independent on the concentration of the substrate. The diastereomeric ratios were determined using GC and ^{1}H-NMR analyses (see Figure 3.17). The structure of the photoadducts were identified from ^{1}H-NMR and ^{13}C-NMR analyses.

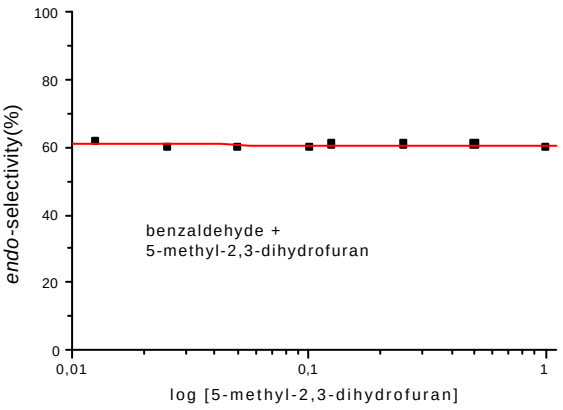


Figure 3.16: Concentration/selectivity profile of the benzaldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

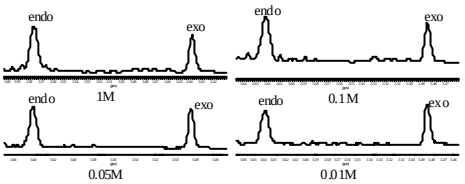
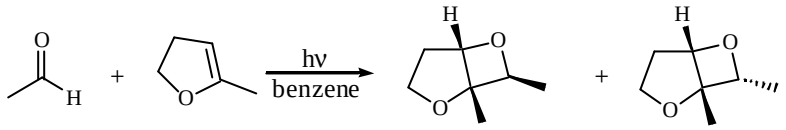


Figure 3.17: ^{1}H-NMR analysis of the benzaldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

3.1.4.2 Reaction with acetaldehyde

The photocycloaddition of electronically excited acetaldehyde to 5-methyl-2,3-dihydrofuran gave the two diastereoisomers *exo*-**9b** and *endo*-**9b**.



1b **8** *exo*-**9b** *endo*-**9b**

Scheme 3.13: Photocycloaddition of acetaldehyde with 5-methyl-2,3-dihydrofuran.

The diastereomeric ratios *endo/exo* were completely inverted when processing from high to low concentration. At high concentration (1 M) the *endo/exo* selectivity was 38 : 62 and changed to 62 : 38 at low concentration (0.025 M) (see Figure 3.19).

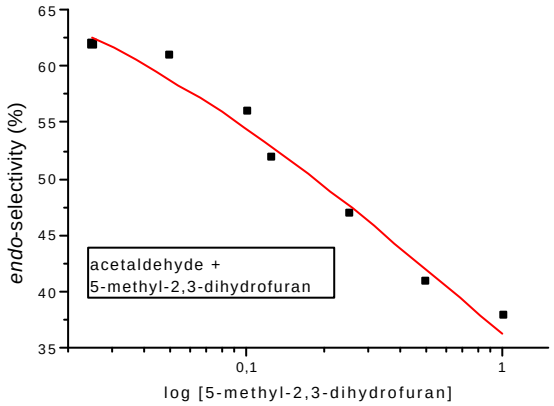


Figure 3.18: Concentration/selectivity profile of the acetaldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

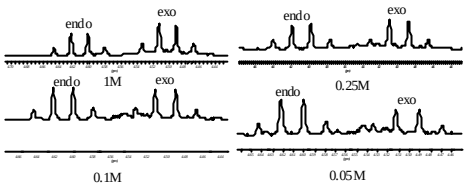
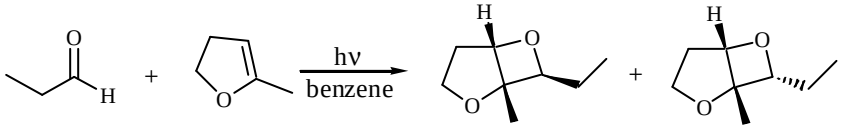


Figure 3.19: ^{1}H-NMR analysis of the acetaldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

3.1.4.3 Reaction with propionaldehyde

Irradiation of propionaldehyde with 5-methyl-2,3-dihydrofuran gave the two diastereoisomers *exo*-**9c** and *endo*-**9c**.



1c **8** *exo*-**9c** *endo*-**9c**

Scheme 3.14: Photocycloaddition of propionaldehyde with 5-methyl-2,3-dihydrofuran.

The diastereomeric *endo/exo* ratio was 50 : 50 at high concentration (1M) and shifted to higher *endo*-selectivity by lowering the substrate concentrations. The *endo/exo* ratio was 67 : 33 at 0.01M. Figure 3.20 shows the concentration/selectivity profile of the photocycloaddition of 5-methyl-2,3-dihydrofuran with propionaldehyde.

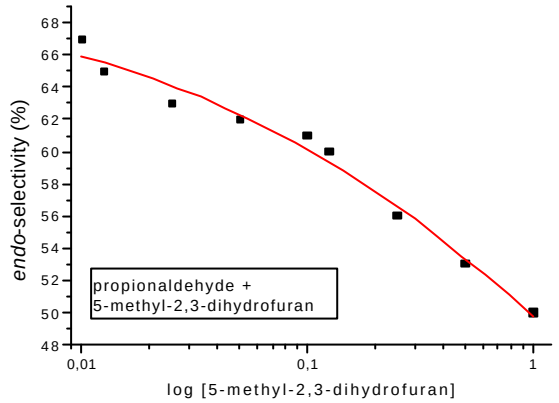


Figure 3.20: Concentration/selectivity profile of the propionaldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

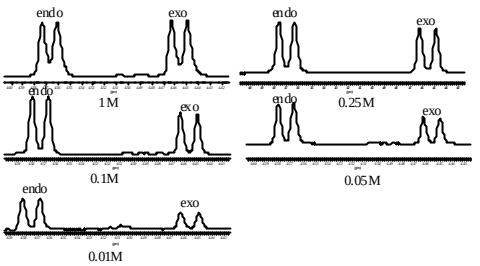
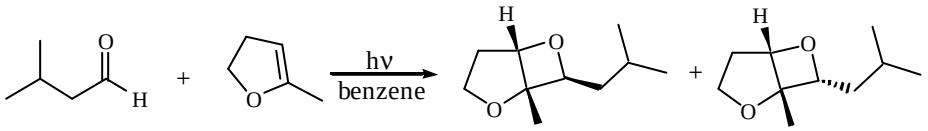


Figure 3.21: ^{1}H-NMR analysis of the propionaldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

3.1.4.3 Reaction with 3-methylbutyraldehyde

The [2+2]-photocycloaddition of 3-methylbutyraldehyde with 5-methyl-2,3-dihydrofuran afforded the mixture of *exo*-**9d** and *endo*-**9d**.



1c **8** *exo*-**9c** *endo*-**9c**

Scheme 3.15: Photocycloaddition of 3-methylbutyraldehyde with 5-methyl-2,3-dihydrofuran.

At high concentration (1M) the *endo/exo* selectivity was 51: 49. By lowering the concentration of the substrate (0.01M) the selectivity switched constantly to 68 : 32 (see Figure 3.23).

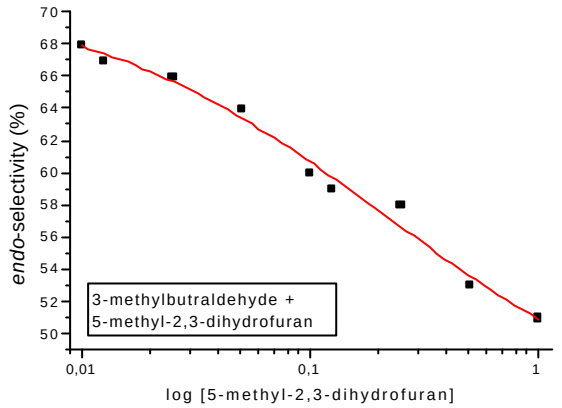


Figure 3.22: Concentration/selectivity profile of the 3-methylbutyraldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

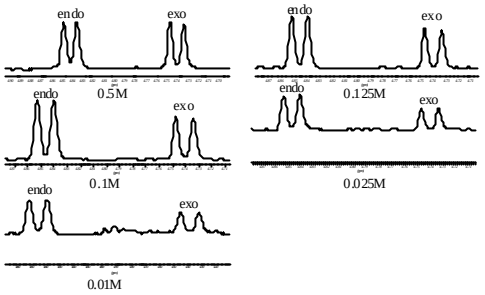
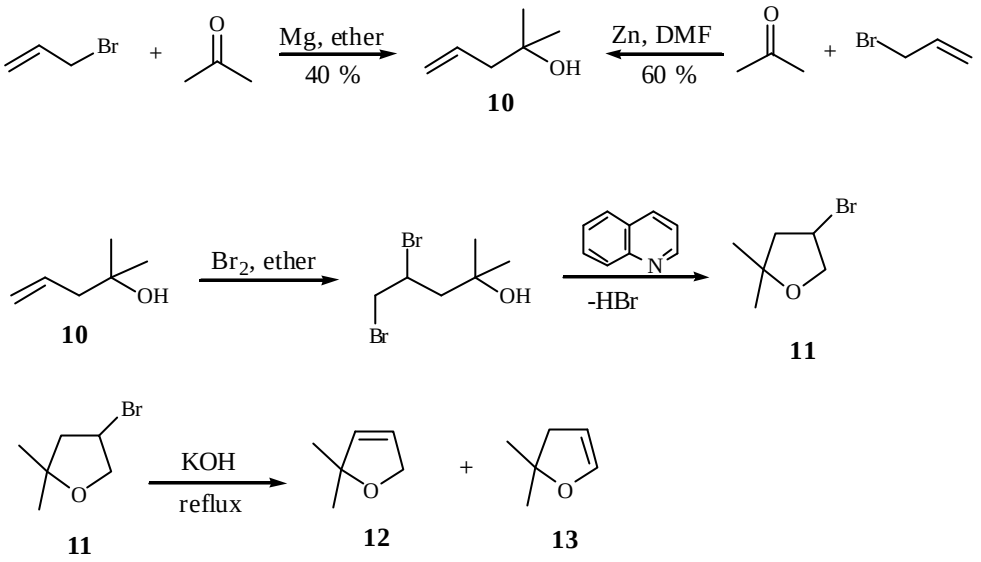


Figure 3.23: ^{1}H-NMR analysis of the 3-methylbutyraldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

3.1.5 Synthesis of 2,2-dimethyl-2,3-dihydrofuran

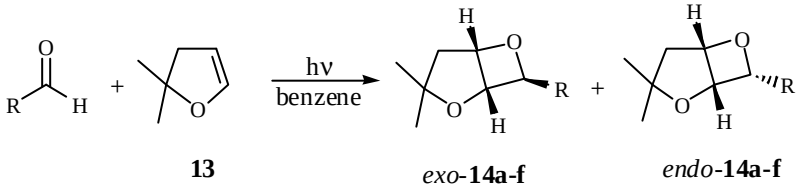
2,2-Dimethyl-2,3-dihydrofuran was not commercially available and was prepared according to a literature procedure as depicted in scheme 3.16.[86] To improve the yield of the primary substrate, 2-methyl-4-penten-2-ol **10**, two different methods were used. The first method required the Grignard addition of allyl magnesium bromide to acetone in ether[87] and the second method used Luche reaction which required the addition of allyl bromide to acetone in DMF and in the presence of zinc dust.[88] The second reaction gave appreciable higher yields. Bromination of 2-methyl-4-penten-2-ol **10** in ether gave 2-methyl-4,5-dibromo-2-pentanol which *in situ* underwent dehydrobromination by refluxing with quinoline to give 2,2-dimethyl-4-bromotetrahydrofuran **11**. Distillation of 2,2-dimethyl-4-bromotetrahydrofuran over KOH pellets furnished the two regioisomers 2,2-dimethyl-2,5-dihydrofuran **12** and 2,2-dimethyl-2,3-dihydrofuran **13**. The ^{1}H-NMR spectra of the products revealed that the ratio of these regioisomers is 1 : 1.5 with preferential formation of the 2,2-dimethyl-2,3-dihydrofuran **13**. The two regioisomers **12** and **13** were successfully separated by column chromatography. The structure of the isolated products were identified using ^{1}H-NMR and ^{13}C-NMR spectral analyses.



Scheme 3.16: Synthesis of 2,2-dimethyl-2,3-dihydrofuran.

3.1.5.1 Photocycloaddition of 2,2-dimethyl-2,3-dihydrofuran with aldehydes

In order to estimate if there is a correlation between spin selectivity and steric effects on the simple diastereoselectivity of the Paternò-Büchi reaction, the photocycloaddition of 2,2-dimethyl-2,3-dihydrofuran **13** with aliphatic and aromatic aldehydes was studied.



13 *exo*-**14a-f** *endo*-**14a-f**

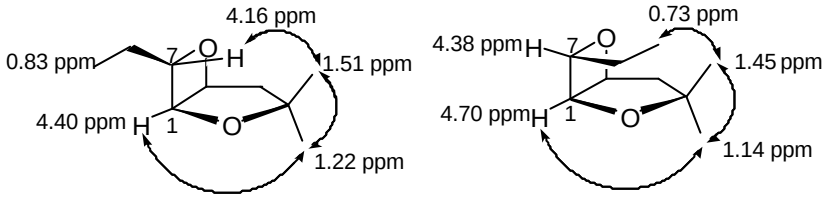
R=Ph,o-Tol, Et, i-Pr, i-Bu, t-Bu

Scheme 3.17: Photocycloaddition of 2,2-dimethyl-2,3-dihydrofuran with aldehydes.

Table 3.4: Simple diastereoselectivity in the Paternò-Büchi reaction of 2,2-dimethyl-2,3-dihydrofuran with aldehydes.

Entry	Conc. (M)	R =	% *exo*-**14**	% *endo*-**14**
1	0.1	Ph	14	86
2	0.1	o-Tol	13	87
3	1.0	Et	38	62
4	0.1	Et	26	74
5	0.1	i-Pr	35	65
6	0.1	i-Bu	30	70
7	0.1	t-Bu	18	82

Firstly, both benzaldehyde and o-tolualdehyde were used as triplet precursor of the photocycloaddition with 2,2-dimethyl-2,3-dihydrofuran. The *endo/exo* selectivity was high in both cases (see Table 3.4, entry 1&2). From concentration studies, we have already learned that aliphatic aldehydes can react from both *singlet* and *triplet* excited state. The photocycloaddition of the electronically excited singlet state of propionaldehyde (1M) to 2,2-dimethyl-2,3-dihydrofuran gave a moderate *endo/exo* selectivity (62 : 38) whereas the triplet excited state of propionaldehyde (0.1M) reacted highly *endo* -selective (74 : 26) (see Table 3.4, entry 3&4). Interestingly, the diastereomeric ratios exhibit a slightly increasing trend in favor of the *endo*-isomers with increasing steric demand of the R-substituent (Et, i-Pr, i-Bu, t-Bu) of the aldehyde. The diastereomeric ratio of the photoadducts were determined from ^{1}H-NMR and the structure of the products were identified from ^{1}H-NMR and ^{13}C-NMR spectral analyses. The relative configuration of the diastereoisomers *exo*-**14c** and *endo*-**14c** were unambiguously determined from NOE difference measurement. In the *exo*-**14c** isomer, irradiation of a methyl hydrogen protons at 1.51 ppm leads to nuclear Overhauser enhancements of both methyl protons signal at 1.22 ppm and methine proton signal, H-7 at 4.16 ppm. In the *endo*-**14c**, irradiation of a methyl protons signal at 1.45 ppm leads to nuclear Overhauser enhancements of the intensity of the methyl protons signal at 1.14 ppm (see Figure 3.24).



exo-**14c** *endo*-**14c**

Figure 3.24: NOE interactions in bicyclic oxetanes *exo*-**14c** and *endo*-**14c**.

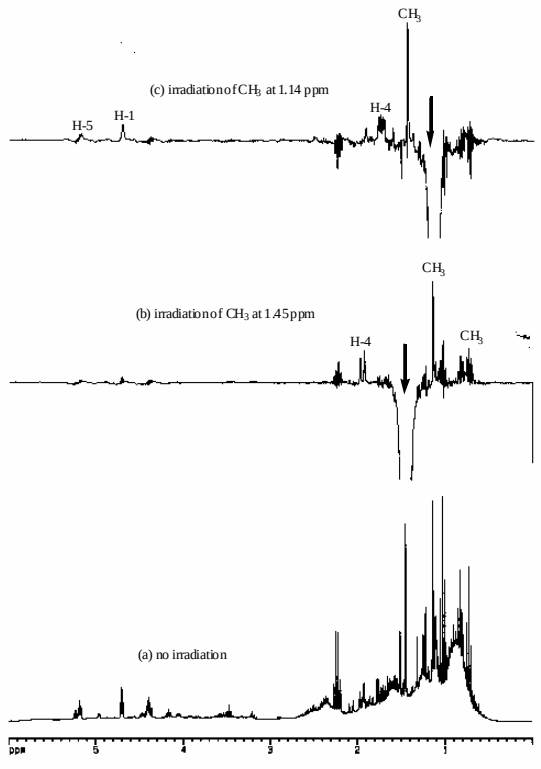


Figure 3.25: NOE difference spectra (300 MHz, $CDCl_3$) of *exo*-**14c**.

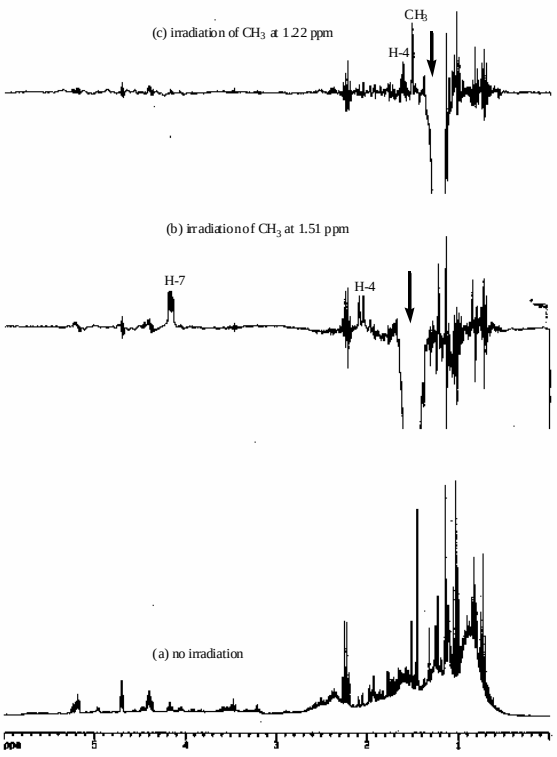


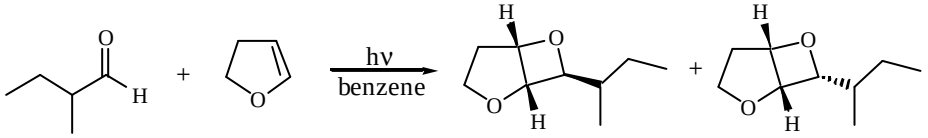
Figure 3.26: NOE difference spectra (300 MHz, $CDCl_3$) of *endo*-**14c**.

3.1.6 Effect of concentration on simple and induced diastereoselectivity of Paternò-Büchi reactions

In order to determine the difference between simple and induced diastereoselectivity in singlet and triplet reactions, the concentration dependence of the photocycloaddition reaction of a chiral aldehyde with 2,3-dihydrofuran and 5-methyl-2,3-dihydrofuran, respectively, was investigated.

3.1.6.1 Photocycloaddition of 2,3-dihydrofuran with 2-methylbutyraldehyde

2-Methylbutyraldehyde is commerically avaliable and was applied in the Paternò-Büchi reaction. The photolysis of 2-methylbutyraldehyde with 2,3-dihydrofuran was performed in benzene at a wide range of concentrations. Two diastereoisomers *exo*-**3g** and *endo*-**3g** were obtained in good yield.



1g **2** *exo*-**3g** *endo*-**3g**

Scheme 3.18: Photocycloaddition of 2-methylbutyraldehyde with 2,3-dihydrofuran.

The asymmetric induction was negligible (i.e. the diastereomeric excessess for both *endo*- and *exo*-isomers was 50 : 50); this might be a reason of the small difference in substituent size at the stereogenic center. The simple *endo/exo* diastereoselectivity was affected by the change of the concentration of the substrate. The results are shown in Figure 3.27: at high alkene concentration (1M), the simple *endo/exo* selectivity was low (47 : 53). In the low concentration region (0.025 M), the *endo*-selectivity became dominant (71 : 29).

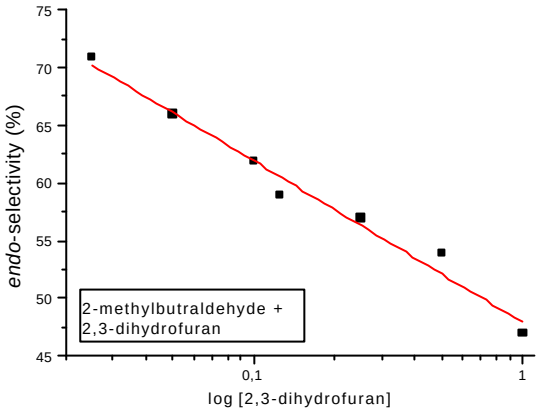
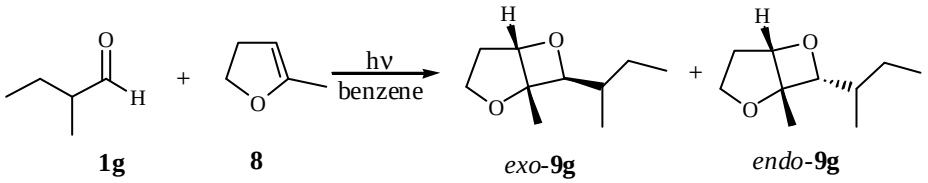


Figure 3.27: Concentration/selectivity profile of the 2-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition.

3.1.6.2 Photocycloaddition of 5-methyl-2,3-dihydrofuran with 2-methylbutyraldehyde

Irradiation of 2-methylbutyraldehyde with 5-methyl-2,3-dihydrofuran in benzene furnished the two diastereoisomers *exo*-**9g** and *endo*-**9g**.



1g **8** *exo*-**9g** *endo*-**9g**

Scheme 3.19: Photocycloaddition of 2-methylbutyraldehyde with 5-methyl-2,3-dihydrofuran.

Again, the asymmetric induction was low and not affected by change of the concentration of the substrate. The simple *endo/exo*-selectivity at 1M was low (52 : 48), increased by dilution and switched to 63 : 37 at 0.025M (see Figure 3.28).

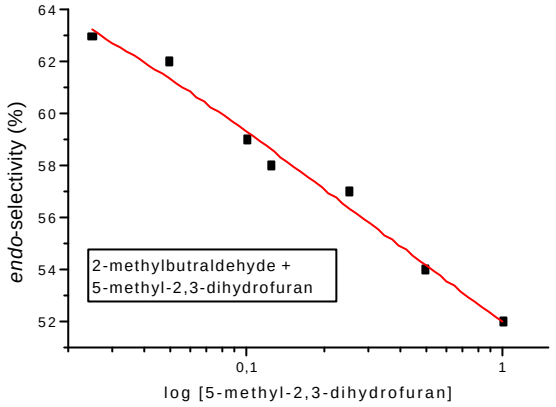
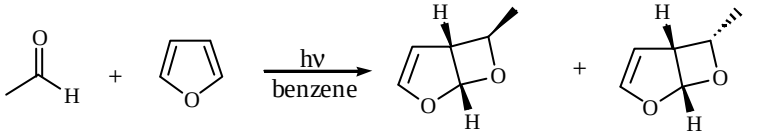


Figure 3.28: Concentration/selectivity profile of the 3-methybutyraldehyde/5-methyl-2,3-dihydrofuran photocycloaddition.

3.1.7 Photocycloaddition of furan with acetaldehyde

The results of the concentration study of the photocycloaddition of aldehydes with electron rich-cycloalkenes have prompted me to investigate the concentration effect also on the stereoselectivity of the furan/acetaldehyde photocycloaddition. Irradiation of acetaldehyde with furan in benzene furnished two diastereoisomers *exo*-**16b** and *endo*-**16b**.



1b **15** *exo*-**16b** *endo*-**16b**

Scheme 3.20: Photocycloaddition of acetaldehyde with furan.

Table 3.5: Simple diastereoselectivity of the photocycloaddition reaction of furan with acetaldehyde.

Conc. (M)	% *exo*	% *endo*
10	92	8
1	86	14
0.1	64	36

Surprisingly, the diastereomeric *exo/endo* ratios were also dependent on the concentration of the substrate (Table 3.5). At high concentration (10M) the simple *exo/endo* selectivity was 92 : 8 wheras at low concentration (0.1M) it decreased to 64 : 36. The diastereomeric ratios were determined from the ^{1}H-NMR analysis of the crude reaction mixture.

3.1.8 Fluorescence quenching

Fluorescence quenching is the most valuable method for determining the probability of carbonyl singlets participation in bimolecular reaction. This measurement uses the intensities of fluorescence (band maxima) in the presence of varying concentrations of a potential quencher and leads to data correlation resolved by the Stern-Volmer equation.

$$F_0/F = 1 + k_q \tau [Q]$$

Where F_0 : unquenched fluorescence intensity

F : quenched fluorescence intensity

k_q : bimolecular quenching rate constant

τ : lifetime of the carbonyl singlet

[Q] : molar concentration of quencher

Solutions of propanal (0.2M) with various concentrations of 2,3-dihydrofuran as quencher (0.02-1M) were measured in benzene; both benzene and 2,3-dihydrofuran showing negligible fluorescence. Solutions were placed in 3 cm^2 quartz cells after deoxygenated by nitrogen bubbling for 30 sec and the fluorescence spectra were recorded. The excitation wavelength was 310 nm, the intensity of the emission (F) at the maximum (~400 nm) for propanal was compared to the intensity (F_0) in the abscence of quencher. A Stern-Volmer plot was drawn of F_0/F *versus* molarity of quencher, and the slope determined at least from four points using linear portion of the curve. The results are shown in Figure 3.29 & 3.30.

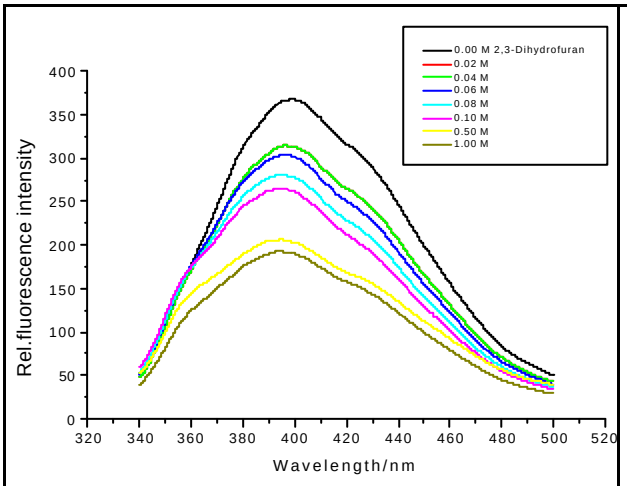


Figure 3.29: Fluorescence quenching of propionaldehyde 0.2M with 2,3-dihydrofuran (0.02–1.00 M) in benzene at 25°C.

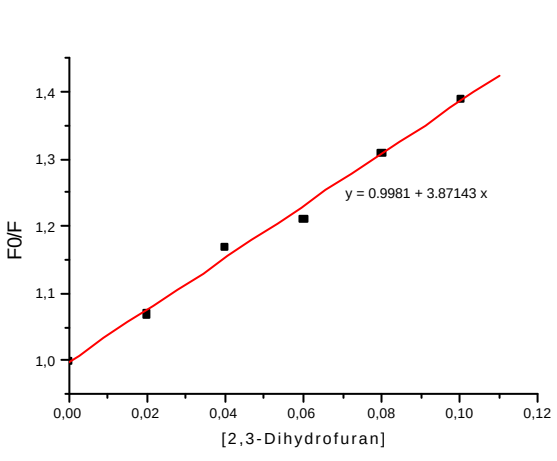


Figure 3.30: Stern-Volmer plot for the fluorescence quenching of propionaldehyde with 2,3-dihydrofuran.

By applying the lifetime of singlet excited state of propanal (τ_s = 1.8 ns),[85] a bimolecular quenching rate constant of $k_q = 2.15 \times 10^9$ m^{-1} s^{-1} was determined. This result clearly shows that the reactivity of singlet excited state of propanal in the photocycloaddition reaction is high and only a factor 5 away from the diffusion limit.

3.1.9 Quantum yield (F)

The quantum yield of the photocycloaddition of benzaldehyde with 2,3-dihydrofuran in benzene was determined by using a merry-go-round apparatus[89] with valerophenone as chemical actinometer.[90] The product composition was measured as a function of time by GC analysis. The conversion of starting material is plotted as a function of time as shown in Figure 3.31.

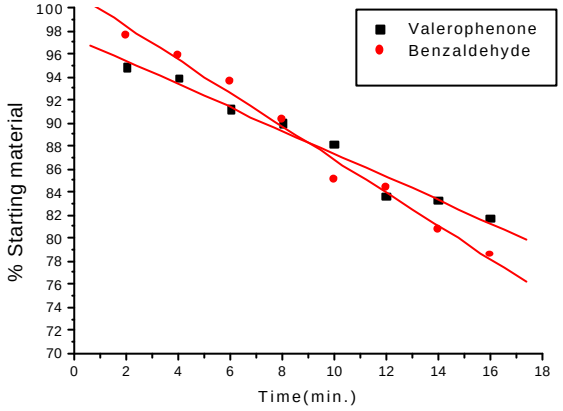


Figure 3.31: The relationship between conversion of the starting material *versus* time for the chemical actinometer and the benzaldehyde/2,3-dihydrofuran system.

The best-fit line for benzaldehyde had a slope -1.43 and for valerophenone a slope of -1.004 resulted. By using the following equation.

$$\frac{\text{slope (valerophenone)}}{\text{slope (benzaldehyde)}} = \frac{\Phi \text{ (valerophenone)}}{\Phi\text{(Paternò-Büchi reaction)}}$$

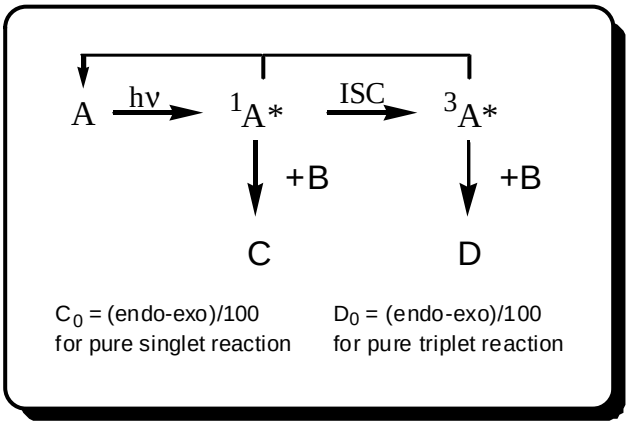
The quantum yield for the triplet photocycloaddition of benzaldehyde with 2,3-dihydrofuran (Φ = 0.48) was determined. The quantum yield is in agreement with literature value for the photocycloaddition of benzaldehyde with tetramethylethylene (Φ = 0.53).[91]

Due to the long lifetimes of the excited triplet carbonyl states, the high concentration of the excited triplet state quencher 2,3-dihydrofuran, and because the slopes are compared in the low conversion region, the method is reliably, albeit uni- and bimolecular photochemistry is compared herein.

Mechanistic analysis

Spin-directed stereoselectivity has been already reported for the photolyses of azoalkenes[92] as well as for Yang cyclization processes following intramolecular hydrogen abstractions.[93] In these cases, however, high diastereoselectivities were observed for singlet reactions and low selectivities for sensitized (triplet) processes. The inverse behavoir, as described herein for the cycloalkene photocycloadditions to aliphatic aldehydes, can be rationalized as follows:

In triplet Paternò-Büchi reactions 1,4-triplet biradicals are generated, which have to undergo intersystem crossing in order to convert into closed-shell products. Obviously, this process requires severe geometrical restrictions and, following the "Griesbeck model",[51] leads to high *endo*-selectivity. The surprising result is the stereoselectivity of the singlet process: very low selectivities were determined even for the reaction of pivalaldehyde with 2,3-dihydrofuran (50 : 50 at high concentration), which gave a 95 : 5 diastereomeric ratio in the triplet channel. Thus, the stereoselectivity of the Paternò-Büchi reaction of singlet excited aldehydes which most likely involves *conical intersections* is not sensitive with respect to carbonyl substituents. The reaction sequence behind the concentration/selectivity plots is given in scheme 3.21.



Scheme 3.21: Mechanistic scenario for singlet and triplet reaction.

The bimolecular photocycloaddition steps resulting in the "spin-characteristic" products C and D competes with unimolecular processes, the ISC to give the triplet excited carbonyl (Φ_{ISC} ca. 0.3-0.5 for aliphatic aldehydes) and the photophysical deactivation of the triplet state. From the correlation shown in the above scheme, C_0 and D_0 were estimated and the D/C+D ratio plotted *versus* the concentration of the trapping reagent B. Nonlinear curve fitting led to the equation $y = [D_0\text{-}C_0/1 + (x/x_0)^p] + C_0$ with y = D/(C+D) and x = B. For the photocycloaddition of propionaldehyde with 2,3-dihydrofuran, the values x_0 = 0.09 and $_p$ = 1.9 were determined (see Figure 3.32).

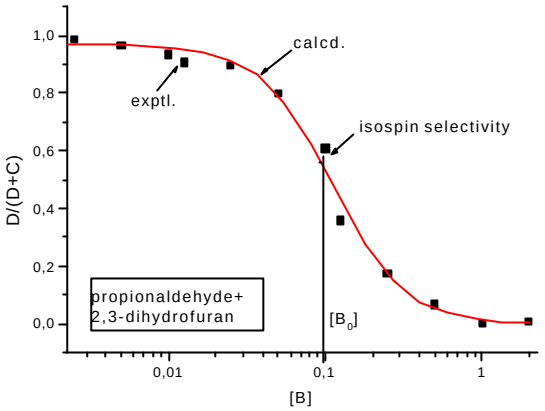
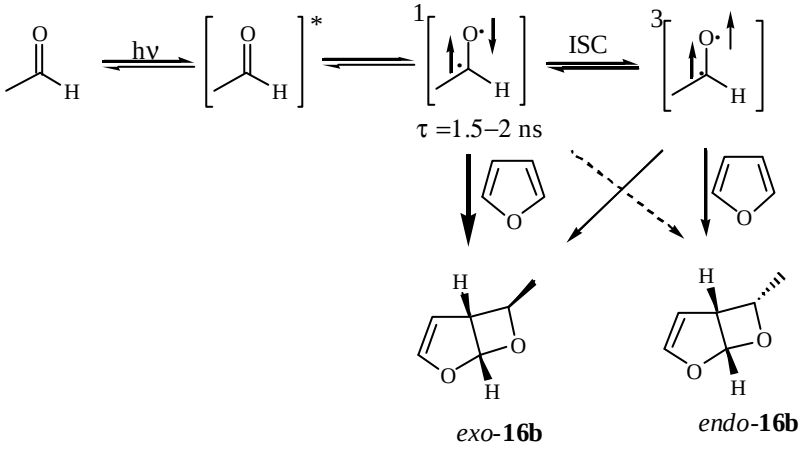


Figure 3.32: Experimental and calculated concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran reaction.

The concentration $B_0(x_0)$ corresponds to a spin (singlet/triplet) selectivity of zero. These values were characteristic for every substrate combination and represent the specific kinetic data. Qualitatively, for carbonyls with shorter lived excited singlets (e.g. aromatic aldehydes), the B_0 value shiftes to higher concentrations, wheras a change in bimolecular rate constants of the cycloaddition steps alters the sigmoidal behavoir of the curve.

Spin selectivity for furan/acetaldehyde photocycloaddition can be explained as depicted in scheme 3.22. At high concentration, the first excited singlet state was quenched rapidly with furan to give high *exo*-adduct wheras at low concentration the singlet excited state undergo ISC to triplet excited state which has relatively long lifetime and then SOC controls geometry of triplet 1,4-biradical.[51]



Scheme 3.22: Mechanistic scenario of furan/acetaldehyde photocycloaddition.

3.2 Effect of solvent polarity on the simple diastereoselectivity of Paternò-Büchi reactions

To get more information on the surprising concentration effect of the simple diastereoselectivity of [2+2] photocycloaddition, solvent polarity effects of the Paternò-Büchi reaction of 2,3-dihydrofuran with aldehydes were studied. As a polar protic solvent, methanol was used, and both acetonitrile and tetrahydrofuran were used as polar aprotic solvent. In addition, n-hexane and benzene were applied as nonpolar solvent.

3.2.1 Solvent polarity effect on the stereoselectivity of the 2,3-dihydrofuran/ propionaldehyde photocycloaddition reaction

The photocycloaddition of propionaldehyde with 2,3-dihydrofuran was investigated in different types of solvent and with a wide range of concentration (1-0.0125M). The diastereomeric *exo/endo* ratios of the photoadducts were determined by using GC and ^{1}H-NMR analyses. Figure 3.33 shows solvent polarity effects on the concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran photocycloaddition. At singlet conditions, i.e. at high concentration range, the *endo*-selectivity was low in the nonpolar solvent n-hexane, and increased with increasing polarity of the solvent. In contrast to the results for the singlet reaction, for the triplet reaction (i.e. at low concentration) the *endo*-selectivity was dominant in the nonpolar solvent benzene whereas polar solvents (methanol and acetonitrile) gave moderate *endo*-selectivity.

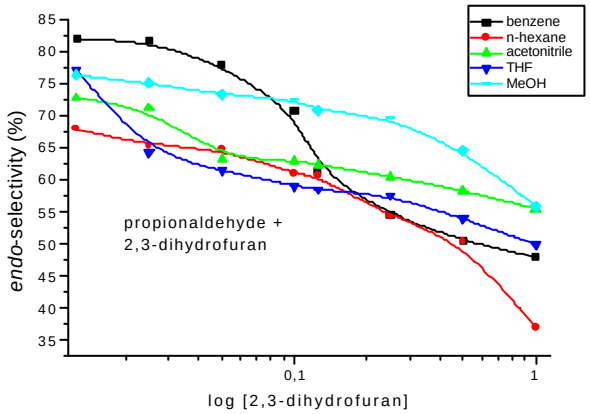


Figure 3.33: Solvent polarity effect on the concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran photocycloaddition.

3.2.2 Solvent polarity effect on the stereoselectivity of the 2,3-dihydrofuran/acetaldehyde photocycloaddition reaction

Next, the effect of solvent polarity on the stereoselectivity of the photocycloaddition of acetaldehyde with 2,3-dihydrofuran was investigated in three solvents (tetrahydrofuran, acetonitile and methanol). The results depicted in Figure 3.34 show, that the *endo*-selectivity in polar solvents (methanol and acetonitrile) was higher than in the less polar tetrahydrofuran solvent at high concentration. By lowering the concentration, the *endo*-selectivity increases parallel with increasing solvent polarity. Surprising, THF showed nearly no concentration effect on the diastereoselectivity in contrast to the propionaldehyde/2,3-dihydrofuran photocycloaddition reaction.

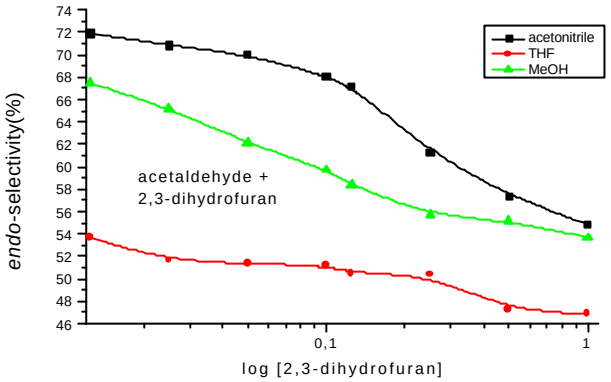


Figure 3.34: Solvent polarity effect on the concentration/selectivity profile of the acetaldehyde/2,3-dihydrofuran photocycloaddition.

Comment

The results of solvent polarity effect suggest that the spin-multiplicity of the excited aldehydes, singlet or triplet, may play an important role for determining the stereoselectivities. The important findings from solvent polarity experiments in the photoreactions of 2,3-dihydrofuran with acetaldehyde and propionaldehyde are as follows:

(a) polar solvents favor the formation of *endo*-diastereoisomers under singlet condition.

(b) nonpolar solvents also favor the formation of *endo*-diastereoisomers under triplet condition.

This results can be explained as follows: At singlet condition, the mechanism of Paternò-Büchi reactions procced *via conical intersections* or *exciplex* which it might be favored in polar solvents than in nonpolar solvent. At triplet condition, SOC controls the geometry of the triplet 1,4-biradical. In polar solvents, there is a competition between biradical formation and photoinduced electron transfer (PET).[42] The PET is favored in polar solvents, so the *endo*-

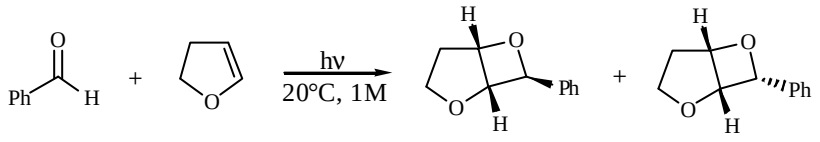
selectivity decreased while the biradical dominants in nonpolar solvent and hence the *endo*-selectivity increased.

3.3 Effect of solvent viscosity on simple diastereoselectivity of Paternò-Büchi reactions

The detection of solvent viscosity dependence on the stereoselectivity of the Paternò-Büchi reaction was essential for demonstrating the difference in simple diastereoselectivites in singlet and in triplet routes. As a model system for this study, the photocycloaddition reaction of 2,3-dihydrofuran with four aldehydes was investigated.

3.3.1 Solvent viscosity effect on the stereoselectivity of the benzaldehyde/2,3-dihydrofuran photocycloaddition reaction

The photocycloaddition of benzaldehyde with 2,3-dihydrofuran was firstly investigated as a typical triplet reaction with concentration-independent diastereoselectivity.



1a **2** *exo*-**3a** *endo*-**3a**

Table 3.6: Viscosity dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with benzaldehyde (1M) at 293K.

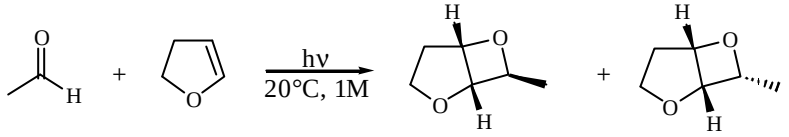
Solvent	η [p]	k_{diff}[a] [$M^{-1}sec^{-1}$]	$k`_{Diff}$[b] [$M^{-1}sec^{-1}$]	*endo/exo*[c]
n-hexane	0.0033	1.8×10^{10}	2.9×10^{10}	82 : 18
acetonitrile	0.0036	1.6×10^{10}	2.6×10^{10}	82 : 18
n-heptane	0.0041	1.4×10^{10}	2.3×10^{10}	85 : 15
methanol	0.0060	9.8×10^{9}	1.6×10^{10}	84 : 16
ethanol	0.012	4.8×10^{9}	7.9×10^{9}	86 : 14
n-propanol	0.023	2.5×10^{9}	4.1×10^{9}	90 : 10
n-butanol	0.029	2.0×10^{9}	3.3×10^{9}	87 : 13
n-octanol	0.085	6.9×10^{8}	1.1×10^{9}	89 : 11
glycol	0.20	2.9×10^{8}	4.7×10^{8}	83 : 17
1,2-propanediol	0.56	1.0×10^{8}	1.6×10^{8}	87 : 13
1,4-butanediol	0.89	6.6×10^{7}	1.1×10^{8}	91 : 9

[a] $k_{diff} = 2 \times 10^5$ T/η. [b] $k`_{Diff} = 8 \times RT/2000\eta$.[95] [c] Determined by means of NMR spectroscopic analysis of the crude product mixture.

The variation of the solvent viscosity over a wide range (η = 0.3 to 89 cp)[94] resulted in a weak but significant increase in *endo*-selectivity from 82% to 91% (Table 3.6, Figure 3.38).

3.3.2 Solvent viscosity effect on the stereoselectivity of the acetaldehyde/2,3-dihydrofuran photocycloaddition reaction

The simple diastereoselectivity of the photocycloaddition reaction of acetaldehyde with 2,3-dihydrofuran (1M substrate concentration) highly influenced by changing the viscosity of the solvent.



1b **2** *exo*-**3b** *endo*-**3b**

Table 3.7: Viscosity dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with acetaldehyde (1M) at 293K.

Solvent	η [p]	k_{diff}[a] [$M^{-1}sec^{-1}$]	$k`_{Diff}$[b] [$M^{-1}sec^{-1}$]	*endo/exo*[c]
n-hexane	0.0033	1.8×10^{10}	2.9×10^{10}	40.0 : 60.0
acetonitrile	0.0036	1.6×10^{10}	2.6×10^{10}	41.6 : 58.4
n-heptane	0.0041	1.4×10^{10}	2.3×10^{10}	44.4 : 55.6
methanol	0.0060	9.8×10^{9}	1.6×10^{10}	44.4 : 55.6
ethanol	0.012	4.8×10^{9}	7.9×10^{9}	44.7 : 55.3
n-propanol	0.023	2.5×10^{9}	4.1×10^{9}	46.1 :53.9
n-butanol	0.029	2.0×10^{9}	3.3×10^{9}	46.5 : 53.5
n-octanol	0.085	6.9×10^{8}	1.1×10^{9}	47.0 : 53.0
glycol	0.20	2.9×10^{8}	4.7×10^{8}	50.3 : 49.7
1,2-propanediol	0.56	1.0×10^{8}	1.6×10^{8}	53.6: 46.4
1,4-butanediol	0.89	6.6×10^{7}	1.1×10^{8}	63.5 : 36.5

[a] $k_{diff} = 2 \times 10^5$ T/η. [b] $k`_{Diff} = 8 \times RT/2000\eta$.[95] [c] Determined by means of GC analysis.

The *endo/exo* selectivity in the low viscous solvent n-hexane was 40 : 60 and increased by increasing solvent viscosity and switched to 63 : 37 in 1,4-butanediol (Table 3.7). The diastereomeric ratios *endo/exo* were determined by using GC analysis (Figure 3.35).

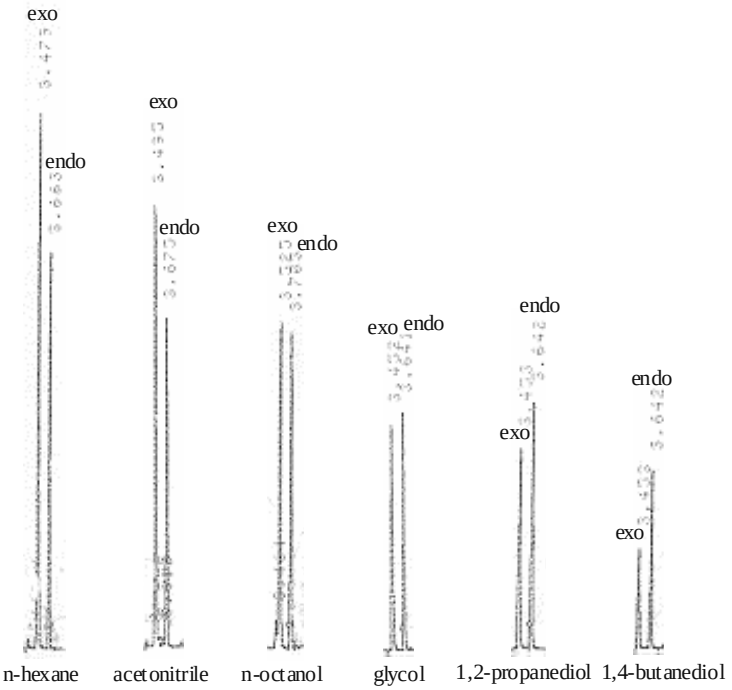
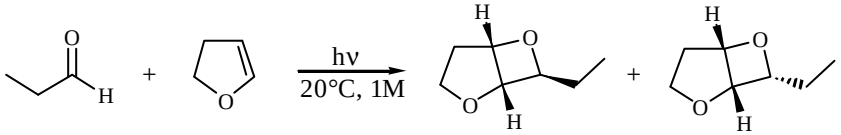


Figure 3.35: GC trace analysis of the diastereoselectivity of acetaldehyde/2,3-dihydrofuran photocycloaddition as a function of solvent viscosity.

3.3.3 Solvent viscosity effect on the stereoselectivity of the propionaldehyde/2,3-dihydrofuran photocycloaddition reaction

The photoaddition of propionaldehyde to 2,3-dihydrofuran was performed in different solvents and with 1M concentration of both substrates.



1c **2** *exo*-**3c** *endo*-**3c**

The variation of the solvent viscosity over a large range (η = 0.3 to 1500 cp) resulted in a substantional increase in *endo* selectivity from 45.3 % to 80.2 % (Table 3.8, Figure 3.36).

Table 3.8 shows, that the *endo*-selectivity changes slightly when going from n-hexane to n-butanol and jumps to moderate selectivity in glycol and is again dramatically increased in glycerol.

Table 3.8: Viscosity dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with propionaldehyde (1M) at 293K.

Solvent	η [p]	K_{diff}[a] [$M^{-1}sec^{-1}$]	$k`_{Diff}$[b] [$M^{-1}sec^{-1}$]	*endo/exo*[c]
n-hexane	0.0033	1.8×10^{10}	2.9×10^{10}	45.3 : 54.7
acetonitrile	0.0036	1.6×10^{10}	2.6×10^{10}	45.3 : 54.7
n-heptane	0.0041	1.4×10^{10}	2.3×10^{10}	48.6 : 51.4
methanol	0.0060	9.8×10^{9}	1.6×10^{10}	49.6 : 50.4
ethanol	0.012	4.8×10^{9}	7.9×10^{9}	50.4 : 49.6
n-propanol	0.023	2.5×10^{9}	4.1×10^{9}	52.1 : 47.9
n-butanol	0.029	2.0×10^{9}	3.3×10^{9}	53.6 : 46.4
n-octanol	0.085	6.9×10^{8}	1.1×10^{9}	57.5 : 42.5
glycol	0.20	2.9×10^{8}	4.7×10^{8}	59.0 : 41.0
1,2-propanediol	0.56	1.0×10^{8}	1.6×10^{8}	60.6: 39.4
1,4-butanediol	0.89	6.6×10^{7}	1.1×10^{8}	72.6 : 27.4
glycerol	15.0	3.9×10^{6}	6.3×10^{6}	80.2 : 19.8

[a] $k_{diff} = 2 \times 10^{5}\ T/\eta$. [b] $k`_{Diff} = 8 \times RT/2000\eta$.[95] [c] Determined by means of GC analysis.

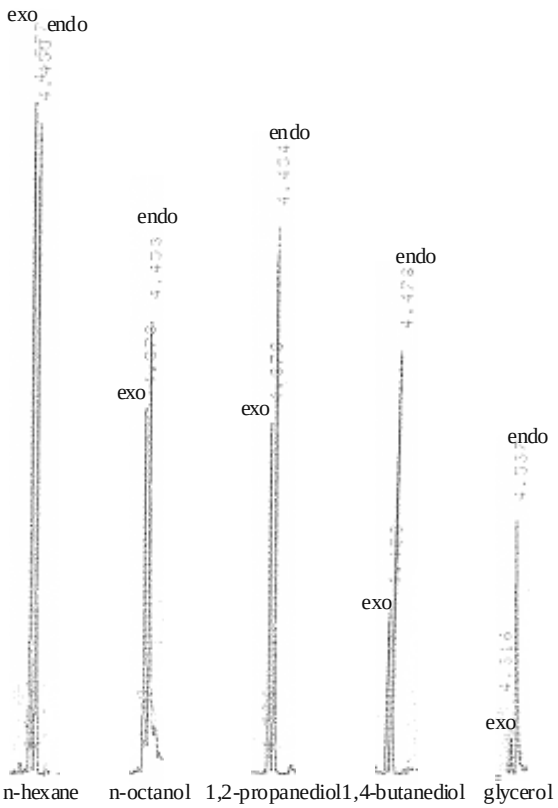
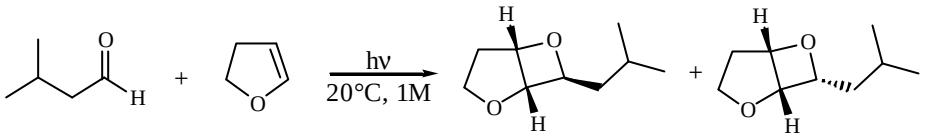


Figure 3.36: GC trace analysis of the diastereoselectivity of propionaldehyde/2,3-dihydrofuran photocycloaddition as a function of solvent viscosity.

3.3.4 Solvent viscosity effect on the stereoselectivity of the 3-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition reaction

The irradiation of 2,3-dihydrofuran in presence of 3-methylbutyraldehyde gave two diastereoisomers, the ratio of which was influenced by changing the solvent viscosity.



1d **2** *exo*-**3d** *endo*-**3d**

Table 3.9: Viscosity dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with 3-methylbutyraldehyde (1M) at 293K.

Solvent	η [p]	k_{diff}[a] [$M^{-1}sec^{-1}$]	$k`_{Diff}$[b] [$M^{-1}sec^{-1}$]	*endo/exo*[c]
n-hexane	0.0033	1.8×10^{10}	2.9×10^{10}	48.8 : 51.2
acetonitrile	0.0036	1.6×10^{10}	2.6×10^{10}	51.2 : 48.8
n-heptane	0.0041	1.4×10^{10}	2.3×10^{10}	51.2 : 48.8
methanol	0.0060	9.8×10^{9}	1.6×10^{10}	51.7 : 48.3
ethanol	0.012	4.8×10^{9}	7.9×10^{9}	51.8 : 48.2
n-propanol	0.023	2.5×10^{9}	4.1×10^{9}	52.4 : 47.6
n-butanol	0.029	2.0×10^{9}	3.3×10^{9}	53.5 : 46.5
n-octanol	0.085	6.9×10^{8}	1.1×10^{9}	55.7 : 44.3
glycol	0.20	2.9×10^{8}	4.7×10^{8}	62.2 : 37.8
1,2-propanediol	0.56	1.0×10^{8}	1.6×10^{8}	65.4: 34.6
1,4-butanediol	0.89	6.6×10^{7}	1.1×10^{8}	73.5 : 26.5

[a] $k_{diff} = 2 \times 10^5$ T/η. [b] $k`_{Diff} = 8 \times RT/2000\eta.^{95}$ [c] Determined by means of GC analysis.

The results in Table 3.9 display, that the *endo/exo* selectivity changes slightly when going from n-hexane to ethanol and increased by increasing solvent viscosity and were switched to 73.5 : 26.5 in 1,4-butanediol.

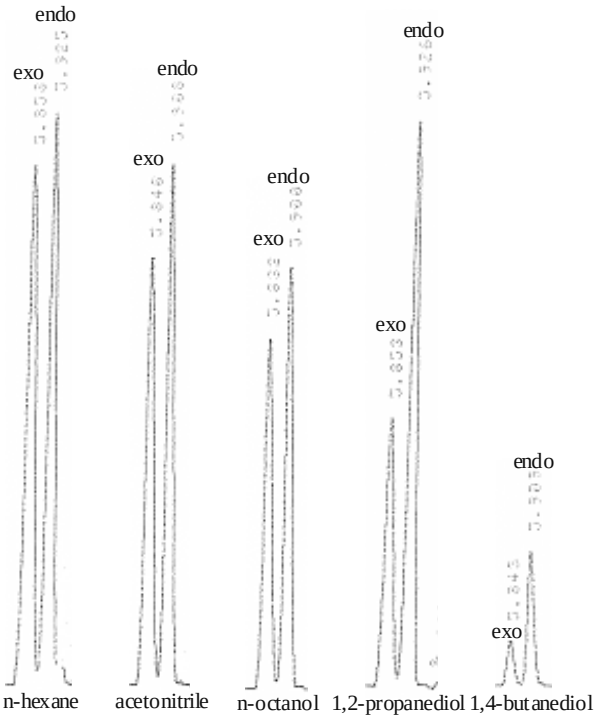


Figure 3.37: GC trace analysis of the diastereoselectivity of 3-methylbutyraldehyde/2,3-dihydrofuran photocycloaddition as a function of solvent viscosity.

The results of the viscosity dependence on the diastereoselectivity of the photocycloaddition reaction of 2,3-dihydrofuran with aliphatic aldehydes suggest that the differences in *endo/exo* selectivity in the singlet reaction are more pronounced than in the triplet reactions (see Figure 3.38).

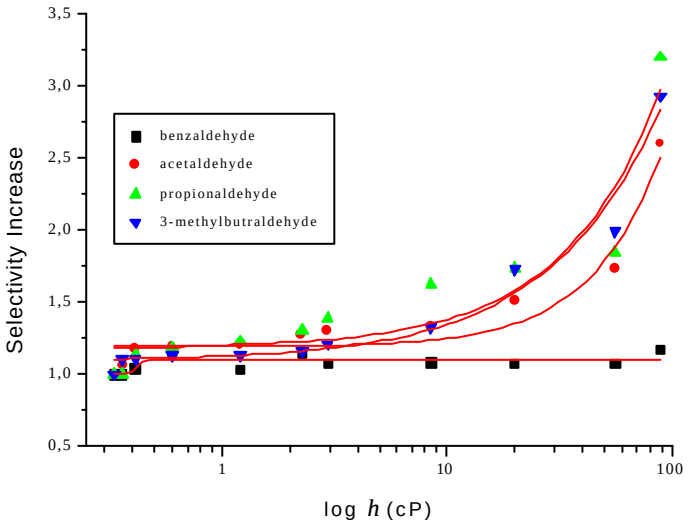


Figure 3.38: Viscosity dependence (normalized) of the Paternò-Büchi reaction of 2,3-dihydrofuran with aldehydes (1M) at 293 K.

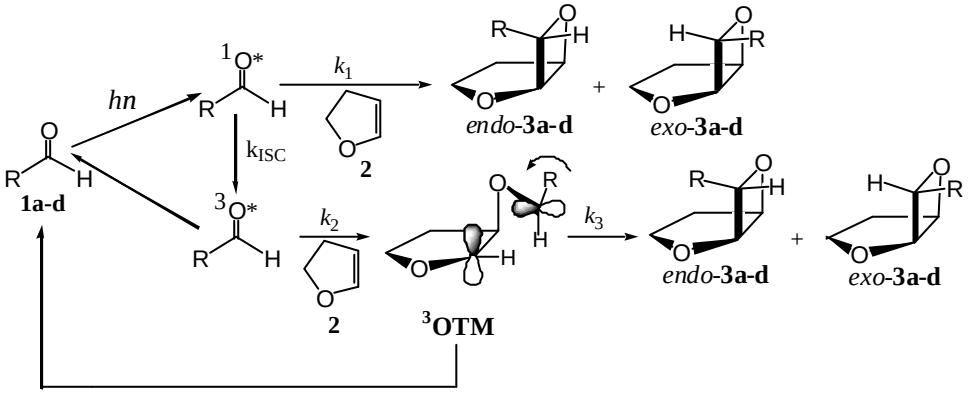
Comment

The results of the viscosity studies can be explained as follows:

An increase in solvent viscosity should favor the triplet channel as a result of a reduction in the diffusion rate limit (about 4 orders of magnitude in the viscosity range).[95] Thus, the viscosity of the medium only slightly influences the diastereoselectivity of the triplet photocycloaddition (k_3) which is controlled by the geometry of 2-oxatetramethylene triplet 1,4-biradical.[32,51] The influence of the solvent viscosity on the diastereoselectivity of singlet reactions which can be estimated from the correlation in Figure 3.38 is more distinct.

Mechanistic analysis

The shape of concentration/diastereoselectivity correlations as well as the viscosity/diastereoselectivity correlations reflects the different kinetic contribution to this complex reaction scenario (Scheme 3.23). Recognize that the difference to Scheme 3.21 is that identical products are now formed *via* the singlet as well as the triplet path, only with different C/D-composition. The *endo/exo* selectivity is controlled by the geometry of the *conical intersections* for the singlet reaction[96] and by the optimal ISC-geometry of the 2-oxatetramethylene biradical ^{3}(OTM) for the triplet path reaction.[51]



Scheme 3.23: Mechanistic scenario for singlet and triplet reaction.

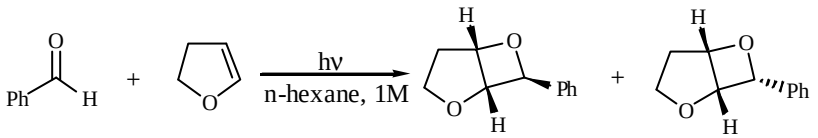
3.4 Effect of temperature on the simple diastereoselectivity of Paternò-Büchi reactions

The effect of temperature on the diastereoselectivity has recently been observed and its influence is not uniform: On increasing the reaction temperature the diastereoselectivity may decline, but it can also be constant or even increase. Scharf *et al*. intensively investigated the effect of temperature on facial selectivities in the triplet photocycloaddition reaction of electron-rich cycloalkenes with chiral phenyl glyoxylates.[68] It was thus of interest to study the influence of excited-state spin multiplicity (singlet *versus* triplet) at different temperatures on

the simple diastereoselectivity of the [2+2] photocycloaddition reaction of 2,3-dihydrofuran with prochiral aldehydes.

3.4.1 Effect of temperature on the simple diastereoselectivity of benzaldehyde/2,3-dihydrofuran photocycloaddition reaction

Firstly, the temperature dependence of the simple diastereoselectivity of the Paternò-Büchi reaction was studied for the triplet reaction between benzaldehyde and 2,3-dihydrofuran. No influence was detected, within the error margin (see Table 3.10). The results of the temperature dependence of the simple diastereoselectivity in the triplet reaction suggest that the reaction is soley controlled by the activation entropy.



1a **2** *exo*-**3a** *endo*-**3a**

Table 3.10: Temperature dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with benzaldehyde (1M) in n-hexane.

Entry	T (°C)	d.r. (*endo* : *exo*)[a]
1	0	90.9 : 9.1
2	-10	90.0 : 10.0
3	-15	91.1 : 8.9
4	-25	88.0 : 12.0
4	-32	87.8 : 12.2
6	-42	90.5 : 9.5
7	-52	90.4 : 9.6
8	-61	86.2 : 13.8
9	-72	89.9 : 10.1
10	-78	90.2 : 9.8

[a] Determined by means of ^{1}H-NMR spectroscopic analysis of the crude product mixture.

3.4.2 Effect of temperature on the concentration/selectivity correlation of propionaldehyde/2,3-dihydrofuran photocycloaddition reaction

In the next experiment, the concentration dependence of the [2+2] photocycloaddition reaction at different temperatures was investigated with the standard system propionaldehyde

and 2,3-dihydrofuran. This substrate combination was used primarily to determine the different simple diastereoselectivities of singlet and triplet photocycloadditions.[97]

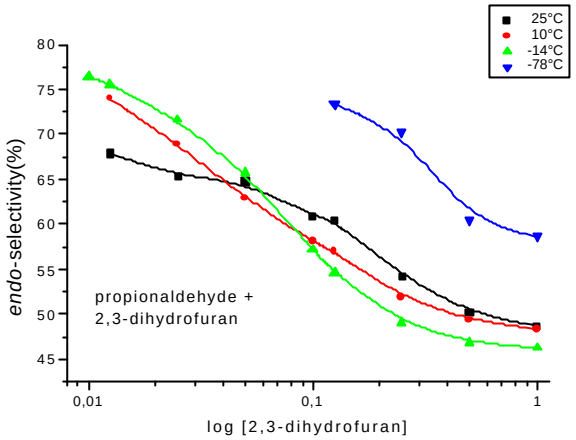
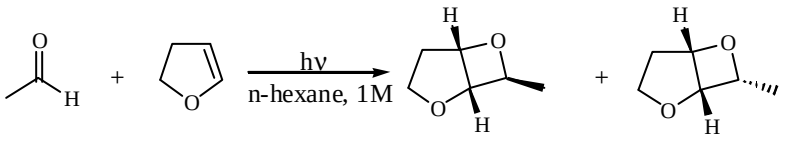


Figure 3.39: Temperature effect on the concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran photocycloaddition in n-hexane.

In the temperature region between –14 and +25 °C, the diastereoselectivity/concentration correlation showed only small changes, whereas at lower (-78 °C) temperatures the point of isospinselectivity is shifted significantly to higher concentrations (see Figure 3.39). This shift is not yet a proof for nonlinear temperature dependence, but a clear indication that not only the concentration, but also the temperature influences the diastereoselectivity of photocycloadditions with carbonyl compounds which can react from initial S_1 and T_1 states.

3.4.3 Effect of temperature on the simple diastereoselectivity of acetaldehyde/2,3-dihydrofuran photocycloaddition reaction

The temperature dependence of the *endo/exo*-selectivity of Paternò-Büchi reaction of acetaldehyde with 2,3-dihydrofuran was investigated at constant concentration (1M) in order to evaluate the difference in spin selectivity in singlet and in triplet reaction. With decreasing temperature, the *endo*-selectivity decreased in the region from +25 °C to –32 °C, and was inverted at –37°C (see Table 3.11 and Figure 3.40).



1b **2** *exo*-**3b** *endo*-**3b**

Table 3.11: Temperature dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with acetaldehyde (1M) in n-hexane.

Entry	T (°C)	d.r. (*endo* : *exo*)[a]
1	25	53.2 : 46.8
2	0	48.6 : 51.4
3	-10	46.3 : 53.7
4	-15	45.5 : 54.5
5	-25	41.0 : 59.0
6	-32	41.5 : 58.5
7	-42	45.5 : 54.5
8	-52	50.0 : 50.0
9	-61	51.4 : 48.6
10	-72	57.9 : 42.1
11	-78	58.3 : 41.7

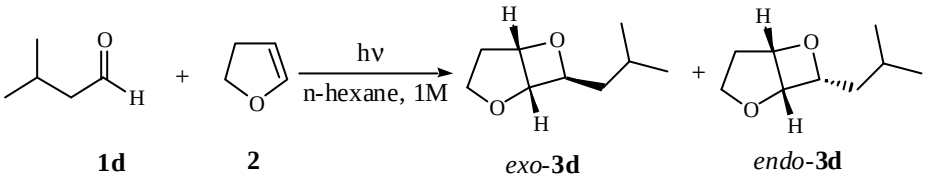
[a] Determined by means of GC and NMR spectroscopic analysis of the crude product mixture.

Furthermore, Figure 3.40 shows the strongest deviation from linearity with an inversion temperature at –37°C. For this specific reaction, we have already detected from concentration studies that the acetaldehyde triplet adds to 2,3-dihydrofuran with high *endo* selectivity (up to 75%) wheras the singlet gives the same products with moderate *exo* selectivity (up to 65%). Thus, the temperature correlation can be interpreted qualitatively as follows: at room temperature under high concentration conditions, the cycloadducts **3b** were formed with low *exo* selectivity, predominantly through the singlet channel. This selectivity increases with decreasing temperature (as intuitively expected) and reaches an inversion point at –37°C (Figure 3.40). At this point, the triplet reactivity gains sufficient influence to increase the *endo* selectivity. The rate of the intersystem crossing process (k_{ISC}) is expected to be nearly temperature-independent.[98]

3.4.4 Effect of temperature on the simple diastereoselectivity of 3-methylbutyraldehyde /2,3-dihydrofuran photocycloaddition reaction

In contrast to the results of acetaldehyde, the temperature dependence of the photocycloaddition of 3-methylbutyraldehyde with 2,3-dihydrofuran showed a positive

deviation from linearity with an inversion temperature at –28°C. In addition, the *endo/exo* selectivity was altered slightly by lowering the temperature (see Table 3.12 and Figure 3.40).



1d **2** *exo*-**3d** *endo*-**3d**

Table 3.12: Temperature dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran (1M) with 3-methylbutyraldehyde (1M) in n-hexane.

Entry	T (°C)	d.r. (*endo* : *exo*)[a]
1	25	51.8 : 48.2
2	0	52.7 : 47.3
3	-10	52.8 : 47.2
4	-15	53.4 : 46.6
5	-25	53.6 : 46.4
6	-32	53.4 : 46.6
7	-42	52.7 : 47.3
8	-52	51.7 : 48.3
9	-61	51.0 : 49.0
10	-72	50.9 : 49.1
11	-78	50.6 : 49.4

[a] Determined by means of GC and NMR spectroscopic analysis of the crude product mixture.

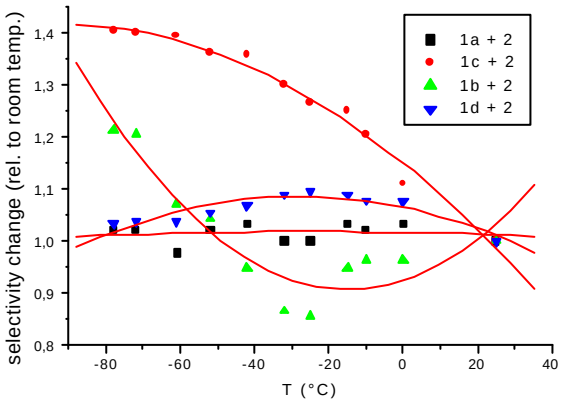
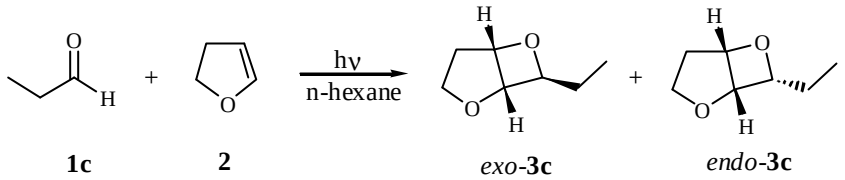


Figure 3.40: Temperature dependence (normalized) of the Paternò-Büchi reaction of 2,3-dihydrofuran with aldehydes in n-hexane (1M both of substrate).

3.4.5 Effect of temperature on the simple diastereoselectivity of propionaldehyde/2,3-dihydrofuran photocycloaddition reaction

The results of the temperature dependence of simple diastereoselectivity of the photocycloaddition reaction of propionaldehyde (1M) with 2,3-dihydrofuran (1M) was surprising. The *endo* selectivity increased gradually with decreasing the temperature and no inversion temperature was detected (see Table 3.13 and Figure 3.40).



1c **2** *exo*-**3c** *endo*-**3c**

Table 3.13: Temperature dependence of the diastereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran with propionaldehyde at (1M & 5M) in n-hexane.

Entry	T (°C)	d.r. (*endo* : *exo*)[a]	d.r. (*endo* : *exo*)[b]
1	25	45.3 : 54.7	47.7 : 52.3
2	0	48.4 : 51.6	43.8 : 56.2
3	-10	50.5 : 49.5	41.4 : 58.6
4	-15	54.6 : 45.4	37.3 : 62.7
5	-25	56.6 : 43.4	35.7 : 64.3
6	-32	57.4 : 42.6	37.1 : 62.9
7	-42	58.9 : 41.1	42.2 : 47.8
8	-52	61.5 : 38.5	48.0 : 52.0
9	-61	61.7 : 38.3	52.4 : 47.6
10	-72	63.2 : 36.8	58.1 : 41.9
11	-78	63.6 : 36.4	63.3 : 36.7

[a] 1M, [b] 5M.

This selectivity reversal could be detected for both acetaldehyde and 3-methylbutyraldehyde-additions to 2,3-dihydrofuran in a temperature region that is experimentally accessible. A marginal change in activation parameter, however, "catapults" this effect out of the experimental window (+40 to –78 °C). This might have been the reason why I did not detect an inversion effect in the propionaldehyde photocycloaddition. If this assumption is true, a change in substrate concentration might shift the inversion region back into the experimentally accessible range. Thus, the temperature dependence of propionaldehyde/2,3-

dihydrofuran system at 5M (both substrates) was measured, and indeed an inversion point at –27°C was detected (see Table 3.13& Figure 3.42).

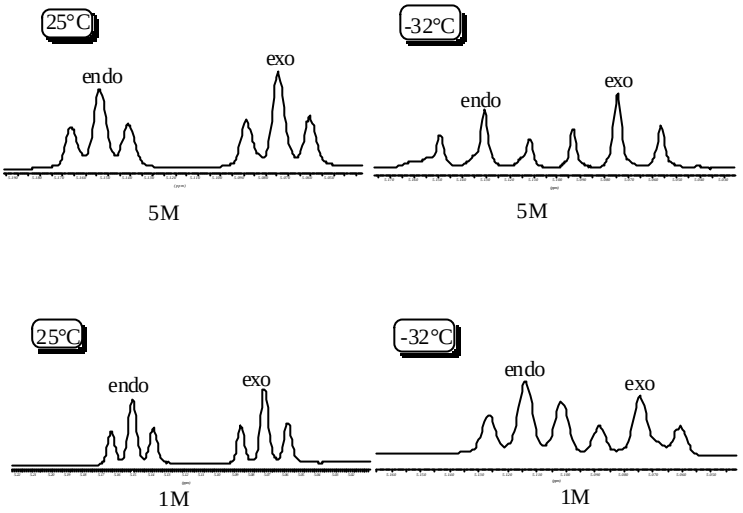


Figure 3.41: ^{1}H-NMR analysis of propionaldehyde/2,3-dihydrofuran photocycloaddition reaction at 1M and 5M.

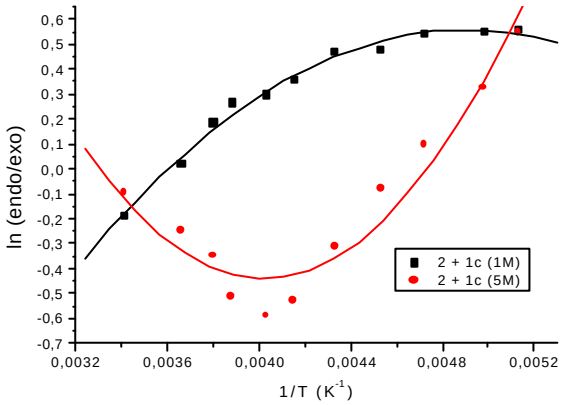


Figure 3.42: Eyring plots of the Paternò-Büchi reaction of 2,3-dihydrofuran **2** with propionaldehyde **1c** at 1M and 5M in n-hexane.

Presumably, in this case an increase in concentration led to a low-temperature shift of the inversion region (Figure 3.42). The reverse should be observed in reactions with their inversion points at low temperatures; which could be shifted to higher temperature with concentration variation.

In order to determine kinetic parameters out of the experimental results, we simulated the curves shown in Figure 3.42 in collaboration with Dr. Gudipati. The simulations have been carried out based on the following considerations: the amount of product P_j formed, which in

the present case is either the *exo* or *endo* oxetane **3** from the singlet and triplet channels, is given by equation (1):

$$P_j = A_j \bullet e^{\frac{-E_j}{RT}} \quad (1)$$

with the four channels (j) being *exo* (j = 1) and *endo* (j = 2) from the singlet state, as well as *exo* (j = 3) and *endo* (j = 4) from the triplet state of the aldehyde. As the lifetime of the S_1 state of aliphatic aldehydes is of the order of ~1 ns,[85] the reaction probability from the singlet channel is further restricted by molecular diffusion in order to encounter the reaction partner during the lifetime of the singlet state in diluted solutions. Under such conditions the photophysical deactivation processes compete with the photochemical channels. Thus, in dilute solutions, the probability of reaction from the singlet channel (R_S) decreases and the probability of triplet population (ϕ_T) increases. On the other hand, when the concentrations of the aldehyde and olefin are increased, though one expects reaction from the singlet channels to dominate, in reality other processes like collisional quenching of the excited singlet and triplet aldehyde by the ground-state aldehyde can not be ignored. If the temperature is lowered, then diffusion controlled diminution of the reaction from the singlet channel is to be expected. Due to the ca. 200 times longer lifetime of the T_1 state of the aldehyde (200-400 ns)[85] the reaction probability (R_T) from the triplet channel should be less dependent on the temperature. From previous studies we know that at concentrations above 1M, the reaction takes place only through the singlet channel at room temperature. Normalized temperature dependent reaction probabilities from the singlet and triplet channels with respect to room temperature (300 K) can be approximated by equation (2a & 2b). Here *n* reflects the non-linearity of the temperature dependent contributions from molecular diffusion, viscosity and concentration.

$$R_S = (T/300K)^n \quad (2a)$$

$$R_T = (1-R_S)\,\phi_T \quad (2b)$$

From the concentration studies at 300K, we know the *endo*/*exo* ratios for pure singlet and pure triplet channels.[97] By using this information we can reduce the number of parameters as follows:

$$S_{endo/exo}^{300K} = \frac{P_2}{P_1} = \frac{A_2}{A_1} \bullet e^{\frac{-(E_2 - E_1)}{300R}} \quad (3)$$

$$E_1 = E_2 + 300R \bullet \ln\left(\frac{S_{endo/exo}^{300K} \bullet A_1}{A_2}\right) \quad (4)$$

similarly, for the triplet channel:

$$E_3 = E_4 + 300R \bullet \ln\left(\frac{S_{endo/exo}^{300K} \bullet A_3}{A_4}\right) \qquad (5)$$

Thus, the temperature-dependent overall *endo*/*exo* ratio Σ is given by equation (6).

$$\Sigma_{endo/exo}^{T} = \frac{R_S P_2 + (1 - R_S)\Phi_T P_4}{R_S P_1 + (1 - R_S)\Phi_T P_3} \qquad (6)$$

The simulated *endo*/*exo* selectivity using these eight parameters for 1M and 5M concentrations of propionaldehyde and dihydrofuran are shown in Figure 3.43.

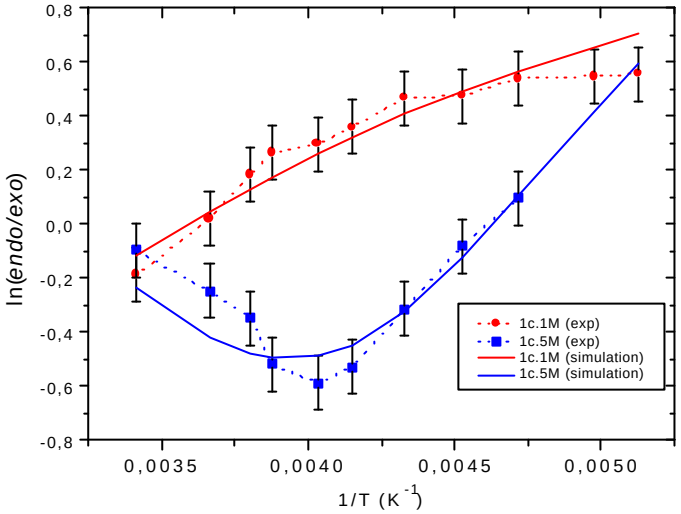


Figure 3.43: Simulation of temperature dependence of the Paternò-Büchi reaction of 2,3-dihydrofuran **2** with propionaldehyde **1c** at 1M and 5M.

The reliability of the present simulations (notwithstanding the high number of parameters) comes from the fact that after fitting the experimental data from 5M solutions, all the other parameters were fixed and only *n* and ϕ_T were varied to simulate the curve for the 1M data. It should be noted that these variable parameters are not independent, but are highly correlated with each other.

Table 3.14: Simulation parameter of the photocycloaddition of propionaldehyde with 2,3-dihydrofuran at 1M and 5M.

Conc.	E_1[a]	E_2	E_3	E_4	A_1	A_2	A_3	A_4	n	ϕ_T
5M	157	8992	-12.5	5.8	0.054	1.599	0.057	0.327	8.99	0.0079
1M	„	„	„	„	„	„	„	„	0.88	0.9975

[a] J/Mol.

The qualitative interpretation of the "selectivity-inversion" is as follows: from the singlet channel the activitation barrier for the formation of the *exo* product is much smaller than for the *endo* product. However, the pre-exponential factor for the *endo* product is larger than for the *exo* product. With decreasing temperature, the exponential part dominates and more *exo* product is formed than the *endo* product.

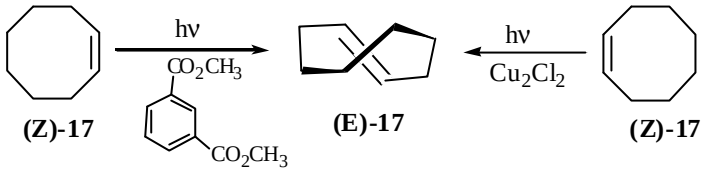
The situation is completely different for triplet channel, namely, the formation of both the *endo* and *exo* products has almost no barrier whereas the pre-exponential factors favor the formation of the *endo* product. Due to the lack of activation barrier for both the products, one should expect no temperature dependence of *endo*/*exo* ratio from the triplet channel. This has been experimentally proven, as discussed earlier, in the case of photocycloaddition of benzaldehyde (**1a**) with **2** (*vide supra*). If in this case the reaction probabilities R_S and R_T were not temperature dependent, then one should not observe any „selectivity inversion". The temperature dependent reaction probabilities R_S and R_T are reflected in the values n and ϕ_T. For the 5M data, n is large, reflecting faster decrease in the reaction probability (R_S) from the singlet channel. This may be due to quenching of the excited singlet aldehyde molecule by the ground-state aldehydes. Similarly, the relative triplet quantum yield, ϕ_T, is very small, implying that at higher concentrations the majority of the excited singlet aldehyde molecules undergo reaction or get deactivated. For the 1M data, n is small and the value R_S decreases less steeply with temperature and ($1-R_S$) increases correspondingly from the initial value of 0 at 300 K. Simultaneously, the relative triplet population ϕ_T is predicted to be close to unity. Thus, both singlet and triplet channels compete with each other at 1M concentration. With decreasing temperature, the triplet contribution increases. Due to larger *endo*/*exo* selectivity from the triplet channels (5.6)[97] with decreasing temperature, the total *endo*/*exo* ratio increases steadily.

The simulations do not indicate an abrupt change in the selectivity correlation like in isoinversion curves,[68] but a inversion region as described by Hale and Ridd.[99]

3.5 Paternò-Büchi reactions of *cis* and *trans* cyclooctene with aliphatic aldehydes

3.5.1 Synthesis of *trans*-cyclooctene

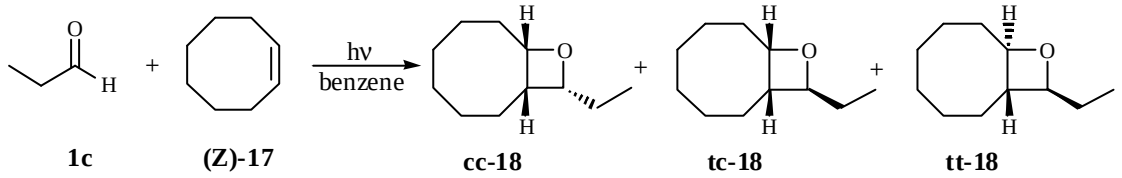
Trans-cyclooctene was not commercially available and was prepared by photoisomerisation of *cis*-cyclooctene using dimethylisophthalate as a sensitizer.[100] Another method was applied to improve the yield.[101] In this method, *trans*-cyclooctene was obtained by irradiation of a solution of Cu_2Cl_2 in a 2.6 fold excess of *cis*-cyclooctene at 250 nm for 24h. Unisomerized *cis*-cyclooctene was removed in *vacuo* and the Cu(I) salts were successively extracted with aqueous ammonia and cyanide. Separation of *trans* from *cis* was accomplished by taking advantage of the better solubility of *trans*-cyclooctene in aqueous silver nitrate solution.



Scheme 3.24: Synthesis of *trans*-cyclooctene.

3.5.2 Irradiation of *cis*-cyclooctene with propionaldehyde

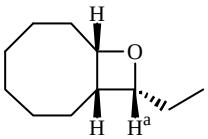
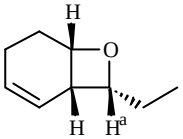
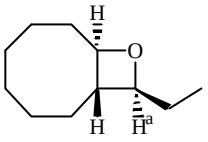
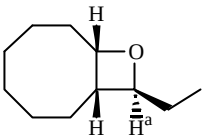
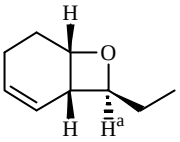
The [2+2]-cycloaddition of propionaldehyde with *cis*-cyclooctene in benzene afforded three products with high chemoselectivity.



Scheme 3.25: Paternò-Büchi reaction of *cis*-cyclooctene with propionaldehyde.

The relative configurations of the *cis*-fused oxetanes **cc-18** and **tc-18** were determined by proton and carbon chemical shift comparison with literature data[57,70,74] and CH-COSY. The assignment of the configuration of the *trans*-fused product **tt-18** resulted from a comparison of chemical shift data of the oxetane ring hydrogen and carbon resonates with the structurally related **tc-18** (see Table 3.15 & experimental section).

Table 3.15: Comparison of the ^{1}H-NMR chemical shift (δ_{ppm}) of H^a of cyclooctene-propionaldehyde photoadducts with cyclohexadiene-propionaldehyde photoadducts.

Compound	 **cc-18**	 **cc**	 **tt-18**	 **tc-18**	 **tc**
δ_{ppm} (H^a)	4.63	4.63	4.25	4.13	3.89

When the substrate concentration was lowered from 5M to 0.01M, a distinct sharp increase in the relative amount of *trans*-fused oxetane **tt-18** resulted between 3 and 1M concentration (Figure 3.44 & 3.45).

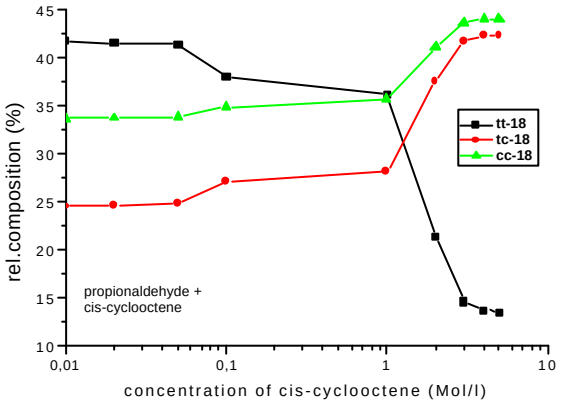


Figure 3.44: Concentration dependence of the photocycloaddition of propionaldehyde to *cis*-cyclooctene.

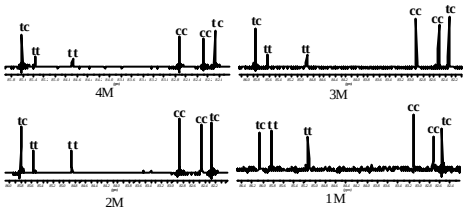


Figure 3.45: ^{13}C-NMR analysis of the stereoismers of propionaldehyde cycloaddition to *cis*-cyclooctene.

Additionally, the ratio between the *cis*-fused *exo* and *endo*-configurated diastereoisomers **cc-18** and **tc-18** did respond to changes in concentrations in a similar fashion as already determined for less complicated cases, i.e. the Paternò-Büchi reaction of aliphatic aldehydes to cyclic enol ether. At high substrate concentrations preferentially singlet reactivity was observed with low (simple) *endo/exo*-selectivity whereas at low concentrations the *endo*-diastereoisomer dominated with a limiting *endo/exo* ratio of 58 : 42.

Fluorescence quenching of propionaldehyde by *cis*-cyclooctene was observed and from the concentration dependence (Stern-Volmer analysis) the bimolecular quenching rate constant of 2.2 x 10^8 m^{-1} s^{-1} was determined (Figure 3.46 & 3.47).[85]

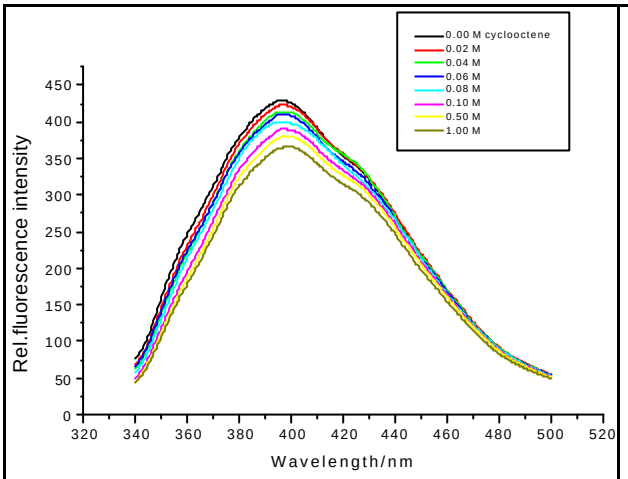


Figure 3.46: Fluorescence quenching of propionaldehyde (0.2M) by *cis*-cyclooctene (0.02 – 1.00 M) in benzene at 25°C.

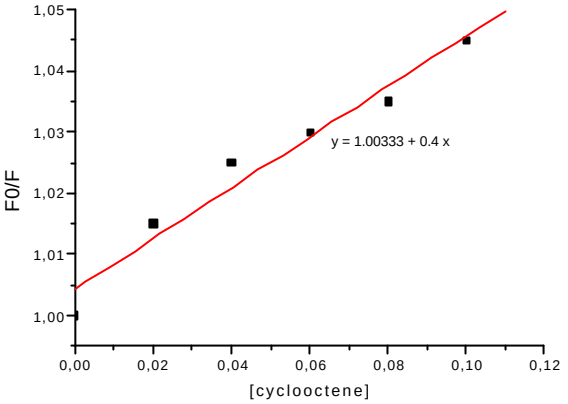
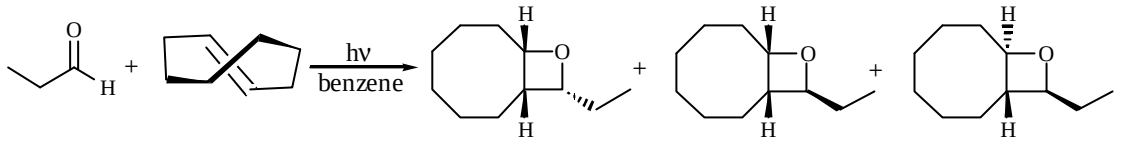


Figure 3.47: Stern-Volmer plot for the fluorescence quenching of propionaldehyde by *cis*-cyclooctene.

The change from the singlet-determined to triplet determined stereoselectivity occurs parallel to the increase in *trans*-isomer **tt-18** formation indicating that the triplet 1,4-biradical involved in the photocycloaddition of the triplet excited aldehyde to **(Z)-17** preferentially converts to the singlet potential energy hypersurface at points which essentialy differ from the corresponding reaction channel involving the singlet excited carbonyl species. It was also striking to find that only one out of the two possible diastereoisomeric *trans*-fused oxetanes was formed: only isomer **tt-18** was detected and none (i.e.< 5 %) of the **ct**-isomer. The low content of **tt-18** at high substrate concentrations (Figure 3.44) indicated that this product is predominantly formed *via* the triplet 1,4-biradical. Thus, the diastereoselectivity of the triplet photocycloaddition path in the reaction of propionaldehyde to *cis*-cyclooctene is remarkably higher for the formation of *trans*-fused products than as for the formation of *cis*-fused products.

3.5.3 Irradiation of *trans*-cyclooctene with propionaldehyde

In order to compare this selectivity behavoir with the reactivity of *trans*-cyclooctene (**(E)-17**), the product pattern of the photocycloaddition of propionaldehyde to mixtures of **(Z)-17** and **(E)-17** with increasing amounts of the *trans*-isomer was investigated.



1c **(E)-17** **cc-18** **tc-18** **tt-18**

Scheme 3.26: Paternò-Büchi reaction of *trans*-cyclooctene with propionaldehyde.

The oxetane compositions of the photoadducts were detected from 2M starting material concentration; the results are depicted in Figure 3.48.

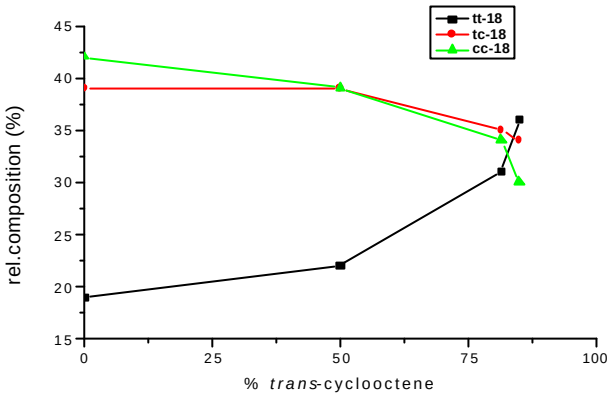
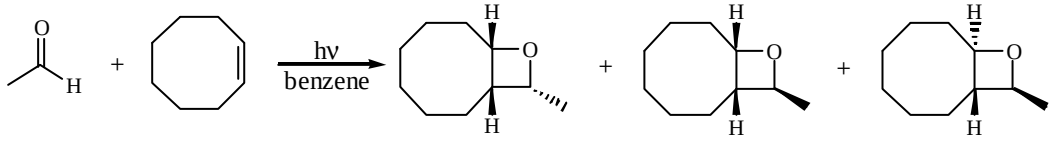


Figure 3.48: Photocycloaddition of propionaldehyde with a mixture of *cis* & *trans*-cyclooctene.

Figure 3.48 shows that, even from high proportions of *trans*-**17**, only the **tt-18** isomer was detected and none of **ct-18**. This shows that the 1,4-triplet biradicals preceding the formation of **tt-18** are identical from *cis*-**17** and *trans*-**17**. The selectivity values have been corrected to low conversions and thus the appearance of **tt-18** is not connected to *cis-trans* isomerisation of *cis*-**17** under the reaction conditions.

3.5.4 Irradiation of *cis*-cyclooctene with acetaldehyde

Analogous to propionaldehyde, the photocycloaddition of cyclooctene with acetaldehyde furnished three diastereoisomers **cc-19**, **tc-19** and **tt-19**.

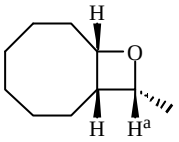
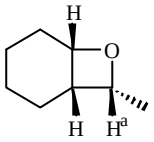
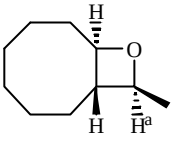
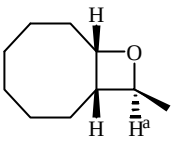
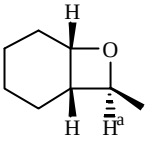


1b **(Z)-17** **cc-19** **tc-19** **tt-19**

Scheme 3.27: Paternò-Büchi reaction of *cis*-cyclooctene with acetaldehyde.

Again, the relative configurations of the photoadducts were unambiguously assigned from the ^{1}H-NMR spectroscopy of the crude reaction mixture and reconfirmed by comparison with data from cyclohexene-acetaldehyde photoadduct (Table 3.16).

Table 3.16: Comparison of the ^{1}H-NMR chemical shift (δ_{ppm}) of H^a of cyclooctene-acetaldehyde photoadducts with cyclohexene-acetaldehyde photoadducts.

Compound	 **cc-19**	 **cc**	 **tt-19**	 **tc-19**	 **tc**
δ_{ppm} (H^a)	4.94	4.94	4.44	4.55	4.36

Under high concentration conditions (> 3M) less than 10 % of **tt-19** was formed beside a 1 : 1 mixture of **cc-19** and **tc-19**, wheras under low concentration conditions (< 0.05M) 62 % of **tt-19** was observed together with 38 % of a 2 : 1 mixture of **cc-19** and **tc-19** (Table 3.17). Thus, the **tt**-isomer is formed by singlet/triplet photocycloaddition of **1b** to *trans*-cyclooctene as well as by triplet photocycloaddition of **1b** to *cis*-cyclooctene.

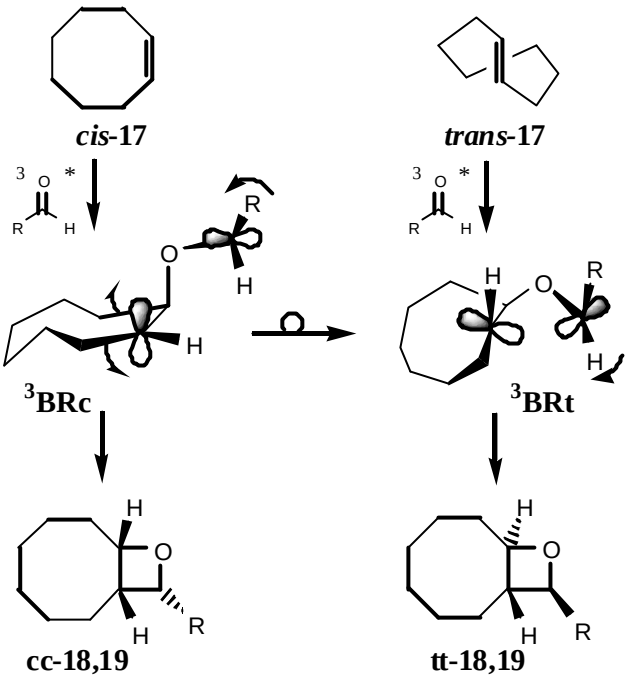
Table 3.17: Concentration dependence of the diastereoselectivity of the acetaldehyde/*cis*-cyclooctene photocycloaddition reaction.

Conc. (M)	d.r. (**cc-19** : **tc-19** : **tt-19**)[a]
5	45.6 : 46.9 : 7.5
3	46.4 : 41.9 : 11.7
2	43.7 : 37.4 : 18.9
1	46.3 : 32.8 : 20.9
0.5	45.6 : 31.2 : 23.2
0.1	43.3 : 26.3 : 30.4
0.05	39.6 : 22.0 : 38.4
0.025	40.6 : 21.2 : 38.2

[a] Determined by means of ^{1}H-NMR spectroscopic analysis of the crude product mixture.

The results indicate a moderate but still significant spin correlation effect in the Paternò-Büchi reaction of cyclooctenes with aliphatic aldehydes; the *exo*-diastereoisomers **tc-18**, **tc-19** were formed with similar probablity than the *endo*-diastereoisomers **cc-18**, **cc-19** in the singlet

manifold of the excited carbonyl species, whereas the triplet excited aldehydes preferred the formation of the *endo*-diastereoisomeres **cc-18**, **cc-19** and the *trans*-fused products **tt-18**, **tt-19**.



Scheme 3.28: Mechanistic scenario for the cyclooctene triplet photocycloaddition reaction from (Z)- and (E)-**17**.

The preference of *endo*-isomers in triplet photocycloaddition reaction can be rationalized on the basis of the already described spin-orbit coupling (SOC) model which controls intersystem crossing geometries favorable for product formation from the triplet 1,4-biradical intermediate,[51] a concept which has recently been corroborated by a profound *ab initio* study.[32] Following the classical " 90° rule " as originally described in the Salem rules,[28] the triplet 2-oxatetramethylene biradical intermediate **^{3}BRc** (Scheme 3.28) is expected to prevail due to minimized steric interactions between the substituent R and the localized hydrogen atom at C-4. The radical-radical combination is coupled to a torque (indicated by the curved arrow) leads to the *endo*-(**cc**) diastereoisomer. In competition with this process, bond rotation about the central C-C single bond driven by release of *gauche* strain generates the isomeric triplet biradical intermediate **^{3}BRt** which exhibits a similar orbital orientation minimizing steric interactions. In this case, however, the formation of the *trans*-*trans*-diastereoisomer is largely preferred because the biradical conformer **^{3}BRt** preceding the terminating bond formation has an optimal substituent orientation. The alternative structure leading to the **ct**-isomer is reasonably expected to be much higher in energy due to severe steric replusion between the R group and the *trans*-cyclooctene ring.

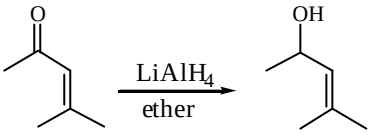
3.6 Paternò-Büchi reactions of allylic alcohols and acetates with aldehydes

The following questions were addressed in this investigation: (a) is there a specific spin-directing effect connected with hydrogen-bonding, (b) do hydrogen-bonding interactions influence induced as well as noninduced (simple diastereoselectivity) of the Paternò-Büchi reaction?, (c) does hydrogen-bonding effects the rate of the Paternò-Büchi reaction?

The role of hydrogen-bonding interactions in the Paternò-Büchi reaction of allylic alcohols can be easily tested by comparison of the free alcohols with O-protected substrates, i.e. the corresponding acetates.

3.6.1 Synthesis of allylic alcohols and acetates

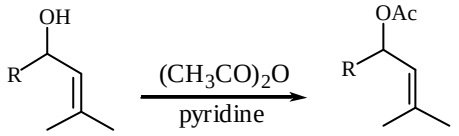
Two allylic alcohols were used in this study, prenol **21**, which was commercially available and mesitylol **22** which was prepared *via* reduction of mesityl oxide in dry ether with $LiAlH_4$.[102]



20 **22**

Scheme 3.29: Synthesis of mesitylol.

Stirring of an equimolar ratio of prenol as well as mesitylol with acetic anhydride in the presence of catalytic amount of pyridine at room temperature, respectively, led to formation of the corresponding allylic acetates **23**[103] and **24,**[104] in high yields.



21 R= H
22 R= CH_3

23 R= H
24 R= CH_3

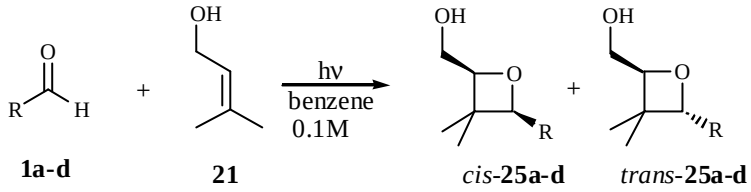
Scheme 3.30: Synthesis of prenyl acetate and mesityl acetate.

3.6.2 Simple diastereoselectivity

3.6.2.1 Photolysis of prenol with aldehydes

As a typical triplet precursor, benzaldehyde **1a** was irradiated in benzene in the presence of prenol **21**. Additionally, three aliphatic aldehydes (acetaldehyde **1b**, propionaldehyde **1c** & 3-

methylbutyraldehyde **1d**) which can react either from their singlet as well as triplet excited states were applied (all substrate 0.1M).



1a-d **21** *cis*-**25a-d** *trans*-**25a-d**

Scheme 3.31: Paternò-Büchi reaction of prenol with aldehydes.

Table 3.18: Simple diastereoselectivity of the photocycloaddition of **1a-d** with **21**.

Entry	R	d.r. (*cis* : *trans*)[a]	Yield (%)
A	Ph	> 97 : 3	80
B	Me	81 : 19	85
C	Et	86 : 14	86
D	Bu^{i}	83 : 17	82

[a] Determined by means of ^{1}H-NMR spectroscopic analysis of the crude product mixture.

The structure of oxetanes were assigned on the basis of the spectroscopic analyses (^{1}H-NMR and ^{13}C-NMR) and mass spectra. In the ^{1}H-NMR spectrum, the hydrogen on the carbon α to oxygen of an oxetane ring has a chemical shift 4.00 - 4.45 ppm which in good agreement with the data reported by Arnold.[105] The mass spectra of compound **25a** and **25c** support the oxetane structure but are not conclusive for their structure. The molecular ion peaks are not observed (usual situation for oxetanes)[106] and the most important fragmentation is cleavage to prenol and a charged carbonyl fragment, the latter then undergoing further decomposition.

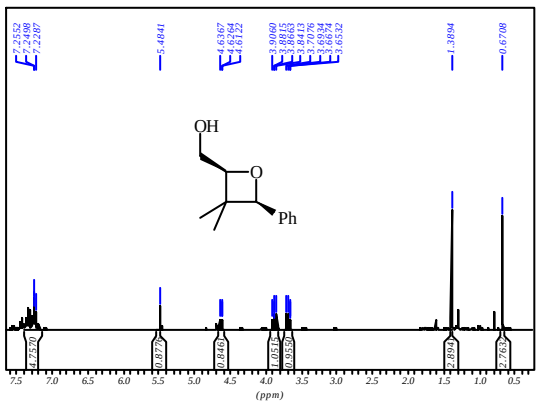


Figure 3.49: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **25a.**

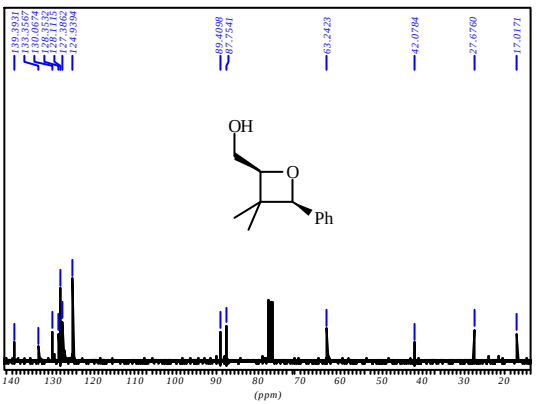


Figure 3.50: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **25a**.

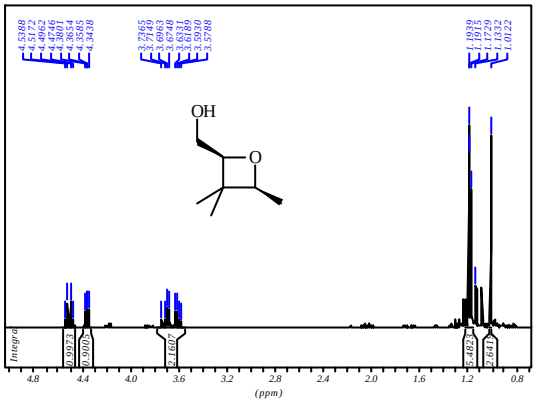


Figure 3.51: ^{1}H-NMR (300MHz, $CDCl_3$) spectrum of **25b**.

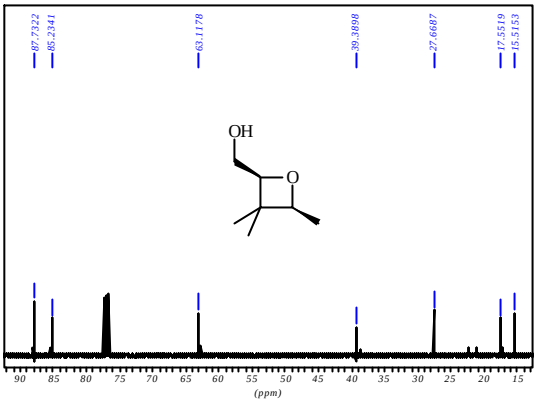


Figure 3.52: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of **25b**.

From all substrate combinations, the *cis*-oxetanes were formed as the major diastereoisomers in good yields. The relative configurations of the major diastereoisomers were unambiguously determined from the NOE effects which were detected for one of the *gem*-methyl groups at the oxetane ring by saturation of both methine hydrogens at C-2 and C-4 of **25c** (Figure 3.53 & 3.54). NOE enhancements were also detected for the methylene hydrogens of the hydroxymethyl and the ethyl substituents at C-2 and C-4 by saturation of the second methyl group. The pseudoaxial methyl group at C-3 (δ = 0.83 ppm) is shifted upfield by ca. 0.2 ppm with respect to the other methyl (δ = 0.98 ppm).

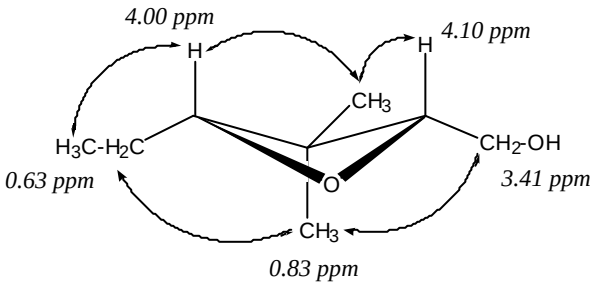


Figure 3.53: NOE-effects for oxetane **25c**.

The diastereomeric values were nearly identical for the three aliphatic aldehydes but higher with benzaldehyde (> 97 : 3) (Table 3.18).

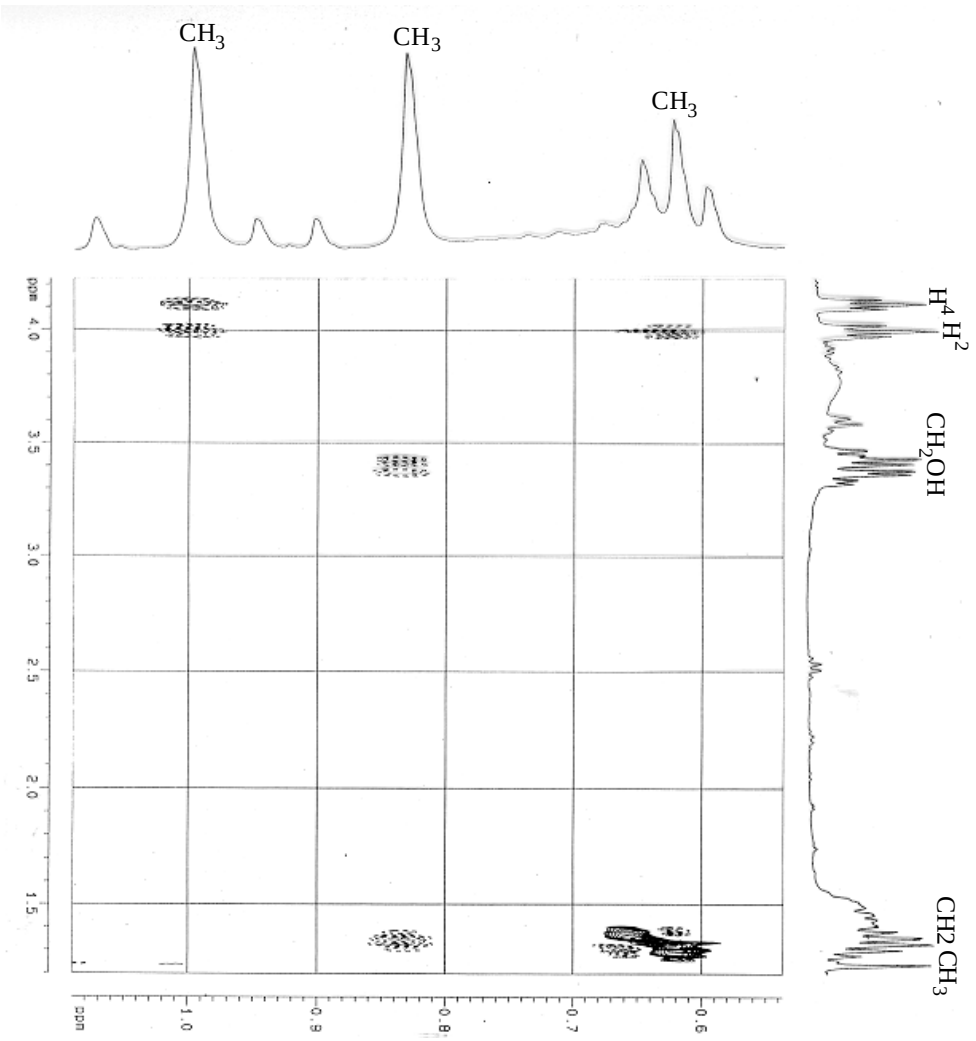
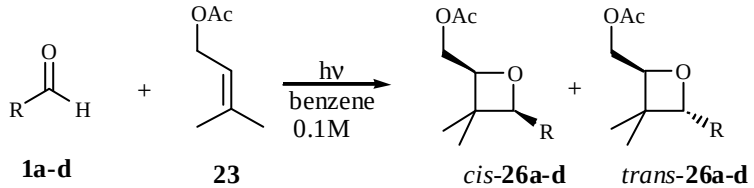


Figure 3.54: NOESY (300 MHz, $CDCl_3$) spectrum of compound **25c**.

3.6.2.2 Photolysis of prenyl acetate with aldehydes

Analogous to prenol, the [2+2] photocycloaddition reaction of prenyl acetate with aldehydes in benzene afforded two diastereoisomers *cis*-**26a-d** and *trans*-**26a-d** in good yield.



1a-d **23** *cis*-**26a-d** *trans*-**26a-d**

Scheme 3.32: Paternò-Büchi reaction of prenylacetate with aldehydes.

Table 3.19: Simple diastereoselectivity of the photocycloaddition of **1a-d** with **23**.

Entry	R =	d.r. (*cis* : *trans*)[a]	Yield (%)
A	Ph	93 : 7	75
B	Me	77 : 23	80
C	Et	81 : 19	83
D	Bu[i]	80 : 20	85

[a] Determined by means of ^{1}H-NMR spectroscopic analysis of the crude product mixture.

The chemical structure of compounds **26a-d** were established by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. The ^{1}H-NMR showed signals at δ 4.53 and 4.64 ppm indicated two methine hydrogens on carbons α of oxetanes ring. The ^{13}C-NMR spectra of compounds **26a-d** showed signal at δ 39 ppm for the quaternary carbon confimed the regioselective addition of aldehydes to prenyl acetate. In the IR spectra, the peak at 1710 cm^{-1} suggests the presence of (C=O) carbonyl ester group.

Interestingly, the diastereomeric *cis/trans* ratio of compounds **26a-d** slightly decreased by comparison with compounds **25a-d** (Table 3.19).

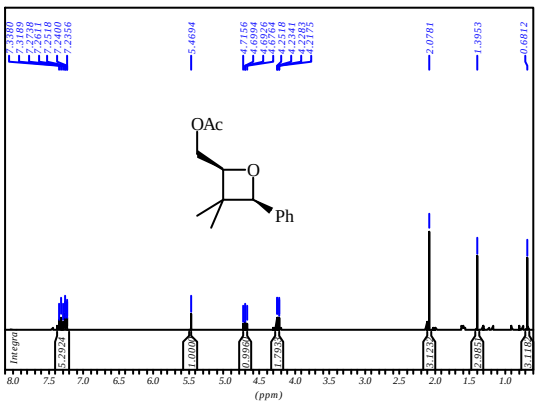


Figure 3.55: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **26a**.

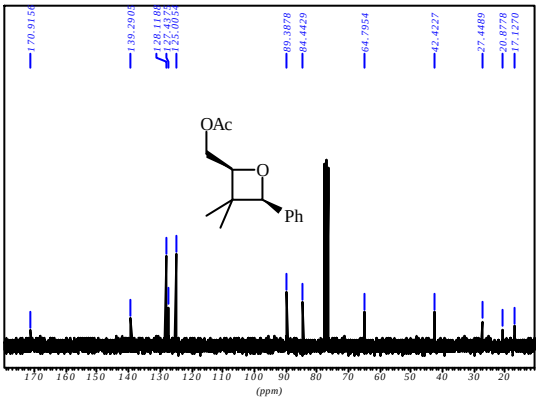


Figure 3.56: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of **26a**.

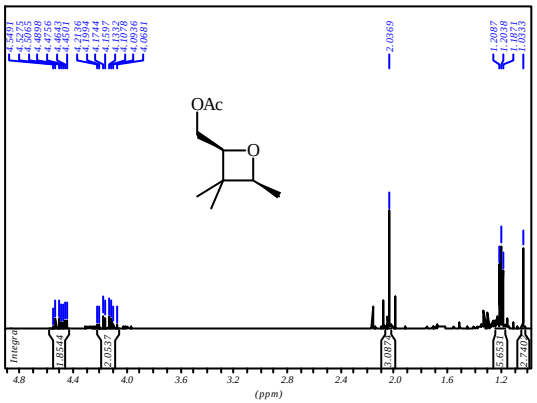


Figure 3.57: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **26b**.

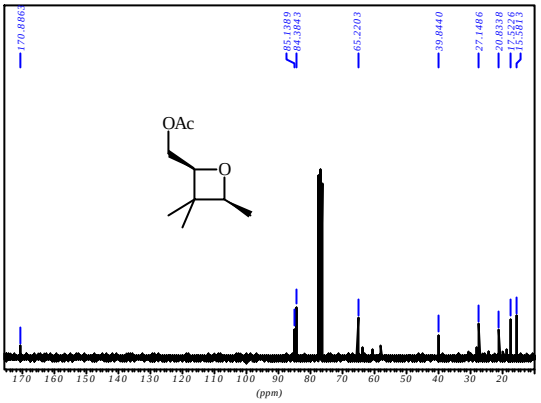
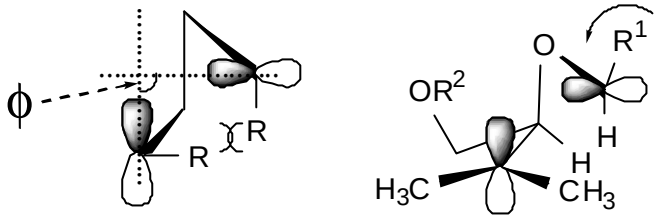


Figure 3.58: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **26b**.

Conclusion I

The regioselectivity of the Paternò-Büchi reaction with prenol as well as prenyl acetate is high and corresponds to the classical biradical stablization concept.[107] The comparison shows that hydrogen-bonding effects are not responsible for controlling the product regioselectivity. The simple diastereoselectivity is moderately high for aliphatic aldehydes reacting with prenol and very high for benzaldehyde with prenol. Comparing these numbers with prenyl acetate shows, that hydrogen-bonding effects might slightly increase the simple diastereoselectivity, but also other reasons like steric effects might explain the marginal differences.

From the numbers in Table 3.18 & 3.19, one can unambiguously derive that the triplet excited carbonyl state reacts highly *cis*-selective with prenol and prenyl acetate. This effect strongly resembles the pronounced *endo*-selectivity which was observed for the Paternò-Büchi reaction of aromatic aldehydes with cycloalkenes. This contrathermodynamic selectivity is again rationalized by the assumption of spin-orbit coupling (SOC) controlled intersystem crossing (ISC) geometries at the stage of the triplet 1,4-biradical (1,4-^{3}BR). Optimal ϕ-values for strong SOC are in the range of 90° ± 10°. This model presupposes conformational mobilty at this intermediate stage in contrast to the reaction of singlet excited carbonyl states where *conical intersections* guide the substrates to the cycloaddition products nearly barrier-free.[51] A view along the central C-C bond of the intermediate triplet 1,4-biradical (Figure 3.59) shows the relevant contribution to this high degree of stereocontrol: increasing *gauche* interactions are expected for biradical approach from the same *half space* as the hydroxymethyl or acetoxymethyl group, respectively.



1,4-^{3}BR

Figure 3.59: Simple diastereoselecectivity: triplet 1,4-biradical geometries from prenol substrates.

Thus, the approach of the two radical centers is expected to proceed preferentially as shown in Figure 3.59 leading to the *cis*-diastereoisomer. An additional internal hydrogen-bonded between the primary hydroxy group and the oxygen atom at position 2 of the 1,4-^{3}BR slightly increases this conformational preference.

3.6.3 Spin-directed simple diastereoselectivity

In order to evaluate the differences in simple diastereoselectivity of the Paternò-Büchi reaction in the singlet and in the triplet channel, the concentration dependence of the reaction of propionaldehyde with prenol and prenyl acetate was investigated. As already described for analogous reactions with 2,3-dihydrofuran as alkene component, the spin profile of a bimolecular photochemical reaction can be traced by variation of substrate concentrations provided that the lifetime of the excited singlet state allows diffusion-controlled processes. This is the case of aliphatic aldehydes which have lifetimes in the 1-2 ns range.[85]

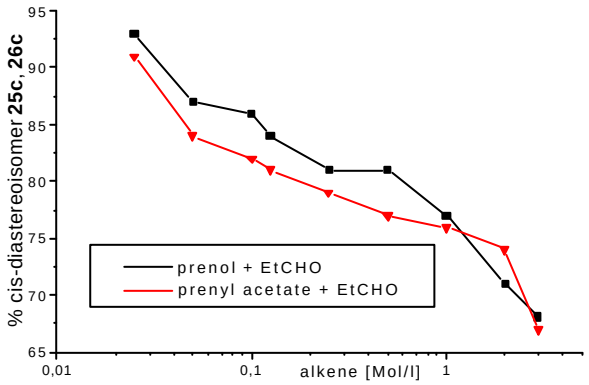


Figure 3.60: Concentration dependence of the propionaldehyde photocycloaddition with prenol and prenyl acetate.

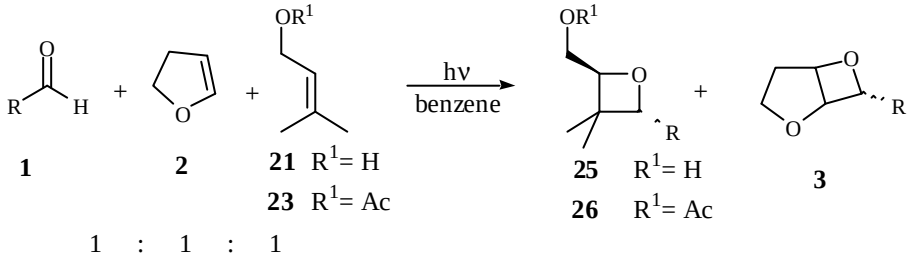
At higher alkene concentration (alkene and aldehyde were used in equimolar concentrations) the simple *cis/trans*-stereoselectivity is identical (ca. 2 : 1) with both substrates prenol and prenyl acetate. In the low concentration region, the selectivity increases constantly to values > 9 : 1 always with the prenol reactions being slightly more selective.

Conclusion II

The curvature of the spin map indicates, that very high selectivities are expected for "pure" triplet reactions, whereas the singlet excited carbonyls only give moderate selectivities. This perfectly corresponds to the results on the spin-directed Paternò-Büchi reaction with cyclic alkenes and clearly shows that the SOC-determined ISC-geometry model is a powerful rationale for explaining simple diastereoselectivites originating from 1,4-triplet biradical combination.

3.6.4 Enhanced reactivity of allylic alcohols

Competition experiments were performed in order to examine the difference in reactivity comparing free and O-protected allylic alcohols. As a standard olefin, 2,3-dihydrofuran in equimolar concentrations (1.0M) as the aldehyde and the acylic alkene was applied.



Scheme 3.33: Competition experiments.

Table 3.20: Results of competition experiment.

Entry	R =	R^1 =	Conc. (M)	**25,26** : **3**[a]
A	Ph	H	1.0	47 : 53
B	Et	H	1.0	55 : 45
C	Et	H	0.01	60 : 40
D	Et	Ac	1.0	13 : 87

[a] Determined by means of ^{1}H-NMR spectroscopic analysis of the crude product mixture.

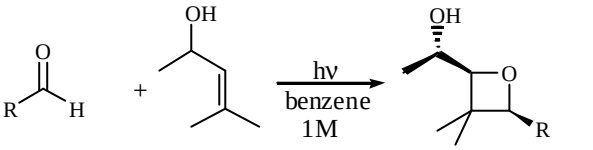
Firstly, benzaldehyde was applied as precursor to a triplet excited carbonyl state: from the ratio of prenol-cycloadduct **25a** and the adduct with dihydrofuran **3**, it was concluded that the

alkenes have similar reactivities toward triplet excited carbonyls (Table 3.20, entry A). In a second experiment, propionaldehyde was used in high (1.0M) and low (0.01M) concentrations in order to trace spin effects. The triplet reactivity of propionaldehyde was slightly higher with prenol than with 2,3-dihydrofuran, an effect which vanished with increasing amount of singlet-derived products (Table 3.20, entry B,C). When prenyl acetate was applied, the adduct **26c** was observed in minor quantities and the dihydrofuran adduct prevailed. Thus, the reactivity difference between prenol and prenyl acetate is about a factor 3 which can originate either from hydrogen bonding interactions or simply from the electronic deactivation of the alkene.

3.6.5 Induced and simple diastereoselectivity with chiral allylic alcohols

3.6.5.1 Photolysis of mesitylol with aliphatic aldehydes

When the aliphatic aldehydes, which gave moderate simple diastereoselectivities with prenol, were irradiated with mesitylol, only one *cis*-diastereoisomers were obtained in high (induced) *threo*-diastereoselectivities (>95 : 5) from the NMR analysis of the crude reaction mixture. This result is fitted well with the results published by Adam in the photocycloaddition of the triplet excited benzophenone with chiral allylic alcohols.[73]



1b-d **22** *threo*-**27b-d**
d.r. > 95 : 5

Scheme 3.34: Paternò-Büchi reaction of mesitylol with aliphatic aldehydes.

The chemical structure of the compounds **27b-d** were assigned by ^{1}H-NMR and ^{13}C-NMR analyses. Again, the ^{13}C-NMR spectrum showed a signal at δ 40.0 ppm for the quaternary carbon and confirmed the regiochemical addition of mesitylol to aldehydes. The IR spectra of compounds **27b-d** exhibit a broad absorption bands at 3300 cm^{-1} to the free OH group.

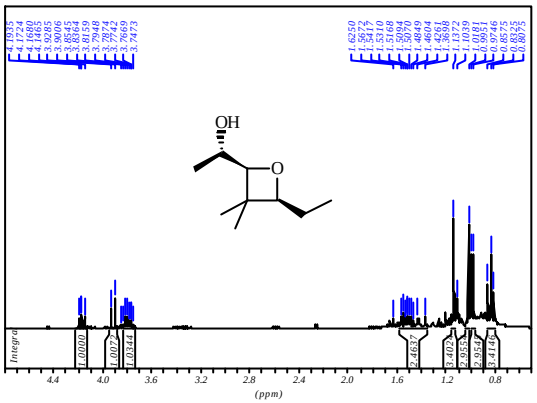


Figure 3.61: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **27c**.

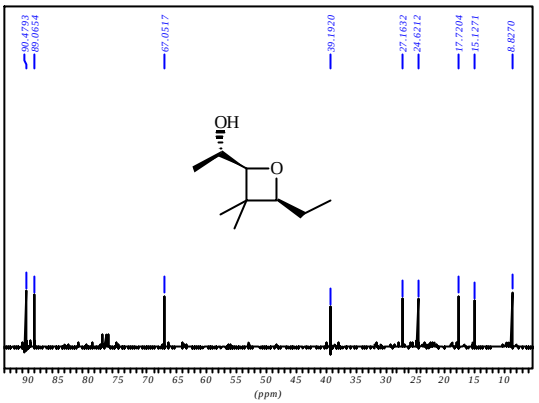
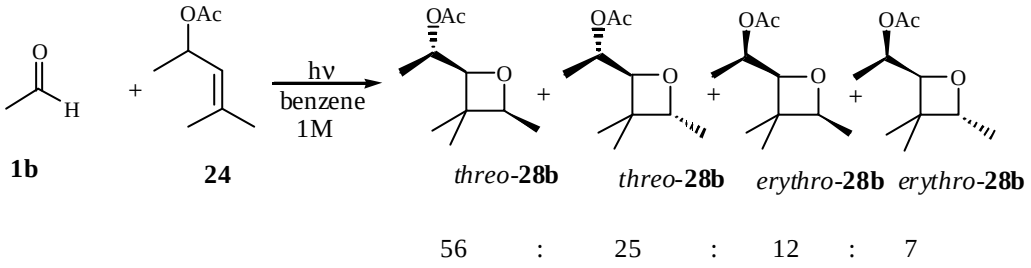


Figure 3.62: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of **27c**.

3.6.5.1 Photolysis of mesityl acetate with acetaldehyde

In contrast to mesitylol, when the mesityl acetate was reacted with acetaldehyde, a mixture of all four diastereoisomers resulted, and the *threo/erythro*-selectivity for the *cis*-isomers dropped.



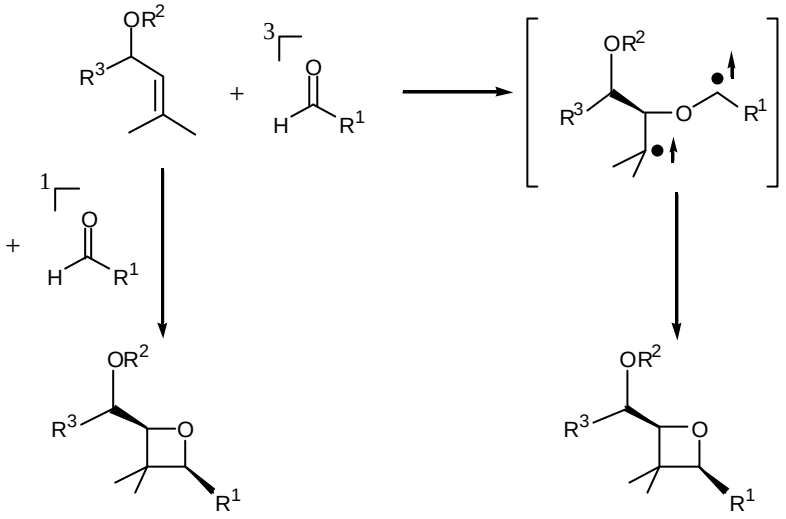
Scheme 3.34: Paternò-Büchi reaction of mesityl acetate with acetaldehyde.

The relative configuration of the four stereoisomers of compound **28b** was assigned by comparing the chemical shifts of the methine hydrogen in the oxetane ring with the literature data from Adam group.[73a,b]

Conclusion III

In light of the mechanistic picture shown in Figure 3.59, an increase in bulk of the hydroxyalkyl chain is expected to lead to an increase in simple diastereoselectivity due to increasing steric interaction in one half-space of the ISC-reactive conformer. This effect was also apparent for the corresponding allylic acetate and thus is not coupled with hydrogen-bonding interactions and also vanishes in the singlet manifold (Figure 3.60). When allylic 1,3-

strain operates (as in substrates **22** & **24**), an additional selectivity increase is observed which is connected with hydrogen-bonding interaction with singlet as well as triplet excited carbonyl states prior to bond formation. Surprisingly, also the induced (*threo*) stereoselectivity was also high with aliphatic aldehydes. This fact, in contrast to the simple diastereoselectivity, cannot be explained by assuming SOC-determined ISC-geometries, because at the given substrate concentrations a noticeable amount of singlet reactivity must be assumed (Scheme 3.36). Also this singlet path gives rise to high selectivity and thus hydrogen bonding interaction in the singlet as well as triplet channel *prior to bond formation* is most probably.



low simple d.s. for R^3 = H
high simple and induced d.s.
for R^3=CH_3 and R^2=H

high simple d.s. for R^3 = H
high simple and induced d.s.
for R^3=CH_3 and R^2=H

Scheme 3.36: Mechanistic scenario for singlet and triplet Paternò-Büchi reaction of allylic alcohols and acetates.

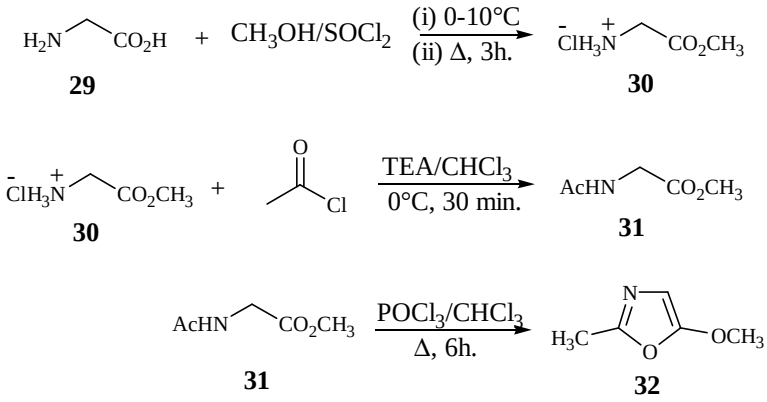
3.7 Diastereoselective photochemical synthesis of a-amino-b-hydroxy carboxylic acid derivatives by photocycloaddition of carbonyl compounds to oxazoles

The interest in α-amino-β-hydroxy acids, a class of primary metabolites, is based on their biological activity as enzyme inhibitors and as starting materials for the synthesis of complex molecules.[108] For example, β-hydroxy tyrosine and β-hydroxy phenylalanine derivatives are found as parts of clinically important glycopeptide antibiotics, which include teicoplanin, ristocetin, actaplanin A4696 and A33512b.[109] The "photoaldol route" has been initially developed by Schreiber *et al*. as a powerful photochemical tool for the synthesis of *threo* β-hydroxy carbonyls compounds.[110] Recently, Griesbeck and Fiege reported on the first example of oxazole-carbonyl photocycloaddition as an efficient route to *erythro* α-amino-β-hydroxy ketones.[81] It was thus of interest to extend the photo aldol route to the synthesis of α-amino-β-hydroxy acids which could be accessible *via* photocycloaddition reaction of 5-methoxy oxazoles with carbonyl compounds.

3.7.1 Synthesis of oxazole substrates

3.7.1.1 Synthesis of 5-methoxy-2-methyl oxazole

5-Methoxy-2-methyl oxazole was prepared from glycine *via* protection as the glycine methyl ester hydrochloride, followed by acylation with acetyl chloride in the presence of triethyl amine to give **31** which upon heating with $POCl_3$ in chloroform afforded oxazole **32** in good yield.[111,112]



Scheme 3.37: Synthesis of 5-methoxy-2-methyl oxazole.

The structure of compound **32** was established on the basis of spectroscopic data. For example, the IR spectrum showed two absorption bands at 1589 and 1625 cm^{-1} correspond to

the presence of C=N and C=C groups, respectively. The ^{1}H-NMR spectrum shows the olefinic hydrogen resonance at 5.87 ppm.

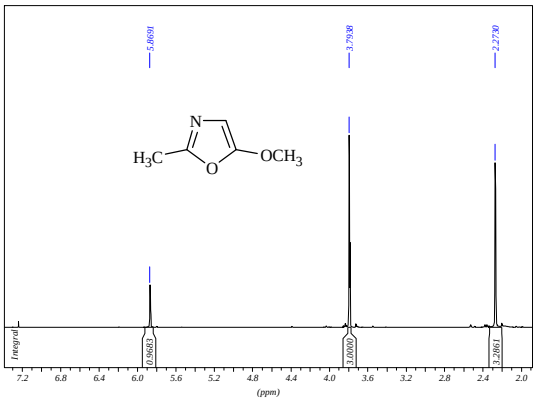


Figure 3.63: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **32**.

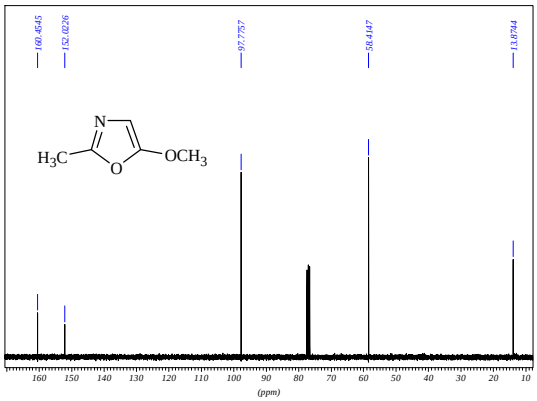
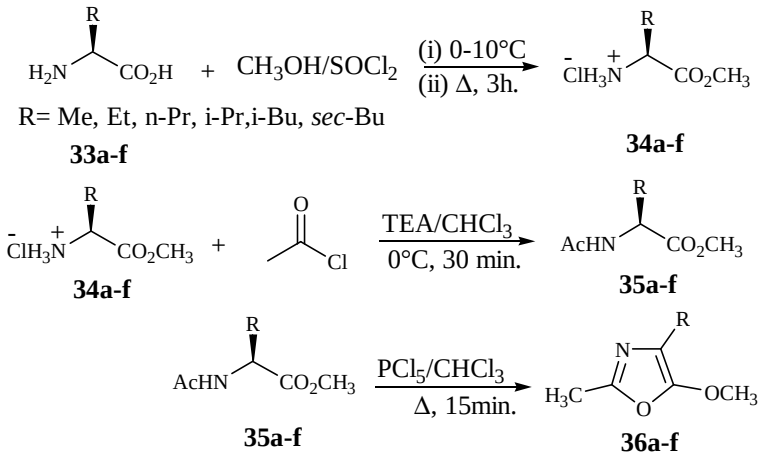


Figure 3.64: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **32**.

3.7.1.2 Synthesis of 4-substituted 2-methyl-5-methoxy oxazoles

A convenient method for the synthesis of 5-methoxy oxazoles with additional substituents at position C-4 is the reaction of an N-acetyl-L-aminoacid methyl ester with PCl_5 as dehydrating agent following a Robinson-Gabriel synthesis as shown in Scheme 3.38.[113,114,115]



Scheme 3.38: Synthesis of 4-substituted 2-methyl-5-methoxy oxazoles.

Table 3.21: Characteristic properties of 4-substituted 2-methyl-5-methoxy oxazoles.

Compound	R =	^{1}H-NMR[a]	^{13}C-NMR[b]	B.p$_{10\ torr}$ (°C)	Yield (%)
36a	Me	3.83	111.2	61-63	60
36b	Et	3.77	117.1	64-67	74
36c	n-Pr	3.77	115.6	75-78	68
36d	i-Pr	3.75	121.1	71-73	65
36e	i-Bu	3.74	114.8	86-88	70
36f	*sec*-Bu	3.79	119.9	89-93	75

[a] chemical shift of OCH_3 in ppm, [b] chemical shift of C-4 in ppm.

The chemical structures of compounds **36a-f** were established on the basis of rigorous spectroscopic (UV, IR, ^{1}H-NMR, ^{13}C-NMR) and elemental analyses. The UV spectra of 5-methoxy-2-methyl oxazoles exhibit one major band of strong intensity at 245-270 nm. Alkyl substitution on oxazole ring has little effect on the position and intensity of this band. The IR spectrum of 2,4-dimethyl-5-methoxy oxazole **36a** shows a strong band at 1555-1598 cm^{-1} which was assigned to the –N=C-O ring stretching frequency. This band is shifted to higher frequency when an additional alkyl substituent is introduced to the oxazole ring either in C-2 or C-4 position. In the ^{1}H-NMR spectra of 5-methoxy oxazoles, the methoxy group absorbs at around 3.7 ppm and the CH_3 at position C-2 absorbs at 2.00 ppm. The ^{13}C-NMR spectra of oxazoles showed two signals at 152 and 154 ppm assigned to the C-2 and C-5, respectively.

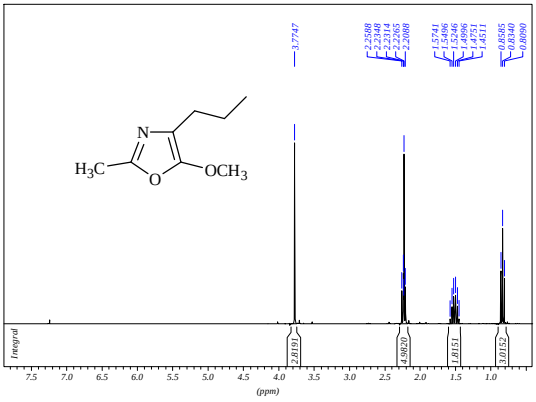


Figure 3.65: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **36c**.

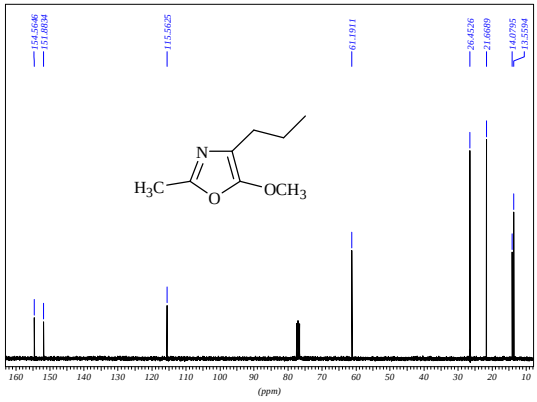


Figure 3.66: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **36c**.

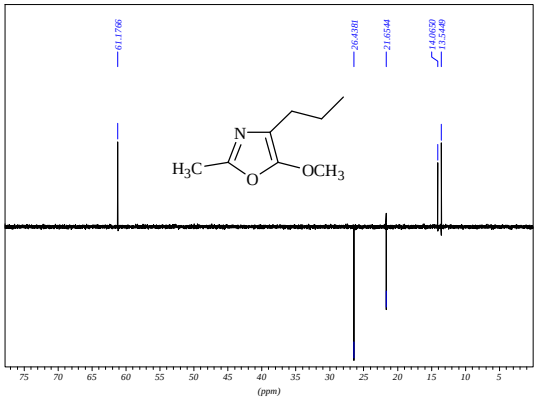
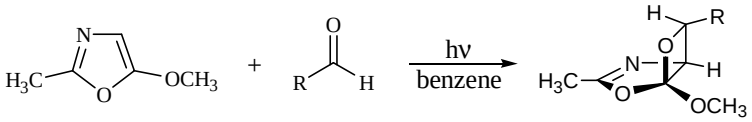


Figure 3.67: DEPT spectrum (75 MHz, $CDCl_3$) of **36c**.

3.7.2 Photoreactions of 5-methoxy-2-methyl oxazole with aldehydes

First of all, the photoreactions (λ_{ex} = 300 nm) of aldehydes (0.05M) with 5-methoxy-2-methyl oxazole (0.05M) were performed in 50 mL benzene at 10°C. In all cases, *exo*-selective (>98 : 2) formation of the 4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-enes **38a-f** was observed in medium yields (Table 3.22).



32 **37a-f** **38a-f**

Scheme 3.40: Paternò-Büchi reaction of 5-methoxy-2-methyl oxazole with aldehydes.

Table 3.22: Results of the photocycloaddition of **32** with **37a-f**.

Compound	R =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
38a	Ph	>98 : 2	87
38b	β-Naph	>98 : 2	85
38c	$BnCH_2$	>98 : 2	87
38d	Et	>98 : 2	90
38e	i-Pr	>98 : 2	86
38f	i-Bu	>98 : 2	88

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture; [b] yield (%) based on conversion of the oxazole.

The formation of the acid-labile bicyclic oxetanes **38a-f** was proven by the characteristic ^{13}C-NMR signals of the orthoester carbon (δ_C ca. 124 ppm). The stereochemical assignment of the

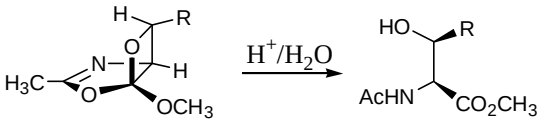
bicyclic oxetanes **38a-f** was performed on the basis of ^{1}H-NMR analysis (especially the strong ring current induced upfield-shift for the aryl-substituted products **38a** and **38b** (Table 3.23).

Table 3.23: Chemical shift (δ_{ppm}) of H-1 and C-5 for compounds **38a-f**.

Compound	R =	H-1	C-5
38a	Ph	4.58	122.9
38b	β-Naph	4.62	123.1
38c	$BnCH_2$	4.87	124.5
38d	Et	5.04	124.6
38e	i-Pr	4.92	124.6
38f	i-Bu	4.97	124.7

3.7.2.1 Ring opening of the bicyclic oxetanes 38a-f

The primary photoadducts **38a-f** were hydrolytically unstable and underwent twofold ring opening to give the α-acetamido-β-hydroxy esters **39a-f**. The diastereomeric ratio of the ring opened products was identical to the diastereomeric ratio of the oxetane precursors except for **39d** (Table 3.24).



38a-f **39a-f**

Scheme 3.40: Synthesis of *erythro* (2S*, 3S*) α-acetamido-β-hydroxy esters.

Table 3.24: Diastereomeric ratio of the compounds **39a-f**.

Compound	R =	d.r. (*erythro* : *threo*)[a]	Yield (%)[b]
39a	Ph	>98 : 2	70
39b	β-Naph	>98 : 2	75
39c	$BnCH_2$	>98 : 2	65
39d	Et	95 : 5	72
39e	i-Pr	>98 : 2	78
39f	i-Bu	>98 : 2	74

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] yield (%) of the isolated mixture of diastereoisomers.

In order to elucidate the relative configuration of the photoaldol adducts **39a-f**, N-acetyl threonine methyl ester **39g** was prepared.[116] Figure 3.68 displays the X-ray analysis of compound **39g**.

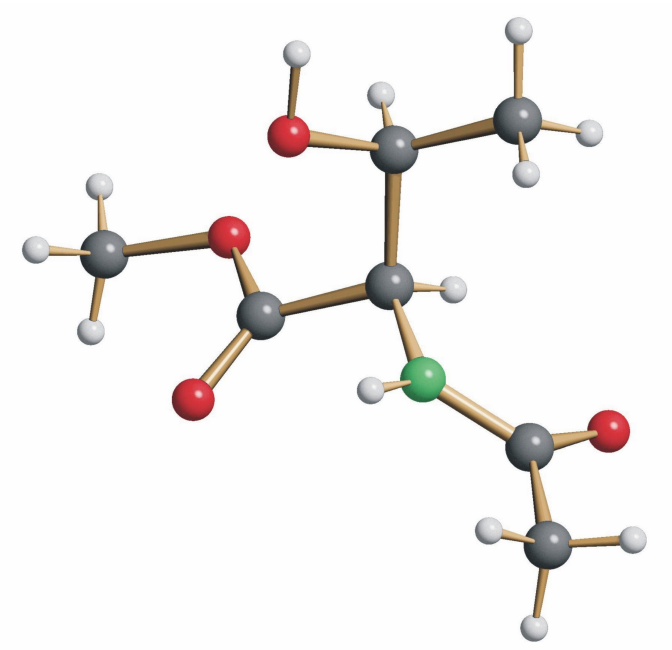
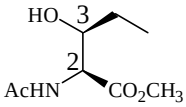
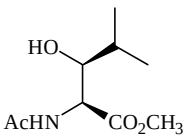
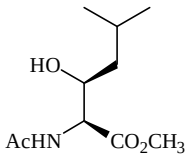
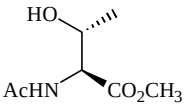
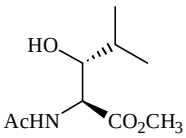


Figure 3.68: X-ray analysis of *threo*-**39g**.

Furthermore, the relative configuration of methyl esters of phenylserine **39a**[117] and β-hydroxyleucine[118] were already elucidated in the literature and, by comparison with our data, the *erythro* (S*, S*) configuration for the major diastereoisomers of **39a-f** was established (Table 3.25).

Table 3.25: Comparsion of NMR spectra of compounds **39d-f** with similar known compounds.

Compound					
δ_{ppm}	**39d**	**39e**	**39f**	**39g**[a]	Lit.[118]
H-2	4.88	4.75	4.87	4.35	4.84
H-3	4.01	3.45	4.18	4.16	3.73
C-2	56.5	54.3	56.8	57.6	54.0
C-3	65.3	69.8	61.8	67.3	77.2

[a] Prepared from (2S*,3R*) threonine.

The structural assignments of compounds **39a-f** were made on the basis of spectroscopic data. The IR spectra of compounds **39a-f** showed characteristic absorption bands for hydroxy, amino, amide and ester groups at 3400, 3320, 1670 and 1720 cm^{-1}, respectively. The ^{13}C-NMR spectra clearly showed resonances which correspond to the carbinol C-3 at 65.3 ppm. Moreover, there appeared two signals at 169.1 and 169.6 ppm pointing out the presence of CON and COO, respectively.

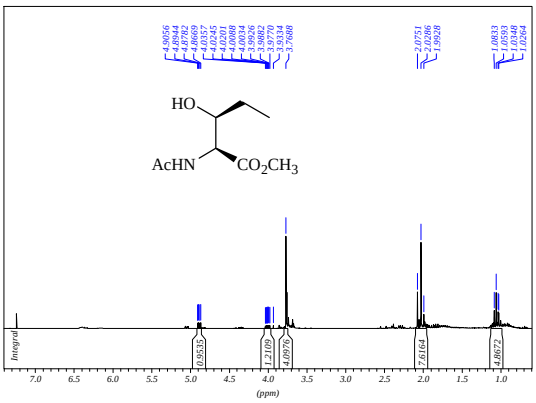


Figure 3.69: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **39c**

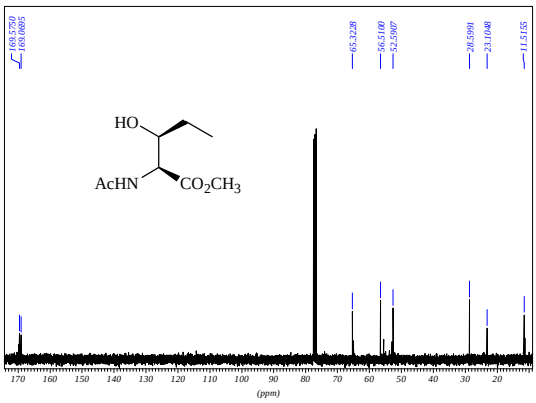
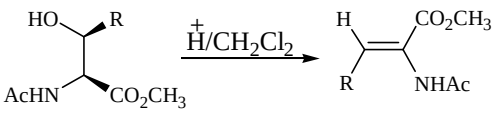


Figure 3.70: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **39c**.

3.7.2.2 Synthesis of (Z)-a, b-didehydroamino acid derivatives

Dehydroamino acids have recently become a topic of increasing interest as important constituents of many fungal metabolites with antibiotic or phytotoxic properties such as nisin and subtilin.[119] In addition, dehydroamino acids are versatile precursors for the asymmetric synthesis of amino acids and peptides.[120] Acid-catalyzed water elimination from the α-acetamido-β-hydroxy esters **39** gave the (Z)-α,β-didehydroamino acid derivatives preferentially.



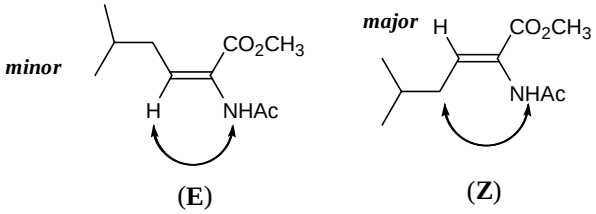
39 **40a-d**

Scheme 3.41: Synthesis of (Z)-α, β-didehydroamino acid derivatives.

Table 3.26: Diastereomeric ratio of the products **40a-d**.

Compound	R =	d.r. (Z : E)	Yield (%)
40a	Ph	>98 : 2	80
40b	Et	97 : 3	75
40c	i-Pr	95 : 5	78
40d	i-Bu	93 : 7	83

The relative configurations of the major and the minor diastereoisomers of the compound **40d** were unambiguously determined by NOE and ROESY analyses at -63°C. The amide proton signal overlaped and exchanged with the deuterium atom from $CDCl_3$ and was not available for NOE measurement at room temperature. At –63°C the NH signal was lowfield-shifted to 7.58 ppm and could be used for saturation experiments.



(**E**) (**Z**)

Figure 3.71: NOE interaction of the major and minor diastereoisomer of compound **40d**.

By irradiation of the amide proton at 7.75 ppm, NOE enhancement was observed for the vinyl proton at 6.95 ppm for the minor diastereoisomer **E-40d**. In the major diastereoisomer **Z-40d**, no enhancement of the vinyl proton signal at 6.75 ppm was observed by irradiation the amide proton at 7.58 ppm (Figure 3.72).

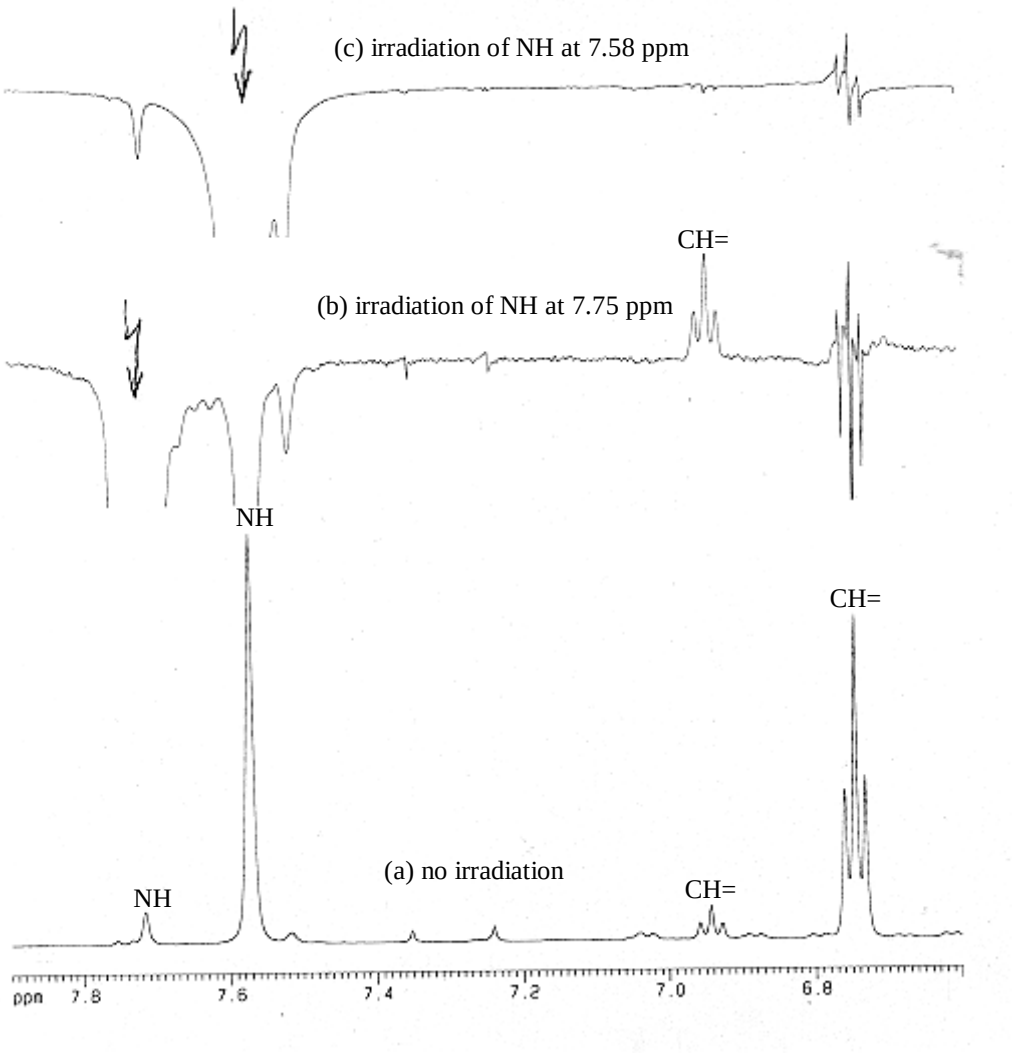


Figure 3.72: The NOE difference spectra (300 MHz, $CDCl_3$) of **Z** & **E - 40d**.

The constitution of the compounds **40a-d** was established by ^{1}H-NMR and ^{13}C-NMR analyses. The ^{1}H-NMR spectra of these compounds show the olefinic hydrogen at around 6.7 ppm and the ^{13}C-NMR spectra show two singlets at around 165 and 168 ppm indicating the presence of two conjugated carbonyl groups.

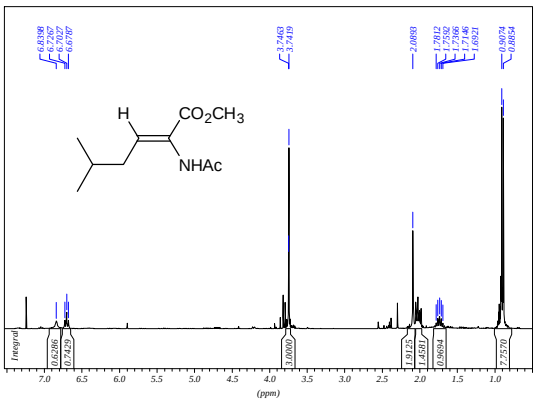


Figure 3.73: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **40d**.

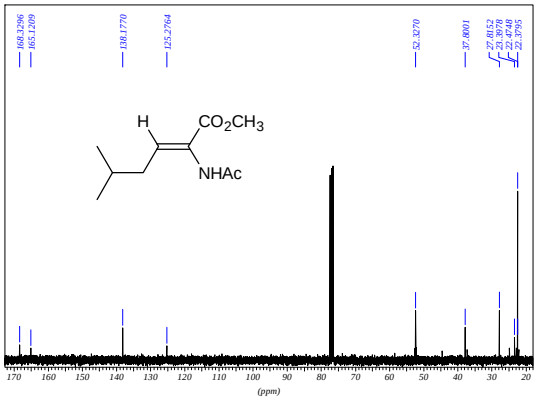
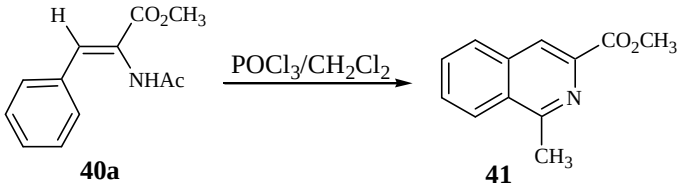


Figure 3.74: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **40d**.

3.7.2.3 Synthesis of methyl 1-methyl isoquinoline-3-carboxylate

Compound **40a** when treated with $POCl_3$ in methylene chloride afforded methyl 1-methyl isoquinoline-3-carboxylate **41** in good yield *via* a Bischler-Napieralski cyclization.



40a **41**

Scheme 3.42: Synthesis of methyl 1-methyl isoquinoline-3-carboxylate **41**.

The structure of compound **41** was confirmed by spectroscopic analysis and by comparsion with literature data.[121] For example, the ^{1}H-NMR spectrum showed two singlets at 2.99, 3.99 ppm attributed to methyl and methoxy groups, respectively. In the ^{13}C-NMR spectrum two signals at 159.4 and 166.5 ppm indicated the presence of conjugated C=N and COOMe groups, respectively.

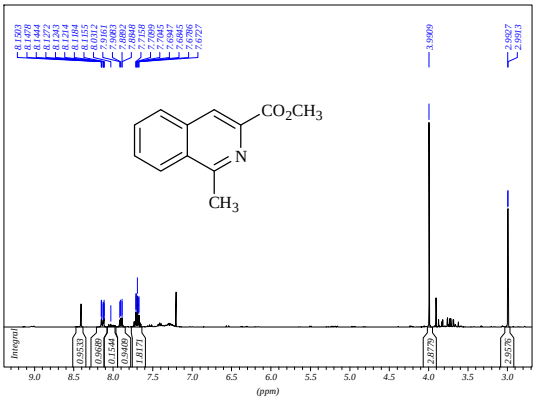


Figure 3.75: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **41**.

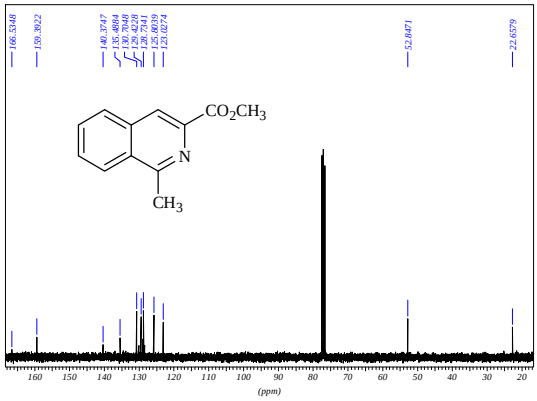
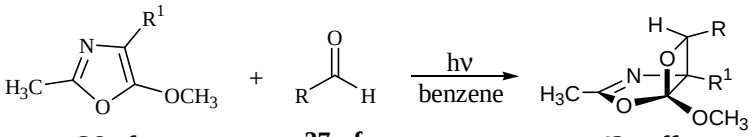


Figure 3.76: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **41**.

3.7.3 Photoreactions of 4-substituted 2-methyl-5-methoxyoxazoles with aldehydes

In order to extend the versatility of 5-methoxyoxazole-carbonyl photocycloaddition as an synthetic approach to α-alkylated-α-amino-β-hydroxy carboxylic acid derivatives, the Paternò-Büchi reaction of 4-substituted 2-methyl-5-methoxyoxazoles with aliphatic and aromatic aldehydes was investigated. The substituents R^1 at position C-4 of the oxazole were varied in order to evaluate the influence of steric bulk and possible electronic effects. Analogous to **32**, photolysis of aliphatic or aromatic aldehydes in presence of oxazole substrates **36a-f** gave the bicyclic oxetanes **42aa-ff** with high regio- and stereoselectivity.



36a-f **37a-f** **42aa-ff**

Scheme 3.43: Paternò-Büchi reaction of aldehydes with oxazole substrates **36a-f**.

Table 3.27: Diastereoselectivity of the photocycloaddition of **36a-f** with **37a-f**.

Compound	R =	R^1 =	d.r.(*exo* : *endo*)[a]	Yield (%)[b]
42aa	Ph	Me	>98 : 2	85
42ab	Ph	Et	>98 : 2	84
42ac	Ph	n-Pr	>98 : 2	86
42ad	Ph	i-Pr	73 : 27	80
42ae	Ph	i-Bu	87 : 13	78
42af	Ph	*sec*-Bu	85 : 15	81
42ba	β-Naph.	Me	>98 : 2	79
42ca	$BnCH_2$	Me	>98 : 2	87
42cd	$BnCH_2$	i-Pr	81 : 19	86
42da	Et	Me	>98 : 2	90
42db	Et	Et	>98 : 2	92
42dc	Et	n-Pr	>98 : 2	95
42dd	Et	i-Pr	>98 : 2	88
42de	Et	i-Bu	>98 : 2	84
42df	Et	*sec*-Bu	>98 : 2	87
42ea	i-Pr	Me	>98 : 2	90
42eb	i-Pr	Et	>98 : 2	87
42ec	i-Pr	n-Pr	>98 : 2	85
42ed	i-Pr	i-Pr	>98 : 2	83
42ee	i-Pr	i-Bu	>98 : 2	80
42ef	i-Pr	*sec*-Bu	>98 : 2	83
42fa	i-Bu	Me	>98 : 2	84
42fb	i-Bu	Et	>98 : 2	84
42fc	i-Bu	n-Pr	>98 : 2	80
42fd	i-Bu	i-Pr	81 : 19	81
42fe	i-Bu	i-Bu	>98 : 2	85
42ff	i-Bu	*sec*-Bu	89 : 11	83

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] yield (%) based on conversion of the oxazole.

From the results in Table 3.27, one can clearly notice that the *exo*-selectivity of the photoadducts was exceedingly high (>98 : 2) except for the benzaldehyde additions to

oxazole substrates with bulky substituents R^1. Again, the formation of the acid-labile bicyclic oxetanes **42aa-ff** was proven by the significant ^{13}C-NMR signals of the orthoester carbon (δ_c ca. 124.5 ppm). The relative configuration of compound **42aa** was unambiguously assigned from NOE measurement. Irradiation of the methine hydrogen at 5.23 ppm leads to nuclear Overhauser enhancement of a methyl signal at 2.03 ppm which clearly confirmed the *exo*-Ph configuration of the bicyclic oxetane. Figure 3.77 summarizes the NOE data recorded for compound **42aa**.

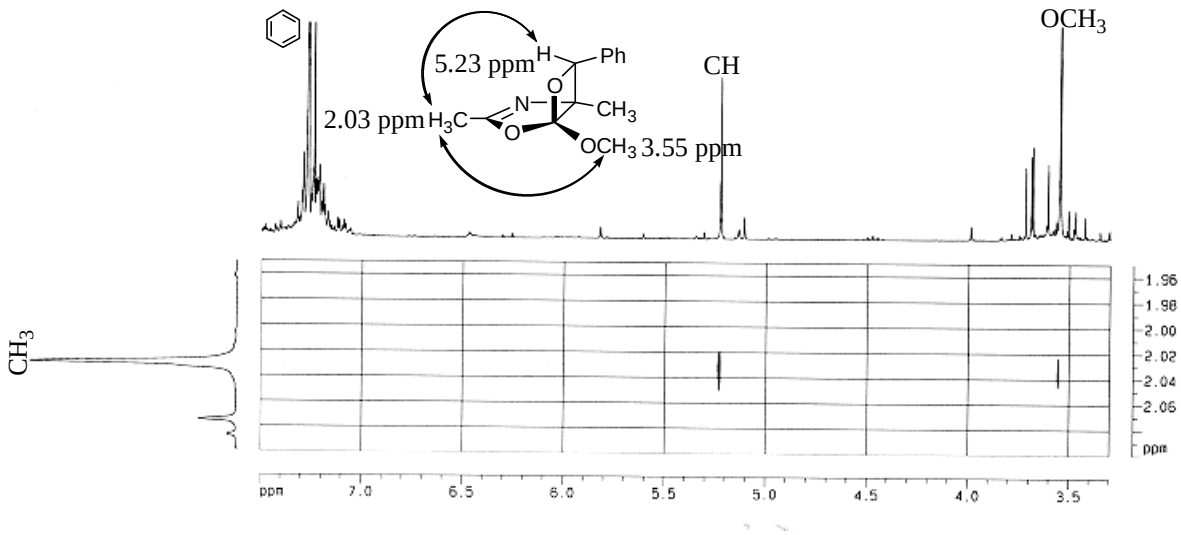
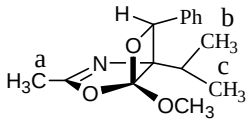
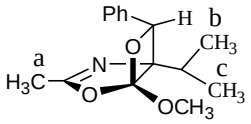


Figure 3.77: NOESY (300 MHz, $CDCl_3$) spectrum of **42aa**.

Moreover, the stereochemical assignment was performed on the basis of ^{1}H-NMR analysis (especially the strong ring current-induced upfield-shift for the C-1 and C-3 methyl groups in the aryl-substituted, see e.g. Table 3.28).

Table 3.28: ^{1}H-NMR chemical shifts of the methyl protons on *exo*-**42ad** & *endo*-**42ad**.





exo-**42ad**			*endo*-**42ad**
δ / ppm	a CH_3	b CH_3	c CH_3
exo-**42ad**	2.00	0.55	0.73
endo-**42ad**	1.67	0.93	0.98

The chemical structures of the photoadducts **42aa-ff** were established on the basis of the spectroscopic data. For example, the ^{1}H-NMR spectrum of compound **42ac** showed three singlets at 2.00, 3.54 and 5.17 ppm corresponding to CH_3 at position C-3, OCH_3 and CH at position C-7, respectively. In the ^{13}C-NMR spectrum, there are three signals characteristic for the oxetane ring at 79.0, 89.9 and 124.6 ppm attributed to C-1, C-7 and C-5, respectively. The signal for C-3 appears down-field shifted at 165.0 ppm (Figure 3.78 & 3.79).

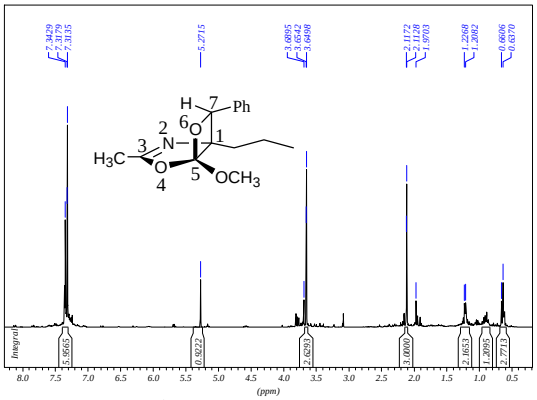


Figure 3.78: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42ac**.

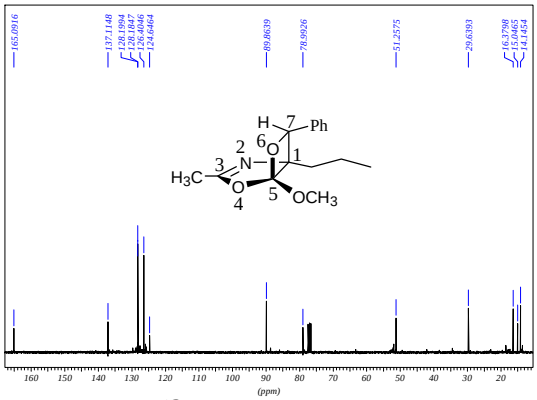


Figure 3.79: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42ac**.

The ^{1}H-NMR spectrum of compound **42ae** showed doublets at 0.58 and 0.69 ppm due to the isopropyl group and confirmed the *exo*-Ph configuration of the photoadduct. In addition, there are three singlets at 2.12, 3.66 and 5.25 ppm corresponding to CH_3, OCH_3 and CH of the oxetane ring, respectively. In the ^{13}C-NMR spectrum, the characteristic signals for the oxetane ring resonate at 78.7, 90.4 and 124.7 ppm due to C-1, C-7 and C-5, respectively.

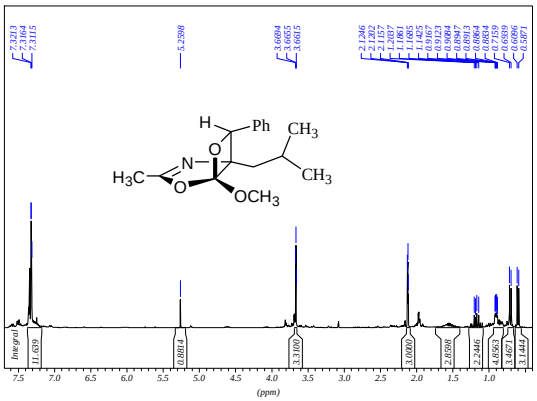


Figure 3.80: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42ae**.

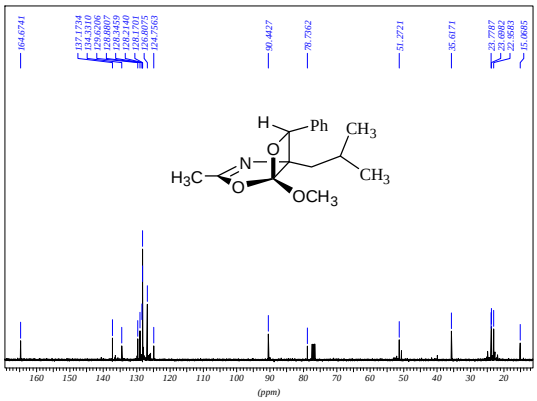


Figure 3.81: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42ae**.

The IR spectrum of compound **42af** showed a strong absorption band at 1620 cm^{-1} attributed to the presence of a C=N group. The mass spectrum showed the base peak at m/z 105 due to the retrocleavage of the photoadduct and formation of the benzoyl cation (PhCO+). The ^{1}H-NMR spectrum showed an upfield-shifted triplet signal at 0.31 ppm corresponding to CH_3 group attached to CH and again strongly supported the *exo*-configuration of the bicyclic oxetane. In the ^{13}C-NMR spectrum, one can clearly show the facial selectivity of the photoadduct is about 50 : 50 with each carbon appears as a signal pair with the same intensity (Figure 3.82 & 3.83).

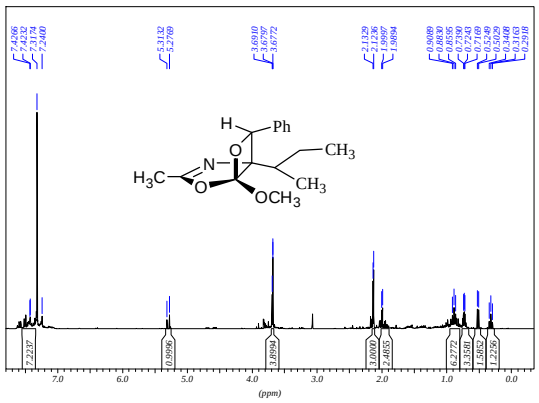


Figure 3.82: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42af**.

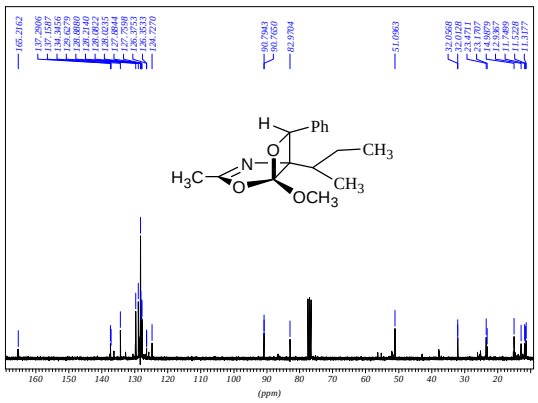


Figure 3.83: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42af**.

The chemical structure of compound **42ca** was established on the basis of ^{1}H-NMR and ^{13}C-NMR analyses. In the ^{1}H-NMR spectrum, there are three singlets absorbing at 1.18, 1.94 and 3.42 ppm corresponding to the CH_3 at position C-1, CH_3 at position C-3, and OCH_3, respectively. In addition there appears a doublet of doublet signal at 4.15 ppm due to the CH of the oxetane ring. The ^{13}C-NMR spectrum revealed, three signals for the oxetane ring at 73.4, 87.9 and 124.5 ppm attributed to C-1, C-7, and C-5, respectively (Figure 3.84 & 3.85).

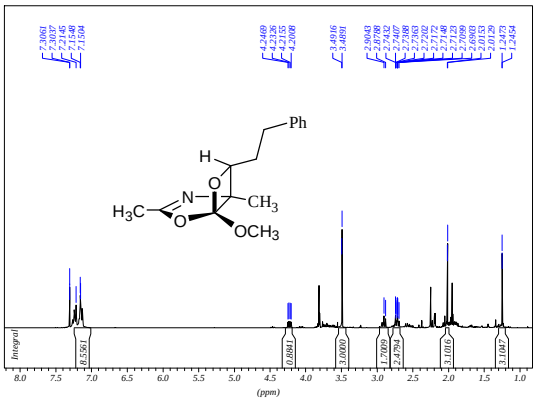


Figure 3.84: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42ca**.

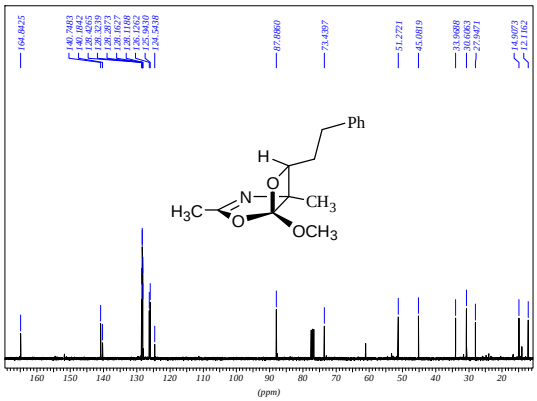


Figure 3.85: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42ca**.

The structural assignment of compound **42dc** was based on the IR spectrum, mass spectrum and NMR analyses. The IR spectrum showed a strong absorption band at 1615 cm^{-1} attributed to a C=N, and a weak absorption band at 1110 cm^{-1} due to a C-O bond. The mass spectrum showed the base peak at 57 corresponding to the (CH_3CH_2CO+) which results after retro cycloaddition of the photoadduct. The ^{1}H-NMR spectrum revealed a doublet of doublet signal at 4.03 ppm attributed to the CH of the oxetane ring. The ^{13}C-NMR spectrum showed three triplet signals at 16.8, 24.9, and 28.3 ppm due to the presence of three methylene groups. In addition three further signals in the aliphatic range (8.9, 14.2, 14.8 ppm) and the OCH_3 group appears at 50.8 ppm.

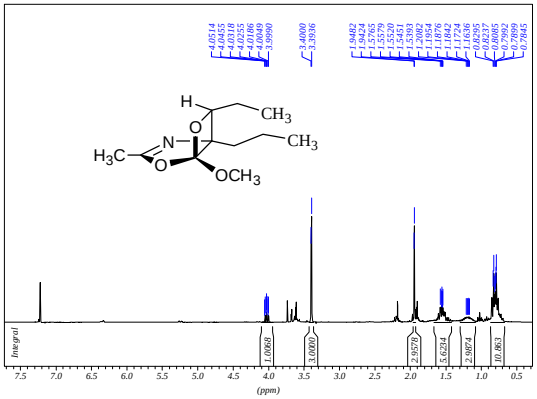


Figure 3.86: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42dc**.

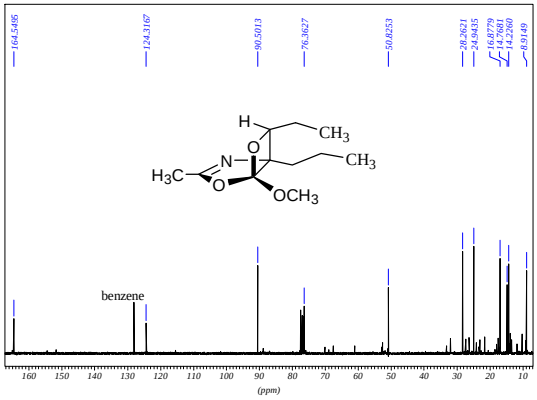


Figure 3.87: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42dc**.

The constitution of compound **42df** was established by IR, mass spectrum and NMR analyses. The IR spectrum showed absorption bands at 987 and 1605 cm^{-1} attributed to a C-O bond and a C=N bond, respectively. In the mass spectrum, the molecular ion peak did not appear and the most important fragments correspond to the retrocycloaddition to oxazole and propionaldehyde which decompose to further fragment. The ^{1}H-NMR spectrum showed two singlets at 2.00 and 3.47 ppm due to the presence of CH_3 and OCH_3, respectively. In addition, the oxetane ring signal absorbs at 4.16 ppm. The ^{13}C-NMR spectrum confirmes the facial selectivity induced by chiral oxazole **36f** is about 50 : 50 as shown from the intensity of the carbon signals. Furthermore, the characteristic signals of the oxetane ring appear at 80.5, 90.9 and 124.5 ppm corresponding to C-1, C-7, and C-5, respectively (Figure 3.88 & 3.89).

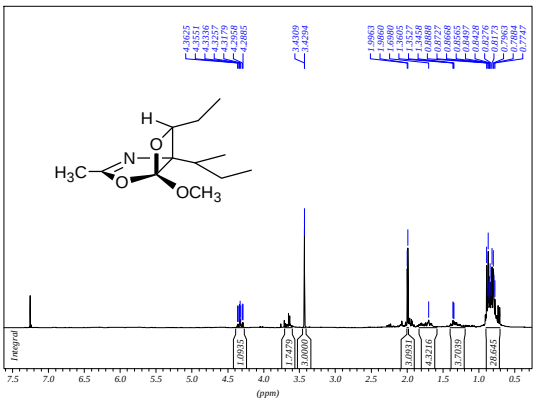


Figure 3.88: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42df**.

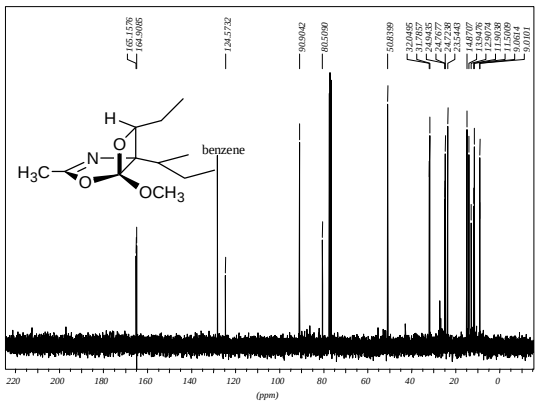


Figure 3.89: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42df**.

The ^{1}H-NMR spectrum of compound **42fe** showed singlets at 2.00 and 3.44 ppm attributed to CH_3 and OCH_3, respectively. In addition a doublet of doublet signal for one proton at 4.25 ppm corresponding to the CH of the oxetane ring. In the ^{13}C-NMR spectrum, there are two triplets at 34.2 and 40.7 ppm indicating the presence of two methylene groups. In addition, three signals appear at 76.3, 88.3, and 124.5 ppm due to C-1, C-7, and C-5, respectively (Figure 3.90& 3.91).

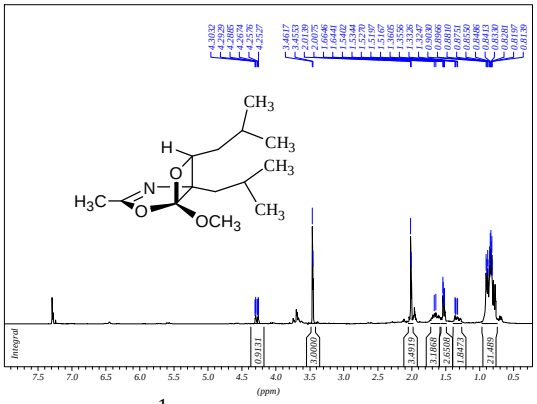


Figure 3.90: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **42fe**.

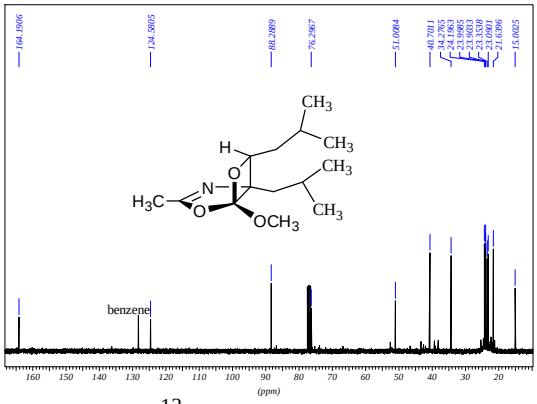
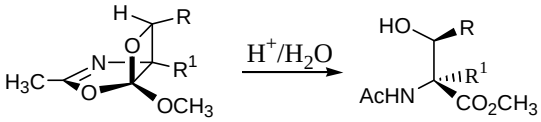


Figure 3.91: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **42fe**.

3.7.3.1 Synthesis of *erythro* (S*,S*) α-alkylated-α-acetamido-β-hydroxy esters

Analogous to **38a-f**, hydrolysis of the bicyclic oxetanes **42aa-ff** resulted in twofold ring-opening and provided a convenient and a high yielding access to *erythro* (S*,S*) α-alkylated-α-acetamido-β-hydroxy esters **43aa-ff**. In most cases, the diastereomeric ratio of the opened products matched the diastereomeric ratio of the bicyclic oxetanes.



42aa-ff **43aa-ff**

Scheme 3.44: Synthesis of *erythro* (S*,S*) α-alkylated-α-acetamido-β-hydroxy esters.

The *erythro* (S*,S*) configuration of compound **43df** was unambiguously determined by single crystal X-ray analysis as depicted in Figure 3.92.

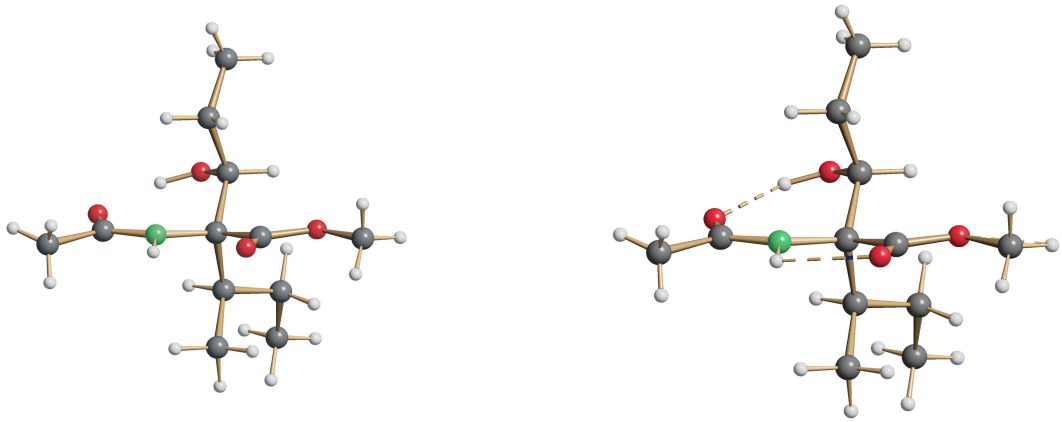


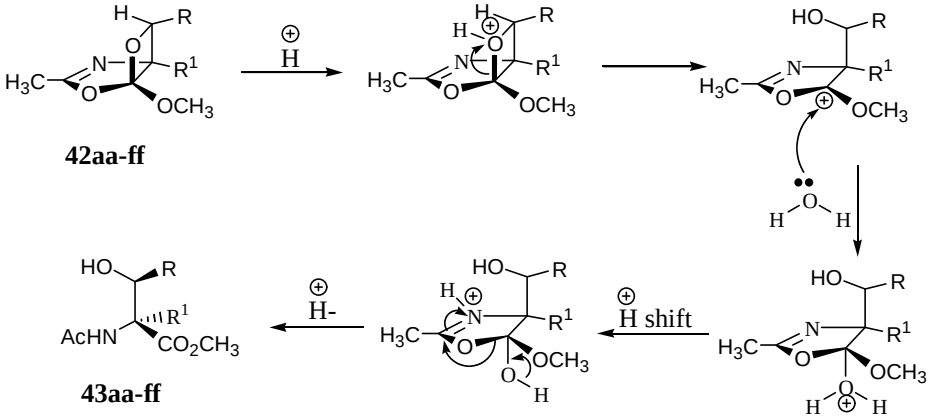
Figure 3.92: X-ray analysis of *erythro*-**43df**: without and with hydrogen-bonds.

Table 3.29: Diastereomeric ratio of compounds **43aa-ff**.

Compound	R =	R^1 =	d.r.(*erythro* : *threo*)[a]	Yield (%)[b]
43aa	Ph	Me	>98 : 2	65
43ab	Ph	Et	93 : 7	73
43ac	Ph	n-Pr	90 : 10	58
43ad	Ph	i-Pr	90 : 10	48
43ae	Ph	i-Bu	90 : 10	58
43af	Ph	*sec*-Bu	92 : 8	40
43ba	β-Naph.	Me	>98 : 2	48
43ca	$BnCH_2$	Me	85 : 15	55
43cd	$BnCH_2$	i-Pr	>98 : 2	55
43da	Et	Me	>98 : 2	70
43db	Et	Et	95 : 5	65
43dc	Et	n-Pr	92 : 8	55
43dd	Et	i-Pr	95 : 5	68
43de	Et	i-Bu	>98 : 2	70
43df	Et	*sec*-Bu	90 : 10	67
43ea	i-Pr	Me	>98 : 2	70
43eb	i-Pr	Et	88 : 12	71
43ec	i-Pr	n-Pr	85 : 15	68
43ed	i-Pr	i-Pr	93 : 7	73
43ee	i-Pr	i-Bu	90 : 10	59
43ef	i-Pr	*sec*-Bu	96 : 4	68
43fa	i-Bu	Me	>98 : 2	55
43fb	i-Bu	Et	93 : 7	66
43fc	i-Bu	n-Pr	>98 : 2	68
43fd	i-Bu	i-Pr	>98 : 2	62
43fe	i-Bu	i-Bu	92 : 8	45
43ff	i-Bu	*sec*-Bu	90 : 10	73

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] yield (%) of the isolated mixture of diastereoisomers.

The mechanism of the ring opening process of bicyclic oxetanes is illustrated in Scheme 3.45. The first step is probably the protonation of the oxetane-oxygen atom followed by opening of the oxetane ring. Then attack of water to the carbenium ion, protonation of the nitrogen atom of the oxazole and the second ring opening follows. Thus, ring opening of the bicyclic oxetanes procceeded with retention of configuration to give the *erythro* (S*,S*) α-alkylated-α-acetamido-β-hydroxy esters **43aa-ff**.



Scheme 3.45: Proposed mechanism for the formation of *erythro* (S*,S*)-α-alkylated-α-acetamido-β-hydroxy esters **43aa-ff**.

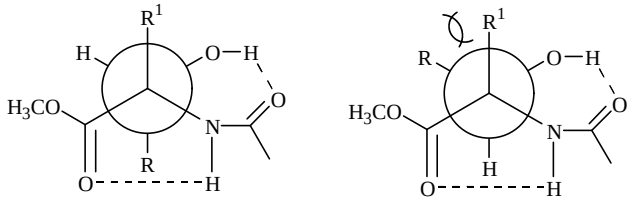
Structural assignment of the photoaldol adduct

The relative configurations of the compounds **43aa-ff** were assigned by using ^{13}C-NMR analysis and also by comparison with similar compounds in the literature.[122] In the ^{13}C-NMR spectra of these compounds, there is a striking difference between *erythro* and *threo* isomers. Both C-2 and C-3 resonate upfield in *erythro*-isomer in compared with the corresponding *threo*-isomer. This phenomena fits well with the results reported by Heathcock who used ^{13}C-NMR as a tool for the assignment of the configuration of β-hydroxy carbonyl compounds (Table 3.30).[123]

Table 3.30: Characterisitic ^{13}C-NMR signals (δ_{ppm}) of photoaldol products in ($CDCl_3$).

Compound	R =	R^1 =	*erythro*		*threo*	
			C-2	C-3	C-2	C-3
43af	Ph	*sec*-Bu	71.9	74.9	82.3	83.9
43ca	$BnCH_2$	Me	75.1	75.6	86.2	87.2
43dc	Et	n-Pr	70.1	78.0	86.1	88.7
43df	Et	*sec*-Bu	69.2	70.3	78.4	86.9
43ea	i-Pr	Me	68.3	71.0	83.3	90.0

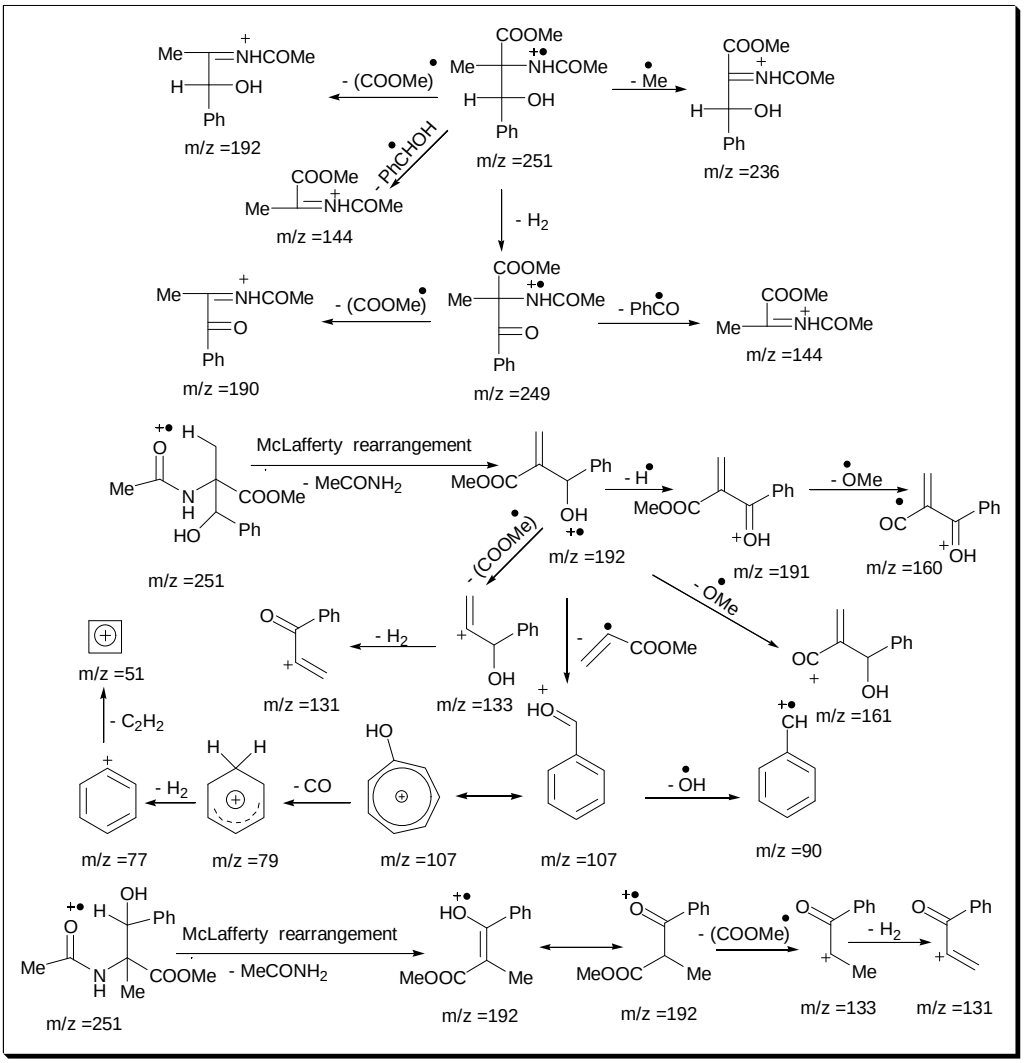
In order to account for the difference in the ^{13}C-NMR shifts in *erythro* and its epimers, I suggest the predominance of a conformation stabilized by an intramolecular hydrogen bond between the hydroxy and amide group (see X-ray structure of compound **43df**). Figure 3.93 shows that such an effect is clearly manifested in the *erythro* and *threo* pairs. However, in the *threo*-isomer, there is a *gauche* interaction between R & R^1 substituents which weakens the the hydrogen bond and might be also responsible for the deshielding effect of C-2 & C-3. If this assumption is true, one should also note the *anti* conformation between the R and R^1 in the *erythro*-isomer resulting in a higher field shift of C-2 and C-3 in comparsion with the *threo*-isomer. In fact, this was proven experimentally. Thus, the ^{13}C-NMR shifts of the C-2 & C-3 in the photoaldol adducts *erythro* & *threo* should unambiguously show correct trends and corroborated the proposed relative configurations.



erythro-isomer *threo*-isomer

Figure 3.93: Newman projection of the *erythro* & *threo*-isomers.

The constitutions of the products **43aa-ff** were established on the basis of IR, mass spectrum, NMR analyses and elemental analysis. For example, the IR spectrum of compound **43aa** displayed absorption bands at 3350, 3220, 1720 and 1680 cm^{-1} corresponding to OH, NH, COO and CON groups, respectively. Scheme 3.46 summarizes the fragmentation pattern of the mass spectrum of compound **43aa**.



Scheme 3.46: Fragmentation pattern of compound **43aa**.

In the ^{1}H-NMR spectrum, there are four singlets at δ 1.22, 2.14, 3.79 and 4.06 ppm attributed to CH_3, $\underline{CH_3}CO$, OCH_3 and $\underline{CH}OH$, respectively. The ^{13}C-NMR showed the disappearence of the orthoester signal and the formation of new signals at δ 47.6, 49.6, 169.9 and 179.4 ppm corresponding to C-2, C-3, CON and COO, respectively (Figure 3.94 & 3.95).

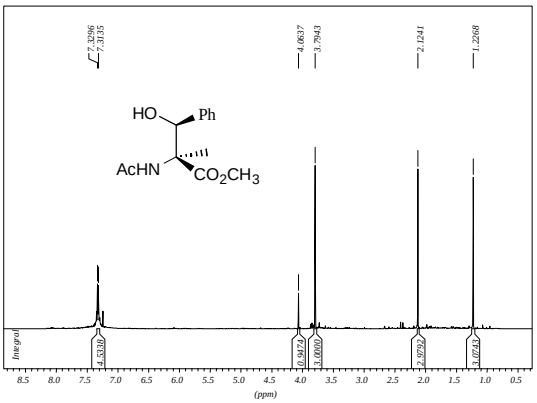


Figure 3.94: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **43aa**.

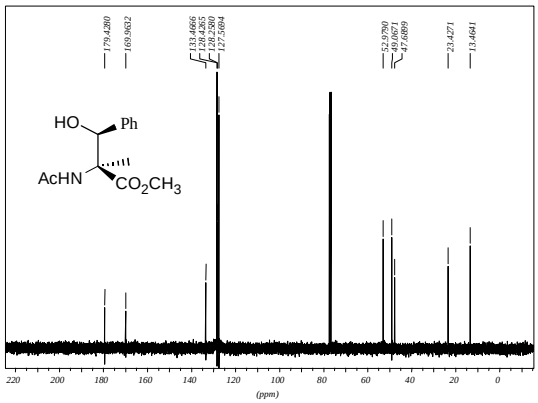


Figure 3.95: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **43aa**.

The IR spectrum of compound **43ca** showed two strong absorption bands at 1735 and 1690 cm^{-1} indicating the presence of ester and amide groups, respectively. In addition, there are two broad bands at 3420 and 3270 cm^{-1} attributed to OH and NH groups, respectively. The ^{1}H-NMR spectrum revealed three singlets at δ 1.35, 2.05, 3.76 ppm corresponding to CH_3, $\underline{CH_3}CO$, and OCH_3, respectively. The carbinol hydrogen absorbs at δ 4.68 ppm (dd, J = 11.2, 3.1Hz). The ^{13}C-NMR spectrum shows signals at δ 75.0, 89.9, 165.2 and 174.3 ppm corresponding to C-2, C-3, CON, and COO, respectively (Figure 3.96 & 3.97).

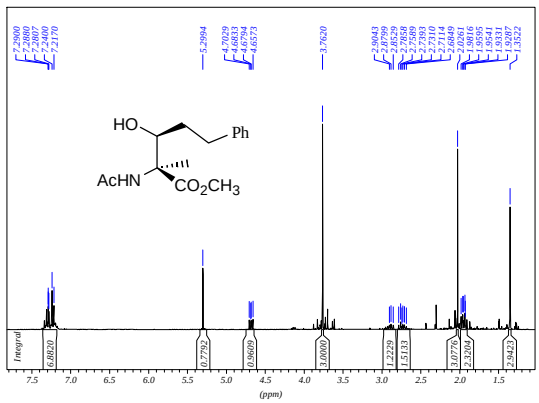


Figure 3.96: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **43ca**.

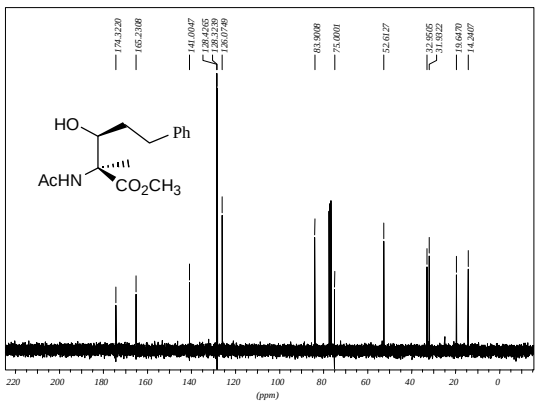
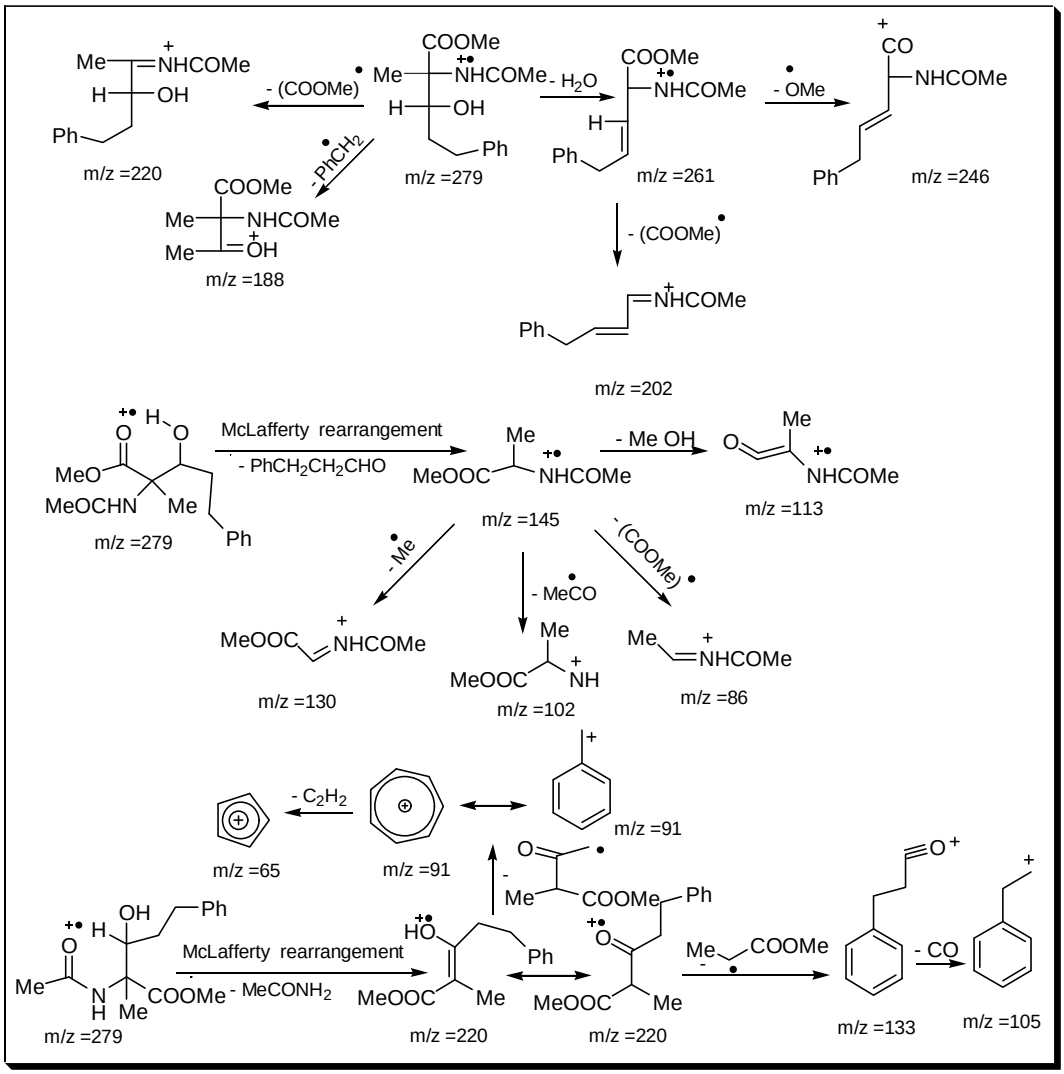


Figure 3.97: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **43ca**.

The mass spectrum showed the molecular ion peak at m/z 279 which strongly supports the structure of compound **43ca**. The fragmentation pattern are summarized in scheme 3.47.



Scheme 3.47: Fragmentation pattern of compound **43ca**.

The constitution of compound **43da** was confirmed by IR and NMR analyses. Analogous to the compounds mentioned above, there are four distinct absorption bands in the infrared spectrum at 3330, 3260, 1720 and 1685 cm^{-1} attributed to OH, NH, ester and amide groups, respectively. The ^{1}H-NMR spectrum revealed three singlets at δ 1.53, 1.95 and 3.71 ppm corresponding to CH_3, $\underline{CH_3}CO$ and OCH_3, respectively. In addition, there is a low-field signal at δ 4.14 ppm for the carbinol proton. In the ^{13}C-NMR spectrum, there are signals resonate at δ 63.5, 69.9, 169.3 and 171.6 ppm for C-2, C-3, CON, and COO, respectively (Figure 3.98 & 3.99).

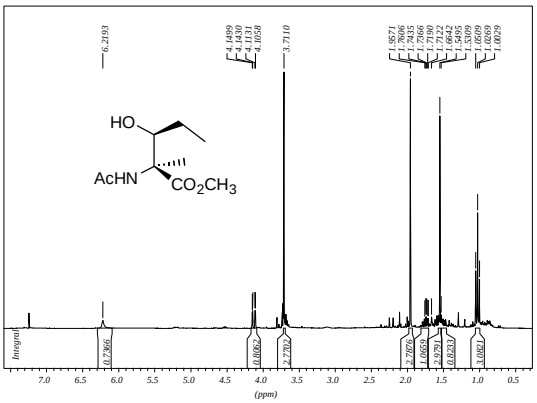


Figure 3.98: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **43da**.

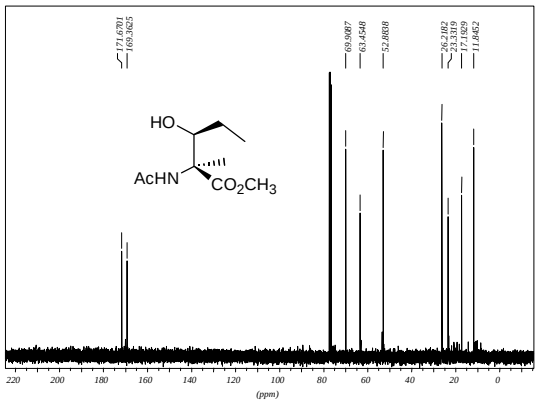


Figure 3.99: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **43da**.

It was possible to separate the two diastereoisomers of compound **43dc**, i.e. *erythro* (S*,S*) and *threo* (S*,R*) by chromatographic purification. The relative configurations of both diastereoisomers were established on the basis of NMR analyses:

There are two main differences in the ^{1}H-NMR spectra of *erythro*- and *threo*-isomer:

(a) both acetyl and methoxy groups in the *threo*-isomer absorb at δ 1.95 and 3.69 ppm, respectively, while in the *erythro*-isomer, this absorption is shifted downfield to 2.00 and 3.77 ppm; (b) the carbinol proton of the *erythro*-isomer resonates at a much higher field (δ = 4.24 ppm, dd, J = 11.6, 2.1 Hz) than in the *threo*-isomer which absorbs at δ 4.34 ppm, dd, J = 10.1, 3.5 Hz.

In the ^{13}C-NMR spectrum, there are also two main differences between the *erythro*- and *threo*-isomers: (a) in the *erythro*-isomer, both C-2 and C-3 resonate at higher field δ 69.1 and 70.3 ppm than in the *threo*-isomer which resonate at δ 78.4 and 86.9 ppm, respectively; (b) the carbonyl of amide and ester appears for the *erythro*-isomer at 169.4 and 172.3 ppm wheras at 165.1 and 174.5 ppm, respectively in the *threo*-isomer (see Figure 3.100, 3.101, 3.102 and 3.103).

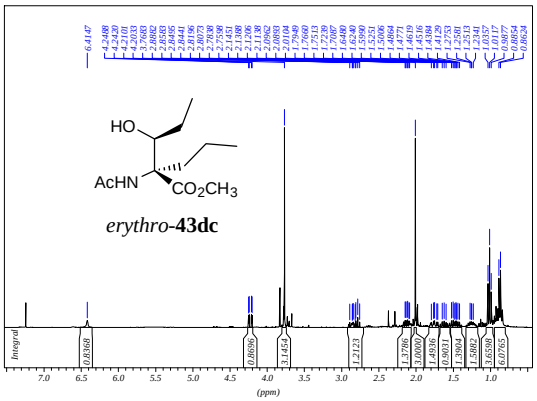


Figure 3.100: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of *erythro*-**43dc**.

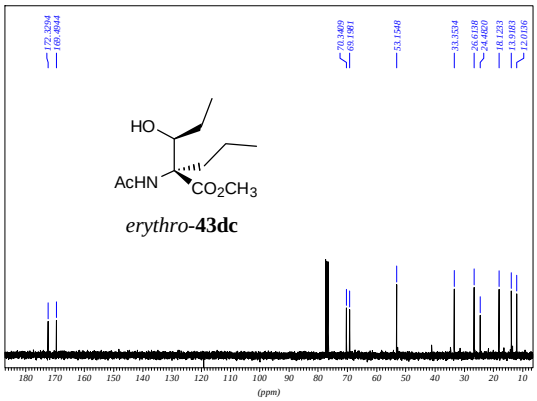


Figure 3.101: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of *erythro*-**43dc**.

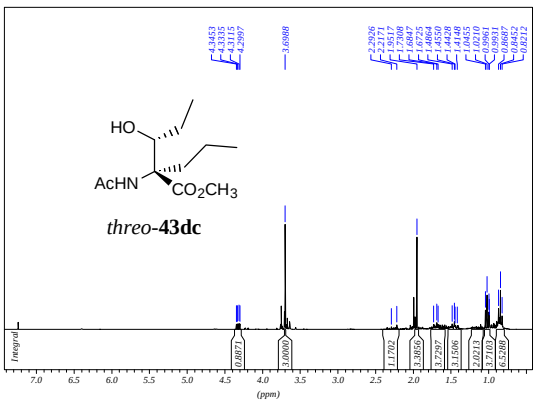


Figure 3.102: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of *threo*-**43dc**.

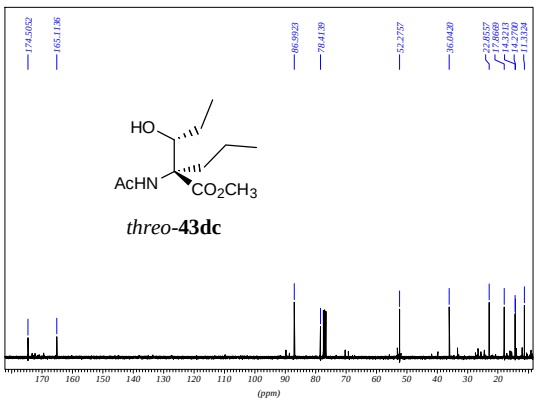
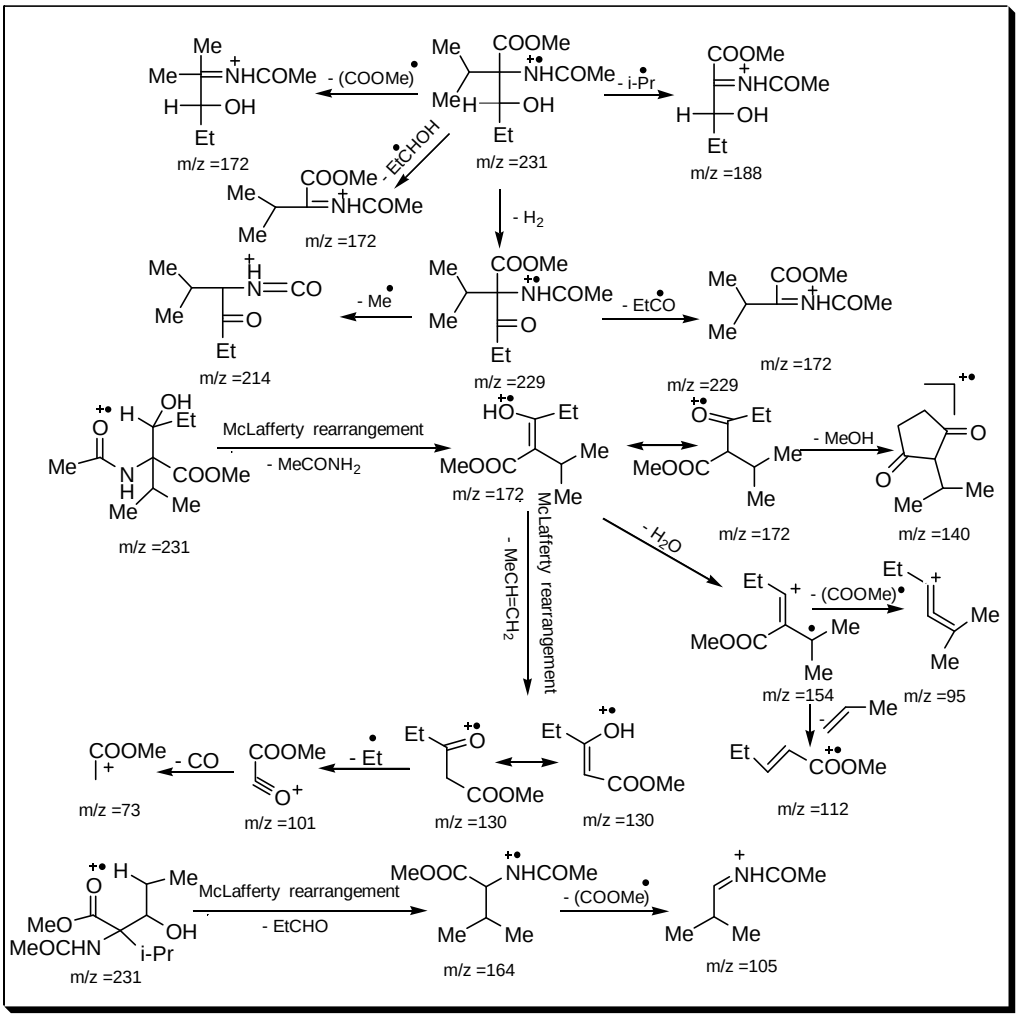


Figure 3.103: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of *threo*-**43dc**.

The constitution determination of the compound **43dd** was based on IR, mass spectrum and NMR analyses. The IR spectrum showed absorption bands characteristic for OH, NH, CON and COO at 3335, 3210, 1745 and 1675 cm^{-1}, respectively. The mass spectrum showed the base peak at m/z 130 due to the formation of methyl propioacetate. Scheme 3.48 illustrates the fragmentation pattern of compound **43dd**.



Scheme 3.48: Fragmentation pattern of compound **43dd**.

In the ^{1}H-NMR spectrum, there are two singlet signals at δ 4.04, 3.79 ppm indicating the presence of $\underline{CH_3}CO$ and OCH_3, respectively. In addition, at δ 4.52 and 6.45 ppm, there are two signals corresponding to $\underline{CH}OH$ and NH, respectively. The ^{13}C-NMR spectrum shows signals at δ 69.9, 73.5, 169.7 and 171.8 ppm attributed to C-2, C-3, CON, and COO, respectively.

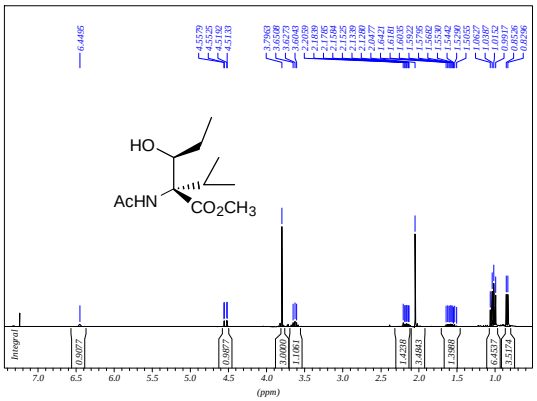


Figure 3.104: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **43dd**.

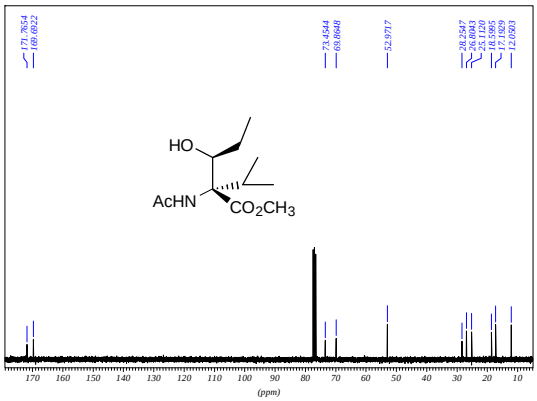


Figure 3.105: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **43dd**.

The constitution of compound **43de** was elucidated by ^{1}H-NMR and ^{13}C-NMR analyses. In the ^{13}C-NMR spectrum, both C-2 and C-3 resonate at lower field in compared with the spectra of the compounds mentioned above indicating the *threo*-configuration of compound **43de**. The ^{1}H-NMR spectrum shows two singlets at δ 3.70 and 1.96 ppm corresponding to OCH_3 and $\underline{CH_3}CO$, respectively. In addition, there appears a doublet of doublet signal at 4.22 ppm dd, J = 10.8, 3.5 Hz for the $\underline{CH}OH$.

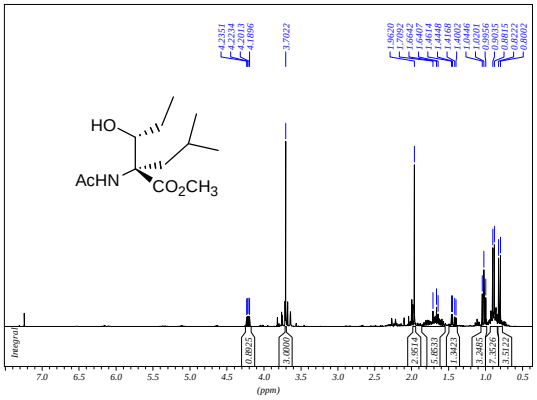


Figure 3.106: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of *threo*-**43de**.

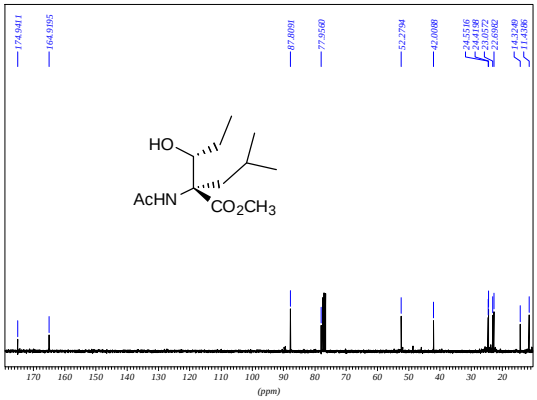


Figure 3.107: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of *threo*-**43de**.

Moreover, the CH-COSY correlation supported the chemical structure of compound **43de** as depicted in Figure 3.108.

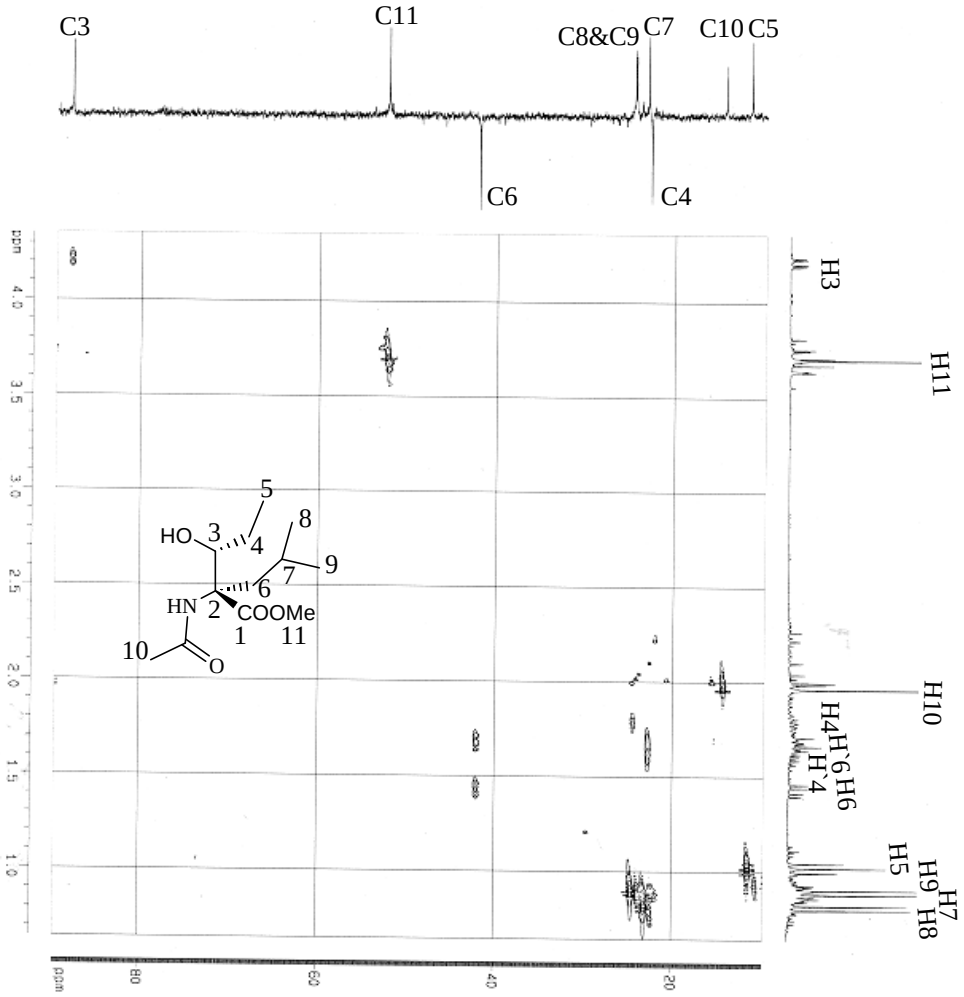


Figure 3.108: HMQC spectrum (300 MHz, $CDCl_3$) of *threo*-**43de**.

The constitution of compound **43fd** was established by IR and NMR analyses. The IR spectrum showed four strong absorption bands at 3452, 3310, 1725 and 1685 cm^{-1} corresponding to the OH, NH, COO and CON groups, respectively. The ^{1}H-NMR spectrum showed singlets at δ 2.04, 3.78 and 6.43 ppm attributed to $\underline{CH_3}CO$, OCH_3 and NH, respectively. The carbinol proton appears at δ 4.73 ppm with doublet of doublet multiplicity (dd, J = 11.2, 2.1 Hz). The ^{13}C-NMR spectrum showed signals at δ 65.9, 73.5, 169.6 and 171.8 pm corresponding to C-2, C-3, CON and COO, respectively. Figure 3.111 shows the HMQC spectrum which also confirmes the NMR assignments.

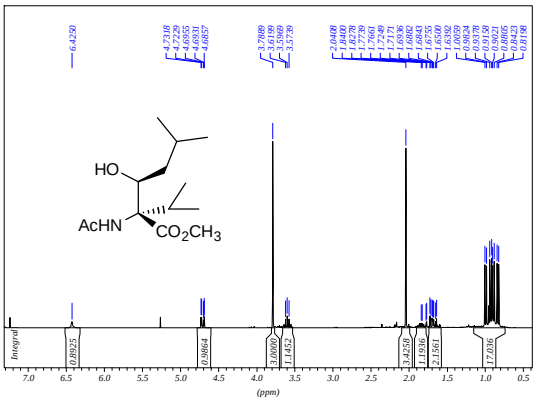


Figure 3.109: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **43fd**.

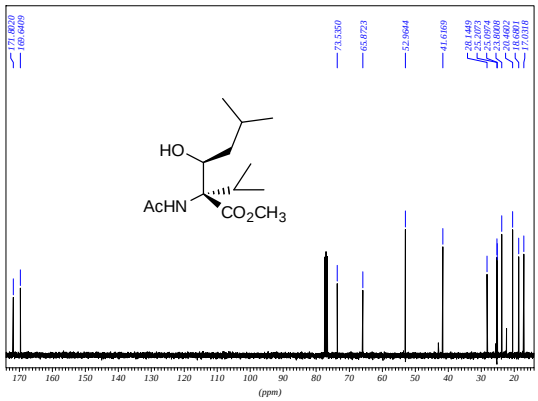


Figure 3.110: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **43fd**.

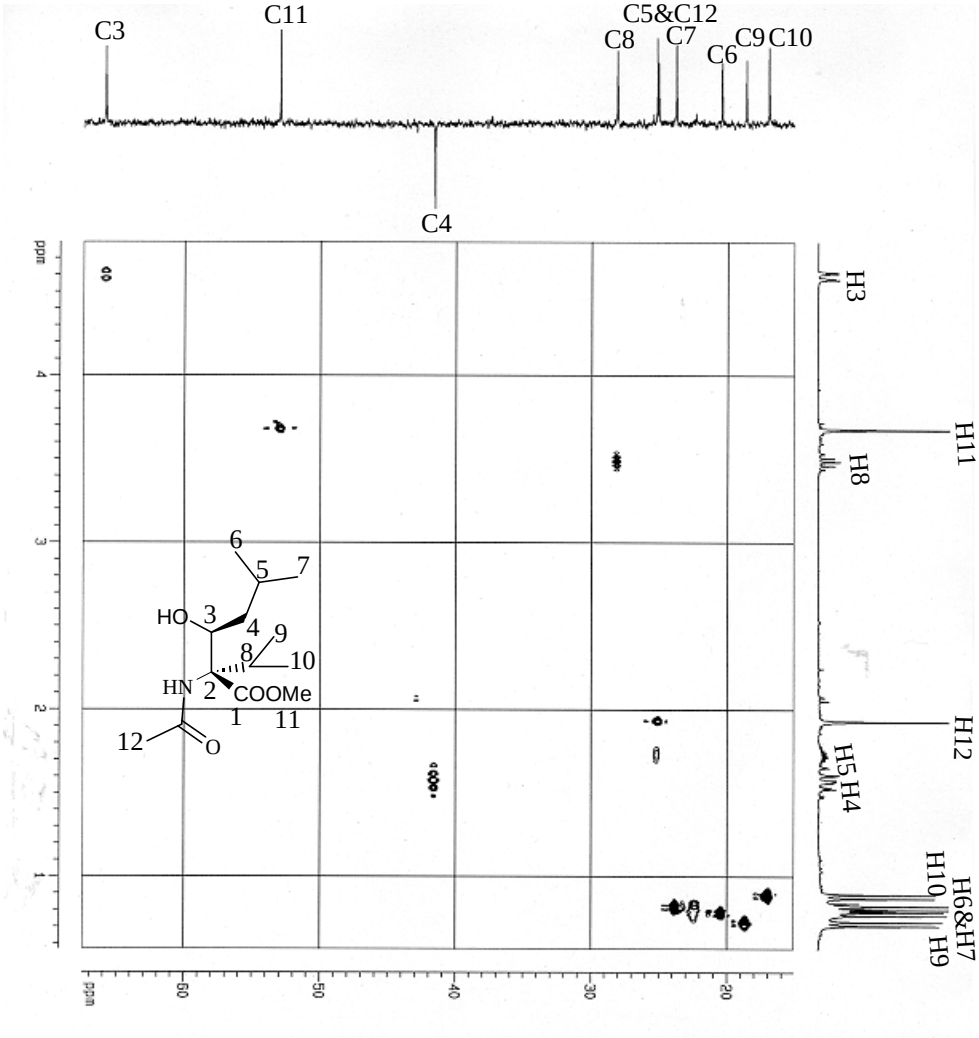


Figure 3.111: HMQC spectrum (300 MHz, $CDCl_3$) of **43fd**.

Analogous to compound **43de**, the relative configuration of compound **43ff** was assigned by using the down-field shift of both C-2 and C-3 as guide for the *threo*-isomer. The constitution

of compound *threo*-**43ff** was established on the basis of IR, mass spectrum and NMR analyses. The IR spectrum revealed bands at 3335, 3225, 1735 and 1680 cm^{-1} attributed to OH, NH, COO, CON groups, respectively. The mass spectrum showed the base peak at m/z 255 due to (M^+-H_2O). In the ^{1}H-NMR spectrum, there are signals at δ 4.40, 3.66 and 1.97 ppm corresponding to CHOH, OCH_3 and CH_3CO, respectively. The ^{13}C-NMR spectrum displayed signals at δ 82.7, 84.6, 165.8 and 174.8 ppm related to C-2, C-3, CON and COO, respectively. Figure 3.114 shows the HH-COSY spectrum of the off-digonal cross peak which correctly correlated the coupled protons.

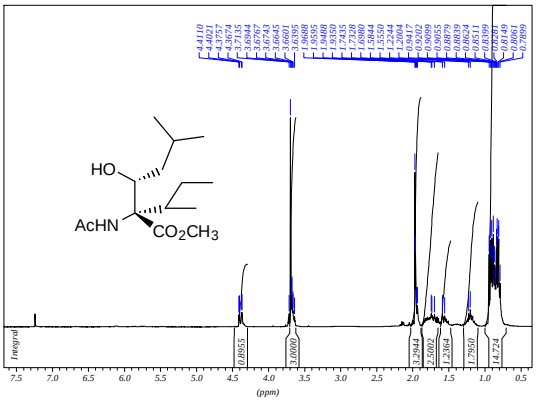


Figure 3.112: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of *threo*-**43ff**.

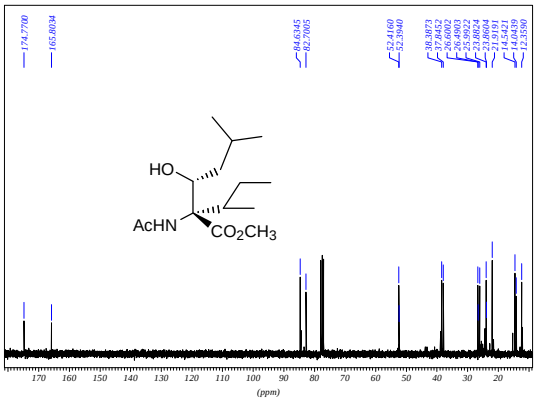


Figure 3.113: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of *threo*-**43ff**.

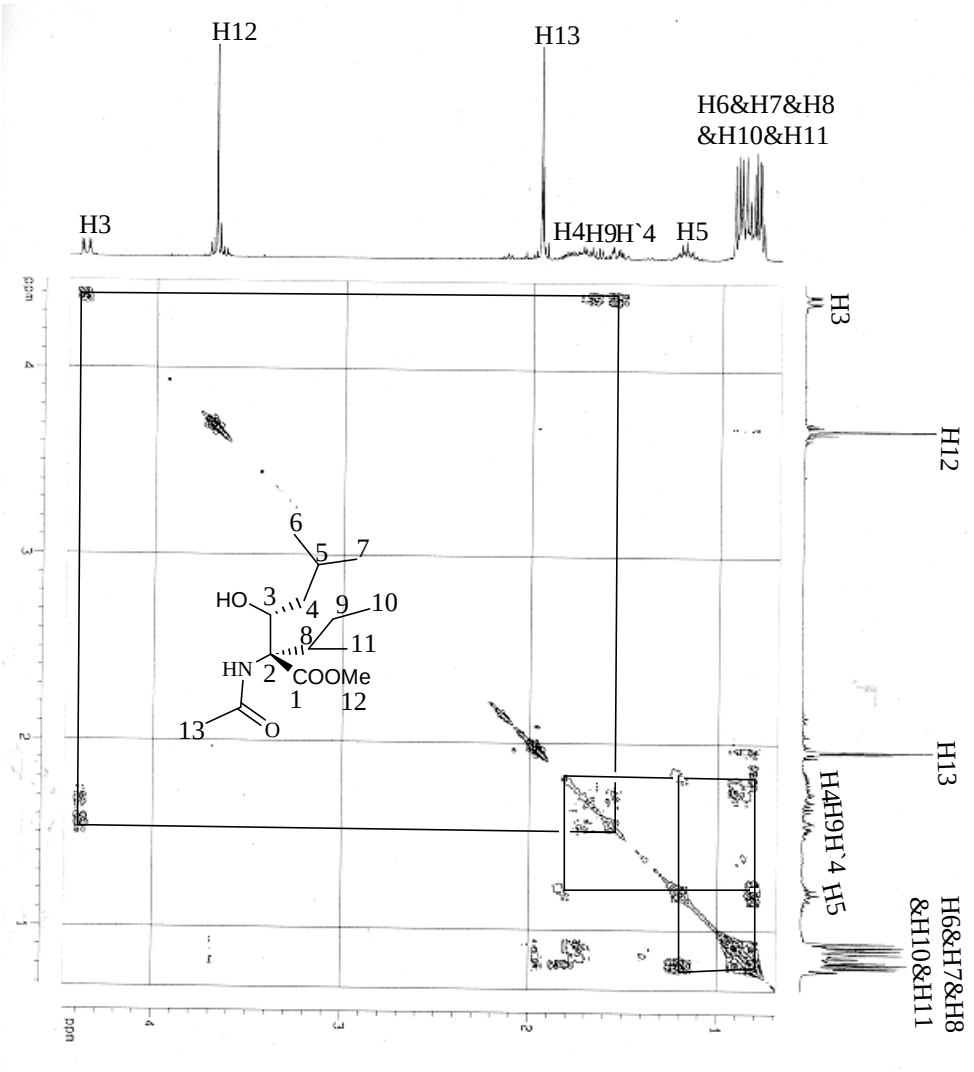
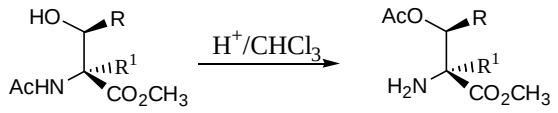


Figure 3.114: HH-COSY spectrum (300 MHz, $CDCl_3$) of *threo*-**43ff**.

3.7.3.2 Transacylation

In order to test the stability of the photoaldol adducts, compounds **43da**, **43dc** and **43fc** were stirred in $CHCl_3$ in the presence of catalytic amount of conc. HCl at r.t. for 24 h.



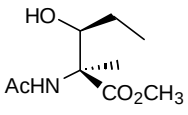
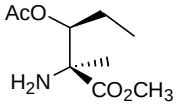
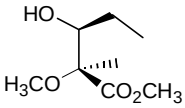
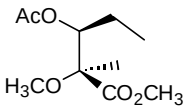
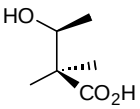
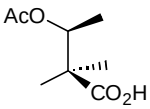
43da, 43dc & 43fc **44da, 44dc & 44fc**

Scheme 3.49: Transacylation.

Thin layer chromatograpy revealed a new spot in addition to the spot of starting material. The result of ^{1}H-NMR analysis indicated that there are a pair of each signals with only small differences in chemical shifts for each proton except for the signal of carbinol hydrogen. These signals were strongly different (about 1.0 ppm). The carbinol proton in the starting

material resonates at higher field than in the new compound. So, I assumed that this may be related to a migration of the acetyl group from amino to hydroxy (i.e transacylation). This assumption was supported by chemical shift comparsion of the carbinol hydrogen with similar compounds in literature (Table 3.31).[124,125]

Table 3.31: Comparison of carbinol ^{1}H-NMR signals of compounds **43da** & **44da** with similar known compounds in the literature.

						
	43da	**44da**	Lit.[124]	Lit.[124]	Lit.[125]	Lit.[125]
δ / ppm	4.15	5.25	3.60	5.12	4.01	5.29

The constitution of compounds **44da**, **44dc** and **44fc** were confirmed by NMR analyses. For example, the ^{1}H-NMR spectrum of compound **44da** showed a signal at δ 5.25 ppm related to CHOAc. In the ^{13}C-NMR spectrum, C-3 resonates at lower field δ 75.1 in comparsion with that in **43da** (Figure 3.115 & 3.116).

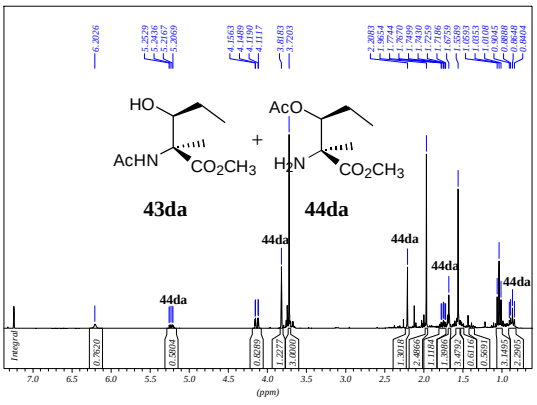


Figure 3.115: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compounds **43da & 44 da**.

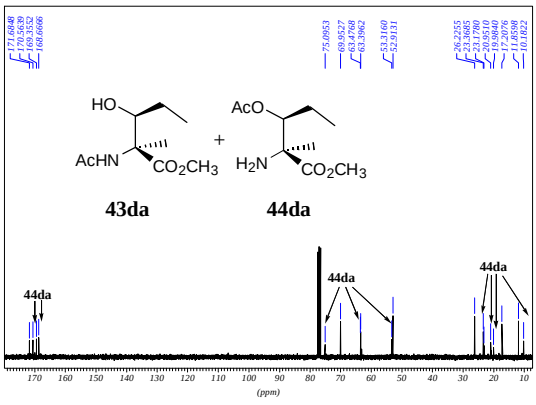
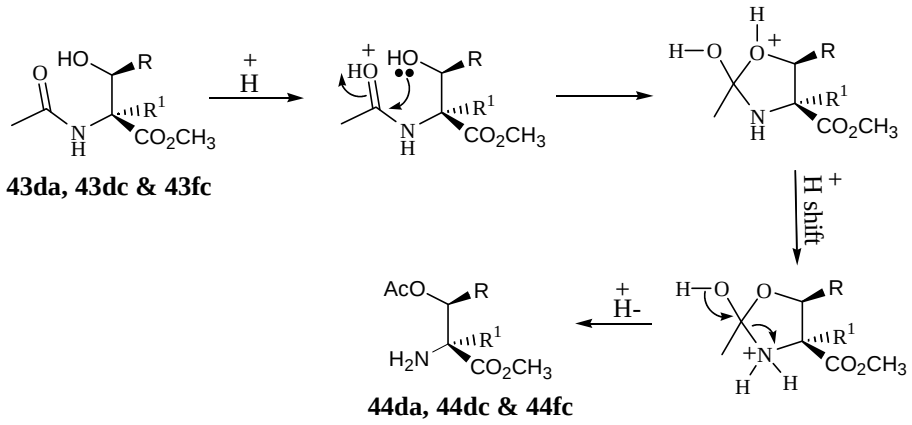


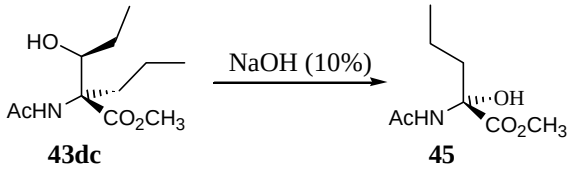
Figure 3.116: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of compounds **43da & 44 da**.

Scheme 3.50 illustrates the suggested mechanism for transacylation *via* formation of an oxazolidine ring intermediate.



Scheme 3.50: Proposed mechanism for transacylation.

In contrast to the result with the photoaldol adducts in acidic medium, treatment of compound **43dc** with aqueous NaOH (10%) led to a cleavage process with the formation of compound **45**. The formation of this product was rather unexpected and may be probably formed *via* nucleophilic substitution by hydroxyl group.



Scheme 3.51: " Retro-aldol" reaction of compound **43dc**.

The structure determination of compound **45** was based on spectroscopic analysis, elemental analysis and X-ray analysis. The IR spectrum showed strong absorption bands at 3400, 3250, 1730 & 1685 cm^{-1} corresponding to OH, NH, COO & CON groups, respectively. The ^{1}H-NMR spectrum showed the disappearence of the carbinol signal at 4.12 ppm. In the ^{13}C-NMR spectrum, there is a new signal at 82.5 ppm related to a quaternary carbon attached to n-Pr, CON &COO groups.

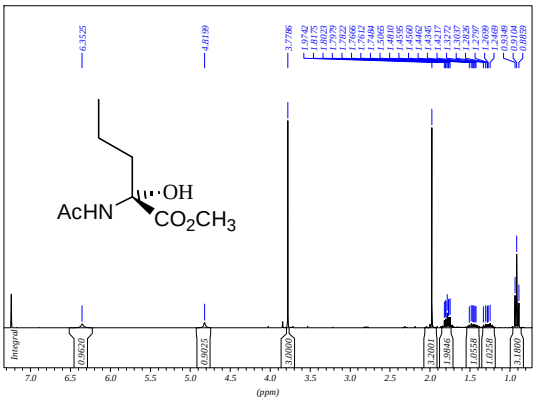


Figure 3.117: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **45**.

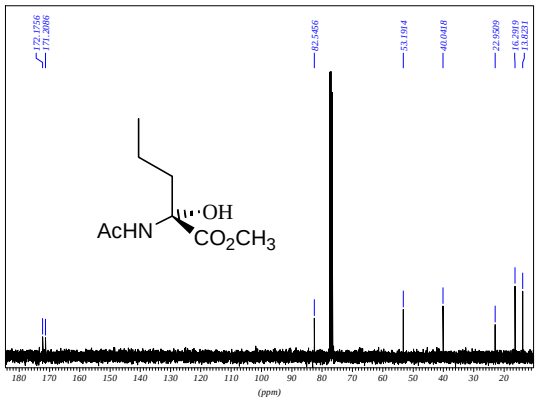


Figure 3.118: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **45**.

Moreover, the elemental analysis confirmed the molecular formular $C_8H_{15}NO_4$ of the compound **45**. The structure determined by single crystal X-ray analysis of compound **45** is shown in Figure 3.119.

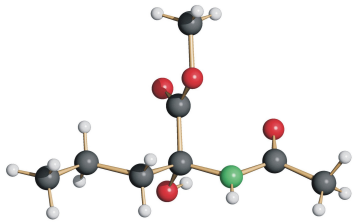
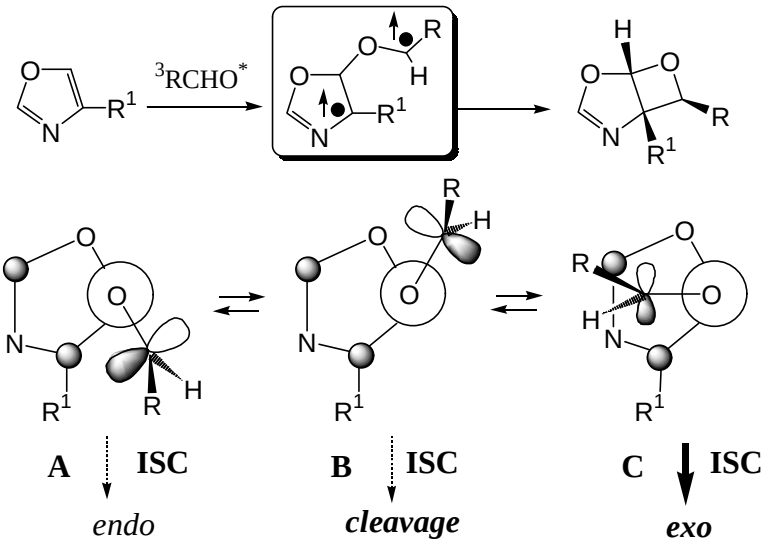


Figure 3.119: X-ray analysis of compound **45**.

Mechanistic analysis

The regioselectivity of the Paternò-Büchi reaction of aldehydes with oxazoles is high (>99 : 1) and corresponds to the classical biradical stablization concept. Wheras the high *exo*-selectivity of the photocycloaddition of electronically excited aldehydes to the C-4 unsubstituted oxazole **32** is analogous to the furan case, the high diastereoselectivity for the trisubstituted oxazoles **36a-f** deserves further explanation. In the triplet photocycloaddition reaction to cycloalkenes,[37] ring alkylation leads to a decrease in selectivity and in some case even to selectivity inversion due to the interference with the spin-orbit coupling geometries.[51] This is obviously not the case for the oxazoles **36a-f** which indicates that the secondary orbital interaction model originally applied for the benzaldehyde-furan reaction is operating.[42] Scheme 3.52 shows the triplet 1,4-biradical conformers **A-C** with reactive spin-orbit coupling geometries.[32] If most of the spin inversion process is directed through the channel **C**, high

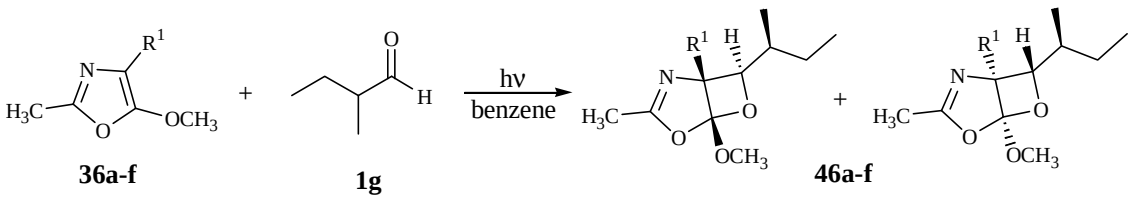
exo-selectivity is expected. The *endo*-contribution from **A** becomes only relevant for bulky groups R and R^1 (as for **42ad-42af**).



Scheme 3.52: Mechanistic scenario for oxazole-carbonyl photocycloaddition.

3.7.4 Asymmetric photocycloaddition between oxazoles and chiral aldehyde

The oxazole-carbonyl photocycloaddition reaction provides a method for the addition of an enolate equivalent (oxazole) to an aldehyde which allows access to *erythro*-aldol products as described above. In the light of the above results photochemical asymmetric synthesis of oxazoles appeared interesting and worth of study. Thus, the photocycloaddition of 4-substituted 2-methyl-5-methoxyoxazoles **36a-f** with 2-methylbutyraldehyde as a chiral carbonyl component was investigated. Irradiation of 2-methylbutyraldehyde in benzene in the presence of oxazole substrates **36a-f** afforded a 1.12 : 1 mixture of the diastereomeric products with high *exo*-selective (> 99 : 1) and in good yields.



36a-f **1g** **46a-f**

Scheme 3.53: Photocycloaddition reaction of 2-methylbutyraldehyde with **36a-f**.

The results in Table 3.32 show that the facial selectivity decreased with increasing size of substituent on the oxazole ring. The high *exo*-selective (relative face selectivity) in combination with the poor diastereotopic face selectivity with regard to the chiral aldehyde was expected on the basis of the results from previous studies.

Table 3.32: Diastereoselectivity of the photocycloaddition of **1g** with **36a-f**.

Compound	R^1 =	d.r.[a]	Yield (%)
46a	Me	63 : 37	75
46b	Et	56 : 44	80
46c	n-Pr	55 : 45	65
46d	i-Pr	47 : 53	84
46e	i-Bu	50 : 50	76
46f	*sec*-Bu	40 : 60	79

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] yield (%) based on converted oxazole.

The stereochemical assignments of the bicyclic oxetanes **46a-f** were based on the configuration of their hydrolysis products, i.e. the aldol type adducts **47a-f** which were easily formed due to the instabilty of the bicyclic oxetanes **46a-f** under the isolation conditions. The constitution of the photoadducts were elucidated by NMR analyses. For example, in the ^{1}H-NMR spectrum of compound **46a** (R^1 = Me), three singlets at δ 3.79, 1.98 and 1.24 ppm appeared corresponding to OCH_3, CH_3 at position C-3 and CH_3 at position C-1, respectively, whereas these signals in the corresponding diastereoisomer (both *exo*-isomers) resonate at δ 3.65, 2.23 and 1.26 ppm. The ^{13}C-NMR spectrum showed one signal at δ 124.1 ppm indicating the presence of the orthoester carbon. At this point, the relative configuration of both diastereoisomer is unknown.

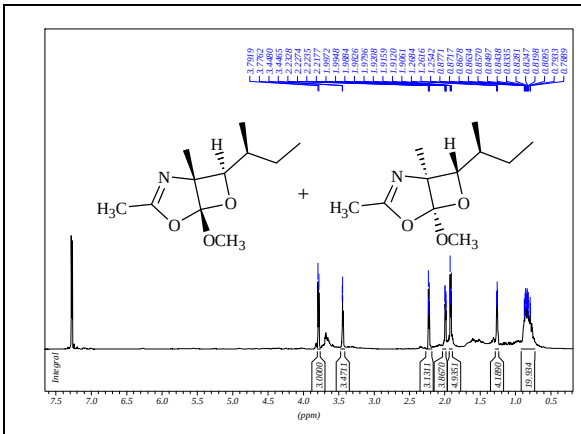


Figure 3.120: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **46a**.

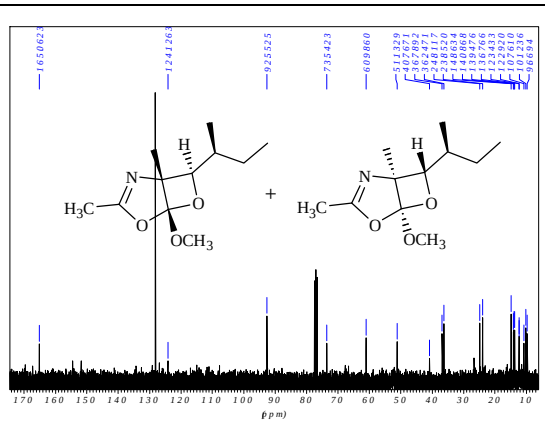
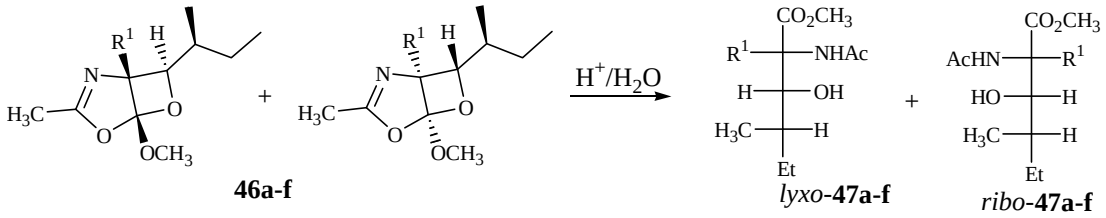


Figure 3.121: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **46a**.

3.7.4.1 Synthesis of *lyxo*-& *ribo*- a-acetamido-b-hydroxy esters

The bicyclic oxetanes **46a-f** possesses an inherent potential as precursors to *lyxo*-& *ribo*- α-acetamido-β-hydroxy esters. Acid treatment of the bicyclic oxetanes **46a-f** afforded a mixture of two diastereoisomers which could not be separated by preparative thick layer chromatograpy.



Scheme 3.54: Ring opening of bicyclic oxetanes **46a-f**.

Table 3.33: Diastereomeric ratio of the photo aldol adducts **47a-f**.

Compound	R^1 =	d.r. (*lyxo* : *ribo*)[a]	Yield (%)[b]
47a	Me	62 : 37	75
47b	Et	56 : 44	80
47c	n-Pr	55 : 45	73
47d	i-Pr	47 : 53	69
47e	i-Bu	49 : 51	80
47f	*sec*-Bu	38 : 62	74

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the product mixture, [b] yield (%) of the crude mixture of diastereoisomers.

The results for the photo aldol adducts are summarized in Table 3.33. The diastereomeric ratio of the ring-opened products matched the diasteremeric excessess of the precursor oxetanes. From the previous studies, the relative configuration of C-2 and C-3 was anticipated to be *erythro*- (S^*,S^*), since the precursor bicyclic oxetanes have *exo*-configurations. The relative configuration of C-3 and C-4 of the products **47a-f** was determined on the basis of ^{1}H-NMR coupling constants between the hydrogens on C-3 and C-4 in each diastereoisomer following Karplus[126] curve analysis. According to Karplus correlation, the coupling constant of two *trans* vicinal protons (having a dihedral angle of about $\phi = 180°$) is expected to be in the range of 9-12 Hz. The coupling constant of the two protons of C-3 and C-4 in the major diastereoisomer was found to be $^3J = 9.1$ Hz which is consistent with the *trans* configuration and assignable to *xylo*-isomer (R*,R*,S*) wheras the minor diastereoisomer had $^3J = 6.1$ Hz which established the *ribo*-configuration (S*,S*,S*).

The constitutions of compounds **47a-f** were determined on the basis of IR, NMR analyses.

For example, the IR spectrum of compound **47c** showed absorption bands at 3455, 3330, 1720 and 1685 cm^{-1} attributed to OH, NH, COO and CON groups, respectively. The ^{1}H-NMR spectrum showed two doublets, one at δ 4.2 ppm (d, J = 9.1 Hz) assigned to the *xylo*-isomer and the second at δ 4.33 ppm (d, J = 6.9 Hz), attributed to the *ribo*-isomer. In the ^{13}C-NMR spectrum, there are signals at δ 78.6, 89.8, 165.1 and 174.7 ppm corresponding to C-2, C-3, CON and COO, respectively.

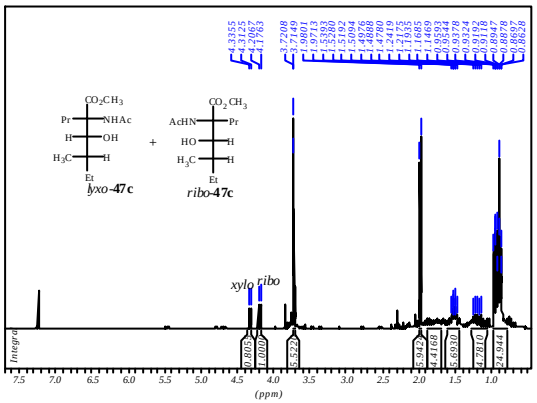


Figure 3.122: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **47c**.

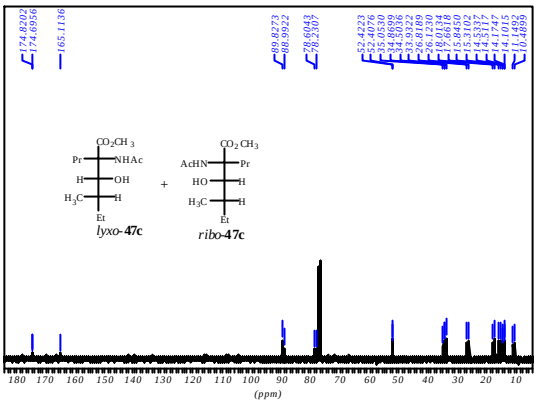


Figure 3.123: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **47c**.

In the ^{1}H-NMR spectrum of compound **47f**, there are two downfield signals at δ 4.42 ppm, (d, J = 6.9 Hz, 1H) and δ 4.16 ppm, (d, J = 9.2 Hz, 1H) attributed to the carbinol protons of *ribo*- and *xylo*-isomers, respectively. The ^{13}C-NMR spectrum showed signals at δ 82.4, 88.9, 174.4 and 179.8 ppm corresponding to C-2, C-3, CON and COO, respectively.

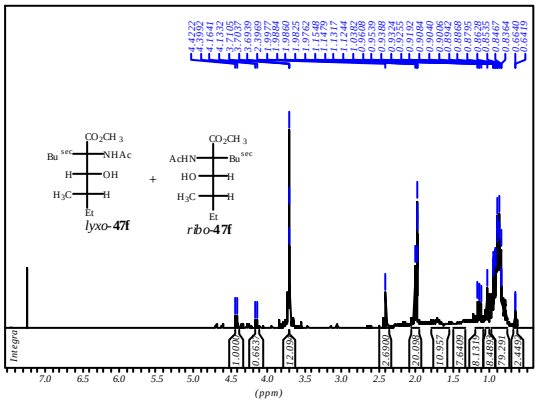


Figure 3.124: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **47f**.

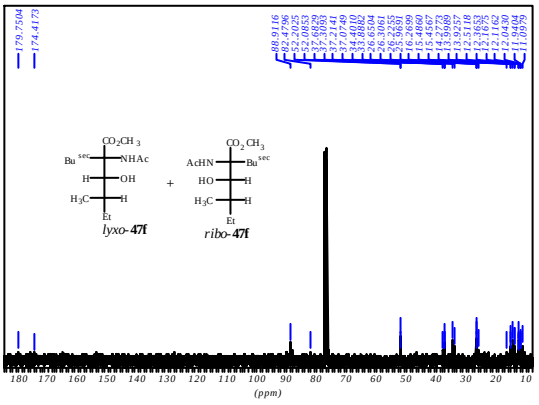
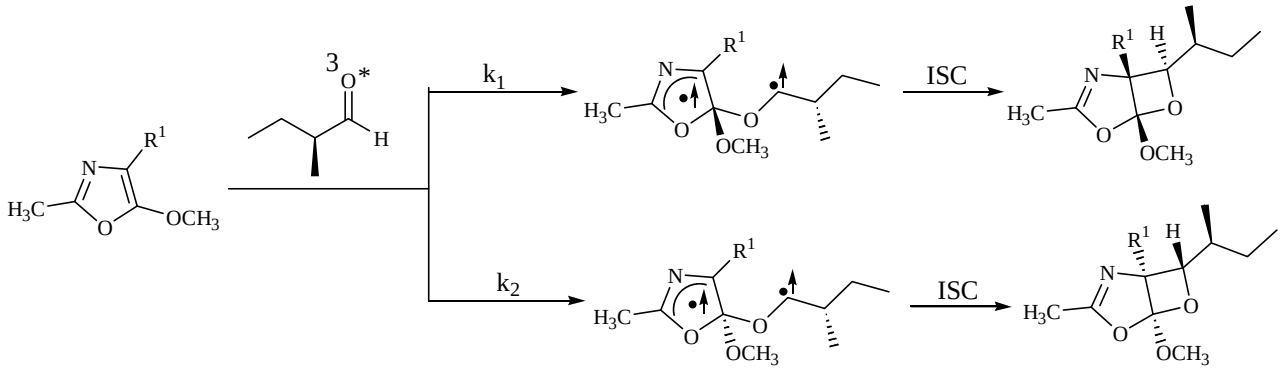


Figure 3.125: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **47f**.

Mechanistic analysis

The lack of facial selectivity in the addition of oxazoles to the excited state of a chiral aldehyde is in contrast to the normal aldol reaction.[127] This feature of the photoreaction suggests a mechanism that is insensitive to the substitution pattern on the chiral aldehyde. One such mechanism is depicted in Scheme 3.53.



Scheme 3.53: Mechanism of the photoaddition of a chiral aldehyde to oxazoles.

The reaction between an triplet excited aldehyde and the oxazole procceds with initial carbon-oxygen bond formation to produce the two biradical species shown above. The k_1/k_2 -ratio represents the amount of induced diastereoselectivity. The asymmetric induction comes from the difference in the distance between the stereocenter of incoming aldehyde and C-5 of oxazole substrates. The top attack (k_1) is slightly favor than the bottom attack (k_2).

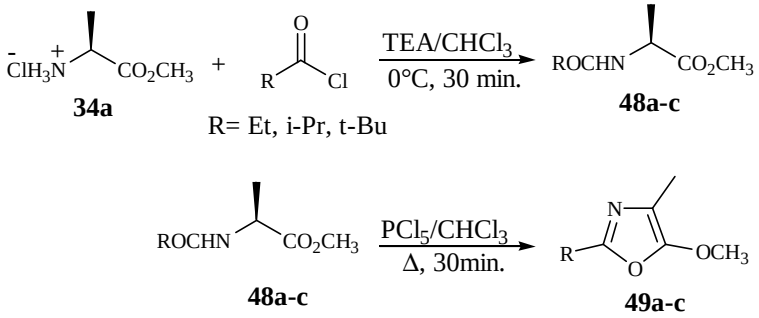
A stereogenic center adjacent to the carbonyl is now in a 1,4-relationship to the newly formed stereogenic center at the acetal carbon and is expected to exert little influence as a stereocontrol device. Two stereogenic centers are present in these intermediates, but the stereogenic center at the acetal carbon is expected to completely dictate the stereochemical outcome of the biradical bond formation. In each case ring closure will produce a *cis* ring fusion with an *exo*-substituted side chain, as in the reaction of achiral aldehydes. The stereogenic center on the side chain is unrelated to the outcome of biradical closure and has minimal influence, stereochemicaly, on the initial acetal formation.

3.8 Photo-Aldol reactions of 5-methoxyoxazoles with a-keto esters: Selectivity pattern and synthetic route to *erythro* (S*,R*) & *threo* (S*,S*) a-amino-b-hydroxy succinic acid derivatives

Photochemical cycloaddition between oxazoles and aldehydes affords, with remarkably high regio- and stereoselectivity, 7-*exo* substituted derivatives of 2-aza-4,6-dioxa-bicyclo[3.2.0] hept-2-enes. Exploring the utility of these highly functionalized compounds for the synthesis of amino acids derivatives seems attractive. The photocycloaddition of oxazoles to α-keto esters appeared to me interesting, not only for mechanistic studies but also from a synthetic point of view, where the photoadducts represent bulding blocks for the synthesis of β-hydroxy aspartic acid derivatives which are known as naturally occuring amino acids.[128]

3.8.1 Synthesis of 2-substituted 4-methyl-5-methoxyoxazoles

Treatment of L-alanine methyl ester hydrochloride with different acid chlorides (propionyl chloride, isobutyrolyl chloride and pivaloyl chloride) in the presence of TEA afforded the amides which cyclized to 2-substitued 4-methyl-5-methoxyoxazoles **49a-c** when heated with PCl_5.[129]



Scheme 3.54: Synthesis of 2-substituted 4-methyl-5-methoxy oxazoles **49a-c**.

Table 3.34: Characteristic properties of 2-substituted 4-methyl-5-methoxy oxazoles **49a-c**.

Compound	R =	^{1}H-NMR[a]	^{13}C-NMR[b]	B.p$_{10\ torr}$ (°C)	Yield (%)
49a	Et	3.78	156.1	80-83	75
49b	i-Pr	3.78	159.2	94-97	80
49c	t-Bu	3.79	161.2	100-102	78

[a] chemical shift of OCH_3 in ppm, [b] chemical shift of C-2 in ppm.

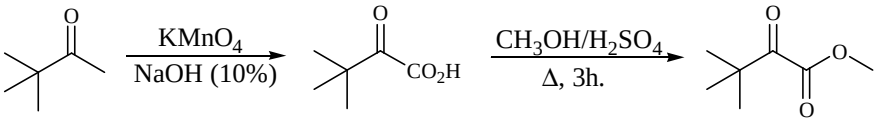
The chemical structures of the compounds **49a-c** were established on the basis of spectroscopic data (UV, IR, ^{1}H-NMR, ^{13}C-NMR) and elemental analyses. The UV spectra of the 2-substitued 4-methyl-5-methoxy oxazoles **49a-c** exhibit one major band of strong

intensity at 245-270 nm. The IR spectra showed strong bands at 1555-1598 cm^{-1} assigned to the –N=C-O ring stretching frequency. The ^{13}C-NMR spectra showed that alkyl substitution at C-2 deshield C-2 in the order t-Bu > i-Pr > Et as depicted in Table 3.34.

3.8.2 Synthesis of a-keto ester substrates

3.8.2.1 Synthesis of methyl trimethylpyruvate

Methyl trimethylpyruvate was prepared from the commercially available methyl *tert*-butyl ketone *via* oxidation with $KMnO_4$ in the presence of sodium hydroxide to give the α-keto acid followed by refluxing with methanol in the presence of conc. H_2SO_4.[130]

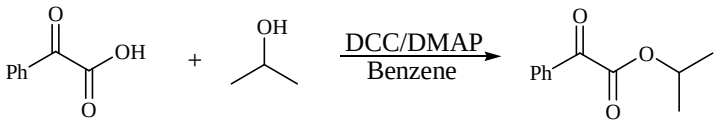


50

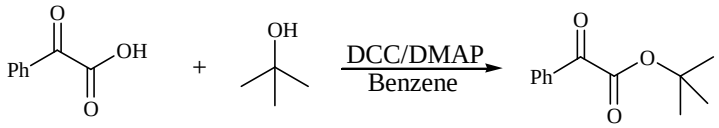
Scheme 3.55: Synthesis of methyl trimethylpyuvate.

3.8.2.2 Synthesis of isopropyl & *tert*-butyl phenylglyoxylates

Both isopropyl and *tert*-butyl phenylglyoxylates were prepared following a procedure described by Neckers[131] from the reaction of phenyl glyoxylic acid with isopropyl alcohol as well as *tert*-butyl alcohol in presence of DCC/DMAP as coupling reagent. The products were isolated as colorless oils after column chromatography.



51

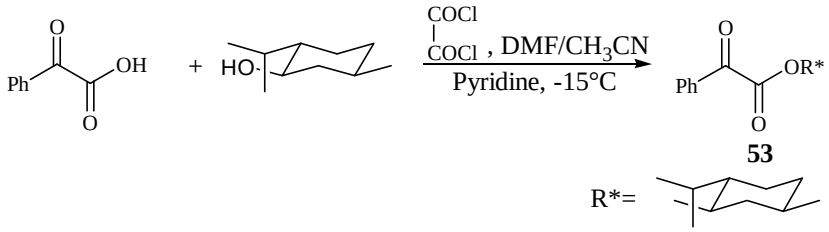


52

Scheme 3.56: Synthesis of isopropyl and *tert*-butyl phenylglyoxylates.

3.8.2.3 Synthesis of (-)-menthyl phenylglyoxylate

Treatment of phenyl glyoxylic acid with (-)-menthol at -15°C in the presence of coupling reagents (oxalyl chloride, DMF/CH_3CN) following the Stadler procedure afforded the (-)-menthyl phenylglyoxylate **53** in high yields.[132]



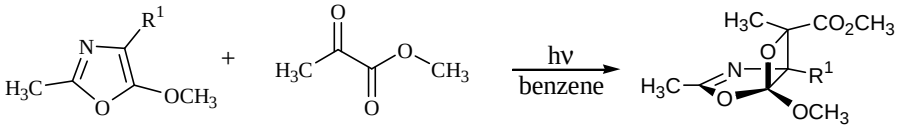
Scheme 3.57: Synthesis of (-)-menthyl phenylglyoxylate **53**.

The structure of the menthyl phenylglyoxylate **53** was confirmed on the basis of the spectroscopic analysis (UV, IR, ^{1}H-NMR, ^{13}C-NMR) and elemental analysis. The UV spectrum showed two absorption bands, one with low intensity at 353 nm and the other with high intensity at 300 nm. The IR spectrum showed two strong signals at 1735 and 1680 cm^{-1} indicating the presence of two carbonyl groups (C=O & OC=O), respectively.

3.8.3 Photocycloaddition reactions of aliphatic a-keto esters with oxazoles 36a-f

3.8.3.1 Reaction with methyl pyruvate

Photolysis of methyl pyruvate with oxazole substrates **36a-f** in benzene using a Rayonet photoreactor (λ = 350 nm) at 10 °C afforded the bicyclic oxetanes **55a-f** with high regio- and stereoselectivity in good yields.



36a-f **54** **55a-f**

Scheme 3.58: Photoreaction of methyl pyruvate with oxazoles **36a-f**.

Table 3.35: Results of the photocycloaddition of methyl pyruvate to oxazole substrates **36a-f**.

Compound	R^1 =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
55a	Me	>98 : 2	85
55b	Et	>98 : 2	87
55c	n-Pr	>98 : 2	90
55d	i-Pr	>98 : 2	92
55e	i-Bu	>98 : 2	84
55f	*sec*-Bu	>98 : 2	88

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] based on the degree of conversion of the oxazole.

The relative configuration of the bicyclic oxetane **55a** was unambiguously determined from NOE effects which were detected for the CH_3 group at C-3 by saturation of both methyl hydrogens at C-7 and the methoxy hydrogens at C-5.

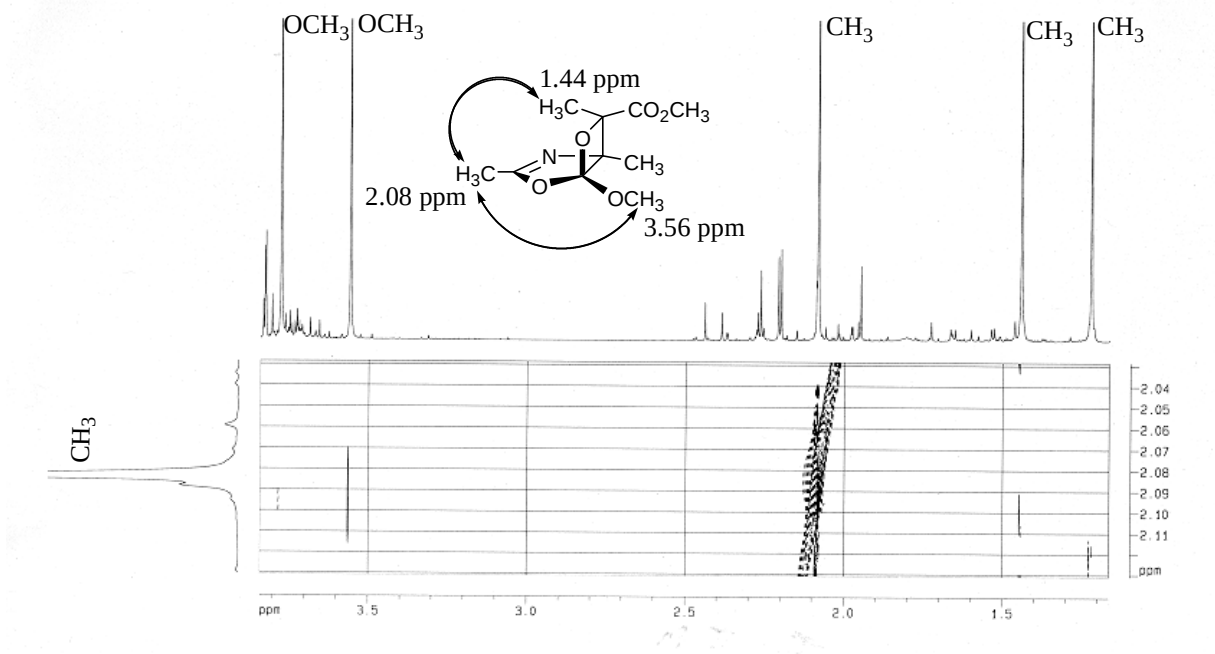


Figure 3.126: NOESY spectrum (300 MHz, $CDCl_3$) of compound **55a**.

The formation of acid-labile bicyclic oxetanes were proven by the characteristic ^{13}C-NMR signals of the orthoester at δ ca. 124.0 ppm. The structure determination of the photoadducts **55a-f** were based on IR, mass spectra and NMR analyses. For example, the IR spectrum of compound **55a** showed absorption bands at 1735 and 1610 cm^{-1} attributed to COO, C=N groups, respectively. The ^{1}H-NMR spectrum showed five singlets at δ 1.22, 1.44, 2.08, 3.56 and 3.78 ppm corresponding to CH_3 at C-1, CH_3 at C-7, CH_3 at C-3, OCH_3 at C-5 and OCH_3 of the ester group, respectively. In the ^{13}C-NMR spectrum, the signals of the oxetane ring resonate at δ 76.0, 88.7 and 123.9 ppm due to C-7, C-1 and C-5, respectively. Additionally, there appeared two signals at low field δ 166.2 and 171.5 ppm attributed to C-3 and the COO group.

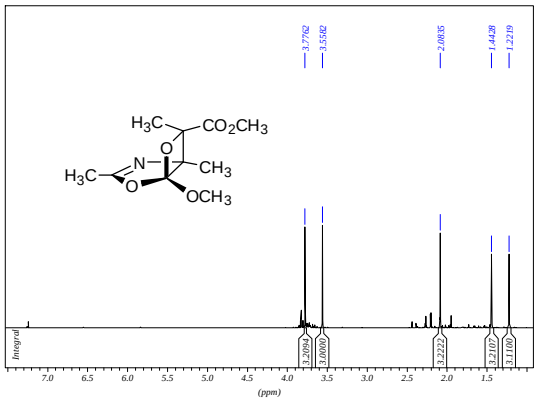


Figure 3.127: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **55a**.

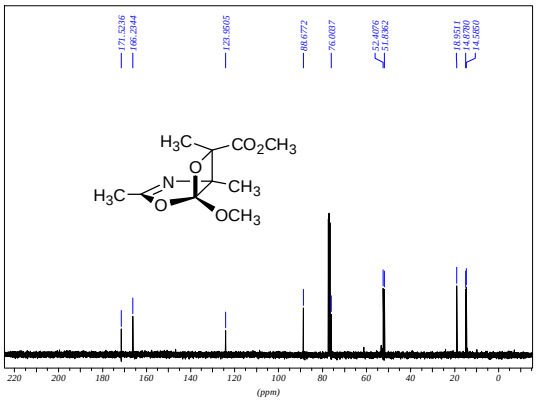
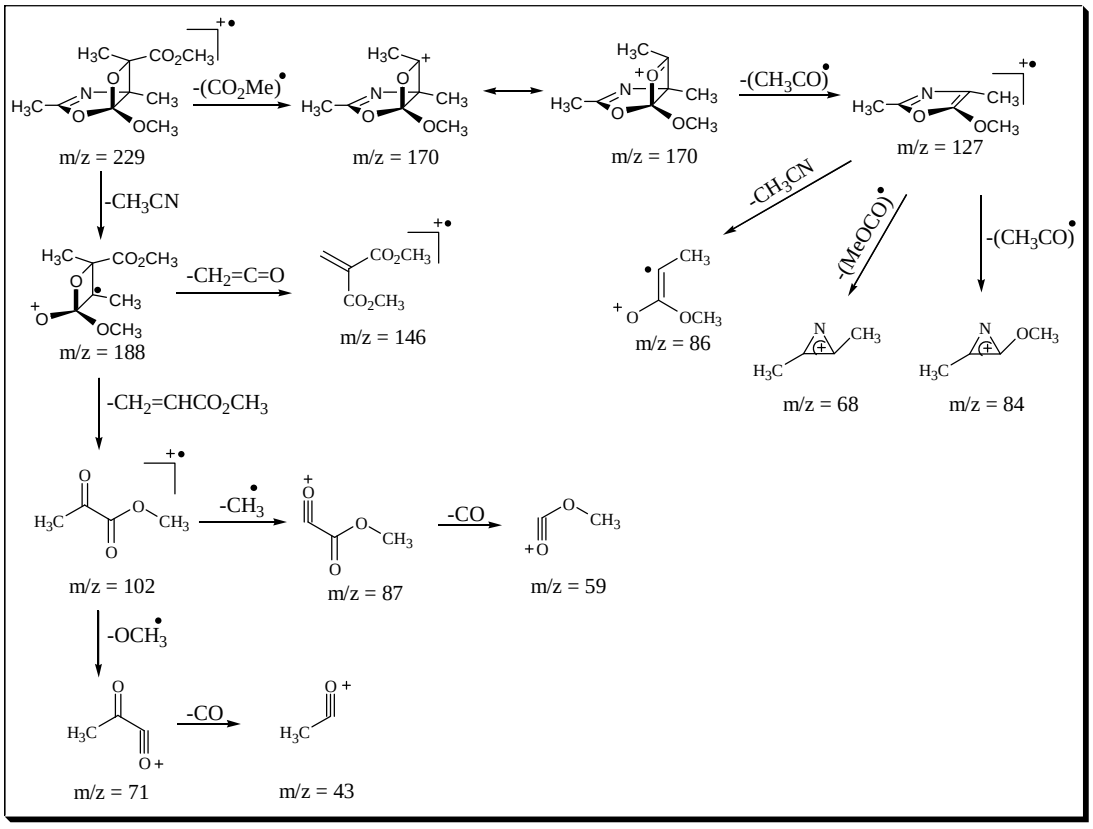


Figure 3.128: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **55a**.

The mass spectrum showed the major peak at m/z = 170 corresponding to (M^+-COOMe). The fragmentation pattern is depicted in Scheme 3.59.



Scheme 3.59: Fragmentation pattern of compound **55a**.

Figure 3.129 shows the HMBC-spectrum of the bicyclic oxetane **55a** which clearly correlates the protons with the corresponding carbon atoms and further assignes the chemical structure of compound **55a**.

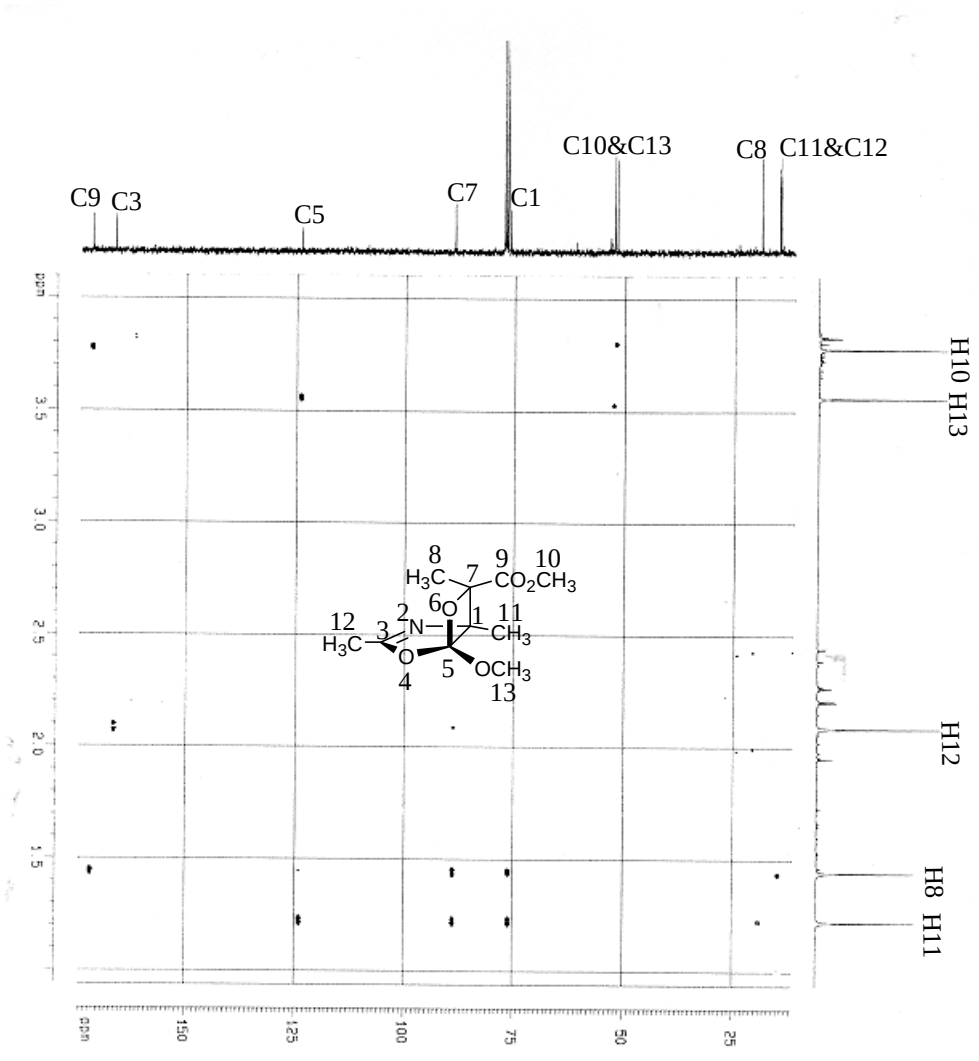


Figure 3.129: HMBC spectrum (300 MHz, $CDCl_3$) of compound **55a**.

The ^{1}H-NMR spectrum of compound **54d** showed two doublets at δ 0.82 ppm (d, J = 6.6 Hz, 3H) and 1.20 ppm (d, J = 6.6 Hz, 3H) corresponding to the two methyl protons of the isopropyl group. In addition, there appeared four singlets at δ 1.55, 2.13, 3.63 and 3.79 ppm attributed to CH_3 at C-1, CH_3 at C-3, OCH_3 at C-5 and OCH_3 of the ester group. The ^{13}C-NMR spectrum revealed signals at δ 82.8, 90.7 and 124.0 ppm due to C-1, C-7 and C-5 of the oxetane ring, respectively. Both C-3 and carbonyl ester resonate at δ 166.4 and 171.2 ppm, respectively.

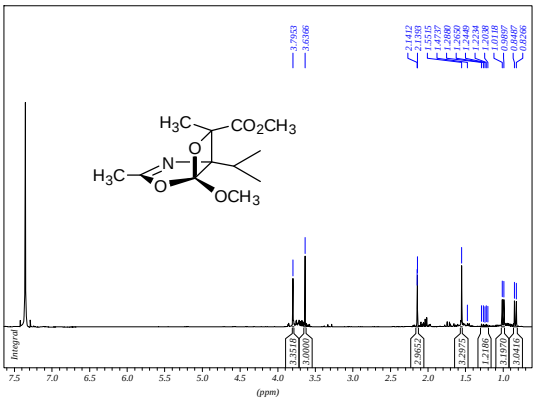


Figure 3.130: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **55d**.

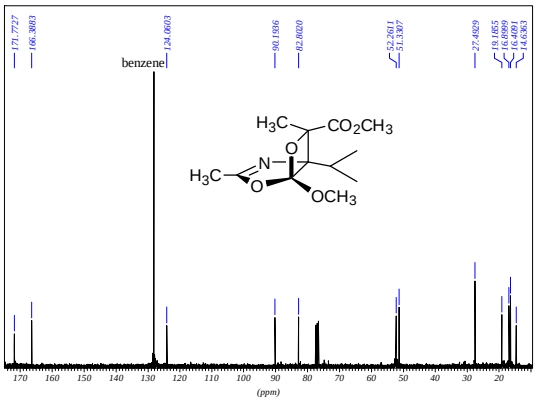


Figure 3.131: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **55d**

Compound **55f** was analyzed by ^{1}H-NMR and ^{13}C-NMR spectroscopy. In the ^{1}H-NMR spectrum at δ 1.47, 2.07, 3.57 and 3.77 ppm, there appeared four singlets attributed to CH_3 at C-1, CH_3 at C-2, OCH_3 at C-5 and OCH_3 of the ester group, respectively. In addition, there appeared a triplet at δ 0.76 and a doublet at δ 0.89 ppm assigned to the CH_3 group attached to CH_2 and CH_3 attached to a CH group, respectively. The ^{13}C-NMR spectrum revealed signals at δ 83.5, 90.5 and 124.2 ppm for the C-1, C-7 and C-5 of the oxetane ring, respectively.

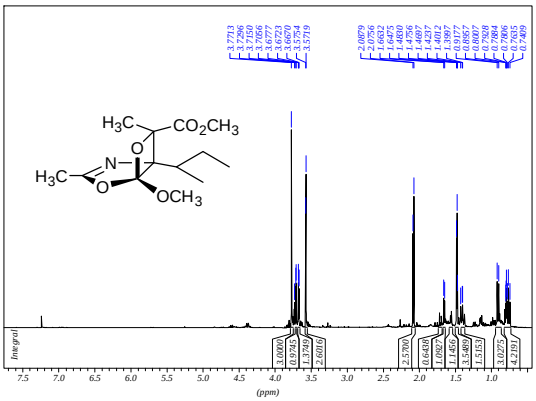


Figure 3.132: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **55f**.

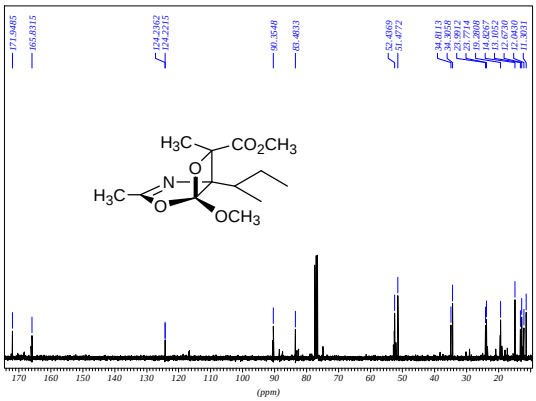
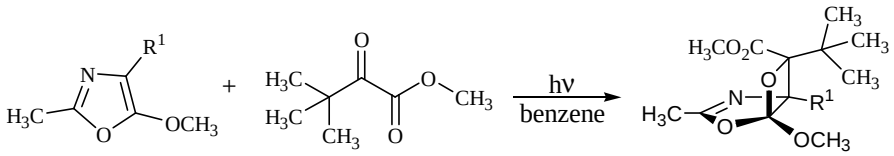


Figure 3.133: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **55f**.

3.8.3.2 Reaction with methyl trimethylpyruvate

In contrast to methyl pyruvate, photolysis of methyl trimethylpyruvate in the presence of oxazole substrates afforded the bicyclic oxetanes **56a-f** with *exo*-*tert*-butyl substituent at position C-7. The diastereomeric ratio was significantly affected by the size of alkyl groups at position C-4 of the oxazole substrates.



36a-f **50** **56a-f**

Scheme 3.60: Photoreaction of methyl trimethylpyruvate with oxazoles **36a-f**.

Table 3.36: Results of the photocycloaddition reaction of methyl trimethylpyruvate with oxazole substrates **36a-f**.

Compound	R^1 =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
56a	Me	>98 : 2	80
56b	Et	>98 : 2	75
56c	n-Pr	>98 : 2	68
56d	i-Pr	49 : 51	79
56e	i-Bu	63 : 37	84
56f	*sec*-Bu	56 : 44	89

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] based on the degree of conversion of the oxazole.

The *exo*-*tert*-butyl configuration of the bicyclic oxetane **56a** was determined by NOE measurement. Irradiation of a methyl protons of the *tert*-butyl group at 1.11 ppm led to NOE enhancement of both signals of CH_3 on C-1 at 1.48 ppm and OCH_3 group on C-5 at 3.55 ppm (see Figure 3.134).

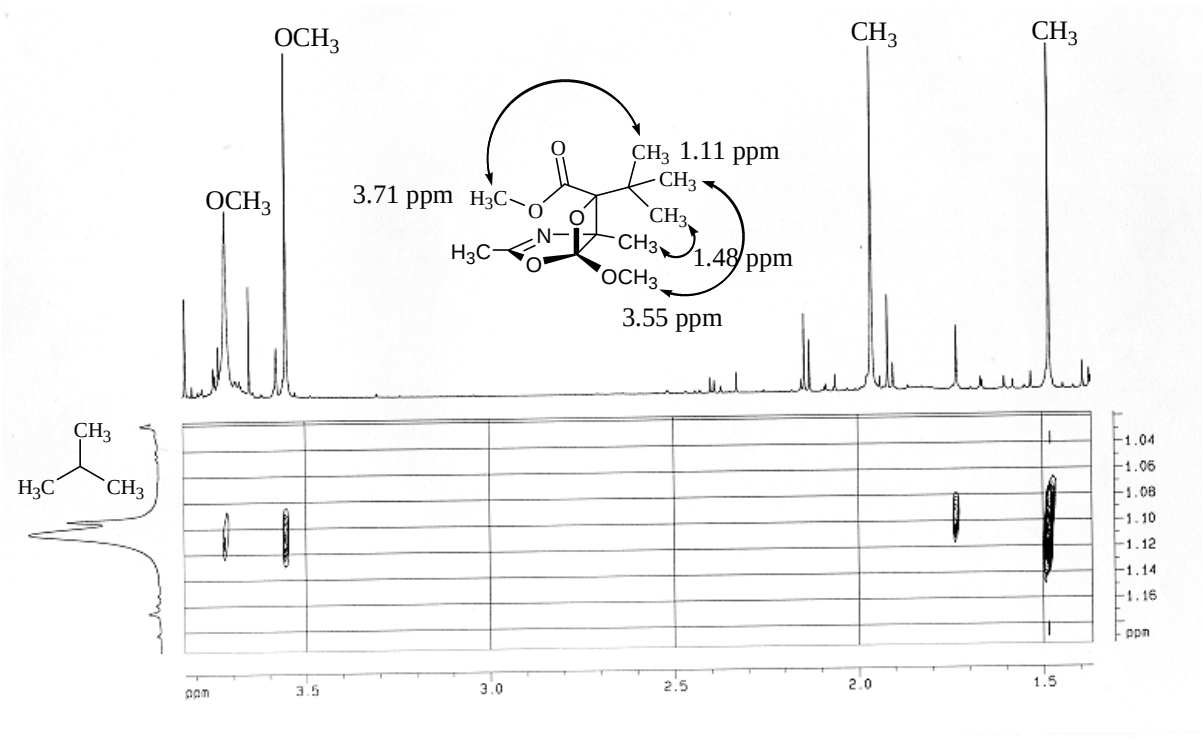


Figure 3.134: NOESY (300 MHz, $CDCl_3$) spectrum of compound **56a**.

The chemical structure determination of the bicyclic oxetanes **56a-f** was based on IR, NMR analyses and mass spectrometry. For example, the infrared spectrum of compound **56a** showed strong absorption bands at 1735 and 1620 cm^{-1} indicating the presence of COO and C=N groups, respectively. Again, the mass spectrum of the bicyclic oxetane did not show the molecular ion peak but peaks which were characteristic for retro-cycloaddition to oxazole and methyl trimethylpyruvate. The ^{1}H-NMR spectrum of compound **56a** showed five singlets at δ1.11, 1.48, 2.01, 3.54 and 3.71 ppm attributed to the *tert*-butyl group, CH_3 at C-1, CH_3 at C-3, OCH_3 at C-5 and OCH_3 of ester group, respectively. The ^{13}C-NMR spectrum revealed signals at δ 80.6, 97.3 and 118.7 ppm corresponding to C-1, C-7 and C-5 of the oxetane ring, respectively. In addition, there appeared two signals at δ 167.8 and 173.3 ppm assigned to C-3 and the carbonyl methyl ester, respectively.

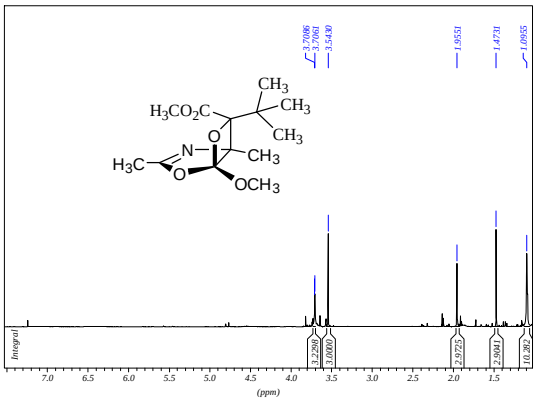


Figure 3.135: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of **56a**.

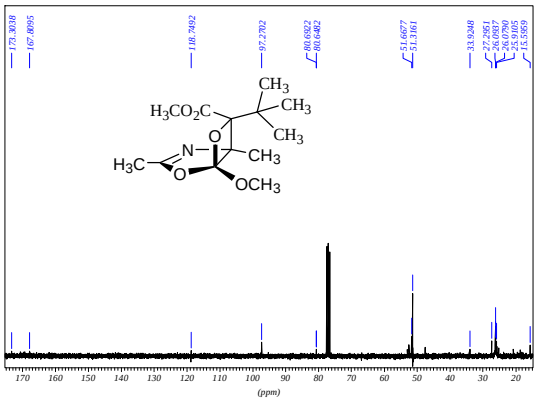


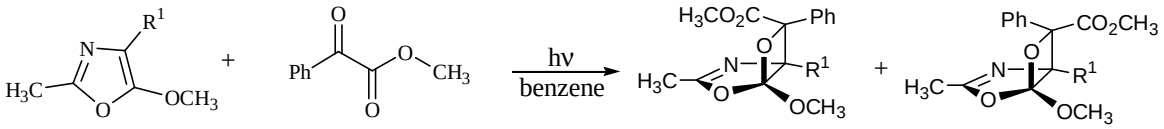
Figure 3.136: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of **56a**.

3.8.4 Photocycloaddition reactions of aromatic a-keto esters with oxazoles 36a-f

In order to evaluate the influence of steric as well as electronic factors on the stereoselectivity of the Paternò-Büchi reaction of oxazoles with aromatic α-keto esters, the photocycloaddition of 4-substituted oxazoles with different types of alkyl phenylglyoxylates was investigated.

3.8.4.1 Reaction with methyl phenylglyoxylate

Photolysis of equimolar amounts of methyl phenylglyoxylate and an oxazole in benzene at 350 nm furnished mixture of diastereoisomers *exo*-**58a-f** and *endo*-**58a-f** in good yields.



36a-f **57** *exo*-**58a-f** *endo*-**58a-f**

Scheme 3.61: Photoreaction of methyl phenylglyoxylate with oxazole substrates **36a-f**.

The *exo/endo* diastereomeric ratios of the photoadducts **58a-f** were slightly affected by changing the alkyl substituent of the oxazole substrates (see Table 3.37).

Table 3.37: Results of the photocycloaddition reaction of methyl phenylglyoxylate with oxazole substrates **36a-f**.

Compound	R^1 =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
58a	Me	79 : 21	86
58b	Et	77 : 23	79
58c	n-Pr	75 : 25	78
58d	i-Pr	71 : 29	85
58e	i-Bu	72 : 28	89
58f	*sec*-Bu	74 : 26	90

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] based on the degree of conversion of the oxazole.

The bicyclic oxetanes **58a-f** were formed with moderate simple diastereoselectivity favoring the *exo*-Ph products. In most examples, the diastereomeric *exo* and *endo* oxetane products were separated by preparative chromatography after treatment with 1% TEA/CH_2Cl_2. No side products were formed except the inevitable pinacol formation, which is due to hydrogen abstraction of the photoexcited methyl phenylglyoxylate and its subsequent addition to another substrate molecule. In order to determine the prefered mode of diastereofacial attack of methyl phenylglyoxylate to the chiral oxazole **36f**, a NOESY experiment was performed with the isolated *endo*-Ph bicyclic oxetane **58f**. Saturation of the methyl hydrogen at 1.22 ppm led to an enhancement of the aromatic proton signal at 7.51 ppm assigned the *lk*-attack (*lk* = *like*) of the methyl phenyglyoxylate whereas irradiation of the methylene proton at 2.09 ppm led to enhancement of the aromatic proton at 7.51 ppm assigned to *ul*-attack (*ul* = unlike) of methyl phenylglyoxylate to the chiral oxazole (see Figure 3.137).

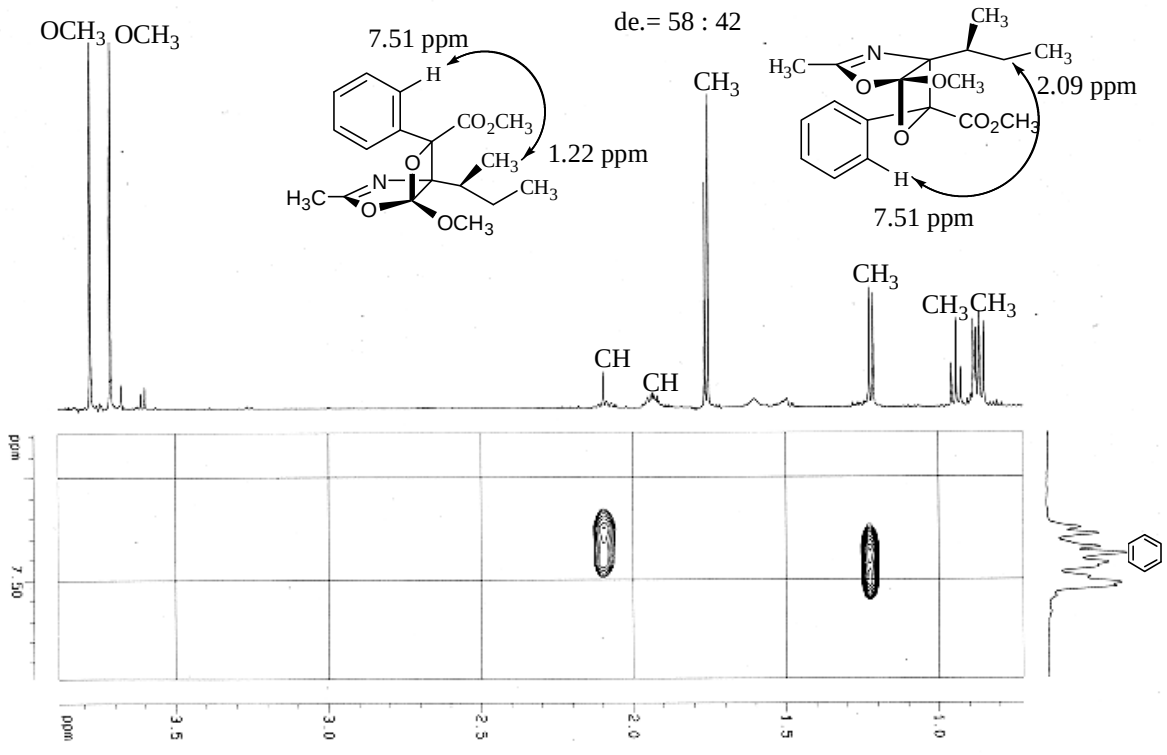
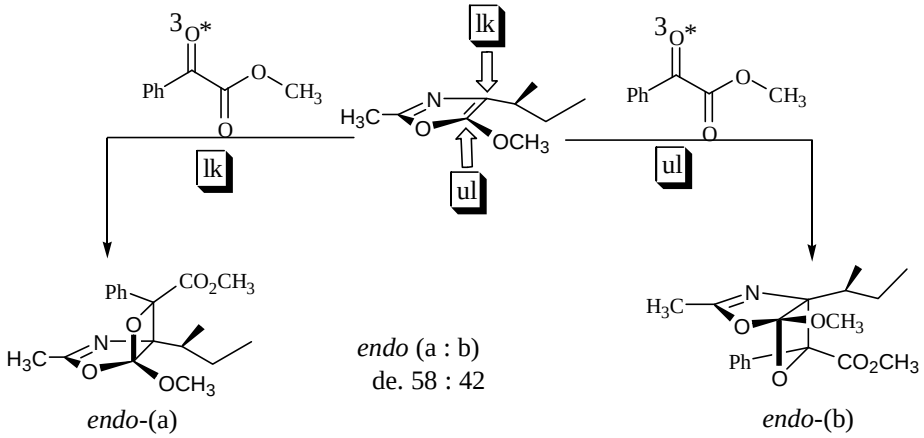


Figure 3.137: NOESY spectrum (300 MHz, $CDCl_3$) of *endo-**58f***.

Scheme 3.62 displays the formation of the two diastereoisomers of the bicyclic oxetanes from the *lk*-attack and *ul*-attack of methyl phenylglyoxylate to the chrial oxazole **36f**.



Scheme 3.62: *lk*- and *ul*- attack of methyl phenylglyoxylate to the chiral oxazole.

The assignment the relative configuration of the two diastereoisomers was possible by ^{1}H-NMR analysis, which showed two main differences between the *exo*-Ph and the *endo*-Ph diastereoisomers in the ^{1}H-NMR spectra: (a) the methyl protons at C-3 in the *exo*-Ph isomer absorb at 2.00 ppm, while in the *endo*-Ph isomer this absorption is shifted upfield to 1.70 ppm due to shielding effect of the benzene ring; (b) the methoxy protons at C-5 in the *exo*-Ph

isomer is shielded by the benzene ring and resonates at much higher field (δ = 3.00 ppm) than the methoxy protons in the *endo*-Ph isomer which absorb at δ = 3.67 ppm.

The constitutions of the bicyclic oxetanes **58a-f** were elucidated on the basis of NMR analyses. For example, the ^{1}H-NMR spectrum of ***exo*-58a** showed four singlets at δ 2.03, 2.08, 3.05 and 3.73 ppm attributed to CH_3 at C-1, CH_3 at C-3, OCH_3 at C-5 and OCH_3 of the ester group, respectively. The ^{13}C-NMR spectrum revealed signals at δ 80.9, 90.9 and 121.7 ppm due to C-1, C-7 and C-5 of the oxetane ring, respectively.

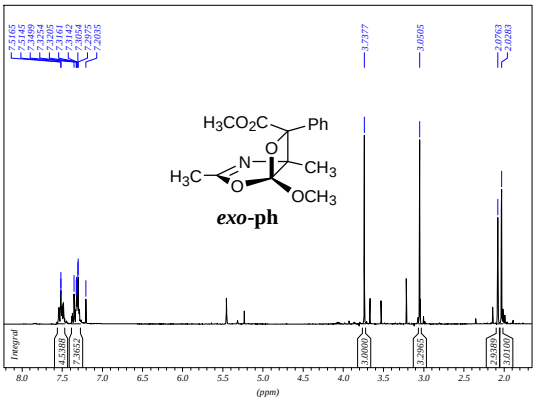


Figure 3.138: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***exo*-58a**.

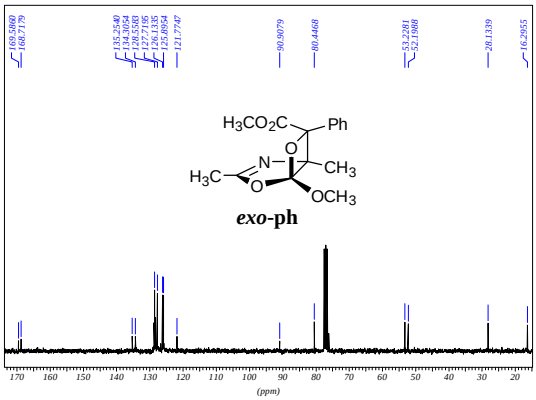


Figure 3.139: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***exo*-58a**.

In the ^{1}H-NMR spectrum of compound **58c**, the methyl protons at C-3 resonates at higher field (δ = 1.66 ppm) influenced by the ring current effect of the benzene ring and assigned to the *endo*-Ph configuration of the bicyclic oxetane. In addition, the two methoxy groups absorb at δ 3.64 and 3.73 ppm. The ^{13}C-NMR spectrum revealed signals at δ 81.6, 91.0, 123.7, 165.2 and 169.8 ppm attributed to C-1, C-7, C-5, C-3 and the carbon of carbonyl ester, respectively.

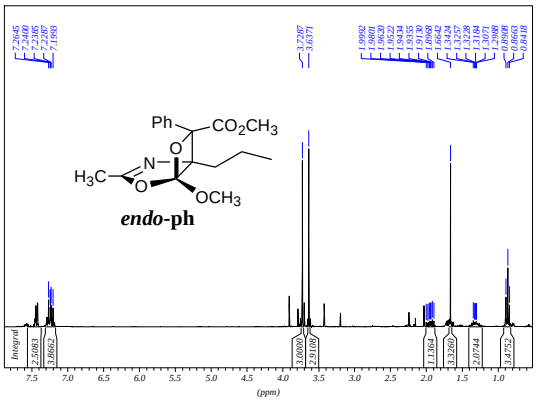


Figure 3.140: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of ***endo*-58c**.

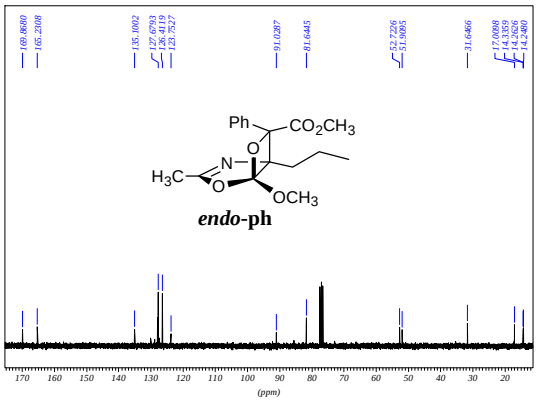


Figure 3.141: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of ***endo*-58c**.

The ^{1}H-NMR spectrum of ***endo*-58e** revealed two doublets at δ 0.79 ppm (d, J = 6.6 Hz, 3H) and 0.92 ppm (d, J = 6.6 Hz, 3H) indicating the presence of an isopropyl group. Again, the methyl protons at C-3 resonate at higher field at δ 1.72 ppm confirming the *endo*-Ph configuration of the bicyclic oxetane. Further prove of the *endo*-Ph configuration came from the chemical shift of OCH_3 group at C-5 (3.69 ppm) indicating that the phenyl group is distant from OCH_3 group. The ^{13}C-NMR spectrum showed signals at δ 81.8, 90.9 and 123.8 ppm due to C-1, C-7 and C-5 of the oxetane ring, respectively. Both C-3 and carbonyl ester resonate at lower field at δ 164.7 and 169.9 ppm, respectively.

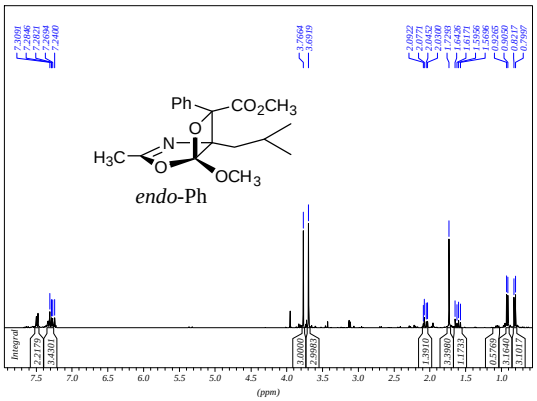


Figure 3.142: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of ***endo*-58e**.

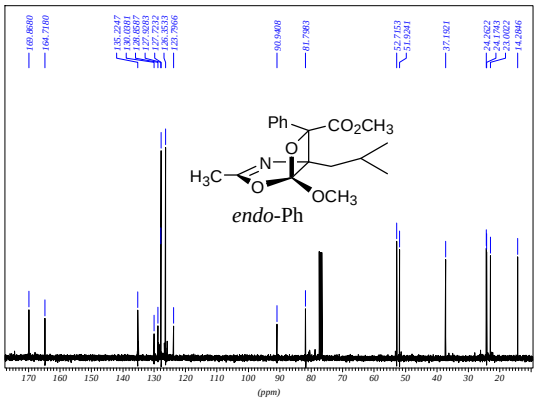


Figure 3.143: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of ***endo*-58e**.

In the ^{1}H-NMR spectrum of ***endo*-58f**, three singlets appeared at δ 1.70, 3.71 and 3.77 ppm related to CH_3 at C-1, OCH_3 at C-5 and OCH_3 of the ester group, respectively. The ^{13}C-NMR spectrum revealed signals at δ 86.3, 92.3 and 123.9 ppm assigned to C-1, C-7 and C-5 of the

oxetane ring, respectively. Moreover, from the intensity of the signals it was detected that the facial selectivity of the photoadduct was low (de. 58 : 42).

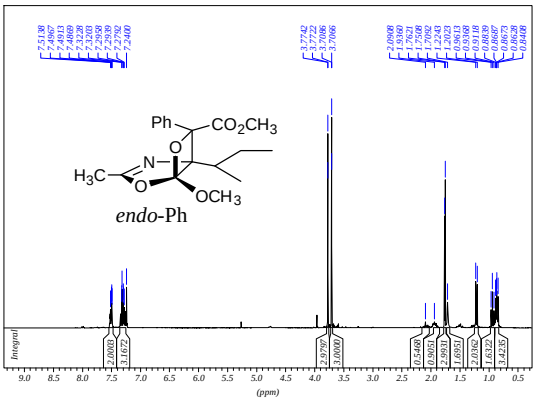


Figure 3.144: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of ***endo*-58f**.

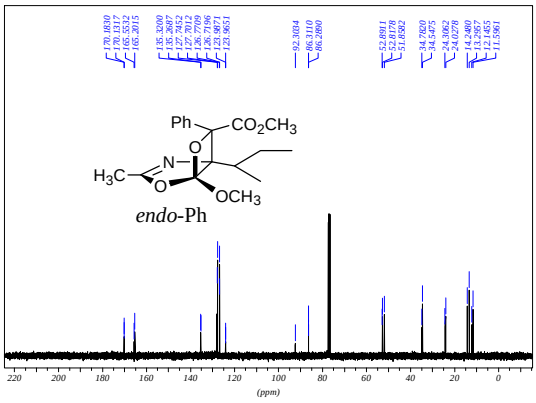
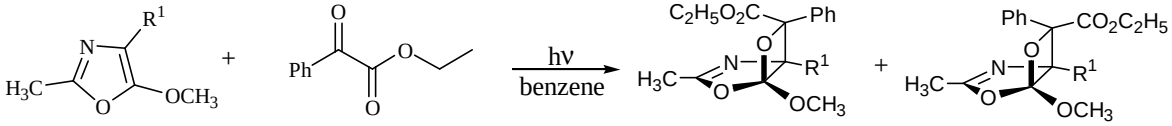


Figure 3.145: ^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of ***endo*-58f**.

3.8.4.2 Reaction with ethyl phenylglyoxylate

Analogous to methyl phenylglyoxylate, irradiation of ethyl phenylglyoxylate in benzene in the presence of the oxazole substrates afforded two diastereoisomers ***exo*-60a-f** and ***endo*-60a-f** in good yields with preferential formation of the *exo*-Ph photoadducts.



36a-f **59** ***exo*-60a-f** ***endo*-60a-f**

Scheme 3.63: Photoreaction of ethyl phenylglyoxylate with oxazole substrates **36a-f**.

The *exo*/*endo* diastereoselectivity of the photoadducts was slightly changed by increasing the size of the alkyl substituent of the oxazole substrates. Comparing the diastereoselectivity of the photoadducts from methyl phenylglyoxylate and ethyl phenylglyoxylate showed that the *exo*/*endo* diastereoselectivity slightly decreased in case of ethyl phenylglyoxylate than for methyl phenylglyoxylate.

Table 3.38: Results of the photocycloaddition reaction of **59** with **36a-f**.

Compound	R^1 =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
60a	Me	73 : 27	89
60b	Et	72 : 28	85
60c	n-Pr	70 : 30	78
60d	i-Pr	67 : 33	75
60e	i-Bu	65 : 35	90
60f	*sec*-Bu	66 : 34	76

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] based on conversion of the oxazole.

The *exo*-Ph and *endo*-Ph bicyclic oxetane diastereoisomers were separated by preparative chromatography although the separation was not always fully successful. The relative configurations of the two separated isomers of compound **60d** were deduced from NOESY studies. The *endo*-Ph diastereoisomer shows strong NOEs effect between the methyl protons at C-3 and aromatic phenyl protons at C-7. This phenomenon is illustrated in Figure 3.147 which summarizes the NOE data recorded for the *endo*-Ph-**60d**. The *exo*-Ph isomer showed a strong nuclear Overhauser enhancement of the aromatic protons signal when both methoxy protons at 3.54 ppm and methyl protons at 0.85 ppm were irradiated (see Figure 3.146).

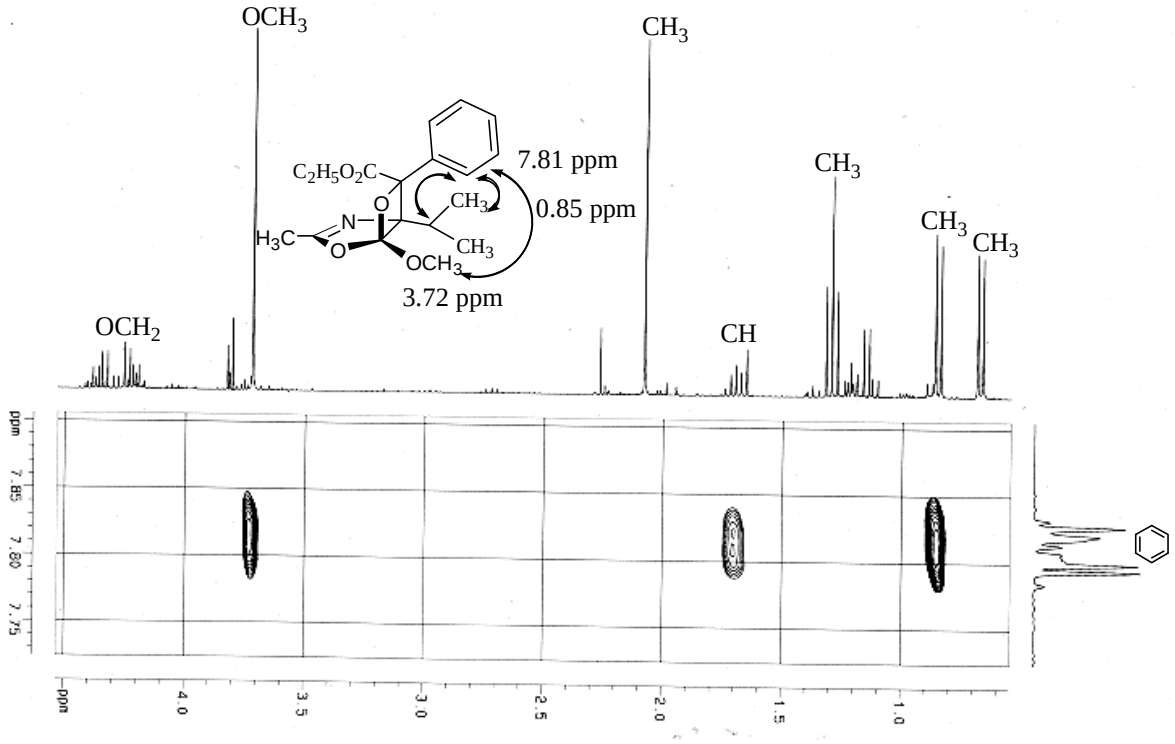


Figure 3.146: NOESY (300 MHz, $CDCl_3$) spectrum of *exo*-**60d**.

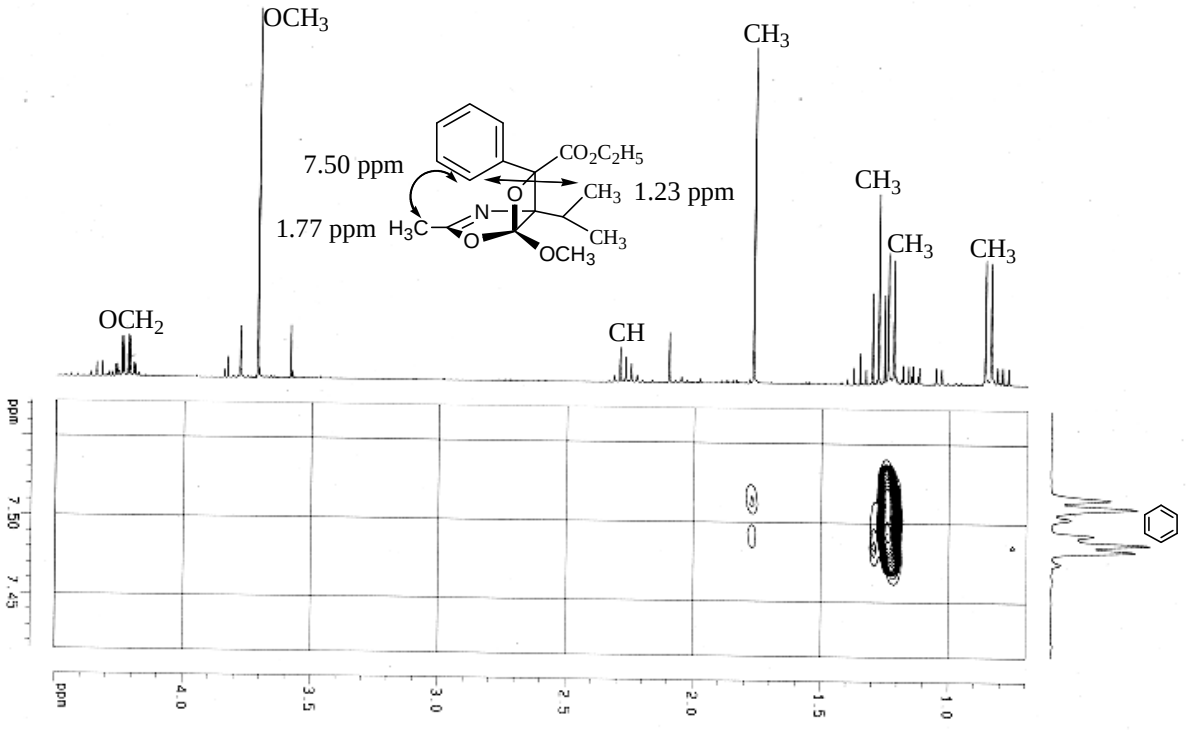


Figure 3.147: NOESY (300 MHz, $CDCl_3$) spectrum of *endo*-**60d**.

The constitutions of the bicyclic oxetanes **60a-f** were confirmed by the ^{1}H-NMR and ^{13}C-NMR analyses. For examples, the ^{1}H-NMR spectrum of *endo*-**60b** showed two triplets at δ 0.93 (t, J = 7.5 Hz, 3H), 1.27 (t, J = 7.4 Hz, 3H) indicating the presence of two ethyl groups. In addition, there appeared two singlets at δ 1.72, 3.69 ppm attributed to methyl protons at C-3 and methoxy protons at C-5, respectively and confirmed the *endo*-Ph configuration of the bicyclic oxetane. The ^{13}C-NMR spectrum revealed signals at δ 81.9, 90.9 and 123.8 ppm attributed to C-1, C-7 and C-5 of the oxetane ring, respectively. Moreover, there appeared two down-field shifted signals at δ 165.4 and 169.3 ppm related to C-3 and carbonyl ester group, respectively.

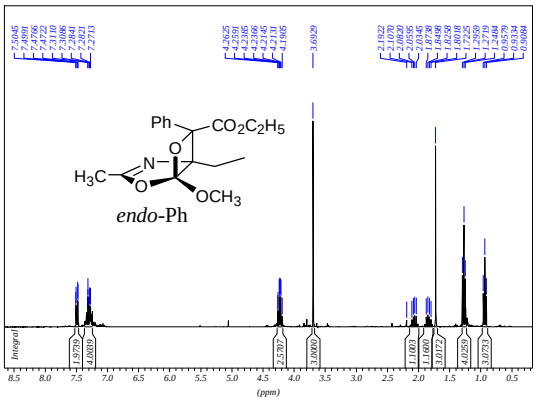


Figure 3.148: ^{1}H-NMR (300 MHZ, $CDCl_3$) spectrum of *endo*-**60b**.

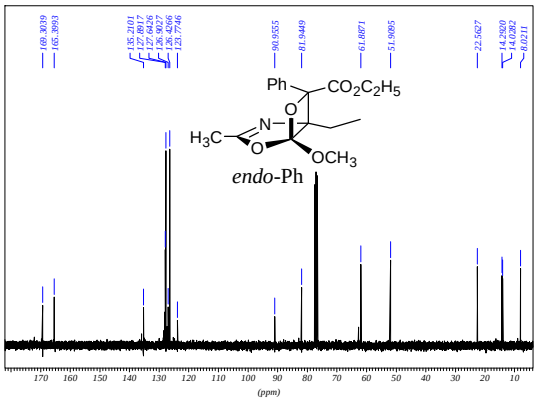


Figure 3.149: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**60b**.

There are two main differences in the ^{1}H-NMR spectra of the *exo*-Ph and *endo*-Ph diastereoisomers of compound **60d**: a) the methyl protons of the isopropyl group in the *exo*-Ph isomer resonate upfield-shifted at δ 0.66 (d, J = 6.6 Hz, 3H), and 0.84 (d, J = 6.6 Hz, 3H) while in the *endo*-Ph isomer the corresponding signals appear at δ 0.84 (d, J = 6.6 Hz, 3H) and 1.22 (d, J = 6.8 Hz, 3H); b) the methyl protons at C-3 absorb at higher field in the *endo*-Ph isomer in comparsion with the *exo*-Ph isomer. The ^{13}C-NMR spectrum revealed, that the methine carbon of isopropyl group in the *exo*-Ph isomer resonate at higher field (δ = 25.9 ppm) than in the *endo*-Ph isomer which resonates at δ 27.8 ppm. This phenomena is related to the ring current effect of the benzene ring which was often used as a tool for the assignement of the relative configuration of the bicyclic oxetanes.

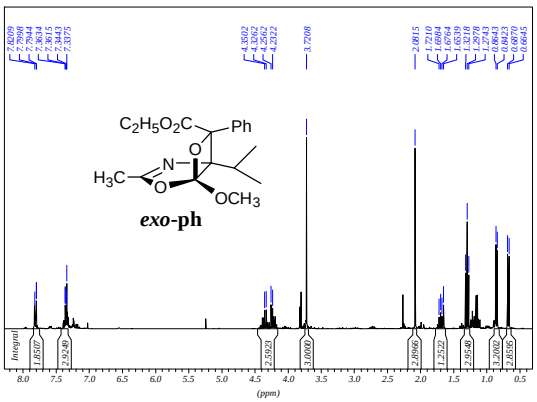


Figure 3.150: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**60d**.

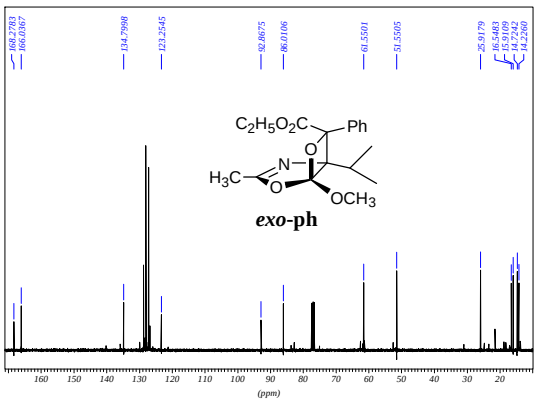


Figure 3.151: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**60d**.

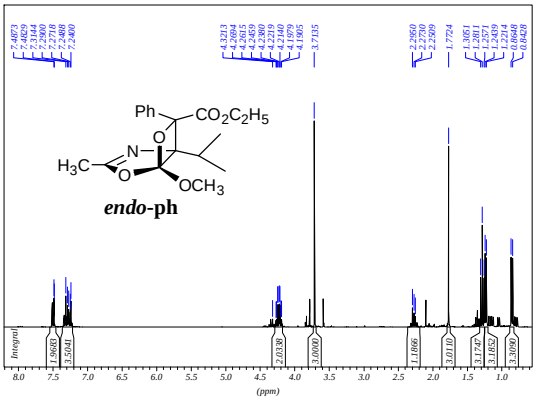


Figure 3.152: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**60d**.

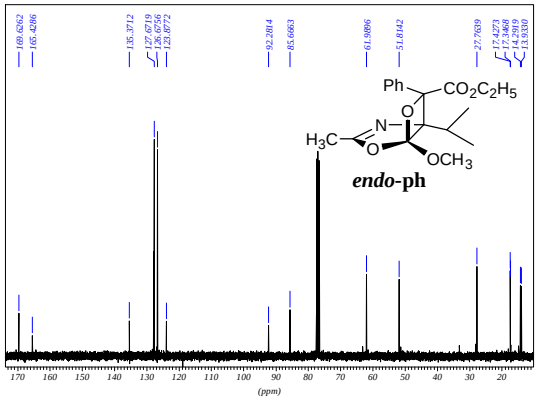


Figure 3.153: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**60d**.

The IR spectrum of compound **60e** showed two strong absorption bands at 1740 and 1620 cm^{-1} attributed to the COO and C=N groups, respectively. The ^{1}H-NMR spectrum showed two singlets at δ 1.72 and 3.69 ppm attributed to methyl protons at C-3 and methoxy protons at C-5, respectively, and confirmed the *endo*-Ph configuration. In the ^{13}C-NMR spectrum, at δ 81.6, 90.8 and 123.8 ppm, there signals appeared corresponding to C-1, C-7 and C-5 of the oxetane ring, respectively.

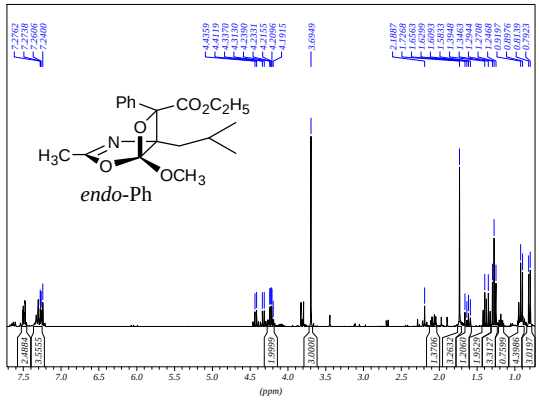


Figure 3.154: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**60e**.

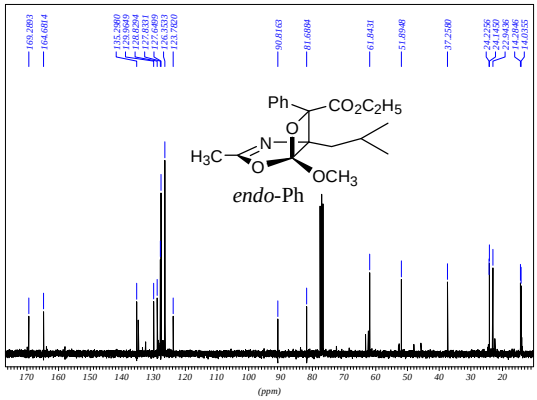
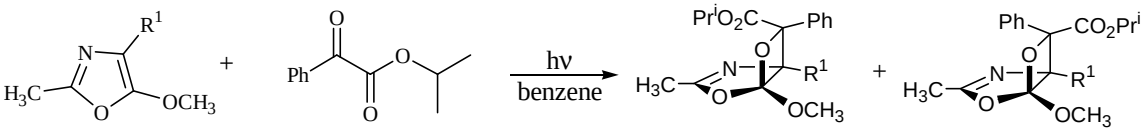


Figure 3.155: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**60e**.

3.8.4.3 Reaction with isopropyl phenylglyoxylate

The [2+2]-photocycloaddition of the electronically excited triplet state of isopropyl phenylglyoxylate with the oxazole substrates **36a-f** afforded two diastereoisomer of the bicyclic oxetanes **61a-f** in high chemical yields.



36a-f **51** *exo*-**61a-f** *endo*-**61a-f**

Scheme 3.64: Photoreaction of isopropyl phenylglyoxylate with oxazole substrates **36a-f**.

The *exo*-Ph / *endo*-Ph diastereomeric ratios exhibited a strong trend disfavoring the *endo*-Ph isomers with increasing steric demand of the R^1 substituent (Me, Et, n-Pr, i-Bu, *sec*-Bu and i-Pr) of the oxazole substrates (see Table 3.39). Interestingly, the *exo*-Ph diastereoisomer is still favored even with the bulky isopropyl substituent.

Table 3.39: Results of the photocycloaddition reaction of isopropyl phenylglyoxylate with oxazole substrates **36a-f**.

Compound	R^1 =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
61a	Me	67 : 33	85
61b	Et	66 : 34	87
61c	n-Pr	63 : 37	80
61d	i-Pr	51 : 49	90
61e	i-Bu	56 : 44	86
61f	*sec*-Bu	55 : 45	84

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] based on conversion of the oxazole.

The *exo*-Ph and *endo*-Ph diastereoisomers of the bicyclic oxetanes **61a-f** were separated by preparative chromatography. The relative configurations of the photoadducts were assgined from the ^{1}H-NMR chemical shift comparsion of the methyl protons at C-3 in both the *exo* and *endo*-isomers similar to the results described above. The chemical structure of the bicyclic oxetanes were elucidated by the ^{1}H-NMR and ^{13}C-NMR analyses. For example, the ^{1}H-NMR spectrum of compound **61a** showed two doublets at δ 1.20 (d, J = 6.2 Hz, 3H), 1.28 (d, J = 6.2 Hz, 3H) indicating the presence of an isopropyl group. In addition, at δ 1.50, 1.69 and 3.67 ppm, three singlets appeared related to CH_3 at C-1, CH_3 at C-3 and OCH_3 at C-5, respectively, and confirmed the *endo*-Ph configuration. In the ^{13}C-NMR spectrum, three signals appeared at δ 78.5, 90.5 and 123.7 ppm attributed to C-1, C-7 and C-5 of the oxetane ring, respectively.

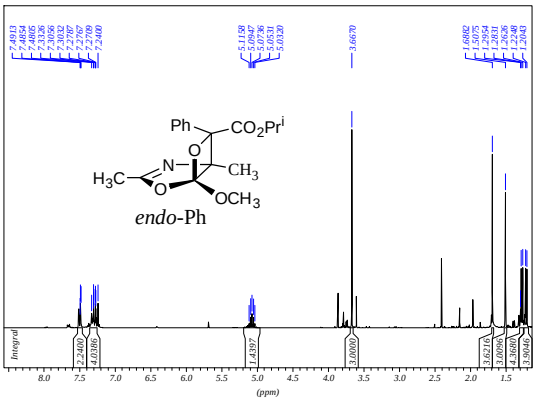


Figure 3.156: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**61a**.

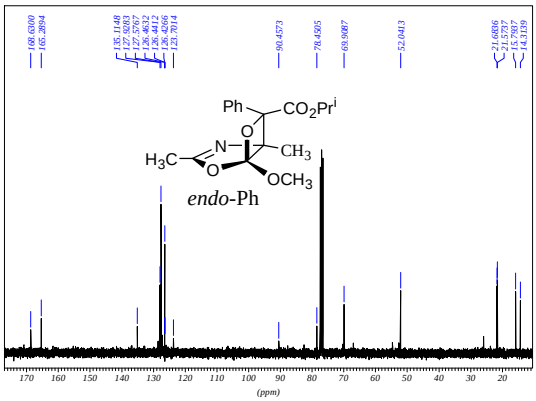
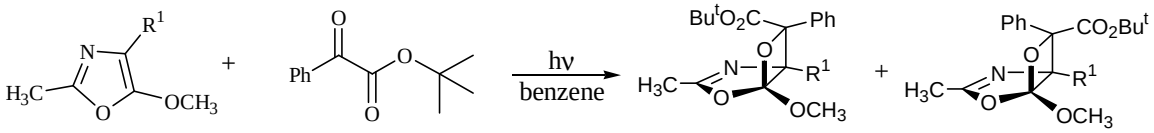


Figure 3.157: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**61a**.

3.8.4.4 Reaction with *tert*-butyl phenylglyoxylate

Analogous to isopropyl phenylglyoxylate, irradiation of *tert*-butyl phenylglyoxylate in benzene in the presence of the oxazole substrates **36a-f** delivered two diastereoisomers of the bicyclic oxetanes **62a-f** in high chemical yields.



36a-f **52** *exo*-**62a-f** *endo*-**62a-f**

Scheme 3.65: Photoreaction of *tert*-butyl phenylglyoxylate with oxazole substrates **36a-f**.

Table 3.40: Results of the photocycloaddition reaction of *tert*-butyl phenylglyoxylate with oxazole substrates **36a-f**.

Compound	R^1 =	d.r. (*exo* : *endo*)[a]	Yield (%)[b]
62a	Me	69 : 31	85
62b	Et	67 : 33	87
62c	n-Pr	61 : 39	80
62d	i-Pr	53 : 47	90
62e	i-Bu	55 : 45	86
62f	*sec*-Bu	55 : 45	84

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectra of the crude product mixture, [b] based on the degree of conversion of the oxazole.

Again, the *exo*-Ph/ *endo*-Ph diastereoselectivities of the photoadducts decreased by increasing size of the substituent at C-4 of the oxazole substrates **36a-f**, albeit the *exo*-Ph isomer is still favored (see Table 3.40).

The two diastereoisomers of the bicyclic oxetanes could be separated by preparative chromatography. The relative configuration of the *endo*-Ph bicyclic oxetane **62a** was clearly assigned by NOESY measurements. Irradiation of the methyl hydrogen protons at 1.67 ppm led to an enhancement of the intensity of the phenyl protons signal at 7.48 ppm. Also, irradiation of the phenyl protons at 7.48 ppm led to an enhancement of the intensity of both the methyl signal at 1.53 ppm and the *tert*-butyl protons signal at 1.44 ppm (see Figure 3.158).

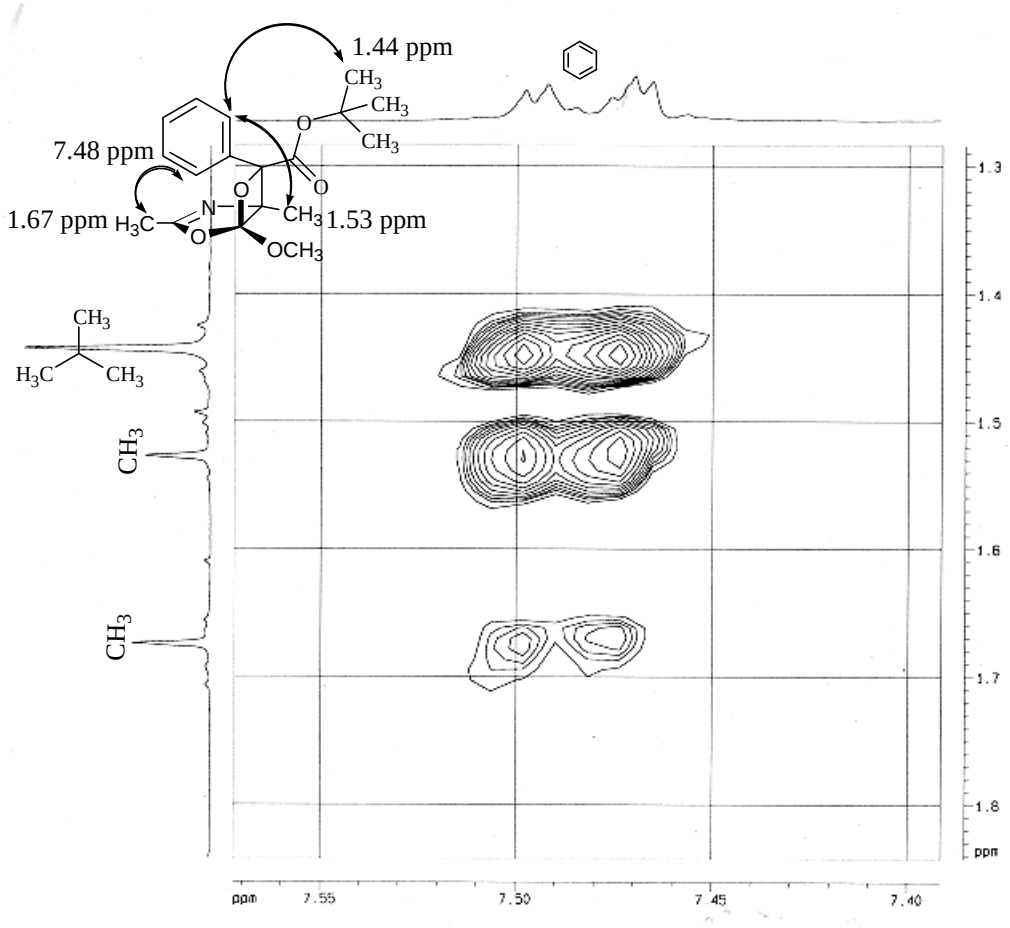
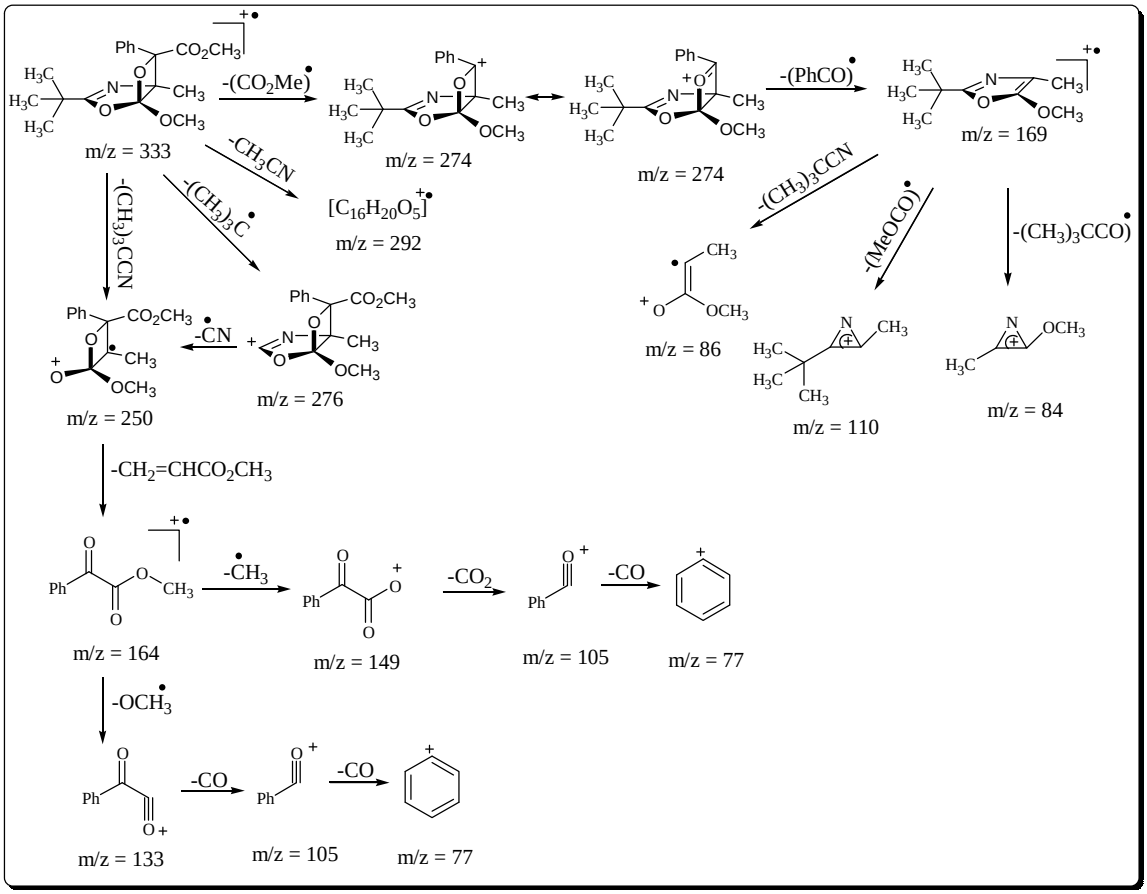


Figure 3.158: NOESY (300 MHz, $CDCl_3$) spectrum of *endo*-**62a**.

The constitutions of compounds **62a-f** were determined by IR, mass spectroscopy and NMR analyses. For example, the IR spectrum of compound **62a** showed two strong absorption bands at 1615 and 1725 cm^{-1} corresponding to the C=N and COO group, respectively. The mass spectrum showed the base peak at m/z 276 due to $[M^+ - (CH_3)_3 C]$, in addition there are two peaks at m/z 127 and 206 related to retrocycloaddition to give 2,4-dimethyl-5-

methoxyoxazole and *tert*-butyl phenylglyoxylate. Scheme 3.66 summarizes the fragmentation pattern of the compound **62a**.



Scheme 3.66: Fragmentation pattern of compound **62a**.

There are two main differences in the ^{1}H-NMR spectra between the *exo*-Ph and the *endo*-Ph diastereoisomer of compound **62a**: (a) the methyl protons at C-3 in the *exo*-Ph isomer absorb at 2.07 ppm, while in the *endo*-Ph isomer this absorption is shifted upfield to 1.67 ppm due to the shielding effect of the benzene ring; (b) the methyl protons at C-1 in the *exo*-Ph isomer are shielded by the benzene ring and resonate at a much higher field (δ = 1.04 ppm) than in the *endo*-Ph which absorbs at 1.52 ppm. The ^{13}C-NMR spectra of both the *exo*- and *endo*-Ph isomers revealed signals at δ 78.8, 91.1 and 123.4 ppm attributed to C-1, C-7 and C-5 of the oxetane ring, respectively. Figure 3.163 shows the DEPT spectrum of the compound *endo*-**62a** which clearly displayes the CH and CH_3 groups.

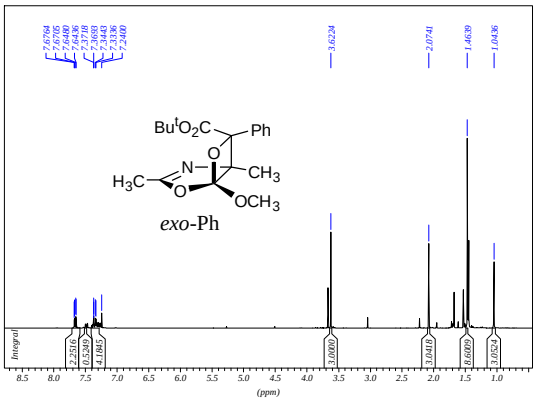


Figure 3.159: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**62a**.

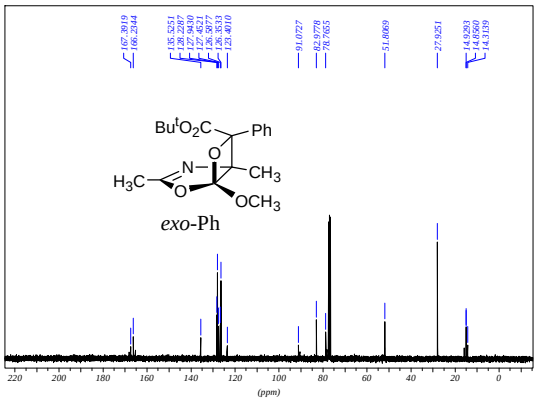


Figure 3.160: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**62a**.

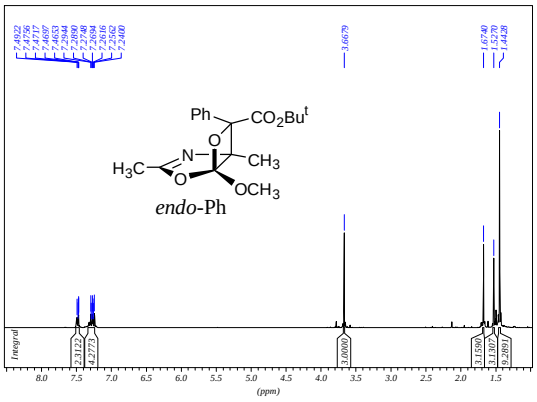


Figure 3.161: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**62a**.

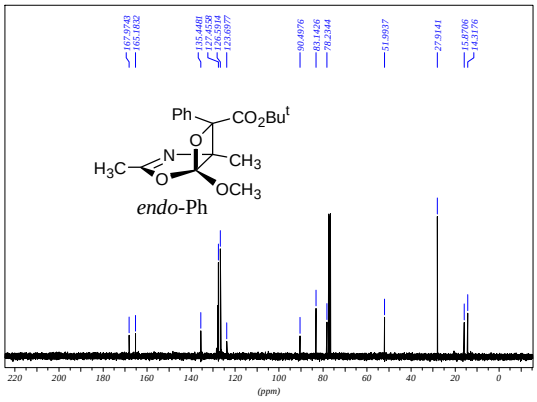


Figure 3.162: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**62a**.

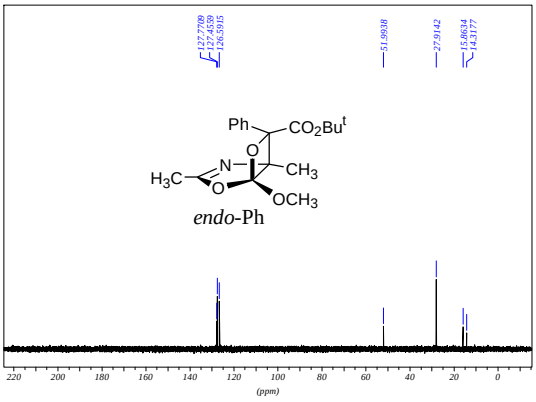


Figure 3.163: DEPT (75MHz, $CDCl_3$) spectrum of *endo*-**62a**.

Proving the chemical structure of compound **62b** was based on NMR analyses. Analogous to compound **62a**, there are also two main differences in the ^{1}H-NMR spectra between the *exo*- and the *endo*-Ph diastereoisomers. The ^{1}H-NMR spectrum of the *exo*-Ph isomer showed a triplet (J = 7.5 Hz, 3H) at higher chemical shift (δ = 0.72 ppm) related to the methyl group attached to the methylene group and assigned to the *exo*-Ph configuration. Additionally, there appeared three singlets at δ 1.47, 2.09 and 3.65 ppm attributed to the *tert*-butyl, methyl, and methoxy groups, respectively. In the ^{1}H-NMR spectrum of the *endo*-Ph isomer, the chemical shift of the methyl protons of ethyl group is shifted downfield to 0.92 ppm, whereas the chemical shift of the methyl protons at C-3 is shifted upfield to 1.70 ppm. The ^{13}C-NMR spectra of both the *exo*-Ph and *endo*-Ph diastereoisomers revealed signals characteristic for the oxetane ring at δ 81.9, 91.3 and 123.3 ppm corresponding to C-1, C-7 and C-5, respectively.

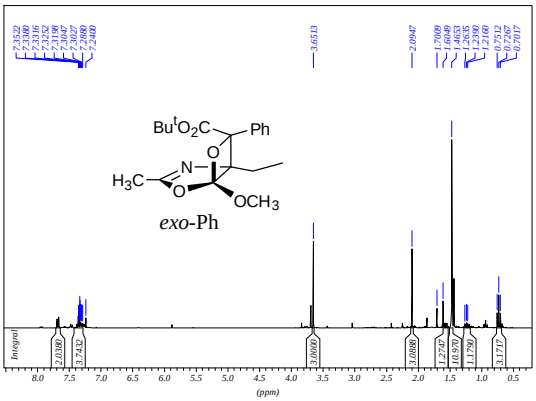


Figure 3.164: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**62b**.

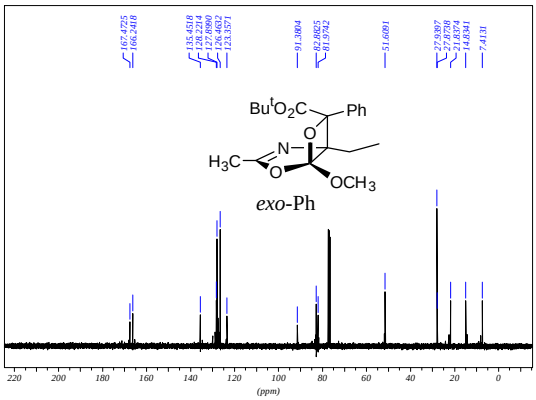


Figure 3.165: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**62b**.

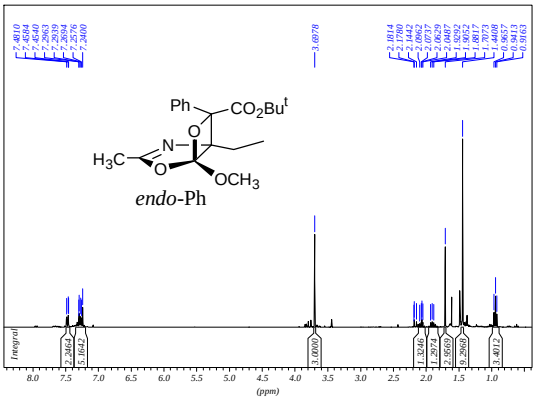


Figure 3.166: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**62b**.

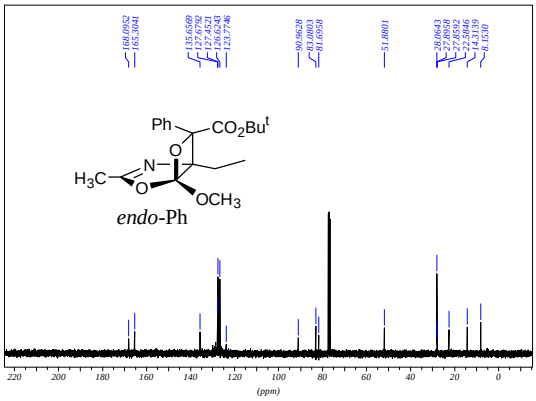


Figure 3.167: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**62b**.

The structure elucidation of both the *exo*- and *endo*-Ph diastereoisomer of compound **62d** was based on their NMR analyses. Analogous to **62a**, there are two main differences between the *exo*- and *endo*-Ph isomers in the ^{1}H-NMR spectra: (a) the methyl protons of the isopropyl group in the *exo*-isomer appears at 0.68 and 0.84 ppm, while in the *endo*-isomer, this absorption is shifted downfield to 0.87 and 1.26 ppm; (b) the methyl protons at C-3 in the *exo*-isomer resonates at 2.09 ppm, while in the *exo*-isomer this absorption is shifted to 1.75 ppm due to shielding effect of the benzene ring. In the ^{13}C-NMR spectra of both the *exo*- and *endo*-isomers, the signals at 85.8, 92.6 and 123.2 ppm correspond to C-1, C-7, and C-7 of the oxetane ring, respectively. In addition, the methine carbon of *exo*-isomer appears at 25.9 ppm, while in the *endo*-isomer this absorption is shifted to 27.6 ppm.

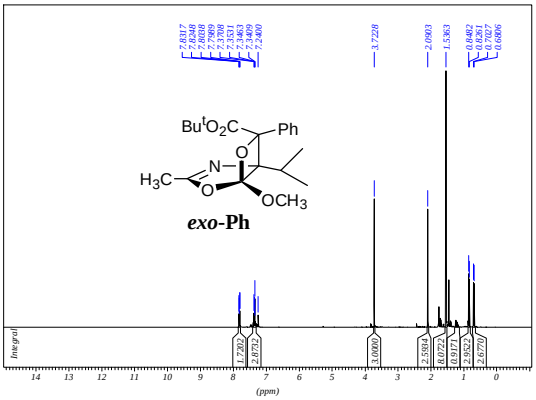


Figure 3.168: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**62d**.

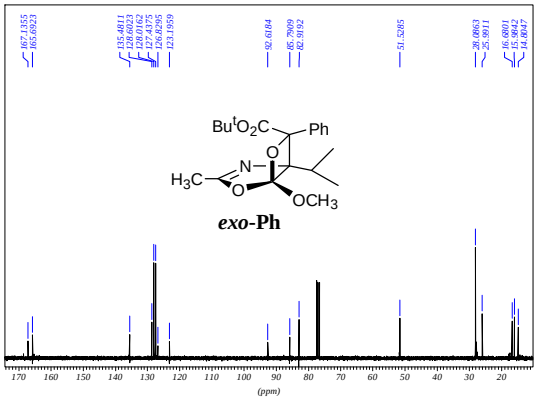


Figure 3.169: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**62d**.

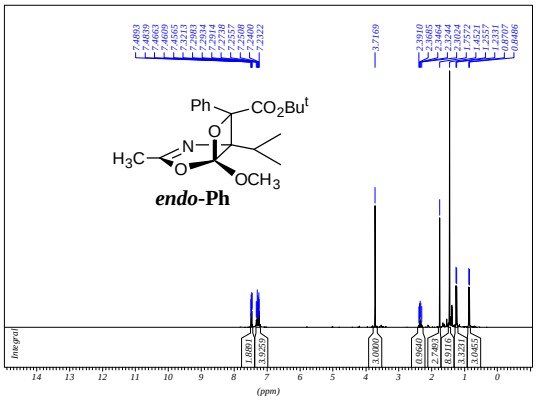


Figure 3.170: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**62d**.

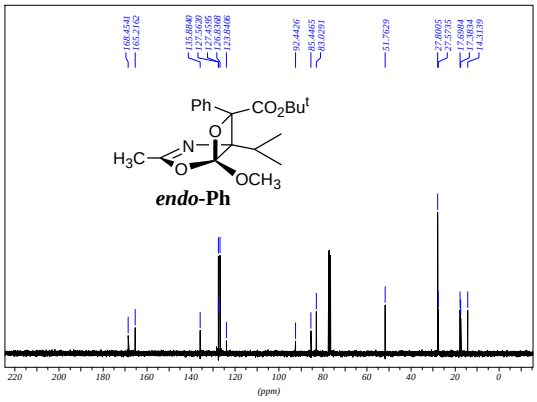


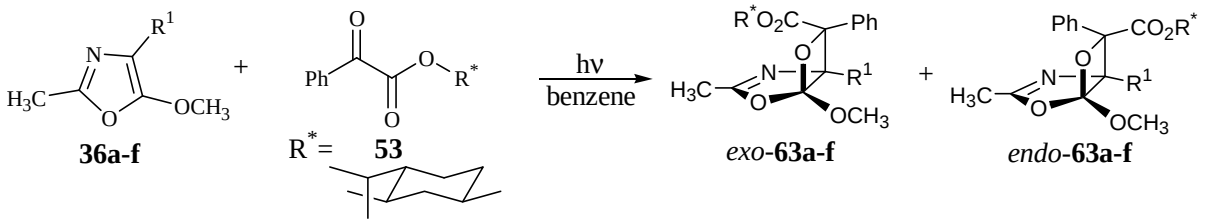
Figure 3.171: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**62d**.

3.8.5 Asymmetric induction

Phenyl glyoxylates derived from chiral alcohols were already described to be excellent substrates for the photocycloaddition to a variety of alkenes.[63] Depending on the facial bias exerted by the auxiliary they yield the corresponding oxetanes with modest to excellent diastereomeric excesses. It was thus of interest to study the asymmetric induction in the Paternò-Büchi reaction of 5-methoxyoxazoles **36a-f** with (-)-menthyl phenylglyoxylate.

3.8.5.1 Photoreactions of menthyl phenylglyoxylate with 5-methoxyoxazoles

When (-)-menthyl phenylglyoxylate was irradiated in benzene in the presence of 5-methoxyoxazoles **36a-f** at 350 nm, mixtures of the *exo*- and *endo*-Ph diastereoisomers **63a-f** were formed in high chemical yields.



Scheme 3.67: Photocycloaddition of (-)-menthyl phenylglyoxylate with 5-methoxyoxazoles **63a-f**.

Table 3.41: Results of the photocycloaddition reaction of menthyl phenylglyoxylate with 5-methoxyoxazoles **36a-f**.

Compound	R^1 =	(*exo* : *endo*)[a]	de. *exo*-Ph	de. *endo*-Ph	Yield (%)[b]
63a	Me	76 : 24	55 : 45	54 : 46	85
63b	Et	69 : 31	53 : 47	53 : 47	92
63c	n-Pr	66 : 34	56 : 44	52 : 48	84
63d	i-Pr	54 : 46	60 : 40	58 : 42	73
63e	i-Bu	64 : 36	52 : 48	53 : 47	92
63f	*sec*-Bu	55 : 45	56 : 44	55 : 45	85

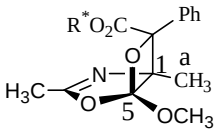
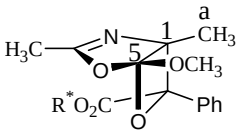
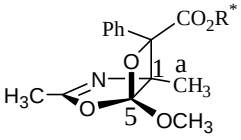
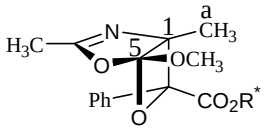
[a] based on the integration of characteristic signals in the ^{1}H-NMR spectrum of the crude products mixture, [b] yield (%) based on the degree of conversion of the oxazole.

Interestingly, the substituent R^1 in the oxazole substrates **36a-f** has significant influence on both the simple *exo*/*endo* diastereoselectivity and and also facial selectivity of the photoadducts. The simple *exo*/*endo* diastereoselectivity decreased with increasing steric demand of the substituent R^1 like the non-induced photocycloaddition of achiral alkyl

phenylglyoxylates with **36a-f**. The facial selectivities of the photoadducts for both *exo*-and *endo*-isomers were low and slightly influenced by increasing size of R^1 groups in oxazole substrates. The low facial selectivity of the photoadducts is similar to furan-menthyl phenylglyoxylate photoadducts which were described by Scharf and coworker.[63] The relatively low diastereomeric excess values observed for both the *exo*- and the *endo*-Ph diastereoisomers might be due to the fact that the bond formation proceeds in an early transition state at high energy of the diabatic reaction coordinate. Another reason for the lack of facial selectivity could be related to the excited menthyl phenyl glyoxylate which attacks the oxazole ring in an *exo*- or *endo*-fashion and might lead to partial cancellation of the inducing effect of the chiral auxiliary.

The relative configurations of the four stereoisomers of the photoadduct **63a** were determined on the basis of the chemical shifts comparsion of the methyl protons at C-1, OCH_3 at C-5 and also the chemical shift of the orthoester carbon (see Table 3.42).

Table 3.42: NMR chemical shifts of the four stereoisomers of compound **63a**.

Compound				
δ ppm	*exo*-(a)	*exo*-(b)	*endo*-(a)	*endo*-(b)
a CH_3	1.04	1.13	1.53	1.55
OCH_3	3.63	3.61	3.64	3.65
C-5	122.9	123.1	123.4	123.5

By use of preparative chromatography both the *exo*- and the *endo*-Ph isomers could be separated. The relative configuration of the major *exo*-Ph diastereoisomer of compound **63a** was determined unambiguously *via* NOE spectroscopy. Significant effects were observed for aromatic phenyl protons (δ = 7.66 ppm) by irradiation of the methyl protons (δ = 1.04 ppm) and the methoxy protons at 3.63 ppm.

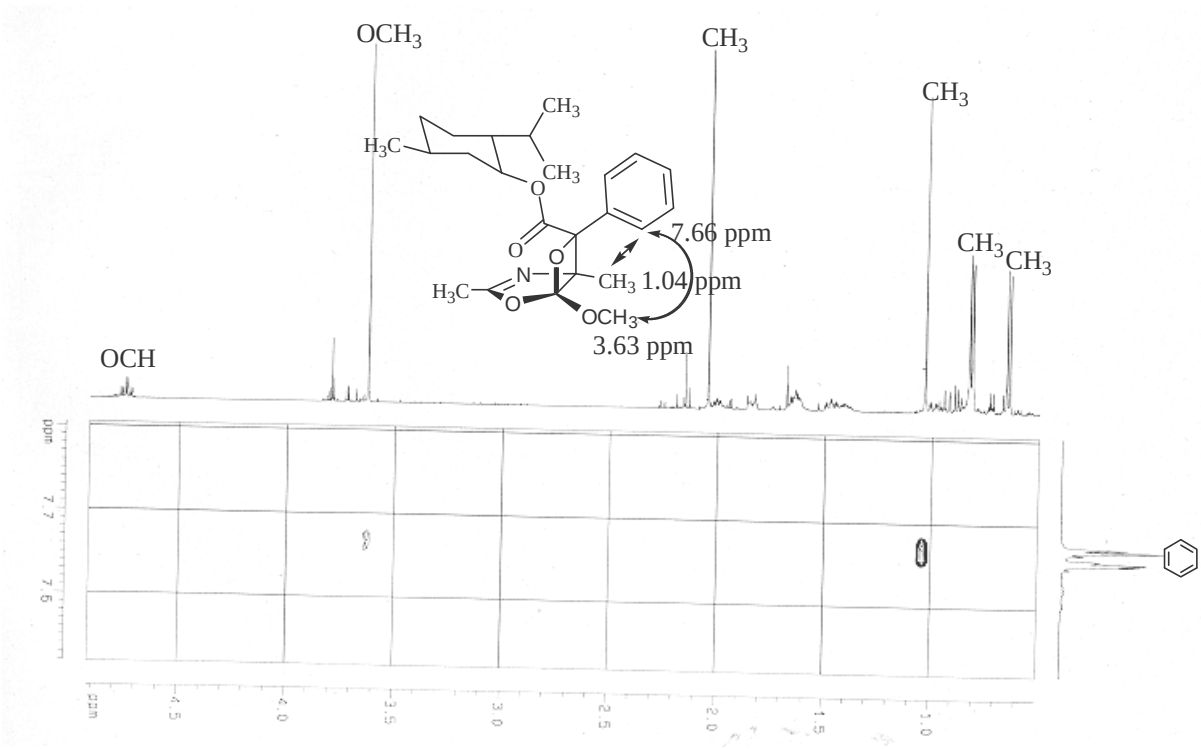


Figure 3.172: NOESY (300 MHz, $CDCl_3$) spectrum of *exo*-**63a**.

Structure elucidation of the bicyclic oxetanes **63a-f** was based on the NMR analyses. For example, the ^{1}H-NMR spectrum of compound **63a** revealed three singlets at δ 1.04, 2.05 and 3.63 ppm corresponding to the methyl protons at C-1, CH_3 at C-3 and OCH_3 at C-5, respectively, and confirmed the *exo*-Ph configuration. In the ^{13}C-NMR spectrum, at δ 79.4, 91.8, 123.7, 166.3 and 168.8 ppm, five signals appeared which were attributed to C-1, C-7, C-5, C-3 and COO group, respectively.

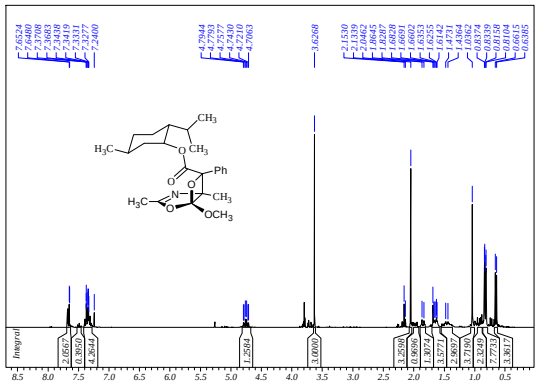


Figure 3.173: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**63a**.

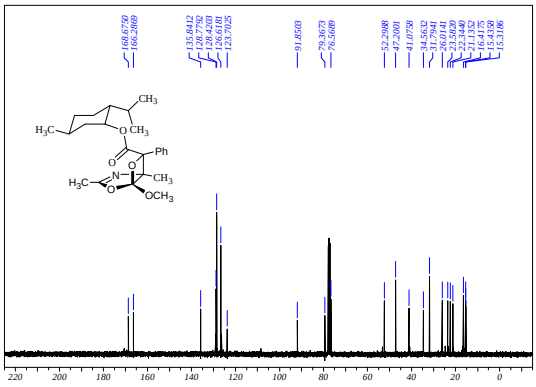


Figure 3.174: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**63a**.

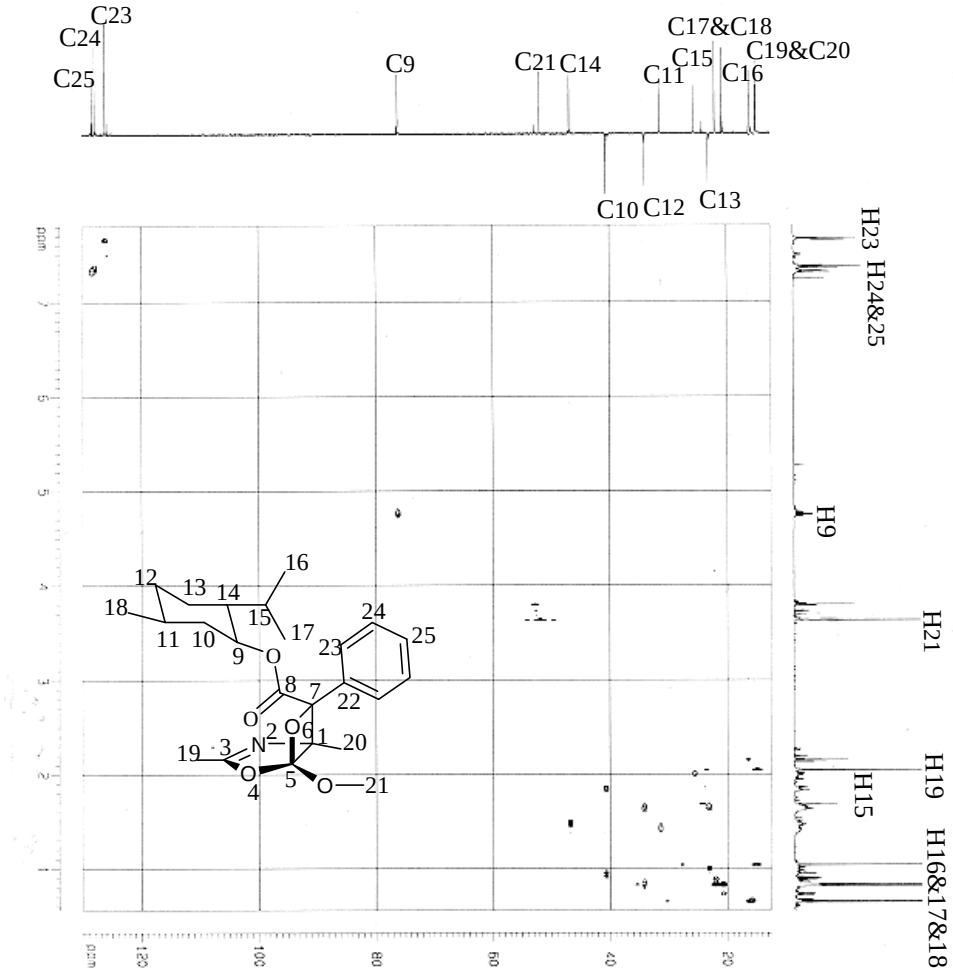


Figure 3.175: HMQC (300 MHz, $CDCl_3$) spectrum of *exo*-**63a**.

The IR spectrum of compound **63c** showed strong absorption bands at 1630 and 1735 cm^{-1} characteristic for the C=N and COO groups, respectively. The ^{1}H-NMR spectrum showed two singlets at δ 2.06 and 3.67 ppm attributed to CH_3 at C-3 and OCH_3 group, respectively, and assigned to the *exo*-Ph configuration. The ^{13}C-NMR spectrum revealed signals at δ 81.9, 91.8 and 123.2 ppm corresponding to C-1, C-7 and C-5 of the oxetane ring, respectively. In addition, two signals appeared down-field shifted at δ 165.4 and 168.3 ppm due to C-3 and CO group, respectively.

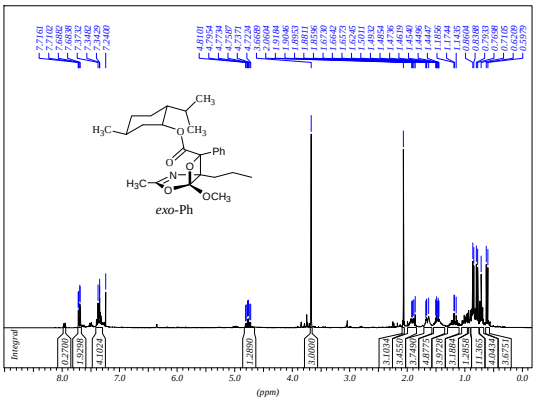


Figure 3.176: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**63c**.

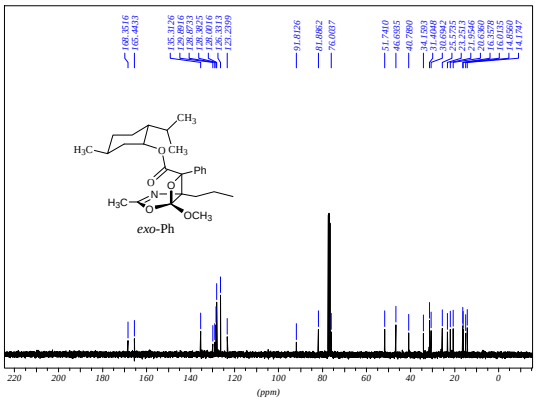


Figure 3.177: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**63c**.

The ^{1}H-NMR spectrum of compound **63f** showed two singlets at δ 2.05 and 3.73 ppm due to CH_3 at C-3 and OCH_3 at C-5, respectively, and were assigned to the *exo*-Ph configuration. In the ^{13}C-NMR spectrum, three signals at δ 86.5, 93.1 and 123.3 ppm appeared which were attributed to C-1, C-7 and C-5 of the oxetane ring, respectively. In addition, both C-3 and CO resonate at lower field at δ 165.1 and 167.8 ppm, respectively.

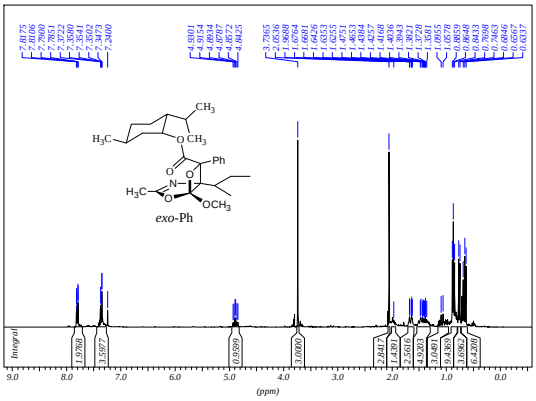


Figure 3.178: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**63f**.

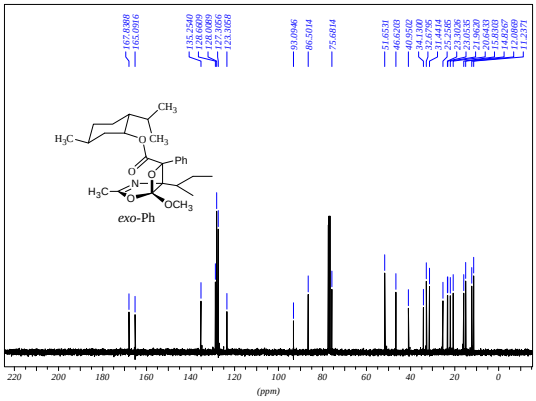


Figure 3.179: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**63f**.

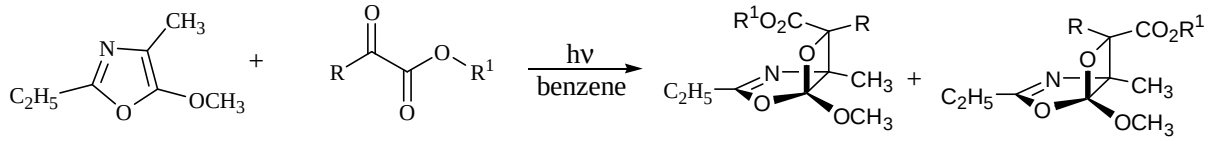
3.8.6 Effect of the substituent at C-2 of the oxazole substrates on the stereoselectivity of the photocycloaddition with α-keto esters

The successful explanation of the strong *endo* preference for a large number of Diels-Alder reactions has been usually considered as an example of secondary orbital interaction (SOI).[133] Recently, Griesbeck *et al.* reported that the *exo* preference for the triplet carbonyl photocycloaddition to dienes could also be related to secondary orbital interactions that

facilitates intersystem crossing by means of an increase in spin-orbit coupling.[42] In order to clarify the role of secondary orbital interactions in controlling the stereoselectivity of the triplet carbonyl-diene photocycloadditions, the Paternò-Büchi reaction of 5-methoxyoxazoles bearing an additional substituent at C-2 with aliphatic and aromatic α-keto esters was investigated.

3.8.6.1 Photocycloaddition reactions of 2-ethyl-4-methyl-5-methoxyoxazole with a-keto esters

Analogous to 2,4-dimethyl-5-methoxyoxazole **36a**, irradiation of aliphatic as well as aromatic α-keto esters in benzene in the presence of 2-ethyl-4-methyl-5-methoxyoxazole **49a** afforded the bicyclic oxetanes **64a-f** in high chemical yields.



49a *exo*-R-**64a-f** *endo*-R-**64a-f**

Scheme 3.68: Photoreaction of **49a** with α-keto esters.

Table 3.43: Simple diastereoselectivity of the Paternò-Büchi reaction of α-keto esters with 2-ethyl-4-methyl-5-methoxy oxazole **49a**.

Compound	R =	R^1 =	d.r.(*exo* : *endo*)[a]	Yield (%)[b]
64a	Me	Me	2 : >98	80
64b	t-Bu	Me	>98 : 2	86
64c	Ph	Me	68 : 32	87
64d	Ph	Et	67 : 33	78
64e	Ph	i-Pr	63 : 37	90
64f	Ph	t-Bu	65 : 35	83

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectrum of the crude products mixture, [b] yield (%) based on the degree of the conversion of the oxazole.

The results in Table 3.43 show that the simple *exo*/*endo* diastereoselectivity of the photoadducts **64a-f** were very high with aliphatic α-keto esters in comparison with the aromatic α-keto esters. From aromatic α-keto esters photoadducts, the simple *exo*/*endo* diastereoselectivity slightly decreased with increasing steric demand of the alkyl phenylglyoxylate substrates. In all cases, the diastereoisomers were successfully separated by preparative chromatography.The structural determination of compounds **64a-f** was based on the ^{1}H-NMR and the ^{13}C-NMR analyses. For example, the ^{1}H-NMR spectrum of compound

64e showed a triplet at a chemical shift δ = 0.68 ppm due to a methyl group attached to methylene group and established the *endo*-Ph configuration of the bicyclic oxetane. Additionally, two singlets at δ 1.53 and 3.66 ppm appeared corresponding to CH_3 at C-1 and OCH_3 at C-5, respectively. In the ^{13}C-NMR spectrum, at δ 78.1, 90.3 and 123.6 ppm, three signals appeared characteristic for C-1, C-7 and C-5 of the oxetane ring, respectively. Moreover, both C-3 and COO group resonate at δ 168.6 and 169.6 ppm, respectively.

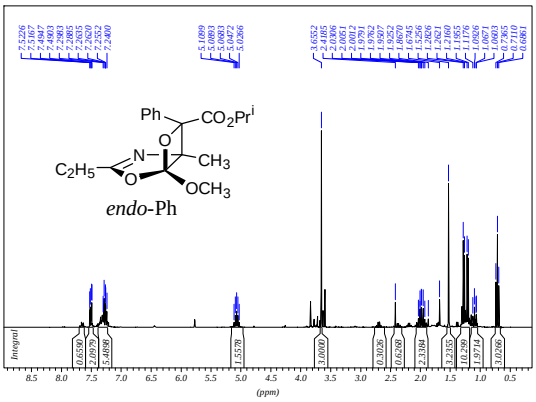


Figure 3.180: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**64e**.

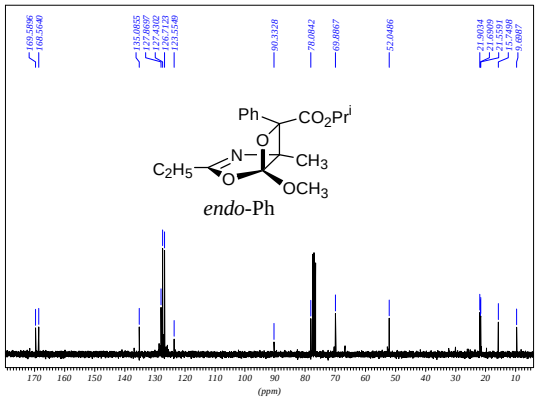


Figure 3.181: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**64e**.

The ^{1}H-NMR spectrum of compound **64f** showed a triplet at 0.67 ppm attributed to the methyl protons of the ethyl group and confirmed the *endo*-Ph configuration. Furthermore, there were three singlets at δ 1.44, 1.54 and 3.66 ppm due to the *tert*-butyl, CH_3 at C-1 and OCH_3 at C-5, respectively. The ^{13}C-NMR spectrum revealed signals at δ 77.9, 90.4, 123.5, 167.9 and 169.5 ppm indicating C-1, C-7, C-5, C-3, and COO group, respectively.

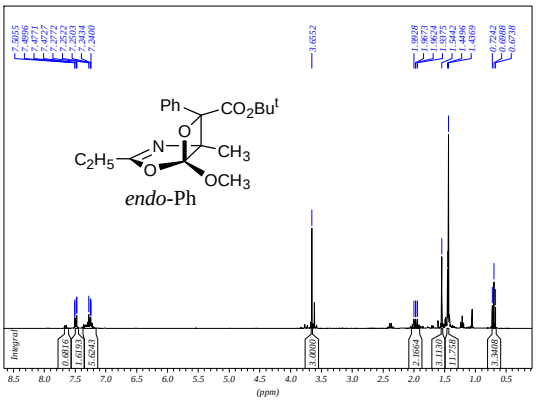


Figure 3.182: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *endo*-**64f**.

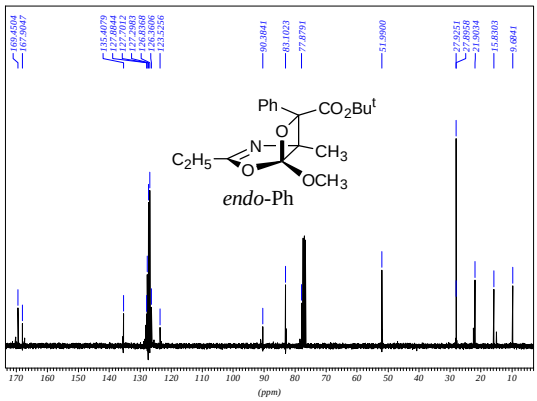
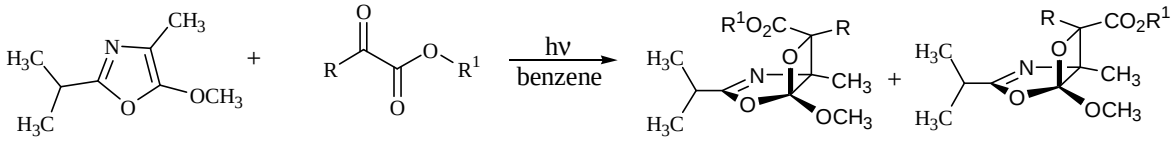


Figure 3.183: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *endo*-**64f**.

3.8.6.2 Photocycloaddition reactions of 2-isopropyl-4-methyl-5-methoxyoxazole with α-keto esters

Irradiation of α-keto ester substrates in benzene in the presence of 2-isopropyl-4-methyl-5-methoxyoxazole resulted in a mixture of diastereoisomers of the bicyclic oxetanes **65a-f** in high chemical yields.



49b *exo*-R-**65a-f** *endo*-R-**65a-f**

Scheme 3.69: Photoreaction of **49b** with α-keto esters.

Table 3.44: Simple diastereoselectivity of the Paternò-Büchi reaction of α-keto esters with 2-isopropyl-4-methyl-5-methoxy oxazole **49b**.

Compound	R =	R^1 =	d.r.(*exo* : *endo*)[a]	Yield (%)[b]
65a	Me	Me	60 : 40	87
65b	t-Bu	Me	70 : 30	90
65c	Ph	Me	69 : 31	94
65d	Ph	Et	67 : 33	80
65e	Ph	i-Pr	42 : 58	83
65f	Ph	t-Bu	37 : 63	85

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectrum of the crude products mixture, [b] yield (%) based on the degree of the conversion of the oxazole.

Surprisingly, the simple *exo*/*endo*-R diastereoselectivity of methyl pyruvate photoadducts **65a** did not only decrease but inverte, compared to the photoadduct from **49a**. For trimethyl methylpyruvate photoadducts **65b**, the *exo*/*endo*-*tert*-butyl diastereoselectivity decreased when compared with the photoadduct from **49a**, but the *exo*-*tert*-butyl isomer still dominated. In case of alkyl phenylglyoxylates photoaddition, by changing the alkyl substituents from Me to Et, the *exo*/*endo*-Ph diastereoselectivity slightly decreased and was complelety inverted when processing from Et to i-Pr and *tert*-Bu. The diastereoisomers of the photoadducts **65a-f** in most cases were isolated by preparative chromatography.

The relative configuration of the major diastereoisomer of compound **65b** was unambiguously determined by NOE experiments. Strong NOE enhancements were detected from *tert*-butyl protons to CH_3 at 1.51 ppm, OCH_3 at 3.57 ppm and OCH_3 at 3.73 ppm, likewise from the methyl protons of isopropyl group at 1.16 ppm to OCH_3 at 3.73 ppm. Thus, the relative configuration is all *exo*- with respect to the *tert*-butyl group at C-7 of the bicyclic oxetane.

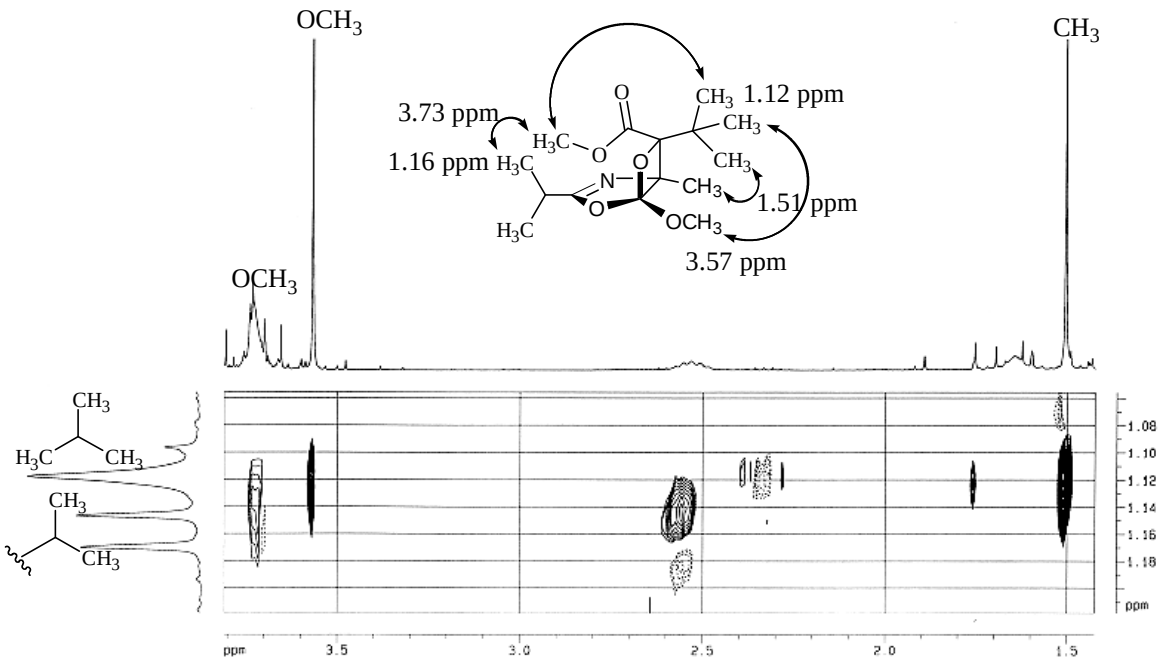


Figure 3.184: NOESY (300 MHz, $CDCl_3$) spectrum of compound **65b**.

The relative configurations of both the *exo*-Ph and the *endo*-Ph diastereoisomers of compound **65f** were determined unambiguously from NOESY studies. For *exo*-Ph isomer, the cross peaks between the phenyl protons resonances at 7.65 ppm and the methyl protons at 1.06 ppm and the methoxy protons at 3.61 ppm indicate a strong NOE-effects and hence spatial proximity (*cis* relationship between Ph, CH_3 and OCH_3 groups) which can be assigned to an *exo*-Ph configuration. Other NOE-effects between the phenyl protons and the *tert*-butyl protons at 1.45 ppm were also detected. For the *endo*-Ph isomer, no interaction between the phenyl protons and the methoxy protons is observable while a weak NOE enhancement is present for the methyl protons at 1.56 ppm and the aromatic protons at 7.27 ppm. Furthermore, cross peaks between a methyl protons of the isopropyl group at 0.72 and 0.79 ppm and the phenyl protons at 7.27 ppm was observed again indicating their spatial proximity.

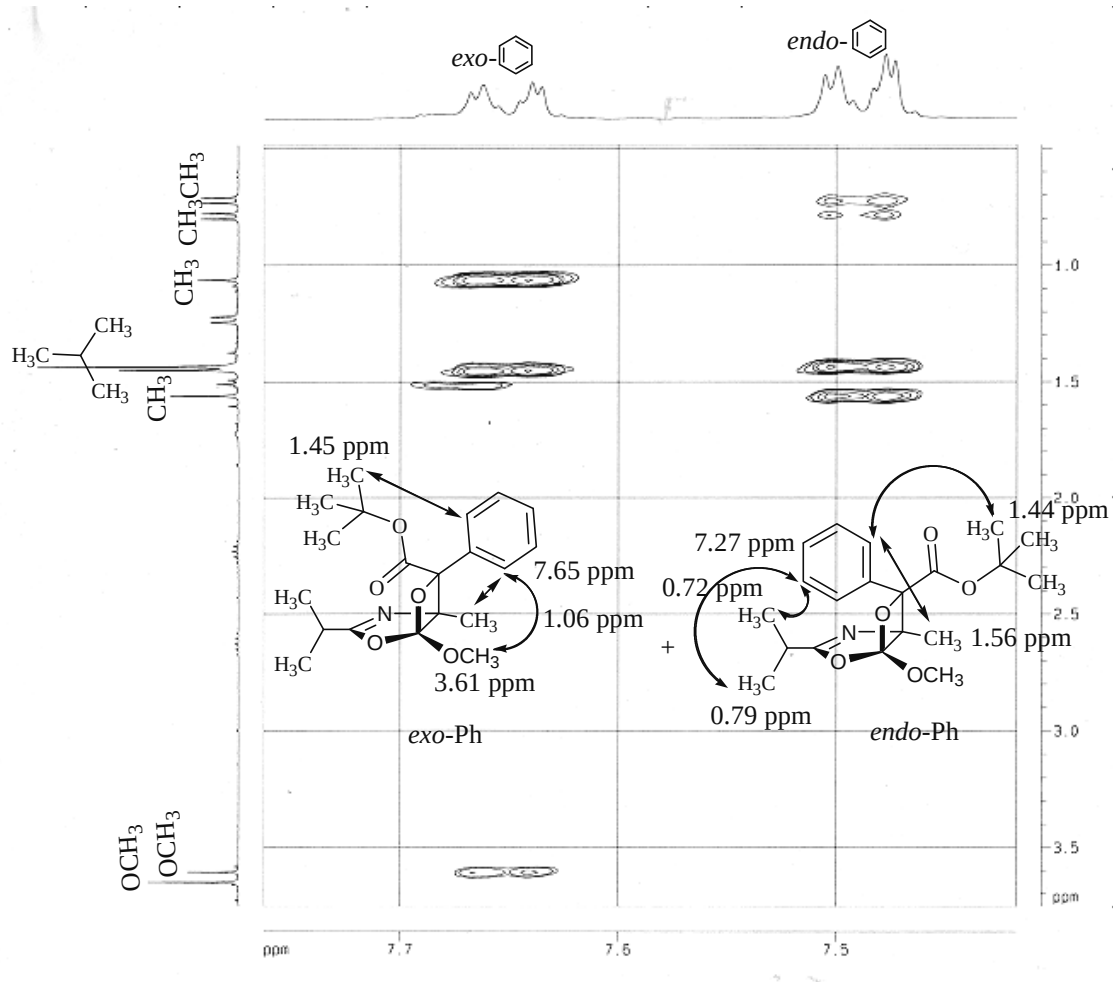


Figure 3.185: NOESY (300 MHz, $CDCl_3$) spectrum of compound **65f**.

The constitutions of compounds **65a-f** were elucidated on the basis of IR, mass spectrometry and NMR analyses. For example, the IR spectrum of compound **65a** showed two strong absorption bands at 1615 and 1740 cm^{-1} corresponding to C=N and ester group, respectively. The ^{1}H-NMR spectrum showed two doublets at δ 0.92 and 1.10 ppm assigned to the isopropyl group. Additionaly, there appeared four singlets at δ 1.44, 1.91, 3.69 and 3.74 ppm corresponding to CH_3 at C-7, CH_3 at C-1, OCH_3 at C-5 and OCH_3 of the ester group, respectively. In the ^{13}C-NMR spectrum, signals at δ 72.4, 87.2, 120.3, 170.4 and 176.2 ppm were attributed to C-1, C-7, C-5, C-3 and COO group, respectively.

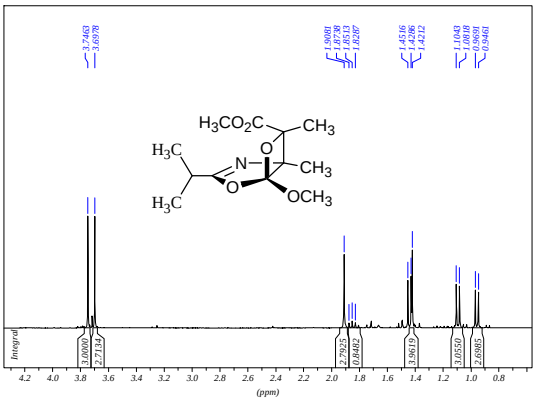


Figure 3.186: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **65a**.

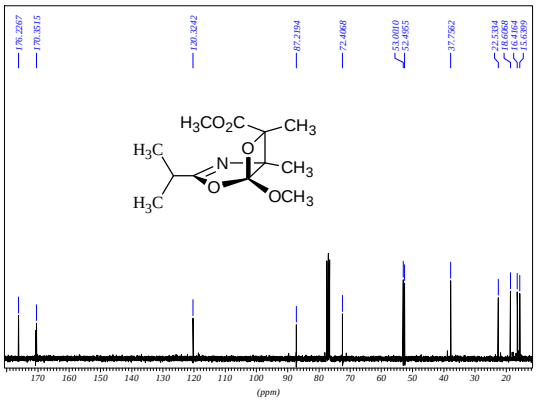


Figure 3.187: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **65a**.

Prove of the chemical structure of compound **65c** was based on NMR analysis. The ^{1}H-NMR spectrum shows two doublets at δ 1.18 and 1.43 ppm due to the isopropyl group. Furthermore, three singlets appeared at δ 1.96, 3.11 and 3.29 ppm attributed to CH_3 at C-1, OCH_3 at C-5 and OCH_3 of ester group, respectively, indicating the *exo*-Ph configuration. In the ^{13}C-NMR spectrum, five signals at 81.3, 92.0, 123.3, 169.1 and 173.4 ppm appeared which were attributed to C-1, C-7, C-5, C-3 and CO, respectively.

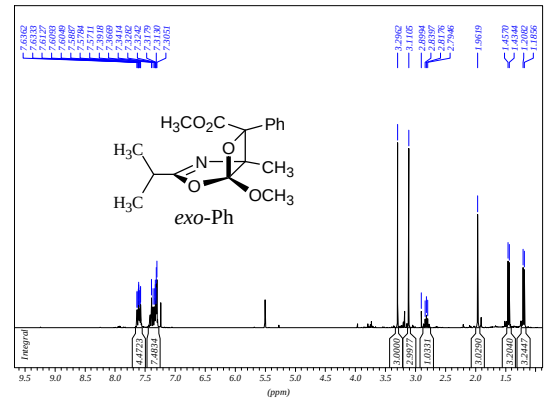


Figure 3.188: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**65c**.

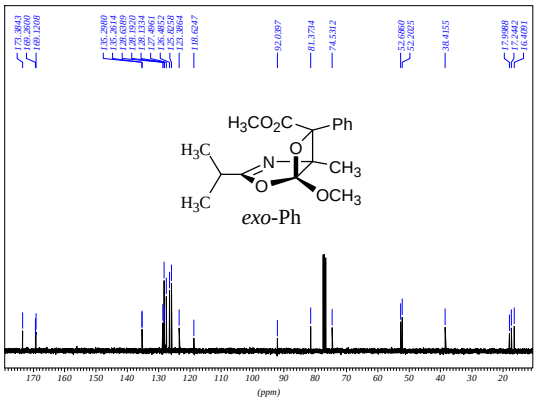


Figure 3.189: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**65c**.

Unfortunately, the diastereoisomers of compound **65e** could not be separated by preparative chromatograpy and hence the constitution of both isomers were determined from the NMR analysis of the diastereoisomer mixture. There are two main differences in the ^{1}H-NMR spectrum between the *exo*- and the *endo*-Ph diastereoisomers as shown in Figure 3.190: (1) the methyl protons of the isopropyl group at C-3 resonates at higher field compared with the

exo-Ph isomer. (2) the methyl protons at C-3 resonates at 2.19 ppm in the *endo*-Ph isomer; while in the *exo*-Ph isomer, this absorption is shifted upfield to 1.06 ppm due to ring current effect of the benzene ring. The ^{13}C-NMR spectrum showed five signals at δ 77.8, 90.2, 123.5, 167.9 and 173.6 ppm related to C-1, C-7, C-5, C-3 and COO group, respectively.

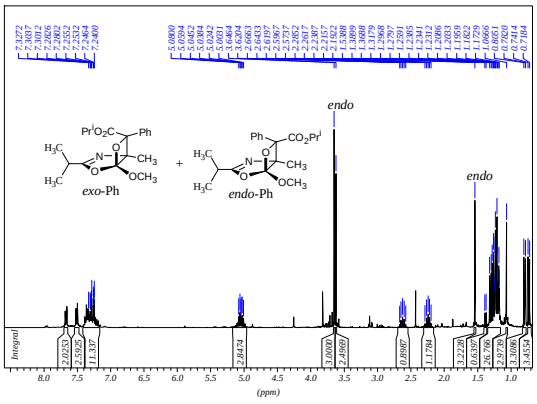


Figure 3.190: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**65e** & *endo*-**65e**.

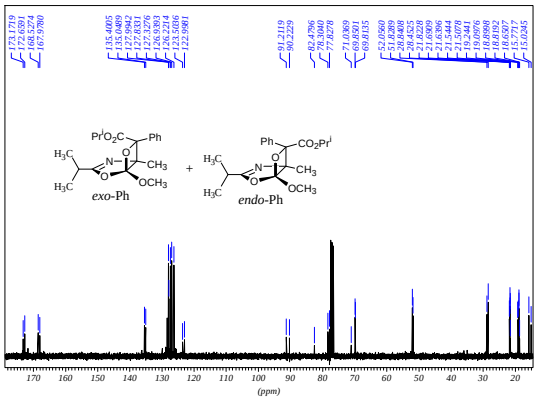


Figure 3.191: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**65e** & *endo*-**65e**.

The diastereoisomers of compound **65f** could not be separated by preparative chromatography and the structure determination was thus based on NMR analysis of the diastereoisomer mixture. Analogous to compound **65e**, there are also two main differences in the ^{1}H-NMR spectrum between the *exo*- and *endo*-isomer: (a) the methyl protons at C-3 in the *exo*-isomer resonates at higher field than in the *endo*-isomer; (b) methyl protons of the isopropyl group at C-3 in the *endo*-isomer appear at 0.71 ppm, while it is shifted in the *exo*-isomer to 1.24 ppm. In the ^{13}C-NMR spectrum three signals appeared at δ 77.6, 90.3, 122.9 ppm corresponding to C-1, C-7 and C-5 of the oxetane ring, respectively.

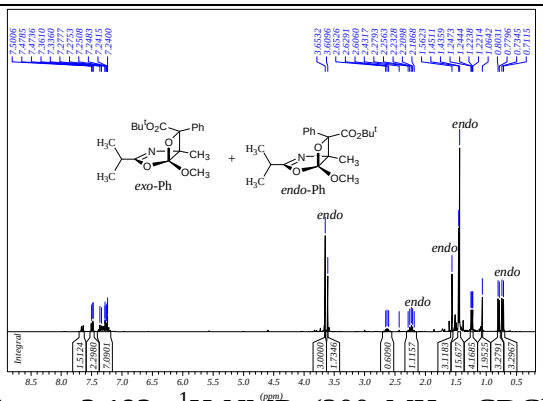


Figure 3.192: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**65f** & *endo*-**65f**.

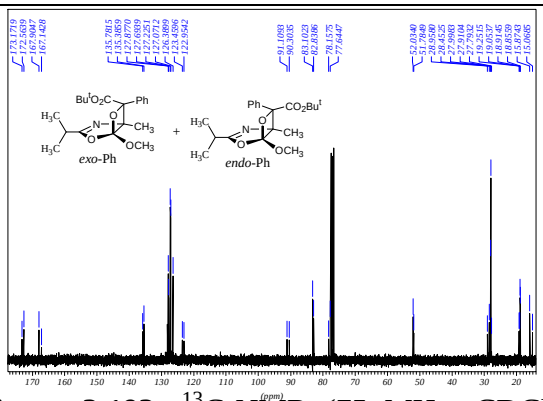
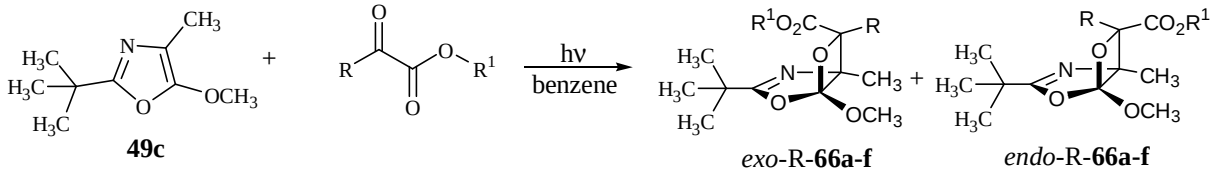


Figure 3.193: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**65f** & *endo*-**65f**.

3.8.6.3 Photocycloaddition reactions of 2-*tert*-butyl-4-methyl-5-methoxyoxazole with α-keto esters

The [2+2]-photocycloaddition of 2-*tert*-butyl-4-methyl-5-methoxyoxazole **49c** with aliphatic and aromatic α-keto esters gave two stereoisomers of the bicyclic oxetanes **66a-f** in high chemical yields.



49c *exo*-R-**66a-f** *endo*-R-**66a-f**

Scheme 3.70: Photoreaction of **49c** with α-keto esters.

Table 3.45: Simple diastereoselectivity of the Paternò-Büchi reaction of α-keto esters with 2-*tert*-butyl-4-methyl-5-methoxy oxazole **49c**.

Compound	R =	R^1 =	d.r.(*exo* : *endo*)[a]	Yield (%)[b]
66a	Me	Me	54 : 46	86
66b	t-Bu	Me	55 : 45	92
66c	Ph	Me	63 : 37	90
66d	Ph	Et	61 : 39	88
66e	Ph	i-Pr	40 : 60	89
66f	Ph	t-Bu	46 : 54	90

[a] based on the integration of characteristic signals in the ^{1}H-NMR spectrum of the crude products mixture, [b] yield (%) based on the degree of conversion of the oxazole.

In case of aliphatic α-keto esters (both methyl pyruvate and trimethyl methylpyruvate) photocycloaddition with **49c**, the simple *exo*/*endo*-R diastereoselectivity substantially decreased compared with the photoadducts of these substrates with **49b**. Whereas, in the case of aromatic α-keto esters, the *exo*/*endo*-Ph diastereoselectivity was inverted when changing the substituents from Et to i-Pr and t-Bu similar to **49b**.

The difference in the heat of formation (ΔH_f) between the *exo*- and *endo*-Ph diastereoisomers of compound **66f** from AM1 is approx. 1.00 kcal/mol. The molecular mechanics calculations revealed, that the observed stereoselectivity corresponds to contrathermodynamic control.

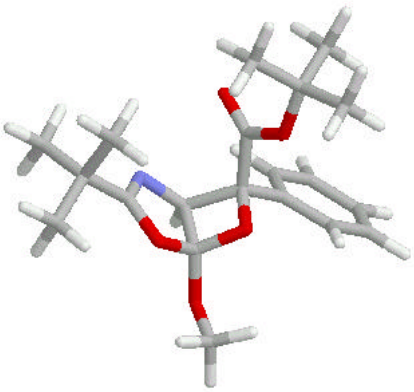


Figure 3.194: PM1 model of *exo*-**66f**.

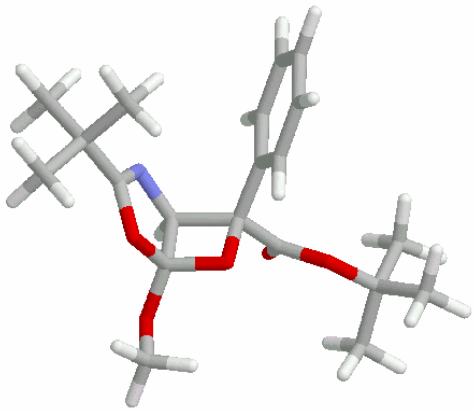


Figure 3.195: PM1 model of *endo*-**66f**.

In most cases, the diastereoisomers of compound **66a-f** were successfully separated by preparative chromatography except compounds **66a** and **66f** which were separated from the crude reaction mixtures as pair of stereoisomers.

The relative configuration of the major diastereoisomer of compound **66b** was unambiguously determined by NOE experiment. Irradiation of the *tert*-butyl protons at 1.12 ppm led to NOE enhancement of both signals of the methyl protons at 1.50 ppm and the methoxy protons at 3.56 ppm. Furthermore, NOE enhancement was observed for *tert*-butyl protons signal at 1.18 ppm when methoxy protons signal at 3.73 ppm irradiated.

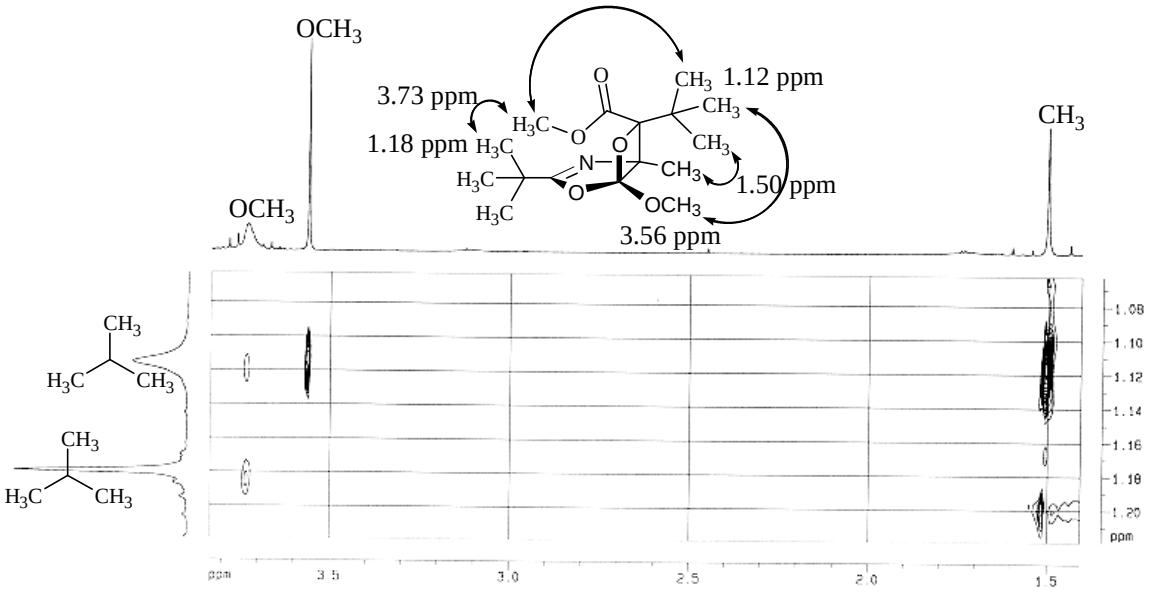


Figure 3.196: NOESY (300 MHz, $CDCl_3$) spectrum of compound **66b**.

The relative configuration of the *exo*- and *endo*-Ph diastereoisomers of compound **66f** were unambiguously determined by NOE measurement. For the *endo*-Ph isomer, cross peaks between the phenyl protons at 7.49 ppm and *tert*-butyl protons at 0.82 ppm indicate a strong NOE-effect and hence spatial proximity (*cis* relationship between Ph and *tert*-butyl group). Other NOE effects between the phenyl protons and the *tert*-butyl at 1.58 ppm and the methyl protons at 1.58 ppm were determined. For the *exo*-Ph isomer, no interaction between the *tert*-butyl protons and phenyl protons is observable while a weak one is present for *tert*-butyl protons at 1.45 ppm and the phenyl protons at 7.65 ppm. Furthermore, a cross peak between the methyl protons at 1.07 ppm and phenyl protons at 7.65 ppm was observed again indicating their spatial proximity.

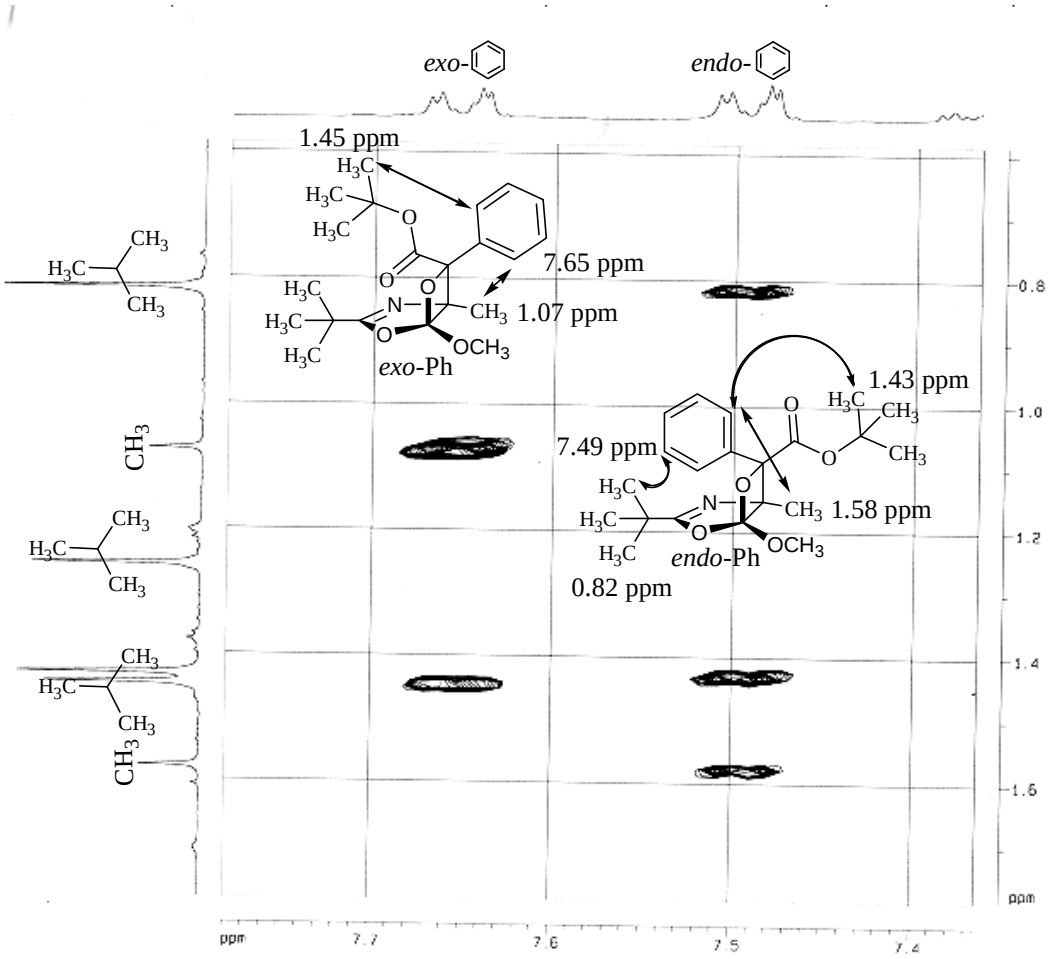


Figure 3.197: NOESY (300 MHz, $CDCl_3$) spectrum of compound **66f**.

The structural assignments of compound **66a-f** were made on the basis of the spectroscopic data. The ^{1}H-NMR spectrum of compound **66a** showed five singlets at δ 0.93, 1.35, 1.81, 3.67 and 3.77 ppm attributed to *tert*-butyl group, CH_3 at C-7, CH_3 at C-1, OCH_3 at C-5 and OCH_3

of ester group respectively. In the ^{13}C-NMR spectrum, there appeared three signals at 74.0, 86.7 and 124.1 ppm attributed to C-1, C-7 and C-5 of the oxetane ring, respectively.

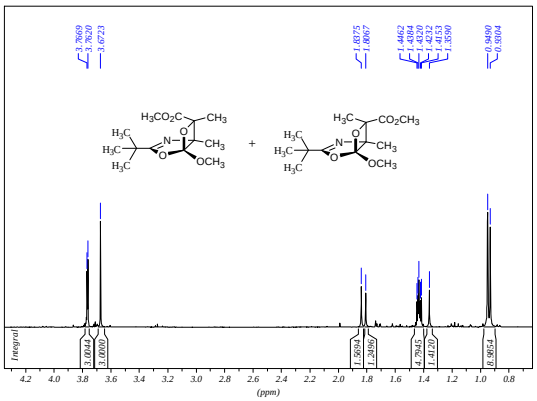


Figure 3.198: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **66a**.

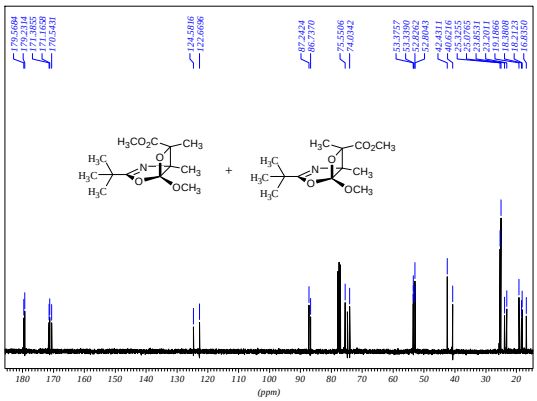
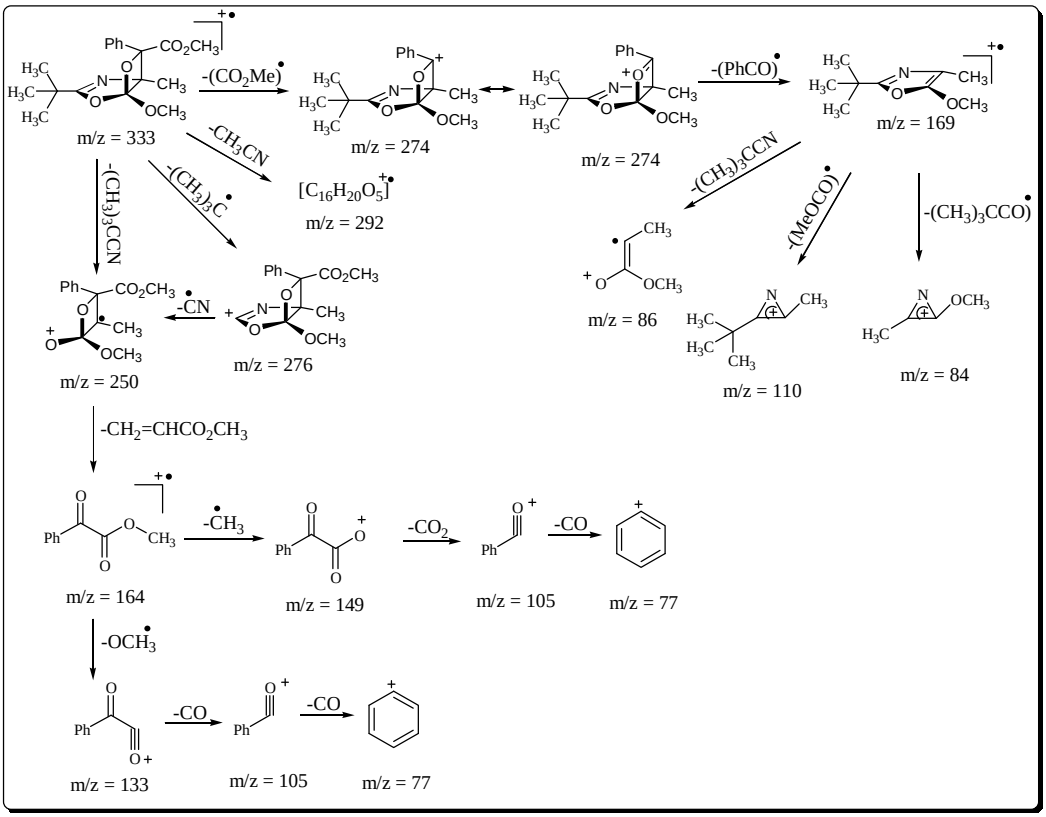


Figure 3.199: ^{13}C-NMR (75 MHz, $CDCl_3$) of compound **66a**.

Prove the chemical structure of compound **66c** was based on IR, mass spectra and NMR analyses. The IR spectrum showed two strong absorption bands at 1617 and 1735 cm^{-1} indicating the presence of an C=N and C=O of ester group, respectively. The mass spectrum showed a base peak at m/z 292 due to [M^+ - CH_3CN]. Furthermore, the fragmentation pattern is summarized in scheme 3.71.



Scheme 3.71: Fragmentation pattern of compound **66c**.

The ^{1}H-NMR spectrum showed four singlets at δ 1.08, 1.25, 3.63 and 3.75 ppm attributed to CH_3 at C-1, *tert*-butyl group at C-3, OCH_3 at C-5 and OCH_3 of the ester group, respectively, and assigned to the *exo*-Ph configuration. In the ^{13}C-NMR spectrum, signals appeared at δ 78.6, 91.6, 123.2 ppm due to C-1, C-7 and C-5 of the oxetane ring, respectively. Moreover, both C-3 and COO resonate at lower field at δ 169.0 and 175.6 ppm, respectively.

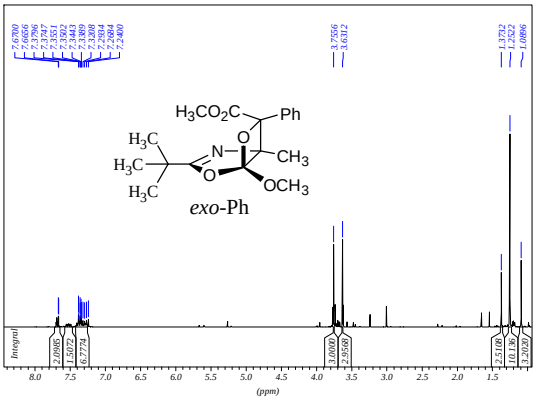


Figure 3.200: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**66c**.

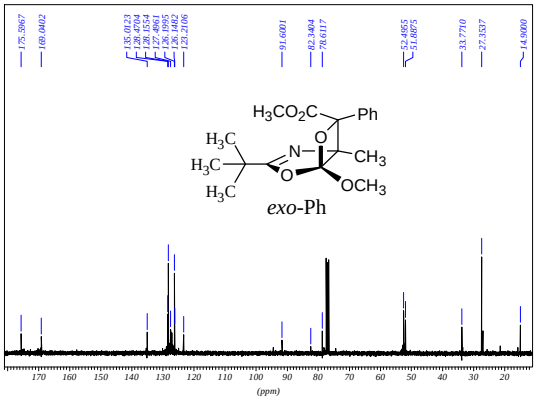


Figure 3.201: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**66c**.

Figure 3.202 shows the ^{1}H-NMR spectrum of the *exo*-Ph and *endo*-Ph diastereoisomers of compound **66f**. The *tert*-butyl protons resonances of the *exo*-isomer appear at 1.22 ppm while in the *endo*-isomer this absorption is shifted upfield to 0.78 ppm due to the ring current effect of the benzene ring. The ^{13}C-NMR spectrum revealed signals at δ 77.8, 90.2 and 123.0 ppm corresponding to C-1, C-7 and C-5 of the oxetane ring, respectively.

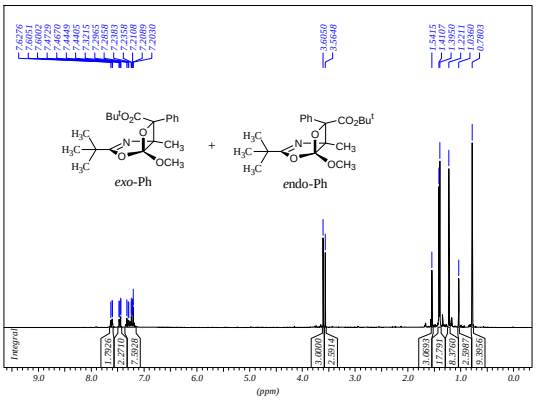


Figure 3.202: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *exo*-**66f** & *endo*-**66f**.

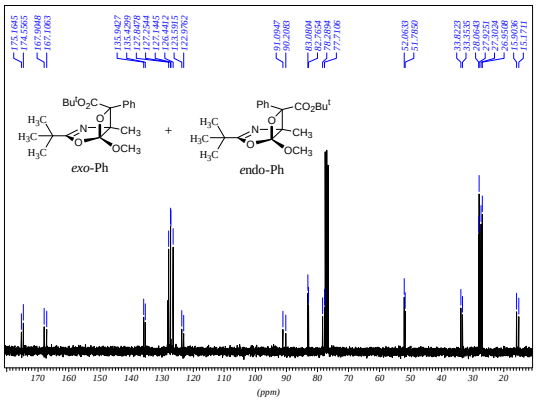
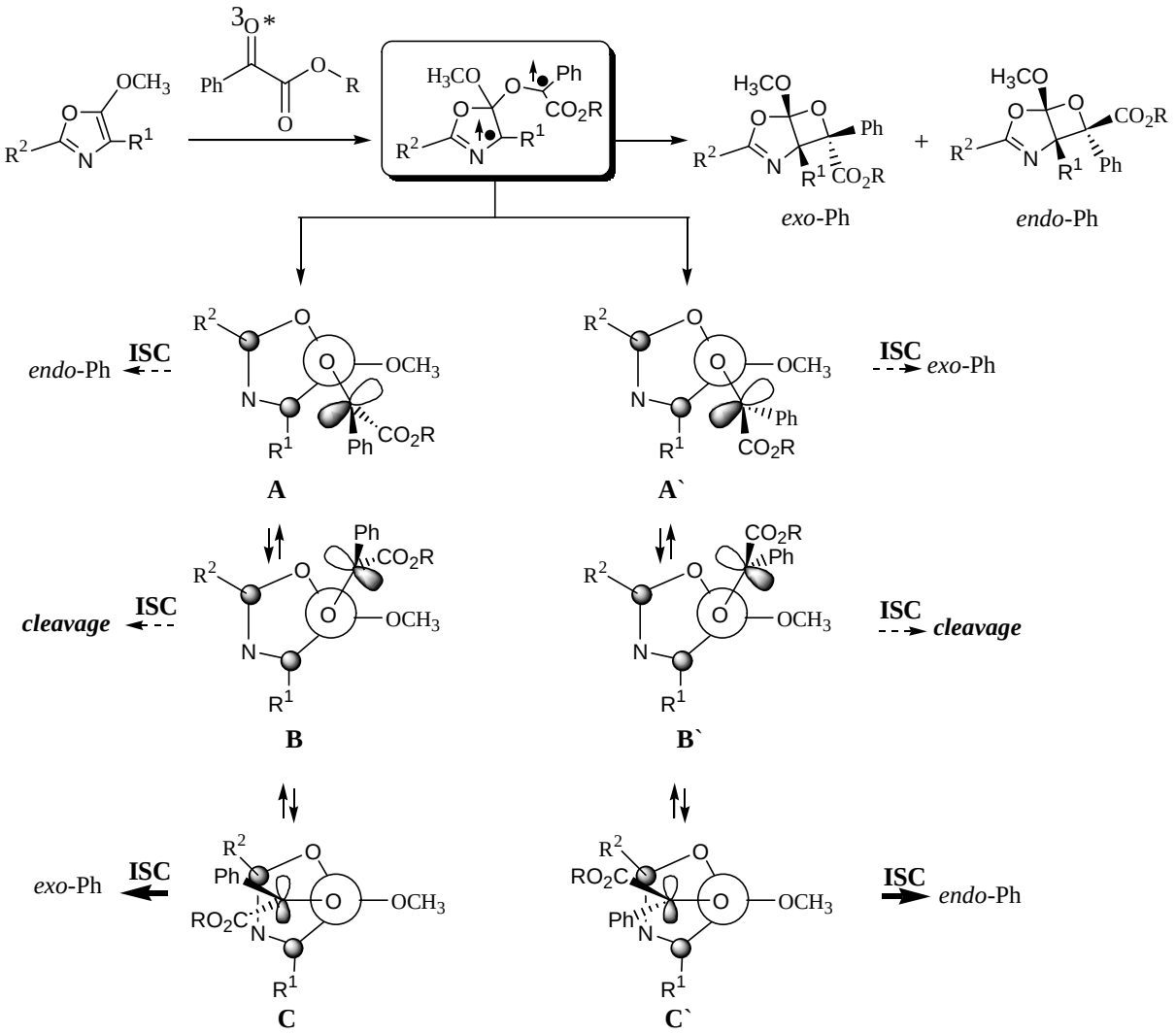


Figure 3.203: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *exo*-**66f** & *endo*-**66f**.

Mechanistic analysis

The regioselectivity of the Paternò-Büchi reaction of aliphatic and aromatic α-keto esters with 5-methoxyoxazoles with additional alkyl substituents either in position C-2 or C-4 is high and corresponds to the classical 1,4-biradical stablization concept. The stereochemistry of the triplet 1,4-biradical is attributed to a conformational memory effect during the intersystem crossing (ISC) process of the triplet 1,4-biradical. According to the Salem-Rowland rules,[28] strong spin-oribt coupling (SOC) occurs when the p-orbitals at the spin-bearing atoms are orthogonal to each other. The possible conformers (**A-C)** of the triplet 1,4-biradical are represented by the Newman projections **A**, **B** and **C**, and **A`** , **B`** and **C`** in Scheme 3.72. Bulky phenyl group prefer to stay away from the former oxazole ring so that conformers **A**-**C** are favored over **A`- C`**. Among **A**-**C**, **A** and **B** are expected to be similary populated wheras **C** is higher in energy. ISC from **A** leads to immediate C-C bond formation, whereby the phenyl group is rotated over the former oxazole ring plane resulting in the *endo*-Ph product. ISC from **B** leads to cleavage of the initially formed C-O bond restoring the starting materials. Similarly, ISC from **C** gives the ***exo***-Ph product. The experimental results show that the *exo*-Ph product is dominant, thus an interaction between the allylic and exocyclic radical in triplet 1,4-biradical (SOI) as depicted in conformer **C** must be crucial for the dominance of this biradical geometry for rapid ISC. The relative stabilities of **A** and **C** depend on the the size of both the substituent R^1 in the oxazole moiety and the size of the α-substituent of the phenyl carbonyl compounds. When the α-substituent is small (such as H) compared to the benzene ring, **C** is the conformer responsible for product formation and the *exo*-Ph is selectively produced. When the α-substituent is large as in the case of COOR, steric interactions between COOR and R^1 disfavor conformer **C**, and hence the amount of *exo*-Ph isomer is expected to be decreased. If only conformers **A**-**C** are responsible for product formation, the *exo*/*endo*-Ph selectivity should not alter significantly with the change of the alkyl group at position C-2 of the oxazole because the same phenyl substituent is involved in all these compounds, and therefore the energy differences between **A** and **C** are expected to be similar with different COOR groups. However, I observed significat changes in the product stereochemisty with variation of the alkyl substituent at position C-2 indicating that the other set of conformers **A`**-**C`** also plays a role in the product formation process. Analogously to the situation in **A**-**C**, **A`** leads to the *exo*-Ph product, **C`** leads to the *endo*-Ph product and **B`** restores the starting materials after ISC. Conformer **C`** is highly congested but still populated because secondary orbital interaction facilitates ISC by means of an increase in spin-orbit coupling and furnishes the *endo*-Ph product. Therefore, when the alkyl substituent at position C-2 in oxazole is small

enough to populate conformer C, *exo*-Ph products results preferentially. Bulky alkyl groups at position C-2 of oxazole favor conformer **C`** and this leads to *endo*-Ph-isomer.



Scheme 3.72: Mechanistic scenario of the oxazoles-α-keto esters photocycloaddition reaction.

Comment

The results of the stereochemistry study of the photocycloaddition of 5-methoxyoxazoles with alkyl phenylglyoxylates are remarkable because the stereochemistry did decrease in contrast to the results described by Scharf and coworkers,[78] and additionally the direction of the stereocontrol has inverted.

The results of the photocycloaddition of α-keto esters with 5-methoxyoxazoles bearing an additional substituent either in position C-2 or C-4 suggest, that secondary orbital interactions (SOI) may play an important role for determining stereoselectivities.

The important findings from the α-keto esters–oxazole photocycloaddition reactions are as follows:

(1) Methyl pyruvate adds photochemically to 5-methoxyoxazole with high regio- and stereoselectivity when the oxazole substrate has small alkyl substituents (Me or Et) in position C-2 and irrespectively of the nature of alkyl substituent in position C-4. The stereoselectivity decreased when bulky alkyl substituents (i-Pr and t-Bu) in position C-2 were employed.

(2) The stereoselectivity of the photocycloaddition of methyl trimethylpyruvate with oxazoles was strongly influenced by the size of alkyl substituent either in position C-2 or C-4.

(3) The *exo*/*endo*-Ph diastereoselectivity of the photocycloaddition of alkyl phenylglyoxylates with 4-substituted oxazoles decreased with increasing steric demand of the alkyl group either in the oxazole moiety or phenylglyoxylate moiety, albeit the *exo*-Ph isomer is still favored.

(4) Using bulky alkyl substituents (i-Pr & t-Bu) either in position C-2 of oxazole substrates or in alkyl phenyl glyoxylates led to an inversion of the *exo*/*endo* diastereoselectivity and the *endo*-Ph isomer was formed preferentially.

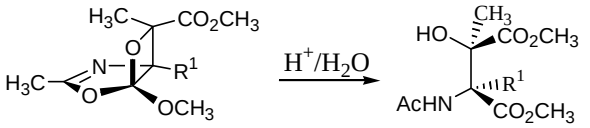
(5) The facial selectivity for both *exo* and *endo* photoadducts of the photocycloaddition of menthyl phenylglyoxylate to oxazole substrates was low, wheras the simple *exo*/*endo*-Ph diastereoselectivity was moderate.

3.9 Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-amino-b-hydroxy succinic acid derivatives

From a synthetic point of view, the bicyclic oxetanes obtained by the Paternò-Büchi reaction of aliphatic and aromatic α-keto esters with 5-methoxyoxazoles are not only interesting by themselves, but also because they might serve as bulding blocks for the stereoselective construction of α-amino-β-hydroxy succinic acid derivatives. Ring opening of the bicyclic oxetanes represents the simplest and straight forward strategy for the stereoselective synthesis of *erythro* (S*,R*) and *threo* (S*,S*) α-amino-β-hydroxy succinic acid derivatives depending on the relative configuration of a substituent at C-7.

3.9.1 Synthesis of *erythro* (S*,R*) a-acetamido-b-hydroxy succinic acid derivatives 67a-f

Acid treatment of the bicyclic oxetanes **54a-f** led to the formation of *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **67a-f** in high chemical yields.



54a-f **erythro (S*,R*)-67a-f**

Scheme 3.73: Synthesis of *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **67a-f**.

The relative configurations of the ring-opened products **67a-f** were expected to be *erythro* (S*,R*) since the bicyclic oxetane precursors had *exo*-CO_2CH_3 configuration as was shown by NOE measurement. As ultimate proof, the *erythro* (S*,R*) stereochemistry of compound **67b** was confirmed by X-ray analysis, depicted in Figure 3.204.

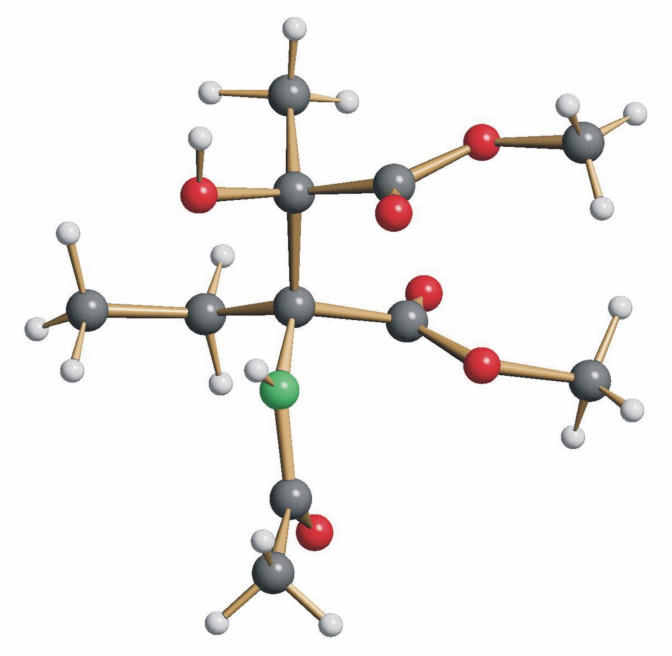


Figure 3.204: X-ray analysis of compound **67b**.

The structure assignments of the photoaldol products **67a-f** were based on IR, mass spectra and NMR analyses. For example, the IR spectrum of compound **67d** showed five strong absorption bands at 3510, 3340, 1745, 1735 and 1685 cm^{-1} indicating the presence of OH, NH, COO, COO and CON groups, respectively. In the ^{1}H-NMR spectrum at δ 0.88 and 1.24 ppm, two doublets appeared assigned to two methyl protons of the isopropyl group. The acetyl methyl protons appears at δ 2.02 ppm. The ^{13}C-NMR spectrum showed signals at δ 73.6, 82.4, 171.1, 171.6 and 174.9 ppm corresponding to C-2, C-3, CON, COO and COO groups, respectively.

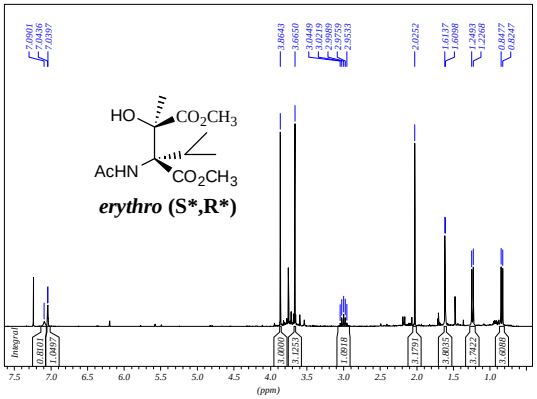


Figure 3.205: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **67d**.

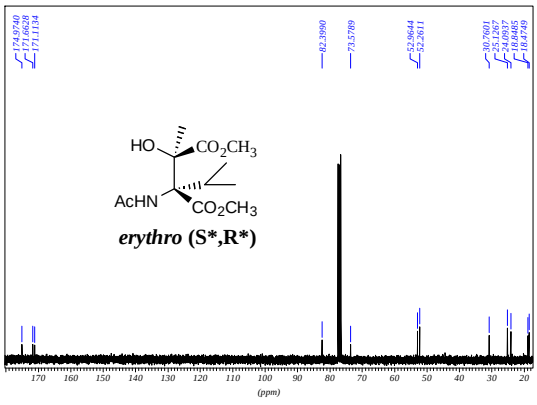


Figure 3.206: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of compound **67d**.

The ^{1}H-NMR spectrum of compound **67f** showed four singlets at δ 1.56, 2.03, 3.56 and 3.65 ppm corresponding to CH_3, $\underline{CH_3}CO$, OCH_3 and OCH_3 groups, respectively. The amide proton absorbs at 6.53 ppm. In the ^{13}C-NMR spectrum, there signals at δ 82.4, 89.7, 164.7, 171.3 and 172.5 ppm appeared which were attributed to C-2, C-3, CON, COO and COO groups, respectively.

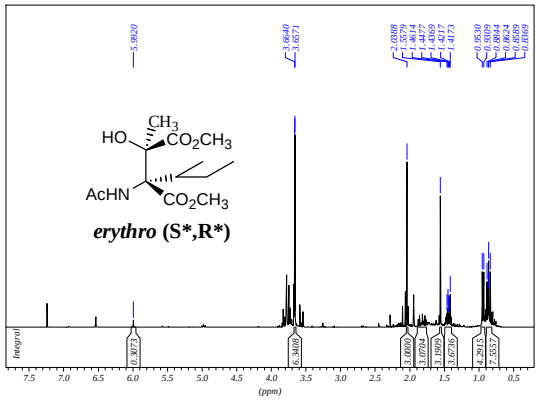


Figure 3.207: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **67f**.

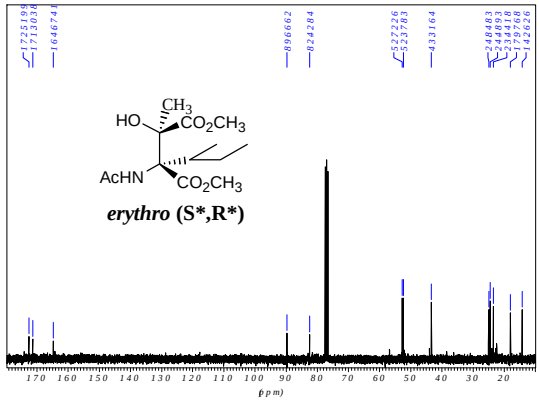
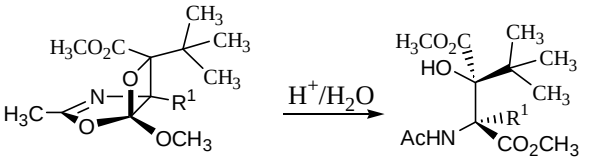


Figure 3.208: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of compound **67f**.

3.9.2 Synthesis of *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 68a-f

The *exo-tert*-butyl bicyclic oxetanes **56a-f** underwent twofold ring opening when treated with a mild acid and led to the formation of *threo* (S*,S*) α-acetamido-β-hydroxy succinic acid derivatives **68a-f** in high chemical yields.



56a-f ***threo* (S*,S*)-68a-f**

Scheme 3.74: Synthesis of *threo* (S*,S*) α-acetamido-β-hydroxy succinic acid derivatives **68a-f**.

The ring-opening reaction is stereospecific; only one stereoisomer is formed. Again, the relative configurations of the products were expected to be *threo* (S*,S*), since the oxetanes precursor had *exo-tert*-butyl configuration as indicated by NOE measurement.

Proving the chemical structure of compounds **68a-f** were based on IR and NMR analyses. For example, the IR spectrum revealed five strong absorption bands at 3490, 3360, 1740, 1735 and 1685 cm^{-1} indicating the presence of OH, NH, COO, COO, CON groups, respectively.

The ^{1}H-NMR spectrum of compound **68a** showed five singlets at δ 1.11, 1.49, 1.97, 3.56 and 3.72 ppm attributed to the *tert*-butyl, CH_3, $\underline{CH_3}CO$, OCH_3 and OCH_3 groups, respectively. In the ^{13}C-NMR spectrum, signals at δ 80.7, 82.3, 169.8, 177.5, 180.9 appeared corresponding to C-2, C-3, CON, COO and COO groups, respectively.

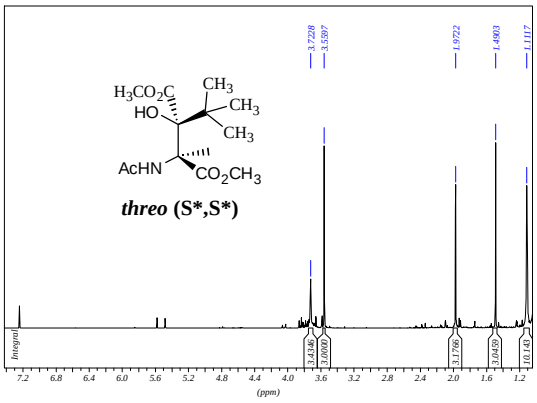


Figure 3.209: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **68a**.

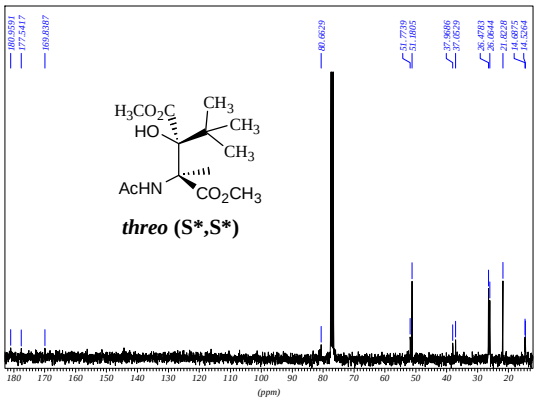
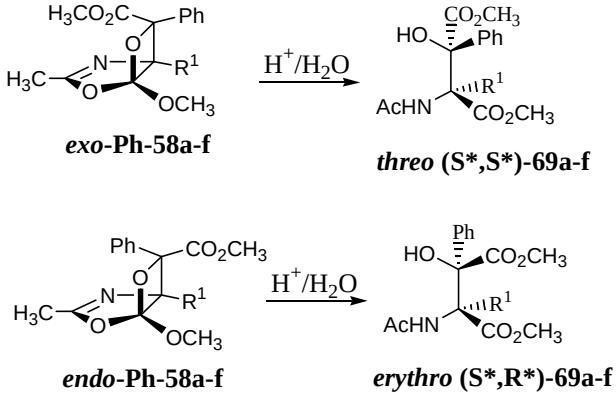


Figure 3.210: ^{13}C-NMR (75MHz, $CDCl_3$) spectrum of compound **68a**.

3.9.3 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 69a-f

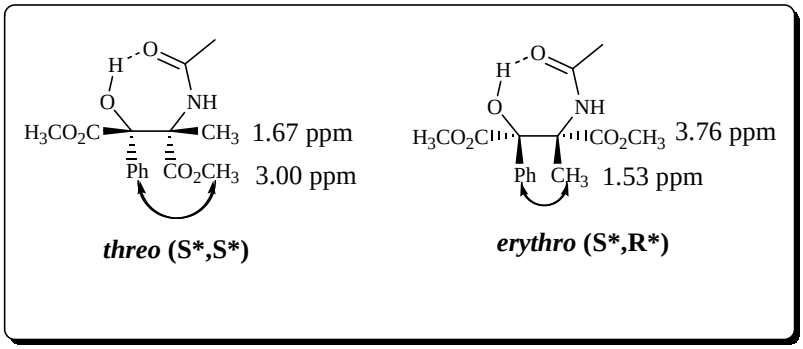
Acid-treatment of the chromatographically separated *exo*-Ph and *endo*-Ph diastereoisomers of the bicyclic oxetanes **58a-f** led to the formation of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **69a-f** in 80-90 % yields, respectively.



Scheme 3.74: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **69a-f**.

The relative configurations of the products **69a-f** were determined on the basis of the characteristic signals in NMR spectra of the diastereoisomeric aldol products. For example, in

the ^{1}H-NMR spectra of the *erythro*-isomer, the methoxy group appears around 3.7 ppm, while in the *threo*-isomer this absorption is shifted upfield to 3.0 ppm due to ring current effect of the benzene ring. Also the chemical shift of the α-alkyl group appears at higher field in the *erythro*-isomer than in the *threo*-isomer. As already described for the photoaldol adduct from aldehydes, both *threo* and *erythro*-isomer favor conformations which are stabilized by hydrogen bonding. This phenomena is displayed in scheme 3.76 and supported by NOE measurement.



Scheme 3.76: Explanation model.

The constitutions of compounds **69a-f** were confirmed by IR, mass spectra and NMR analyses. For example, the IR spectrum of compound **69b** showed absorption bands at 3500, 3340, 1745, 1735, 1670, 1600 cm^{-1} indicating the presence of the OH, NH, COO, COO, CON, and Ph groups, respectively.

In the ^{1}H-NMR spectrum of compound **69b**, there are two striking differences between the *erythro*- and the *threo*-isomers: (a) the methoxy carbonyl group at C-2 in the *threo*-isomer appears at higher field (δ = 3.0 ppm) than in the *erythro*- isomer which resonates at 3.76 ppm; (b) the diastereotopic protons of the methylene group at C-2 appear down-field shifted in the *threo*-isomer at 2.46 ppm, while in the *erythro*-isomer this resonance is shifted upfield to 2.0 ppm. The ^{13}C-NMR spectra revealed that a significant difference in the chemical shifts of C-2 and C-3 by ca. 10 ppm depending on the configuration; the *threo*-isomer shows the low-field shifted signals (see Figure 3.212 and 3.214).

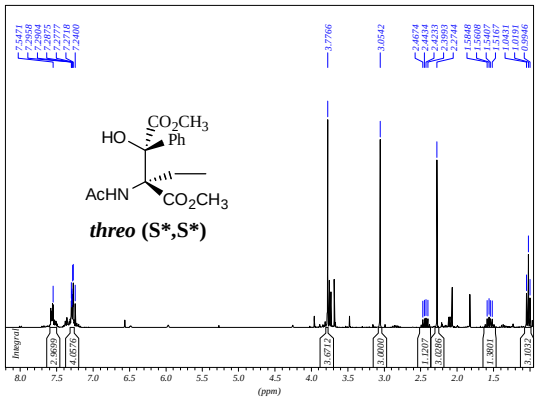


Figure 3.211: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***threo*-69b**.

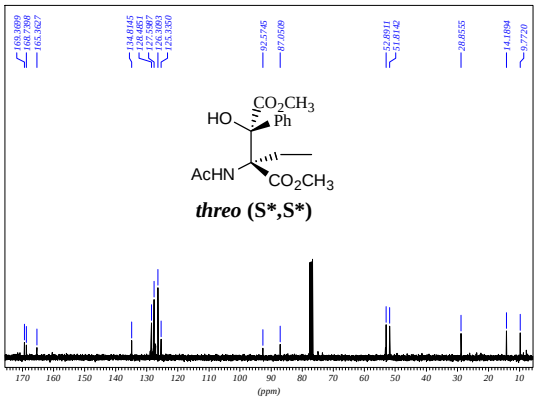


Figure 3.212: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***threo*-69b**.

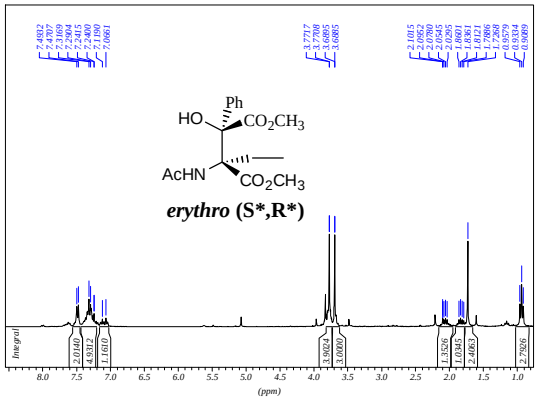


Figure 3.213: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***erythro*-69b**.

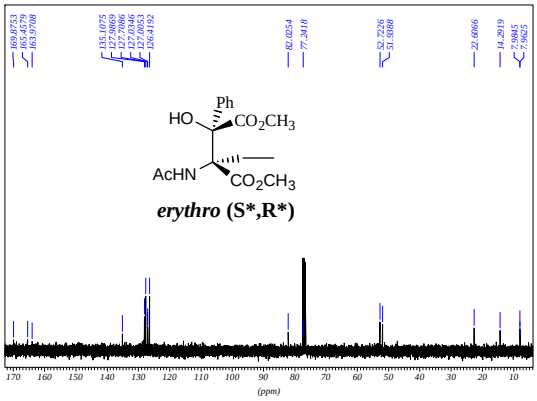


Figure 3.214: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***threo*-69b**.

The ^{1}H-NMR spectrum of compound **69c** showed three singlets at δ 2.23, 3.00 and 3.75 ppm attributed to $\underline{CH_3}CO$, OCH_3 and OCH_3 groups, respectively, and confirmed the *threo*-configuration. In the ^{13}C-NMR spectrum, five signals at δ 86.6, 92.6, 165.2, 168.7, 169.5 ppm appear corresponding to C-2, C-3, CON, COO and COO groups, respectively.

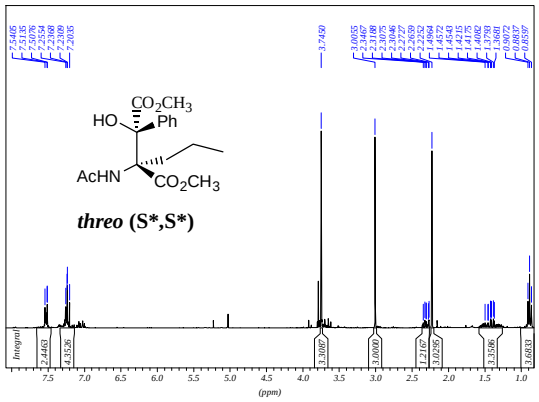


Figure 3.215: ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) spectrum of ***threo*-69c**.

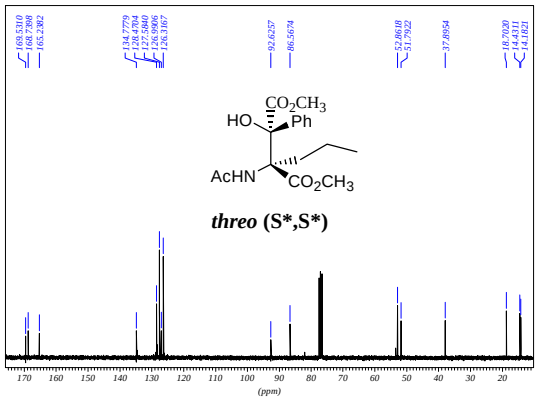


Figure 3.216: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***threo*-69c**.

Figure 3.217 shows the HMQC spectrum which also confirmes the NMR assignments. Figure 3.218 shows the HH-COSY spectrum; the off-diagonal cross peak correctly correlate the coupled protons.

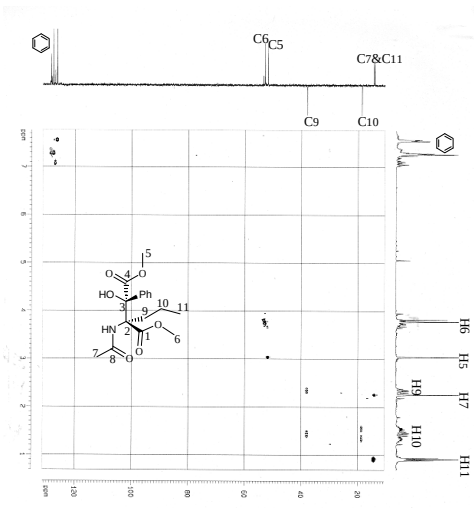


Figure 3.217: HMQC (300 MHz, $CDCl_3$) spectrum of compound **69c**.

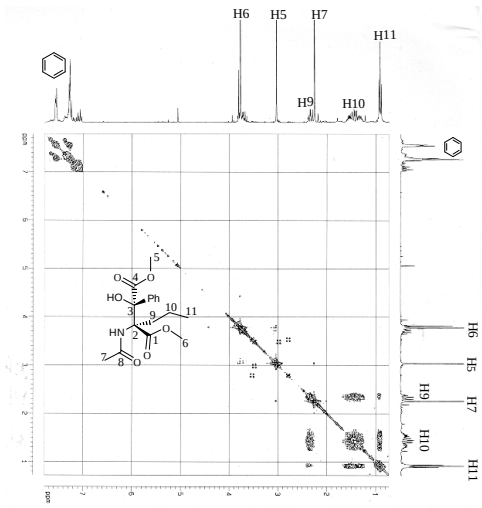
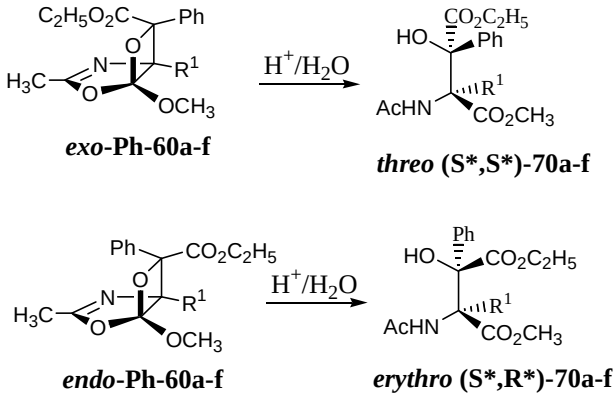


Figure 3.218: HH-COSY (300 MHz, $CDCl_3$) spectrum of compound **69c**.

3.9.4 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 70a-f

Analogous to compounds **58a-f**, ring opening of the *exo*- and *endo*-Ph bicyclic oxetanes **59a-f** procceeded with retention of configuration and gave the *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **70a-f** in high chemical yields, respectively.



Scheme 3.77: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **70a-f**.

The constitution of compounds **70a-f** was established on the basis of IR and NMR analyses. For example the IR spectrum of compound **70e** exhibits five strong absorption bands at 3490, 3360, 1755, 1729 and 1680 cm^{-1} indicating the presence of the OH, NH, COO, COO and CON groups, respectively. Additionally, a band at 1580 cm^{-1} suggests the presence of phenyl group. The ^{1}H-NMR spectrum revealed two singlet signals at 2.26 and 3.05 ppm due to $\underline{CH_3}CO$ and OCH_3 groups, respectively, and indicates the *threo*-configuration. In addition, a quartet at 4.24 ppm appeared which was attributed to the $O\underline{CH_2}$ group. In the ^{13}C-NMR spectrum five signals at δ 86.4, 92.9, 164.7, 168.1 and 170.1 ppm appear attributed to C-2, C-3, CON, COOEt and COOMe groups, respectively.

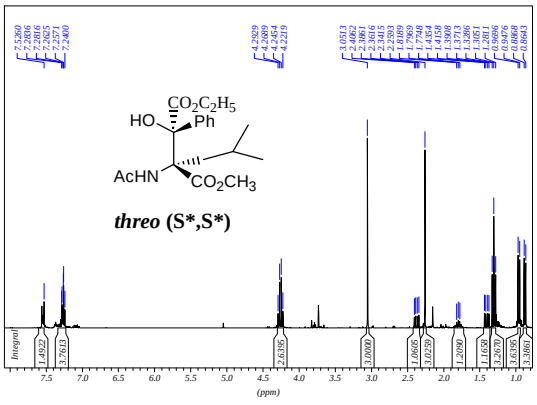


Figure 3.219: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***threo*-70e**.

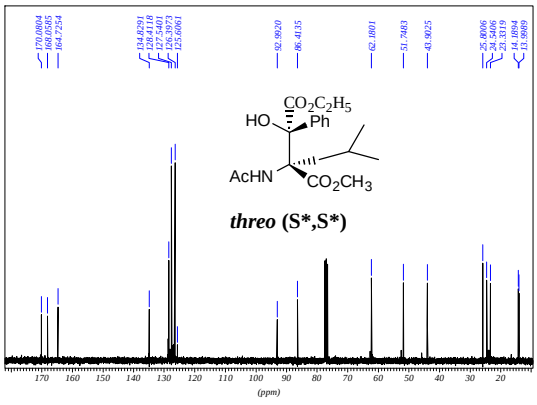


Figure 3.220: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***threo*-70e**.

Figure 3.221 shows the HMQC spectrum which also confirmes the NMR assignments.

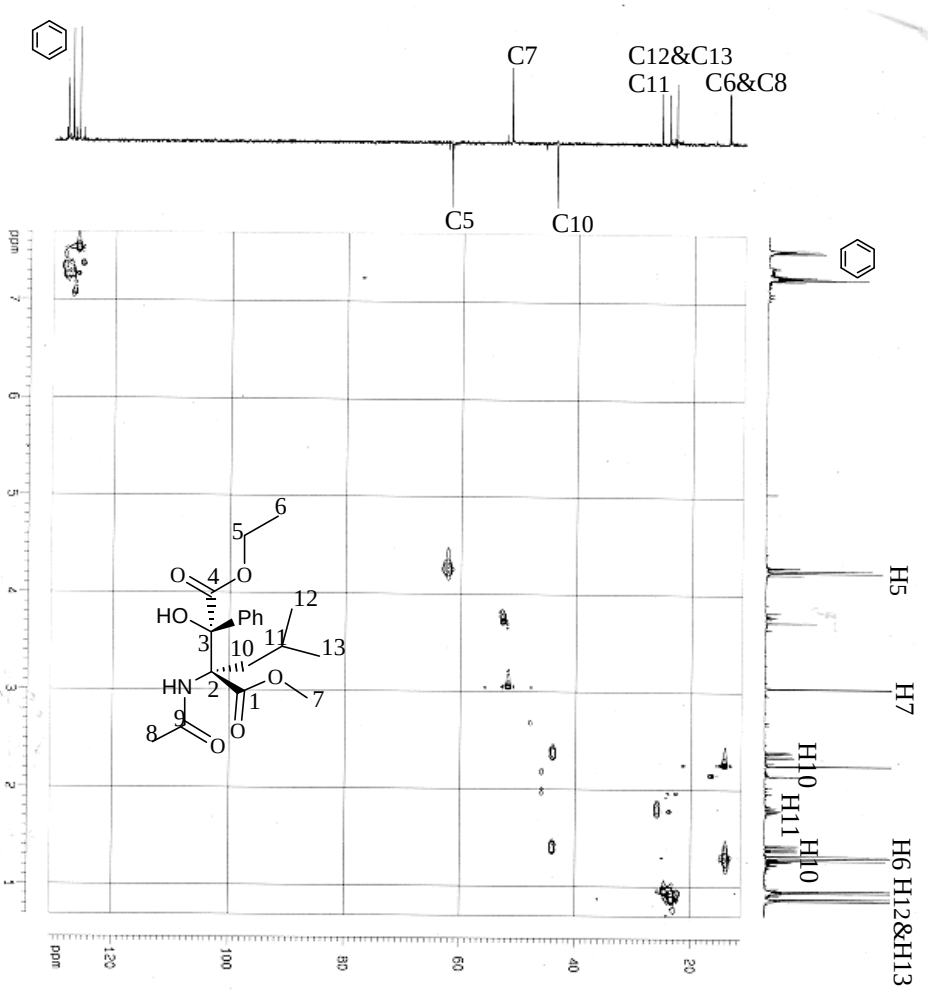
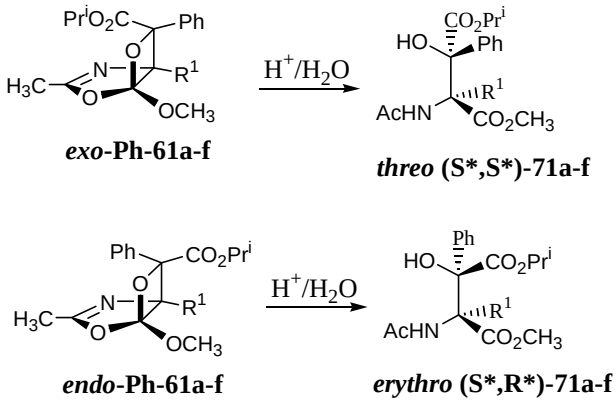


Figure 3.221: HMQC (300 MHz, $CDCl_3$) spectrum of compound **70e**.

3.9.5 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-amino-b-hydroxy succinic acid derivatives 71a-f

Acid hydrolysis of the chromatographically separated *exo*-Ph and *endo*-Ph bicyclic oxetanes **61a-f** furnished *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **71a-f** in high chemical yields, respectively.



***exo*-Ph-61a-f** ***threo* (S*,S*)-71a-f**

***endo*-Ph-61a-f** ***erythro* (S*,R*)-71a-f**

Scheme 3.78: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **71a-f**.

The chemical structures of compounds **71a-f** were established on the basis of NMR analyses. For example, the ^{1}H-NMR spectrum of compound **71c** revealed two singlets at δ 2.26 and 3.04 ppm indicating the presence of $\underline{CH_3}CO$ and OCH_3 groups, respectively, and assigned the *threo*-configuration. Additionally, the methine proton appears at 5.03 ppm. In the ^{13}C-NMR spectrum, five signals at 86.3, 92.5, 165.4, 167.6 and 169.7 ppm appeared, corresponding to C-2, C-3, CON, COO and COO groups, respectively, and reconfirmed the *threo* assignment (see Figure 3.222 & 3.223).

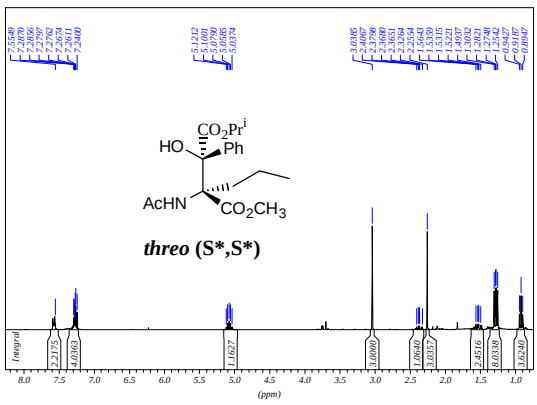


Figure 3.222: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**71c**.

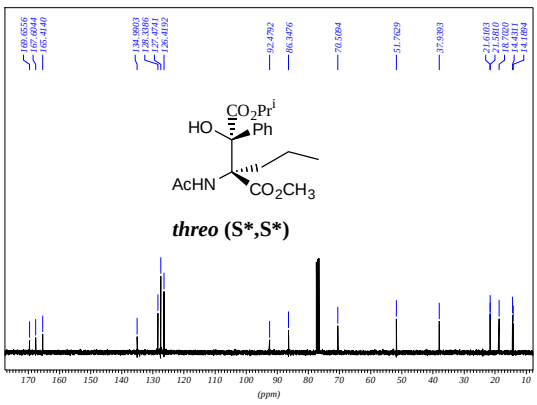


Figure 3.223: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***threo*-71c**.

The IR spectrum of compound **71e** showed six strong absorption bands at 3500, 3370, 1745, 1728, 1645 and 1600 cm^{-1} suggesting the presence of OH, NH, COO, COO, CON and Ph groups, respectively. In the ^{1}H-NMR spectrum, the methoxy group appears as a singlet at 3.05 ppm assigning the *threo*- configuration as already described for the compound

mentioned above. Additionally, four doublets appeared upfield-shifted at δ 0.86, 0.97, 1.27 ppm indicating the presence of two isopropyl groups. The ^{13}C-NMR spectrum showed signals at δ 86.3, 92.9, 164.9, 167.5 and 170.1 ppm attributed to C-2, C-3, CON, COO and COO groups, respectively (see Figure 3.224 and 3.225).

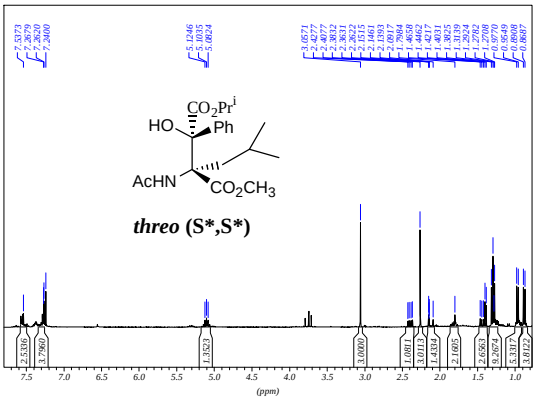


Figure 3.224: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**71e**.

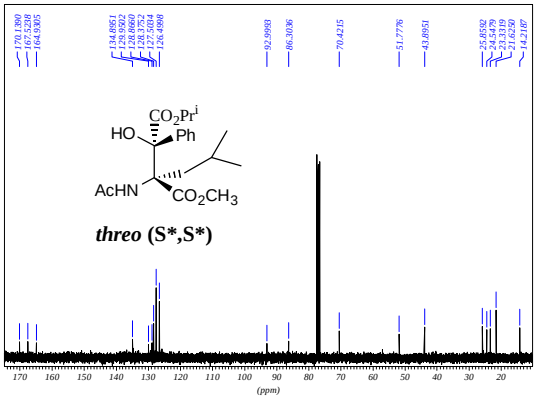
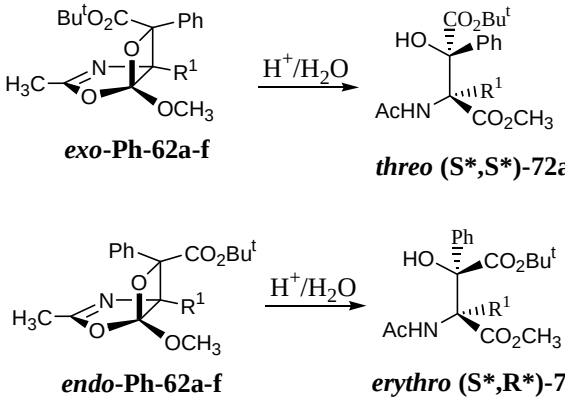


Figure 3.225: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***threo*-71e**.

3.9.6 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 72a-f

Analogous to the compounds mentioned above, ring-opening of the chromatographically separated *exo*-Ph and *endo*-Ph of the bicyclic oxetanes **62a-f** proceeds smoothly and leads to the formation of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **72a-f** in (80-90 %) yields, respectively.



Scheme 3.79: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **72a-f**.

The assignment of the relative configurations of the photoaldol adducts were based on characteristic signals in NMR analyses. For example, in the ^{1}H-NMR spectra of the *threo*- and *erythro*-isomers of compound **72a**, there is a pronouncing difference: the methyl protons resonance in the *threo*-isomer appears at 1.71 ppm, while in the *erythro*-isomer, this resonance is shifted upfield to 1.50 ppm influencing by a ring current effect of the phenyl group. The ^{13}C-NMR spectra showed also a strong chemical shift difference of C-2 and C-3 of about 30 ppm, the *threo*-isomer absorbs at lower-field chemical shift (see Figure 3.226, 3.227, 3.228 & 3.229). The mass spectrum showed the base peak at m/z 145 due to retro aldol fragment of N-acetyl alanine methyl ester. Scheme 3.80 summarizes the fragmentation pattern of compound **72a**.

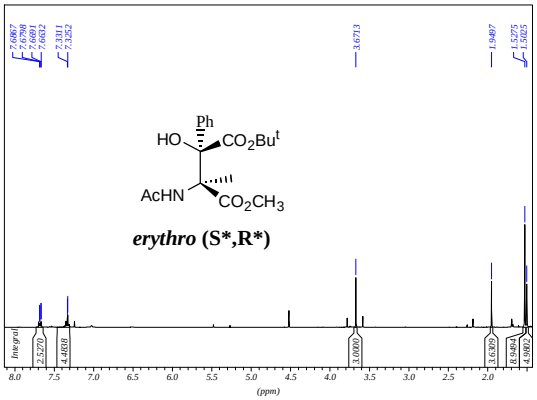


Figure 3.226: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ery*thro*-**72a**.

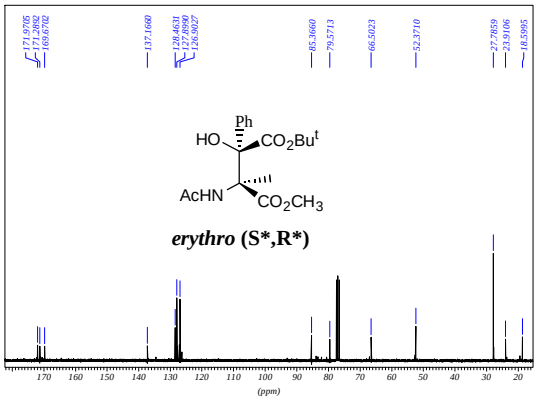


Figure 3.227: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *erythro*-**72a**.

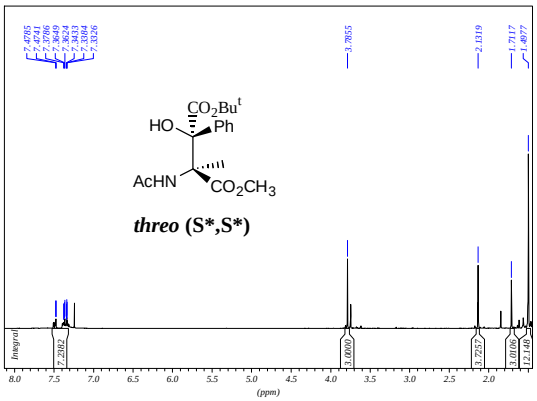


Figure 3.228: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**72a**.

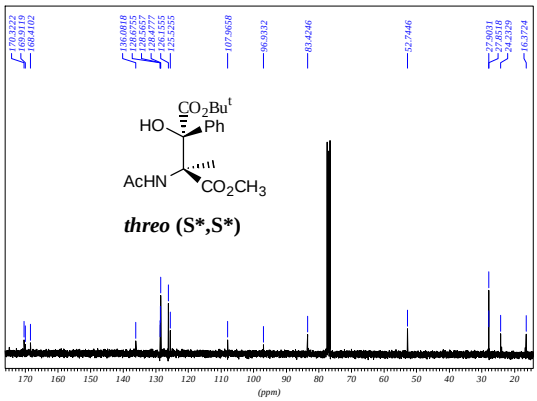
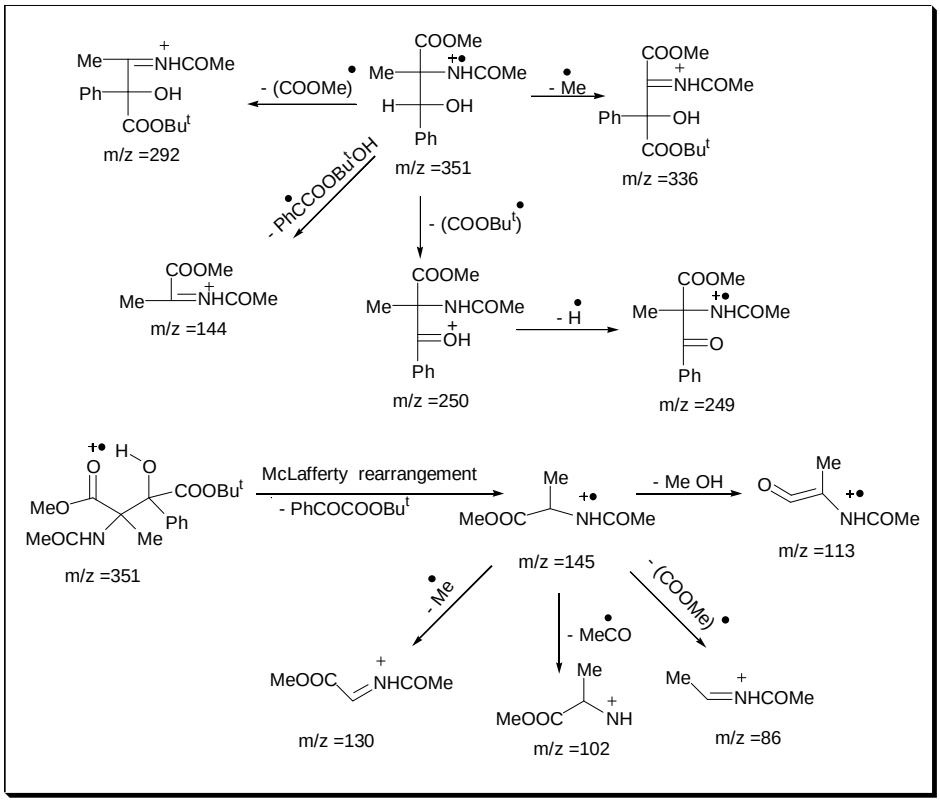


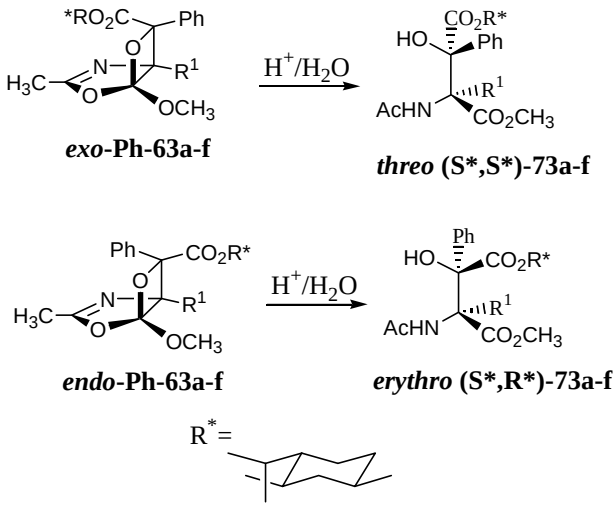
Figure 3.229: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**72a**.



Scheme 3.80: Fragmentation pattern of compound **72a**.

3.9.7 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 73a-f

Despite of the relatively low diastereoselection in the photocycloaddition of menthyl phenyl glyoxylate with 5-methoxyoxazoles, the ring-opening reaction is a simple and versatile preparative method to synthesize diastereomerically pure oxetane derivatives, since the four stereoisomers obtained have quite different physical properties and can be separated by HPLC. The bicyclic oxetanes are valuable chiral bulding blocks for natural product synthesis because the degree of chemical yields and conversion allow to produce them in large amounts. Hydrolysis of the chromatographically separated *exo*-Ph and *endo*-Ph oxetanes **63a-f** resulted in the *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **73a-f**, respectively, as depicted in scheme 3.81.



Scheme 3.81: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives **73a-f**.

The constitutions of compounds **73a-f** were analyzed on grounds of IR, mass spectra and NMR spectral analyses. For example, the IR spectrum of compound **73a** showed strong absorption bands at 3540, 3370, 1736, 1725, 1670, 1595 cm^{-1} characteristic for the OH, NH, COO, COO, CON and Ph groups, respectively. The mass spectrum revealed the base peak at m/z 374 for the fragment [M^+-COOMe]. In the ^{1}H-NMR spectrum, the methoxy protons resonance which used as guide for assignment of the relative configuration of the photoaldol adducts appeared at 3.06 ppm indicating the compound has *threo*-configuration. The ^{13}C-NMR spectrum showed signals at δ 82.1, 92.7, 166.2, 167.9 and 170.3 ppm attributed to C-2, C-3, CON, COO and COO groups, respectively (see Figure 3.230 and 3.231).

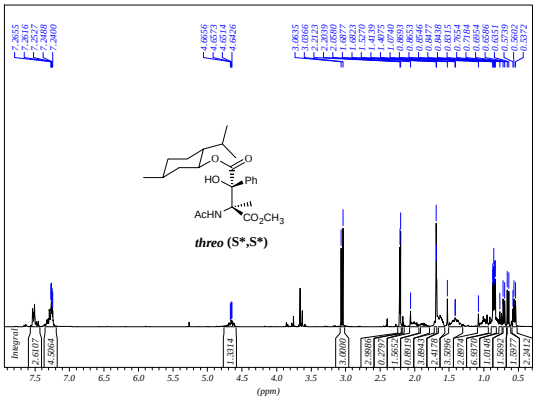


Figure 3.230: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**73a**.

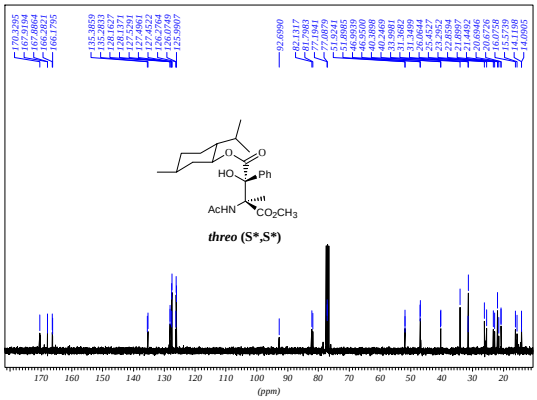


Figure 3.231: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**73a**.

There are two main differences in the ^{1}H-NMR spectra of compound **73d** between the *erythro*- and the *threo*-isomers: (1) the methoxy group in the *threo*-isomer absorbs at δ 3.15 ppm, while in the *erythro*-isomer, this absorption is shifted downfield to 3.82 ppm; (2) the methine proton of the isopropyl group in the *erythro*-isomer resonates at a much higher field (δ = 1.53 ppm) than in the *threo*-isomer which resonates at (δ = 1.79 ppm).

In the ^{13}C-NMR spectrum, five signals at δ 89.9, 91.2, 163.4, 167.1 and 170.3 ppm appeared attributed to C-2, C-3, CON, COO and COO groups, respectively (see Figure 3.232, 3.233, 3.234 and 3.235).

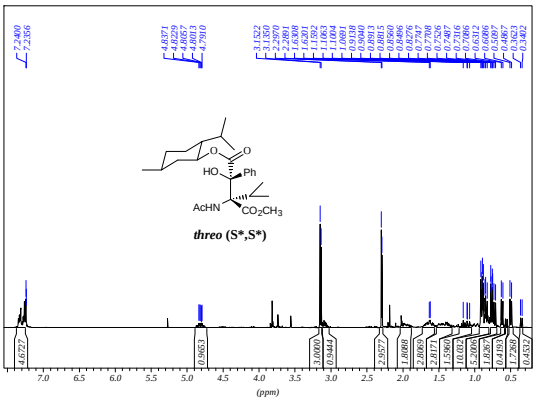


Figure 3.232: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**73d**.

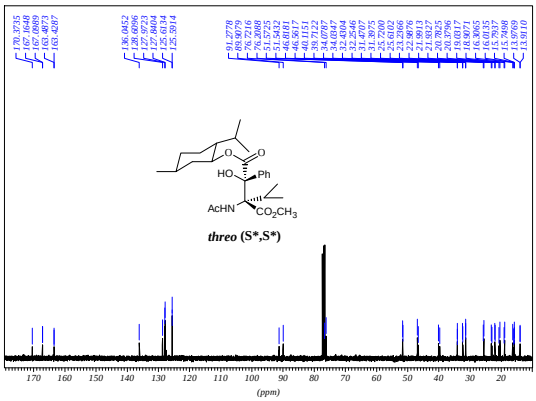


Figure 3.233: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**73d**.

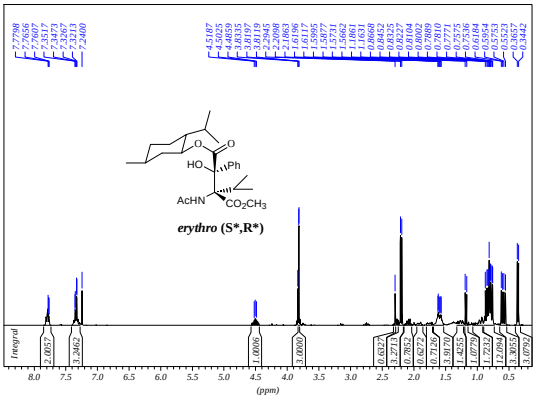


Figure 3.234: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *erythro*-**73d**.

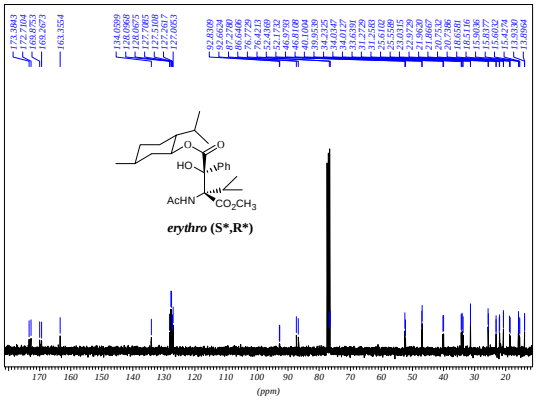
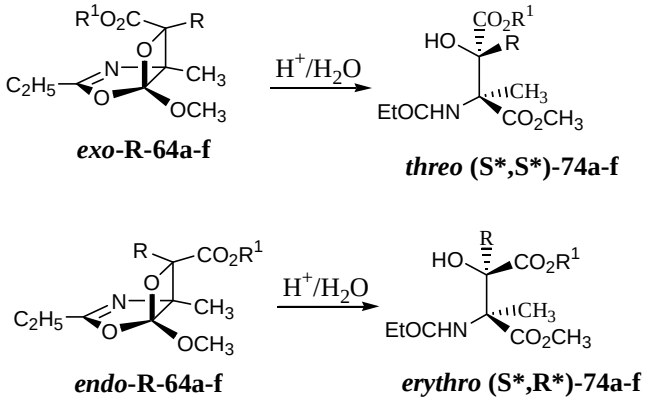


Figure 3.235: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *erythro*-**73d**.

3.9.8 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-propionylamino-b-hydroxy succinic acid derivatives 74a-f

The chromatographically separated *exo*-R and *endo*-R bicyclic oxetanes **64a-f** underwent two fold ring-opening when treated with acid and led to the formation of *threo* (S*,S*) and *erythro* (S*,R*) α-propionylamino-β-hydroxy succinic acid derivatives **74a-f**, respectively, in high chemical yields.



Scheme 3.82: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-propionylamino-β-hydroxy succinic acid derivatives **74a-f**.

Again, the relative configuration of the photoaldol adducts **74a-f** was determined on the basis of NMR anaylses (especially the chemical shift of both methoxy and methyl groups). The results are summarized in Table 3.46.

Table 3.46: Characterisitic ^{1}H-NMR signals (δ_{ppm}) of photo-aldol products **74c-f** in ($CDCl_3$).

compound	R =	R^1 =	*erythro*		*threo*	
			CH_3	OCH_3	CH_3	OCH_3
74c	Ph	Me	1.58	3.62	1.87	2.99
74d	Ph	Et	1.67	3.61	1.83	3.00
74e	Ph	i-Pr	1.54	3.65	1.69	3.05
74f	Ph	t-Bu	1.57	3.67	1.72	3.03

The constitutions of compounds **74a-f** were determined on the basis of IR and NMR analyses. For example, the IR spectrum of compound **74d** revealed strong bands at 3490, 3365, 1743, 1720 and 1650 cm^{-1} indicating the presence of OH, NH, COO, COO and CON groups, respectively. The ^{1}H-NMR spectrum exhibits two singlets at δ 1.67 and 3.61 ppm attributed to methyl and methoxy groups, respectively, and assigned to the *erythro*- configuration. In the

^{13}C-NMR spectrum, there signals at δ 66.2, 82.9, 172.1, 172.4 and 174.7 ppm appeared corresponding to C-2, C-3, CON, COO, COO groups, respectively (see Figure 3.236 and 3.237).

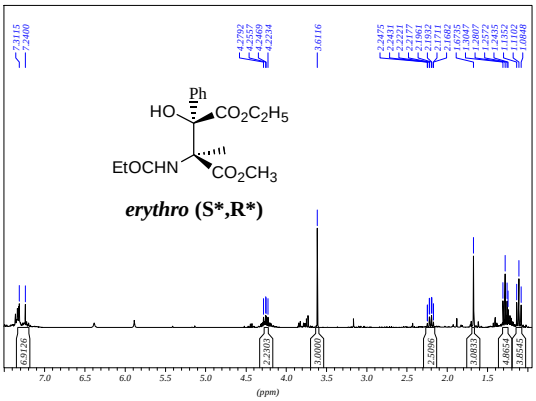


Figure 3.236: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *erythro*-**74d**.

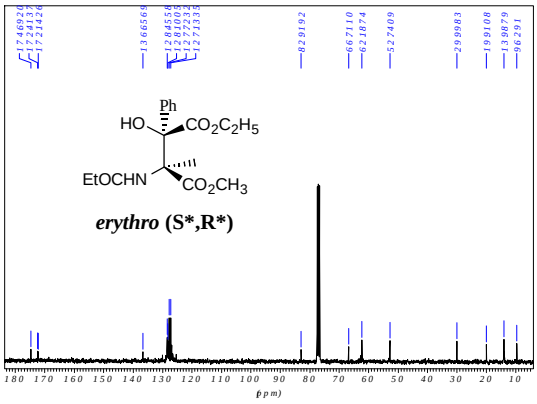
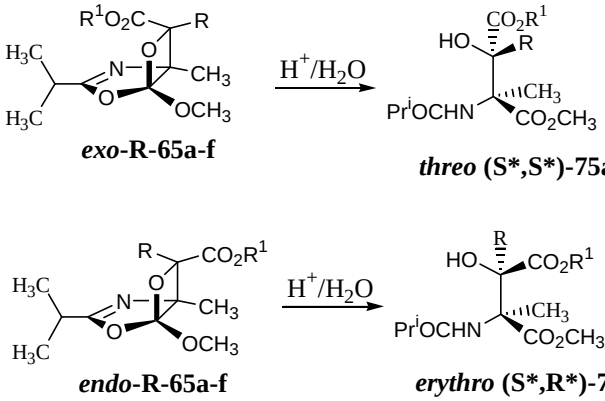


Figure 3.237: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *erythro*-**74d**.

3.9.9 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-isobutyrylamino-b-hydroxy succinic acid derivatives 75a-f

Analogous to compounds **64a-f**, ring opening of the *exo*- and *endo*-R bicyclic oxetanes **65a-f** procceeded with retention of configuration and gave the *threo* (S*,S*) and *erythro* (S*,R*) α-isobutyrylamino-β-hydroxy succinic acid derivatives **75a-f** in high chemical yields, respectively.



Scheme 3.83: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-isobutyrylamino-β-hydroxy succinic acid derivatives **75a-f**.

The structure determination of compounds **75a-f** were made on the basis of IR, mass spectra and NMR analyses. For example, the IR spectrum of compound **75e** showed strong

absorption bands at 3525, 3370, 1756, 1730 and 1645 cm^{-1} suggesting the presence of OH, NH, COO, COO and CON groups, respectively. The ^{1}H-NMR spectra revealed that there is a striking differences between the *threo*- and *erythro* isomer: (a) the methoxy group in the *threo*- isomer resonates at higher field chemical shift (δ = 3.00 ppm) than in the *erythro*-isomer which appears at 3.68 ppm; (b) the methyl group at C-2 absorbs down-field shifted in the *threo*- isomer at 1.68 ppm, while in the *erythro*-isomer this absorption is shifted upfield to 1.54 ppm.

Also, the ^{13}C-NMR spectra showed a pronouncing differences in the chemical shifts of C-2 and C-3 by ca. 10 ppm depending on the relative configuration, the *threo*-isomer has low-field shifted signals (see Figure 3.238, 3.239, 3.240 and 3.241).

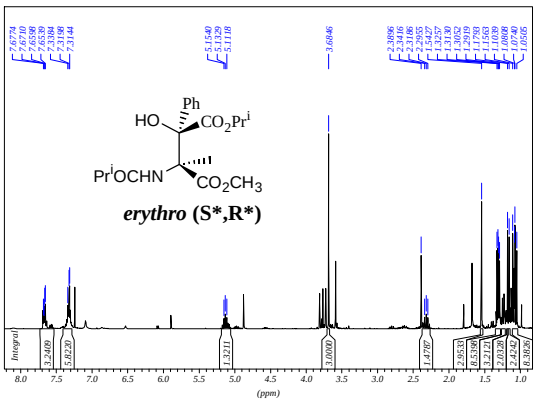


Figure 3.238: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *erythro*-**75e**.

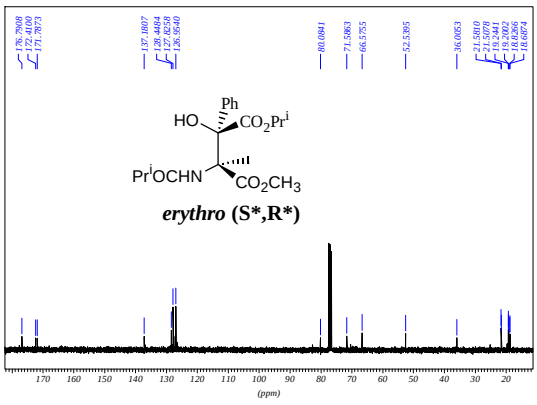


Figure 3.239: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *erythro*-**75e**.

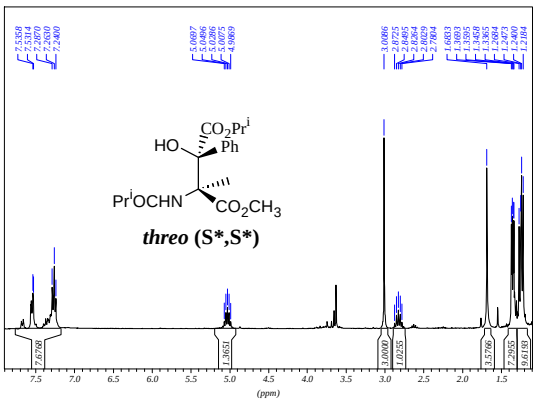


Figure 3.240: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**75e**.

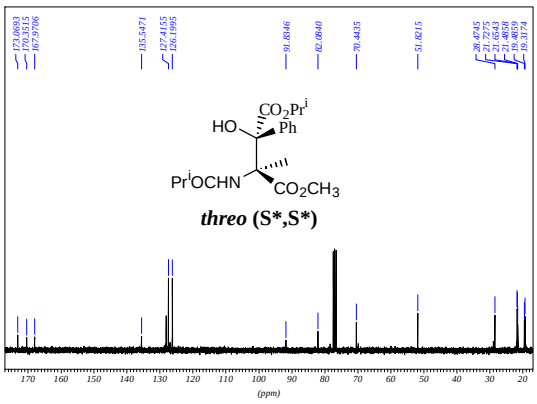


Figure 3.241: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**75e**.

In the ^{1}H-NMR spectrum of compound **75f** three singlets at δ 1.44, 1.72 and 3.00 ppm appeared which are characteristic for *tert*-butyl, methyl and methoxy groups, respectively, and confirmed the *threo*- configuration. Additionally, there a doublet at 1.34 ppm appears for the isopropyl group. In the ^{13}C-NMR spectrum, there signals at δ 82.1, 91.9, 167.3, 170.5 and 173.0 ppm appeared attributed to C-2, C-3, CON, COO and COO groups, respectively (see Figure 3.242 and 3.243).

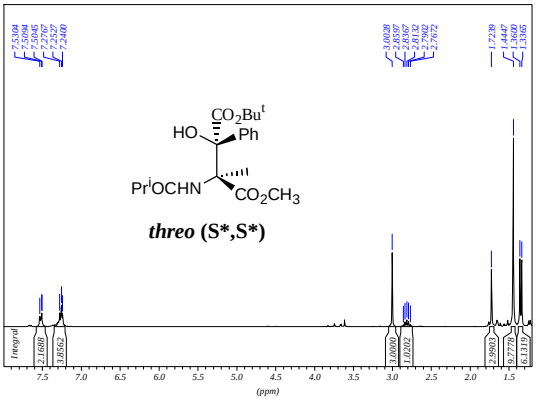


Figure 3.242: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**75f**.

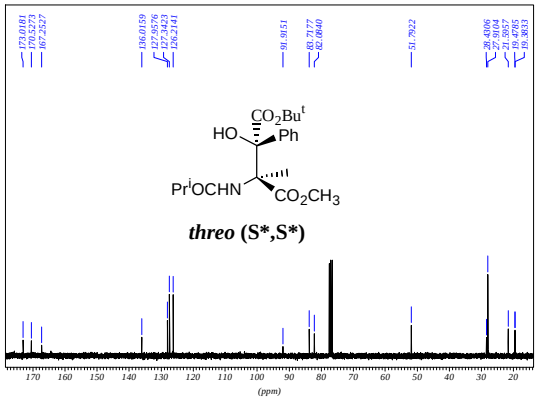
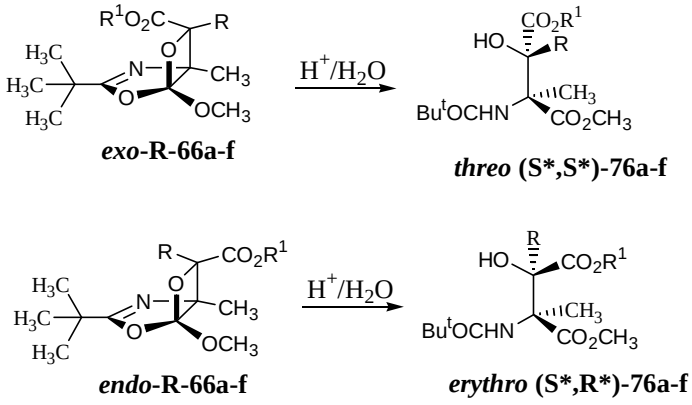


Figure 3.243: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**75f**.

3.9.10 Synthesis of *erythro* (S*,R*) and *threo* (S*,S*) a-(2,2-dimethyl-propionylamino)-b-hydroxy succinic acid derivatives 76a-f

Acid hydrolysis of the chromatographically separated *exo*-R and *endo*-R bicyclic oxetanes **66a-f** furnished *threo* (S*,S*) and *erythro* (S*,R*) α-(2,2-dimethyl-propionylamino)-β-hydroxy succinic acid derivatives **76a-f** in high chemical yields.



Scheme 3.84: Synthesis of *threo* (S*,S*) and *erythro* (S*,R*) α-(2,2-dimethyl-propionylamino)-β-hydroxy succinic acid derivatives **76a-f**.

The structure of the compounds **76a-f** were established on the basis of IR, mass spectra and NMR anaylses. For example, the IR spectrum of compound **76d** exhibits five strong absorption bands at 3530, 3420, 1755, 1724, 1675 cm^{-1} characteristic for OH, NH, COO, COO and CON groups, respectively. The mass spectrum showed the base peak at m/z 306 due to [M^+ - COOMe]. In the ^{1}H-NMR spectra, there are two distinct differences between the *erythro*- and *threo*- isomers: (a) in the *threo*-isomer, the methoxy resonance appears at 3.00 ppm, while in the *erythro*-isomer appears down-field shifted to 3.70 ppm; (b) the methyl protons in the *threo*-isomer absorbs at 1.67 ppm, whereas in the *erythro*-isomer this absorption is shifted upfield to 1.55 ppm. The ^{13}C-NMR spectra also revealed two significant differences between the *threo*- and *erythro*- isomers. Both C-2 and C-3 in the *threo*-isomer resonate lower-field shifted than in the *erythro*- isomer (see Figure 3.244, 3.245, 3.246 and 3.248).

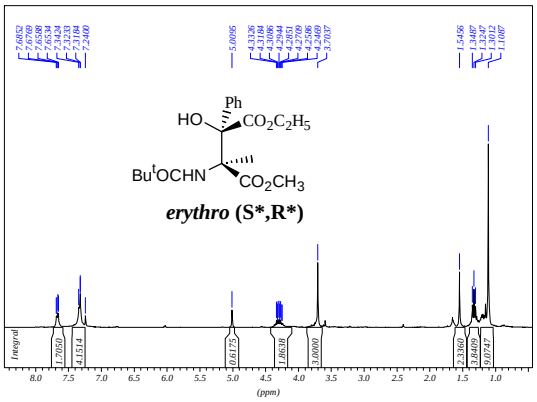


Figure 3.244: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *erythro*-**76d**.

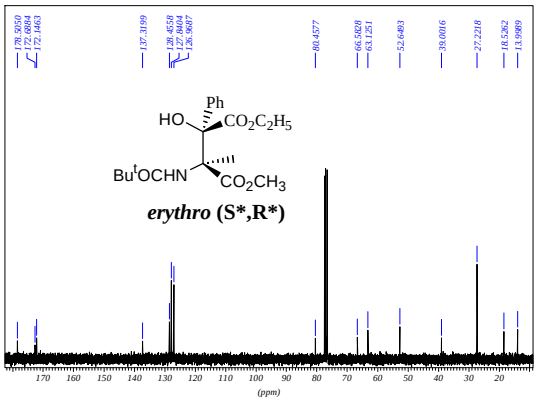


Figure 3.245: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *erythro*-**76d**.

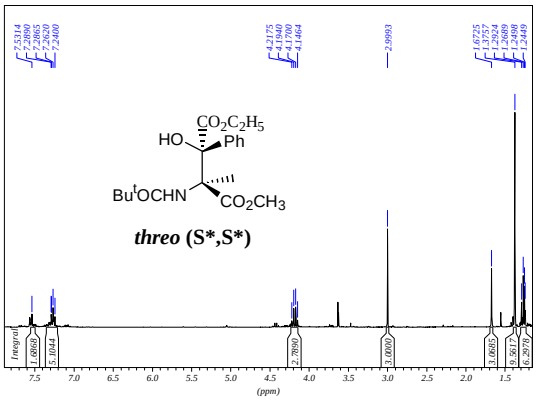


Figure 3.246: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**76d**.

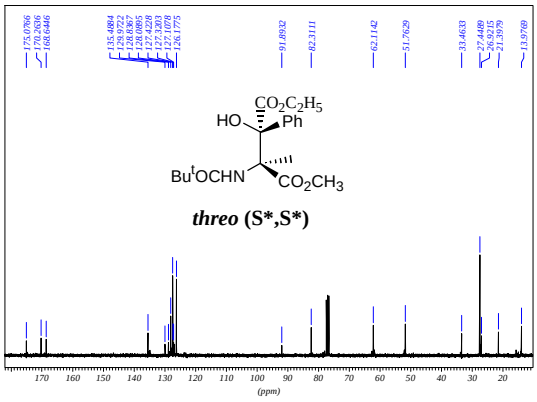


Figure 3.247: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**76d**.

The ^{1}H-NMR spectrum of compound **76e** exhibits three singlets at δ 1.38, 1.69 and 2.99 ppm characteristic for *tert*-butyl, methyl and methoxy groups, respectively, and supports the *threo*-configuration. Furthermore, two doublets at δ 1.23 ppm appeared attributed to the isoropyl group. The ^{13}C-NMR spectrum showed signals at δ 82.3, 91.7, 168.1, 170.3 and 175.1 ppm corresponding to C-2, C-3, CON, COO and COO groups, respectively, and reconfirmed the *threo*- configuration (see Figure 3.248 and 3.249).

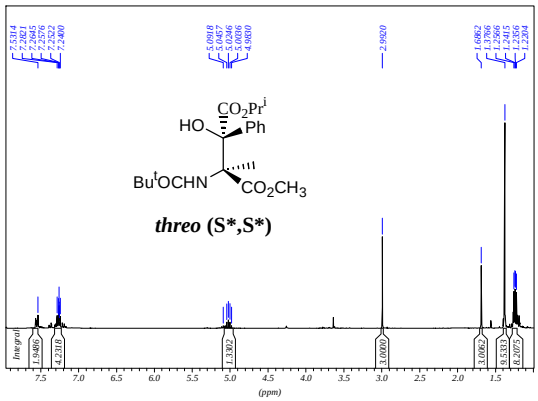


Figure 3.248: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**76e**.

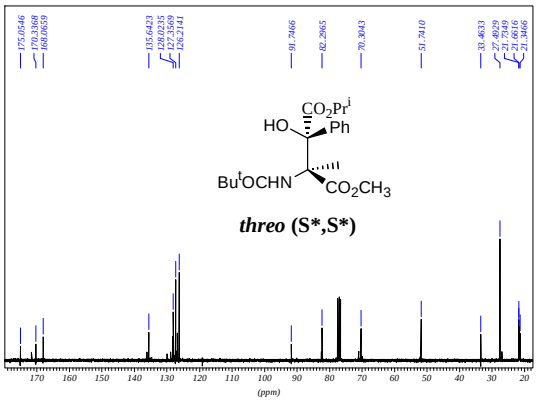


Figure 3.249: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**76e**.

Proving the constitution of compound **76f** was made on the basis of IR, mass spectrum and NMR analyses. The IR spectrum showed absorption bands at 3510, 3450, 1740, 1735, 1670 and 1605 cm^{-1} indicating the presence of OH, NH, COO, COO, CON and Ph groups, respectively. The mass spectrum showed the base peak at m/z 187 due to retro aldol cleavage and formation of 2,2-dimethylpropionylamino alanine methyl ester. As already mentioned above, there are two striking differences in the ^{1}H-NMR spectra between the *threo*- and *erythro*- isomer: (a) the methoxy group resonates in the *threo*- isomer at a higher chemical shift (δ = 2.99 ppm) than in the *erythro*- isomer which resonates at 3.78 ppm; (b) the methyl group resonance in the *threo*- isomer appears at 1.73 ppm, while in the *erythro*- isomer this resonance is shifted upfield to 0.96 ppm.

The ^{13}C-NMR spectrum showed signals at δ 82.4, 91.8, 167.4, 170.6 and 174.9 ppm attributed to C-2, C-3, CON, COO and COO groups, respectively (see Figure 3.250, 3.251, 3.252 and 3.253).

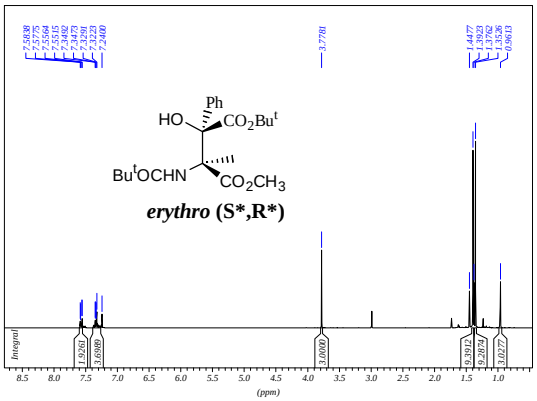


Figure 3.250: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *erythro*-**76f**.

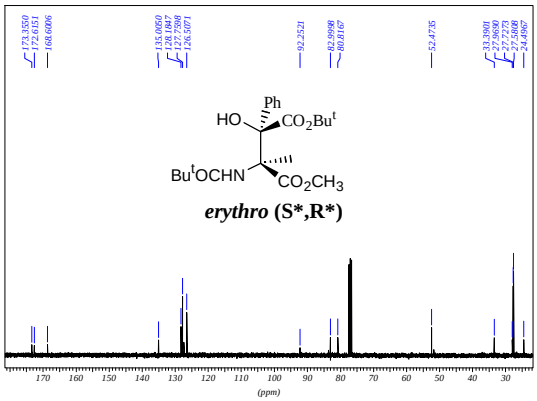


Figure 3.251: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *erythro*-**76f**.

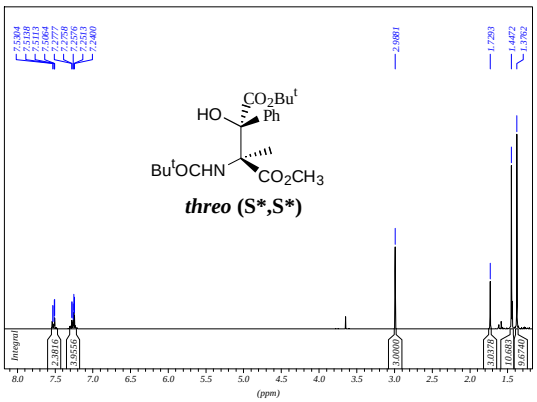


Figure 3.252: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of *threo*-**76f**.

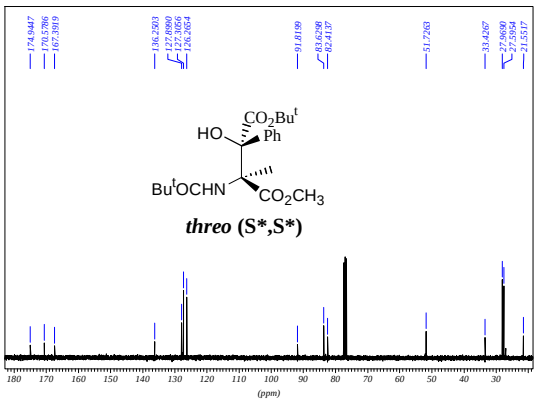


Figure 3.253: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of *threo*-**76f**.

3.10 Magnetic isotope effects on the diastereoselectivity of the triplet photocycloaddition reactions

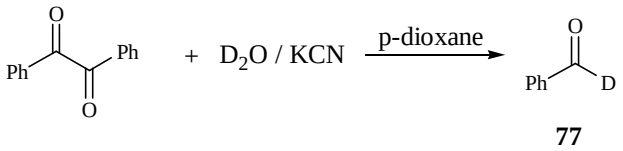
Studies of isotope effects are exceedingly important for our understanding of reaction mechanism. Primary and secondary kinetic isotope effects (KIE) as well as equilibrium isotope effects (EIE) are frequently discussed as central features. In recent years, spectacular reinvestigation of numerous basic organic reactions have been performed by Singleton and coworkers demonstrating the significance of kinetic isotope effects.[134] Less often have isotope effects been used in photochemical reactions,[135] partly due to the larger diffculties in determining reaction rate constants. Furthermore, photochemical reactions present an additional degree of complexity, the appearance of different spin states which only slowly interconvert. As already been stated by Turro and Kräuter in a seminal review in 1980, difference in the nuclear–spin hyperfine coupling constants (HFC) might leads to substantial differences in process where spin states are interchanging.[136] This speculation has created a new concept, *spin chemistry* as defined and described in several reviews by Buchachenko.[137] In the first part of my dissertation, I have described *spin chemistry* effects in the photocycloaddition reactions which were generated by spin-orbit coupling (SOC) phenomena determining the geometries of triplet biradical intermediates when crossing into singlet potential hypersurface.[51] Spin-orbit coupling is thought to be the dominant factor for triplet biradicals connected by short hydrocarbon chains as in tetramethylenes or in 2-oxatetramethylenes. Additional effects may arise from HFC differences and manifest themselves in substantial magnetic isotope effects (MIE).

To test the magnetic isotope effect (MIE) on the stereoselectivity of the [2+2] carbonyl-ene photocycloaddition (Paternò-Büchi reaction), benzaldehyde-1-d, propanal-1d, and 5-d-2,3-dihydrofuran were prepared in more than 96 % isomeric purity. These substrates are ideal for this purpose because they bear a deuterium α- to carbonyl and / or double bond, which allow estimation of a possible magnetic isotope effect.

3.10.1 Synthesis of starting materials

3.10.1.1 Synthesis of benzaldehyde-1-d

Benzaldehyde-1d was prepared in 60 % yield from benzil when treated with deuterium oxide and potasium cyanide in p-dioxane following a literature procedure.[138]



77

Scheme 3.85: Synthesis of benzaldehyde-1d.

The structure assignment of compound **77** was based on NMR analyses and also on comparsion with literature data (see Figure 3.254 and 3.255).

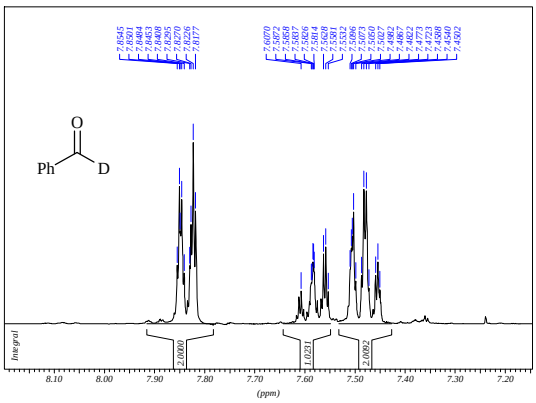


Figure 3.254: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **77**.

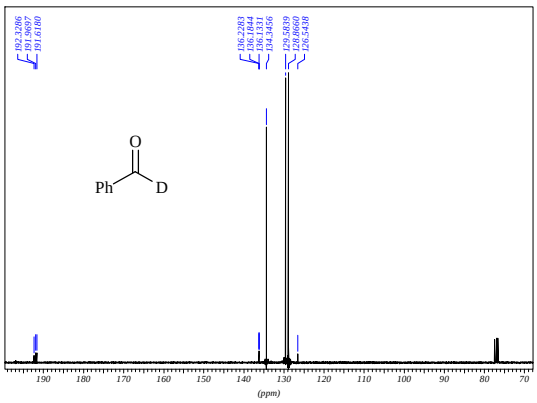
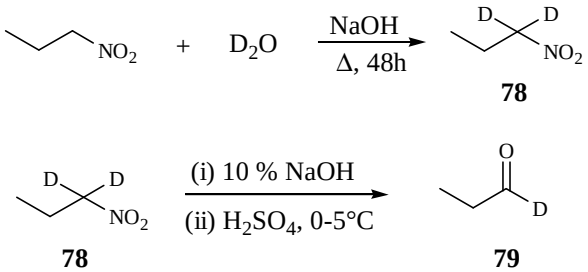


Figure 3.255: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **77**.

3.10.1.2 Synthesis of propanal-1-d

Propanal-1d was synthesized in higher than 96 % isomeric purity by a minor modification of the Nef reaction[139] with nitropropane-1,1-d_2 which was prepared by H/D exchange of nitropropane using deuterium oxide in the presence of sodium hydroxide as depicted in Scheme 3.86.



Scheme 3.86: Synthesis of propanal-1d.

The constitution of propanal-1-d was confirmed by spectroscopic analysis. The ^{1}H-NMR spectrum showed two signals, one appears as a triplet at 0.87 ppm and the other appears as a quartet at 2.25 ppm, indicating the presence of ethyl group. In the ^{13}C-NMR spectrum, there

appeared three signals at 6.0, 37.0, and 202.8 ppm (triplet) attributed to CH_3, CH_2, and COD group, respectively.

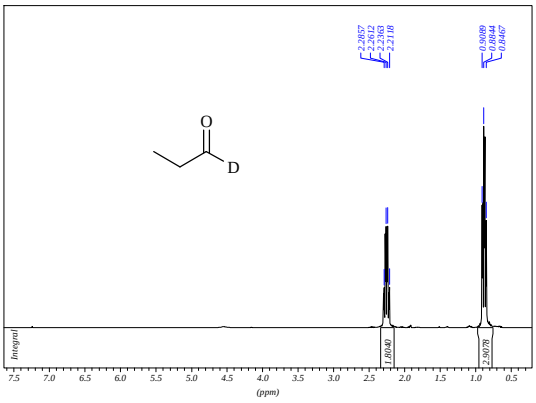


Figure 3.256: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **79**.

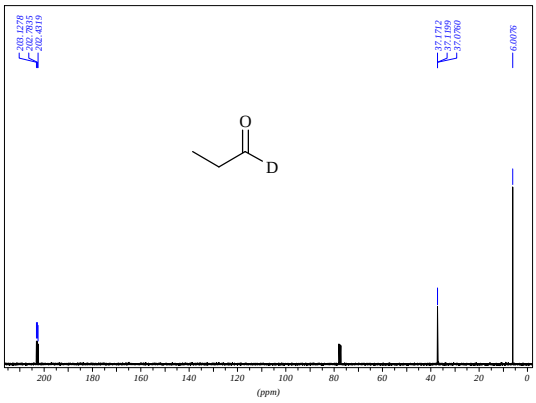
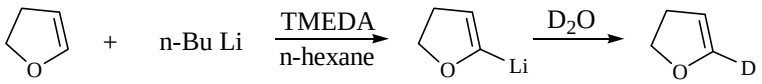


Figure 3.257: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of compound **79**.

3.10.1.3 Synthesis of 5-deuterio-2,3-dihydrofuran

When 2,3-dihydrofuran **2** was allowed to react with n-butyllithium in n-hexane in the presence of catalytic amounts of tetramethylethylenediamine (TMEDA) at room temperature, 5-litho-2,3-dihydrofuran was formed immediately, which upon quenching with deuterium oxide afforded 5-deuterio-2,3-dihydrofuran **80** in good yield.[140]



2 **80**

Scheme 3.85: Synthesis of 5-deuterio-2,3-dihydrofuran **80**.

The constitution of compound **80** was established by NMR analyses and also by comparsion with the literature data. The ^{13}C-NMR spectrum of compound **80** displays a triplet signal down-field shifted for C-5 and confirmed the attachment of C-5 to a deuterium atom. In the ^{1}H-NMR spectrum the disappearance of the H-5 signal proved complete deuteration (see Figure 3.258 & 3.259).

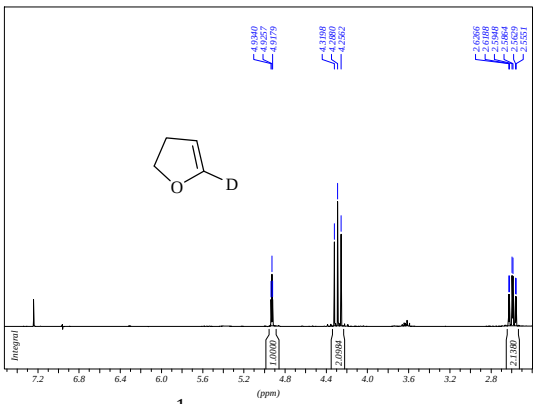


Figure 3.258: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **80**.

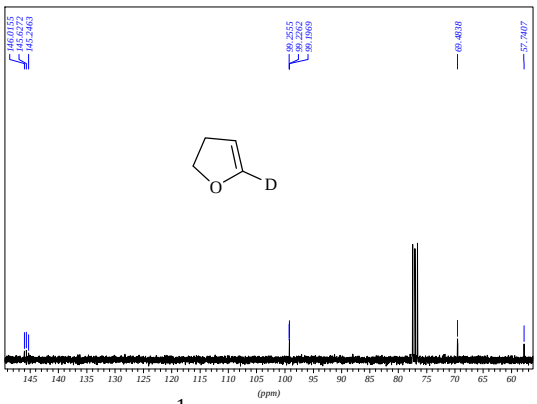
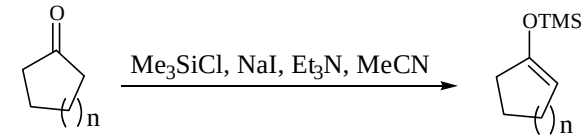


Figure 3.258: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **80**.

3.10.1.4 Synthesis of 1-trimethylsilyloxy cycloalkenes

Treatment of cyclic ketones (cyclopentanone, cyclohexanone, cycloheptanone) with the trimethylchlorosilane-sodium iodide-triethylamine reagent in acetonitrile was a convenient method for the preparation of 1-trimethylsilyloxycycloalkenes in excellent yields as depicted in Scheme 3.88.[141, 142, 143, 144]



n = 1,2, 3

81, n = 1
82, n = 2
83, n = 3

Scheme 3.88: Synthesis of 1-trimethylsilyloxy cycloalkenes **81-83**.

Table 3.47: Characteristic properties of 1-trimethylsilyloxy cycloalkenes **81-83**.

Compound	^{1}H-NMR[a]	^{13}C-NMR[b]	B.p$_{10\ torr}$ (°C)	Yield (%)
83	4.58	154.9	55-57	75
84	4.98	150.2	78-80	82
85	4.82	155.9	78-81	85

[a] chemical shift of CH= in ppm, [b] chemical shift of C-1 in ppm.

The constitutions of compounds **81-83** were confirmed by NMR analyses. For example, the ^{1}H-NMR spectrum of compound **82** showed a down-field shifted signal at 4.82 ppm attributed to the olefinic proton. In addition, there appeared a singlet upfield shifted at 0.14 ppm characteristic for the trimethylsilyl group. In the ^{13}C-NMR spectrum, the olefinic carbons

appear at 104.1 and 150.3 ppm corresponding to C-2 and C-1, respectively (see Figure 3.260 and 3.261).

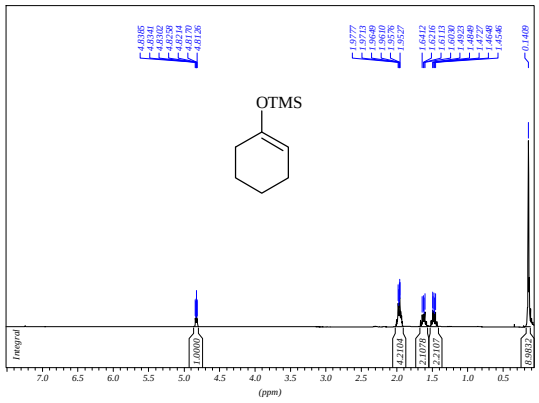


Figure 3.260: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of compound **82**.

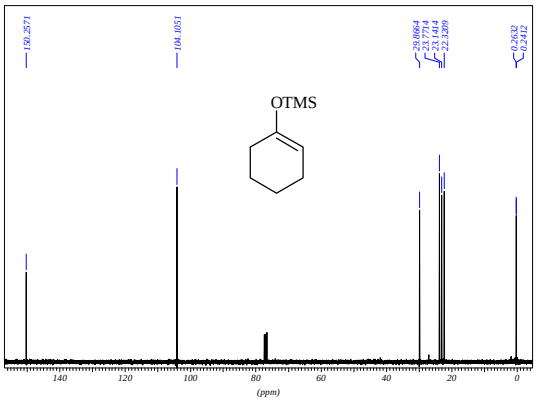
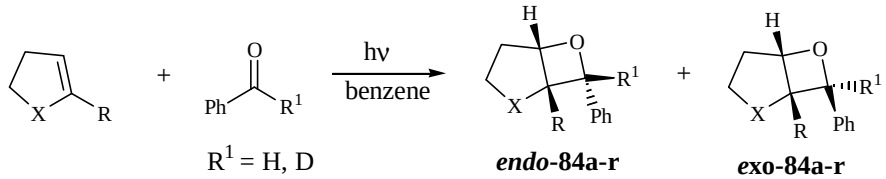


Figure 3.261: ^{13}C-NMR (300 MHz, $CDCl_3$) spectrum of compound **82**.

3.10.2 Photoreactions of benzaldehyde and benzaldehyde-1-d with cyclic alkenes

In order to evaluate isotope effects on the diastereoselectivity of "pure" triplet photocycloadditions, benzaldehyde and benzaldehyde-1-d were used as carbonyl substrates. These carbonyl substrates have high intersystem crossing rates (ISC) (for benzaldehyde, $k_{ISC} \cong 10^{11}$ sec^{-1} and ΔE_{ST} = 4 kcal/mol) which excludes singlet reactivity.[145] As olefinic reaction partners two sets of cycloalkenes were employed: unsubstituted cycloalkenes (2,3-dihydrofuran, 5-deuterio-2,3-dihydrofuran, cyclopentene, cyclohexene) and substituted cycloalkenes (5-methyl-2,3-dihydrofuran, 1-methylcyclohexene, 1-trimethylsilyloxy-cyclopentene, 1-trimethylsilyloxycyclohexene, 1-trimethylsilyloxycycloheptene). Photolysis of benzaldehyde as well as benzaldehyde-1-d with substituted and unsubstituted cycloalkenes in benzene gave mixtures of two diastereoisomers as depicted in Scheme 3.89.



R^1 = H, D

***endo*-84a-r** ***exo*-84a-r**

Scheme 3.89: Photoreaction of benzaldehyde and benzaldehyde-1-d with cyclic alkenes.

The *exo*/*endo* diastereomeric ratios of the photoadducts **84a-r** were determined by ^{1}H-NMR and GC analyses, for reactions with benzaldehyde-1-d additionally by ^{2}H-NMR analysis. The results are presented in Table 3.48.

Table 3.48: Simple diastereoselectivity of the photocycloaddition of benzaldehyde and benzaldehyde-1-d with cyclic alkenes.

Entry	Compound	X =	R =	R^1 =	d.r. (*endo* : *exo*)[a]
A	**84a**	O	H	H	82 : 18
B	**84b**	O	H	D	93 : 07
C	**84c**	O	D	H	89 : 11
D	**84d**	O	D	D	90 : 10
E	**84e**	O	Me	H	65 : 35
F	**84f**	O	Me	D	67 : 33
G	**84g**	CH_2	H	H	61 : 39
H	**84h**	CH_2	H	D	87 : 13
I	**84i**	$(CH_2)_2$	H	H	74 : 26
J	**84j**	$(CH_2)_2$	H	D	85 : 15
K	**84k**	$(CH_2)_2$	Me	H	67 : 33
L	**84l**	$(CH_2)_2$	Me	D	75 : 25
M	**84m**	CH_2	OTMS	H	60 : 40
N	**84n**	CH_2	OTMS	D	63 : 37
O	**84o**	$(CH_2)_2$	OTMS	H	80 : 20
P	**84p**	$(CH_2)_2$	OTMS	D	83 : 17
Q	**84q**	$(CH_2)_3$	OTMS	H	60 : 40
R	**84r**	$(CH_2)_3$	OTMS	D	70 : 30

[a] based on integration of the characteristic signals in the ^{1}NMR spectra of the crude reaction mixture and also on the GC analysis.

In agreement with literature results, the *endo*-selectivity of the triplet Paternò-Büchi reaction of benzaldehyde and benzaldehyde-1-d with substituted cycloalkenes was moderate and high with unsubstituted cycloalkenes (see Table 3.48, entry A, E).

The comparsion between benzaldehyde with benzaldehyde-1-d photoadducts revealed that:

(a) the *endo*-selectivity increases when the reaction partner contains deuterium;

(b) from the four possible combinations of benzaldehyde/2,3-dihydrofuran (entry A, B, C & D), the *endo*-selectivity of benzaldehyde-1-d/2,3-dihydrofuran was the highest one;

(c) the *endo/exo*-selectivity of the benzaldehyde-1-d/cyclopentene photoadduct increases by a factor of 4.2 in comparsion with the benzaldehyde/cyclopentene photoadduct (see entry H & I);

(d) the same trend appeared in the substituted cycloalkene series; the diastereoselectivity (favoring the *endo*-photoadduct) increases with benzaldehyde-1-d compared to benzaldehyde.

The structure determination of the deuterated photoadducts were based on NMR analyses and mass spectrometry. For example, Figure 3.262A displays ^{1}H-NMR traces of H-7, H-5 and H-1 for benzaldehyde/2,3-dihydrofuran photoadduct (top) *versus* benzaldehyde-1-d/2,3-dihydrofuran photoadduct (bottom). In the bottom spectrum, one can clearly see the disappearance of H-7 signal at 5.72 ppm and the appearance of H-1 at 4.95 ppm as a doublet which confirmed again the regioselectivity.

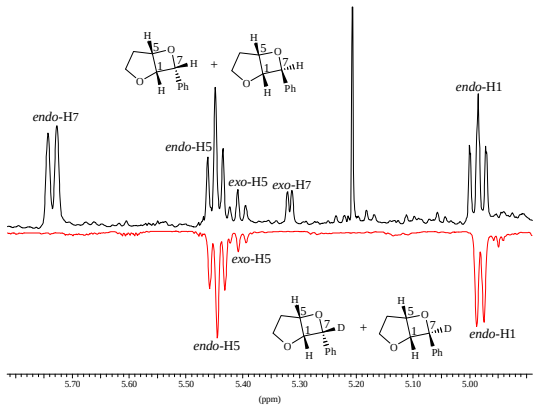


Figure 3.262A: ^{1}H-NMR spectra of **84a** & **84b**.

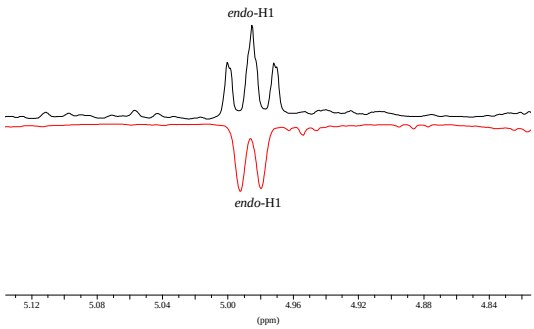


Figure 3.262B: ^{1}H-NMR spectra of H-1 for **84a** & **84b**.

There are two main differences in the ^{1}H-NMR spectra of benzaldehyde/2,3-dihydrofuran and benzaldehyde/5-deuterio-2,3-dihydrofuran photoadducts:

(1) in the bottom spectrum, H-7 appears as singlet and H-5 as doublet whereas in the top spectrum H-7 appears as doublet and H-5 appears as a doublet of doublet; (2) the disappearance of the H-1 signal in the bottom spectrum confirmed again the regioselectivity (see Figures 3.263A & 3.263B).

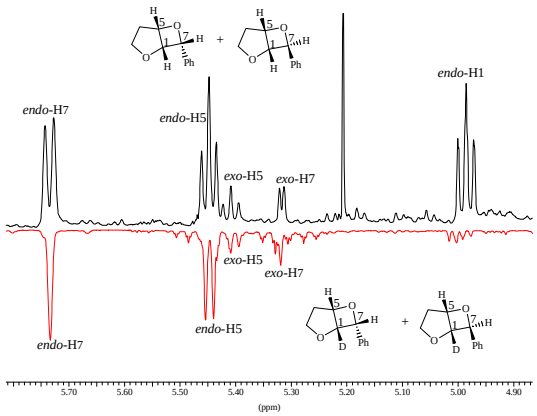


Figure 3.263A: ^{1}H-NMR spectra of **84a** & **84c**.

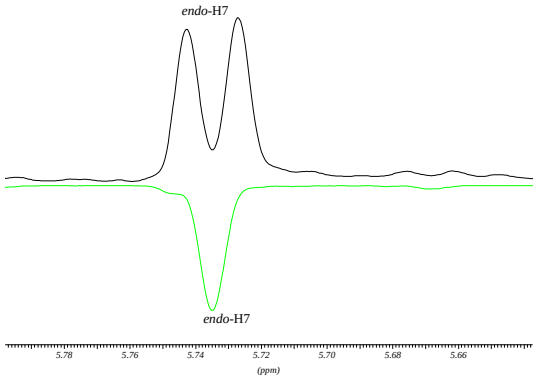


Figure 3.263B: ^{1}H-NMR spectra of H-7 for **84a** & **84c**.

Figures 3.264A & 3.264B display the ^{1}H-NMR spectra of benzaldehyde-1-d/5-deuterio-2,3-dihydrofuran photoadducts. As can be seen in the bottom spectrum, the disappearance of both the H-7 and H-1 signals and the appearance of the H-5 signal as doublet reveal the correct regiochemistry.

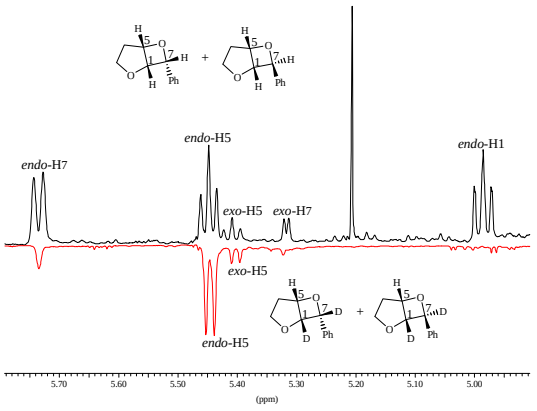


Figure 3.264A: ^{1}H-NMR spectra of **84a** & **84d**.

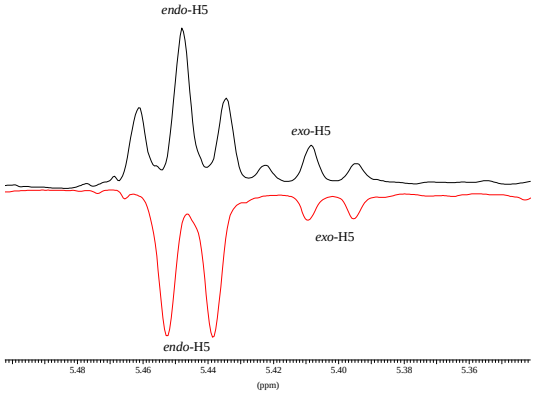


Figure 3.264B: ^{1}H-NMR spectra of H-1 for **84a** & **84d**.

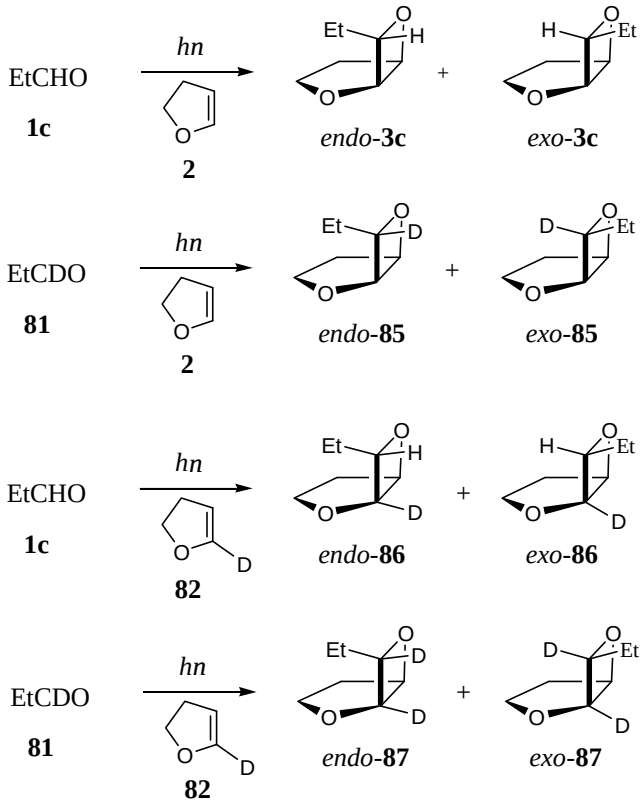
In order to obtain further information on kinetic isotope effects, the reactivity differences between benzaldehyde and benzaldehyde-1-d competing for the 2,3-dihydrofuran was determined. The k_H/k_D values from ^{1}H-NMR analyses for competition reactions with initial concentrations of 1 : 1 : 1 and 2 : 2 : 1 for benzaldehyde : benzaldehyde-1d : 2,3-dihydrofuran were *1.05* and *1.1*, respectively. Thus, benzaldehyde-1-d is only slightly less reactive with 2,3-dihydrofuran than benzaldehyde, but gives significantly higher diastereomeric ratios. The effect on k_H/k_D might also be due to the reduced triplet benzaldehyde lifetimes. An alternative

explanation is an amplification of the cleavage channel from the intermediate 1,4-biradical. The quantum yield for the photocycloaddition of benzaldehyde to 2,3-dihydrofuran was estimated as 0.45.[146] Thus, the cleavage channel can compete with product formation with similar probability in the non-deuterated case.

3.10.3 Photoreactions of propanal and propanal-1-d with 2,3-dihydrofuran and 5-deuterio-2,3-dihydrofuran

In order to obtain more evidence for magnetic isotope effects (MIE), the concentration dependence of the [2+2] photocycloaddition of propanal and propanal-1d with 2,3-dihydrofuran as well as 5-deuterio-2,3-dihydrofuran was investigated. This unlabelled combination (propanal/2,3-dihydrofuran) was used primarily to determine the different in simple diastereoselectivities of singlet and triplet photocycloadditions.[146]

The addition of 2,3-dihydrofuran or 5-deuterio-2,3-dihydrofuran to electronically excited propanal-1-d in hexane at a wide range of substrate concentrations afforded two diastereoisomers. The *endo/exo* diastereomeric ratios of the photoadducts were strongly influenced by the concentration of substrates. The diastereomeric ratios of the photoadducts were determined by GC and ^{1}H-NMR analyses.



Scheme 3.90: Photocycloaddition reactions of propanal, propanal-1d with 2,3-dihydrofuran and 5-deuterio-2,3-dihydrofuran in n-hexane.

Table 3.49: Concentration dependence of the simple diastereoselectivity of the photocycloaddition reactions of propanal and propanal-1-d with 2,3-dihydrofuran as well as 5-deuterio-2,3-dihydrofuran in hexane.

Conc. (M)	d.r.(*endo* : *exo*)[a]	d.r.(*endo* : *exo*)[b]	d.r.(*endo* : *exo*)[c]	d.r.(*endo* : *exo*)[d]
1	47.3 : 52.7	46.1 : 53.9	46.9 : 53.1	45.2 : 54.8
0.5	50.2 : 49.8	49.9 : 50.1	50.9 : 49.9	48.3 : 51.7
0.25	54.9 : 45.1	55.1 : 44.9	55.8 : 44.2	53.2 : 46.8
0.125	60.4 : 39.6	60.2 : 39.8	61.4 : 38.6	57.6 : 42.4
0.1	62.8 : 37.2	60.7 : 39.3	62.9 : 37.1	60.3 : 39.7
0.05	64.3 : 35.7	67.8 : 32.2	67.1 : 32.9	66.7 : 33.3
0.025	66.3 : 33.7	70.1 : 29.9	70.3 : 29.7	66.9 : 33.1
0.0125	69.2 : 30.8	73.5 : 26.5	71.4 : 28.6	72.9 : 27.1

[a] simple diastereoselectivity of propanal/2,3-dihydrofuran photocycloaddition reaction determined by ^{1}H-NMR analysis, [b] simple diastereoselectivity of propanal-1-d/2,3-dihydrofuran photocycloaddition reaction determined by ^{1}H-NMR analysis, [c] simple diastereoselectivity of propanal/5-deuterio-2,3-dihydrofuran photocycloaddition reaction determined by ^{1}H-NMR analysis, [d] simple diastereoselectivity of propanal-1-d/5-deuterio-2,3-dihydrofuran photocycloaddition reaction determined by ^{1}H-NMR analysis.

As can be seen from Table 3.49, in all combinations, at higher concentration, the *endo/exo* selectivity levels oft around 46 : 54 whereas at lower concentration, the selectivity reached a maximum value of 74 : 26 with preferential formation of the *endo*-diastereoisomer. Comparing the *endo/exo* selectivity of propanal-1-d/2,3-dihydrofuran, propanal/5-deuterio-2,3-dihydrofuran and propanal-1-d/5-deuterio-2,3-dihydrofuran photoadducts with propanal/2,3-dihydrofuran photoadducts showed that the selectivity of the singlet reaction is the same for all combinations whereas the triplet reaction gave higher *endo*-selectivities when one or two reaction partners bear a deuterium atom.

In the triplet region (low substrate concentration), a similar isotope effect on the *endo/exo*-ratio was determined for the 5-deuterio-2,3-dihydrofuran/propanal and the 2,3-dihydrofuran/propanal-1-d combinations (Figure 3.265). An average isotope selectivity effect of 1.2 resulted for both reactions at 0.01M. These results orginate from several factors, all in connection with intersystem crossing processes: ISC-rates are reduced and thus singlet as well as triplet lifetimes are increased. This effect seems to be balanced out for the 2,3-dihydrofuran/propanal reaction: the inversion regions are nearly identical for all combinations.

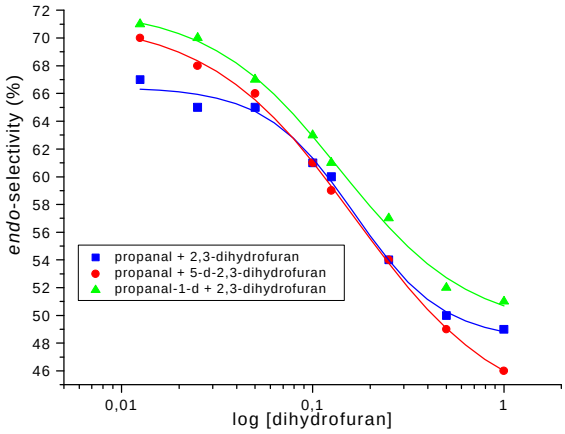
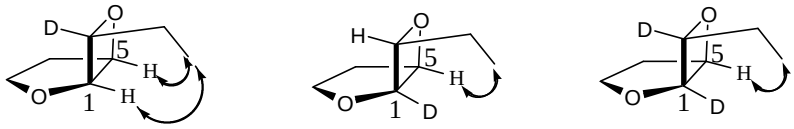


Figure 3.265: Concentration / selectivity profiles for the photocycloaddition of propanal with 2,3-dihydrofuran and deuterated substrate combination.

The stereochemistry of all deuterated photoadducts was confirmed *via* NOE spectroscopy for the *exo*-stereoisomers. A common feature of the NOE measurements was the enhancement of oxetane ring hydrogen (H-5) resonances following saturation of the methyl group.



exo-**85** *exo*-**86** *exo*-**87**

Figure 3.266: NOE interactions of the deuterated *exo*-diastereoisomers.

The structure assignments of the bicyclic oxetanes were based on the NMR analyses. Table 3.50 summerizes the characteristic signals of all possible photoadducts.

Table 3.50: Characteristic ^{1}H-NMR and ^{13}C-NMR signals of compounds **3c**, **85, 86**, **87**.

Compound	H-7	H-5	H-1	C-7	C-5	C-1
***exo*-3c**	4.19	5.17	4.42	88.3	84.2	80.7
***endo*-3c**	4.50	5.22	4.66	86.4	84.1	78.6
***exo*-85**	-	5.15	4.41	87.5	84.0	80.4
***endo*-85**	-	5.22	4.64	85.7	83.8	78.3
***exo*-86**	4.24	5.19	-	88.2	84.2	80.4
***endo*-86**	4.53	5.27	-	86.4	84.0	78.3
***exo*-87**	-	5.14	-	87.6	84.1	80.2
***endo*-87**	-	5.22	-	85.8	83.9	78.1

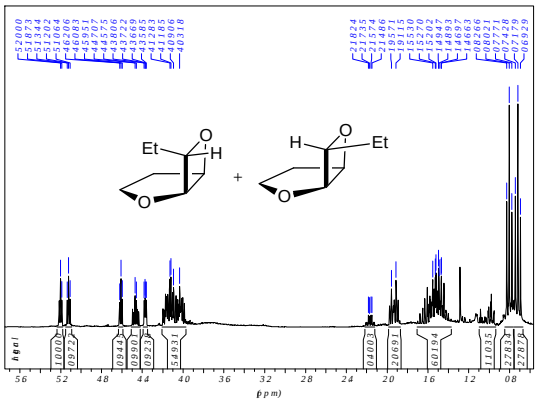


Figure 3.267: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***exo*- & *endo*-3c**.

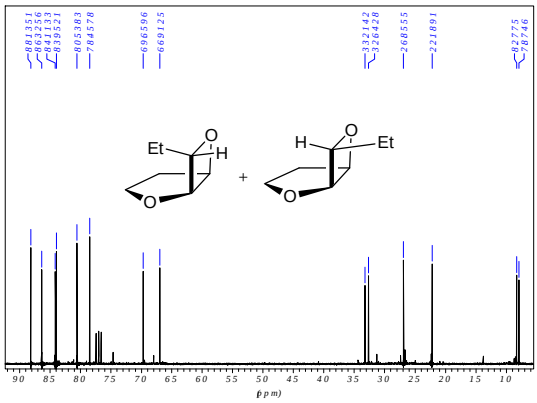


Figure 3.268: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***exo*- & *endo*-3c**.

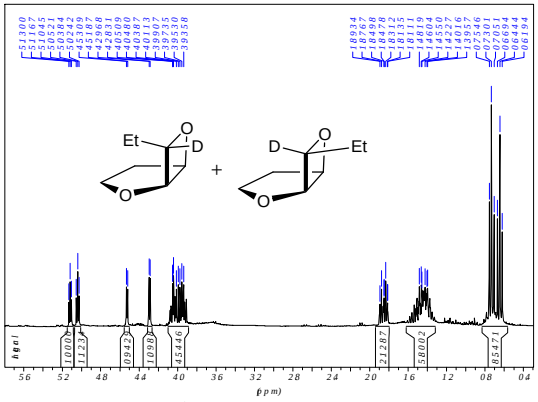


Figure 3.269: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***exo* & *endo*-85**.

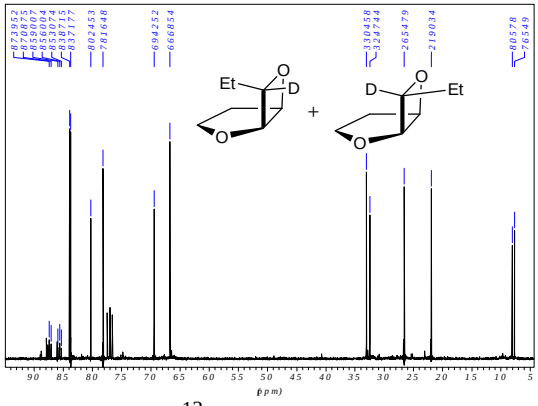


Figure 3.270: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***exo* & *endo*-85**.

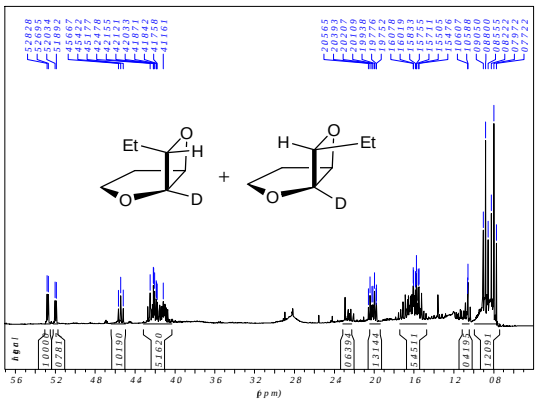


Figure 3.271: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***exo* & *endo*-86**.

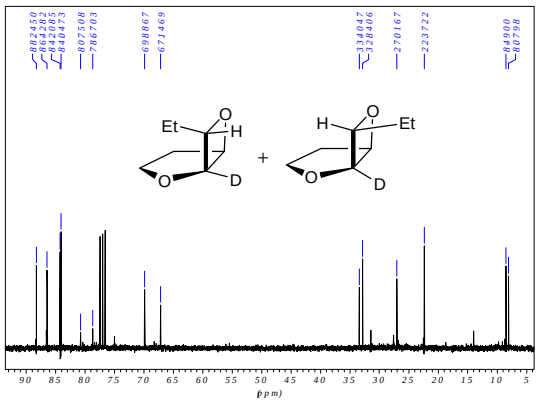


Figure 3.272: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***exo* & *endo*-86**.

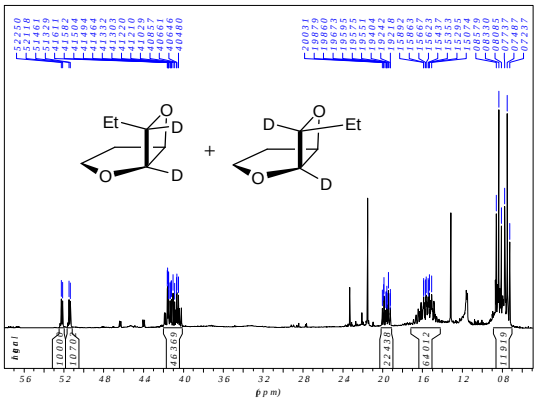


Figure 3.273: ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of ***exo* & *endo*-87**.

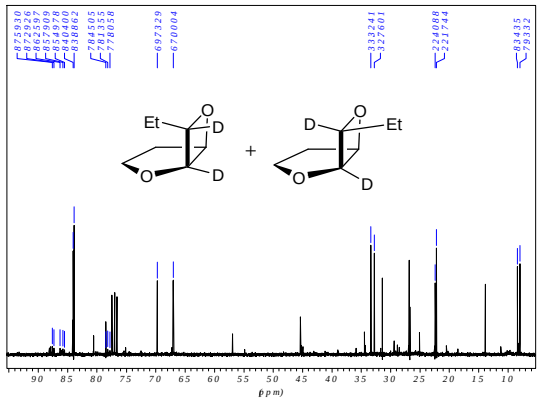


Figure 3.274: ^{13}C-NMR (75 MHz, $CDCl_3$) spectrum of ***exo* & *endo*-87**.

Mechanistic analysis

The formation of the thermodynamically unfavored *endo*-products in the triplet photocycloaddition of a carbonyl to a cyclic alkene was rationalized by assuming spin-orbit coupling (SOC) controlled intersystem crossing (ISC) geometries at the stage of triplet 1,4-biradical.[42] Figure 3.275 shows the triplet 1,4-biradical conformer with all possible three spin-orbit coupling-active geometries.

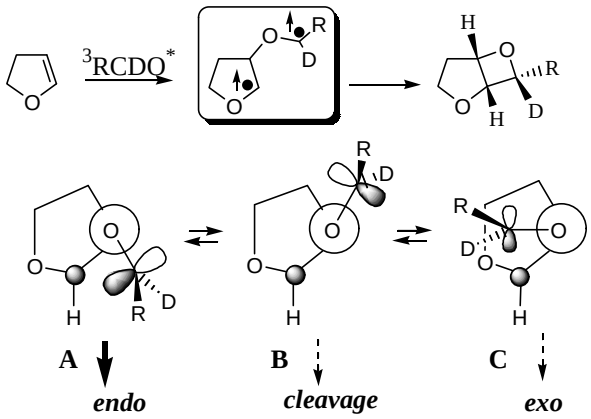


Figure 3.275: Conformers of 1,4-biradical intermediates.

The significant increase in *endo*-selectivity of the deuterated benzaldehyde/2,3-dihydrofuran-photoadducts can be explained as follows: If the radical centers in the triplet biradicals are separated by distance of several Å or more (like in conformer B), the singlet (S)-triplet (T) energy gap ΔE_{ST} decreases and intersystem crossing (ISC) is more strongly controlled by the weak hyperfine coupling (HFC) induced by nuclear-electron-spin interactions which are isotope dependent.

As easily recognized from the gyromagnetic ratios of ^{1}H and ^{2}H, hyperfine coupling is stronger by a factor of 6 for ^{1}H than for ^{2}H interaction with adjacent carbon radical. Thus, HFC-induced ISC is more relevant for ^{1}H-substituted radicals and consequently the alternative (strong) SOC-mechanism is expected to dominate for ^{2}H-substituted biradicals. As the *endo*-selectivity was interpreted (*vide supra*) as a mechanistic signature for SOC-mechanism, it appears logical, that *endo*-selectivity increases for ^{2}H-substituted 1,4-biradicals. Basically one has to assume, that the triplet 1,4-biradical lifetime is decreased when going from deuterated to non-deuterated intermediates, and this expectation has been also revealed.[136]

It was reported that the effect of deuterium substitution on the singlet and triplet lifetimes of carbonyl compounds in the vapor phase is dramatic. For example, the fluorescence quantum yield of formaldehyde[147] increases by a factor of about 20 upon going from CH_2=O to CD_2=O. The effect of deutration on acetone lifetime[148] is less apparent (τ_s acetone $-h_6$ is 1.7 ns, acetone-d_6 is 2.3 ns) but nonetheless significant. The substitution of D for H decreases the magnitude of k_{ISC} or IC. It is not yet clear whether a spin-orbit or Franck-Condon inhibition is involved

The lifetime of triplet propanal-1-d [149] is increased in comparsion with undeuterated propanal in vapor phase by a factor of 4.4. Thus, one should expect the rate of ISC from T_1 to S_1 will be decreased on going from propanal to propanal-1-d. However, our experiment did not at all visualize this effect, i.e. the *endo*-selectivity of “pure” triplet propanal-1d photoaddition was higher than for the propanal/2,3-dihydrofuran reaction. The results of propanal-1d/dihydrofuran photocycloaddition supported the results of benzaldehyde-1-d/cycloalkene photocycloaddition and may shed some light on the role of SOC and HFC on ISC.

4. Experimental part

4.1 General Remarks

Spectroscopic methods:

UV/VIS: Electronic spectra were recorded in acetonitrile unless otherwise stated, using a Perkin-Elmer Lambda 7 spectrophotometer and are listed as absorbance maxima (nm) followed by the extinction coefficient ε (cm^{-1} M^{-1}).

IR: Infrared spectra were recorded as KBr or CsI disc for solids or as neat films between sodium chloride plates for liquids using a Perkin-Elmer 1600 Series FTIR spectrophotometer.

^{1}H-NMR: The ^{1}H-NMR spectra were recorded on a Brucker AC 300 (300 MHz) spectrometer. The ^{1}H NMR chemical shifts are reported in δ_{ppm} using residual $CHCl_3$ (δ 7.24) in the perdeuterated solvent as the internal standard. Multiplicities were reported as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants J are given in Hz.

^{13}C-NMR: The ^{13}C-NMR spectra were recorded on Brucker AC 300 (75.5 MHz) spectrometer. ^{13}C NMR chemical shifts are reported in δ_{ppm} relative to the internal standard $CDCl_3$ (δ 77). Carbon multiplicities were determined by distortionless enhancement by polarization transfer (DEPT).

MS: Mass spectra were recorded using Finnigan Incos 500 instrument using positive ion electron impact (EI) techniques at 20 and 70 eV. Ions are quoted as an m/z value followed by intensity (%).

HRMS: High resolution mass spectra were recorded on a Finnigan MAT H-SQ 30 (FAB) spectrometer.

Chromatographic methods:

CC: Column chromatography was performed using SiO_2 60 (0.063 – 0.200 mm) as stationary phase. As a mobile phase, a mixture of n-hexane and ethyl acetate were used.

TLC: Thin layer chromatography was conducted on commercially precoated polygram® SIL – G/UV 254 plates (Macherey – Nagel) and also on precoated silica gel foils 60 F_{254} supplied by Merck and the chromatograms were visulized under a 254 nm UV lamp and / or with 5 % I_2 solution.

PLC: Preparative thick layer chromatography was carried out on 20 x 20 cm glass plates coated with silica gel (Merck Kieselgel G F_{254}) and eluted with the solvent system indicated. The separated compounds were located under 254 nm UV light and extracted using methylene chloride.

GC: Gas chromatography was performed on a Hewlett-Packard 5890 Series II instrument equipped with a capillary HP-5 cross-linked phenylmethylpolysiloxane (30 m x 0.32 mm) column, connected to FI- Detector and a HP 3395 calculating integrator, temperature program, 60-250°C in 20°C/min steps (1 min initial time), N_2 was used as flow gas.

Analytical methods:

X-ray analysis: The X – ray anaylsis was performed on an Enraf-Nonius CAD4 diffractometer at the Institute of Organic Chemistry-University of Cologne.

Elemental analysis: Combustion analyses were conducted at a Elementar Vario El. Instrument.

Melting points (M.p °C): All melting points were determined with a Büchi melting point apparatus (type Nr. 535) and are uncorrected.

Photolyses:

Glas apparatus: Quartz and pyrex® vessel were used for irradiation.

Reactors: Rayonet chamber photoreactors PRR- 208 (8 x 3000 Å lamps, ca. 800 W, $\lambda = 300 \pm 10$ nm), RPR – 100 (16 x 3500 Å lamps, ca. 400 W, $\lambda = 350 \pm 20$ nm) were used for irradiation and high pressure mercury lamp($\lambda > 290$ nm).

Solvent and Reagents: Benzene was purchased from Fluka and used without purification. All reagents were purchased from standard chemical supplies and purified to match the reported physical and spectral data.

Solvent and Reagents:

Solvents were dried by distillation over drying agents as follows: acetonitrile (P_2O_5), dichloromethane, chloroform, dimethyl formamide and pentane (CaH_2), diethylether, THF (Na / benzophenone), methanol, ethanol, propanol (Mg), pyridine and triethyl amine (KOH).

Conversion and Yield (%):

The conversion and yield % were determined by integration of characteristic signals in the crude ^{1}NMR spectra with an approx. error ± 5%.

Nomenclature:

All new compounds were named according to the Autonom program.[150]

4.2 General procedure for the photolyses of aldehydes and alkenes on the analytical scale: (Concentration study):

The mechanistic studies of carbonyl-ene photoreaction including concentration effect were carried out on a merry-go-round apparatus. This equipment consists of a rotating turntable having nine holes in an inner ring surrounding a quartz immersion well. The light source was a high pressure mercury lamp. Use of the merry-go-round apparatus ensured that all the samples recieve the same light quantity. The quartz tubes that were used were of a uniform quality, the samples to be irradiated always contained the same concentration of both aldehydes and alkenes so that equal light quantity were absorbed by all samples in any given run. Samples were made up in 10 mL volumetric flasks, then transfered to the tubes which were deoxygenated using N_2, corked and placed in the merry-go-round for irradiation at 10°C for 10 h. After photolysis the samples were analysed by GC and spectroscopic data. There are several common features in the spectral data of these bicyclic oxetane products. In the IR spectra, the two asymmetric C-O-C stretching bands of the oxetane ring are at ≅ 980 and 1030 cm^{-1}.[151] In the mass spectrum, retro-cycloaddition leads to the cation-radical peak for the carbonyl compound.

4.2.1 General procedure for the photolyses of aldehydes and alkenes on the preparative scale:

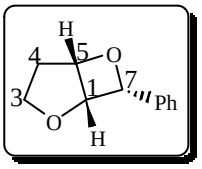
Alkenes (5 mmol) and aldehydes (5 mmol) were dissolved in 100 mL benzene, the solution transfered to a vacum – jacket pyrex tube and deoxygenated with a steady stream of N_2 gas. The reaction mixture was cooled to 10°C by means of a cold finger and irradiated in a Rayonet photoreactor (RPR 300 nm). The solvent was evaporated (40 °C, 20 torr) and the residue was purified by bulb-to-bulb distillation.

4.2.1.1 Photolyses of 2,3-dihydrofuran with aldehydes 1a-f:

Irradiation of 2,3-dihydrofuran with benzaldehyde (sbo-157)

A solution of 2,3-dihydrofuran (0.35 g, 5 mmol) and benzaldehyde (0.53 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.76 g (86 %) of inseparable mixture of oxetanes as a pale yellow viscous oil.

***endo*-7-Phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3a)**[152]



IR: (Nujol, mixture of *endo* & *exo*)

$\tilde{n}$ (cm^{-1}) = 3020, 2920, 1605, 1505, 1470, 1400, 1050, 835, 778.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.64 (ddd, J = 8.4, 11.2, 13.4 Hz, 1H, 4-H), 2.12 (dd, J = 5.4, 13.7 Hz, 1H, 4-H), 3.73 (ddd, J = 5.4, 8.6, 11.2 Hz, 1H, 3-H), 3.97 (dd, J = 8.4, 8.6 Hz, 1H, 3-H), 5.05 (dd, J = 4.5, 4.5 Hz, 1H, 1-H), 5.51 (dd, J = 4.5, 4.5 Hz, 1H, 5-H), 5.80 (d, J = 4.5 Hz, 1H, 7-H), 7.15-7.35 (m, 5H, $H_{arom.}$).

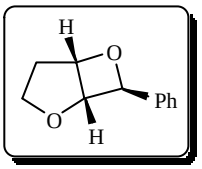
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.9 (t, C-4), 69.0 (t, C-3), 79.7 (d, C-1), 85.2 (d, C-5), 85.3 (d, C-7), 124.6 (d, $CH_{arom.}$), 127.0 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 137.6 (s, $Cq_{arom.}$).

MS: (EI, 20 eV)

m/z (%) = 176 (M^+, 27), 120 (40), 105 (20), 104 (25), 91 (100), 77 (20), 70 (20).

***exo*-7-Phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-3a)**[152]



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.77 (dddd, J = 4.2, 8.8, 10.8, 13.7 Hz, 1H, 4-H), 2.24 (dd, J = 4.5, 13.7 Hz, 1H, 4-H), 4.37 (m, 2H, 3-H & 3-H), 4.64 (dd, J = 2.4, 4.0 Hz, 1H, 1-H), 5.41 (d, J = 2.4 Hz, 1H, 1-H), 5.50 (dd, J = 4.2, 4.2 Hz, 1H, 5-H), 7.20-7.50 (m, 5H, $H_{arom.}$).

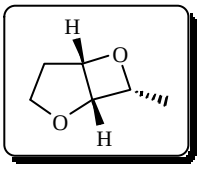
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.9 (t, C-4), 69.0 (t, C-3), 79.7 (d, C-1), 85.2 (d, C-5), 85.3 (d, C-7), 124.6 (d, $CH_{arom.}$), 127.0 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 137.6 (s, $Cq_{arom.}$).

Irradiation of 2,3-dihydrofuran with acetaldehyde (sbo-167)

A solution of 2,3-dihydrofuran (0.35 g, 5 mmol) and acetaldehyde (0.22 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.55 g (91 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3b)**[153]



GC: R_t = 3.5 min.

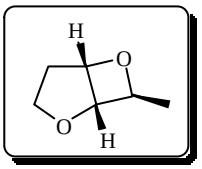
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.10 -1.85 (m, 2H, 4-H), 1.25 (d, J = 6.5 Hz, 3H, CH_3), 3.65 – 4.40 (m, 2H, 3-H), 4.58 (dq, J = 2.8, 6.5 Hz, 1H, 7-H), 4.73 (dd, J = 3.8, 3.8 Hz, 1H, 5-H), 5.36 (dd, J = 2.8, 3.8 Hz, 1H, 1-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 20.1 (q, CH_3), 33.3 (t, C-4), 67.2 (t, C-3), 79.2 (d, C-1), 82.2 (d, C-5), 83.9 (d, C-7).

***exo*-7-Methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-3b)**[153]



GC: R_t = 3.4 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.10 -1.85 (m, 2H, 4-H), 1.41 (d, J = 6.4 Hz, 3H, CH_3), 3.65–4.40 (m, 2H, 3-H), 4.49 (dd, J = 2.6, 4.0 Hz, 1H, 5-H), 4.93 (dq, J = 4.2, 6.4 Hz, 1H, 7-H), 5.32 (dd, J = 4.0, 4.2 Hz, 1H, 1-H).

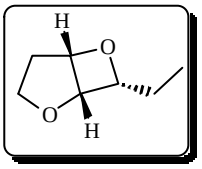
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 20.5 (q, CH_3), 32.8 (t, C-4), 69.8 (t, C-3), 81.6 (d, C-1), 83.8 (d, C-5), 84.4 (d, C-7).

Irradiation of 2,3-dihydrofuran with propionaldehyde (sbo-P2)

A solution of 2,3-dihydrofuran (0.35 g, 5 mmol) and propionaldehyde (0.29 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.51 g (80 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7 -Ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3c)**[154]



GC: R_t = 6.5 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (t, J = 7.4 Hz, 3H, CH_3), 1.59 - 1.65 (m, 2H, $\underline{CH_2}CH_3$), 1.66 - 2.06 (m, 2H, 4-H), 4.17-4.27 (m, 2H, 3-H), 4.60 (ddd, J = 4.1, 4.0, 4.1 Hz, 1H, 7-H), 4.75 (dd, J = 3.8, 4.0 Hz, 1H, 1-H), 5.34 (dd, J = 3.8, 3.8 Hz, 1H, 5-H).

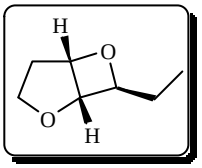
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.6 (q, CH_3), 22.5 (t, CH_2), 32.9 (t, C-4), 70.0 (t, C-3), 78.8 (d, C-1), 84.3 (d, C-5), 86.6 (d, C-7).

MS: (EI, 20 eV)

m/z (%) = 128 (M^+, 20), 99 (100), 86 (43), 71 (50), 70 (68), 58 (60), 57 (78).

***exo*-7- Ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-3c)**[154]



GC: R_t = 6.4 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.94 (t, J = 7.4 Hz, 3H, CH_3), 1.67-1.76 (m, 2H, $\underline{CH_2}CH_3$), 1.77 - 2.08 (m, 2H, 4-H), 4.17 - 4.26 (m, 2H, 3-H), 4.31 (dd, J = 2.5, 2.9 Hz, 1H, 7-H), 4.51 (dd, J = 4.1, 4.3 Hz, 1H, 1-H), 5.25 (dd, J = 3.8, 3.8 Hz, 1H, 5-H).

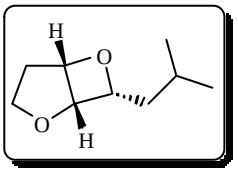
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.2 (q, CH_3), 27.2 (t, CH_2), 33.5 (t, C-4), 67.3 (t, C-3), 80.9 (d, C-1), 84.4 (d, C-5), 88.5 (d, C-7).

Irradiation of 2,3-dihydrofuran with 3-methylbutyraldehyde (sbo-P4)

A solution of 2,3-dihydrofuran (0.35 g, 5 mmol) and 3-methylbutyraldehyde (0.43 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.68 g (87 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Isobutyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3d)**



GC: R_t = 9.2 min.

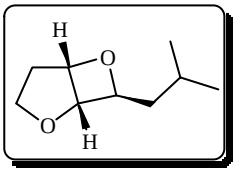
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.6 Hz, 6H, $2CH_3$), 1.43 (m, 1H, CH), 1.54 - 1.61 (m, 2H, CH_2), 1.96 - 2.16 (m, 2H, 4-H), 4.18 (m, 2H, 3-H), 4.73 (dd , J = 3.8, 4.0 Hz, 1H, 1-H), 4.78 (ddd, J = 4.0, 4.0, 3.5 Hz, 1H, 7-H), 5.33 (dd, J = 3.7, 3.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.7 (q, CH_3), 22.8 (q, CH_3), 22.9 (d, CH), 33.3 (t, C-4) , 38.4 (t, CH_2), 70.2 (t, C-3), 79.9 (d, C-1), 84.8 (d, C-5) , 84.9 (d, C-7).

***exo*-7-Isobutyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-3d)**



GC: R_t = 9.1 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (d, J = 6.7 Hz, 6H, $2CH_3$), 1 .43 - 1.48 (m, 2H, CH_2), 1.96 - 2.10 (m, 2H, 4-H), 2.11-2.13 (m, 1H, CH) , 4.12(m , 2H , 3-H), 4.30 (dd, J = 4.1, 2.6 Hz, 1H, 1-H), 4.5 (ddd, J = 2.8, 1.3, 2.2 Hz, 1H, 7-H), 5.27 (dd, J = 4.1, 4.1 Hz, 1H, 5-H).

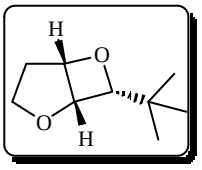
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.8 (q, CH_3), 22.9 (q, CH_3), 23.0 (d, CH), 33.9 (t, C-4) , 43.3 (t, CH_2), 68.6 (t, C-3), 82.2 (d, C-1), 84.8 (d, C-5), 86.6 (d, C-7).

Irradiation of 2,3-dihydrofuran with pivalaldehyde (sbo-P16)

A solution of 2,3-dihydrofuran (0.35 g, 5 mmol) and pivalaldehyde (0.43 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.62 g (80 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-*tert*-Butyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3e)**



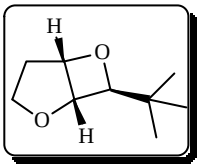
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.98 (s, 9H, $3CH_3$), 1.99 (m, 2H, 4-H) , 3.50-3.66 (m, 2H, 3-H), 3.82 (d, J = 3.5Hz, 1H, 7-H), 4.60 (dd, J = 3.7, 3.5 Hz, 1H, 1-H), 5.10 (dd, J = 3.7, 4.0 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.4 (q, CH_3), 24.8 (q, CH_3), 26.7 (q, CH_3), 31.3 (s, Cq), 37.8 (t, C-4) , 69.3 (t, C-3), 81.1 (d, C-1), 86.5 (d, C-5), 90.6 (d, C-7).

***exo*-7-*tert*-Butyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-3e)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.67 (s, 9H , $3CH_3$), 1.88 (m, 2H, 4-H), 3.50 - 3.66 (m, 2H, 3-H), 4.05 (d, J = 3.67 Hz, 1H, 7-H), 4.45 (dd, J = 3.7, 4.1 Hz, 1H, 1-H), 5.0 (dd, J = 4.1, 4.1 Hz, 1H, 5-H).

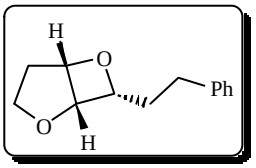
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.4 (q, CH_3), 24.8 (q, CH_3), 26.7 (q, CH_3), 32.7 (s, Cq), 33.3 (t, C-4), 66.6 (t, C-3), 83.0 (d, C-1) , 83.8 (d, C-5), 83.9 (d, C-7).

Irradiation of 2,3-dihydrofuran with 3-phenylpropionaldehyde (sbo-P6)

A solution of 2,3-dihydrofuran (0.35 g, 5 mmol) and 3-phenylpropionaldehyde (0.67 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.76 g (75 %) of inseparable mixture of oxetanes as a pale yellow viscous oil.

***endo*-7-Phenethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3f)**



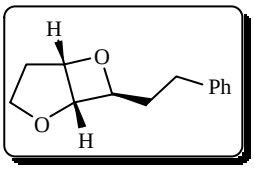
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.15 (t, J = 7.7 Hz, 2H, CH_2), 1.45 (m, 2H, CH_2), 1.98 (m, 2H, 4-H), 4.05 (m, 2H, 3-H), 4.60 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.70 (dt, J = 4.1, 4.0, 4.0 Hz, 1H, 7-H), 5.30 (dd, J = 3.7, 3.7 Hz, 1H, 5-H), 7.21 - 7.77 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 29.9 (t, CH_2), 30.3 (t, CH_2), 35.4 (t, C-4), 69.4 (t, C-3), 78.3 (d, C-1), 83.8 (d, C-5), 84.0 (d, C-7), 125.4 (d, $CH_{arom.}$), 127.8 (d, CH_{arom}), 129.3 (d, $CH_{arom.}$), 140.7 (s, $Cq_{arom.}$).

***exo*-7-Phenethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-3f)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.15 (t, J = 7.7 Hz, 2H, CH_2), 1.45 (m, 2H, CH_2), 1.98 (m, 2H, 3-H), 4.20 (m, 2H, 4-H), 4.38 (dddd, J = 2.5, 2.5, 2.4, 2.2 Hz, 1H, 7-H), 4.49 (dd, J = 2.5, 2.5 Hz, 1H, 1-H), 5.27 (dd, J = 4.1, 4.0 Hz, 1H, 5-H), 7.20 - 7.45 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

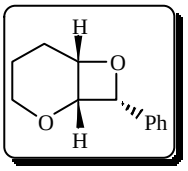
δ_{ppm} = 29.9 (t, CH_2), 32.4 (t, CH_2), 32.9 (t, C-4), 66.7 (t, C-3), 80.5 (d, C-1), 83.9 (d, C-5), 85.9 (d, C-7), 126.4 (d, $CH_{arom.}$), 127.4 (d, $CH_{arom.}$), 128.4 (d, $CH_{arom.}$), 140.8 (s, $Cq_{arom.}$).

4.2.1.2 Photolyses of 2,3-dihydropyran with aldehydes 1a-d:

Irradiation of 2,3-dihydropyran with benzaldehyde (sbo-68)

A solution of 2,3-dihydropyran (0.42 g, 5 mmol) and benzaldehyde (0.53 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.84 g (88 %) of inseparable mixture of oxetanes as a pale yellow viscous oil.

***endo*-8-Phenyl-2,7-dioxa-bicyclo[4.2.0]octane (*endo*-5a)**[152]



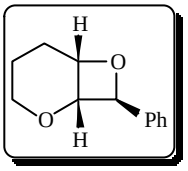
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.50 – 2.20 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.66 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.91 (m, 1H, 6-H), 5.70 (d, J = 4.0 Hz, 1H, 8-H), 7.20 – 7.50 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

20.9 (t, C-4), 26.0 (t, C-5), 63.5 (t, C-3), 73.5 (d, C-1), 74.8 (d, C-6), 82.9 (d, C-8), 126.7 (d, $CH_{arom.}$), 127.7 (d, $CH_{arom.}$), 128.9 (d, $CH_{arom.}$), 136.9 (s, $Cq_{arom.}$).

***exo*-8-Phenyl-2,7-dioxa-bicyclo[4.2.0]octane (*exo*-5a)**[152]



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.52 – 2.20 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.36 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.91 (m, 1H, 6-H), 5.62 (d, J = 4.1 Hz, 1H, 8-H), 7.20 – 7.50 (m, 5H, $H_{arom.}$).

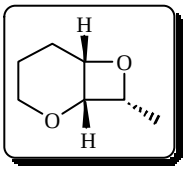
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

20.5 (t, C-4), 26.2 (t, C-5), 64.5 (t, C-3), 73.6 (d, C-1), 74.5 (d, C-6), 82.8 (d, C-8), 126.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.2 (d, $CH_{arom.}$), 136.9 (s, $Cq_{arom.}$).

Irradiation of 2,3-dihydropyran with acetaldehyde (sbo-67)

A solution of 2,3-dihydropyran (0.42 g, 5 mmol) and acetaldehyde (0.22 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.64 g (86 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-8-Methyl-2,7-dioxa-bicyclo[4.2.0]octane (*endo*-5b)**[153]



GC: R_t = 4.5 min.

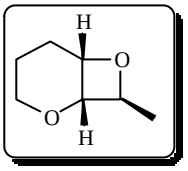
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.21 (d, J = 5.2 Hz, 3H, CH_3), 1.52 – 2.20 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.36 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.69 (d, J = 5.2 Hz, 1H, 6-H), 5.41 (dq, J = 4.1, 5.2 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

19.9 (q, CH_3), 21.5 (t, C-4), 28.2 (t, C-5), 67.5 (t, C-3), 79.6 (d, C-1), 84.5 (d, C-6), 89.8 (d, C-8).

***exo*-8-Methyl-2,7-dioxa-bicyclo[4.2.0]octane (*exo*-5b)**[153]



GC: R_t = 4.6 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.35 (d, J = 6.5 Hz, 3H, CH_3), 2.34 (m, 2H, 5-H), 2.37 (m, 2H, 4-H), 3.58 – 3.73 (m, 2H, 3-H), 4.36 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.64 (dq, J = 3.4, 6.5 Hz, 1H, 8-H), 5.54 (d, J = 4.3 Hz, 1H, 6-H).

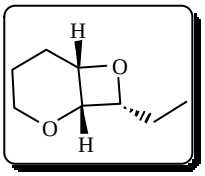
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

20.8 (q, CH_3), 26.2 (t, C-5), 33.7 (t, C-4), 62.5 (t, C-3), 72.6 (d, C-1), 78.5 (d, C-6), 83.8 (d, C-8).

Irradiation of 2,3-dihydropyran with propionaldehyde (sbo-66)

A solution of 2,3-dihydropyran (0.42 g, 5 mmol) and propionaldehyde (0.29 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.53 g (75 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-8-Ethyl-2,7-dioxa-bicyclo[4.2.0]octane (*endo*-5c)**[153]



GC: R_t = 5.3 min.

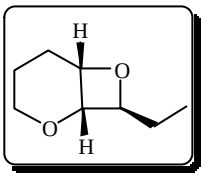
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (t, J = 7.4 Hz, 3H, CH_3), 1.74 (dq, J = 2.0, 7.4 Hz, 2H, CH_2), 1.82 – 2.20 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.41 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.98 (m, 1H, 6-H), 5.35 (d, J = 4.1 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

8.5 (q, CH_3), 22.4 (t, CH_2), 23.5 (t, C-4), 26.2 (t, C-5), 64.5 (t, C-3), 73.6 (d, C-1), 78.5 (d, C-6), 92.8 (d, C-8).

***exo*-8-Ethyl-2,7-dioxa-bicyclo[4.2.0]octane (*exo*-5c)**[153]



GC: R_t = 5.4 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (t, J = 7.3 Hz, 3H, CH_3), 1.67 (dq, J = 2.6, 7.3 Hz, 2H, CH_2), 1.82 – 2.25 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.44 (dd, J = 4.2, 4.2 Hz, 1H, 1-H), 4.87 (m, 1H, 6-H), 5.45 (dd, J = 4.2, 4.1 Hz, 1H, 8-H).

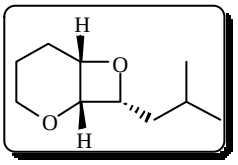
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

8.6 (q, CH_3), 23.2 (t, CH_2), 25.8 (t, C-4), 26.9 (t, C-5), 69.5 (t, C-3), 78.6 (d, C-1), 79.5 (d, C-6), 86.8 (d, C-8).

Irradiation of 2,3-dihydropyran with 3-methylbutyraldehyde (sbo-74)

A solution of 2,3-dihydropyran (0.42 g, 5 mmol) and 3-methylbutyraldehyde (0.43 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.68 g (80 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-8-Isobutyl-2,7-dioxa-bicyclo[4.2.0]octane (*endo*-5d)**



GC: R_t = 6.6 min.

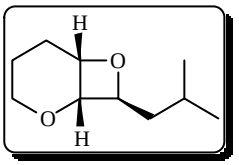
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.87 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.12 (m, 1H, CH), 1.34 - 1.43 (m, 2H, CH_2), 1.52 – 2.20 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.41 (dd, J = 4.1, 4.0 Hz, 1H, 1-H), 4.96 (m, 1H, 6-H), 5.52 (d, J = 4.1 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

16.3 (q, CH_3), 17.4 (q, CH_3), 20.9 (t, C-4), 25.3 (d, CH), 26.8 (t, C-5), 37.5 (t, CH_2), 67.5 (t, C-3), 78.6 (d, C-1), 79.5 (d, C-6), 87.8 (d, C-8).

***exo*-8-Isobutyl-2,7-dioxa-bicyclo[4.2.0]octane (*exo*-5d)**



GC: R_t = 6.7 min.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (d, J = 6.6 Hz, 6H, $2CH_3$), 1.18 (m, 1H, CH), 1.38-1.48 (m, 2H, CH_2), 1.52 – 2.20 (m, 4H, 4-H & 5-H), 3.25 (dt, J = 2.2, 11.2 Hz, 2H, 3-H), 4.36 (dd, J = 4.0, 4.0 Hz, 1H, 1-H), 4.91 (m, 1H, 6-H), 5.62 (d, J = 4.1 Hz, 1H, 8-H).

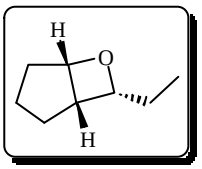
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

18.6 (q, CH_3), 18.9 (q, CH_3), 20.5 (t, C-4), 24.7 (d, CH), 26.2 (t, C-5), 64.5 (t, C-3), 73.6 (d, C-1), 74.5 (d, C-6), 82.8 (d, C-8).

4.1.2.3 Photolysis of cyclopentene with propionaldehyde (sbo-P1)

A solution of propionaldehyde (0.29 g, 5 mmol) and cyclopentene (0.34 g, 5 mmol) in 100 mL benzene was irradiated following the general procedure for 24 h. Distillation of the residue after evapouation of the solvent afforded 0.52 g (83 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Ethyl-6-oxa-bicyclo[3.2.0]heptane (*endo*-7c)**



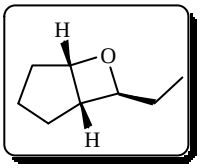
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (t, 3H, CH_3), 1.59 - 1.65 (m, 2H, CH_2), 1.70-2.38 (m, 6H, $3CH_2$), 3.93 (ddd, J = 4.2, 4.1, 4.0 Hz, 1H, 1-H), 4.55 (dd, J = 7.2, 7.1 Hz, 1H, 7-H), 5.10 (dd, J = 4.2, 4.3 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.6 (q, CH_3), 25.4 (t, CH_2), 29.8 (t, C-2), 30.1 (t, C-3), 33.85 (t, C-4), 40.3 (d, C-5), 82.1 (d, C-1), 84.4 (d, C-7).

***exo*-7-Ethyl-6-oxa-bicyclo[3.2.0]heptane (*exo*-7c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.94 (t, 3H, CH_3), 1.67 - 1.76 (m, 2H, CH_2), 1.77 - 2.38 (m, 6H, $3CH_2$), 3.50 (m, 1H, 1-H), 4.05 (dd, J = 4.1, 4.3 Hz, 1H, 7-H), 4.99 (dd, J = 5.0, 4.3 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

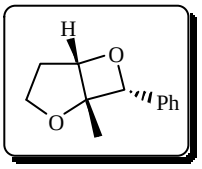
δ_{ppm} = 7.9 (q, CH_3), 25.8 (t, CH_2), 26.6(t, C-2), 30.8 (t, C-3), 34.4 (t, C-4), 42.9 (d, C-5), 84.5 (d, C-1), 86.4 (d, C-7).

4.2.1.4 Photolyses of 5-methyl-2,3-dihydrofuran with aldehydes 1a-d:

Irradiation of 5-methyl-2,3-dihydrofuran with benzaldehyde (sbo-268)

A solution of 5-methyl-2,3-dihydrofuran (0.42 g, 5 mmol) and benzaldehyde (0.53 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.8 g (84 %) of inseparable mixture of oxetanes as a pale yellow viscous oil.

***endo*-7-Phenyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-9a)**[152]



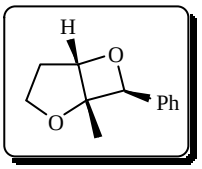
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.52 (s, 3H, CH_3), 1.68 (dddd, J = 4.2, 8.2, 11.2, 13.8 Hz, 1H, 4-H), 2.04 (dd, J = 5.3, 13.8 Hz, 1H, 4-H), 3.71 (ddd, J = 5.3, 8.8, 11.2 Hz, 1H, 3-H), 3.88 (dd, J = 8.2, 8.8 Hz, 1H, 3-H), 5.10 (d, J = 4.5 Hz, 1H, 5-H), 5.58 (s, 1H, 7-H), 7.17 - 7.32 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.4 (q, CH_3), 33.0 (t, C-4), 69.1 (t, C-3), 77.2 (s, C-1), 89.1 (d, C-5), 89.6 (d, C-7), 124.3 (d, $CH_{arom.}$), 127.0 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 137.8 (s, $Cq_{arom.}$).

***exo*-7-Phenyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-9a)**[152]



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (s, 3H, CH_3), 1.80 (m, 1H, 4-H), 2.14 (m, 1H, 4-H), 4.29-4.36 (m, 2H, 3-H), 4.99 (d, J = 4.0 Hz, 1H, 5-H), 5.44 (s, 1H, 7-H), 7.19 - 7.33 (m, 5H, $H_{arom.}$).

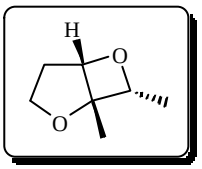
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.8 (q, CH_3), 34.1 (t, C-4), 67.7 (t, C-3), 89.3 (d, C-5), 89.5 (s, C-1), 90.9 (d, C-7), 125.3 (d, $C_{arom.}$), 127.6 (d, $C_{arom.}$), 128.4 (d, $C_{arom.}$), 138.8 (s, $Cq_{aroms.}$).

Irradiation of 5-methyl-2,3-dihydrofuran with acetaldehyde (sbo-203)

A solution of 5-methyl-2,3-dihydrofuran (0.42 g, 5 mmol) and acetaldehyde (0.22 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.59 g (92 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-1,7-Dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-9b)**



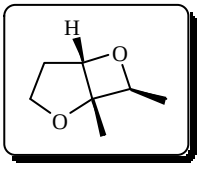
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.10 (d, J = 6.5 Hz, 3H, CH_3), 1.21 (s, 3H, CH_3), 2.35 (dd, J = 6.9, 6.9 Hz, 2H, 4-H), 4.15 - 4.21 (m, 2H, 3-H), 4.62 (q, J = 6.5 Hz, 1H, 7-H), 4.87 (d, J = 3.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 19.8 (q, CH_3), 32.6 (t, C-4), 69.5 (t, C-3), 85.2 (s, C-1), 85.5 (d, C-5), 88.0 (d, C-7).

***exo*-1,7-Dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-9b)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.22 (s, 3H, CH_3), 1.28 (d, J = 6.5 Hz, 3H, CH_3), 2.43 (dd, J = 7.2, 7.2 Hz, 2H, 4-H), 4.15 - 4.21 (m, 2H, 3-H), 4.54 (q, J = 6.5 Hz, 1H, 7-H), 4.77 (d, J = 4.1 Hz, 1H, 5-H).

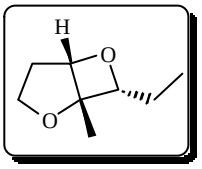
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.4 (q, CH_3), 18.2 (q, CH_3), 33.8 (t, C-4), 67.0 (t, C-3), 85.3 (s, C-1), 85.6 (d, C-5), 87.9 (d, C-7).

Irradiation of 5-methyl-2,3-dihydrofuran with propionaldehyde (sbo-251)

A solution of 5-methyl-2,3-dihydrofuran (0.42 g, 5 mmol) and propionaldehyde (0.29 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.72 g (88 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Ethyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-9c)**



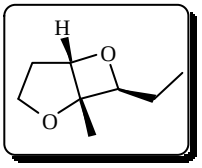
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (t, J = 7.5 Hz, 3 H, CH_3), 1.34 (s, 3H, CH_3), 1.63 - 1.78 (m, 2H, CH_2), 1.85 - 2.00 (m, 2H, CH_2), 4.05 - 4.15 (m, 2H, 3-H), 4.45 (dd, J = 7.2, 7.35 Hz, 1H, 7-H), 4.93 (d , J = 3.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.4 (q, CH_3), 19.8 (q, CH_3), 21.8 (t, CH_2), 33.1 (t, C-4), 66.2 (t, C-3), 84.4 (s, C-1), 86.9 (d, C-5), 89.8 (d, C-7).

***exo*-7-Ethyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-9c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (t, J = 7.5 Hz, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.63 - 1.78 (m, 2H, CH_2), 1.85 - 2.00 (m, 2H, 4-H), 4.05 (m, 2H, 3-H), 4.30 (dd, J =5.6, 5.4 Hz, 1H, 7-H), 4.82 (d, 4.0 Hz, 1H, 5-H).

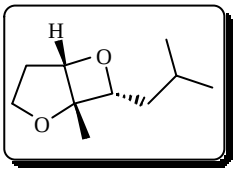
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.8 (q, CH_3), 15.2 (q, CH_3), 25.3 (t, CH_2), 32.0 (t, C-4), 68.9 (t, C-3), 84.8 (s, C-1), 87.2 (d, C-5), 89.9 (d, C-7).

Irradiation of 5-methyl-2,3-dihydrofuran with 3-methylbutyraldehyde (sbo-260)

A solution of 5-methyl-2,3-dihydrofuran (0.42 g, 5 mmol) and 3-methylbutyraldehyde (0.43 g, 5 mmol) in 100 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue after evaporation of the solvent afforded 0.69 g (81 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Isobutyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-9d)**



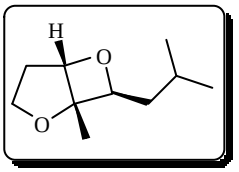
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.6 Hz, $2CH_3$), 0.85 - 0.93 (m, 1H, CH), 1.25 (s, 3H, CH_3), 1.55 - 1.65 (m, 2H, CH_2), 1.92 (m, 2H, 4-H), 4.10 - 4.19 (m, 2H, 3-H), 4.56 (dd, J = 6.8, 6.6 Hz, 1H, 7-H), 4.85 (d, J = 3.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.9 (q, CH_3), 21.8 (q, CH_3), 22.3 (q, CH_3), 24.0 (d, CH), 32.4 (t, C-4), 37.6 (t, CH_2), 69.1 (t, C-3), 85.0 (s, C-1), 87.4 (d, C-5), 87.4 (d, C-7).

***exo*-7-Isobutyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-9d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

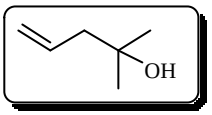
δ_{ppm} = 0.83 (d, J = 6.7 Hz, 6 H, $2CH_3$), 1.25 (s, 3H, CH_3), 1.55 - 1.65 (m, 2H, CH_2), 2.12 (m, 2H, 4-H), 4.10 - 4.20 (m, 2H, 3-H), 4.44 (dd, J = 3.7, 9.7 Hz, 1H, 7-H), 4.74 (d, J = 4.0 Hz,1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 21.5 (q, CH_3), 22.5 (q, CH_3), 24.2 (d, CH), 33.4 (t, C-4), 41.4 (t, CH_2), 66.6 (t, C-3), 85.4 (s, C-1), 87.4 (d, C-5), 87.6 (d, C-7).

4.3 Synthesis of 2,2-dimethyl-2,3-dihydrofuran

Preparation of 2-methyl-pent-4-en-2-ol (10) (sbo-211)



Method A:[87]

A 250 mL three neck round-bottomed flask, containing a magnetic stirring bar, was equipped with a dropping funnel, and a reflux condenser. Finely powdered magnesium of good quality (18.3 g, 0.75 mol) was covered with dry ether (50 mL), and allyl bromide (30.3 g, 0.25 mol) dissolved in ether (150 mL), was added with vigrous stirring during 4 h, the solvent continued in gentle boiling through the reaction, and stirred for further 3h, then heated to reflux for 30 min. After cooling to room temperature, acetone (14.5 g, 0.25 mol) in ether (25 mL) was added dropwise and the stirring is continued further for 1h. Then the mixture was added dropwise into a cold saturated solution of ammonium chloride, extracted with ether, washed with brine solution and dry over anhydrous Mg SO_4. Then evaporated the solvent under reduced pressure and the remainder solution was subjected to long column distillation to give the pure product in 40 % yield, (B.p = 117 – 118 °C, Lit,[87] 115-118°C).

Method B:[88]

Into a stirred solution of acetone (7.34 g, 0.127 mol) and allyl bromide (19.88 g, 0.127 mol) in a 125 mL dimethylformamide, zinc dust (12.5 g) was added at room temperature under the atmosphere. An exothermic reaction started within 10 min. and it ceased in 30 min, Then the reaction mixture was poured into a saturated aqueous solution of ammonium chloride (100 mL), extracted with ether (30 mL x 3), and the combined organic phase was dried over anhydrous Mg SO_4. Rotoevaporation of the solvent (20 °C, 15 torr) yielded 8.3 g (70%) of a yellow liquid, which on distillation (B.p = 117-118 °C) afforded 7.5 g (68 %) of the allylic alcohol as a colorless liquid.

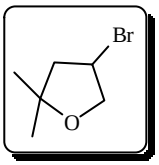
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.13 (s, 6H, $2CH_3$), 2.00 (s, 1H, OH), 2.15 (d, J = 7.5 Hz, 2H, CH_2), 5.04 (m, 2H, 5-H), 5.83 (m, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 28.9 (q, $2CH_3$), 48.1 (t, CH_2), 70.18 (s, Cq), 118.2 (t, C-5), 134.2 (d, C-4).

Preparation of 4-bromo-2,2-dimethyl-tetrahydrofuran (11)[86] (sbo-215)



A 250- mL two-necked round-bottomed flask, containing stirring bar, is equipped with a dropping funnel, reflux condenser. The dropping funnel is charged with Br_2 (8.8 g, 55 mmol). The flask is charged with dimethyl allyl carbinol (5.5 g, 55 mmol) with 100 mL of dry ether and cooled with an ice-water bath (0-5°C). Bromine is added dropwise over a period of 8 min. The solution is stirred for a further 2h, then quinoline (7.8 g) is added in one portion and the solution is slowly heated to reflux. The reflux is continued for 2h, (notice the separation of a white ppt from quinoline hydrobromide salt during the heating). Then the solution is allowed to cool to room temperature and the precipitate was filtered, washed with dry ether and the solvent was evaporated under *vacum*. Fractional distillation of the residue (B.p 62 °C, 10 torr) yielded 3.5 g (70 %) of 4-bromo-2,2-dimethyl-tetrahydrofuran **11** as a colorless liquid.

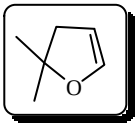
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.20 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 2.12 (dd, J = 13.8, 5.6 Hz, 1H, 3-H), 2.33 (dd, J = 13.8, 7.7 Hz, 3-H), 4.0 (dd, J = 10.0, 5.6 Hz, 1H, 5-H), 4.16 (dd, J = 10.1, 5.7 Hz, 1H, 5-H), 4.36 (dddd, J = 13.2, 11.2, 7.7, 5.6 Hz, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 28.4 (q, CH_3), 28.5 (q, CH_3), 45.2 (t, C-3), 48.9 (d, C-4) , 74.6 (t, C-5) , 81.2 (s, C-2).

Preparation of 2,2-dimethyl-2,3-dihydrofuran (13)[86] (sbo-216)



Distillation of 2,2-dimethyl-4-bromotetrahydrofuran (3.58 g, 20 mmol) with 2 g of potassium hydroxide pellets gave a mixture of two regioisomers of dihydrofuran at B.p 78 –82 °C which separated by column chromatography using a mixture of ethyl acetate and n-hexane as eluent, the less polar being the major product, 2,2-dimethyl-2,3-dihydrofuran (**13**).

Yield: 0.9 g (46 %)

TLC: R_f = 0.23 (EA/n-HE 1 : 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.31 (s, 6H, $2CH_3$), 2.37 (m, 2H, 3-H), 4.73 (m, 1H, 4-H), 6.61 (m, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 28.1 (q, CH_3), 28.1 (q, CH_3), 42.2 (t, C-3), 73.9 (s, C-2), 98.2 (d, C-4), 144.0 (d, C-5).

2,2-Dimethyl-2,5-dihydrofuran (12)[86]

Yield: 0.23 g (12 %)

TLC: R_f = 0.43 (EA/n-HE 1 : 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.31 (s, 6H, $2CH_3$), 4.59 (m, 2H, 5-H), 5.71 (m, 2H, 3-H & 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 27.6 (q, CH_3), 29.0 (q, CH_3), 84.3 (t, C-5), 87.4 (s, C-2), 124.6 (d, C-3), 135.2 (d, C-4).

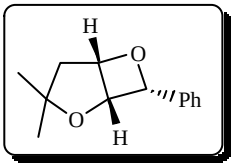
4.3.1 Photolyses of 2,2-dimethyl-2,3-dihydrofuran with aldehydes; General procedure:

Under a nitrogen atmosphere, a solution of 2,2-dimethyl-2,3-dihydrofuran (3 mmol) and aldehyde (3 mmol) in 30 mL benzene in a quartz tube was irradiated in a Rayonet Photoreactor (300 nm) at room temperature. The solvent was removed in *vacuo*, and the residue was purified by bulb to bulb distillation.

Irradiation of 2,2-dimethyl-2,3-dihydrofuran with benzaldehyde (sbo-220)

A solution of 2,2-dimethyl-2,3-dihydrofuran (0.29 g, 3 mmol) and benzaldehyde (0.31 g, 3 mmol) in 30 mL benzene was irradiated for 24 h following the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.45 g (74 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-3,3-Dimethyl-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-14a)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.15 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.74 - 1.94 (m, 2H, 4-H), 4.38 (dd, J = 3.7, 3.8 Hz, 1H, 1-H), 5.30 (dd, J = 3.8, 3.8 Hz, 1H,5-H), 5.73 (d, J = 3.8 Hz, 1H, 7-H), 7.25 - 7.32 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

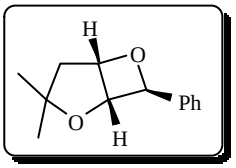
δ_{ppm} = 29.3 (q, CH_3), 29.9 (q, CH_3), 46.8 (t, C-4), 79.8 (s, C-3), 80.4 (d, C-1), 85.2 (d, C-5), 89.4 (d, C-7), 126.4 (d, $CH_{arom.}$), 128.4 (d, $CH_{arom.}$), 129.2 (d, $CH_{arom.}$), 134.3 (s, $Cq_{arom.}$).

HRMS: ($C_{13}H_{16}O_2$, M = 204.12)

Calcd: 204.1178

Found: 204.1176

***exo*-3,3-Dimethyl-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-14a)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.21 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.79 - 1.98 (m, 2H, 4-H), 4.64 (dd, J = 3.8, 3.8 Hz, 1H, 1-H), 4.97 (d, J = 3.8 Hz, 1H,7-H), 5.23 (dd, J = 3.8, 3.8 Hz, 1H, 5-H), 7.26 – 7.33 (m, 5H, $H_{arom.}$).

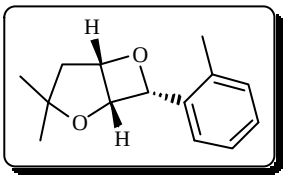
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 29.2 (q, CH_3), 30.7 (q, CH_3), 49.4 (t, C-4), 76.3 (s, C-3), 86.4 (d, C-1), 89.0 (d, C-5), 90.4 (s, C-7), 126.8 (d, $CH_{arom.}$), 128.9 (d, $CH_{arom.}$), 129.6 (d, $CH_{arom.}$), 135.3 (s, $Cq_{arom.}$).

Irradiation of 2,2-dimethyl-2,3-dihydrofuran with o-tolualdehyde (sbo-224g)

A solution of 2,2-dimethyl-2,3-dihydrofuran (0.29 g, 3 mmol) and o-tolualdehyde (0.36 g, 3 mmol) in 30 mL benzene was irradiated for 24 h following the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.42 g (64 %) of inseparable mixture of oxetanes as a pale yellow viscous oil.

***endo*-3,3-Dimethyl-7-*o*-tolyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-14b)**



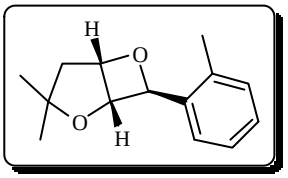
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.17 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.76 - 1.96 (m, 2H, 4-H), 2.12 (s, 3H, CH_3), 4.41 (dd, J = 3.9, 3.9 Hz, 1H, 1-H), 5.35 (dd, J = 3.8, 3.8 Hz, 1H, 5-H), 5.65 (d, J = 3.8 Hz, 1H, 7-H), 7.25 - 7.32 (m, 4H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 20.9 (q, CH_3), 29.6 (q, CH_3), 30.9 (q, CH_3), 49.8 (t, C-4), 76.3 (s, C-3), 87.4 (d, C-1), 89.6 (d, C-5), 91.4 (s, C-7), 126.5 (d, $CH_{arom.}$), 128.2 (d, $CH_{arom.}$), 129.9 (d, $CH_{arom.}$), 135.1 (s, $Cq_{arom.}$).

***exo*-3,3-Dimethyl-7-*o*-tolyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-14b)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.27 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 1.78 – 2.05 (m, 2H, 4-H), 2.15 (s, 3H, CH_3), 4.67 (dd, J = 4.0, 3.9 Hz, 1H, 1-H), 5.15 (d, J = 3.9 Hz, 1H, 7-H), 5.35 (dd, J = 3.8, 3.9 Hz, 1H, 5-H), 7.28 - 7.35 (m, 4H, $H_{arom.}$).

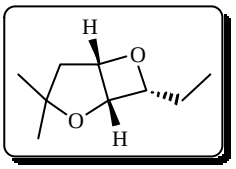
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.1 (q, CH_3), 29.4 (q, CH_3), 33.5 (q, CH_3), 50.8 (t, C-4), 79.3 (s, C-3), 88.3 (d, C-1), 89.8 (d, C-5), 91.6 (s, C-7), 126.8 (d, $CH_{arom.}$), 128.4 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 135.4 (s, $Cq_{arom.}$).

Irradiation of 2,2-dimethyl-2,3-dihydrofuran with propionaldehyde (sbo-235)

A solution of 2,2-dimethyl-2,3-dihydrofuran (0.29 g, 3 mmol) and propionaldehyde (0.17 g, 3 mmol) in 30 mL benzene was irradiated for 24 h following the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.41 g (88 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Ethyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-14c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.73 (t, J = 7.5 Hz, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.58 - 1.67 (m, 2H, CH_2), 1.74 - 1.94 (m, 2H, 4-H), 4.38 (dd, J = 3.7, 3.8 Hz, 1H, 7-H), 4.70 (dd, J = 3.8, 3.8 Hz, 1H,1-H), 5.18 (ddd, J = 8.4, 5.7, 3.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

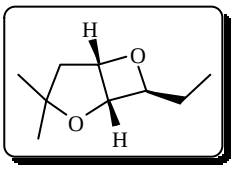
δ_{ppm} = 8.2 (q, CH_3), 22.4 (t, CH_2), 29.0 (q, CH_3), 29.7 (q, CH_3), 46.4 (t, C-4), 79.3 (s, C-3), 84.4 (d, C-1), 85.0 (d, C-5), 86.4 (d, C-7).

HRMS: ($C_9H_{16}O_2$, M = 156.12)

Calcd: 156.1264

Found: 156.1256

***exo*-7-Ethyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-14c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (t, J = 7.5 Hz, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.55 - 1.63 (m, 2H, CH_2), 1.60 - 2.07 (m, 2H, 4-H), 4.16 (dd, J = 3.7, 3.8 Hz, 1H, 7-H), 4.4 (dd, J = 6.5, 6.8 Hz, 1H, 1-H), 5.23 (dd, J = 5.0, 4.9 Hz, 1H, 5-H).

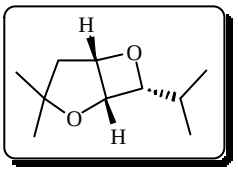
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.1 (q, CH_3), 26.9 (t, CH_2), 29.1 (q, CH_3), 29.9 (q, CH_3), 45.5 (t, C-4), 82.0 (s, C-3), 85.7 (d, C-1), 86.8 (d, C-5), 89.8 (d, C-7).

Irradiation of 2,2-dimethyl-2,3-dihydrofuran with isobutyraldehyde (sbo-224c)

A solution of 2,2-dimethyl-2,3-dihydrofuran (0.29 g, 3 mmol) and isobutyraldehyde (0.22 g, 3 mmol) in 30 mL benzene was irradiated for 24 h following the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.37 g (75 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Isopropyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-14d)**



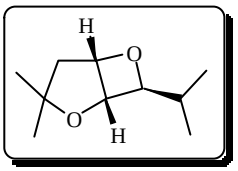
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.24 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.55 - 1.63 (m, 1H, CH), 1.78 - 2.07 (m, 2H, 4-H), 4.21 (dd, J = 3.8, 3.8 Hz, 1H, 7-H), 4.41 (dd, J = 5.0, 6.8 Hz, 1H,1-H), 5.25 (dd, J = 5.0, 4.9 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.3 (q, CH_3), 18.9 (q, CH_3), 25.4 (d, CH), 29.1 (q, CH_3), 29.7 (q, CH_3), 46.5 (t, C-4), 82.6 (s, C-3), 86.7 (d, C-1), 88.8 (d, C-5), 89.9 (d, C-7).

***exo*-7-Isopropyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-14d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.17 (m, 1H, CH), 1.21 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.64 - 2.06 (m, 2H, 4-H), 4.18 (dd, J = 4.0, 6.8 Hz, 1H, 7-H), 4.46 (dd, J = 4.0, 5.0 Hz, 1H,1-H), 5.29 (dd, J = 5.0, 4.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.1 (q, CH_3), 18.6 (q, CH_3), 25.4 (d, CH), 29.5 (q, CH_3), 30.4 (q, CH_3), 48.5 (t, C-4), 84.7 (s, C-3), 85.9 (d, C-1), 87.8 (d, C-5), 90.8 (d, C-7).

HRMS: ($C_{10}H_{18}O_2$, M = 170.13)

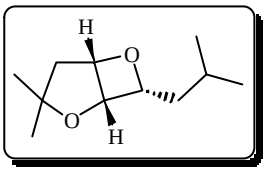
Calcd: 170.1264

Found: 170.1269

Irradiation of 2,2-dimethyl-2,3-dihydrofuran with 3-methylbutyraldehyde (sbo-224e)

A solution of 2,2-dimethyl-2,3-dihydrofuran (0.29 g, 3 mmol) and 3-methylbutyraldehyde (0.26 g, 3 mmol) in 30 mL benzene was irradiated for 24 h following the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.46 g (83 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-Isobutyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-14e)**



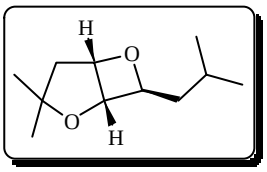
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.2 Hz, 6H, $2CH_3$), 0.88 (m, 2H, CH_2), 1.14 (s, 3H, CH_3), 1.29 (m, 1H, CH), 1.45 (s, 3H, CH_3), 1.74 - 1.94 (dd, J = 13.9, 4.7 Hz, 2H, 4-H), 4.57 (dd, J = 3.7, 3.8 Hz, 1H, 7-H), 4.68 (dd, J = 4.3, 3.8 Hz, 1H,1-H), 5.15 (dd, J = 4.3 , 4.3 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.4 (q, CH_3), 22.9 (q, CH_3), 24.4 (d, CH), 29.1 (q, CH_3), 29.8 (q, CH_3), 38.0 (t, CH_2), 45.6 (t, C-4), 80.30 (s, C-3), 82.9 (d, C-1), 85.7 (d, C-5), 86.3 (d, C-7).

***exo*-7-Isobutyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-14e)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.18 Hz, 6H, $2CH_3$), 0.88 (m, 2H, CH_2), 1.14 (s, 3H, CH_3), 1.29 (m, 1H, CH), 1.45 (s, 3H, CH_3), 1.74 - 1.94 (dd, J = 13.9, 4.7 Hz, 2H, 4-H), 4.30 (ddd, J = 2.1, 4.1, 6.0 Hz, 1H, 7-H), 4.38 (dd, J = 4.9, 4.6 Hz, 1H,1-H), 5.23 (dd, J = 4.9, 4.9 Hz, 1H, 5-H).

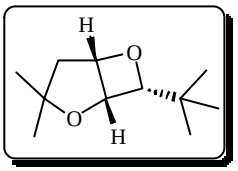
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.2 (q, CH_3), 22.4 (q, CH_3), 24.4 (d, CH), 29.9 (q, CH_3), 30.0 (q, CH_3), 42.9 (t, CH_2), 46.4 (t, C-4), 79.3 (s, C-3), 80.0 (d, C-), 85.0 (d, C-5), 87.5 (d, C-7).

Irradiation of 2,2-dimethyl-2,3-dihydrofuran with pivalaldehyde (sbo-224f)

A solution of 2,2-dimethyl-2,3-dihydrofuran (0.29 g, 3 mmol) and pivalaldehyde (0.26 g, 3 mmol) in 30 mL benzene was irradiated for 24 h following the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.35 g (78 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***endo*-7-*tert*-Butyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-14f)**



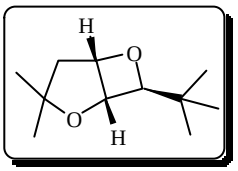
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.90 (s, 9H, $3CH_3$), 1.45 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.79 - 2.04 (dd, J = 13.9, 4.7 Hz, 2H, 4-H), 4.27 (d, J = 4.0 Hz, 1H, 7-H), 4.54 (dd, J = 4.0, 4.3 Hz, 1H,1-H), 5.33 (dd, J = 4.0, 5.0 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.2 (q, CH_3), 22.4 (q, CH_3), 23.8 (q, $3CH_3$), 33.7 (s, Cq), 48.9 (t, C-4), 80.6 (s, C-3), 83.4 (d, C-1), 85.0 (d, C-5), 87.5 (d, C-7).

***exo*-7-*tert*-Butyl-3,3-dimethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-14f)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (s, 9H, $3CH_3$), 1.21 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.83 - 2.34 (dd, J = 13.9, 4.7 Hz, 2H, 4-H), 4.17 (d, J = 4.0 Hz, 1H, 7-H), 4.34 (dd, J = 4.0, 4.3 Hz, 1H,1-H), 5.30 (dd, J = 4.0, 4.9 Hz, 1H, 5-H).

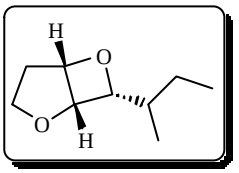
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.4 (q, CH_3), 22.8 (q, CH_3), 24.8 (q, $3CH_3$), 33.9 (s, Cq), 49.7 (t, C-4), 81.6 (s, C-3), 85.4 (d, C-1), 86.2 (d, C-5), 88.5 (d, C-7).

4.4 Photolysis of 2,3-dihydrofuran with 2-methylbutyraldehyde (sbo-237)

Under a nitrogen atmosphere, a solution of 2,3-dihydrofuran (0.7 g, 10 mmol) and 2-methylbutyraldehyde (0.82 g, 10 mmol) in 100 mL benzene was irradiated in Rayonet Photoreactor (300 nm) for 24 h. Distillation of the solvent under *vacum*, followed by Büchi distillation of the residue afforded 0.9 g (90 %) of inseparable mixture of oxetanes as a colorless oil.

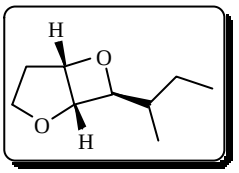
***endo*-7-*sec*-Butyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-3g)**[153]



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 - 0.97 (m, 6H, $2CH_3$), 1.28 - 1.83 (m, 4H), 2.02 (dd, J = 4.7, 5.0 Hz, 1H, 4-H), 4.03 - 4.29 (m , 3H, 3-H & 5-H), 4.71 (dd, J = 3.4, 6.6 Hz, 1H, 7-H), 5.26 (dd, J = 3.2, 3.4 Hz, 1H, 1-H).

***exo*-7-*sec*-Butyl-2,6-dioxa-bicyclo[3,2,0]heptane (*exo*-9g)**[153]



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 - 0.97 (m, 6H, 2 CH_3), 1.28 - 1.83 (m, 4H), 2.08 (dd, J = 4.7, 5.0 Hz, 1H, 4-H), 4.03 - 4.29 (m, 3H, 3-H & 5-H), 4.55 (m, 1H, 7-H), 5.18 (dd, J = 4.2, 6.7 Hz, 1H, 1-H).

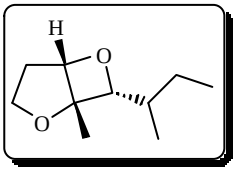
^{13}C-NMR: (75.5 MHz, $CDCl_3$) (*endo* & *exo* mixture)

δ_{ppm} = 10.6, 10.9, 11.0, 11.3 (each q), 12.5, 13.2, 13.4, 13.6 (each q), 23.7, 23.8, 23.9, 24.3 (each t), 32.9, 33.4, 33.9, 34.0 (each t), 38.0 (d, 2C), 67. 1, 67.5, 69.7, 69.9 (each t), 78.7 (d , 2C), 79.9 (d), 80.0 (d), 83.4 (d), 83.5 (d), 84.1 (d), 84.2 (d), 89.0 (d), 89.6 (d), 90.9 (d), 91.0 (d).

4.4.1 Photolysis of 5-methyl-2,3-dihydrofuran with 2-methylbutyraldehyde (sbo-261)

Under a nitrogen atmosphere, a solution of 5-methyl-2,3-dihydrofuran (0.84 g, 10 mmol) and 2-methylbutyraldehyde (0.82 g, 10 mmol) in 100 mL benzene was irradiated in Rayonet Photoreactor (300 nm) for 24 h. Distillation of the solvent under *vacum*, followed by Büchi distillation of the residue afforded 0.94 g (87 %) of inseparable mixture of oxetanes as a colorless oil.

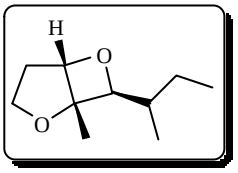
***endo*-7-*sec*-Butyl-1-methyl-2,6-dioxabicyclo[3.2.0]heptane (*endo*-9g)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.73 (s, 3H, CH_3), 0.81 - 0.91 (m, 6H, 2 CH_3), 1.26 - 1.33 (m, 4H), 2.31 (dd, J = 7.4, 7.2 Hz, 2H, 4-H), 4.15 (dd, J = 7.7, 7.9 Hz, 1H, 3-H), 4.19 (m, 1H, 5-H), 4.81 (dd, J = 4.0, 4.0 Hz, 1H, 7-H).

***exo*-7-*sec*-Butyl-1-methyl-2,6-dioxabicyclo[3.2.0]heptane (*exo*-9g)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (s, 3H, CH_3), 0.81-0.91 (m, 6H, 2CH_3), 1.26 - 1.33 (m, 4H), 2.42 (dd, J = 6.9, 7.1 Hz, 2H, 4-H), 4.00 (dd, 3.5, 3.0 Hz, 1H, 3-H), 4.19 (m, 1H, 5-H), 4.65 (d, 1H, J = 3.97 Hz, 1H, 7-H).

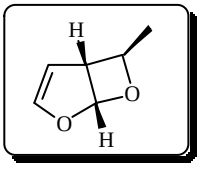
^{13}C-NMR: (75.5 MHz, $CDCl_3$) (*endo* & *exo* mixture)

δ_{ppm} = 9.7, 9.8, 9.9, 10.2 (each q), 12.6, 12.7, 13.1, 13.4 (each q), 16.0 (q), 23.2, 23.5, 23.6, 24.1 (each t), 32.1, 33.2, 33.2, 33.8 (each t), 37.2 (d, 2C), 38.1 (d, 2C), 66.3, 66.5, 69.1, 69.2 (each t), 84.3 (d, 2C), 84.5 (d), 85.1 (d), 86.3 (d), 86.7 (d), 86.8 (d), 91.8 (d), 86.7 (d).

4.5 Photolysis of furan with acetaldehyde (sbo-192)

A solution of furan (0.34 g, 5 mmol) and acetaldehyde (0.22 g, 5 mmol) in 25 mL benzene was degassed by N_2 bubbling. The test-tube shaped reaction apparatus was equipped parallel to Rayonet lamp (300 nm) and irradiated for 24 h. The solvent was removed using a rotary evaporator to give the products. The photolysate was analysed by ^{1}H-NMR in order to determine the product ratios. Distillation of the residue yielded 0.5 g (89 %) of oxetane as a colorless liquid.

***exo*-6 Methyl-2,7-dioxa-bicyclo[3.2.0]hept-3-ene (*exo*-16b)**[155]



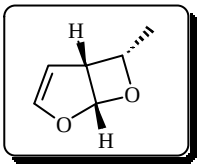
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.52 (d, J = 6.3 Hz, 3H, CH_3), 3.42 (dddd, J = 1.2, 2.9, 3.1, 4.3 Hz, 1H, 5-H), 4.71 (ddq, J = 0.6, 3.1, 6.3 Hz, 1H, 6-H), 5.33 (dd, J = 2.9, 2.9 Hz, 1H, 4-H), 6.31 (d, J = 4.3 Hz, 1H, 1-H), 6.61 (dd, J = 1.0, 2.9 Hz, 1H, 3-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.3 (q, CH_3), 50.2 (d, C-5), 88.8 (d, C-6), 104.1 (d, C-4), 107.5 (d, C-1), 147.9 (d, C-3).

***endo*-6 Methyl-2,7-dioxa-bicyclo[3.2.0]hept-3-ene (*endo*-16b)**[155]



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.52 (d, J = 6.3 Hz, 3H, CH_3), 3.42 (dddd, J = 1.2, 2.9, 3.1, 4.3 Hz, 1H, 5-H), 4.71 (ddq, J = 0.6, 3.1, 6.3 Hz, 1H, 6-H), 5.13 (dd, J = 2.9, 2.9 Hz, 1H, 4-H), 6.21 (d, J = 4.3 Hz, 1H, 1-H), 6.61 (dd, J = 1.0, 2.9 Hz, 1H, 3-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.1 (q, CH_3), 50.7 (d, C-5), 88.9 (d, C-6), 104.4 (d, C-4), 107.9 (d, C-1), 147.3 (d, C-3).

4.6 Determination of solvent polarity effects on the stereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran with aldehydes 1b & 1c: (sbo-90, sbo-93, sbo-94, sbo-95, sbo-96, sbo-97, sbo-98)

A solution of an equimolar ratio of aldehydes and 2,3-dihydrofuran in different solvents (acetonitrile, THF, methanol, n-hexane, benzene) was irradiated in Rayonet Photoreactor (300 nm) until complete conversion of the aldehydes. The product composition was determined directly from crude mixture by both GC and ^{1}H-NMR analyses.

4.7 Determination of solvent viscosity effects on the stereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran with aldehydes 1a-d: (sbo-127, sbo-141, sbo-156, sbo-158, sbo-159, sbo-162)

A solution of 1M of aldehydes **1a-d** and 1M of 2,3-dihydrofuran in 10 mL solvent (benzene, n-hexane, acetonitrile, methanol, ethanol, propanol, octanol, glycol, 1,2-propandiol, 1,4-butanediol, glycerol) was irradiated in quartz tube using Rayonet Photoreactor (300 nm) for 8 h. The product composition was determined from crude mixture by GC anaylsis.

4.8 Determination of temperature effects on the stereoselectivity of the Paternò-Büchi reaction of 2,3-dihydrofuran with aldehydes 1a-d: (sbo-114, sbo-116, sbo-120, sbo-166, sbo-167, sbo-168, sbo-198, sbo-204)

A quartz tube was charged with equimolar ratio of aldehydes and 2,3-dihydrofuran in 10 mL n-hexane (both substrates 1M). The samples were put in a dewar had a window and irradiated at > 290 nm using using high pressure mercury lamp at a wide range of temperature (from 30 °C to – 78 °C) for 8 h. The product distribution was determined directly by both GC and ^{1}H-NMR analyses.

4.9 Fluorescence quenching study: (sbo-272)

Solutions of propionaldehyde (0.2 M) with various concentrations of 2,3-dihydrofuran as quencher (0.02 – 1.00 M) were measured in benzene; both benzene and quencher showing negligible fluorescence. Solutions were placed in 3 cm^2 quartz cells after deoxygenated by N_2 bubbling for 30 sec and the fluorescence spectra were recorded. The exciation wavelength was 310 nm, the intensity of the emmision (F) at the maximum (~ 400 nm) for propionaldehyde was compared to the intensity (F_0) in the abscence of quencher. A stern – Volmer plot was drawn of F_0 / F versus molarity of quencher, and the slope determined at least from four points using linear portion of the curve.

4.10 Quantum yield determination: (sbo-201)

A benzene solution of valerophenone (0.1 M) as chemical actiometer ($\Phi_{acetophenone}$ = 0.33)[90] was irradiated parallel to the sample solution (1M of 2,3-dihydrofuran & 0.1 M of benzaldehyde) on a merry – go – round apparatus. The reactions were monitored by GC. The intergration of the peaks from GC were callibrated with n-undecane as internal standard. Quantum yield reported are average of three measurement.

4.11 Preparation of *trans*-cyclooctene (E-17) (sbo-122)

Method (A):[100]

A pentane solution (150 mL) of 6.6 g (0.06 mol, 7.8 mL) of cyclooctene and 1.0 g (3.65 mmol) of dimethylisophthalate placed in quartz photoreactor and then irradiated at 254 nm under N_2 with cooling to 10°C. The irradiation was occured with RPR (254 nm) for 72 h. The irradiated

solution was extracted with three 25 mL portions of 20% aq. Ag NO_3 solution at < 5°C. The aqueous extracts were combined, washed with two 10 mL portions of pentane at < 5°C, and then added dropwise into a stirred conc. aq. NH_3 solution (100 mL) at 0°C. The resulting mixture was extracted with three 25 mL portions of pentane. The combined pentane extracts were washed with water, dried over Mg SO_4, and concentrated at a reduced presure (50-100 torr) to give an almost pure product, which was finally trap to trap distilled in *vacuo* to afford *trans*-cyclooctene in 13 % yield (Lit.[100], 18 %).

Method (B):[101] (sbo-152)

A 150 mL quartz irradiation vessel was charged with 25 mL of *cis*-cyclooctene, (0.18mol) and 7.0 g of freshly cuprous chloride (0.07 mol). The vessel was fitted with a condenser and nitrogen bubbler was purged, the mixture was irradiated at 253 nm for 24 h. The solution was then evaporated at 1.0 mmHg to a thick oil. To this oil was added concentrated ammonia and pentane, and it was shaken, decolorized with sodium cyanide and separted. The aqueous layer was then extracted twice with pentane, and all pentane solutions were combined, dried over Mg SO_4, and concentrated by distillation to ca. 50 mL. The solution was then extracted with 20% aqueous Ag NO_3 and the aqueous layer was washed once with pentane. Treatment of the aqueous layer with concentrated ammonia followed by extractions three time with pentane. Evapouation of the solvent and distillation of the residue under *vacum* yielded *trans*-cyclooctene 1.4 g (19 %).[101]

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 - 0.84 (m, 2H), 1.38 - 1.56 (m, 2H), 1.79 - 1.84 (m, 2H), 1.91 - 2.00 (m, 4H), 2.35 - 2.39 (m, 2H), 5.48-5.52 (m, 2H, CH=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 29.3 (t), 35.7 (t), 35.8 (t), 133.9 (d, CH=).

4.11.1 General procedure for the photolyses of aldehydes (1b & 1c) with cyclooctene (Z-17 & E-17) on the analytical scale:

An equimolar ratio of cyclooctene (**Z-17** or **E-17**) and aldehydes (**1b** or **1c**) were dissolved in 10 mL benzene, and transfered to quartz tube. The samples were degassed for 2 min with a steady stream of N_2 gas, the quartz tubes were sealed and placed into a Rayonet Photoreactor (λ = 300 nm), and irradiated for 24 h. The solvent was evaporated (40°C, 20 torr) and the residue were analyzed by ^{1}H-NMR spectroscopy to determine the diastereomeric ratios from the relative areas of the relevant ^{1}H-NMR peaks.

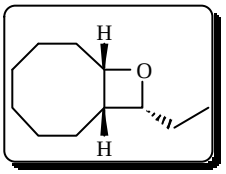
4.11.2 General procedure for the photolyses of aldehydes (1b & 1c) with cyclooctene (Z-17 & E-17) on the preparative scale:

The cyclooctene (1.1 g, 0.01 mol) and aldehydes (0.01 mol) were dissolved in 50 mL benzene, the solution transfered to a vacum-jacket pyrex tube and degassed with a steady stream of nitrogen gas. The reaction mixture was cooled to 10°C by means of a cold finger and irradiated in a Rayonet Photoreactor (RPR λ = 300 nm) for 48 h. The solvent was evaporated (40°c, 20 torr) and the residue was purified by bulb to bulb distillation.

Irradiation of cyclooctene with propionaldehyde (sbo-107)

A solution of cyclooctene (1.1 g, 10 mmol) and propionaldehyde (0.58 g, 10 mmol) in 50 mL benzene was irradiated for 48 h according to the above general procedure. Distillation of the residue after evaporation of the solvent yielded 1.2 g (71 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***cis, cis*-10-Ethyl-9-oxa-bicyclo[6.2.0]decane (cc-18)**



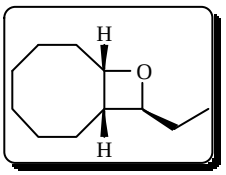
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.90 (t, J = 7.5 Hz, 3H, CH_3), 1.64 (m, 2H, CH_2), 0.82 - 1.92 (m, 12H, 2-H to 7-H), 2.78 (ddd, J = 11.8, 7.5, 3.4 Hz, 1H, 1-H), 4.63 (dt, J = 7.5, 6.5 Hz, 1H, 10-H), 4.76 (ddd, J = 11.8, 7.5, 2.8 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.2 (q), 24.8, 25.5, 25.8, 25.9, 26.6, 28.9, 30.7 (7 t), 40.7 (d, C-1), 82.5 (d, C-10), 82.9 (d, C-8).

***trans, cis*-10-Ethyl-9-oxa-bicyclo[6.2.0]decane (tc-18)**



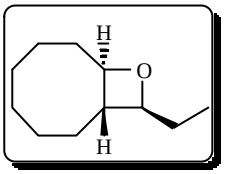
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J=7.5 Hz, 3H, CH_3), 1.73 (m, 2H, CH_2), 0.54 - 1.77 (m, 12H, 2-H to 7-H), 2.44 (ddd, J = 11.8, 7.5, 3.4 Hz, 1H, 1-H), 4.13 (dt, J = 6.5, 6.5 Hz, 1H, 10-H), 4.64 (ddd, J = 11.8, 7.9, 2.7 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.23 (q), 22.7, 25.6, 25.6, 26.7, 28.3, 29.6, 32.2 (7 t), 43.0 (d, C-1), 82.3 (d, C-8), 85.9 (d, C-10).

***trans, trans*-10-Ethyl-9-oxa-bicyclo[6.2.0]decane (tt-18)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.91 (t, J = 6.5 Hz, 3H, CH_3), 1.68 (m, 2H, CH_2), 0.82 - 1.95 (m, 12H, 2-H to 7-H), 2.33 (ddd, J = 10.9, 7.5, 3.2 Hz, 1H, 1-H), 4.25 (dt, J = 7.5, 6.6 Hz, 1H, 10-H), 4.53 (ddd, J = 10.9, 7.5, 3.3 Hz, 1H, 8-H).

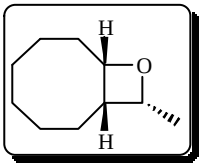
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.07 (q), 26.9, 28.3, 28.4, 29.0, 29.2, 30.0, 38.5 (7 t), 48.7 (d, C-1), 84.9 (d, C-8), 85.6 (d, C-10).

Irradiation of cyclooctene with acetaldehyde (sbo-113)

A solution of cyclooctene (1.1 g, 10 mmol) and acetaldehyde (0.44 g, 10 mmol) in 50 mL benzene was irradiated for 48 h according to the above general procedure. Distillation of the residue after evaporation of the solvent yielded 0.98 g (68 %) of inseparable mixture of oxetanes as a colorless viscous oil.

***cis, cis*-10-Methyl-9-oxa-bicyclo[6.2.0]decane (cc-19)**



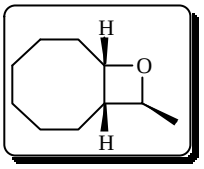
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 - 1.92 (m, 12H, 2-H to 7-H), 1.24 (d, J = 6.03 Hz, 3H, CH_3), 2.76 (ddd, J = 11.8, 7.4, 2.8 Hz, 1H, 1-H), 4.77 (ddd, J = 11.8, 7.5, 2.8 Hz, 1H, 8-H), 4.94 (dq, J = 7.5, 6.0 Hz, 1H, 10-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.28 (q), 22.0, 24.9, 25.8, 25.9, 26.9, 28.8 (6 t), 40.8 (d, C-1), 77.3 (d, C-10), 83.7 (d, C-8).

***trans*, *cis*-10-Methyl-9-oxa-bicyclo[6.2.0]decane (tc-19)**



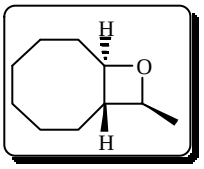
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.06 (m, 1H), 1.15 - 1.33 (m, 6H), 1.37 (m, 1H), 1.40 (d, J = 6.2 Hz, 3H, CH_3), 1.86 (m, 1H), 4.36 (dq, J = 7.9, 6.2 Hz, 1H, 10-H), 4.66 (ddd, J = 11.8, 7.9, 2.7 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.6 (q), 24.8, 25.8, 25.9, 26.6, 28.9, 30.7 (6 t), 45.2 (d, C-1), 81.3 (d, C-10), 82.5 (d, C-8).

***trans*, *trans*-10-Methyl-9-oxa-bicyclo[6.2.0]decane (tt-19)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.34 (d, J = 6.5 Hz, 3H, CH_3), 0.82 - 1.96 (m, 12H, 2-H to 7-H), 2.76 (ddd, J = 10.9, 7.5, 3.4 Hz, 1H, 1-H), 4.44 (dq, J = 7.5, 6.5 Hz, 1H, 10-H), 4.52 (ddd, J = 10.9, 7.5, 3.2 Hz, 1H, 8-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

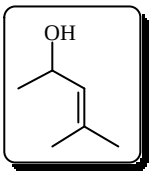
δ_{ppm} = 22.8 (q), 26.9, 28.3, 28.4, 29.0, 29.2, 38.5 (6 t), 51.1 (d, C-1), 80.9 (d, C-10), 85.2 (d, C-8).

Fluorescence Quenching: (sbo-273)

A propanal solution 0.2 M was prepared in benzene. A known volume of the propanal solution was pipetted into a quartz fluorescence cell and the fluorescence was obseved using excitation wavelength of 310 nm. Aliquots of cyclooctene was added to the solution by means of a micro syringe while monitoring the decrease in fluoresence intensity at 420 nm.

4.12 Synthesis of allylic alcohols and acetates

Preparation of mesitylol (22)[102] (sbo-85)



Under a N_2 atmosphere, a solution of (50.0 g, 0.51 mol) of mesityl oxide in 100 mL of dry ether was added dropwise to a suspention of (9.8 g, 0.26 mol) of $LiAlH_4$ in dry ether. After stirring for 1h at room temperature (ca. 20°C), the reaction was stopped by adding carefully 15 mL of ice water, 15 mL of a 15% NaOH solution and 50 mL of water. The phases were separated, the aqueous phase was extracted with ether (3 x 50 mL), the combined organic phases were dried over $MgSO_4$, and the solvent was rotoevaporated (20°C, 30 torr). Fractional distillation of the residue (B.p 52°C, 22 torr) yielded 35.0 g (70%) of 4-methyl-pent-3-en-2-ol **(22)** as a colorless liquid.

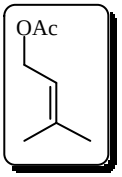
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 1.15 (d, J = 6.3 Hz, 3H, CH_3), 1.62 (d, J = 1.2 Hz, 3H, CH_3), 1.65 (d, J = 1.2 Hz, 3H, CH_3), 2.41 (brs, 1H, OH), 4.48 (dq, J = 8.5, 6.3 Hz, 1H, CHOH) , 5.13 (d , J= 8.5Hz ,1H, CH=)

^{13}C-NMR: ($CDCl_3$)

δ = 17.9 (q, CH_3), 23.5 (q, CH_3), 25.5 (q, CH_3), 64.5 (d, CHO), 129.3 (d, CH), 133.7 (s, Cq)

Preparation of prenyl acetate (23)[103] (sbo-535)



To prenol (4.3 g, 0.05 mol), in 20 mL of dry pyridine, acetic anhydride (10 g, 0.09 mol) was added at room temperature with stirring. After stirring overnight, the reaction mixture was poured into water from which the product was recovered by ether extraction. Washing of the combined extracts with 10% HCl, saturated $NaHCO_3$, and saturated NaCl, drying ($MgSO_4$), and

evaporation left the product as a yellow oil. Distillation gave a colorless oil: B.p 74°C (55 mmHg); yield 85% .

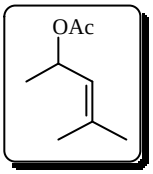
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 1.59 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.92 (s, 3H, $\underline{CH_3}CO$), 4.46 (d, J = 7.4 Hz, 2H, CH_2), 5.24 (m, 1H, CH=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ = 17.6 (q, CH_3), 20.6 (q, CH_3), 25.4 (q, CH_3), 61.1 (t, CH_2), 118.6 (d, CH), 138.6 (s, Cq), 170.8 (s, CO).

Preparation of mesityl acetate (24)[104] (sbo-536)



To 4-methyl-3-penten-2-ol (5.0 g, 0.05 mol), in 20 mL of dry pyridine, acetic anhydride (10.0 g, 0.09 mol) was added at room temperature with stirring. After stirring overnight, the reaction mixture was poured into water from which the product was recovered by ether extraction. Washing of the combined extracts with 10% HCl, saturated $NaHCO_3$, and saturated NaCl, drying ($MgSO_4$), and evaporation left the product as a yellow oil. Distillation gave a colorless oil: B.p 50-52°C (15 mmHg); yield 87% .

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 1.25 (d, J = 6.0 Hz, 3H, CH_3), 1.70 (d, J = 1.5 Hz, 6H, $2CH_3$), 1.95 (s, 3H, $\underline{CH_3}CO$), 4.40 (dq, J = 9.0, 6.0 Hz, 1H, $\underline{CH}O$), 4.85 (d, J = 9.0 Hz, 1H, CH=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ =18.2 (q, CH_3), 20.9 (q, CH_3), 21.4 (q, CH_3), 25.6 (q, CH_3), 68.1 (d, CHO), 124.9 (d, CH), 136.2 (s, Cq), 170.4 (s, CO).

4.12.1 General procedure for the photolyses of propionaldehyde and allylic substrates (21&23) on the analytical scale: (sbo-83, sbo-89, sbo-105)

An equimolar ratio of both allylic substrates (**21** or **23**) and propionaldehyde were dissolved in 10 mL benzene, and transfered to a quartz tube. The samples were degassed for 2 min with a steady stream of N_2 gas, the quartz tubes were sealed and placed into a merry-go-round system equiped with a 125 W high pressure mercury lamp (λ > 290 nm), cooled to 13°C, and irradiated

for 24h. The solvent was evaporated (40 °C, 20 torr) and the residue were analyzed by ^{1}H-NMR spectroscopy to determine the diastereomeric ratios from the relative areas of the relevant ^{1}H-NMR peaks .

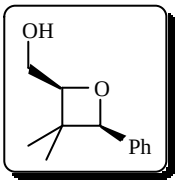
4.12.2 General procedure for the photolyses of aldehydes and the allylic substrates on the preparative scale:

The allylic substrates (2.9 mmol) and aldehydes (2.9 mmol) were dissolved in 50 mL benzene, the solution transfered to a vacuum-jacket pyrex vessel and degassed with a steady stream of nitrogen gas. The reaction mixture was cooled to 10 °C by means of a cold finger and irradiated in a Rayonet photoreactor (RPR, λ = 300 nm). The solvent was evaporated (40°C, 20 torr) and the residue was purified by Kugelrohr distillation or by silica gel preparative chromatography using a mixture of ethyl acetate and n-hexane as eluent.

Irradiation of prenol with benzaldehyde (sbo-534a)

A solution of (0.25 g, 2.9 mmol) of prenol and (0.31 g, 2.9 mmol) of benzaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Preparative chromatography of the residue yielded 0.32 g (65 %) of oxetane as colorless oil.

***cis*- (3,3-Dimethyl-4-phenyl-oxetan-2-yl)-methanol (*cis*-25a)**



TLC: R_f = 0.36 (ethyl acetate/n-hexane 1: 3)

IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 3500, 3055, 1559, 1445, 1035, 975, 835, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.54 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.55 (bs, 1H, OH), 3.51 (dd, J = 12.0, 4.3 Hz, 1H, CHOH), 3.72 (dd, J = 12.0, 7.4 Hz, 1H, CHOH), 4.52 (dd, J = 4.3, 7.4 Hz, 1H, 2-H) , 5.31 (s, 1H, 4-H), 7.12 - 7.14 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.9 (q, CH_3), 27.5 (q, CH_3), 42.0 (s, C-3), 62.9 (t, CH_2O) , 87.8 (d, C-2), 89.3 (d, C-4), 124.9 (d, $CH_{arom.}$), 125.4 (d, $CH_{arom.}$), 127.3 (d, $CH_{arom.}$), 128.0 (d, $CH_{arom.}$), 139.4 (s, Cq_{arom}).

MS: (EI, 70 eV)

m/z (%) = 191 (M^+-1, 38), 161 (25), 105 (75), 91 (24), 85 (42), 77 (45), 71 (100).

HRMS: ($C_{12}H_{16}O_2$, M = 192.11 g/mol)

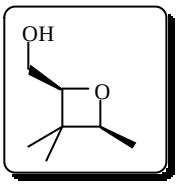
Calcd: 192.1072

Found: 192.1070

Irradiation of prenol with acetaldehyde (sbo-548)

A solution of (0.25 g, 2.9 mmol) of prenol and (0.13 g, 2.9 mmol) of acetaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue (B.p = 65-68 °C, 10 torr) yielded 0.28 g (75 %) of oxetane as a colorless oil.

***cis*- (3,3,4-Trimethyl-oxetan-2-yl)-methanol (*cis*-25b)**



IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 3515, 30330, 1538, 1425, 1055, 972, 885, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.01 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.19 (d, J = 6.5 Hz, 3H, CH_3), 1.25 (bs, 1H, OH), 3.60 (dd, J =12.1, 4.8 Hz, 1H, CHOH), 3.70 (dd, J =12.1, 6.5 Hz, 1H, CHOH), 4.37 (dd, J = 4.3, 6.5 Hz, 1H, 2-H), 4.52 (q, J = 6.5 Hz, 1H, 2-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

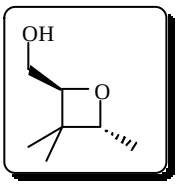
δ_{ppm} = 15.5 (q, CH_3), 17.6 (q, CH_3), 27.7 (q, CH_3), 39.4 (s, C-3), 63.1 (t, CH_2O), 85.2 (d, C-2), 87.7 (d, C-4).

Anal: ($C_7H_{14}O_2$, M = 140.1 g/mol)

Calcd: C 64.58 H 10.84

Found: C 63.98 H 10.37

***trans*- (3,3,4-Trimethyl-oxetan-2-yl)-methanol (*trans*-25b)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.02 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.26 (d, J = 4.4Hz, 3H, CH_3), 3.73 (dd, J = 12.0, 6.9 Hz, 1H, CHOH), 3.77 (dd, J = 12.0, 4.3Hz, 1H, CHOH), 4.12 (dd, J = 4.3, 6.9 Hz, 1H, 4-H), 4.75 (q, J = 4.4 Hz, 1H, 2-H).

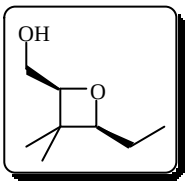
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 20.5 (q, CH_3), 24.6 (q, CH_3), 30.3 (q, CH_3), 40.1 (s, C-3), 67.2 (t, CH_2O), 90.2 (d, C-2), 95.7 (d, C-4).

Irradiation of prenol with propionaldehyde (sbo-529)

A solution of (0.25 g, 2.9 mmol) of prenol and (0.17 g, 2.9 mmol) of propionaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue (B.p = 73-75 °C, 10 torr) yielded 0.32 g (78 %) of oxetane as a colorless oil.

***cis*- 4-Ethyl-(3,3-dimethyl-oxetan-2-yl)-methanol (*cis*-25c)**



IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 3508, 3058, 1534, 1445, 1035, 970, 865, 778.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (t, J = 7.4 Hz, 3H, CH_3), 0.81 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.25 (s, 1H, OH), 1.35 (m, 2H, CH_2), 3.33 (dd, J = 12.0, 4.9 Hz, 1H, CHOH), 3.44 (dd, J = 12.0, 6.6Hz, 1H, CHOH), 4.15 (dd, J = 4.9, 6.6 Hz, 1H, 2-H), 4.23 (dd, J = 6.3, 7.8 Hz, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.2 (q, CH_3), 14.3 (q, CH_3), 24.3 (t, CH_2), 38.6 (s, C-3), 61.9 (t, CH_2O), 86.6 (d, C-2), 89.4 (d, C-4).

MS: (EI, 70 eV)

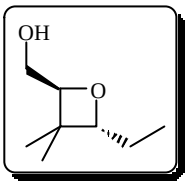
m/z (%) = 127 (M^+-OH, 30), 111 (25), 109 (30), 97 (27), 85 (87), 71 (50), 69 (82), 59 (23), 57 (100).

Anal: ($C_8H_{16}O_2$, M = 144.2 g/mol)

Calcd: C 66.63 H 11.18

Found: C 66.61 H 11.20

***trans*- 4-Ethyl-(3,3-dimethyl-oxetan-2-yl)-methanol (*trans*-25c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (t, J = 7.5 Hz, 3H, CH_3), 0.87 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 1.30 (m, 2H, CH_2), 3.53 (dd, J = 12.0, 3.8, 1H, CHOH), 3.62 (dd, J = 12.0, 6.8, 1H, CHOH), 3.83 (dd, J = 7.4, 9.0 Hz, 1H, 4-H), 3.93 (dd, J = 3.8, 6.8 Hz, 1H, 2-H).

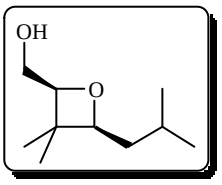
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.0 (q, CH_3), 20.0 (q, CH_3), 23.5 (t, CH_2), 29.0 (q, CH_3), 37.3 (s, C-3), 56.4 (t, CH_2O), 87.0 (d, C-2), 90 (d, C-4).

Irradiation of prenol with 3-methylbutyraldehyde (sbo-530)

A solution of (0.25 g, 2.9 mmol) of prenol and (0.25 g, 2.9 mmol) of 3-methylbutyraldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue (B.p = 84 °C, 10 torr) yielded 0.37 g (80 %) of oxetane as a pale yellow oil.

***cis*- (4-Isobutyl-3,3-dimethyl-oxetan-2-yl)-methanol (*cis*-25d)**



IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3406, 2956, 2871, 1467, 1385, 1169, 1042, 997.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.5 Hz, 3H, CH_3), 0.88 (d, J = 6.5Hz, 3H, CH_3), 0.89 (m, 1H, CH), 1.02 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.25 (bs, 1H, OH), 1.35 (m, 2H, CH_2), 3.55 (dd, J = 12.0, 4.4 Hz, 1H, CHOH), 3.65 (dd, J =12.0, 6.5 Hz, 1H, CHOH), 4.31 (dd, J = 4.4, 6.5 Hz, 1H, 2-H), 4.5 (dd, J = 4., 8.5 Hz, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

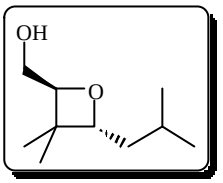
δ_{ppm} = 15.67 (q, CH_3), 22.4 (q, CH_3), 23.2 (q, CH_3), 24.6 (d, CH), 27.7 (q, CH_3), 39.7 (t, CH_2), 41.1 (s, C-3), 63.0 (t, CH_2O), 87.3 (d, C-2), 87.5 (d, C-4).

Anal: ($C_{10}H_{20}O_2$, M = 172.2 g/mol)

Calcd: C 69.72 H 11.70

Found: C 69.45 H 12.00

***trans*- (4-Isobutyl-3,3-dimethyl-oxetan-2-yl)-methanol (*trans*-25d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.5 Hz, 6H, $2CH_3$), 0.91 (m, 1H), 1.13 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.35 (bs, 1H, OH), 1.42 (m, 2H, CH_2), 3.70 (dd, J = 12.0, 4.0 Hz, 1H, CHOH), 3.75 (dd, J = 12.0, 6.5 Hz, 1H, CHOH), 3.82 (dd, J = 4.0, 6.5 Hz, 1H, 2-H), 4.2 (dd, J = 4.5, 8.0 Hz, 1H, 4-H).

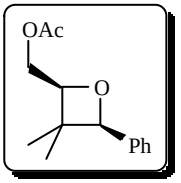
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 22.4 (q, CH_3), 23.2 (q, CH_3), 24.6 (d, CH), 27.7 (q, CH_3), 39.7 (t, CH_2), 41.1 (s, C-3), 63.0 (t, CH_2O), 87.3 (d, C-2), 87.5 (d, C-4).

Irradiation of prenyl acetate with benzaldehyde (sbo-537a)

A solution of (0.35 g, 3.0 mmol) of prenyl acetate and (0.32 g, 3.0 mmol) of benzaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Preparative chromatography of the residue yielded 0.37 g (75 %) of oxetane as a colorless oil.

***cis*-3,3-Dimethyl-4-phenyl-oxetan-2-ylmethylacetate (*cis*-26a)**



TLC: R_f = 0.43 (ethyl acetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3100, 2989, 1742, 1559, 1445, 1035, 975, 835, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 2.08 (s, 3H, $\underline{CH_3}CO$), 4.18 (dd, J = 12.0, 6.9 Hz, 1H, $\underline{CH}OAc$), 4.23 (dd, J =12.0, 4.9 Hz, 1H, $\underline{CH}OAc$), 4.70 (dd, J = 6.9, 4.9 Hz, 1H, 2-H), 5.47 (s, 1H, 4-H), 7.12 - 7.28 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.1 (q, CH_3), 20.9 (q, CH_3), 27.4 (q, CH_3), 42.5 (s, C-3), 64.8 (t, $\underline{CH_2}OAc$), 84.5 (d, C-2) , 89.4 (d, C-4), 125.7 (d, $CH_{arom.}$), 127.3 (d, $CH_{arom.}$), 136.4 (s, $Cq_{arom.}$), 170.7 (s, CO).

Anal: ($C_{14}H_{18}O_3$, M = 234.2 g/mol)

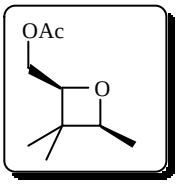
Calcd: C 71.77 H 7.74

Found: C 71.64 H 7.70

Irradiation of prenyl acetate with acetaldehyde (sbo-549b)

A solution of (0.35 g, 3.0 mmol) of prenyl acetate and (0.32 g, 3.0 mmol) of acetaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Preparative chromatography of the residue yielded 0.33 g (65 %) of oxetane as a colorless oil.

***cis*-3,3,4-Trimethyl-oxetan-2-ylmethylacetate (*cis*-26b)**



TLC: R_f = 0.40 (ethyl acetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2965, 1737, 1547, 1462, 1380, 1020, 970, 855, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.03 (s, 3H, CH_3), 1.18 (d, J = 6.5 Hz, 3H, CH_3), 1.20 (s, 3H, CH_3), 2.04 (s, 3H, $\underline{CH_3}CO$), 4.10 (dd, J = 12.0, 7.6 Hz, 1H, $\underline{CH}OAc$), 4.17 (dd, J = 12.0, 4.3 Hz, 1H, $\underline{CH}OAc$), 4.64 (dd, J = 7.6, 4.3 Hz, 1H, 2-H), 4.53 (q, J = 6.5 Hz, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

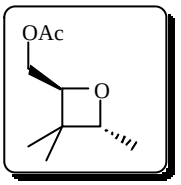
δ_{ppm} = 15.6 (q, CH_3), 17.5 (q, CH_3), 20.8 (q, CH_3), 27.1 (q, CH_3), 39.8 (s, C-3), 65.2 (t, $\underline{CH_2}OAc$), 84.4 (d, C-2), 85.1 (d, C-4), 170.9 (s, CO).

Anal: ($C_{10}H_{18}O_3$, M = 186.3 g/mol)

Calcd: C 64.49 H 9.74

Found: C 64.87 H 9.68

***trans*-3,3,4-Trimethyl-oxetan-2-ylmethylacetate (*trans*-26b)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.00 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.26 (d, J = 6.4Hz, 3H, CH_3), 1.97 (s, 3H, $\underline{CH_3}CO$), 3.98 (dd, J = 12.0, 6.9 Hz, 1H, $\underline{CH}OH$), 4.17 (dd, J = 12.0, 4.4 Hz, 1H, $\underline{CH}OH$), 4.12 (dd, J = 4.4, 6.9 Hz, 1H, 4-H), 4.65 (q, J = 6.4 Hz, 1H, 2-H).

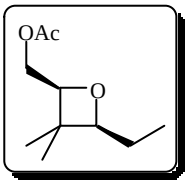
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.4 (q, CH_3), 20.8 (q, CH_3), 24.8 (q, CH_3), 32.3 (q, CH_3), 40.0 (s, C-3), 67.7 (t, $\underline{C}H_2O$), 86.6 (d, C-2), 87.7 (d, C-4), 171.3 (s, CO).

Irradiation of prenyl acetate with propionaldehyde (sbo-543)

A solution of (0.35 g, 3.0 mmol) of prenyl acetate and (0.20 g, 3.0 mmol) of propionaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Preparative chromatography of the residue yielded 0.36 g (70 %) of oxetane as a colorless oil.

***cis*-4-Ethyl-3,3-dimethyl-oxetan-2-ylmethylacetate (*cis*-26c)**



TLC: R_f = 0.48 (ethyl acetate/n-hexane 1: 4)

IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 3085, 2980, 1740, 1490, 1475, 1380, 1245, 1035, 970, 865, 710.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.77 (t, J = 7.5 Hz, 3H, CH_3), 0.84 (m, 2H, CH_2), 1.00 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.95 (s, 3H, $\underline{CH_3}CO$), 4.12 (dd, J = 12.0, 7.6 Hz, 1H, $\underline{CH}OAc$), 4.16 (dd, J =12.0, 4.4 Hz, 1H, $\underline{CH}OAc$), 4.22 (dd, J = 6.2, 7.8Hz, 1H, 2-H), 4.43 (dd, J = 4.4, 7.6 Hz, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

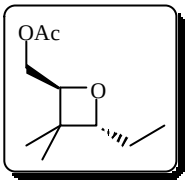
δ_{ppm} = 9.1 (q, CH_3), 15.3 (q, CH_3), 20.7 (q, CH_3), 27.4 (q, CH_3), 32.0 (t, CH_2), 39.9 (s, C-3), 64.9 (t, $\underline{CH_2}OAc$), 83.9 (d, C-2), 90.3 (d, C-4), 170.1 (s, CO).

Anal: ($C_{10}H_{18}O_3$, M = 186.13 g/mol)

Calcd: C 64.49 H 9.74

Found: C 64.38 H 9.48

***trans*-4-Ethyl-3,3-dimethyl-oxetan-2-ylmethylacetate (*trans*-26c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (t, J = 7.5 Hz, 3H, CH_3), 0.87 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 1.30 (m, 2H, CH_2), 2.12 (s, 3H, CH_3CO), 3.59 (dd, J = 12.0, 3.8 Hz, 1H, $\underline{CH}OAc$), 3.64 (dd, J = 12.0, 7.8, 1H, $\underline{CH}OAc$), 3.89 (dd, J = 7.8, 9.0 Hz, 1H, 4-H), 3.99 (dd, J = 3.8, 7.8 Hz, 1H, 2-H).

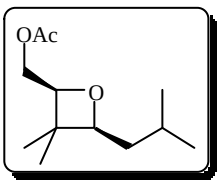
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.4 (q, CH_3), 20.4 (q, CH_3), 22.8 (q, CH_3), 23.8 (t, CH_2), 29.3 (q, CH_3), 39.3 (s, C-3), 59.4 (t, $\underline{C}H_2O$), 84.8 (d, C-2), 90.6 (d, C-4), 171.2 (s, CO).

Irradiation of prenyl acetate with 3-methylbutyraldehyde (sbo-546d)

A solution of (0.35 g, 3.0 mmol) of prenyl acetate and (0.26 g, 3.0 mmol) of 3-methylbutyraldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Preparative chromatography of the residue yielded 0.39 g (80 %) of oxetane as a colorless oil.

***cis*-4-Isobutyl-3,3-dimethyl-oxetan-2-ylmethylacetate (*cis*-26d)**



TLC: R_f = 0.54 (ethyl acetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.5 Hz, 6H, $2CH_3$), 0.99 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 1.30 (m, 1H, CH), 1.55 (m, 2H, CH_2), 2.04 (s, 3H, $\underline{CH_3}CO$), 4.05 (dd, J = 12.0, 7.6 Hz, 1H,

CHOAc), 4.17 (dd, J = 12.0, 4.4 Hz, 1H, CHOAc) , 4.43 (dd, J = 4.4, 7.6 Hz, 1H, 2-H), 4.46 (dd, J = 4.7, 7.9 Hz, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

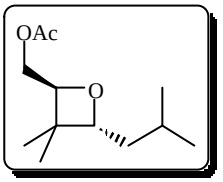
δ_{ppm} = 15.7 (q, CH_3), 22.3 (q, CH_3), 20.9 (q, CH_3), 22.4 (q, CH_3), 24.4 (d, CH), 27.1 (q, CH_3), 40.2 (s, C-3), 41.0 (t, C-2), 65.1 (t, CH_2OAc), 84.1 (d, C-2), 87.4 (d, C-4), 170.9 (s, CO).

Anal: ($C_{12}H_{22}O_3$, M = 214.16 g/mol)

Calcd: C 67.26 H 10.35

Found: C 67.17 H 10.32

***trans*-4-Isobutyl-3,3-dimethyl-oxetan-2-ylmethylacetate (*trans*-26d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.5 Hz, 6H, $2CH_3$), 0.91 (m, 1H), 1.13 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.42 (m, 2H, CH_2), 2.00 (s, 3H, CH_3CO), 4.05 (dd, J = 12.0, 4.0 Hz, 1H, CHOAc), 4.17 (dd, J = 12.0, 6.5 Hz, 1H, CHOAc), 4.28 (dd, J = 4.0, 6.5 Hz, 1H, 2-H), 4.44 (dd, J = 4.5, 8.0 Hz, 1H, 4-H).

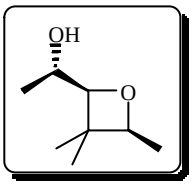
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 21.3 (q, CH_3), 22.4 (q, CH_3), 23.2 (q, CH_3), 24.6 (d, CH), 27.7 (q, CH_3), 39.8 (s, C-3), 41.1 (t, CH_2), 63.9 (t, CH_2O), 85.3 (d, C-2), 87.5 (d, C-4), 171.3 (s, CO).

Irradiation of mesitylol with acetaldehyde (sbo-554)

A solution of (0.3 g, 3.0 mmol) of mesitylol and (0.25 g, 3.5 mmol) of acetaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue (B.p = 80-82 °C, 10 torr) yielded 0.32 g (68 %) of oxetane as a colorless oil.

***threo*-1-(3,3,4-Trimethyl-oxetan-2-yl)-ethanol (*threo*-27b)**



IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 3514, 3068, 1536, 1453, 1031, 975, 868, 777.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.91 (s, 3H, CH_3), 0.93 (d, J = 6.5 Hz, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.09 (d, J = 6.5Hz, 3H, CH_3), 3.75 (dq, J = 8.4, 6.2 Hz, 1H, CHOH), 3.92 (d, J = 8.4Hz, 1H, 2-H), 4.42 (q, J = 6.5 Hz, 1H, 2-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.7 (q, CH_3), 16.8 (q, CH_3), 17.1 (q, CH_3), 26.2 (q, CH_3), 38.5 (s, C-3), 66.5 (d, CHOH), 83.1 (d, C-2), 90.5 (d, C-4).

Anal: ($C_8H_{16}O_2$, M = 144.12 g/mol)

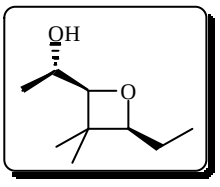
Calcd: C 66.63 H 11.18

Found: C 66.60 H 11.12

Irradiation of mesitylol with propionaldehyde (sbo-104)

A solution of (0.3 g, 3.0 mmol) of mesitylol and (0.20 g, 3.0 mmol) of propionaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue (B.p = 76-78 °C, 10 torr) yielded 0.34 g (60 %) of oxetane as a colorless oil.

***threo*-1-(4-Ethyl-3,3-dimethyl-oxetan-2-yl)-ethanol (*threo*-27c)**



IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 3510, 3050, 1544, 1435, 1039, 978, 885, 773.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.77 (t, J = 7.5 Hz, 3H, CH_3), 0.91 (d , J = 6.2 Hz, 3H, CH_3), 0.95 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.45 (m, 2H, CH_2), 3.73 (dq, J = 8.4, 6.2 Hz, 1H, CHOH), 3.92 (d, J = 8.4 Hz, 1H, 2-H), 4.12 (dd, J = 6.4, 7.7 Hz, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.4 (q, CH_3), 14.7 (q, CH_3), 17.3 (q, CH_3), 24.2 (t, CH_2), 26.7 (q, CH_3), 38.8 (s, C-3), 66.6 (d, CHO), 88.6 (d, C-2), 90.0 (d, C-4).

Anal: ($C_9H_{18}O_2$, M = 158.2 g/mol)

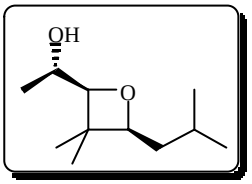
Calcd: C 68.31 H 11.47

Found: C 68.57 H 11.32

Irradiation of mesitylol with 3-methylbutyraldehyde (sbo-559a)

A solution of (0.3 g, 3.0 mmol) of mesitylol and (0.25 g, 3.0 mmol) of 3-methylbutyraldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue (B.p = 80-82 °C, 10 torr) yielded 0.43 g (84 %) of oxetane as a colorless oil.

***threo*-1-(4-Isobutyl-3,3-dimethyl-oxetan-2-yl)-ethanol (*threo*-27d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.02 (d, J = 6.2 Hz, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.30 (m, 1H, CH), 1.53 (m, 2H, CH_2), 3.83 (dq, J = 8.1, 6.2 Hz, 1H, CHOH), 3.92 (d, J = 8.1 Hz, 1H, 2-H), 4.42 (dd, J = 4.7, 8.7 Hz, 1H, 2-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 18.2 (q, CH_3), 22.3 (q, CH_3), 23.3 (q, CH_3), 24.5 (d, CH), 27.7 (q, CH_3), 39.5 (s, C-3), 41.0 (t, CH_2), 67.6 (d, CHO), 86.47 (d, C-2), 90.6 (d, C-4).

Anal: ($C_{11}H_{12}O_2$, M = 186.2 g/mol)

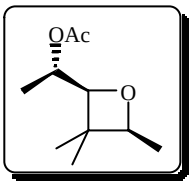
Calcd: C 70.92 H 11.90

Found: C 70.43 H 11.64

Irradiation of mesityl acetate with acetaldehyde (sbo-134)

A solution of (0.47 g, 3.0 mmol) of mesityl acetate and (0.32 g, 3.8 mmol) of acetaldehyde in 50 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the residue afforded 0.42 g (75 %) of the product as a pale yellow oil.

***threo*-1-(3,3,4-Trimethyl-oxetan-2-yl)-ethylacetate (*threo*-28b)**



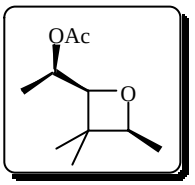
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.02 (d, J = 6.5 Hz, 3H, CH_3),1.13 (s, 3H, CH_3), 1.20 (d, J = 6.5 Hz, 3H, CH_3), 1.25 (s, 3H, CH_3), 4.12 (dq, J = 9.2, 6.5 Hz, 1H, CHOAc), 4.46 (d, J = 9.2 Hz, 1H, 2-H), 4.55 (q, J = 6.5 Hz, 1H, 2-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 17.4 (q, CH_3), 20.9 (q, CH_3), 27.8 (q, CH_3), 39.5 (s, C-3), 66.2 (d, CHOAc), 86.4 (d, C-2), 98.2 (d, C-4), 171.4 (s, CO).

***erythro*-1-(3,3,4-Trimethyl-oxetan-2-yl)-ethylacetate (*erythro*-28b)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

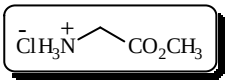
δ_{ppm} = 1.05 (d, J = 6.5 Hz, 3H, CH_3),1.17 (s, 3H, CH_3), 1.26 (d, J = 6.5 Hz, 3H, CH_3), 1.29 (s, 3H, CH_3), 4.32 (dq, J = 6.2, 6.5 Hz, 1H, CHOAc), 4.47 (d, J = 6.2 Hz, 1H, 2-H), 4.62 (q, J = 6.5 Hz, 1H, 2-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 17.6 (q, CH_3), 21.4 (q, CH_3), 27.4 (q, CH_3), 40.5 (s, C-3), 65.8 (d, CHOAc), 88.4 (d, C-2), 97.6 (d, C-4), 171.7 (s, CO).

4.13 Synthesis of oxazole substrates

Preparation of glycine methyl ester hydrochloride (30)[156] (sbo-370)



A 250 mL two necked round bottomed flask containing a magnetic stirring bar, is equipped with a dropping funnel, reflux condenser protected from moisture by a $CaCl_2$ tube and a rubber septum. The dropping funnel is charged with (4.2 mL, 60 mmol) of thionyl chloride. The flask is charged with 50 mL of absolute methanol and cooled with ice-salt bath to -10°C. Thionyl chloride is added dropwise over a period of 5 min. The solution is stirred for a further 5 min, then glycine (2.25 g, 30 mmol) is added in one portion and the solution is slowly heated to reflux. The reflux is continued for 3 h, then the solution is allowed to cool to room temperature and the solvent is removed under reduced pressure to give glycine methyl ester hydrochloride as a white crystalline material.

Yield: 92 %

M.p: 175-176 °C (Lit.[156], 180°C).

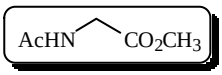
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 3.54 (s, 3H, OCH_3), 3.97 (s, 2H, CH_2), 8.64 (s, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 42.5 (t, CH_2), 52.1 (q, OCH_3), 170.1 (s, CO).

Preparation of N-acetyl glycine methyl ester (31)[157] (sbo-370a)



To a stirred suspension of glycine methyl ester hydrochloride (3.0 g, 24 mmol) in chloroform (50 mL) was added triethyl amine (6.7 mL, 53 mmol) at 0°C and the mixture was stirred for 5 min at room temperature. The acetyl chloride (2.1 g, 26 mmol) was added dropwise and stirring was continued for 30 min, the solvent was removed under reduced pressure; ethyl acetate (300 mL) was added and the mixture was filtered through a pad of silica gel. Evaporation of the solvent under reduced pressure afforded 3.0 g of N-acetyl glycine methyl ester as white solid.

Yield: 96 %

M.p: 53-55 °C (Lit.[157], 58-59°C).

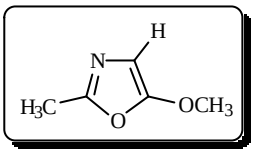
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.90 (s, 3H, $\underline{CH_3}CO$), 3.52 (s, 3H, OCH_3), 3.75 (d, J = 5.7 Hz, 2H, CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.0 (q, CH_3), 40.7 (t, CH_2), 51.7 (q, OCH_3), 170.2 (s, CON), 170.9 (s, CO).

Synthesis of 2-methyl-5-methoxyoxazole (32)[111] (sbo-417)



Method (A):[112]

A mixture of (13.1 g, 0.1 mol) N-acetyl glycine methyl ester and (40.0 g, 0.15 mol) of phosphorous pentoxide in (100 mL) chloroform was heated to reflux with mechanical stirring for a period of 24 h. After cooling to room temperature, the residual phosphorous pentoxide was carefully crushed, and the resulting thick suspension was slowly added, in small portions, to ice-cold saturated sodium bicarbonate maintaining the pH of 6-7. The organic layer was separated and the aqueous layer was extracted with 4 x 75 mL of methylene chloride. The combined extracts were then washed with brine, dried over anhydrous magnesium sulphate, concentrated and distilled to afford 10.0 g (80 %) as a colorless oil.

Method (B):[111]

N-Acetyl glycine methyl ester (655 mg, 5 mmol) was added to phosphorous oxychloride (2.3 mL, 25 mmol) and heated at reflux temperature for 4 h. After cooling to room temperature, the reaction mixture was poured onto crushed ice with stirring and neutralized with 20% aq. KOH solution. It was extracted with chloroform (3 x 15 mL), washed with water (2 x 15 mL), and brine solution (20 mL). The organic phase was dried over anhydrous Na_2SO_4, the solvent was removed in *vacuo* and the residual oil was distilled over Kugelrohr apparatus to give the product (**32**) as a colorless liquid.

Yield: 70 %

B.p: 64-66°C, 10 torr (Lit.,[113] 60°C, 0.2 mmHg).

UV/Vis: (CH_3CN, c = 1.6 x 10^{-4} mol/l, d = 1 cm)

λ_{max} (nm, log ε) = 220 (4.18).

IR: (Nujol)

$\tilde{n}$ (cm^{-1}) = 2984, 1623, 1580, 1283, 1084, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.27 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 5.87 (s, 1H, CH).

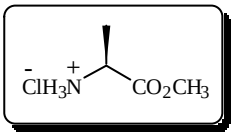
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 58.4 (q, OCH_3), 97.8 (d, C-4), 152.0 (s, C-5), 160.5 (s, C-2).

Synthesis of amino acid methyl ester hydrochloride 34a-f ; General procedure:

A 250 mL, two-necked, round-bottomed flask, contanining a magnetic stirring bar, is equipped with a dropping funnel, reflux condenser protected from moisture by a calcium chloride-filled drying tube and a rubber septum. The dropping funnel is charged with (4.2 mL, 60 mmol) of thionyl chloride. The flask is charged with 50 mL of absolute methanol and cooled with ice-salt bath to (-10°C). Thionyl chloride is added dropwise over a period of 5 min. The solution is stirred for a further 5 min, then solid (L)-amino acid (30 mmol) is added in one portion and the solution is slowly heated to reflux. The reflux is continued for 3 h, then the solution is allowed to cool to room temperature and the solvent is removed under reduced pressure to give aminoacid methyl ester hydrochloride as a white crystalline solid that is used without further purification.

L-Alanine methyl ester hydrochloride (34a)[158] (sbo-289)



The reaction was carried out according to the above general procedure using L-alanine (2.67 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give 3.85 g of the product as a white powder.

Yield: 92 %

M.p: 151-153°C (Lit.[158], 154-155°C).

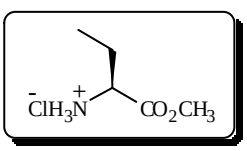
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.72 (d, J = 7.2 Hz, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.26 (m, 1H, CHN), 8.67 (bs, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.0 (q, CH_3), 49.3 (d, CHN), 53.2 (q, OCH_3), 170.5 (s, CO).

2-Amino butyric acid methyl ester hydrochloride (34b)[159] (sbo-363)



The reaction was carried out according to the above general procedure using 2-amino butyric acid (3.1 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give 4.4 g of the product as a white powder.

Yield: 96 %

M.p: 1444-146 °C (Lit.[159], 145-146°C).

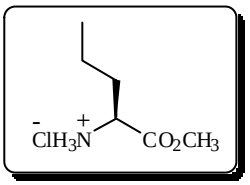
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.06 (t, J = 6.8 Hz, 3H, CH_3), 2.06 (quintet, J = 6.8 Hz, 2H, CH_2), 3.77 (s, 3H, OCH_3), 4.12 (d, J = 6.8 Hz, 1H, CHN), 8.69 (bs, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.6 (q, CH_3), 23.7 (t, CH_2), 52.9 (q, OCH_3), 54.4 (d, CHN), 169.8 (s, CO).

L-Norvaline methyl ester hydrochloride (34c)[160] (sbo-330)



The reaction was carried out according to the above general procedure using norvaline (3.51 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give 4.76 g of the product as a white powder.

Yield: 95 %

M.p: 86-88°C (Lit.[160], 85°C).

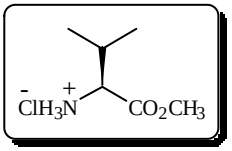
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (t, J = 7.5 Hz, 3H, CH_3), 1.14 (sextet, J = 7.5 Hz, 2H, CH_2), 1.43 (m, 2H, CH_2), 3.56 (s, 3H, OCH_3), 4.41 (m, 1H, CHN), 8.61 (bs, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.0 (q, CH_3), 22.1 (t, CH_2), 33.7 (t, CH_2), 51.6 (q, OCH_3), 51.7 (d, CHN), 173.0 (s, CO).

L-Valine methyl ester hydrochloride (34d)[161] (sbo-315)



The reaction was carried out according to the above general procedure using L-valine (3.51 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give 4.5 g of the product as a white powder.

Yield: 90 %

M.p: 178-179°C (Lit.[161], 180°C).

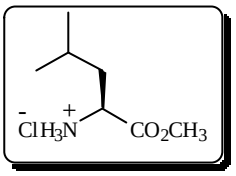
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 7.5 Hz, 6H, $2CH_3$), 2.0 (m, 1H, CH), 3.70 (s, 3H, OCH_3), 4.51 (m, 1H, CHN), 8.50 (bs, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.7 (q, CH_3), 18.7 (q, CH_3), 30.0 (d, CH), 51.9 (q, OCH_3), 56.0 (d, CHN), 173.0 (s, CO).

L-Leucine methyl ester hydrochloride (34e)[162] (sbo-329a)



The reaction was carried out according to the above general procedure using L-leucine (3.93 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give 5.0 g of the product as a white powder.

Yield: 93 %

M.p: 151-153°C (Lit.[162], 153-154°C).

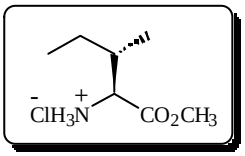
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (d, J = 6.0 Hz, 6H, $2CH_3$), 1.47 (m, 1H, CH), 1.57 (m, 2H, CH_2), 3.71 (s, 3H, OCH_3), 4.41 (m, 1H, CH), 8.64 (bs, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.8 (q, CH_3), 22.6 (q, CH_3), 24.7 (d, CH), 41.9 (t, CH_2), 51.0 (q, OCH_3), 52.3 (d, CHN), 173.7 (s, CO).

L-Isoleucine methyl ester hydrochloride (34f)[163] (sbo-327)



The reaction was carried out according to the above general procedure using L-isoleucine (3.93 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give 5.1 g of the product as a white powder.

Yield: 94 %

M.p: 118-120°C (Lit.[163], 117-119°C).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.87 (d, J = 7.0 Hz, 6H, $2CH_3$), 1.17 (m, 2H, CH_2), 1.90 (m, 1H, CH), 3.67 (s, 3H, OCH_3), 4.51 (m, 1H, CHN), 8.70 (bs, 3H, NH_3).

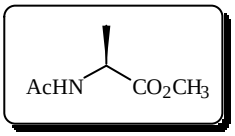
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.0 (q, CH_3), 15.3 (q, CH_3), 25.2 (t, CH_2), 37.0 (d, CH), 51.0 (q, OCH_3), 56.0 (d, CHN), 173.0 (s, CO).

Synthesis of N-acetylamino acid methy ester 35a-f; General procedure:

To a stirred suspension of amino acid methyl ester hydrochloride (100 mmol) in absolute chloroform (150 mL) was added triethyl amine (28 mL , 200 mmol) at 0°C and the mixture was stirred for 15 min at room temperature. The acetyl chloride (7.2 mL, 100 mmol) was added dropwise and stirring was continued for 45 min. The solvent was removed under reduced pressure; ethyl acetate (750 mL) was added and the mixture was filtered through a pad of silica gel. Evaporation of the solvent under reduced pressure afforded the amide in high purity.

Methyl 2-acetylaminopropionate (35a)[164] (sbo-292)



Alanine methyl ester hydrochloride (13.96 g, 0.1 mol) and acetyl chloride (7.2 mL, 0.1 mol) were allowed to react according to the above general procedure to give 13.1 g of methyl 2-acetylaminopropionate as a white powder.

Yield: 90 %

M.p: 45-47 °C (Lit.[164], 47-48°C).

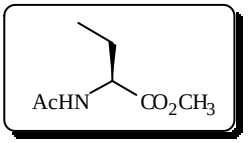
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.34 (d, J = 7.2 Hz, 3H, CH_3), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.70 (s, 3H, OCH_3), 4.51 (m, 1H, CHN).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.3 (q, CH_3), 22.2 (q, CH_3), 47.6 (d, CHN), 51.8 (q, OCH_3), 170.0 (s, CON), 173.2 (s, CO).

Methyl 2-acetylaminobutyrate (35b)[165] (sbo-364)



2-Acetylamino butyric acid methyl ester hydrochloride (15.4 g, 0.1 mol) and acetyl chloride (7.2 mL, 0.1 mol) were allowed to react according to the above general procedure to give 14.9 g of methyl 2-acetylaminopentanoate as a white powder.

Yield: 94 %

M.p: 43-45 °C (Lit.[165], 44-45°C).

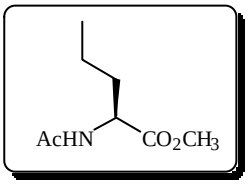
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (t, J = 7.5 Hz, 3H, CH_3), 1.45 (septet, J = 7.4 Hz, 1H, CH), 1.66 (d, J = 7.5 Hz, 1H, CH), 1.82 (s, 3H, $\underline{CH_3}CO$), 3.52 (s, 3H, OCH_3), 4.29 (m, 1H, CHN), 6.94 (d, J = 7.7 Hz, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.4 (q, CH_3), 22.4 (q, CH_3), 24.8 (t, CH_2), 51.7 (q, OCH_3), 53.1 (d, CHN), 170.3 (s, CON), 172.7 (s, CO).

Methyl 2-acetylaminopentanoate (35c)[166] (sbo-342)



Norvaline methyl ester hydrochloride (16.8 g, 0.1 mol) and acetyl chloride (7.2 mL, 0.1 mol) were allowed to react according to the above general procedure to give 15.6 g of methyl 2-acetylaminopentanoate as a white powder.

Yield: 90 %

M.p: 78-79 °C (Lit.[166], 78°C).

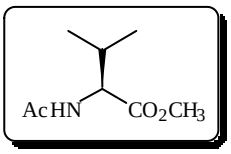
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (t, J = 7.5 Hz, 3H, CH_3), 1.16 (sextet, J = 7.5 Hz, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.83 (s, 3H, $\underline{CH_3}CO$), 3.53 (s, 3H, OCH_3), 4.38 (m, 1H, CHN), 6.94 (d, J = 7.2 Hz, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.2 (q, CH_3), 18.3 (q, CH_3), 22.3 (t, CH_2), 33.7 (t, CH_2), 51.7 (d, CHN), 51.8 (q, OCH_3), 170.3 (s, CON), 173.0 (s, CO).

Methyl 2-acetylamino-3-methylbutyrate (35d)[167] (sbo-315a)



Valine methyl ester hydrochloride (16.8 g, 0.1 mol) and acetyl chloride (7.2 mL, 0.1 mol) were allowed to react according to the above general procedure to give 15.9 g of methyl 2-acetylamino-3-methylbutyrate as a white powder.

Yield: 92 %

M.p: 67-68 °C (Lit.[167], 68-69°C).

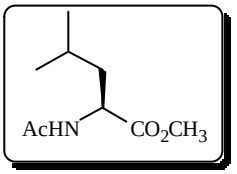
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 9.4 Hz, 3H, CH_3), 0.86 (d, J = 9.4 Hz, 3H, CH_3), 1.97 (s, 3H, $\underline{CH_3}CO$), 2.06 (m, 1H, CH), 3.67 (s, 3H, OCH_3), 4.49 (dd, 1H, J = 5.1, 2.5 Hz, 1H, CHN), 6.13 (d, J = 5.1Hz, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.7 (q, CH_3), 18.7 (q, CH_3), 23.0 (q, CH_3), 31.1 (d, CH), 51.9 (q, OCH_3), 56.9 (d, CHN), 169.9 (s, CON), 172.6 (s, CO).

Methyl 2-acetylamino-4-methylpentanoate (35e)[168] (sbo-329)



Leucine methyl ester hydrochloride (18.2 g, 0.1 mol) and acetyl chloride (7.2 mL, 0.1 mol) were allowed to react according to the above general procedure to give 17.6 g of methyl 2-acetylamino-4-methylpentanoate as a white powder.

Yield: 94 %

M.p: 75-77 °C (Lit.[168], 77°C).

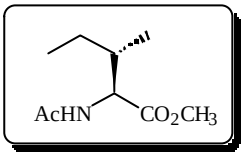
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 5.9 Hz, 6H, $2CH_3$), 1.45 (m, 1H, CH), 1.55 (m, 2H, CH_2), 1.95 (s, 3H, $\underline{CH_3}CO$), 3.66 (s, 3H, OCH_3), 4.56 (ddd, J = 7.8, 5.2, 4.9 Hz, 1H, CHN), 6.30 (d, 1H, J = 7.8 Hz, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.8 (q, CH_3), 22.6 (q, CH_3), 22.9 (q, CH_3), 24.7 (d, CH), 41.4 (t, CH_2), 50.6 (q, OCH_3), 52.1 (d, CHN), 170.0 (s, CON), 173.7 (s, CO).

Methyl 2-acetylamino-3-methylpentanoate (35f)[169] (sbo-332)



Isoleucine methyl ester hydrochloride (18.2 g, 0.1 mol) and acetyl chloride (7.2 mL, 0.1 mol) were allowed to react according to the above general procedure to give 17.77 g of methyl 2-acetylamino-3-methylpentanoate as a white powder.

Yield: 95 %

M.p: 54-56 °C (Lit.[169], 54-55°C).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (d, J = 7.1 Hz, 6H, $2CH_3$), 1.13 (m, 1H, CH), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.70 (s, 3H, OCH_3), 4.57 (m, 1H, CH), 6.14 (bs, 1H, NH).

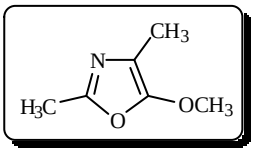
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.5 (q, CH_3), 15.3 (q, CH_3), 23.1 (q, CH_3), 25.2 (t, CH_2), 37.9 (d, CH), 52.0 (q, OCH_3), 56.4 (d, CHN), 169.9 (s, CON), 172.6 (s, CO).

Synthesis of 4-substituted 2-methyl-5-methoxyoxazoles (36a-f); General procedure:

N-Acetyl-L-amino acid methyl ester (0.1 mol) was dissolved in 20 ml of chloroform in a 250 ml flask, 20.8 g (0.1 mol) of phosphorous pentachloride was added and the flask was fitted with a calcium chloride tube. The solution was gently warmed by means of a water bath (ca. 60 °C) with stirring until the HCl gas evolution ceased and the solution became intensively yellow. Then, the flask was cooled by an ice-salt bath and 50 ml of absolute ether was added. To the cooled mixture, 20 % aqueous KOH was added dropwise until neutralization with vigorous stirring. The mixture was stirred at room temperature for 30 min. The organic layer was subsequently separated and the aqueous layer was extracted with 2 x 200 mL of ether. The combined organic extracts were washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvents under vacum, the remaining oil was distilled by a Büchi Kugelrohr apparatus to give the product **36a-f**.

2,4-Dimethyl-5-methoxyoxazole (36a)[170](sbo-295)



Reaction of methyl N-acetylamino alaninate (14.5 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 7.6 g of 2,4-dimethyl-5-methoxyoxazole as a colorless liquid.

Yield: 60 %

B.p: 61-63 °C, 10 torr.

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2943, 1625, 1598, 1440, 1341, 1052, 967.

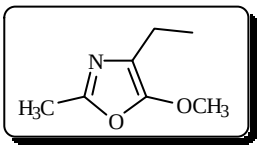
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.96 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.8 (q, CH_3), 14.1 (q, CH_3), 61.2 (q, OCH_3), 111.2 (s, C-4), 151.9 (s, C-5), 154.6 (s, C-2).

4-Ethyl-2-methyl-5-methoxyoxazole (36b)[115] (sbo-365)



Reaction of methyl 2-acetylamino butyrate (15.9 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 10.4 g of 4-ethyl-2-methyl-5-methoxyoxazole as a colorless liquid.

Yield: 74 %

B.p: 64-67 °C, 10 torr (Lit.[115], 65 °C, 10 torr).

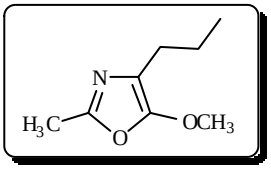
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.07 (t, J = 7.5 Hz, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.28 (q, J=7.5 Hz, 2H, CH_2), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.0 (q, CH_3), 14.1 (q, CH_3), 17.9 (t, CH_2), 61.2 (q, OCH_3), 117.1 (s, C-4), 151.8 (s, C-5), 154.0 (s, C-2).

2-Methyl-4-propyl-5-methoxyoxazole (36c) (sbo-343)



Reaction of methyl N-acetylamino norvalinate (17.3 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 10.5 g of 2-methyl-4-propyl-5-methoxyoxazole as a colorless liquid.

Yield: 68 %

B.p: 75-78 °C, 10 torr.

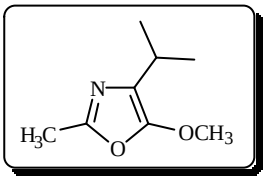
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (t, J = 7.5 Hz, 3H, CH_3), 1.52 (sextet, J = 7.5 Hz, 2H, CH_2), 2.21 (t, J = 7.5 Hz, 2H, CH_2), 2.22 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.6 (q, CH_3), 14.1 (q, CH_3), 21.7 (t, CH_2), 26.5 (t, CH_2), 115.6 (s, C-4), 151.9 (s, C-5), 154.6 (s, C-2).

4-Isopropyl-2-methyl-5-methoxyoxazole (36d)[115] (sbo-322)



Reaction of methyl N-acetylamino valinate (17.3 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 10.0 g of 4-isopropyl-2-methyl-5-methoxyoxazole as a colorless liquid.

Yield: 65 %

B.p: 71-73 °C, 10 torr (Lit.,[115] 72°C, 10 torr).

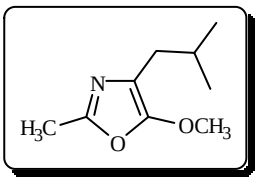
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.09 (d, J=7.1 Hz, 6H,2CH_3), 2.20 (s, 3H, CH_3), 2.65 (septet, J=7.1 Hz, 1H, CH), 3.75 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 21.5 (q, CH_3), 24.7 (d, CH), 61.2 (q, OCH_3), 121.1 (s, C-4), 151.8 (s, C-5), 153.2 (s, C-2).

4-Isobutyl-2-methyl-5-methoxyoxazole (36e)[115] (sbo-331)



Reaction of methyl N-acetylamino leucinate (18.7 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 11.8 g of 4-isobutyl-2-methyl-5-methoxyoxazole as a colorless liquid.

Yield: 70 %

B.p: 86-88 °C, 10 torr (Lit.[115], 88°C, 10 torr).

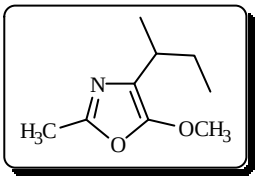
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.79 (sextet, J = 6.6 Hz, 1H, CH), 2.08 (d, J = 6.8 Hz, 2H, CH_2), 2.19 (s, 3H, CH_3), 3.74 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 22.1 (q, CH_3), 22.2 (q, CH_3), 27.6 (t, CH_2), 33.5 (d, CH), 60.9 (q, OCH_3), 114.8 (s, C-4), 151.7 (s, C-5), 154.9 (s, C-2).

4-*sec*-Butyl-2-methyl-5-methoxyoxazole (36f) (sbo-333)



Reaction of methyl N-acetylamino isoleucinate (18.7 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 12.7 g of 4-*sec*-butyl-2-methyl-5-methoxyoxazole as a colorless liquid.

Yield: 75 %

B.p: 89-93 °C, 10 torr.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.77 (t, J = 7.4 Hz, 3H, CH_3), 1.12 (d, J = 7.1 Hz, 3H, CH_3), 1.50 (m, 2H, CH_2), 2.26 (s, 3H, CH_3), 2.42 (m, 1H, CH), 3.79 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

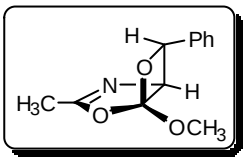
δ_{ppm} = 11.9 (q, CH_3), 14.1 (q, CH_3), 19.3 (q, CH_3), 28.6 (d, CH), 31.5 (t, CH_2), 61.3 (q, OCH_3), 119.9 (s, C-4), 152.1 (s, C-5), 154.1 (s, C-2).

4.14 Photolyses of 2-methyl-5-methoxyoxazole (32) with aldehydes (37a-f); General procedure:

2-Methyl-5-methoxyoxazole **32**, (0.56 g, 0.005 mol) and aldehydes (0.005 mol) were dissolved in 50 mL benzene, the solution transfered to a vacuum-jacket quartz tube and degassed with a steady stream of N_2 gas. The reaction mixture was irradiated at 10°C in a

Rayonet photoreactor (RPR 300 nm) for 24 h. The solvent was evaporated (40°C, 20 torr) and the residue was submitted to ^{1}H-NMR analysis to determine the diastereomeric ratio of the photoadducts. Purification was carried out by bulb to bulb distillation. The thermally and hydrolytically unstable primary products could in most cases not be characterized by combustion analysis and were hydrolyzed subsequently to the more stable α-amino-β-hydroxy esters.

***exo*-5-Methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-38a)** (sbo-419)



A solution of benzaldehyde (0.53 g, 5 mmol) and 2-methyl-5-methoxyoxazole (0.57 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.82 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 75 %

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2987, 1635, 1600, 1558, 1440, 1341, 1012, 967.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.11 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.58 (d, J = 7.7 Hz, 1H, 1-H), 5.68 (d, J = 7.7 Hz, 1H, 7-H), 7.26-7.31 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

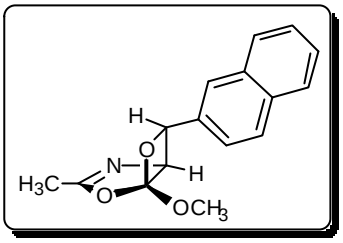
δ_{ppm} = 15.9 (q, CH_3), 52.8 (q, OCH_3), 76.2 (d, C-1), 83.0 (d, C-7), 122.9 (s, C-5), 125.4 (d, CH_{arom}), 126.2 (d, CH_{arom}), 128.1 (d, CH_{arom}), 134.3 (s, Cq_{arom}), 167.7 (s, C-3).

HRMS: ($C_{12}H_{13}NO_3$, M = 219.09 g/mol)

Calcd: 219.0892

Found: 219.0886

***exo*-5-Methoxy-3-methyl-7-naphthalen-2-yl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-38b)** (sbo-428)



A solution of 2-naphthaldehyde (0.78 g, 5 mmol) and 2-methyl-5-methoxyoxazole (0.57 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.1 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 82 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

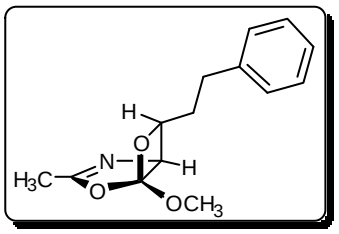
δ_{ppm} = 2.00 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 4.62 (d, J = 7.8 Hz, 1H, 1-H), 5.91 (d, J = 7.8 Hz, 1H, 7-H), 7.25-8.00 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.5 (q, CH_3), 51.9 (q, OCH_3), 78.0 (d, C-1), 84.1 (d, C-7), 123.1 (s, C-5), 126.1 (d, CH_{arom}), 128.1 (d, CH_{arom}), 129.3 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 137.1 (s, Cq_{arom}), 139.1 (s, Cq_{arom}), 168.0 (s, C-3).

***exo*-5-Methoxy-3-methyl-7-phenethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-38c)**

(sbo-439)



A solution of 3-phenylpropionaldehyde (0.67 g, 5 mmol) and 2-methyl-5-methoxyoxazole (0.57 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.98 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 79 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

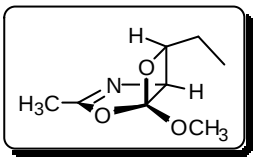
δ_{ppm} = 1.99 (s, 3H, CH_3), 2.08 (m, 2H, CH_2), 2.82 (m,2H, CH_2), 3.69 (s, 3H, OCH_3), 4.87 (d, J = 5.2 Hz, 1H, 1-H), 4.91 (dd, J = 5.2, 3.4 Hz, 1H, 7-H), 7.20-7.28 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 27.9 (t, CH_2), 35.1 (t, CH_2), 52.2 (q, OCH_3), 73.3 (d, C-1), 73.6 (d, C-7), 124.5 (s, C-5), 125.7 (d, C_{arom}), 127.6 (d, C_{arom}), 135.5 (s, Cq_{arom}), 169.6 (s, C-3).

***exo*-7-Ethyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-38d)**

(sbo-422)



A solution of propionaldehyde (0.29 g, 5 mmol) and 2-methyl-5-methoxyoxazole (0.57 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.76 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 89 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

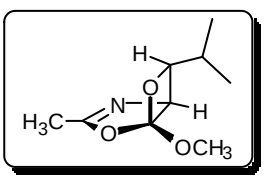
δ_{ppm} = 0.98 (t, J = 7.5 Hz, 3H, CH_3), 1.25 (m, 2H, CH_2), 2.07 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 5.04 (d, J = 7.4 Hz, 1H, 1-H), 5.24 (ddd, J = 11.6, 7.4, 4.7 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.7 (q, CH_3), 14.7 (q, CH_3), 24.7 (t, CH_2), 52.2 (q, OCH_3), 73.3 (d, C-1), 75.5 (d, C-7), 124.6 (s, C-5), 167.5 (s, C-3).

***exo*-7-Isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-38e)**

(sbo-435)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 2-methyl-5-methoxyoxazole (0.57 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.78 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 84 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

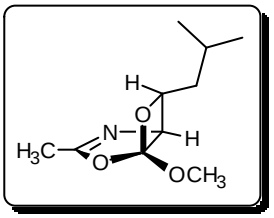
δ_{ppm} = 1.05 (d, J = 6.2 Hz, 6H, $2CH_3$), 1.54 (m, 1H, CH), 1.95 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 4.52 (d, J = 3.5 Hz, 1H, 1-H), 4.64 (dd, J=3.5, 7.9 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 18.8 (q, CH_3), 18.9 (q, CH_3), 31.1 (d, CH), 52.0 (q, OCH_3), 78.4 (d, C-1), 87.3 (d, C-7), 124.6 (s, C-5), 170.3 (s, C-3).

***exo*-7-Isobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-38f)**

(sbo-427)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 2-methyl-5-methoxyoxazole (0.57 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.85 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 85 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.6 Hz, 6H, $2CH_3$), 1.62 (m, 1H, CH), 1.90 (m, 2H, CH_2), 1.97 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 4.32 (d, J = 4.2 Hz, 1H, 1-H), 4.44 (dd, J = 4.2, 6.8 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.4 (q, CH_3), 22.2 (q, CH_3), 24.2 (q, CH_3), 27.5 (d, CH), 37.2 (t, CH_2), 51.7 (q, OCH_3), 80.8 (d, C-1), 84.5 (d, C-7), 144.7 (s, C-5), 167.4 (s, C-3).

HRMS: ($C_{10}H_{17}NO_3$, M = 199.12 g/mol)

Calcd: 199.1275

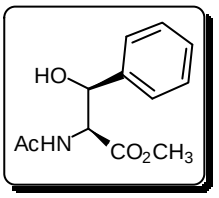
Found: 199.1271

4.14.1 Ring opening of the bicyclic oxetanes (*exo*-38a-f); General procedure:

A (0.002 mol) of bicyclic oxetanes **38a-f** was dissolved in 20 mL of methylene chloride and 0.5 ml of conc. HCl was added. The mixture is stirred in an open flask at room temperature for 2 h and the reaction was controled by TLC. When the reaction is finished, the reaction mixture was poured into water and extract with methylene chloride. The organic layer was washed with 5 % $NaHCO_3$, brine, dried over anhydrous $MgSO_4$. The solvent was removed in *vacuo* and the residual oil was purified by preparative chromatography using a mixture of ethyl acetate and n-hexane as eluent.

Synthesis of *erythro* (S*,S*) a -acetamido-b -hydroxy esters 39a-f:

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-3-phenylpropionate (*erythro*-39a)**[117] (sbo-419a)



According to the the above general procedure, the bicyclic oxetane **38a** (0.44 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.33 g of the product as a colorless oil.

Yield: 70 %

TLC: R_f = 0.34 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.07 (s, 3H, $\underline{CH_3}CO$), 3.97 (s, 3H, OCH_3), 4.45 (d, J = 9.7 Hz, 1H, $\underline{CH}N$), 5.85 (d, J = 9.7 Hz, 1H, $\underline{CH}OH$), 6.37 (bs, 1H, NH), 7.28-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

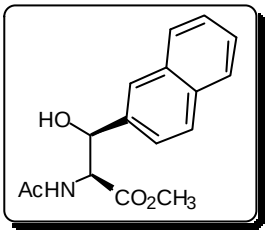
δ_{ppm} = 23.7 (q, CH_3), 52.4 (q, OCH_3), 75.4 (d, C-2), 81.6 (d, C-3), 126.2 (d, CH_{arom}), 128.9 (d, CH_{arom}), 129.6 (d, CH_{arom}), 134.3 (s, Cq_{arom}), 169.3 (s, CON), 170.3 (s, COO).

Anal: ($C_{12}H_{15}NO_4$, M = 237.10 g/mol)

Calcd: C 60.75 H 6.37 N 5.90

Found: C 60.86 H 6.52 N 6.00

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-3-naphthalen-2-yl-propionate (*erythro*-39b)** (sbo-428a)



According to the the above general procedure, the bicyclic oxetane **38b** (0.54 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.43 g of the product as a colorless oil.

Yield: 75 %

TLC: R_f = 0.41 (ethylacetate/n-hexane 1: 4)

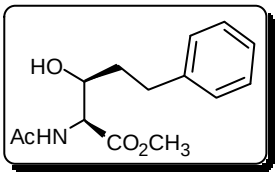
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.12 (s, 3H, $\underline{CH_3}CO$), 3.85 (s, 3H, OCH_3), 4.47 (d, J = 9.6 Hz, 1H, $\underline{CH}N$), 5.91 (d, J = 9.6 Hz, 1H, $\underline{CH}OH$), 6.24 (bs, 1H, NH), 7.25-8.04 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.0 (q, CH_3), 51.9 (q, OCH_3), 76.1 (d, C-2), 83.1 (d, C-3), 126.7 (d, CH_{arom}), 128.5 (d, CH_{arom}), 129.1 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 135.7 (s, Cq_{arom}), 139.1 (s, Cq_{arom}), 169.3 (s, CON), 172.0 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-5-phenylpentanoate (*erythro*-39c)** (sbo-439a)



According to the the above general procedure, the bicyclic oxetane **38c** (0.49 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.35 g of the product as a colorless oil.

Yield: 65 %

TLC: R_f = 0.32 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.97 (s, 3H, $\underline{CH_3}CO$), 2.43 (m, 2H, CH_2), 2.89 (m,2H, CH_2), 3.74 (s, 3H, OCH_3), 4.84 (dd, J=3.2, 8.2 Hz, 1H, $\underline{CH}N$), 5.06 (dd, J = 3.2, 7.4 Hz, 1H, $\underline{CH}OH$), 6.24 (bs, 1H, NH), 7.12-7.28 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.1 (q, CH_3), 30.6 (t, CH_2), 36.4 (t, CH_2), 52.6 (q, OCH_3), 55.0 (d, C-2), 73.8 (d, C-3), 126.2 (d, CH_{arom}), 128.5 (d, CH_{arom}), 129.3 (d, CH_{arom}), 140.6 (s, Cq_{arom}), 169.8 (s, CON), 172.8 (s, COO).

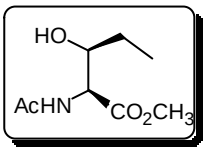
HRMS: ($C_{15}H_{21}NO_4$, M = 279.15 g/mol)

Calcd: 279.1465

Found: 279.1458

***erythro*-Methyl (2S*, 3S*) 2-acetylamino-3-hydroxy pentanoate (*erythro*-39d)**[171]

(sbo-422b)



According to the the above general procedure, the bicyclic oxetane **38d** (0.34 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.27 g of the product as a colorless oil.

Yield: 72 %

TLC: R_f = 0.36 (ethylacetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3320, 3300, 2989, 1725, 1648, 1440, 1341, 1052, 967.

^{1}H-NMR: (300 MHz, $CDCl_3$)

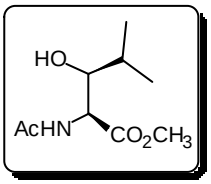
δ_{ppm} = 1.06 (t, J = 7.5 Hz, 3H, CH_3), 1.67 (m, 2H, CH_2), 2.03 (s, 3H, $\underline{CH_3}CO$), 3.77 (s, 3H, OCH_3), 4.01 (dd, J = 8.2, 4.7 Hz, 1H, $\underline{CH}N$), 4.88 (dd, J = 8.2, 3.4 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.5 (q, CH_3), 23.1 (q, CH_3), 28.6 (t, CH_2), 52.6 (q, OCH_3), 56.5 (d, C-2), 65.3 (d, C-3), 169.1 (s, CON), 169.6 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-4-methylpentanoate (*erythro*-39e)**[118]

(sbo-435a)



According to the the above general procedure, the bicyclic oxetane **38e** (0.37 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 78 %

TLC: R_f = 0.44 (ethylacetate/n-hexane 1: 4)

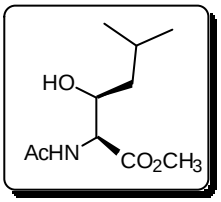
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (d, J = 6.6 Hz, 3H, CH_3), 0.98 (d, J = 6.8 Hz, 3H, CH_3), 1.67 (m, 1H, CH), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.76 (s, 3H, OCH_3), 4.45 (dd, J = 8.6, 3.3 Hz, 1H, $\underline{CH}N$), 4.75 (dd, J = 7.4, 3.3 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.5 (q, CH_3), 19.9 (q, CH_3), 20.5 (q, CH_3), 32.7 (d, CH), 53.1 (q, OCH_3), 54.3 (d, C-2), 69.8 (d, C-3), 169.3 (s, CON), 171.1 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-5-methylhexanoate (*erythro*-39f)** (sbo-427b)



According to the the above general procedure, the bicyclic oxetane **38f** (0.4 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 74 %

TLC: R_f = 0.51 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.98 (d, J = 6.6 Hz, 6H, $2CH_3$), 1.25 (m, 1H, CH), 1.54 (m, 2H, CH_2), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.75 (s, 3H, OCH_3), 4.18 (ddd, J = 7.6, 3.2, 4.7 Hz, 1H, $\underline{CH}N$), 4.87 (dd, J = 8.2, 3.2 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.5 (q, CH_3), 21.3 (q, CH_3), 21.4 (q, CH_3), 28.3 (d, CH), 34.1 (t, CH_2), 52.7 (q, OCH_3), 56.8 (d, C-2), 61.8 (d, C-3), 169.3 (s, CON), 171.3 (s, COO)

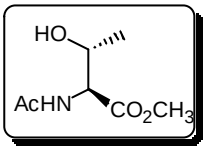
HRMS: ($C_{10}H_{19}NO_4$, M = 217.13 g/mol)

Calcd: 217.1287

Found: 217.1281

Independent synthesis of methyl (2S*,3R*) 2-acetylamino-3-hydroxy butanoate (*threo*-39g)[116]

(sbo-425a)



A 100 mL, three-necked, round bottomed flask, containing a magnetic stirring bar, is equipped with a dropping funnel and reflux condenser. The dropping funnel is charged with 7.8 mL of acetyl chloride. The flask is charged with 50 mL of methanol and cooled with an ice-bath to 0°C. Acetyl chloride is added dropwise over a period of 10 min. The solution is stirred for a further 5 min, then L-threonine (4.5 g, 38 mmol) is added in one portion and the solution is slowly heated to reflux. Reflux is continued for 3h, then the solution is allowed to cool to room temperature and the solvent is reomved under reduced pressure to give 4.8 g (94 %) of methyl threoniate hydrochloride.

A 250 mL two necked flask, is equipped with a magnetic stirring bar, reflux condenser and a pressure-equalizing dropping funnel that is charged with acetyl chloride (2.1 mL, 30 mmol). Methyl threoniate hydrochloride (4.6 g, 30 mmol) is placed in the flask and suspended in 100 mL of chloroform and triethyl amine (7.6 mL, 60 mmol). The resulting white suspension is cooled with an ice-bath and the solution of acetyl chloride is added dropwise over a period of 30 min. After 15 min of additional stirring, the ice-bath is removed and the suspension is stirred for a further 2h. The solvent was removed under vacuo, ethylacetate (150 mL) was added and the mixture was filtered through a pad of silica gel, evapouation of the solvent under reduced pressure afforded 4.9 g (89 %) of N-acetyl methyl threoniate as white crystal.

M.p: 106-108°C (Lit.[116], 105-106°C).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (d, J = 6.4 Hz, 3H, CH_3), 1.97 (s, 3H, $\underline{CH_3}CO$), 3.59 (s, 3H, OCH_3), 4.16 (ddq, J = 2.6, 6.0, 6.4 Hz, 1H, $\underline{CH}OH$), 4.35 (dd, J = 8.8, 2.6 Hz, 1H, $\underline{CH}N$).

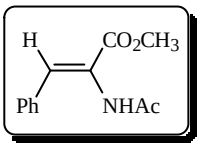
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.4 (q, CH_3), 20.2 (q, CH_3), 52.1 (q, OCH_3), 57.6 (d, C-2), 67.3 (d, C-3), 171.3 (s, CON), 171.4 (s, COO).

4.14.2 Synthesis of (Z)-a,b-didehydroamino acid derivatives (40a-d); General procedure:

The aldol product (1 mmol) was added to methylene chloride (15 mL) previously saturated with conc. HCl for 5 min and the solution stirred at room temperature until TLC indicated completion of the reaction. The reaction mixture was then washed with saturated $NaHCO_3$, saturated NaCl, dried over anhydrous Na_2SO_4 and then evaporated. The residue was purified by preparative thick-layer chromatography.

Methyl 2-acetylamino-3-phenylacrylate (Z-40a)[172] (sbo-419b)



According to the the above general procedure, methyl 2-acetylamino-3-hydroxy-3-phenylpropionate **39a** (0.24 g, 1 mmol) was dehydrated in 20h. Preparative chromatography yielded 0.17 g of the product as a colorless oil which was solidified from a mixture of chloroform and petroleum ether as a white powder.

Yield: 80 %

M.p: 122-124°C (Lit.[172], 125°C).

TLC: R_f = 0.52 (ethylacetate/n-hexane 1:4)

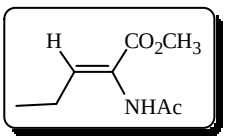
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.05 (s, 3H, $\underline{CH_3}CO$), 3.82 (s, 3H, OCH_3), 6.73 (s, 1H, CH=), 7.23-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.5 (q, CH_3), 52.1 (q, OCH_3), 123.6 (d, CH_{olefin}), 125.2 (d, CH_{arom}), 126.2 (d, C_{arom}), 127.3 (d, CH_{arom}), 135.5 (s, Cq_{olefin}), 135.9 (s, Cq_{arom}), 165.1 (s, CON), 168.3 (s, COO).

Methyl 2-acetylamino-pent-2-enoate (Z-40b)[173] (sbo-422c)



According to the the above general procedure, methyl 2-acetylamino-3-hydroxypentanoate **39d** (0.19 g, 1 mmol) was dehydrated in 24h. Preparative chromatography yielded 0.13 g of

the product as a colorless oil which was solidified by treatment with petroleum ether as a white powder.

Yield: 75 %

M.p: 55-56°C (Lit.[173], 58-60°C).

TLC: R_f = 0.44 (ethylacetate/n-hexane 1:4)

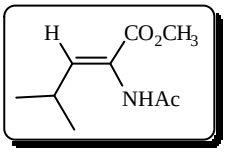
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.98 (t, J = 7.5 Hz, 3H, CH_3), 1.65 (m, 2H, CH_2), 2.08 (s, 3H, $\underline{CH_3}CO$), 3.83 (s, 3H, OCH_3), 6.84 (t, J=7.5 Hz, 1H, CH=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.5 (q, CH_3), 21.7 (q, CH_3), 24.5 (t, CH_2), 52.1 (q, OCH_3), 125.1 (d, CH_{olefin}), 138.1 (s, Cq_{olefin}), 165.1 (s, CON), 167.1 (s, COO).

Methyl 2-acetylamino-4-methyl-pent-2-enoate (Z-40c)[174] (sbo-435b)



According to the the above general procedure, methyl 2-acetylamino-3-hydroxy-4-methylpentanoate **39e** (0.2 g, 1 mmol) was dehydrated in 24h. Preparative chromatography yielded 0.14 g of the product as a colorless oil which was solidified by treatment with petroleum ether as a white powder.

Yield: 78 %

M.p: 71-72°C (Lit.[174], 73-75°C).

TLC: R_f = 0.49 (ethylacetate/n-hexane 1:4)

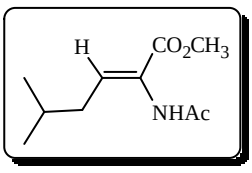
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.98 (d, J = 6.8 Hz, 6H, 2 CH_3), 1.35 (m, 1H, CH), 2.06 (s, 3H, $\underline{CH_3}CO$), 3.82 (s, 3H, OCH_3), 6.54 (d, J = 6.6 Hz, 1H, CH=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.3 (q, CH_3), 21.3 (q, CH_3), 21.5 (q, CH_3), 28.1 (d, CH), 52.1 (q, OCH_3), 124.1 (d, CH_{olefin}), 139.1 (s, Cq_{olefin}), 165.1 (s, CON), 167.5 (s, COO).

Methyl 2-acetylamino-5-methyl-hex-2-enoate (Z-40d)[175] (sbo-427c)



According to the the above general procedure, methyl 2-acetylamino-3-hydroxy-5-methylhexanoate **39f** (0.22 g, 1 mmol) was dehydrated in 24h. Preparative chromatography yielded 0.17 g of the product as a colorless oil which was solidified by treatment with petroleum ether as a white powder.

Yield: 83 %

M.p: 66-68°C (Lit.[175], 70-71°C).

TLC: R_f = 0.45 (ethylacetate/n-hexane 1: 3)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3305, 2978, 1698, 1627, 1580, 1440, 1340, 1062, 987.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.90 (d, J = 6.6 Hz, 6H, $2CH_3$), 1.74 (m, 1H, CH), 2.03 (m, 2H, CH_2), 3.74 (s, 3H, OCH_3), 6.70 (t, J = 7.2 Hz, 1H, CH=), 6.84 (s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 22.4 (q, CH_3), 22.5 (q, CH_3), 23.4 (q, CH_3), 27.9 (d, CH), 37.8 (t, CH_2), 52.5 (q, OCH_3), 125.3 (s, Cq_{olefin}), 138.2 (d, CH_{olefin}), 165.1 (s, CON), 168.3 (s, COO).

MS: (EI, 70 eV)

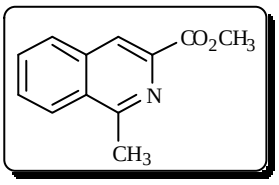
m/z (%) = 199 (M^+, 5), 168 (M^+-OMe, 8), 167 (M^+-MeOH, 13), 156 (M^+-COMe, 22), 125 (10), 114 (100), 97 (12), 55 (17), 54 (65).

HRMS: ($C_{10}H_{17}NO_3$, M = 199.12 g/mol)

Calcd: 199.1208

Found: 199.1203

4.14.3 Synthesis of methyl 1-methyl isoquinoline-3-carboxylate (41)[121] (sbo-419c)



To a solution of (Z)-2-acetylamino-3-phenylacrylate (0.21 g, 0.001 mol) in methylene chloride (20 mL), phosphorous oxychloride (0.2 g, 0.0015 mol) was added, and the mixture was warmed at 60 °C for 2 h. After the reaction was quenched with saturated sodium bicarbonate (25 mL), the mixture was extracted with methylene chloride (3 x 10 mL) and dried over $MgSO_4$. After removal of the solvent, the residue was purified by preparative chromatography to give 0.29 g of the product as a white powder.

Yield: 78 %

M.p: 105-107°C (Lit.,[121] 104-105°C).

TLC: R_f = 0.43 (ethylacetate/n-hexane 1:4)

IR: (CsI)

$\tilde{n}$ (cm^{-1}) = 2985, 1685, 1620, 1600, 1550, 1013, 970.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 3.03 (s, 3H, CH_3), 4.03 (s, 3H, OCH_3), 7.72 (t, J = 1.7 Hz, 1H, 7-H_{arom}), 7.74 (t, J = 1.7 Hz, 1H, 6-H_{arom}), 7.93 (dd, J = 1.7, 2.2 Hz, 1H, 5-H_{arom}), 8.17 (m, 1H, 8-H_{arom}), 8.44 (s, 1H, 4-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

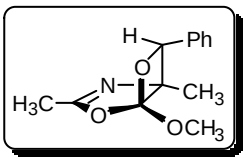
δ_{ppm} = 22.7 (q, CH_3), 52.9 (q, OCH_3), 125.8 (d, CH_{arom}), 128.7 (d, CH_{arom}), 128.9 (s, Cq_{arom}),129.4 (d, CH_{arom}), 130.7 (d, CH_{arom}), 135.5 (s, Cq_{arom}), 140.4 (s, C-3), 159.4 (s, C-1), 166.5 (s, CO).

4.15 Photolyses of 4-substituted 2-methyl-5-methoxyoxazoles 36a-f with aldehydes 37a-f; General procedure:

5-Methoxyoxazoles (0.005 mol) and aldehydes (0.005 mol) were dissolved in 50 mL of benzene, the solution transfered to a vacuum-jacket quratz vessel and degassed with a steady stream of N_2 gas. The reaction mixture was irradiated at 10°C in a Rayonet photoreactor (RPR 300 nm) for 24 h. The solvent was evaporated (40°C , 20 torr) and the residue was analyzed by ^{1}H-NMR analysis. Purification was carried out by bulb to bulb distillation. The thermally and hydrolytically unstable primary products could in most cases not be characterized by combustion analysis and were hydrolyzed subsequently to the more stable α-amino-β-hydroxy esters.

Photolyses of benzaldehyde with 5-methoxyoxazoles 36a-f:

***exo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42aa)** (sbo-573)



A solution of benzaldehyde (0.53 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.96 g of the oxetane as a pale yellow oil.

The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 82 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 3.52 (s, 3H, OCH_3), 5.19 (s, 1H, 7-H), 7.21-7.25 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

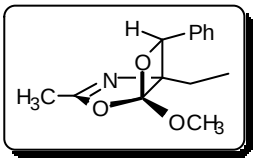
δ_{ppm} = 13.4 (q, CH_3), 14.8 (q, CH_3), 51.2 (q, OCH_3), 75.8 (s, C-1), 89.3 (d, C-7), 124.5 (s, C-5), 125.7 (d, CH_{arom}), 128.6 (d, CH_{arom}), 129.3 (d, CH_{arom}), 136.9 (s, Cq_{arom}), 164.9 (s, C-3).

HRMS: ($C_{13}H_{15}NO_3$, M = 233.1 g/mol)

Calcd: 233.0762

Found: 233.0758

***exo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ab)** (sbo-400)



A solution of benzaldehyde (0.53 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.31 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (t, J = 7.2 Hz, 3H, CH_3), 1.06 (q, J = 7.2 Hz, 2H, CH_2), 2.00 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 5.79 (s, 1H, 7-H), 7.26-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

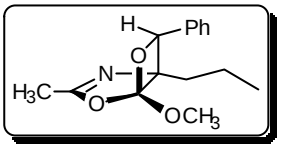
δ_{ppm} = 8.5 (q, CH_3), 23.7 (q, CH_3), 24.9 (t, CH_2), 51.7 (q, OCH_3), 79.2 (s, C-1), 82.0 (d, C-7), 124.5 (s, C-5), 125.6 (d, CH_{arom}), 127..3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 136.5 (s, Cq_{arom}), 164.9 (s, C-3).

HRMS: ($C_{14}H_{17}NO_3$, M = 247.12 g/mol)

Calcd: 247.1204

Found: 247.1197

***exo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ac)** (sbo-348)



A solution of benzaldehyde (0.53g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.14 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2992, 1628, 1598, 1440, 1348, 1042, 960.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.55 (t, J = 7.1 Hz, 3H, CH_3), 0.78 (sextet, J = 7.1 Hz, 2H, CH_2), 1.12 (t, J = 7.1 Hz, 2H, CH_2), 2.00 (s, 3H, CH_3), 3.55 (s, 3H, OCH_3), 5.17 (s, 1H, 7-H), 7.25-7.32 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

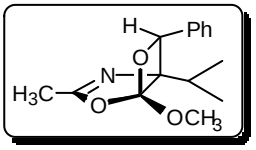
δ_{ppm} = 14.1 (q, CH_3), 15.1 (q, CH_3), 16.4 (t, CH_2), 29.6 (t, CH_2), 51.3 (q, OCH_3), 78.9 (s, C-1), 89.9 (d, C-7), 124.6 (s, C-5), 126.4 (d, CH_{arom}), 128.2 (d, CH_{arom}), 137.1 (s, Cq_{arom}), 165.1 (s, C-3).

HRMS: ($C_{15}H_{19}NO_3$, M = 261.14 g/mol)

Calcd: 261.1360

Found: 261.1356

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ad)** (sbo-326)



A solution of benzaldehyde (0.53g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general

procedure. Distillation of the solvent under vaccum afforded 1.1 g of the oxetane as a pale yellow oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 85 %

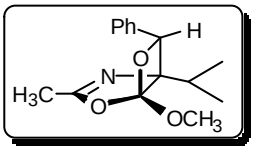
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.53 (d, J = 6.8 Hz, 3H, CH_3), 0.76 (d, J = 6.8 Hz, 3H, CH_3), 1.89 (m, 1H, CH), 2.02 (s, 3H, CH_3), 3.61 (s, 3H, OCH_3), 5.26 (s, 1H, 7-H), 7.28-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.5 (q, CH_3), 15.3 (q, CH_3), 16.3 (q, CH_3), 24.9 (d, CH), 50.5 (q, OCH_3), 82.2 (s, C-1), 90.2 (d, C-7), 124.3 (s, C-5), 127.4 (d, CH_{arom}), 127.8 (d, CH_{arom}), 128.2 (d, C_{arom}), 135.9 (s, Cq_{arom}), 164.8 (s, C-3).

***endo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*endo*-42ad) (sbo-326)**



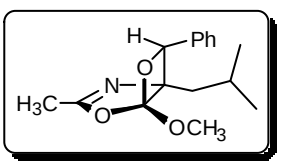
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (d, J = 6.8 Hz, 3H, CH_3), 0.98 (d, J = 6.9 Hz, 3H, CH_3), 1.95 (m, 1H, CH), 1.67 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 5.28 (s, 1H, 7-H), 7.30-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.7 (q, CH_3), 15.4 (q, CH_3), 16.3 (q, CH_3), 24.7 (d, CH), 50.8 (q, OCH_3), 82.7 (s, C-1), 90.7 (d, C-7), 124.3 (s, C-5), 127.3 (d, CH_{arom}), 127.8 (d, CH_{arom}), 128.2 (d, CH_{arom}), 135.5 (s, Cq_{arom}), 165.1 (s, C-3).

***exo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ae)** (sbo-338)



A solution of benzaldehyde (0.53 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general

procedure. Distillation of the solvent under vaccum afforded 1.16 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 84 %

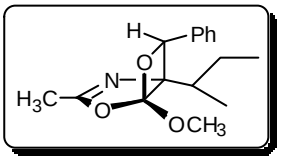
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.58 (d, J = 6.8 Hz, 3H, CH_3), 0.72 (d, J = 6.6 Hz, 3H, CH_3), 0.90 (m, 1H, CH), 1.20 (dd, J = 5.3, 7.8 Hz, 2H, CH_2), 2.21 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 5.26 (s, 1H, 7-H), 7.30-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.1 (q, CH_3), 22.9 (q, CH_3), 23.7 (q, CH_3), 23.8 (d, CH), 35.6 (t, CH_2), 51.3 (q, OCH_3), 78.7 (s, C-1), 90.4 (d, 7-H), 124.8 (s, C-5), 126.8 (d, C_{arom}), 127.9 (d, C_{arom}), 128.8 (d, C_{arom}), 164.7 (s, C-3).

***exo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42af)** (sbo-344)



A solution of benzaldehyde (0.53 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.24 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 90 %

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2985, 1620, 1600, 1550, 1108, 1042, 980.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.34 (t, J = 7.4 Hz, 3H, CH_3), 0.52 (d, J = 6.6 Hz, 3H, CH_3), 0.73 (m, 2H, CH_2), 0.91 (m, 1H, CH), 2.13 (s, 3H, CH_3), 3.68 (s, 3H, OCH_3), 5.27 (s, 1H, 7-H), 7.30-7.53 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

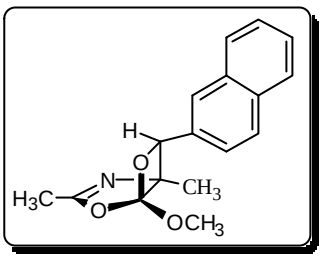
δ_{ppm} = 11.3 (q, CH_3), 11.5 (q, CH_3), 11.7 (t, CH_2), 20.9 (d, CH), 32.0 (t, CH_2), 51.1 (q, OCH_3), 82.9 (s, C-1), 90.8 (d, CH), 124.7 (s, C-5), 126.4 (d, C_{arom}), 127.9 (d, C_{arom}), 128.5 (d, C_{arom}), 137.3 (s, Cq_{arom}), 165.2 (s, C-3).

MS: (EI, 70 eV)

m/z (%) = 234 (M^+-CH_3CN, 15), 218 (M^+-Bu^{sec}, 10), 198 (28), 169 (100), 168 (52), 155 (32), 144 (75), 126 (63), 112 (43), 99 (20), 95 (15), 84 (55), 70 (18), 57 (60).

Photolysis of 2-naphthaldehyde with 2,4-dimethyl-5-methoxyoxazole 36a:

***exo*-5-Methoxy-1,3-dimethyl-7-naphth-2-yl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ba)** (sbo-304)



A solution of 2-naphthalaldehyde (0.64 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.3 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 92 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

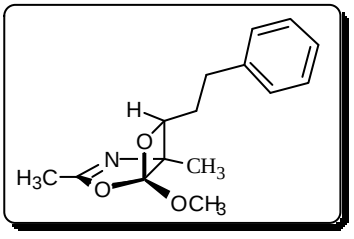
δ_{ppm} = 0.82 (s, 3H, CH_3), 2.00 (s, 3H , CH_3), 3.54 (s, 3H, OCH_3), 5.21 (s, 1H, 7-H), 7.42-7.81 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.6 (q, CH_3), 14.9 (q, CH_3), 51.4 (q, OCH_3), 75.9 (s, C-1), 89.5 (d, C-7), 124.6 (s, C-5), 125.9 (d, CH_{arom}), 128.2 (d, CH_{arom}), 129.5 (d, CH_{arom}), 134.3 (s, Cq_{arom}), 136.2 (s, Cq_{arom}), 137.0 (s, Cq_{arom}), 165.3 (s, C-3).

Photolyses of 3-phenylpropionaldehyde with 5-methoxyoxazoles 36a & 36d:

***exo*-5-Methoxy-1,3-dimethyl-7-phenethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ca)** (sbo-313)



A solution of 3-phenylpropionaldehyde (0.67 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.27 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.18 (s, 3H, CH_3), 1.95 (s, 3H, CH_3) , 2.70 (m, 2H, CH_2), 2.92 (m, 2H, CH_2), 3.43 (s, 3H, OCH_3), 4.15 (dd, J = 4.3, 9.5 Hz, 1H, 7-H), 7.26 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

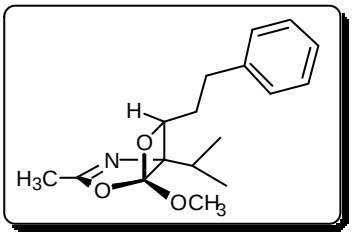
δ_{ppm} = 12.1 (q, CH_3), 14.9 (q, CH_3), 27.9 (t, CH_2), 45.1 (t, CH_2), 51.3 (q, OCH_3), 73.4 (s, C-1), 87.9 (d, C-7), 124.5 (s, C-5), 128.0 (d, CH_{arom}), 128.8 (d, CH_{arom}), 129.5 (d, CH_{arom}), 140.7 (s, Cq_{arom}), 164.8 (s, C-3).

HRMS: ($C_{15}H_{19}NO_3$, M = 261.14 g/mol)

Calcd: 261.1360

Found: 261.1358

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42cd)** (sbo-313)



A solution of 3-phenylpropionaldehyde (0.67 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.27 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (d, J = 6.6 Hz, 3H, CH_3), 0.85 (d, J = 6.8 Hz, 3H, CH_3), 1.87 (m, 2H, CH_2), 1.95 (s, 3H, CH_3), 2.44 (m, 2H, CH_2), 2.75 (m, 1H, CH), 3.46 (s, 3H, OCH_3), 4.18 (dd, J = 11.2, 2.7 Hz, 1H, 7-H), 7.21-7.34 (m, 5H, H_{arom}).

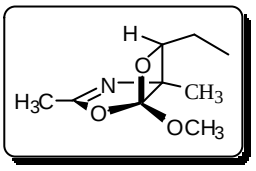
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 14.8 (q, CH_3), 16.6 (q, CH_3), 17.7 (d, CH), 30.6 (t, CH_2), 33.4 (t, CH_2), 50.8 (q, OCH_3), 79.9 (s, C-1), 88.3 (d, C-7), 124.5 (s, C-5), 125.6 (d, CH_{arom}), 126.1 (d, CH_{arom}), 128.9 (d, CH_{arom}), 140.2 (s, Cq_{arom}), 165.2 (s, C-3).

Photolyses of propionaldehyde with 5-methoxyoxazoles 36a-f:

***exo*-1-Ethyl-5-methoxy-1,3-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42da)**

(sbo-300)



A solution of propionaldehyde (0.29 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.78 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 84 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (t, J = 7.2 Hz, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.55 (dt, J = 7.8, 7.2 Hz, 2H, CH_2), 1.95 (s, 3H, CH_3), 3.41 (s, 3H, OCH_3), 4.05 (dd, J = 7.8, 6.3 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.7 (q, CH_3), 11.8 (q, CH_3), 14.7 (q, CH_3), 25.1 (t, CH_2), 51.0 (q, OCH_3), 73.2 (s, C-1), 90.1 (d, C-7), 124.3 (s, C), 164.7 (s, C-3).

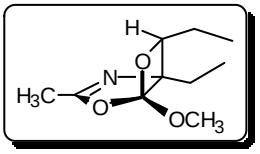
HRMS: ($C_9H_{15}NO_3$, M = 185.11 g/mol)

Calcd: 185.1048

Found: 185.1039

***exo*-1-Diethyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42db)**

(sbo-410)



A solution of propionaldehyde (0.29 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general

procedure. Distillation of the solvent under vaccum afforded 0.9 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 90 %

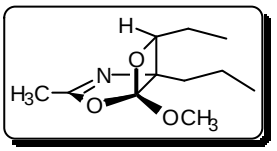
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.76 (t, J = 7.5 Hz, 3H, CH_3), 0.82 (t, J = 7.4 Hz, 3H, CH_3), 1.55 (q, J = 7.5 Hz, 2H, CH_2), 1.58 (m, 2H, CH_2), 1.93 (s, 3H, CH_3), 3.58 (s, 3H, OCH_3), 4.03 (dd, J = 5.7, 8.3 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.8 (q, CH_3), 8.9 (q, CH_3), 14.7 (q, CH_3), 19.0 (t, CH_2), 24.9 (t, CH_2), 50.8 (q, OCH_3), 76.7 (s, C-1), 90.4 (d, C-7), 124.3 (s, C-5), 164.8 (s, C-3).

***exo*-7-Ethyl-5-methoxy-3-methyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42dc)** (sbo-349)



A solution of propionaldehyde (0.29 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.92 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 86 %

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2998, 1615, 1440, 1110, 967.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (t, J = 7.1 Hz, 3H, CH_3), 0.84 (t, J = 7.5 Hz, 3H, CH_3), 0.85 (t, J = 7.1 Hz, 2H, CH_2), 1.21 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 1.96 (s, 3H, CH_3), 3.41 (s, 3H, OCH_3), 4.07 (dd, J = 6.0, 8.0 Hz, 1H, 7-H).

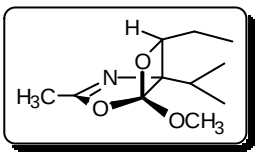
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.9 (q, CH_3), 14.2 (q, CH_3), 16.9 (t, CH_2), 24.9 (t, CH_2), 28.3 (t, CH_2), 50.8 (q, OCH_3), 76.4 (s, C-1), 90.5 (d, C-7), 124.3 (s, C-5), 164.5 (s, C-3).

MS: (EI, 70 eV)

m/z (%) = 184 (M^+-Et, 12), 172 (M^+-CH_3CN, 16), 155 (80), 144 (75), 126 (34), 112 (43), 99 (20), 95 (15), 86 (55), 68 (88), 57 (100).

***exo*-7-Ethyl-1-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42dd)** (sbo-324)



A solution of propionaldehyde (0.29 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.88 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 83 %

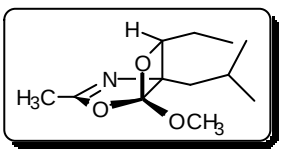
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (d, J = 6.8 Hz, 3H, CH_3), 0.87 (t, J = 7.5 Hz, 3H, CH_3), 1.65 (m, 2H, CH_2), 1.97 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 3.42 (s, 3H, OCH_3), 4.10 (dd, J = 9.4, 4.4 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.0 (q, CH_3), 14.9 (q, CH_3), 16.6 (q, CH_3), 17.7 (q, CH_3), 21.5 (d, CH), 24.7 (t, CH_2), 50.7 (q, OCH_3), 80.0 (s, C-1), 90.8 (d, C-7), 124.5 (s, C-5), 164.9 (s, C-3).

***exo*-7-Ethyl-1-isobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42de)** (sbo-337)



A solution of propionaldehyde (0.29 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.99 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (d, J = 6.6 Hz, 3H, CH_3), 0.86 (d, J = 7.4 Hz, 3H, CH_3), 1.05 (m, 1H, CH), 1.54 (t, J = 7.5 Hz, 3H, CH_3), 1.67 (m, 2H, CH_2), 1.88 (m, 2H, CH_2), 1.95 (s, 3H, CH_3), 3.42 (s, 3H, OCH_3), 4.05 (dd, J = 7.6, 6.2 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

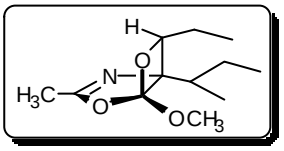
δ_{ppm} = 8.9 (q, CH_3), 13.9 (q, CH_3), 14.8 (q, CH_3), 20.8 (d, CH), 22.9 (q, CH_3), 27.6 (t, CH_2), 34.1 (t, CH_2), 50.8 (q, OCH_3), 76.9 (s, C-1), 90.9 (d, C-7), 124.4 (s, C-5), 164.0 (s, C-3).

HRMS: ($C_{12}H_{21}NO_3$, M = 227.15 g/mol)

Calcd: 227.1516

Found: 227.1512

***exo*-1-*sec*-Butyl-7-ethyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42df)** (sbo-341)



A solution of propionaldehyde (0.29 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.0 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 88 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.76 (d, J = 6.6 Hz, 3H, CH_3), 0.83 (m, 3H, CH_3), 0.92 (t, J = 7.4 Hz, 3H, CH_3), 1.43 (m, 1H, CH), 1.83 (m, 2H, CH_2), 2.10 (s, 3H, CH_3), 3.47 (s, 3H, OCH_3), 4.16 (dd, J = 3.7, 7.5 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

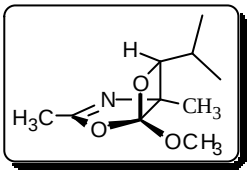
δ_{ppm} = 9.0 (q, CH_3), 11.5 (q, CH_3), 12.9 (q, CH_3), 13.9 (q, CH_3), 23.5 (d, CH), 24.9 (t, CH_2), 32.0 (t, CH_2), 51.8 (q, OCH_3), 80.4 (s, C-1), 91.0 (d, C-7), 124.6 (s, C-5), 164.9 (s, C-3).

MS: (EI, 70 eV)

m/z (%) = 216 (M^+-Et, 10), 196 (5), 186 (18), 170 (20), 169 (35), 168 (52), 155 (32), 144 (75), 126 (100), 112 (43), 99 (20), 95 (15), 84 (55), 70 (18), 57 (60).

Photolyses of isobutyraldehyde with 5-methoxyoxazoles 36a-f:

***exo*-7-Isopropyl-5-methoxy-1,3-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ea)** (sbo-320)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.93 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 93 %

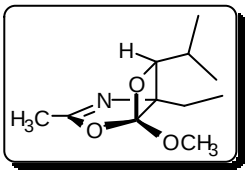
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 7.5 Hz, 3H, CH_3), 0.85 (d, J = 7.2 Hz, 3H, CH_3), 0.87 (m,1H, CH), 1.31 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 3.48 (s, 3H, OCH_3), 4.28 (d, J = 3.4 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.4 (q, CH_3), 14.9 (q, CH_3), 17.7 (q, CH_3), 19.3 (q, CH_3), 23.8 (d, CH), 52.5 (q, OCH_3), 73.0 (s, C-1), 93.9 (d, C-7), 124.6 (s, C-5), 165.0 (s, C-3).

***exo*-1-Ethyl-7-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42eb)** (sbo-415)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.93 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

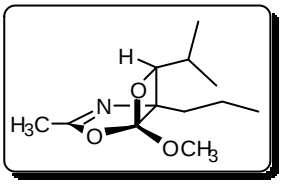
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (d, J = 7.2 Hz, 6H, $2CH_3$), 0.85 (m, 1H, CH), 1.00 (t, J = 7.5 Hz, 3H, CH_3), 1.58 (m, 2H, CH_2), 2.15 (s, 3H, CH_3), 3.60 (s, 3H, OCH_3), 4.04 (d, J = 8.4 Hz, 1H, CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.7 (q, CH_3), 15.0 (q, CH_3), 18.3 (q, CH_3), 18.9 (q, CH_3), 21.2 (t, CH_2), 27.8 (d, CH), 50.8 (q, OCH_3), 78.3 (s, C-1), 85.1 (d, C-7), 124.1 (s, C-5), 164.1 (s, C-3).

***exo*-7-Isopropyl-5-methoxy-3-methyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ec)** (sbo-353)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.98 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 86 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (d, J = 6.8 Hz, 6H, $2CH_3$), 0.82 (t, J = 7.2 Hz, 3H, CH_3), 1.12 (m, 2H, CH_2), 1.23 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 1.78 (m, 1H, CH), 2.21 (s, 3H, CH_3), 3.44 (s, 3H, OCH_3), 3.66 (d, J = 12.2 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

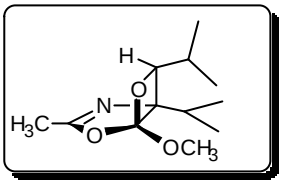
δ_{ppm} = 13.5 (q, CH_3), 13.9 (q, CH_3), 14.3 (q, CH_3), 16.7 (q, CH_3), 17.7 (d, CH), 26.3 (t, CH_2), 28.6 (t, CH_2), 50.8 (q, OCH_3), 90.7 (s, C-1), 94.1 (d, C-7), 124.1 (s, C-5), 164.8 (s, C-3).

HRMS: ($C_{12}H_{21}NO_3$, M = 227.15 g/mol)

Calcd: 227.1516

Found: 227.1509

***exo*-1,7-Diisopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ed)** (sbo-p38)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.92 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 81 %

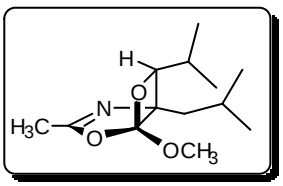
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.78 (d, J = 6.6 Hz, 6H, $2CH_3$), 0.82 (m, 1H, CH), 0.85 (d, J = 7.2 Hz, 3H, CH_3), 0.92 (t, J = 7.4 Hz, 3H, CH_3), 1.43 (m, 1H, CH), 1.85 (m, 2H, CH_2), 2.00 (s, 3H, CH_3), 3.62 (s, 3H, OCH_3), 4.18 (d, J = 8.4 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.7 (q, CH_3), 11.3 (q, CH_3), 11.9 (t, CH_2), 14.5 (q, CH_3), 19.3 (q, CH_3), 19.5 (q, CH_3), 22.3 (d, CH), 27.2 (d, CH), 52.0 (q, OCH_3), 82.3 (s, C-1), 88.1 (d, C-7), 124.3 (s, C-5), 165.7 (s, C-3).

***exo*-1-Isobutyl-7-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ee)** (sbo-340)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.1 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 91 %

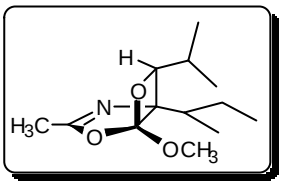
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.8 Hz, 6H, $2CH_3$), 0.85 (d, J = 7.2 Hz, 6H, $2CH_3$), 1.12 (m, 2H, 2CH), 1.78 (m, 2H, CH_2), 1.98 (s, 3H, CH_3), 3.46 (s, 3H, OCH_3), 3.79 (d, J = 12.1 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.9 (q, CH_3), 17.7 (q, CH_3), 18.6 (q, CH_3), 18.9 (q, CH_3), 29.7 (d, CH), 34.4 (d, CH), 40.6 (t, CH_2), 50.8 (q, OCH_3), 91.5 (s, C-1), 94.1 (d, C-7), 124.3 (s, C-5), 164.5 (s, C-3).

***exo*-1-*sec*-Butyl-7-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ef)** (sbo-346)



A solution of isobutyraldehyde (0.36 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.97 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 83 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.6 Hz, 3H, CH_3), 0.84 (d, J = 6.8 Hz, 3H, CH_3), 0.89 (d, J = 7.2 Hz, 3H, CH_3), 0.91 (t, J = 7.1 Hz, 3H, CH_3), 1.10 (m, 2H, CH_2), 1.43 (m, 1H, CH), 2.00 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 4.17 (d, J = 4.2 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.3 (q, CH_3), 11.8 (q, CH_3), 12.7 (q, CH_3), 19.3 (q, CH_3), 19.4 (q, CH_3), 23.3 (d, CH), 24.2 (t, CH_2), 27.3 (d, CH), 52.3 (q, OCH_3), 80.0 (s, C-1), 81.3 (d, C-7), 124.3 (s, C-5), 164.7 (s, C-3).

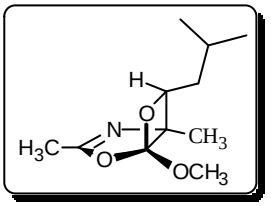
HRMS: ($C_{13}H_{23}NO_3$, M = 241.17 g/mol)

Calcd: 241.1672

Found: 241.1667

<u>Photolyses of 3-methylbutyraldehyde with 5-methoxyoxazoles 36a-f:</u>

***exo*-7-Isobutyl-5-methoxy-1,3-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42fa)** (sbo-312)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.89 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 84 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.6 Hz, 3H, CH_3), 0.86 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (m, 1H, CH), 1.23 (s, 3H, CH_3), 1.43 (m, 2H, CH_2), 2.02 (s, 3H, CH_3), 3.47 (s, 3H, OCH_3), 4.32 (dd, J = 4.0, 8.5 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

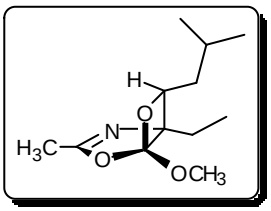
δ_{ppm} = 12.2 (q, CH_3), 14.9 (q, CH_3), 21.9 (q, CH_3), 23.2 (d, CH), 24.4 (q, CH_3), 40.8 (t, CH_2), 51.3 (q, OCH_3), 73.6 (s, C-1), 82.8 (d, C-7), 124.6 (s, C-5), 165.0 (s, C-3).

HRMS: ($C_{11}H_{19}NO_3$, M = 213.14 g/mol)

Calcd: 213.1360

Found: 213.1353

***exo*-1-Ethyl-7-isobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42fb)** (sbo-412)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.98 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 86 %

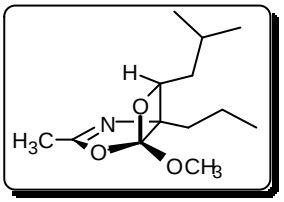
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.8 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.02 (t, J = 7.5 Hz, 3H, CH_3), 1.23 (m, 1H, CH), 1.43 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 2.03 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 4.12 (dd, J = 9.2, 2.1 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.0 (q, CH_3), 15.4 (q, CH_3), 19.2 (q, CH_3), 19.7 (q, CH_3), 23.1 (t, CH_2), 27.3 (d, CH), 34.1 (t, CH_2), 50.2 (q, OCH_3), 79.2 (s, C-1), 88.3 (d, C-7), 124.2 (s, C-5), 164.7 (s, C-3).

***exo*-7-Isobutyl-5-methoxy-3-methyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42fc)** (sbo-350)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.0 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 83 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (d, J = 7.1 Hz, 6H, $2CH_3$), 0.83 (t, J = 7.2 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 1.73 (m, 1H, CH), 1.98 (s, 3H, CH_3), 3.41 (s, 3H, OCH_3), 4.27 (dd, J = 10.2, 4.9 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

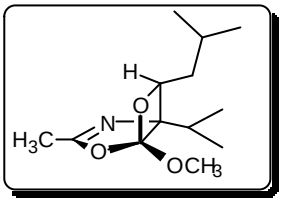
δ_{ppm} = 14.3 (q, CH_3), 14.9 (q, CH_3), 16.9 (t, CH_2), 21.7 (d, CH), 23.2 (q, CH_3), 24.2 (q, CH_3), 28.4 (t, CH_2), 40.4 (t, CH_2), 50.9 (q, OCH_3), 76.5 (s, C-1), 87.8 (d, C-7), 124.4 (s, C-5), 164.7 (s, C-3).

HRMS: ($C_{13}H_{23}NO_3$, M = 241.17 g/mol)

Calcd: 241.1764

Found: 241.1762

***exo*-7-Isobutyl-1-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42fd)** (sbo-325)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.1 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

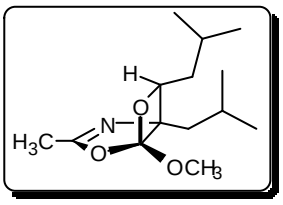
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (d, J = 6.6 Hz, 3H, CH_3), 0.81 (d, J = 6.5 Hz, 3H, CH_3), 0.88 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.35 (m, 2H, 2CH), 1.76 (m, 2H, CH_2), 1.98 (s, 3H, CH_3), 3.42 (s, 3H, OCH_3), 4.29 (dd, J = 11.2, 2.3 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.8 (q, CH_3), 16.6 (q, CH_3), 17.7 (q, CH_3), 21.3 (q, CH_3), 23.5 (q, CH_3), 23.9 (d, CH), 24.7 (d, CH), 40.1 (t, CH_2), 50.7 (q, OCH_3), 80.0 (s, C-1), 87.9 (d, C-7), 124.4 (s, C-5), 164.9 (s, C-3).

***exo*-1,7-Diisobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42fe)** (sbo-339)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.12 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 88 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.8 Hz, 3H, CH_3), 0.83 (d, J = 6.7 Hz, 3H, CH_3), 0.85 (d, J = 7.1 Hz, 3H, CH_3), 0.89 (d, J = 7.5 Hz, 3H, CH_3), 1.53 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 2.00 (s, 3H, CH_3), 3.46 (s, 3H, OCH_3), 4.27 (dd, J = 1.3, 7.7 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

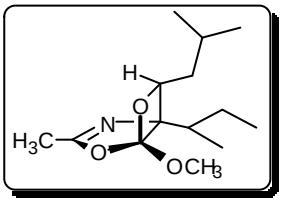
δ_{ppm} = 15.0 (q, CH_3), 21.6 (q, CH_3), 23.1 (q, CH_3), 23.4 (q, CH_3), 23.9 (q, CH_3), 24.2 (d, CH), 24.4 (d, CH), 34.3 (t, CH_2), 40.7 (t, CH_2), 51.0 (q, OCH_3), 76.3 (s, C-1), 88.3 (d, C-7), 124.6 (s, C-5), 164.2 (s, C-3).

HRMS: ($C_{14}H_{25}NO_3$, M = 255.18 g/mol)

Calcd: 255.1828

Found: 255.1822

***exo*-1-*sec*-Butyl-7-isobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-42ff)** (sbo-345)



A solution of 3-methylbutyraldehyde (0.43 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.89 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 88 %

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2984, 1605, 1445, 1009, 980.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (t, J = 7.4 Hz, 3H, CH_3), 0.83 (d, J = 6.8 Hz, 3H, CH_3), 0.89 (d, J = 7.2 Hz, 3H, CH_3), 0.91 (d, J = 7.1 Hz, 3H, CH_3), 1.10 (m, 2H, CH_2), 1.43 (m, 1H, CH), 1.65 (m, 2H, CH_2), 2.0 (s, 3H, CH_3), 2.35 (m, 1H, CH), 3.47 (s, 3H, OCH_3), 4.25 (dd, 1H, J = 5.3, 6.0 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.0 (q, CH_3),11.5 (q, CH_3), 11.9 (q, CH_3), 12.9 (q, CH_3), 13.9 (q, CH_3), 14.9 (q, CH_3), 23.5 (d, CH), 24.7 (d, CH), 24.8 (t, CH_2), 32.1 (t, CH_2), 50.8 (q, OCH_3), 80.5 (s, C-1), 80.9 (d, C-7), 124.6 (s, C-5), 165.2 (s, C-3).

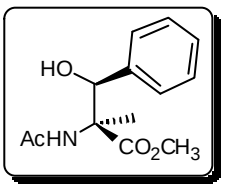
MS: (EI, 70 eV)

m/z (%) = 214 (M^+-CH_3CN, 5), 198 (M^+-Bu^i, 23), 169 (55), 168 (32), 155 (52), 144 (75), 126 (100), 112 (43), 99 (20), 95 (15), 86 (55), 68 (18), 57 (40).

4.15.1 Synthesis of *erythro* (2S*,3S*)-a -acetamido-a -alkylated-b -hydroxy esters 43aa-ff; General procedure:

To a solution of the bicyclic oxetane **42aa-ff** (0.002 mol) in 20 mL of methylene chloride, 0.5 ml of conc. HCl was added. The mixture is stirred in an open flask at room temperature for 2 h and the reaction was controled by TLC. The reaction mixture was quenched with water and extracted with methylene chloride (3 x 20 mL). The organic layer was washed with 5 % $NaHCO_3$, brine, and dried over anhydrous $MgSO_4$. The solvent was removed in *vacuo* and the residual oil was purified by preparative chromatography.

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-3-hydroxy-2-methyl-3-phenylpropanoate (*erythro*-43aa)** (sbo-305b)



Following the above general procedure, the bicyclic oxetane **42aa** (0.47 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.33 g of the product as a colorless oil.

Yield: 65 %

TLC: R_f = 0.33 (ethylacetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3350, 3320, 2988, 1720, 1680, 1580, 1440, 1340, 1062, 987.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.23 (s, 3H, CH_3), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.79 (s, 3H, OCH_3), 4.06 (s, 1H, $\underline{CH}OH$), 7.32 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.5 (q, CH_3), 21.4 (q, CH_3), 23.4 (q, CH_3), 47.7 (s, C-2), 49.1 (d, C-3), 52.9 (q, OCH_3), 127.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 133.5 (s, Cq_{arom}), 169.9 (s, CON), 179.4 (s, COO).

MS: (EI, 70 eV)

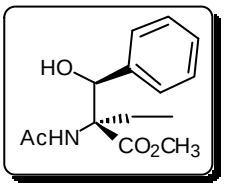
m/z (%) = 249 (M^+-H_2, 4), 236 (M^+-Me, 8), 202 (8), 192 (M^+-CO_2Me, 15), 191 (78), 160 (10), 132 (12), 131 (100), 105 (50), 91 (20), 77 (30), 51 (10).

HRMS: ($C_{13}H_{17}NO_4$, M = 251.12 g/mol)

Calcd: 251.1254

Found: 251.1249

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-2-ethyl-3-hydroxy-3-phenylpropanoate (*erythro*-43ab)** (sbo-400a)



Following the above general procedure, the bicyclic oxetane **42ab** (0.49 g, 2 mmol) was hydrolytically cleaved in 5h. Preparative chromatography yielded 0.39 g of the product as a colorless oil.

Yield: 73 %

TLC: R_f = 0.36 (ethylacetate/n-hexane 1: 4)

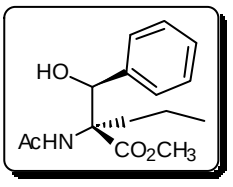
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.08 (t, J = 7.5 Hz, 3H, CH_3), 1.35 (q, J = 7.5 Hz, 2H, CH_2), 1.99 (s, 3H, $\underline{CH_3}CO$), 3.89 (s, 3H, OCH_3), 4.35 (s, 1H, $\underline{CH}OH$), 7.26-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.8 (q, CH_3), 24.1 (q, CH_3), 25.4 (t, CH_2), 53.0 (q, OCH_3), 63.2 (s, C-2), 70.2 (d, C-3), 126.1 (d, CH_{arom}), 128.1 (d, CH_{arom}), 129.3 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 170.3 (s, CON), 171.5 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)pentanoate (*erythro*-43ac)** (sbo-348a)



Following the above general procedure, the bicyclic oxetane **42ac** (0.52 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 58 %

TLC: R_f = 0.21 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.4 Hz, 3H, CH_3), 1.27 (m, 2H, CH_2), 1.51-1.81(m, 2H, CH_2), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.78 (s, 3H, OCH_3), 4.02 (s, 1H, $\underline{CH}OH$), 6.21 (bs, 1H, NH), 7.22-7.26 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.6 (q, CH_3), 18.5 (q, CH_3), 23.1 (t, CH_2), 34.6 (t, CH_2), 52.2 (q, OCH_3), 70.1 (s, C-2), 78.0 (d, C-3), 125.7 (d, CH_{arom}), 126.9 (d, CH_{arom}), 128.1 (d, CH_{arom}), 136.4 (s, Cq_{arom}), 169.8 (s, CON), 173.3 (s, COO).

MS: (EI, 70 eV)

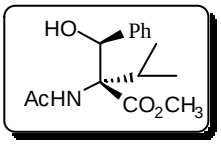
m/z (%) = 278 (M^+-1, 5), 262 (M^+-OH, 7), 202 (8), 220 (M^+-CO_2Me, 10), 219 (55), 155 (78), 127 (100), 105 (43), 91 (15), 77 (30), 59 (13).

Anal: ($C_{15}H_{21}NO_4$, M = 279.33 g/mol)

Calcd: C 64.50 H 7.58 N 5.01

Found: C 64.72 H 7.42 N 5.16

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)-3-methylbutanoate (*erythro*-43ad)** (sbo-336c)



Following the above general procedure, the bicyclic oxetane **42ad** (0.52 g, 2 mmol) was hydrolytically cleaved in 4h. Preparative chromatography yielded 0.27 g of the *erythro*-isomer and 0.12 g of the *threo*-isomer, both as a colorless oil.

Yield: 48 %

TLC: R_f = 0.47 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.76 (d, J = 6.9 Hz, 3H, CH_3), 1.23 (d, J = 6.8 Hz, 3H, CH_3), 1.43 (sextet, J = 6.8 Hz, 1H, CH), 2.13 (s, 3H, $\underline{CH_3}CO$), 3.78 (s, 3H, OCH_3), 4.14 (s, 1H, $\underline{CH}OH$), 7.32-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

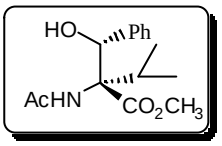
δ_{ppm} = 17.5 (q, CH_3), 18.2 (q, CH_3), 23.7 (q, CH_3), 30.3 (d, CH), 52.8 (q, OCH_3), 75.1 (s, C-2), 75.6 (d, C-3), 125.8 (d, CH_{arom}), 127.8 (d, CH_{arom}), 128.8 (d, CH_{arom}), 141.2 (s, Cq_{arom}), 170.2 (s, CON), 171.4 (s, COO).

Anal: ($C_{15}H_{21}NO_4$, M = 279.33 g/mol)

Calcd: C 64.50 H 7.58 N 5.01

Found: C 64.65 H 7.38 N 4.98

***threo*-Methyl (2S*,3R*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)-3-methyl butanoate (*threo*-43ad)** (sbo-326a)



Yield: 25 %

TLC: R_f = 0.31 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.95 (d, J = 6.8 Hz, 3H, CH_3), 0.99 (d, J = 6.6 Hz, 3H, CH_3), 2.19 (s, 3H, $\underline{CH_3}CO$), 2.33 (sextet, J = 6.8 Hz, 1H, CH), 3.09 (s, 3H, OCH_3), 3.83 (s, 1H, $\underline{CH}OH$), 7.14-7.26 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

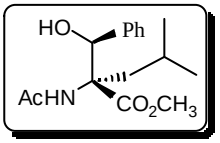
δ_{ppm} = 13.8 (q, CH_3), 15.7 (q, CH_3), 18.2 (q, CH_3), 35.9 (d, CH), 51.3 (q, OCH_3), 86.2 (s, C-2), 87.2 (d, C-3), 125.8 (d, CH_{arom}), 127.8 (d, CH_{arom}), 128.8 (d, CH_{arom}), 137.4 (s, Cq_{arom}), 165.9 (s, CON), 171.3 (s, COO).

HRMS: ($C_{15}H_{21}NO_4$, M = 279.15 g/mol)

Calcd: 279.1465

Found: 279.1460

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)-4-methylpentanoate (*erythro*-43ae)** (sbo-338a)



Following the above general procedure, the bicyclic oxetane **42ae** (0.55 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.34 g of the *erythro*-isomer and 0.13 g of the *threo*-isomer, both as a colorless oil.

Yield: 58 %

TLC: R_f = 0.39 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.6 Hz, 3H, CH_3), 0.83 (d, J = 6.6 Hz, 3H, CH_3), 0.90 (m, 1H, CH), 1.89 (dd, J = 13.4, 6.7 Hz, 1H, CH), 1.92 (s, 3H, $\underline{CH_3}CO$), 2.72 (dd, J = 13.4 Hz, 4.5 Hz, 1H, CH), 3.80 (s, 3H, OCH_3), 3.82 (s, 1H, $\underline{CH}OH$), 7.25-7.38 (m, 5H, H_{arom}).

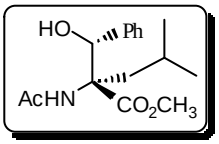
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.7 (q, CH_3), 21.9 (q, CH_3), 23.9 (q, CH_3), 24.6 (q, CH_3), 40.8 (t, CH_2), 52.8 (q, OCH_3), 68.3 (s, C-2), 71.0 (d, C-3), 126.1 (d, CH_{arom}), 129.8 (d, CH_{arom}), 137.2 (s, Cq_{arom}), 169.6 (s, CON), 172.9 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 278 (M^+-1, 5), 261 (M^+-H_2O, 8), 218 (10), 202 (12), 156 (15), 155 (100), 140 (38), 127 (80), 112 (45), 105 (65), 84 (27), 77 (30), 55 (8).

***threo*-Methyl (2S*,3R*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)-4-methyl pentanoate (*threo*-43ae)** (sbo-338b)



Yield: 24 %

TLC: R_f = 0.33 (ethylacetate/n-hexane 1: 3)

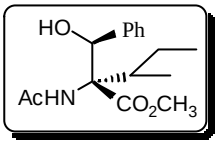
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.8 Hz, 3H, CH_3), 1.00 (d, J = 6.6 Hz, 3H, CH_3), 1.33 (m, 1H, CH), 1.70 (dd, J = 13.5, 5.6 Hz, 1H, CH), 2.17 (s, 3H, $\underline{CH_3}CO$), 2.80 (dd, J = 13.5, 5.6 Hz, 1H, CH), 3.09 (s, 3H, OCH_3), 3.77 (s, 1H, $\underline{CH}OH$), 7.23-7.36 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 22.9 (q, CH_3), 24.3 (q, CH_3), 24.5 (q, CH_3), 24.9 (t, CH_2), 52.9 (q, OCH_3), 83.3 (s, C-2), 90.0 (d, C-3), 125.8 (d, CH_{arom}), 126.1 (d, CH_{arom}), 128.6 (d, CH_{arom}), 140.6 (s, Cq_{arom}), 165.7 (s, CON), 171.5 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)-3-methylpentanoate (*erythro*-43af)** (sbo-344c)



Following the above general procedure, the bicyclic oxetane **42af** (0.55 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.23 g of the *erythro*-isomer and 0.11 g of the *threo*-isomer, both as a colorless oil.

Yield: 40 %

TLC: R_f = 0.36 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.77 (d, J = 6.9 Hz, 3H, CH_3), 0.87 (d, J = 7.4 Hz, 3H, CH_3), 1.32 (m, 2H, CH_2), 1.94 (s, 3H, $\underline{CH_3}CO$), 2.67 (m, 1H, CH), 3.82 (s, 3H, OCH_3), 4.13 (s, 1H, $\underline{CH}OH$), 6.65 (bs, 1H, NH), 7.05-7.16 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

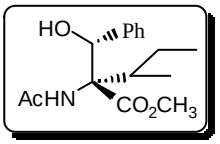
δ_{ppm} = 12.8 (q, CH_3), 14.1 (q, CH_3), 23.6 (q, CH_3), 24.9 (t, CH_2), 36.9 (d, CH), 52.7 (q, OCH_3), 74.7 (s, C-2), 75.8 (d, C-3), 125.7 (d, CH_{arom}), 127.9 (d, CH_{arom}), 128.6 (d, CH_{arom}), 141.2 (s, Cq_{arom}), 171.5 (s, CON), 171.9 (s, COO).

Anal: ($C_{16}H_{23}NO_4$, M = 293.3 g/mol)

Calcd: C 65.51 H 7.90 N 4.77

Found: C 65.66 H 7.53 N 4.74

***threo*-Methyl (2S*,3R*) 2-(N-acetylamino)-2-(hydroxy-phenyl-methyl)-3-methylpentanoate (*threo*-43af)** (sbo-344b)



Yield: 19 %

TLC: R_f = 0.27 (ethylacetate/n-hexane 1: 4)

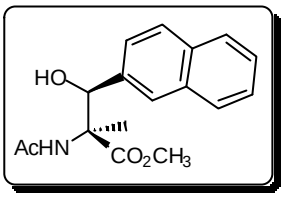
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.89 (d, J = 7.5 Hz, 3H, CH_3), 0.94 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (m, 1H, CH), 1.47 (m, 2H, CH_2), 2.20 (s, 3H, $\underline{CH_3}CO$), 3.08 (s, 3H, OCH_3), 3.84 (s, 1H, $\underline{CH}OH$), 7.21-7.53 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.9 (q, CH_3), 12.1 (q, CH_3), 13.8 (q, CH_3), 22.3 (d, CH), 42.9 (t, CH_2), 51.3 (q, OCH_3), 78.1 (s, C-2), 86.8 (d, C-3), 126.4 (d, CH_{arom}), 128.5 (d, CH_{arom}), 128.6 (d, CH_{arom}), 133.3 (s, Cq_{arom}), 169.9 (s, CON), 185.7 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-(N-acetylamino)-3-hydroxy-2-methyl-3-naphthen-2-ylpropanoate (*erythro*-43ba)** (sbo-304c)



Following the above general procedure, the bicyclic oxetane **42ba** (0.57 g, 2 mmol) was hydrolytically cleaved in 7h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 48 %

TLC: R_f = 0.47 (ethylacetate/n-hexane 1: 2)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25 (s, 3H, CH_3), 2.17 (s, 3H, $\underline{CH}_3CO$), 3.82 (s, 3H, OCH_3), 4.22 (s, 1H, $\underline{CH}OH$), 7.46-7.92 (m, 7H, H_{arom}).

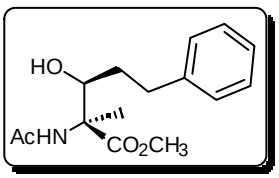
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.5 (q, CH_3), 23.5 (q, CH_3), 47.9 (s, C-2), 49.3 (d, C-3), 53.0 (q, OCH_3), 126.3 (d, CH_{arom}), 127.8 (d, CH_{arom}), 128.3 (d, CH_{arom}), 129.3 (d, CH_{arom}), 133.2 (s, C_{arom}), 136.9 (s, Cq_{arom}), 166.9 (s, CON), 180.0 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 299 (M^+-H_2, 5), 242 (4), 241 (50), 207 (28), 206 (30), 182 (19), 181 (100), 140 (30), 139 (48), 102 (10), 89 (5), 63 (4).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-methyl-5-phenylpentanoate (*erythro*-43ca)** (sbo-313a)



Following the above general procedure, the bicyclic oxetane **42ca** (0.52 g, 2 mmol) was hydrolytically cleaved in 4h. Preparative chromatography yielded 0.31 g of the product as a colorless oil.

Yield: 55 %

TLC: R_f = 0.41 (ethylacetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3420, 3270, 2986, 1735, 1690, 1600, 1550, 1340, 1062, 957.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.35 (s, 3H, CH_3), 1.94 (dd, J = 6.3, 14.0 Hz, 2H, CH_2), 2.03 (s, 3H, $\underline{CH}_3CO$), 2.68-2.92 (dd, J = 7.4, 14.0 Hz, 2H, CH_2), 3.76 (s, 3H, OCH_3), 4.66 (dd, J = 7.4, 6.3 Hz, 1H, $\underline{CH}OH$), 5.30 (s, 1H, NH), 7.21-7.31 (m, 5H, H_{arom}).

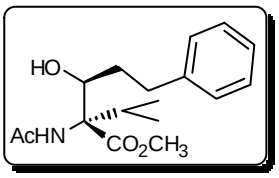
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 19.6 (q, CH_3), 31.9 (t, CH_2), 32.9 (t, CH_2), 52.6 (q, OCH_3), 75.0 (s, C-2), 83.9 (d, C-3), 126.1 (d, C_{arom}), 128.3 (d, C_{arom}), 129.3 (d, C_{arom}), 141.0 (s, Cq_{arom}), 165.2 (s, CON), 174.3 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 279 (M^+, 5), 261 (M^+-H_2O, 6), 220 (M^+-CO_2Me, 5), 178 (8), 145 (45), 119 (8), 113 (40), 102 (100), 92 (10), 91 (78), 77 (15), 51 (7).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-isopropyl-5-phenylpentanoate (*erythro*-43cd)** (sbo-328b)



Following the above general procedure, the bicyclic oxetane **42cd** (0.58 g, 2 mmol) was hydrolytically cleaved in 5h. Preparative chromatography yielded 0.34 g of the product as a colorless oil.

Yield: 55 %

TLC: R_f = 0.48 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (m, 1H, CH), 2.02 (s, 3H, $\underline{CH}_3CO$), 2.13 (dd, J = 7.4, 14.0 Hz, 2H, CH_2), 2.63-2.92 (dd, J = 6.4, 14.0 Hz, 2H, CH_2), 3.68 (s, 3H, OCH_3), 4.32 (dd, J = 10.4, 3.3 Hz, 1H, $\underline{CH}OH$), 7.21-7.33 (m, 5H, H_{arom}).

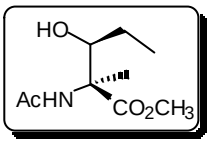
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 17.5 (q, CH_3), 18.8 (q, CH_3), 30.7 (d, CH), 31.3 (t, CH_2), 33.5 (t, CH_2), 52.1 (q, OCH_3), 67.5 (s, C-2), 75.1 (d, C-3), 126.1 (d, CH_{arom}), 128.3 (d, CH_{arom}), 129.3 (d, CH_{arom}), 141.0 (s, Cq_{arom}), 169.5 (s, CON), 171.3 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 307 (M^+, 5), 290 (M^+-OH, 4), 289 (M^+-H_2O, 10), 246 (M^+-CO_2Me, 8), 231 (15), 230 (100), 214 (20), 188 (13), 141 (10), 133 (28), 130 (40), 105 (60), 91 (78), 79 (7), 70 (10), 55 (8).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-methylpentanoate (*erythro*-43da)** (sbo-300a)



Following the above general procedure, the bicyclic oxetane **42da** (0.37 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 70 %

TLC: R_f = 0.15 (ethylacetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3330, 3260, 2983, 1720, 1685, 1448, 1345, 1042, 987.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.03 (t, J = 7.2 Hz, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.76 (dq, J = 2.1, 7.2 Hz, 2H, CH_2), 1.96 (s, 3H, $\underline{CH_3}CO$), 3.71 (s, 3H, OCH_3), 4.15 (dd, J = 11.1, 2.1 Hz, 1H, $\underline{CH}OH$), 6.22 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

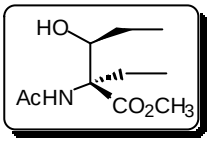
δ_{ppm} = 11.8 (q, CH_3), 17.2 (q, CH_3), 23.3 (q, CH_3), 26.2 (t, CH_2), 52.9 (q, OCH_3), 63.5 (s, C-2), 69.9 (d, C-3), 169.4 (s, CON), 171.7 (s, COO).

HRMS: ($C_9H_{17}NO_4$, M = 203.12 g/mol)

Calcd: 203.1248

Found: 203.1247

***erythro*-Methyl (2S*,3S*) 2-acetylamino-2-ethyl-3-hydroxypentanoate (*erythro*-43db)** (sbo-410b)



Following the above general procedure, the bicyclic oxetane **42db** (0.4 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 65 %

TLC: R_f = 0.19 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (t, J = 7.4 Hz, 3H, CH_3), 1.03 (t, J = 7.4 Hz, 3H, CH_3), 1.50 (m, 2H, CH_2), 2.07 (s, 3H, $\underline{CH_3}CO$), 2.13 (sextet, J = 7.4 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 4.23 (dd, J = 11.6, 2.1 Hz, 1H, $\underline{CH}OH$), 6.40 (bs, 1H, NH).

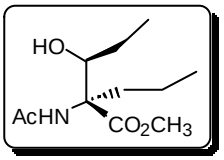
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.0 (q, CH_3), 12.0 (q, CH_3), 24.5 (t, CH_2), 26.7 (t, CH_2), 53.2 (q, OCH_3), 69.9 (s, C-2), 70.2 (d, C-3), 169.5 (s, CON), 172.2 (s, COO).

Anal: ($C_{10}H_{19}NO_4$, M = 217.3 g/mol)

Calcd:	C 55.28	H 8.81	N 6.46
Found:	C 55.85	H 8.22	N 6.41

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-propylpentanoate (*erythro*-43dc)** (sbo-349b)



Following the above general procedure, the bicyclic oxetane **42dc** (0.43 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.35 g of the *erythro*-isomer and 0.08 g of the *threo*-isomer, both as a colorless oil.

Yield: 75 %

TLC: R_f = 0.19 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (t, J = 6.9 Hz, 3H, CH_3), 1.00 (t, J = 7.2 Hz, 3H, CH_3), 1.53 (m, 2H, CH_2), 1.64 (dd, J = 7.2, 2.1 Hz, 1H, CH), 1.76 (ddd, J = 7.2, 4.6, 3.2 Hz, 1H, CH), 2.00 (s, 3H, $\underline{CH_3}CO$), 2.15 (m, 1H, CH), 2.85 (m, 1H, CH), 3.77 (s, 3H, OCH_3), 4.21 (dd, J = 11.6, 2.1 Hz, 1H, $\underline{CH}OH$), 6.41 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

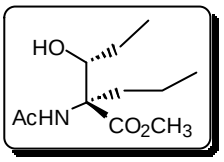
δ_{ppm} = 12.0 (q, CH_3), 13.9 (q, CH_3), 18.1 (q, CH_3), 24.5 (t, CH_2), 26.6 (t, CH_2), 33.4 (t, CH_2), 53.2 (q, OCH_3), 69.2 (s, C-2), 70.3 (d, C-3), 169.5 (s, CON), 172.3 (s, COO).

HRMS: ($C_{11}H_{21}NO_4$, M = 231.15 g/mol)

Calcd: 231.1465

Found: 231.1461

***threo*-Methyl (2S*,3R*) 2-acetylamino-3-hydroxy-2-propylpentanoate (*threo*-43dc)** (sbo-349a)



Yield: 12 %

TLC: R_f = 0.15 (ethylacetate/n-hexane 1: 4)

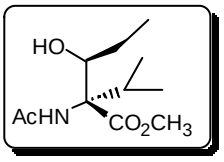
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (t, J = 7.2 Hz, 3H, CH_3), 1.02 (t, J = 7.4 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.48 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 1.95 (s, 3H, $\underline{CH_3}CO$), 3.69 (s, 3H, OCH_3), 4.33 (dd, J = 10.1, 3.5 Hz, 1H, $\underline{CH}OH$), 6.41 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.3 (q, CH_3), 14.2 (q, CH_3), 14.3 (q, CH_3), 17.9 (t, CH_2), 22.9 (t, CH_2), 36.0 (t, CH_2), 52.3 (q, OCH_3), 78.4 (s, C-2), 86.9 (d, C-3), 165.1 (s, CON), 174.5 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-isopropylpentanoate (*erythro*-43dd)** (sbo-324b)



Following the above general procedure, the bicyclic oxetane **42dd** (0.43 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.31 g of the product as a colorless oil.

Yield: 67 %

TLC: R_f = 0.47 (ethylacetate/n-hexane 1: 4)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3339, 3220, 2998, 1740, 1665, 1450, 1355, 1042, 980.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.9 Hz, 3H, CH_3), 1.00 (d, J = 7.1 Hz, 3H, CH_3), 1.05 (t, J = 7.2 Hz, 3H, CH_3), 1.56 (ddq, J = 7.2, 7.1, 4.4 Hz, 1H, CH), 2.01 (s, 3H, $\underline{CH_3}CO$), 2.14 (dd, J = 7.2, 1.6 Hz, 1H, CH), 2.71 (sextet, J = 6.9 Hz, 1H, CH), 3.79 (s, 3H, OCH_3), 4.51 (dd, J = 11.7, 1.7 Hz, 1H, $\underline{CH}OH$), 6.45 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.1 (q, CH_3), 17.2 (q, CH_3), 18.6 (q, CH_3), 25.1 (q, CH_3), 26.8 (t, CH_2), 52.9 (q, OCH_3), 69.9 (s, C-2), 73.5 (d, C-3), 169.7 (s, CON), 171.8 (s, COO).

MS: (EI, 70 eV)

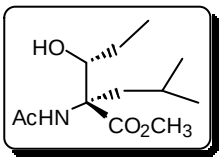
m/z (%) = 215 (M^+-H_2O, 27), 214 (M^+-OH, 21), 172 (29), 164 (42), 154 (50), 130 (100), 112 (48), 98 (25), 95 (30), 70 (87), 60 (67), 57 (50).

HRMS: ($C_{11}H_{21}NO_4$, M = 231.15 g/mol)

Calcd: 231.1465

Found: 231.1463

***threo*-Methyl (2S*,3R*) 2-acetylamino-3-hydroxy-2-isobutylpentanoate (*threo*-43de)** (sbo-337a)



Following the above general procedure, the bicyclic oxetane **42de** (0.45 g, 2 mmol) was hydrolytically cleaved in 5h. Preparative chromatography yielded 0.34 g of the product as a colorless oil.

Yield: 70 %

TLC: R_f = 0.40 (ethylacetate/n-hexane 1: 3)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3335, 3210, 2978, 1745, 1675, 1453, 1355, 1042, 980.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (d, J = 6.6 Hz, 3H, CH_3), 0.88 (d, J = 6.6 Hz, 3H , CH_3), 1.02 (t, J = 7.4 Hz, 3H, CH_3), 1.41 (dd, J = 13.4, 5.0 Hz, 1H, CH), 1.62 (m, 2H, CH_2), 1.87 (m, 1H, CH), 1.96 (s, 3H, $\underline{CH_3}CO$), 2.03 (dd, J = 13.9, 3.5Hz, 1H, CH), 3.64 (s, 3H, OCH_3), 4.20 (dd, J = 10.1, 3.5 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

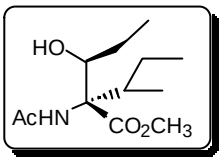
δ_{ppm} = 11.4 (q, CH_3), 14.3 (q, CH_3), 22.7 (q, CH_3), 23.7 (q, CH_3), 24.4 (d, CH), 24.6 (t, CH_2), 42.0 (t, CH_2), 52.3 (q, OCH_3), 77.9 (s, C-2), 87.8 (d, C-3), 164.9 (s, CON), 174.9 (s, COO).

Anal: ($C_{12}H_{23}NO_4$, M = 245.16 g/mol)

Calcd: C 58.75 H 9.45 N 5.71

Found: C 58.52 H 9.27 N 5.49

***erythro*-Methyl (2S*,3S*) 2-acetylamino-2-(1-hydroxy-propyl)-3-methylpentanoate (*erythro*-43df)** (sbo-341d)



Following the above general procedure, the bicyclic oxetane **42df** (0.45 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.37 g of the product as a colorless oil. A crystalline sample for X-ray crystal structure analysis could be obtained by crystallization of the product from chloroform.

Yield: 75 %

M.p: 43-45 °C

TLC: R_f = 0.55 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.76 (d, J = 6.9, Hz, 3H, CH_3), 0.85 (t, J = 7.2, Hz, 3H, CH_3), 0.96 (t, J = 7.1 Hz, 3H, CH_3), 1.21 (m, 1H, CH), 2.08 (s, 3H, $\underline{CH_3}CO$), 2.42 (m,1H, CH), 3.77 (s, 3H, OCH_3), 4.62 (dd, J = 11.7, 1.7 Hz, 1H, $\underline{CH}OH$), 6.90 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

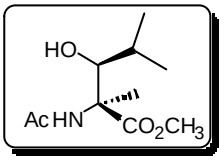
δ_{ppm} = 10.8 (q, CH_3), 12.3 (q, CH_3), 13.3 (q, CH_3), 13.9 (q, CH_3), 23.7 (d, CH), 27.3 (t, CH_2), 37.4 (t, CH_2), 52.9 (q, OCH_3), 73.7 (s, C-2), 74.2 (d, C-3), 170.8 (s, CON), 172.8 (s, COO).

Anal: ($C_{12}H_{23}NO_4$, M = 245.32 g/mol)

Calcd: C 58.75 H 9.45 N 5.71

Found: C 59.03 H 9.38 N 5.62

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2,4-dimethylpentanoate (*erythro*-43ea)** (sbo-320a)



Following the above general procedure, the bicyclic oxetane **42ea** (0.4 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.3 g of the product as a colorless oil.

Yield: 70 %

TLC: R_f = 0.51 (ethylacetate/n-hexane 1: 3)

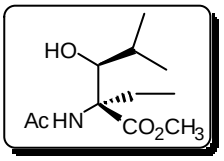
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.6 Hz, 3H, CH_3), 0.90 (d, J = 6.8 Hz, 3H, CH_3), 1.25 (m, 1H, CH), 1.43 (s, 3H, CH_3), 2.10 (s, 3H, $\underline{CH_3}CO$), 3.78 (s, 3H, OCH_3), 4.43 (d, J = 9.2 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.7 (q, CH_3), 18.9 (q, CH_3), 19.3 (q, CH_3), 23.9 (q, CH_3), 27.3 (d, CH), 52.3 (q, OCH_3), 68.1 (s, C-2), 78.1 (d, C-3), 169.1 (s, CON), 170.3 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-2-ethyl-3-hydroxy-4-methylpentanoate (*erythro*-43eb)** (sbo-415a)



Following the above general procedure, the bicyclic oxetane **42eb** (0.43 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.33 g of the product as a colorless oil.

Yield: 71 %

TLC: R_f = 0.45 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.90 (t, J = 7.4 Hz, 3H, CH_3), 0.95 (d, J = 6.9 Hz, 6H, $2CH_3$), 1.31 (m, 1H, CH), 1.59 (m, 2H, CH_2), 1.99 (s, 3H, $\underline{CH_3}CO$), 3.74 (s, 3H, OCH_3), 4.16 (d, J = 8.4 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

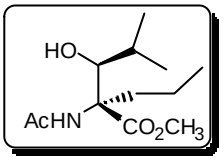
δ_{ppm} = 8.9 (q, CH_3), 14.1 (q, CH_3), 19.8 (q, CH_3), 19.9 (q, CH_3), 25.6 (t, CH_2), 27.9 (d, CH), 52.4 (q, OCH_3), 78.6 (s, C-2), 90.8 (d, C-3), 165.2 (s, CON), 174.5 (s, COO).

Anal: ($C_{11}H_{21}NO_4$, M = 231.29 g/mol)

Calcd: C 57.12 H 9.12 N 6.06

Found: C 56.92 H 8.96 N 5.87

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-4-methyl-2-propylpentanoate (*erythro*-43ec)** (sbo-353a)



Following the above general procedure, the bicyclic oxetane **42ec** (0.45 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.36 g of the product as a colorless oil.

Yield: 73 %

TLC: R_f = 0.47 (ethylacetate/n-hexane 1: 3)

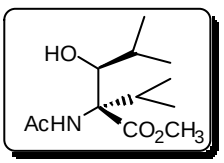
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.6 Hz, 3H, CH_3), 0.87 (d, J = 6.8 Hz, 3H, CH_3), 1.00 (t, J = 7.5 Hz, 3H, CH_3), 1.21 (m, 1H, CH), 1.24 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 2.05 (s, 3H, $\underline{CH_3}CO$), 3.74 (s, 3H, OCH_3), 4.34 (d, J = 8.9 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.7 (q, CH_3), 23.7 (q, CH_3), 24.5 (q, CH_3), 24.7 (q, CH_3), 27.1 (t, CH_2), 28.1 (d, CH), 39.2 (t, CH_2), 52.0 (q, OCH_3), 68.2 (s, C-2), 74.1 (d, C-3), 169.1 (s, CON), 172.1 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-isopropyl-4-methylpentanoate (*erythro*-43ed)** (sbo-p39a)



Following the above general procedure, the bicyclic oxetane **42ed** (0.45 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 59 %

TLC: R_f = 0.42 (ethylacetate/n-hexane 1: 3)

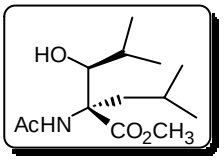
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.8 Hz, 6H, $2CH_3$), 0.89 (d, J = 6.5 Hz, 3H, CH_3), 0.93 (d, J = 6.6 Hz, 3H, CH_3), 1.03 (m, 2H, 2CH), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.79 (s, 3H, OCH_3), 4.44 (d, J = 8.4 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.0 (q, CH_3), 18.7 (q, CH_3), 19.2 (q, CH_3), 19.7 (q, CH_3), 20.3 (q, CH_3), 23.8 (d, CH), 27.2 (d, CH), 52.7 (q, OCH_3), 66.3 (s, C-2), 73.5 (d, C-3), 170.1 (s, CON), 171.8 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-isobutyl-4-methylpentanoate (*erythro*-43ee)** (sbo-340a)



Following the above general procedure, the bicyclic oxetane **42ee** (0.48 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.34 g of the product as a colorless oil.

Yield: 65 %

TLC: R_f = 0.42 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.65 (dd, J = 6.6, 6.6 Hz, 6H, $2CH_3$), 0.75 (dd, J = 7.5, 7.5 Hz, 6H , $2CH_3$), 1.30 (m, 1H, CH), 1.65 (dd, J = 1.6, 3.4 Hz, 1H, CH), 1.94 (s, 3H, $\underline{CH_3}CO$), 2.42 (dd, J = 7.5, 1.5 Hz, 1H, CH), 3.50 (m, 1H, CH), 3.72 (s, 3H, OCH_3), 3.92 (dd, J = 4.5, 1.6 Hz, 1H, $\underline{CH}OH$), 6.97 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

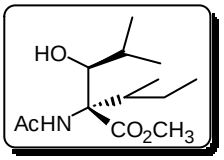
δ_{ppm} = 19.8 (q, CH_3), 23.5 (q, CH_3), 23.6 (q, CH_3), 23.7 (q, CH_3), 24.4 (d, CH), 24.6 (d, CH), 41.1 (t, CH_2), 52.8 (q, OCH_3), 69.0 (s, C-2), 78.0 (d, C-3), 171.3 (s, CON), 174.5 (s, COO).

HRMS: ($C_{13}H_{25}NO_4$, M = 259.18 g/mol)

Calcd: 259.1777

Found: 259.1773

***erythro*-Methyl (2S*,3S*) 2-acetylamino-2-*sec*-butyl-3-hydroxy-4-methylpentanoate (*erythro*-43ef)** (sbo-346b)



Following the above general procedure, the bicyclic oxetane **42ef** (0.48 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.35 g of the product as a colorless oil.

Yield: 68 %

TLC: R_f = 0.42 (ethylacetate/n-hexane 1: 3)

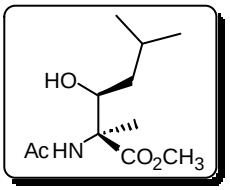
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.9 Hz, 3H, CH_3), 0.84 (d, J = 6.8 Hz, 3H, CH_3), 0.88 (d, J = 6.5 Hz, 3H, CH_3), 0.99 (t, J = 7.5 Hz, 3H, CH_3), 1.43 (m, 1H, CH), 1.55 (m, 2H, 2CH), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.19 (dd, J = 8.4 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.9 (q, CH_3), 12.5 (q, CH_3), 13.7 (q, CH_3), 14.5 (q, CH_3), 24.3 (q, CH_3), 25.2 (t, CH_2), 27.1 (d, CH), 29.3 (d, CH), 52.9 (q, OCH_3), 74.3 (s, C-2), 79.3 (d, C-3), 169.5 (s, CON), 172.0 (s, COO).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2,5-dimethylhexanoate (*erythro*-43fa)** (sbo-312a)



Following the above general procedure, the bicyclic oxetane **42fa** (0.43 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.25 g of the product as a colorless oil.

Yield: 55 %

TLC: R_f = 0.43 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.5 Hz, 3H, CH_3), 0.91 (d, J = 6.5 Hz, 3H, CH_3), 0.94 (m, 1H, CH), 1.24 (dd, J = 1.9, 1.8 Hz, 1H, CH), 1.54 (s, 3H, CH_3), 1.87 (m, 1H, CH), 1.96 (s, 3H, $\underline{CH_3}CO$), 3.71 (s, 3H, OCH_3), 4.25 (dd, J = 11.4, 1.8 Hz, 1H, $\underline{CH}OH$), 6.20 (bs, 1H, NH).

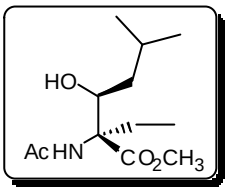
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.1 (q, CH_3), 20.4 (q, CH_3), 23.3 (q, CH_3), 23.5 (q, CH_3), 25.1 (d, CH), 41.6 (t, CH_2), 52.8 (q, OCH_3), 63.4 (s, C-2), 65.9 (d, C-3), 169.2 (s, CON), 171.5 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 299 (M^+-H_2, 5), 214 (M^+-OH, 4), 190 (15), 172 (8), 154 (18), 148 (52), 112 (22), 102 (100), 85 (20), 70 (18), 57 (18).

***erythro*-Methyl (2S*,3S*) 2-acetylamino-2-ethyl-3-hydroxy-5-methylhexanoate (*erythro*-43fb)** (sbo-412c)



Following the above general procedure, the bicyclic oxetane **42fb** (0.45 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 66 %

TLC: R_f = 0.44 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (t, J = 7.5 Hz, 3H, CH_3), 0.84 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (m, 1H, CH), 1.63 (ddd, J = 10.1, 2.1, 2.1 Hz, 2H, CH_2), 1.85 (m, 1H, CH), 2.12 (s, 3H, $\underline{CH_3}CO$), 2.80 (sextet, J = 7.5 Hz, 1H, CH), 3.76 (s, 3H, OCH_3), 4.40 (dd, J = 11.5 , 2.1 Hz, 1H, $\underline{CH}OH$), 6.39 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

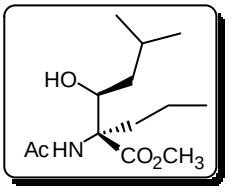
δ_{ppm} = 9.0 (q, CH_3), 20.5 (q, CH_3), 23.7 (q, CH_3), 24.4 (q, CH_3), 24.5 (t, CH_2), 25.1 (d, CH), 42.0 (t, CH_2), 53.1 (q, OCH_3), 65.7 (s, C-2), 69.7 (d, C-3), 169.3 (s, CON), 172.2 (s, COO).

HRMS: ($C_{12}H_{23}NO_4$, M = 245.16 g/mol)

Calcd: 245.1621

Found: 245.1618

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-5-methyl-2-propylhexanoate (*erythro*-43fc)** (sbo-350b)



Following the above general procedure, the bicyclic oxetane **42fc** (0.48 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.35 g of the product as a colorless oil.

Yield: 68 %

TLC: R_f = 0.48 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.5 Hz, 3H, CH_3), 0.86 (t, J = 4.3 Hz, 3H, CH_3), 0.91 (d, J = 6.6 Hz, 3H, CH_3), 1.52 (dddd, J = 3.1, 3.2, 3.1, 3.2 Hz, 2H, CH_2), 1.65 (ddd, J = 6.5, 2.1, 1.9 Hz, 1H, CH), 1.81 (m, 2H, CH_2), 2.00 (s, 3H, $\underline{CH_3}CO$), 3.77 (s, 3H, OCH_3), 4.39 (dd, J = 11.5, 2.1 Hz, 1H, $\underline{CH}OH$), 6.39 (bs, 1H, NH).

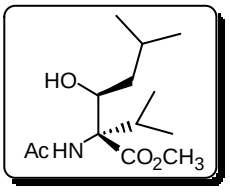
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 18.1 (q, CH_3), 20.5 (q, CH_3), 23.7 (q, CH_3), 25.1 (t, CH_2), 33.4 (t, CH_2), 41.9 (t, CH_2), 53.1 (q, OCH_3), 65.9 (s, C-2), 69.0 (d, C-3), 169.3 (s, CON), 172.3 (s, COO).

Anal: ($C_{13}H_{25}NO_4$, M = 259.18 g/mol)

Calcd:	C 60.21	H 9.72	N 5.40
Found:	C 59.98	H 9.61	N 5.32

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-isopropyl-5-methylhexanoate (*erythro*-43fd)** (sbo-325c)



Following the above general procedure, the bicyclic oxetane **42fd** (0.48 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 62 %

TLC: R_f = 0.63 (ethylacetate/n-hexane 1: 3)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3396, 2919, 1738, 1668, 1471, 1056, 1031, 978, 680.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.8 Hz, 3H, CH_3), 0.89 (d, J = 6.5 Hz, 3H, CH_3), 0.93 (d, J = 6.6 Hz, 3H, CH_3), 1.00 (d, J = 7.1 Hz, 3H, CH_3), 1.70 (m, 2H, CH_2), 1.86 (m, 1H, CH), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.57 (sextet, J = 6.9 Hz, 1H, CH), 3.79 (s, 3H, OCH_3), 4.69 (dd, J = 11.2, 2.4 Hz, 1H, $\underline{CH}OH$), 6.43 (bs, 1H, NH).

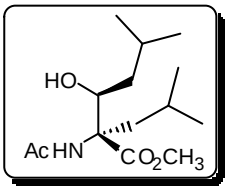
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.0 (q, CH_3), 18.7 (q, CH_3), 20.5 (q, CH_3), 23.8 (q, CH_3), 25.1 (d, CH), 28.1 (d, CH), 41.6 (t, CH_2), 52.9 (q, OCH_3), 65.9 (s, C-2), 73.5 (d, C-3), 169.6 (s, CON), 171.8 (s, COO).

Anal: ($C_{13}H_{25}NO_4$, M = 259.3 g/mol)

Calcd:	C 60.21	H 9.72	N 5.40
Found:	C 59.89	H 9.64	N 5.27

***erythro*-Methyl (2S*,3S*) 2-acetylamino-3-hydroxy-2-isobutyl-5-methylhexanoate (*erythro*-43fe)** (sbo-339c)



Following the above general procedure, the bicyclic oxetane **42fe** (0.51 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.26 g of the *erythro*-isomer and 0.09 g of the *threo*-isomer, both as a colorless oil.

Yield: 45 %

TLC: R_f = 0.33 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.74 (d, J = 6.5 Hz, 3H, CH_3), 0.81 (d, J = 6.6 Hz, 3H , CH_3), 0.86 (d, J = 6.6, Hz, 3H, CH_3), 0.95 (d, J = 6.8 Hz, 3H, CH_3), 1.51 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 1.94 (s, 3H, $\underline{CH_3}CO$), 2.21 (m, 1H, CH), 2.26 (dd, J = 13.5, 3.5 Hz, 1H, CH), 2.81 (dd, J = 13.5, 1.8 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 4.43 (dd, J = 11.6, 1.8 Hz, 1H, $\underline{CH}OH$), 6.50 (bs, 1H, NH).

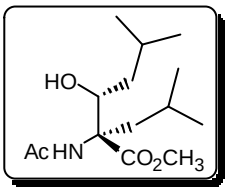
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.4 (q, CH_3), 20.5 (q, CH_3), 21.5 (q, CH_3), 23.2 (q, CH_3), 25.1 (d, CH), 28.1 (d, CH), 37.9 (t, CH_2), 52.8 (q, OCH_3), 68.0 (s, C-2), 73.9 (d, C-3), 169.3 (s, CON), 172.9 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 271 (M^+-H_2, 5), 256 (M^+-H_2O, 7), 214 (M^+-CO_2Me, 12), 196 (22), 187 (60), 170 (20), 154 (30), 112 (26), 102 (100), 85 (70), 57 (52).

***threo*-Methyl (2S*,3R*) 2-acetylamino-3-hydroxy-2-isobutyl-5-methylhexanoate (*threo*-43fe)** (sbo-339a)



Yield: 13 %

TLC: R_f = 0.23 (ethylacetate/n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.8 Hz, 3H, CH_3), 0.88 (d, J = 6.6 Hz, 3H , CH_3), 0.93 (dd, J = 7.5, 7.4 Hz, 6H, $2CH_3$), 1.00 (dd, J = 6.9 Hz, 1H, CH), 1.12 (dd, J = 7.0, 1.8 Hz, 1H, CH), 1.53 (m, 1H, CH), 2.00 (s, 3H, $\underline{CH_3}CO$), 2.43 (dd, J = 7.5, 1.5 Hz,1H, CH), 3.67 (s, 3H, OCH_3), 4.00 (dd, J = 8.5, 1.4 Hz, 1H, $\underline{CH}OH$), 6.97 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

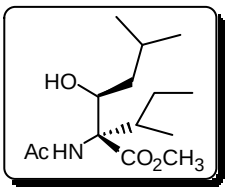
δ_{ppm} = 14.0 (q, CH_3), 20.0 (q, CH_3), 23.3 (q, CH_3), 23.8 (q, CH_3), 24.7 (d, CH), 27.9 (d, CH), 40.6 (t, CH_2), 52.3 (q, OCH_3), 80.0 (s, C-2), 91.5 (d, C-3), 164.9 (s, CON), 174.9 (s, COO).

Anal: ($C_{14}H_{27}NO_4$, M = 273.2 g/mol)

Calcd: C 61.51 H 9.96 N 5.12

Found: C 61.62 H 9.86 N 4.97

***erythro*-Methyl (2S*,3S*) 2-acetylamino-2-*sec*-butyl-3-hydroxy-5-methylhexanoate (*erythro*-43ff)** (sbo-345a)



Following the above general procedure, the bicyclic oxetane **42ff** (0.51 g, 2 mmol) was hydrolytically cleaved in 3h. Preparative chromatography yielded 0.4 g of the *erythro*-isomer and 0.11 g of the *threo*-isomer, all as a colorless oil.

Yield: 73 %

TLC: R_f = 0.61 (ethylacetate/n-hexane 1: 3)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3305, 2874, 1732, 1673, 1455, 1051, 1031, 960, 670.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.9, Hz, 3H, CH_3), 0.88 (d, J = 6.5, Hz, 3H , CH_3), 0.94 (d, J = 6.6 Hz, 3H, CH_3), 0.99 (t, J = 7.5 Hz, 3H, CH_3), 1.43 (m, 1H, CH), 1.53 (m, 2H, 2CH), 1.97 (s, 3H, $\underline{CH_3}CO$), 3.71 (s, 3H, OCH_3), 4.15 (dd, J = 11.2, 1.6 Hz, 1H, $\underline{CH}OH$), 6.33 (bs, 1H, NH).

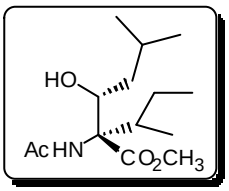
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.9 (q, CH_3), 12.7 (q, CH_3), 13.4 (q, CH_3), 14.3 (q, CH_3), 21.3 (q, CH_3), 24.7 (d, CH), 25.5 (d, CH), 34.3 (t, CH_2), 39.7 (t, CH_2), 52.6 (q, OCH_3), 71.9 (s, C-2), 74.2 (d, C-3), 169.4 (s, CON), 173.0 (s, COO).

Anal: ($C_{14}H_{27}NO_4$, M = 273.2 g/mol)

Calcd:	C 61.51	H 9.96	N 5.12
Found:	C 61.67	H 9.66	N 5.12

***threo*-Methyl (2S*,3R*) 2-acetylamino-2-*sec*-butyl-3-hydroxy-5-methylhexanoate (*threo*-43ff)** (sbo-345c)



Yield: 15 %

TLC: R_f = 0.46 (ethylacetate/n-hexane 1: 3)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3340, 2956, 1738, 1682, 1471, 1056, 1031, 978, 680.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 7.5, Hz, 3H, CH_3), 0.84 (d, J = 7.5, Hz, 3H , CH_3), 0.88 (t, J = 6.5 Hz, 3H, CH_3), 0.93 (d, J = 6.5 Hz, 3H, CH_3), 1.21 (m, 2H, CH_2), 1.53 (m, 1H, CH),

1.75 (m, 2H, CH_2), 2.00 (s, 3H, $\underline{CH_3}CO$), 3.69 (s, 3H, OCH_3), 4.38 (dd, J = 10.5, 2.5 Hz, 1H, $\underline{CH}OH$), 6.33 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.9 (q, CH_3), 13.6 (q, CH_3), 14.1 (q, CH_3), 21.5 (q, CH_3), 23.4 (q, CH_3), 24.8 (d, CH), 26.5 (d, CH), 37.4 (t, CH_2), 37.9 (t, CH_2), 51.9 (q, OCH_3), 82.3 (s, C-2), 83.9 (d, C-3), 165.4 (s, CON), 174.3 (s, COO).

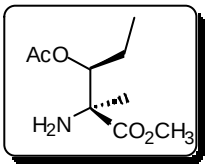
MS: (EI, 70 eV)

m/z (%) = 255 (M^+-H_2O, 15), 218 (M^+-CO_2Me, 18), 196 (20), 187 (68), 170 (20), 154 (30), 112 (26), 102 (100), 86 (70), 68 (52).

4.15.2 Transacylation; General procedure:

To a solution of α-acetamido-β-hydroxy ester (0.3 g, 15 mmol) in chloroform (15 mL), 1N aq. HCl (0.2 mL) was added at room temperature, the mixture was left to stirr overnight. After the reaction was quenched with water, (15 mL), the mixture was extracted with methylene chloride (3 x 15 mL) and the organic extract was washed with 5% sodium bicarbonate solution, dried (Mg SO_4) and the solvent was removed under vacum. The residue was purified by preparative chromatography.

Methyl (2S*,3S*) 3-acetoxy-2-amino-2-methylpentanoate (*erythro*-44da) (sbo-300b)



Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.51 (ethylacetate/n-hexane 1: 3)

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3336, 2919, 1760, 1738, 1471, 1056, 1031, 978, 680.

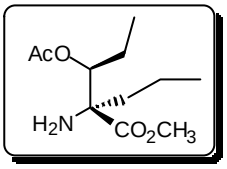
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 0.81 (t, J = 7.2, Hz, 3H, CH_3), 1.62 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 2.21 (s, 3H, $\underline{CH_3}CO$), 3.85 (s, 3H, OCH_3), 5.24 (dd, J = 10.9, 2.9 Hz, 1H, $\underline{CH}OAc$), 6.20 (bs, 2H, NH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ = 11.0 (q, CH_3), 20.8 (q, CH_3), 21.9 (q, CH_3), 23.2 (t, CH_2), 53.9 (q, OCH_3), 63.7 (s, Cq), 76.0 (d, $\underline{CH}OAc$), 171.9 ($\underline{CO}OCH_3$), 173.0 (s, $O\underline{CO}CH_3$).

Methyl (2S*,3S*) 3-acetoxy-2-amino-2-propyl pentanoate (*erythro*-44dc) (sbo-349d)



Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 79 %

TLC: R_f = 0.57 (ethylacetate/ n-hexane 1: 3)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 0.78 (t, J = 7.4, Hz, 3H, CH_3), 0.84 (t, J = 6.0 Hz, 2H, CH_2), 1.10 (t, J = 7.6 Hz, 3H, CH_3), 1.42 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.69 (s, 3H, OCH_3), 5.30 (dd, J = 10.9, 2.6 Hz, 1H, $\underline{CH}OAc$), 6.38 (bs, 2H, NH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ = 9.2 (q, CH_3), 11.3 (q, CH_3), 13.3 (t, CH_2), 17.6 (q, CH_3), 23.7 (t, CH_2), 36.0 (t, CH_2), 52.8 (q, OCH_3), 67.8 (s, Cq), 77.6 (d, $\underline{CH}OAc$), 172.9 ($\underline{CO}OCH_3$), 173.6 (s, $O\underline{CO}CH_3$).

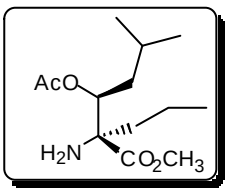
HRMS: ($C_{11}H_{21}NO_4$, M = 231.15 g/mol)

Calcd: 231.1473

Found: 231.1471

Methyl (2S*,3S*) 3-acetoxy-2-amino-5-methyl-2-propylhexanoate (*erythro*-44fc)

(sbo-350c)



Preparative chromatography yielded 0.17 g of the product as a colorless oil.

Yield: 72 %

TLC: R_f = 0.55 (ethylacetate/n-hexane 1: 3)

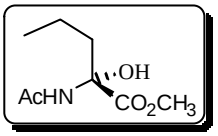
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 0.84 (t, J = 6.5, Hz, 3H, CH_3), 0.85 (m, 2H, CH_2), 0.91 (dd, J = 6.5, 6.5 Hz, 6H, $2CH_3$), 1.23 (m, 1H, CH), 1.54 (m, 2H, CH_2), 1.99 (s, 3H, $\underline{CH_3}CO$), 3.70 (s, 3H, OCH_3), 5.49 (dd, J = 7.7, 3.9 Hz, 1H, CHOAc), 6.36 (bs, 2H, NH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ = 13.9 (q, CH_3), 17.6 (q, CH_3), 21.3 (q, CH_3), 23.6 (q, CH_3), 24.3 (t, CH_2), 32.1 (d, CH), 39.1 (t, CH_2), 43.3 (t, CH_2), 52.8 (q, OCH_3), 67.7 (s, Cq), 74.3 (d, CHOAc), 172.3 ($COOCH_3$), 172.9 (s, $OCOCH_3$).

Synthesis of methyl 2-acetylamino-2-hydroxypentanoate (45) (sbo-392)



To a solution of methyl 2-acetylamino-3-hydroxy-2-propylpentanoate **43dc** (0.22 g, 1 mmol) in methanol (20 mL), 10 % sodium hydroxide (20 mL) was added, and the mixture was heated under reflux for 6h. After the reaction mixture was neutralized with 1N HCl, the solvent was evaporated in *vacuo* and the residue was purified by preparative chromatography to give 0.15 g of **45** as a white needle crystal.

Yield: 85 %

M.p: 123-124 °C.

TLC: R_f = 0.34 (ethylacetate/n-hexane 1: 4)

IR: (CsI)

$\tilde{n}$ (cm^{-1}) = 3329, 2971, 2878, 1738, 1660, 1445, 1097, 1031, 968, 684.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ = 0.91 (t, J = 7.4, Hz, 3H, CH_3), 1.27 (m, 1H, CH), 1.46 (m, 1H, CH), 1.78 (m, 2H, CH_2), 1.97 (s, 3H, CH_3CO), 3.78 (s, 3H, OCH_3), 4.82 (bs, 1H, OH), 6.35 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ = 13.8 (q, CH_3), 16.3 (t, CH_2), 22.9 (q, CH_3), 40.0 (t, CH_2), 53.2 (q, OCH_3), 82.5 (s, Cq), 171.2 (CON), 172.2 (s, COO).

Anal: ($C_8H_{15}NO_4$, M = 189.2 g/mol)

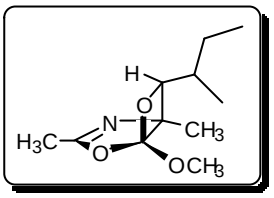
Calcd:	C 50.78	H 7.99	N 7.40
Found:	C 50.76	H 7.94	N 7.42

4.16 Photolyses of 5-methoxyoxazoles 36a-f with 2-methylbutyraldehyde; Genernal procedure:

A mixture of 5-methoxyoxazoles **36a-f** (5 mmol) and 2-methylbutyraldehyde (5 mmol) in 50 mL benzene was irradiated (λ = 300 nm) in a pyrex vessel for 24 h while purging with a slow stream of nitrogen and cooling to ca. 15 °C. After irradiation, the solvent was evaporated at

40°C/200 torr and the residue was submitted to ^{1}H-NMR analysis to determine the diastereomeric ratio of the product. Purification was carried out by Büchi distillation. The thermally and hydrolytically unstable primary products could in most cases not be characterized by combustion analysis and were hydrolyzed subsequently to the more stable α-amino-β-hydroxy esters.

***exo*-7-*sec*-Butyl-5-methoxy-1,3-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-46a)** (sbo-372)



A solution of 2-methylbutyraldehyde (0.43 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.95 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 90 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.76 (d, J = 6.8, Hz, 3H, CH_3), 0.78 (t, J = 7.4, Hz, 3H , CH_3), 0.92 (m, 2H, CH_2), 1.43 (s, 3H, CH_3), 1.58 (m, 1H, CH), 2.05 (s, 3H, CH_3), 3.56 (s, 3H, OCH_3), 3.68 (d, J = 4.6 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

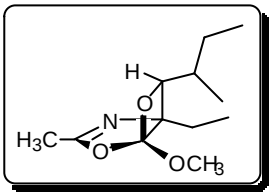
δ_{ppm} = 9.7 (q, CH_3), 10.7 (q, CH_3), 13.9 (q, CH_3), 14.8 (q, CH_3), 23.4 (d, CH), 36.2 (t, CH_2), 51.1 (q, OCH_3), 73.5 (s, C-1), 92.5 (s, C-7), 124.1 (s, C-5), 165.1 (s, C-3).

HRMS: ($C_{11}H_{19}NO_3$, M = 213.14 g/mol)

Calcd: 213.1360

Found: 213.1352

***exo*-7-*sec*-Butyl-1-ethyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*- 46b)** (sbo-369)



A solution of 2-methylbutyraldehyde (0.43 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 0.99 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

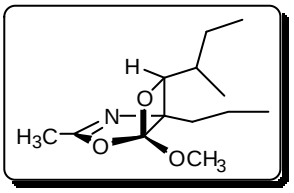
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (t, J = 7.5, Hz, 3H, CH_3), 0.78 (d, J = 6.8, Hz, 3H , CH_3), 0.81 (m, 2H, CH_2), 1.13 (m, 2H, CH_2), 1.17 (m, 1H, CH), 2.12 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 3.72 (d, J = 4.2 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.7 (q, CH_3), 10.8 (q, CH_3), 12.9 (q, CH_3), 14.8 (q, CH_3), 23.9 (d, CH), 25.9 (t, CH_2), 35.8 (t, CH_2), 52.1 (q, OCH_3), 77.1 (s, C-1), 92.7 (s, C-7), 124.2 (s, C-5), 165.1 (s, C-3).

***exo*-7-*sec*-Butyl-5-methoxy-3-methyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*- 46c)** (sbo-393)



A solution of 2-methylbutyraldehyde (0.43 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.12 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 90 %

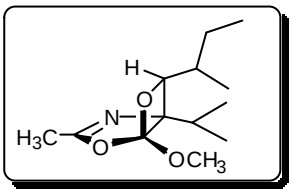
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.77 (t, J = 7.4, Hz, 3H, CH_3), 0.79 (d, J = 6.9, Hz, 3H , CH_3), 0.83 (t, J = 6.5 Hz, 3H, CH_3), 0.87 (m, 2H, CH_2), 1.49 (m, 1H, CH), 1.53 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 2.00 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 3.67 (d, J = 4.4 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.1 (q, CH_3), 10.8 (q, CH_3), 16.7 (q, CH_3), 23.9 (q, CH_3), 25.1 (d, CH), 28.6 (t, CH_2), 35.8 (t, CH_2), 36.4 (t, CH_2), 50.8 (q, OCH_3), 77.8 (s, C-1), 92.8 (s, C-7), 124.2 (s, C-5), 164.7 (s, C-3).

***exo*-7-*sec*-Butyl-1-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-46d)** (sbo-396)



A solution of 2-methylbutyraldehyde (0.43 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.1 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 87 %

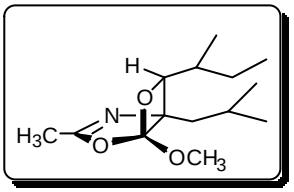
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.74 (d, J = 6.6 Hz, 3H, CH_3), 0.78 (d, J = 6.8, Hz, 3H , CH_3), 0.80 (t, J = 7.4 Hz, 3H, CH_3), 0.83 (d, J = 7.2 Hz, 3H, CH_3), 1.12 (m, 1H, CH), 1.23 (m, 2H, CH_2), 2.10 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 4.12 (d, J = 4.7 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.7 (q, CH_3), 11.1 (q, CH_3), 14.0 (q, CH_3), 18.4 (q, CH_3), 18.9 (q, CH_3), 21.4 (d, CH), 25.4 (d, CH), 27.5 (t, CH_2), 50.4 (q, OCH_3), 80.4 (s, C-1), 93.1 (s, C-7), 124.4 (s, C-5), 164.7 (s, C-3).

***exo*-7-*sec*-Butyl-1-isobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-46e)** (sbo-398)



A solution of 2-methylbutyraldehyde (0.43 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.0 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 78 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 6H, $2CH_3$), 0.88 (t, J = 7.4, Hz, 3H , CH_3), 0.93 (t, J = 6.5 Hz, 3H, CH_3), 1.12 (m, 1H, CH), 1.23 (m, 2H, CH_2), 1.43 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 2.12 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.12 (d, J = 4.8 Hz, 1H, 7-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

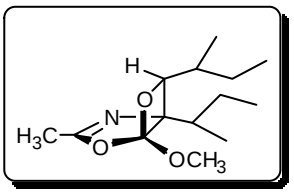
δ_{ppm} = 10.3 (q, CH_3), 11.0 (q, CH_3), 12.7 (q, CH_3), 16.0 (q, CH_3), 16.5 (q, CH_3), 24.7 (d, CH), 24.9 (t, CH_2), 31.0 (d, CH), 40.7 (t, CH_2), 50.9 (q, OCH_3), 78.0 (s, C-1), 90.3 (s, C-7), 124.5 (s, C-5), 164.9 (s, C-3).

HRMS: ($C_{14}H_{25}NO_3$, M = 255.18 g/mol)

Calcd: 255.1825

Found: 255.1822

***exo*-1,7-Di-*sec*-butyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene (*exo*-46f)** (sbo-397)



A solution of 2-methylbutyraldehyde (0.43 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24h according to the above general procedure. Distillation of the solvent under vaccum afforded 1.09 g of the oxetane as a pale yellow oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 85 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.6 Hz, 6H, $2CH_3$), 0.87 (t, J = 6.5, Hz, 6H , $2CH_3$), 0.97 (m, 2H, CH_2), 1.23 (m, 2H, 2CH), 2.12 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 4.27 (d, J = 6.2 Hz, 1H, 7-H).

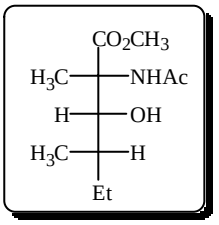
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.9 (q, CH_3), 9.5 (q, CH_3), 10.2 (q, CH_3), 10.7 (q, CH_3), 14.7 (q, CH_3), 20.4 (d, CH), 25.1 (d, CH), 27.1 (t, CH_2), 29.1 (t, CH_2), 51.2 (q, OCH_3), 79.4 (s, C-1), 89.1 (s, C-7), 124.3 (s, C-5), 164.1 (s, C-3).

4.16.1 Synthesis of *lyxo*- & *ribo*- a-acetamido-b-hydroxy esters (47a-f); General procedure:

To a solution of bicyclic oxetanes **46a-f** (1 mmol) in 20 mL of methylene chloride, 0.3 mL of 1N HCl was added, and the mixture was stirred at room temperature for 6 h. The reaction was quenched by the addition of water (20 mL), the mixture was extracted with methylene chloride (3 x 15 mL) and the organic extract was washed with saturated $NaHCO_3$, brine, dried ($MgSO_4$). After removal of the solvent, the residue was purified by preparative thick-layer chromatography.

***lyxo*-Methyl (2R*,3R*,4S*) 2-acetylamino-3-hydroxy-2,4-dimethylhexanoate (*lyxo*-47a)** (sbo-372a)



Following the above general procedure, bicyclic oxetane **46a** (0.43 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.35 g of the two inseparable diastermeric *lyxo*-& *ribo*-isomers as a colorless oil.

Yield: 75 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.39 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.69 (d, J = 6.8 Hz, 3H, CH_3), 0.85 (t, J = 7.5 Hz, 3H, CH_3), 1.12 (m, 1H, CH), 1.48 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.73 (s, 3H, OCH_3), 4.40 (d, J = 9.9 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

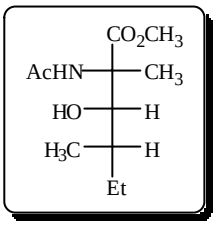
δ_{ppm} = 10.4 (q, CH_3), 14.1 (q, CH_3), 15.4 (q, CH_3), 18.4 (q, CH_3), 26.2 (t, CH_2), 34.0 (d, CH), 52.8 (q, OCH_3), 74.5 (s, C-2), 88.9 (s, C-3), 165.5 (s, CON), 174.4 (s, COO).

Anal: ($C_{11}H_{21}NO_4$, M = 231.15 g/mol)

Calcd: C 57.12 H 9.15 N 6.06

Found: C 57.08 H 8.98 N 5.97

***ribo*-Methyl (2S*,3S*,4S*) 2-acetylamino-2-ethyl-3-hydroxy-4-methylhexanoate (*ribo*-47a)** (sbo-372a)



Yield: 75 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.39 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.69 (d, J = 6.8 Hz, 3H, CH_3), 0.85 (t, J = 7.5 Hz, 3H, CH_3), 1.12 (m, 1H, CH), 1.48 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.73 (s, 3H, OCH_3), 4.44 (d, J = 8.5 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

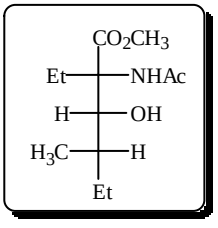
δ_{ppm} = 10.9 (q, CH_3), 14.2 (q, CH_3), 15.7 (q, CH_3), 18.7 (q, CH_3), 26.2 (t, CH_2), 34.7 (d, CH), 52.8 (q, OCH_3), 74.5 (s, C-2), 88.9 (s, C-3), 165.4 (s, CON), 174.5 (s, COO).

HRMS: ($C_{11}H_{21}NO_4$, M = 231.15 g/mol)

Calcd: 231.1519

Found: 231.1513

***lyxo*-Methyl (2R*,3R*,4S*) 2-acetylamino-2-ethyl-3-hydroxy-4-methylhexanoate (*lyxo*-47b)** (sbo-369a)



Following the above general procedure, bicyclic oxetane **46b** (0.45 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.39 g of the two inseparable diastermeric *lyxo*-& *ribo*-isomers as a colorless oil.

Yield: 80 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.31 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 0.89 (t, J = 7.4 Hz, 3H, CH_3), 1.24 (m, 2H, CH_2), 1.54 (m, 4H, $2CH_2$), 1.68 (m, 1H, CH), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.22 (d, J = 9.3 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

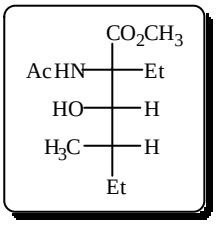
δ_{ppm} = 8.1 (q, CH_3), 9.1 (q, CH_3), 11.1 (q, CH_3), 14.1 (q, CH_3), 15.3 (q, CH_3), 25.5 (d, CH), 33.9 (t, CH_2), 52.4 (q, OCH_3), 78.5 (s, C-2), 88.9 (s, C-3), 165.4 (s, CON), 174.6 (s, COO).

HRMS: ($C_{12}H_{23}NO_4$, M = 245.16 g/mol)

Calcd: 245.1621

Found: 245.1613

***ribo*-Methyl (2S*,3S*,4S*) 2-acetylamino-3-hydroxy-4-methyl-2-propylhexanoate (*ribo*-47b)** (sbo-369a)



Yield: 80 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.31 (ethylacetate/n-hexane 1: 4)

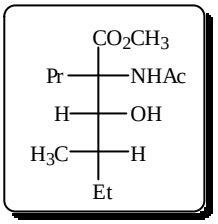
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 0.89 (t, J = 7.4 Hz, 3H, CH_3), 1.24 (m, 2H, CH_2), 1.54 (m, 4H, $2CH_2$), 1.68 (m, 1H, CH), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.33 (d, J = 7.1 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.8 (q, CH_3), 10.4 (q, CH_3), 11.4 (q, CH_3), 14.4 (q, CH_3), 15.8 (q, CH_3), 23.6 (d, CH), 34.5 (t, CH_2), 52.4 (q, OCH_3), 78.9 (s, C-2), 88.8 (s, C-3), 165.2 (s, CON), 174.5 (s, COO).

***lyxo*-Methyl (2R*,3R*,4S*) 2-acetylamino-3-hydroxy-4-methyl-2-propylhexanoate (*lyxo*-47c)** (sbo-393a)



Following the above general procedure, bicyclic oxetane **46c** (0.48 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.38 g of the two inseparable diastermeric *lyxo*-& *ribo*-isomers as a colorless oil.

Yield: 73 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.36 (ethylacetate/n-hexane 1: 4)

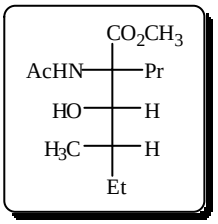
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (t, J = 7.5 Hz, 3H, CH_3), 0.90 (t, J = 7.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.68 (m, 1H, CH), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.20 (d, J = 9.2 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.5 (q, CH_3), 14.1 (q, CH_3), 14.5 (q, CH_3), 15.3 (q, CH_3), 17.7 (t, CH_2), 26.1 (d, CH), 33.9 (t, CH_2), 34.9 (t, CH_2), 52.4 (q, OCH_3), 78.2 (s, C-2), 88.9 (s, C-3), 165.1 (s, CON), 174.7 (s, COO).

***ribo*-Methyl (2S*,3S*,4S*) 2-acetylamino-3-hydroxy-4-methyl-2-propylhexanoate (*ribo*-47c)** (sbo-393a)



Yield: 73 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.36 (ethylacetate/n-hexane 1: 4)

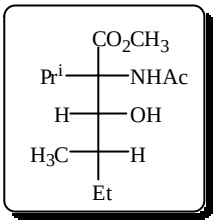
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (t, J = 7.5 Hz, 3H, CH_3), 0.90 (t, J = 7.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.68 (m, 1H, CH), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.33 (d, J = 6.9 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.1 (q, CH_3), 14.2 (q, CH_3), 14.6 (q, CH_3), 15.8 (q, CH_3), 18.0 (t, CH_2), 26.8 (d, CH), 34.5 (t, CH_2), 35.1 (t, CH_2), 52.5 (q, OCH_3), 78.6 (s, C-2), 89.8 (s, C-3), 165.1 (s, CON), 174.8 (s, COO).

***lyxo*-Methyl (2R*,3R*,4S*) 2-acetylamino-3-hydroxy-2-isopropyl-4-methylhexanoate (*lyxo*-47d)** (sbo-396b)



Following the above general procedure, bicyclic oxetane **46d** (0.48 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.36 g of the two inseparable diastermeric *lyxo*-& *ribo*-isomers as a colorless oil.

Yield: 69 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.45 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 6.5 Hz, 3H, CH_3), 0.96 (d, J = 6.6 Hz, 3H, CH_3), 1.02 (d, J = 6.6 Hz, 3H, CH_3), 1.16 (d, J = 6.9 Hz, 3H, CH_3), 1.72 (m, 2H, CH_2), 1.99 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.06 (d, J = 10.0 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

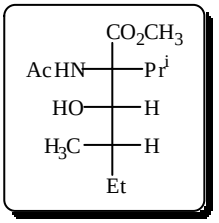
δ_{ppm} = 10.3 (q, CH_3), 13.9 (q, CH_3), 16.0 (q, CH_3), 17.6 (q, CH_3), 19.1 (q, CH_3), 26.3 (d, CH), 30.4 (d, CH), 33.7 (t, CH_2), 52.1 (q, OCH_3), 81.9 (s, C-2), 89.1 (s, C-3), 167.2 (s, CON), 173.9 (s, COO).

HRMS: ($C_{13}H_{25}NO_4$, M = 259.18 g/mol)

Calcd: 259.1777

Found: 259.1770

***ribo*-Methyl (2S*,3S*,4S*) 2-acetylamino-3-hydroxy-2-isopropyl-4-methylhexanoate (*ribo*-47d)** (sbo-396b)



Yield: 69 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.45 (ethylacetate/n-hexane 1: 4)

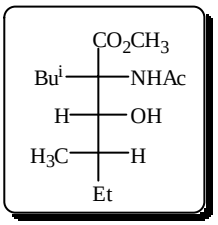
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 6.5 Hz, 3H, CH_3), 0.96 (d, J = 6.6 Hz, 3H, CH_3), 1.02 (d, J = 6.6 Hz, 3H, CH_3), 1.16 (d, J = 6.9 Hz, 3H, CH_3), 1.72 (m, 2H, CH_2), 1.99 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.28 (d, J = 8.1 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.0 (q, CH_3), 15.9 (q, CH_3), 17.9 (q, CH_3), 18.9 (q, CH_3), 21.6 (q, CH_3), 26.7 (d, CH), 30.3 (d, CH), 34.3 (t, CH_2), 52.1 (q, OCH_3), 81.9 (s, C-2), 89.1 (s, C-3), 167.2 (s, CON), 173.9 (s, COO).

***lyxo*-Methyl (2R*,3R*,4S*) 2-acetylamino-3-hydroxy-2-isobutyl-4-methylhexanoate (*lyxo*-47e)** (sbo-398b)



Following the above general procedure, bicyclic oxetane **46e** (0.51 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.44 g of the two inseparable diastermeric *lyxo*-& *ribo*-isomer as a colorless oil.

Yield: 80 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.40 (ethylacetate/n-hexane 1: 4)

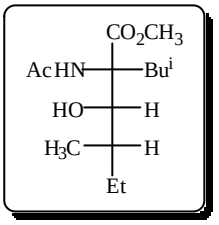
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.6 Hz, 6H, $2CH_3$), 0.88 (t, J = 7.4 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.12 (m, 2H, 2CH), 1.54 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 1.96 (s, 3H, $\underline{CH_3}CO$), 3.81 (s, 3H, OCH_3), 4.05 (d, J = 9.3 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.4 (q, CH_3), 14.2 (q, CH_3), 15.3 (q, CH_3), 22.2 (q, CH_3), 23.3 (q, CH_3), 24.6 (d, CH), 26.2 (d, CH), 33.8 (d, CH), 40.7 (t, CH_2), 52.3 (q, OCH_3), 78.1 (s, C-2), 89.6 (s, C-3), 164.8 (s, CON), 175.2 (s, COO).

***ribo*-Methyl (2S*,3S*,4S*) 2-acetylamino-3-hydroxy-2-isobutyl-4-methylhexanoate (*ribo*-47e)** (sbo-398b)



Yield: 80 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.40 (ethylacetate/n-hexane 1: 4)

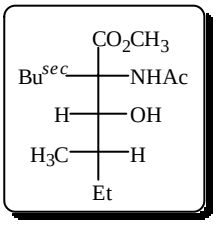
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.6 Hz, 6H, $2CH_3$), 0.88 (t, J = 7.4 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.12 (m, 2H, 2CH), 1.54 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 1.96 (s, 3H, $\underline{CH_3}CO$), 3.81 (s, 3H, OCH_3), 4.22 (d, J = 6.9 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.0 (q, CH_3), 14.1 (q, CH_3), 15.6 (q, CH_3), 22.3 (q, CH_3), 23.7 (q, CH_3), 24.8 (d, CH), 26.7 (d, CH), 34.2 (d, CH), 40.7 (t, CH_2), 52.4 (q, OCH_3), 78.1 (s, C-2), 89.6 (s, C-3), 164.8 (s, CON), 175.2 (s, COO).

***lyxo*-Methyl (2R*,3R*,4S*) 2-acetylamino-2-*sec*-butyl-3-hydroxy-4-methylhexanoate (*lyxo*-47f)** (sbo-397b)



Following the above general procedure, bicyclic oxetane **46f** (0.51 g, 2 mmol) was hydrolytically cleaved in 6h. Preparative chromatography yielded 0.40 g of the two inseparable diastermeric *lyxo*-& *ribo*-isomers as a colorless oil.

Yield: 74 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.51 (ethylacetate/n-hexane 1: 4)

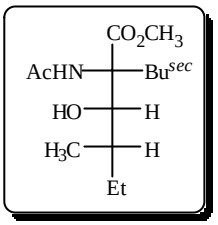
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (t, J = 6.6 Hz, 3H, CH_3), 0.85 (d, J = 6.8 Hz, 3H, CH_3), 0.87 (t, J = 7.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.05 (m, 2H, CH_2), 1.15 (m, 2H, CH_2), 1.54 (m, 1H, CH), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.15 (d, J = 9.2 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.1 (q, CH_3), 12.1 (q, CH_3), 13.9 (q, CH_3), 14.2 (q, CH_3), 15.5 (q, CH_3), 25.9 (d, CH), 26.2 (d, CH), 33.7 (t, CH_2), 37.9 (t, CH_2), 52.1 (q, OCH_3), 82.5 (s, C-2), 88.9 (s, C-3), 174.4 (s, CON), 179.8 (s, COO).

***ribo*-Methyl (2S*,3S*,4S*) 2-acetylamino-2-*sec*-butyl-3-hydroxy-4-methylhexanoate (*ribo*-47f)** (sbo-397b)



Yield: 74 % (*lyxo*- & *ribo*-isomer)

TLC: R_f = 0.51 (ethylacetate/n-hexane 1: 4)

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (t, J = 6.6 Hz, 3H, CH_3), 0.85 (d, J = 6.8 Hz, 3H, CH_3), 0.87 (t, J = 7.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.05 (m, 2H, CH_2), 1.15 (m, 2H, CH_2), 1.54 (m, 1H, CH), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.72 (s, 3H, OCH_3), 4.28 (d, J = 8.1 Hz, 1H, $\underline{CH}OH$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.8 (q, CH_3), 12.4 (q, CH_3), 13.6 (q, CH_3), 14.8 (q, CH_3), 15.9 (q, CH_3), 25.4 (d, CH), 26.7 (d, CH), 33.1 (t, CH_2), 37.4 (t, CH_2), 52.4 (q, OCH_3), 81.9 (s, C-2), 88.5 (s, C-3), 174.2 (s, CON), 179.1 (s, COO).

Anal: ($C_{14}H_{27}NO_4$, M = 273.17 g/mol)

Calcd: C 61.51 H 9.96 N 5.12

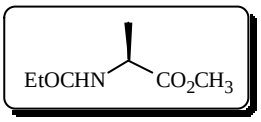
Found: C 61.42 H 9.64 N 5.04

4.17 Synthesis of 2-substituted 4-methyl-5-methoxyoxazoles

Synthesis of N-acylalanine methyl ester 48a-c; General procedure:

To a stirred suspension of alanine methyl ester hydrochloride (13.96 g, 100 mmol) in absolute chloroform (150 mL) was added triethylamine (28 mL, 200 mmol) at 0°C and the mixture was stirred for 15 min at room temperature. The appropriate acid chloride (100 mmol) was added dropwise and stirring was continued for 45 min. The solvent was removed under reduced pressure; ethyl acetate (750 mL) was added and the mixture was filtered through a pad of silica gel. Evaporation of the solvent under reduced pressure afforded the amide in high purity.

Methyl 2-propionylaminopropionate (48a)[129] (sbo-420)



Alanine methyl ester hydrochloride (13.96 g, 0.1 mol) and propionyl chloride (8.74 mL, 0.1 mol) were allowed to react according to the above general procedure to give 14.3 g of methyl 2-propionylaminopropionate as a colorless viscous oil.

Yield: 90 %

B.p: 130-132 °C, 10 torr (Lit.[129], 129-129.5°C, 10 torr).

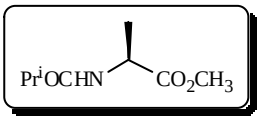
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.03 (t, J = 7.5 Hz, 3H, CH_3), 1.26 (d, J = 7.2 Hz, 3H, CH_3), 2.12 (q, J = 7.5 Hz, 2H, CH_2), 3.62 (s, 3H, OCH_3), 4.46 (quintet, J = 7.2 Hz, 1H, CHN), 6.39 (d, J = 5.3 Hz, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.4 (q, CH_3), 17.9 (t, CH_2), 29.1 (q, CH_3), 47.7 (d, CHN), 52.1 (q, OCH_3), 173.4 (s, CON), 173.5 (s, CO).

Methyl 2-isobutyrylaminopropionate (48b)[176] (sbo-448)



Alanine methyl ester hydrochloride (13.96 g, 0.1 mol) and isobutyryl chloride (10.55 mL, 0.1 mol) were allowed to react according to the above general procedure to give 16.6 g of methyl 2-isobutyrylaminopropionate as a colorless white solid.

Yield: 96 %

M.p: 55-57 °C (Lit.[176], 55.5-57°C).

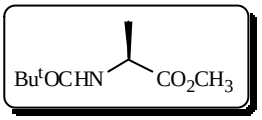
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (d, J = 6.9 Hz, 6H, $2CH_3$), 1.28 (d, J = 7.2 Hz, 3H, CH_3), 2.32 (septet, J = 6.9 Hz, 1H, CH), 3.64 (s, 3H, OCH_3), 4.48 (quintet, J = 7.2 Hz, 1H, CHN), 6.26 (d, J = 5.6 Hz, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.1 (q, CH_3), 19.1 (q, CH_3), 19.2 (q, CH_3), 35.1 (d, CH), 47.6 (d, CHN), 52.2 (q, OCH_3), 173.6 (s, CON), 176.5 (s, CO).

Methyl 2-(2,2-dimethyl-propionylamino)propionate (48c) (sbo-413)



Alanine methyl ester hydrochloride (13.96 g, 0.1 mol) and pivaloyl chloride (12.3 mL, 0.1 mol) were allowed to react according to the above general procedure to give 16.84 g of methyl 2-(2,2-dimethyl-propionylamino)propionate as a colorless white solid.

Yield: 90 %

M.p: 61-63 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.03 (s, 9H, $3CH_3$), 1.22 (d, J = 7.2 Hz, 3H, CH_3), 3.56 (s, 3H, OCH_3), 4.34 (quintet, J = 7.2 Hz, 1H, CHN), 6.23 (bs, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

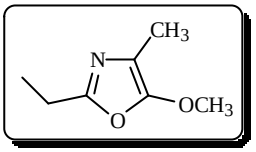
δ_{ppm} = 17.8 (q, CH_3), 27.0 (q, $3CH_3$), 38.2 (s, Cq), 47.6 (d, CHN), 51.9 (q, OCH_3), 173.4 (s, CON), 177.8 (s, CO).

Synthesis of 2-substituted 4-methyl-5-methoxyoxazoles (49a-c); General procedure:

N-Acyl-L-alanine methyl ester (0.1 mol) was dissolved in 20 ml of chloroform in a 250 ml flask, 20.8 g (0.1 mol) of phosphorous pentachloride was added and the flask was fitted with a calcium chloride tube. The solution was gently warmed by means of a water bath (ca. 60 °C) with stirring until the HCl gas evolution ceased and the solution became intensively yellow. Then, the flask was cooled by an ice-salt bath and 50 ml of absolute ether was added. To the cooled mixture, 20 % aqueous KOH was added until neutralization dropwise with vigorous stirring. The mixture was stirred at room temperature for 30 min. The organic layer was subsequently separated and the aqueous layer was extracted with 2 x 200 mL of ether. The

combined organic extracts were washed with water, brine and dried over anhydrous $MgSO_4$. After removal of the solvents under vacuum, the remaining oil was distilled by a Büchi Kugelrohr apparatus to give the product **49a-f**.

2-Ethyl-4-methyl-5-methoxyoxazole (49a)[129] (sbo-421)



Reaction of methyl 2-propionylaminopropionate (15.9 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 10.6 g of 2-ethyl-4-methyl-5-methoxyoxazole as a colorless liquid.

Yield: 75 %

B.p: 80-83 °C, 10 torr (Lit.,[129] 81°C, 31 torr).

UV/Vis: (CH_3CN, c = 1.64 x 10^{-4} mol/l, d = 1 cm)

λ_{max} (nm, log ε) = 228 (4.18), 236 (4.28).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2987, 1625, 1598, 1448, 1348, 1052, 963.

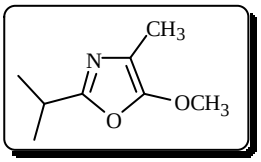
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.18 (t, J = 7.5 Hz, 3H, CH_3), 1.92 (s, 3H, CH_3), 2.54 (q, J = 7.5 Hz, 2H, CH_2), 3.78 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.8 (q, CH_3), 10.8 (q, CH_3), 21.7 (t, CH_2), 61.0 (q, OCH_3), 111.0 (s, C-4), 154.4 (s, C-5), 156.1 (s, C-2).

2-Isopropyl-4-methyl-5-methoxyoxazole (49b) (sbo-449)



Reaction of methyl 2-isobutyrylaminopropionate (17.3 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 12.4 g of 2-isopropyl-4-methyl-5-methoxyoxazole as a pale yellow liquid.

Yield: 80 %

B.p: 94-97 °C, 10 torr.

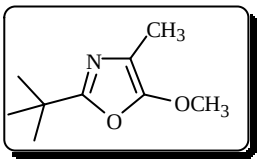
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.19 (d, J = 6.9 Hz, 6H, $2CH_3$), 1.92 (s, 3H, CH_3), 2.82 (septet, J = 7.1 Hz, 1H, CH), 3.78 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.7 (q, CH_3), 19.9 (q, $2CH_3$), 28.3 (d, CH), 60.8 (q, OCH_3), 110.7 (s, C-4), 154.1 (s, C-5), 159.2 (s, C-2).

2-*tert*-Butyl-4-methyl-5-methoxyoxazole (49c) (sbo-414)



Reaction of methyl 2-(2,2-dimethyl-propionylamino)propionate (18.7 g, 0.1 mol) and PCl_5 (20.8 g, 0.1 mol) according to the above general procedure afforded 13.2 g of 2-*tert*-butyl-4-methyl-5-methoxyoxazole as a pale yellow liquid.

Yield: 78 %

B.p: 100-102 °C, 10 torr.

UV/Vis: (CH_3CN, c = 1.64 x 10^{-4} mol/l, d = 1 cm)

λ_{max} (nm, log ε) = 234 (4.15), 245 (3.94).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2972, 1672, 1567, 1480, 1395, 1332, 995.

^{1}H-NMR: (300 MHz, $CDCl_3$)

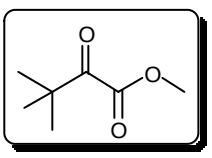
δ_{ppm} = 1.24 (s, 9H, $3CH_3$), 1.94 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.8 (q, CH_3), 28.2 (q, $3CH_3$), 33.5 (s, Cq), 60.9 (q, OCH_3), 110.6 (s, C-4), 154.2 (s, C-5), 161.4 (s, C-2).

4.18 Synthesis of a -keto ester substrates

Synthesis of methyl trimethyl pyruvate (50)[130] (sbo-466)



3,3-Dimethyl-2-butanone (10 g, 0.1 mol) was rapidly added to $KMnO_4$ (31.6 g, 0.2 mol) in 750 mL of water containing 10g of sodium hydroxide at room temperature. The mixture was

stirred for 5h, then filtered on a Büchner funnel (eliminating MnO_2) and concentrated until one-fifth of the initial volume remained. Concentrated HCl (38 mL) was slowly added in small amounts. The supernatant oily liquid was decanted and the aqueous layer was salted out with sodium chloride and concentrated. The obtained ketoacid was stirred with 15 g of methanol and 7.5 g of conc. H_2SO_4. The mixture was heated under reflux for 2h. After cooling, the mixture was decanted, extracted three times with pentane, and the organic layer was neturalized with 5% sodium bicarbonate solution and dried over sodium sulfate. The solvents were evapourated under reduced pressure and the ketoester was distilled to give 7.5 g of pure methyl trimethylpyruvate.

Yield: 70 %

B.p: 65-67 °C, 10 torr (Lit.,[130] 68-70 °C, 1o torr).

UV/Vis: (CH_3CN, c = 1.64 x 10^{-4} mol/l, d = 1 cm)

λ_{max} (nm, log ε) = 352 (2.18), 296 (3.34).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2974, 2875, 1742, 1716, 1480, 1463, 1435, 1368, 833.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.20 (s, 9H, $3CH_3$), 3.79 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

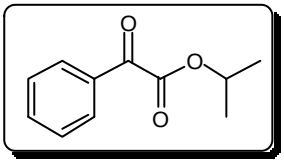
δ_{ppm} = 25.6 (q, $3CH_3$), 42.5 (s, Cq), 52.1 (q, OCH_3), 163.9 (s, COO), 201.6 (s, CO).

Anal: ($C_7H_{12}O_3$, M = 144.2 g/mol)

Calcd: C 58.32 H 8.39

Found: C 58.15 H 8.17

Synthesis of isopropyl phenyl glyoxylate (51)[131b] (sbo-452)



To a stirring solution of benzoyl formic acid (2.60 g, 17.3 mmol) in 40 mL of dry benzene were added 4-(dimethylamino)pyridine (DMAP) (213 mg, 1.7 mmol) and 2.21 g, 35 mmol of isopropyl alcohol and N,N-dicyclohexylcarbodiimide (DCC) (3.57 g, 17.3 mmol) was added to the reaction mixture kept in ice-bath. The mixture was stirred in the ice bath for 10 min and then stirred at room temperature for another 10 h. Precipitated urea was filtered by vacuum filteration. The resulting solution was washed with water, 0.5N HCl, and saturated sodium

bicarbonate solution three times and chromatographed with eluent (ethylacetate/hexane, 1/5) to yield 2.74 g of pure isopropyl phenylglyoxylate as a colorless viscous oil.

Yield: 90 %

TLC: R_f = 0.45 (ethylacetate/n-hexane 1: 5)

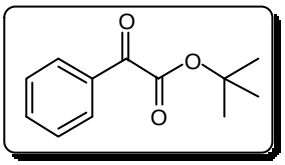
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.37 (d, J = 6.3Hz, 6H, $2CH_3$), 5.30 (septet, J = 6.3 Hz, 1H, CH), 7.43 (m, 2H, H_{arom}), 7.59 (m, 1H, H_{arom}), 7.99 (d, J = 6.0 Hz, 2H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.6 (q, $2CH_3$), 70.6 (d, OCH), 128.8 (d, CH_{arom}), 129.8 (d, CH_{arom}), 132.4 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 163.6 (s, COO), 186.6 (s, CO).

Synthesis of *tert*-butyl phenylglyoxylate (52)[131a] (sbo-440)



To a stirring solution of benzoyl formic acid (2.60 g, 17.3 mmol) in 40 mL of dry benzene were added 4-(dimethylamino)pyridine (DMAP) (213 mg, 1.7 mmol) and 2.22 g, 30 mmol of *tert*-butyl alcohol and N,N-dicyclohexylcarbodiimide (DCC) (3.57 g, 17.3 mmol) was added to the reaction mixture kept in ice-bath. The mixture was stirred in the ice bath for 10 min and then stirred at room temperature for another 10 h. Precipitated urea was filtered by vacuum filteration. The resulting solution was washed with water, 0.5N HCl, and saturated sodium bicarbonate solution, dried ($MgSO_4$). After removal of the solvent under vacum, the residue was purified by columm chromatography using a mixture of ethyl acetate and n-hexane as eluent to give 3.54 g of *tert*-butyl phenylglyoxylate as a colorless viscous oil.

Yield: 92 %

TLC: R_f = 0.42 (ethylacetate/n-hexane 1: 10)

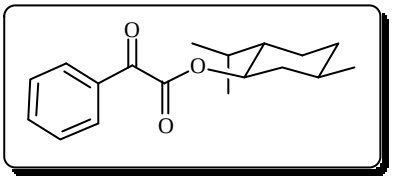
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.63 (s, 9H, $3CH_3$), 7.50 (t, J = 6.0 Hz, 2H, H_{arom}), 7.64 (t, J = 6.0 Hz, 1H, H_{arom}), 7.79 (d, J = 6.0 Hz, 2H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 27.9 (q, $3CH_3$), 84.6 (s, C_q), 128.7 (d, CH_{arom}), 129.7 (d, CH_{arom}), 132.4 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 163.6 (s, COO), 186.7 (s, CO).

Synthesis of (-)-menthyl phenylglyoxylate (53)[132] (sbo-360)



Oxalyl chloride (9.45 mL, 0.11 mol) in acetonitrile (10 mL) is added dropwise to a solution of dimethylformamide (25 mL) in acetonitrile (120 mL) at –15°C under nitrogen. After 15min, phenyl glyoxylic acid (15.0 g, 0.1 mol) is added with stirring and stirring is continued until the precipitate dissolves (~30 min). Menthol (15.6 g, 0.1 mol) dissolved in acetonitrile (15 mL) is added and the mixture is stirred at room temperature for 6h. The mixture is then cooled to 0°C, pyridine (15 mL) in acetonitrile (30 mL) is added dropwise, and the mixture is stirred for 1h. Dichloromethane (300 mL) is added, the solution is washed with sodium carbonate solution (300 mL), extracted with dichloromethane (300mL). The extract is dried with magnesium sulfate and the solvent is evaporated. The residue is cooled to – 25°C and mixed with an equal volume of 1/1 ether/pentane. After 5-10 h, the crystals are filtered, washed with pentane and the mother liquor is again evaporated and collected to give 24.5 g of menthyl phenylglyoxylate as a colorless needles.

Yield: 85 %

M.p: 64-67°C.

UV/Vis: (CH_3CN, c = 1.60 x 10^{-5} mol/l, d = 1 cm)

λ_{max} (nm, log ε) = 348 (2.34), 310 (3.49).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2957, 2937, 2900, 2876, 1733, 1685, 1594, 1450, 1387, 1296, 1177, 980.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.9 Hz, 3H, CH_3), 0.89 (d, J = 6.9 Hz, 3H, CH_3), 0.95 (d, J = 6.5 Hz, 3H, CH_3), 1.10 (m, 1H, CH), 1.20 (m, 1H, CH), 1.53 (m, 2H, CH_2), 1.73 (m, 2H, CH_2), 2.19 (m, 1H, CH), 4.98 (ddd, J = 11.0, 4.6, 4.4 Hz, 1H, OCH), 7.49 (m, 2H, H_{arom}), 7.65 (m, 1H, H_{arom}), 7.97 (m, 2H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.2 (q, CH_3), 20.7 (q, CH_3), 22.0 (q, CH_3), 23.4 (t, CH_2), 26.2 (d, CH), 31.6 (d, CH), 40.6 (t, CH_2), 46.8 (d, CH), 77.0 (d, OCH), 128.9 (d, CH_{arom}), 129.9 (d, CH_{arom}), 132.6 (s, Cq_{arom}), 163.9 (s, COO), 186.8 (s, CO).

Anal: ($C_{18}H_{24}O_3$, M = 288.38 g/mol)

Calcd: C 74.97 H 8.39

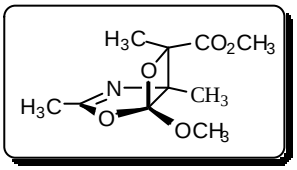
Found: C 74.89 H 8.31

4.19 Photolyses of a -keto esters with 5-methoxyoxazoles; General procedure:

Under a nitrogen atmosphere, a solution of α-keto ester substrates (5 mmol) and 5-methoxyoxazole substrates (5 mmol) in 50 mL of benzene was irradiated in a Rayonet photoreactor (350 nm) at 10°C for 24. The solvent was evaporated in *vacuo*, and the residue was analyzed by ^{1}H-NMR spectroscopy to determine the diastereoselectivity. Purification was carried out by preparative chromatography using silica gel which was firstly neutralized by elution with 1% TEA/CH_2Cl_2. The thermally and hydrolytically unstable primary products could in most cases not be characterized by combustion analysis and were hydrolyzed subsequently to the more stable α-amino-β-hydroxy esters.

Photolyses of methyl pyruvate with 5-methoxyoxazoles 36a-f:

5-Methoxy-1,3,7-trimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (55a) (sbo-494c)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.62 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 0.98 g of a yellow oil. Preparative chromatography on silica gel yielded 0.85 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 74 %

TLC: R_f = 0.37 (ethylacetate/n-hexane 1: 4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2989, 2895, 1725, 1610, 1600, 1445, 1095, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.22 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 3.56 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

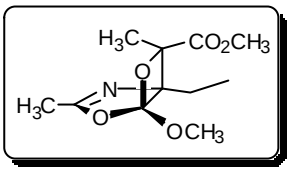
δ_{ppm} = 14.6 (q, CH_3), 14.9 (q, CH_3), 18.0 (q, CH_3), 51.8 (q, OCH_3), 52.4 (q, OCH_3), 76.0 (s, C-7), 88.7 (s, C-1), 123.9 (s, C-5), 166.2 (s, C-3), 171.5 (s, COO).

HRMS: ($C_{10}H_{15}NO_5$, M = 229.10 g/mol)

Calcd: 229.0946

Found: 229.0941

1-Ethyl-5-methoxy-3,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (55b) (sbo-399e)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 0.96 g of a yellow oil. Preparative chromatography on silica gel yielded 0.80 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 66 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

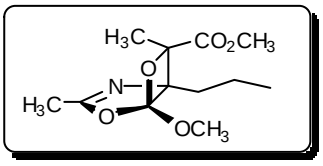
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (t, J = 7.5 Hz, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.58 (m, 1H, CH), 1.68 (m, 1H, CH), 2.13 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.7 (q, CH_3), 14.9 (q, CH_3), 19.9 (q, CH_3), 21.6 (t, CH_2), 51.7 (q, OCH_3), 52.4 (q, OCH_3), 79.5 (s, C-7), 89.0 (s, C-1), 124.0 (s, C-5), 166.3 (s, C-3), 171.7 (s, COO).

5-Methoxy-3,7-dimethyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (55c) (sbo-405b)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general

procedure to give 1.1 g of a yellow oil. Preparative chromatography on silica gel yielded 0.92 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 73 %

TLC: R_f = 0.33 (ethyl acetate/n-hexane 1:4).

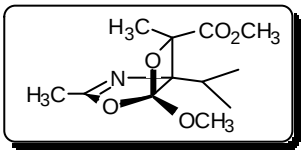
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (t, J = 7.5 Hz, 3H, CH_3), 1.33 (t, J = 7.1 Hz, 2H, CH_2), 1.47 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.14 (sextet, J = 7.5 Hz, 2H, CH_2), 3.74 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.6 (q, CH_3), 16.0 (q, CH_3), 22.4 (q, CH_3), 23.4 (t, CH_2), 34.6 (t, CH_2), 52.3 (q, OCH_3), 52.4 (q, OCH_3), 63.6 (s, C-7), 73.3 (s, C-1), 124.2 (s, C-5), 165.2 (s, C-3), 168.4 (s, COO).

1-Isopropyl-5-methoxy-3,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (55d) (sbo-406)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.0 g of a yellow oil. Preparative chromatography on silica gel yielded 0.75 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 60 %

TLC: R_f = 0.37 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (d, J = 6.6 Hz, 3H, CH_3), 1.01 (d, J = 6.6 Hz, 3H, CH_3), 1.23 (septet, J = 6.6 Hz, 1H, CH), 1.55 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

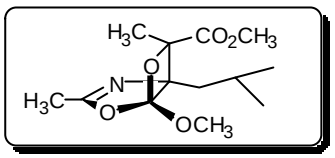
δ_{ppm} = 14.6 (q, CH_3), 16.4 (q, CH_3), 16.9 (q, CH_3), 19.2 (q, CH_3), 27.5 (d, CH), 51.3 (q, OCH_3), 52.3 (q, OCH_3), 82.8 (s, C-7), 90.2 (s, C-1), 124.1 (s, C-5), 166.4 (s, C-3), 171.8 (s, COO).

HRMS: ($C_{12}H_{19}NO_5$, M = 257.13 g/mol)

Calcd: 257.1374

Found: 257.1371

1-Isobutyl-5-methoxy-3,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (55e) (sbo-407d)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.12 g of a yellow oil. Preparative chromatography on silica gel yielded 0.98 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 72 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

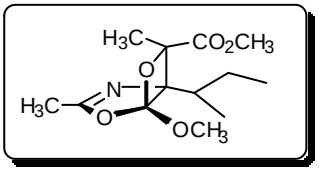
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (d, J = 6.6 Hz, 3H, CH_3), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 1.00 (m, 1H, CH), 1.18 (m, 2H, CH_2), 1.46 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.9 (q, CH_3), 18.8 (q, CH_3), 22.2 (q, CH_3), 23.9 (q, CH_3), 27.8 (d, CH), 36.1 (t, CH_2), 51.7 (q, OCH_3), 52.4 (q, OCH_3), 78.9 (s, C-7), 89.3 (s, C-1), 124.1 (s, C-5), 165.6 (s, C-3), 171.7 (s, COO).

1-*sec*-Butyl-5-methoxy-3,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (55f) (sbo-408b)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.0 g of a yellow oil. Preparative chromatography on silica gel yielded 0.92

g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 68 %

TLC: R_f = 0.42 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

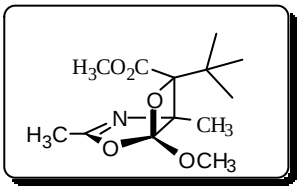
δ_{ppm} = 0.76 (t, J = 6.8 Hz, 3H, CH_3), 0.90 (d, J = 6.6 Hz, 3H, CH_3), 1.47 (m, 2H, CH_2), 1.48 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 3.67 (m, 1H, CH), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.3 (q, CH_3), 12.6 (q, CH_3), 14.8 (q, CH_3), 19.3 (q, CH_3), 23.8 (t, CH_2), 34.3 (d, CH), 51.5 (q, OCH_3), 52.4 (q, OCH_3), 83.5 (s, C-7), 90.4 (s, C-1), 124.2 (s, C-5), 165.8 (s, C-3), 171.9 (s, COO).

Photolyses of methyl trimethylpyruvate with 5-methoxyoxazoles 36a-f:

7-*tert*-Butyl-5-methoxy-1,3-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (56a) (sbo-480a)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.32 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.58 g of a yellow oil. Preparative chromatography on silica gel yielded 0.5 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 74 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.03 (s, 3H, CH_3), 1.11 (s, 9H, $3CH_3$), 1.49 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 3.56 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

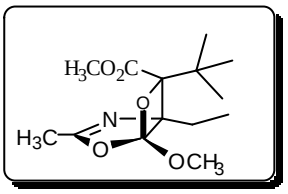
δ_{ppm} = 14.7 (q, CH_3), 15.6 (q, CH_3), 25.7 (q, $3CH_3$), 36.6 (s, Cq), 51.3 (q, OCH_3), 51.7 (q, OCH_3), 86.8 (s, C-1), 87.1 (s, C-7), 122.2 (s, C-5), 168.1 (s, C-3), 176.0 (s, COO).

HRMS: ($C_{13}H_{21}NO_5$, M = 271.14 g/mol)

Calcd: 271.1381

Found: 271.1386

7-*tert*-Butyl-1-ethyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (56b) (sbo-390)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.35 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.63 g of a yellow oil. Preparative chromatography on silica gel yielded 0.6 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 84 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

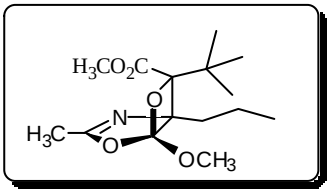
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.77 (t, J = 7.5 Hz, 3H, CH_3), 0.94 (m, 2H, CH_2), 1.04 (s, 9H, $3CH_3$), 1.99 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.0 (q, CH_3), 14.6 (q, CH_3), 21.8 (q, $3CH_3$), 27.0 (s, Cq), 33.7 (t, CH_2), 34.6 (s, Cq), 51.6 (q, OCH_3), 53.1 (q, OCH_3), 80.6 (s, C-1), 81.2 (s, C-7), 122.9 (s, C-5), 166.2 (s, C-3), 171.8 (s, COO).

7-*tert*-Butyl-5-methoxy-3-methyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (56c) (sbo-389)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.38 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.68 g of a yellow oil. Preparative chromatography on silica gel yielded 0.52 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 70 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 4:1).

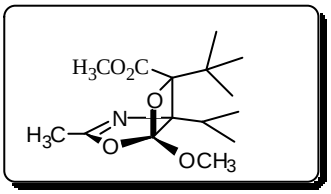
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 0.98 (t, J = 7.1 Hz, 2H, CH_2), 1.05 (s, 9H, $3CH_3$), 1.55 (m, 1H, CH), 1.78 (m, 1H, CH), 2.11 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.3 (q, CH_3), 14.6 (q, CH_3), 21.4 (q, CH_3), 25.8 (q, $3CH_3$), 27.3 (t, CH_2), 36.7 (t, CH_2), 38.2 (s, Cq), 50.8 (q, OCH_3), 51.3 (q, OCH_3), 92.3 (s, C-1), 97.3 (s, C-7), 123.9 (s, C-5), 165.6 (s, C-3), 172.1 (s, COO).

7-*tert*-Butyl-1-isopropyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (56e) (sbo-574)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.38 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.63 g of a yellow oil. Preparative chromatography on silica gel yielded 0.51 g of oxetane as a colorless oil.

Yield: 69 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

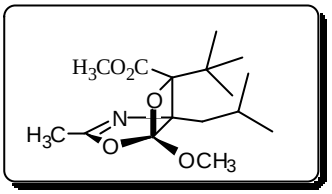
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (d, J = 6.5 Hz, 3H, CH_3), 0.87 (d, J = 6.6 Hz, 3H, CH_3), 1.03 (s, 9H, $3CH_3$), 1.45 (m, 1H, CH), 2.12 (s, 3H, CH_3), 3.58 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.7 (q, CH_3), 16.6 (q, CH_3), 16.7 (q, CH_3), 26.1 (q, $3CH_3$), 27.2 (d, C), 36.7 (s, Cq), 50.5 (q, OCH_3), 51.8 (q, OCH_3), 90.7 (s, C-1), 94.2 (s, C-7), 124.1 (s, C-5), 168.2 (s, C-3), 173.4 (s, COO).

7-*tert*-Butyl-1-isobutyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (56e) (sbo-575)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 2-isobutyl-4-methyl-5-methoxyoxazole (0.42 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.68 g of a yellow oil. Preparative chromatography on silica gel yielded 0.55 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 70 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.85 (d, J = 6.8 Hz, 3H, CH_3), 0.92 (d, J = 6.9 Hz, 3H, CH_3), 1.08 (s, 9H, $3CH_3$), 1.52 (m, 1H, CH), 1.78 (m, 2H, CH_2), 2.07 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

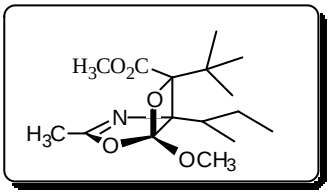
δ_{ppm} = 13.4 (q, CH_3), 18.9 (q, CH_3), 19.4 (q, CH_3), 25.8 (q, $3CH_3$), 27.3 (d, CH), 39.7 (s, Cq), 40.2 (t, Cq), 51.2 (q, OCH_3), 51.8 (q, OCH_3), 92.4 (s, C-1), 96.2 (s, C-7), 124.4 (s, C-5), 169.2 (s, C-3), 173.4 (s, COO).

HRMS: ($C_{16}H_{27}NO_5$, M = 313.19 g/mol)

Calcd: 313.1927

Found: 313.1924

7-*tert*-Butyl-1-*sec*-butyl-5-methoxy-3-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (56f) (sbo-576)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.42 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.68 g of a yellow oil. Preparative chromatography on silica gel yielded 0.54 g of oxetane as a colorless oil.

Yield: 69 %

TLC: R_f = 0.34 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

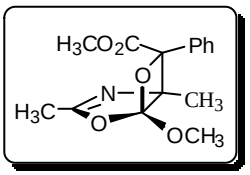
δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 1.00 (d, J = 7.4 Hz, 3H, CH_3), 1.05 (s, 9H, $3CH_3$), 1.23 (m, 2H, CH_2), 1.56 (m, 1H, CH), 2.06 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.3 (q, CH_3), 14.6 (q, CH_3), 21.4 (q, CH_3), 25.8 (q, $3CH_3$), 26.2 (t, CH_2), 28.7 (d, CH), 38.2 (s, Cq), 50.2 (q, OCH_3), 51.9 (q, OCH_3), 90.6 (s, C-1), 95.8 (s, C-7), 124.0 (s, C-5), 167.6 (s, C-3), 173.4 (s, COO).

Photolyses of methyl phenylglyoxylate with 5-methoxyoxazoles 36a-f:

***exo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-58a)** (sbo-35a)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.62 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.23 g of a yellow oil. Preparative chromatography on silica gel yielded 0.75 g of the *exo*-isomer (and 0.4 g of the *endo*-isomer) as a colorless oil.The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 51 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2994, 2898, 1728, 1615, 1605, 1550, 1440, 1065, 980, 775.

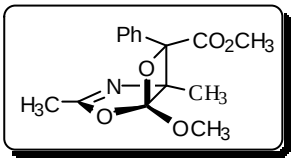
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.09 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 7.23-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.7 (q, CH_3), 28.1 (q, CH_3), 51.8 (q, OCH_3), 52.6 (q, OCH_3), 82.3 (s, C-1), 91.5 (s, C-7), 123.3 (s, C-5), 125.6 (d, CH_{arom}), 126.2 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 165.5 (s, C-3), 169.6 (s, COO).

***endo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-58a)** (sbo-359)



Yield: 28 %

TLC: R_f = 0.50 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.53 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 3.68 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.23-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

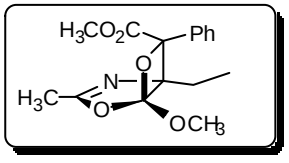
δ_{ppm} = 14.7 (q, CH_3), 26.4 (q, CH_3), 51.9 (q, OCH_3), 52.7 (q, OCH_3), 80.4 (s, C-1), 90.2 (s, C-7), 124.1 (s, C-5), 126.5 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 166.6 (s, C-3), 172.4 (s, COO).

HRMS: ($C_{15}H_{17}NO_5$, M = 291.11 g/mol)

Calcd: 291.1123

Found: 291.1118

***exo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-58b)** (sbo-368)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.35 g of a yellow oil. Preparative chromatography on silica gel yielded 0.8 g of the *exo*-isomer (and 0.35 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 52 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

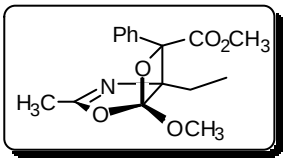
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (t, J = 7.5 Hz, 3H, CH_3), 1.00 (m, 1H, CH), 1.26 (m, 1H, CH), 2.08 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 7.26-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.3 (q, CH_3), 14.3 (q, CH_3), 21.2 (t, CH_2), 51.7 (q, OCH_3), 52.6 (q, OCH_3), 82.1 (s, C-1), 91.8 (s, C-7), 123.4 (s, C-5), 126.3 (d, CH_{arom}), 127.1 (d, CH_{arom}), 128.1 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 166.6 (s, C-3), 171.1 (s, COO).

***endo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-58b)** (sbo-368a)



Yield: 23 %

TLC: R_f = 0.57 (ethyl acetate/n-hexane 1:4).

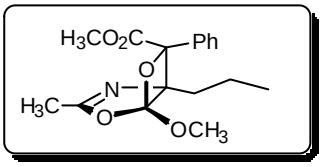
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (t, J = 7.5 Hz, 3H, CH_3), 1.55 (m, 1H, CH), 1.72 (s, 3H, CH_3), 1.87 (m, 1H, CH), 3.74 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 7.21-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.2 (q, CH_3), 14.8 (q, CH_3), 23.9 (t, CH_2), 52.7 (q, OCH_3), 53.1 (q, OCH_3), 84.4 (s, C-1), 92.1 (s, C-7), 124.1 (s, C-5), 126.1 (d, CH_{arom}), 127.1 (d, CH_{arom}), 128.1 (d, CH_{arom}), 137.6 (s, Cq_{arom}), 169.1 (s, C-3), 173.0 (s, COO).

***exo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicylo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-58c)** (sbo-361a)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.40 g of a yellow oil. Preparative chromatography on silica gel yielded 0.82 g of the *exo*-isomer (and 0.42 g of the *endo*-isomer) as a colorless oil.The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 52 %

TLC: R_f = 0.35 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (t, J = 7.1 Hz, 3H, CH_3), 1.25 (m, 2H, CH_2), 1.52 (m, 2H, CH_2), 2.08 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 7.25-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

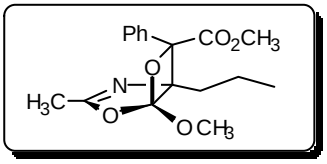
δ_{ppm} = 14.0 (q, CH_3), 14.4 (q, CH_3), 16.4 (t, CH_2), 30.5 (t, CH_2), 51.6 (q, OCH_3), 52.7 (q, OCH_3), 83.0 (s, C-1), 92.6 (s, C-7), 123.3 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 165.7 (s, C-3), 168.2 (s, COO).

HRMS: ($C_{17}H_{21}NO_5$, M = 319.14 g/mol)

Calcd: 319.1367

Found: 319.1363

***endo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicylo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-58c)** (sbo-361d)



Yield: 27 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

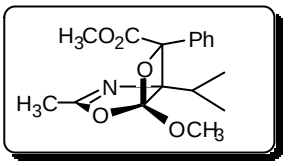
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.87 (t, J = 7.5 Hz, 3H, CH_3), 1.32 (m, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.95 (m, 2H, CH_2), 3.64 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 7.25-7.45 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.3 (q, CH_3), 17.0 (t, CH_2), 31.6 (t, CH_2), 51.9 (q, OCH_3), 52.7 (q, OCH_3), 81.6 (s, C-1), 91.0 (s, C-7), 123.8 (s, C-5), 126.4 (d, CH_{arom}), 127.8 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 165.2 (s, C-3), 169.9 (s, COO).

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-58d)** (sbo-362)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.42 g of a yellow oil. Preparative chromatography on silica gel yielded 0.76 g of the *exo*-isomer (and 0.48 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 48 %

TLC: R_f = 0.33 (ethyl acetate/n-hexane 1:4).

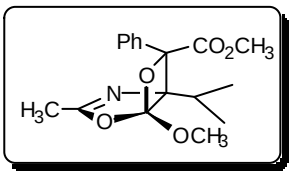
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (d, J = 6.6 Hz, 3H, CH_3), 0.88 (d, J = 6.8 Hz, 3H, CH_3), 0.98 (septet, J = 6.8 Hz, 1H, CH), 2.04 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.33-7.62 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.3 (q, CH_3), 23.1 (q, CH_3), 25.5 (q, CH_3), 27.1 (d, CH), 52.1 (q, OCH_3), 52.8 (q, OCH_3), 82.7 (s, C-1), 90.7 (s, C-7), 124.1 (s, C-5), 127.2 (d, CH_{arom}), 128.0 (d, CH_{arom}), 128.7 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 166.1 (s, C-3), 168.2 (s, COO).

***endo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-58d)** (sbo-362a)



Yield: 31 %

TLC: R_f = 0.33 (ethyl acetate/n-hexane 1:4).

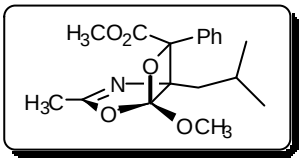
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.89 (d, J = 6.9 Hz, 3H, CH_3), 1.23 (d, J = 6.8 Hz, 3H, CH_3), 1.28 (septet, J = 6.8 Hz, 1H, CH), 1.78 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 7.27-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 17.3 (q, CH_3), 17.4 (q, CH_3), 27.8 (d, CH), 51.8 (q, OCH_3), 52.3 (q, OCH_3), 85.7 (s, C-1), 92.1 (s, C-7), 123.5 (s, C-5), 126.7 (d, CH_{arom}), 127.7 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.4 (s, Cq_{arom}), 165.7 (s, C-3), 169.1 (s, COO).

***exo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-58e)** (sbo-366a)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.82 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.55 g of a yellow oil. Preparative chromatography on silica gel yielded 0.84 g of the *exo*-isomer (and 0.42 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 50 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:4).

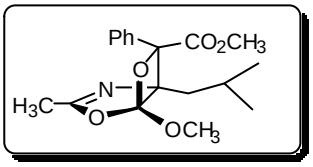
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.64 (d, J = 6.7 Hz, 3H, CH_3), 0.74 (d, J = 6.6 Hz, 3H, CH_3), 0.78 (m, 1H, CH), 1.35 (dd, J = 13.4, 5.7 Hz, 1H, CH), 2.08 (s, 3H, CH_3), 2.33 (dd, J = 13.4, 6.1 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 7.27-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.8 (q, CH_3), 22.7 (q, CH_3), 23.6 (q, CH_3), 25.7 (d, CH), 36.6 (t, CH_2), 52.5 (q, OCH_3), 53.3 (q, OCH_3), 81.9 (s, C-2), 91.8 (s, C-7), 123.4 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 165.8 (s, C-3), 169.2 (s, COO).

***endo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-58e)** (sbo-366c)



Yield: 25 %

TLC: R_f = 0.59 (ethyl acetate/n-hexane 1:4).

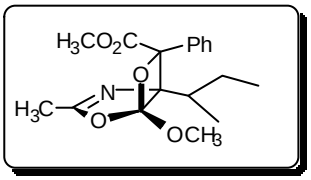
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.80 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.06 (m, 1H, CH), 1.62 (dd, J = 14.2, 7.8 Hz, 1H, CH), 1.73 (s, 3H, CH_3), 2.07 (dd, J = 14.2, 4.7 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 7.24-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 23.0 (q, CH_3), 24.2 (q, CH_3), 24.3 (d, CH), 37.2 (t, CH_2), 51.9 (q, OCH_3), 52.7 (q, OCH_3), 81.8 (s, C-1), 90.9 (s, C-7), 123.8 (s, C-5), 126.4 (d, CH_{arom}), 127.8 (d, CH_{arom}), 129.9 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 164.7 (s, C-3), 169.9 (s, COO).

***exo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methylester (*exo*-58f)** (sbo-367a)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.50 g of a yellow oil. Preparative chromatography on silica gel yielded 0.8 g of the *exo*-isomer (and 0.39 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 48 %

TLC: R_f = 0.59 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.50 (t, J = 7.4 Hz, 3H, CH_3), 0.68 (quintet, J = 7.4 Hz, 2H, CH_2), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 1.35 (m, 1H, CH), 2.09 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 7.26-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

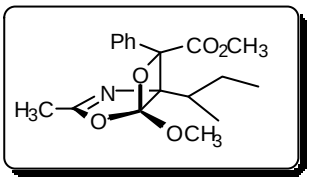
δ_{ppm} = 11.3 (q, CH_3), 13.7 (q, CH_3), 14.6 (q, CH_3), 25.0 (d, CH), 37.2 (t, CH_2), 52.3 (q, OCH_3), 53.3 (q, OCH_3), 86.5 (s, C-1), 93.2 (s, C-7), 123.3 (s, C-5), 126.9 (d, CH_{arom}), 127.4 (d, CH_{arom}), 128.8 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 166.7 (s, C-3), 169.0 (s, COO).

HRMS: ($C_{18}H_{23}NO_5$, M = 333.16 g/mol)

Calcd: 333.1578

Found: 333.1572

***endo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methylester (*endo*-58f)** (sbo-367d)



Yield: 24 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

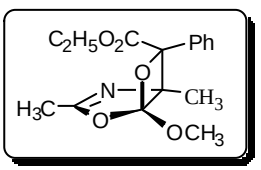
δ_{ppm} = 0.86 (d, J = 6.8 Hz, 3H, CH_3), 0.94 (t, J = 7.5 Hz, 3H, CH_3), 1.25 (m, 1H, CH), 1.77 (s, 3H, CH_3), 1.93 (m, 2H, CH_2), 3.71 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.27-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.2 (q, CH_3), 13.3 (q, CH_3), 14.3 (q, CH_3), 24.3 (d, CH), 34.8 (t, CH_2), 51.9 (q, OCH_3), 52.9 (q, OCH_3), 86.3 (s, C-1), 92.4 (s, C-7), 124.0 (s, C-5), 126.7 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.9 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 165.4 (s, C-3), 170.2 (s, COO).

<u>Photolyses of ethyl phenylglyoxylate with 5-methoxyoxazoles 36a-f:</u>

***exo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-60a)** (sbo-351)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general

procedure to give 1.42 g of a yellow oil. Preparative chromatography on silica gel yielded 0.65 g of the *exo*-isomer (and 0.41 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 43 %

TLC: R_f = 0.39 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.06 (s, 3H, CH_3), 1.24 (t, J = 7.2 Hz, 3H, CH_3), 2.06 (s, 3H, CH_3), 3.63 (s, 3H, OCH_3), 4.21 (q, J = 7.2 Hz, 2H, OCH_2), 7.23-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

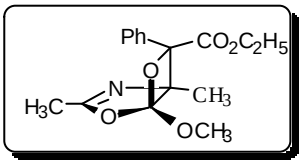
δ_{ppm} = 13.8 (q, CH_3), 14.0 (q, CH_3), 15.6 (q, CH_3), 51.7 (q, OCH_3), 61.7 (t, OCH_2), 78.4 (s, C-1), 90.4 (s, C-7), 123.3 (s, C-5), 126.2 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 166.3 (s, C-3), 168.5 (s, COO).

HRMS: ($C_{16}H_{19}NO_5$, M = 305.13 g/mol)

Calcd: 305.1271

Found: 305.1268

***endo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-60a)** (sbo-351b)



Yield: 27 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

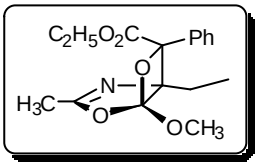
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.27 (t, J = 7.2 Hz, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.22 (q, J = 7.2 Hz, 2H, OCH_2), 7.27-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.3 (q, CH_3), 15.7 (q, CH_3), 52.1 (q, OCH_3), 61.9 (t, OCH_2), 78.5 (s, C-1), 90.5 (s, C-7), 123.7 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 166.3 (s, C-3), 168.5 (s, COO).

***exo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-60b)** (sbo-371a)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.39 g of a yellow oil. Preparative chromatography on silica gel yielded 0.68 g of the *exo*-isomer (and 0.38 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.35 (ethyl acetate/n-hexane 1:4).

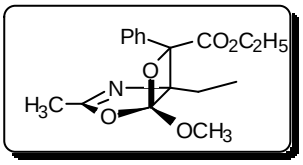
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25 (t, J = 7.5 Hz, 6H, $2CH_3$), 1.58 (q, J = 7.5 Hz, 2H, CH_2), 2.09 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.23 (q, J = 7.5 Hz, 2H, OCH_2), 7.25-7.71 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.3 (q, CH_3), 9.8 (q, CH_3), 14.1 (q, CH_3), 28.8 (t, CH_2), 51.7 (q, OCH_3), 61.8 (t, OCH_2), 82.1 (s, C-1), 86.9 (s, C-7), 123.4 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 165.4 (s, C-3), 166.4 (s, COO).

***endo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-60b)** (sbo-371b)



Yield: 24 %

TLC: R_f = 0.55 (ethyl acetate/n-hexane 1:4).

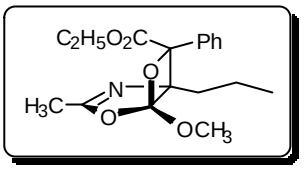
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.5 Hz, 3H, CH_3), 1.27 (t, J = 7.2 Hz, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.85 (sextet, J = 7.5 Hz, 1H, CH), 2.08 (sextet, J = 7.5 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 4.22 (q, J = 7.2 Hz, 2H, OCH_2), 7.27-7.31 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.0 (q, CH_3), 14.0 (q, CH_3), 14.3 (q, CH_3), 22.6 (t, CH_2), 51.9 (q, OCH_3), 61.9 (t, OCH_2), 81.9 (s, C-1), 90.9 (s, C-7), 123.8 (s, C-5), 126.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 129.0 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 165.4 (s, C-3), 169.3 (s, COO).

***exo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-60c)** (sbo-354a)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.49 g of a yellow oil. Preparative chromatography on silica gel yielded 0.73 g of the *exo*-isomer (and 0.37 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 44 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

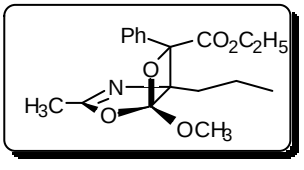
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (t, J = 6.8 Hz, 3H, CH_3), 0.92 (t, J = 7.5 Hz, 3H, CH_3), 1.47 (m, 2H, CH_2), 2.06 (s, 3H, CH_3), 2.33 (m, 2H, CH_2), 3.64 (s, 3H, OCH_3), 4.20 (q, J = 7.5 Hz, 2H, OCH_2), 7.25-7.67 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 14.1 (q, CH_3), 14.8 (q, CH_3), 16.4 (t, CH_2), 30.7 (t, CH_2), 51.6 (q, OCH_3), 61.7 (t, OCH_2), 86.4 (s, C-1), 92.5 (s, C-7), 123.4 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 165.3 (s, C-3), 168.2 (s, COO).

***endo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-60c)** (sbo-354)



Yield: 23 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

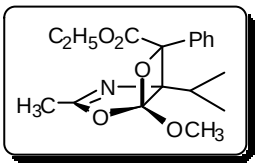
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (t, J = 6.9 Hz, 3H, CH_3), 0.93 (t, J = 7.5 Hz, 3H, CH_3), 1.49 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.25 (q, J = 7.5 Hz, 2H, OCH_2), 7.27-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.3 (q, CH_3), 14.9 (q, CH_3), 16.5 (t, CH_2), 31.2 (t, CH_2), 51.7 (q, OCH_3), 61.8 (t, OCH_2), 84.3 (s, C-1), 91.7 (s, C-7), 123.7 (s, C-5), 127.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 166.0 (s, C-3), 169.1 (s, COO).

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-60d)** (sbo-352b)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.44 g of a yellow oil. Preparative chromatography on silica gel yielded 0.69 g of the *exo*-isomer (and 0.35 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2983, 2895, 1725, 1612, 1600, 1558, 1435, 1085, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.66 (d, J = 6.8 Hz, 3H, CH_3), 0.86 (d, J = 6.6 Hz, 3H, CH_3), 1.16 (septet, J = 6.8 Hz, 1H, CH), 1.29 (t, J = 6.8 Hz, 3H, CH_3), 2.08 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 4.25 (q, J = 6.8 Hz, 2H, OCH_2), 7.33-7.82 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.7 (q, CH_3), 15.9 (q, CH_3), 16.5 (q, CH_3), 25.9 (d, CH), 51.6 (q, OCH_3), 61.6 (t, OCH_2), 86.0 (s, C-1), 92.9 (s, C-7), 123.3 (s, C-5), 127.2 (d,

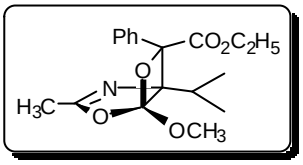
CH_{arom}), 128.0 (d, CH_{arom}), 128.7 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 166.0 (s, C-3), 168.3 (s, COO).

HRMS: ($C_{18}H_{23}NO_5$, M = 333.16 g/mol)

Calcd: 333.1570

Found: 333.1561

***endo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-60d)** (sbo-352d)



Yield: 21 %

TLC: R_f = 0.57 (ethyl acetate/n-hexane 1:4).

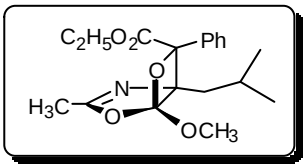
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 3H, CH_3), 1.24 (d, J = 6.8 Hz, 3H, CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.27 (septet, J = 6.6 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 4.22 (q, J = 7.2 Hz, 2H, OCH_2), 7.25-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 14.3 (q, CH_3), 17.4 (q, CH_3), 17.4 (q, CH_3), 27.8 (d, CH), 51.8 (q, OCH_3), 61.9 (t, OCH_2), 86.3 (s, C-1), 91.9 (s, C-7), 123.9 (s, C-5), 126.7 (d, CH_{arom}), 127.7 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.4 (s, Cq_{arom}), 165.4 (s, C-3), 169.6 (s, COO).

***exo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-60e)** (sbo-355a)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.60 g of a yellow oil. Preparative chromatography on silica gel yielded 0.75 g of the *exo*-isomer (and 0.37 g of the *endo*-isomer) as a colorless oil. The

products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 43 %

TLC: R_f = 0.34 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (d, J = 6.6 Hz, 3H, CH_3), 0.72 (d, J = 6.6 Hz, 3H, CH_3), 1.27 (t, J = 7.5 Hz, 3H, CH_3), 1.56 (m, 2H, CH_2), 1.58 (m, 1H, CH), 2.04 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 4.22 (q, J = 7.5 Hz, 2H, OCH_2), 7.26-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

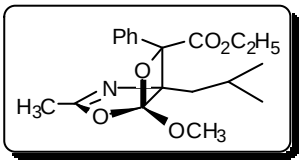
δ_{ppm} = 13.8 (q, CH_3), 14.0 (q, CH_3), 22.6 (q, CH_3), 23.5 (q, CH_3), 25.7 (d, CH), 36.5 (t, CH_2), 51.6 (q, OCH_3), 62.1 (t, OCH_2), 81.7 (s, C-2), 91.5 (s, C-3), 123.3 (s, C-5), 126.3 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.2 (s, Cq_{arom}), 165.5 (s, C-3), 169.9 (s, COO).

HRMS: ($C_{19}H_{25}NO_5$, M = 347.17 g/mol)

Calcd: 347.1717

Found: 347.1716

***endo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-60e)** (sbo-355d)



Yield: 21%

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

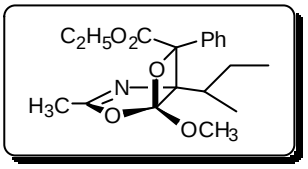
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (d, J = 6.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.18 (m, 1H, CH), 1.27 (t, J = 7.2 Hz, 3H, CH_3), 1.38 (m, 2H, CH_2), 1.72 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 4.24 (q, J = 7.5 Hz, 2H, OCH_2), 7.26-7.80 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 14.3 (q, CH_3), 22.9 (q, CH_3), 24.1 (q, CH_3), 24.2 (d, CH), 37.3 (t, CH_2), 51.9 (q, OCH_3), 61.8 (t, OCH_2), 81.8 (s, C-2), 90.8 (s, C-3), 123.8 (s, C-5), 126.4 (d, CH_{arom}), 127.8 (d, CH_{arom}), 129.9 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 164.7 (s, C-3), 169.3 (s, COO).

***exo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethylester (*exo*-60f)** (sbo-356b)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.62 g of a yellow oil. Preparative chromatography on silica gel yielded 0.71 g of the *exo*-isomer (and 0.36 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 41 %

TLC: R_f = 0.31 (ethyl acetate/n-hexane 1:4).

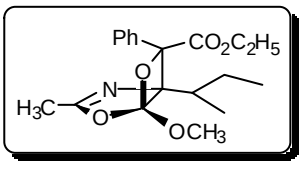
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.67 (t, J = 6.8 Hz, 3H, CH_3), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 1.23 (t, J = 7.5 Hz, 3H, CH_3), 1.31 (m, 2H, CH_2), 1.47 (m, 1H, CH), 2.08 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.25 (q, J = 7.5 Hz, 2H, OCH_2), 7.22-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.2 (q, CH_3), 12.1 (q, CH_3), 13.8 (q, CH_3), 14.2 (q, CH_3), 23.4 (d, CH), 32.6 (t, CH_2), 51.6 (q, OCH_3), 61.6 (t, OCH_2), 86.6 (s, C-1), 93.1 (s, C-7), 123.4 (s, C-5), 126.9 (d, CH_{arom}), 127.4 (d, CH_{arom}), 128.8 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 165.8 (s, C-3), 168.3 (s, COO).

***endo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethylester (*endo*-60f)** (sbo-356d)



Yield: 21 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

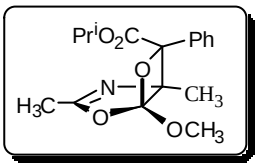
δ_{ppm} = 0.78 (d, J = 6.8 Hz, 3H, CH_3), 0.86 (t, J = 7.5 Hz, 3H, CH_3), 1.18 (t, J = 7.4 Hz, 3H, CH_3), 1.28 (m, 2H, CH_2), 1.69 (s, 3H, CH_3), 1.98 (m, 1H, CH), 3.64 (s, 3H, OCH_3), 4.24 (q, J = 7.5 Hz, 2H, OCH_2), 7.17-7.45 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.6 (q, CH_3), 13.2 (q, CH_3), 13.9 (q, CH_3), 14.2 (q, CH_3), 23.9 (d, CH), 34.5 (t, CH_2), 51.8 (q, OCH_3), 61.9 (t, OCH_2), 86.2 (s, C-1), 92.3 (s, C-7), 123.9 (s, C-5), 126.7 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.9 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 165.1 (s, C-3), 169.6 (s, COO).

Photolyses of isopropyl phenylglyoxylate with 5-methoxyoxazoles 36a-f:

***exo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-61a)** (sbo-582a)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.40 g of a yellow oil. Preparative chromatography on silica gel yielded 0.74 g of the *exo*-isomer (and 0.43 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 46 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

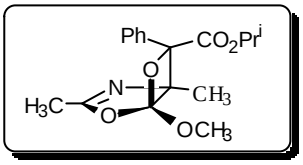
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.2 Hz, 3H, CH_3), 0.95 (d, J = 6.2 Hz, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 5.3 (septet, J = 6.2 Hz, 1H, OCH), 7.24-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.5 (q, CH_3), 15.9 (q, CH_3), 21.8 (q, CH_3), 21.9 (q, CH_3), 52.2 (q, OCH_3), 70.0 (d, OCH), 79.5 (s, C-1), 92.5 (s, C-7), 124.3 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 166.3 (s, C-3), 168.5 (s, COO).

***endo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-61a)** (sbo-582b)



Yield: 27 %

TLC: R_f = 0.45 (ethyl acetate/n-hexane 1:4).

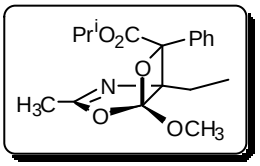
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.26 (d, J = 6.2 Hz, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 5.08 (septet, J = 7.2 Hz, 1H, OCH), 7.27-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 15.8 (q, CH_3), 21.6 (q, CH_3), 21.7 (q, CH_3), 52.0 (q, OCH_3), 69.9 (d, OCH), 78.5 (s, C-1), 90.5 (s, C-7), 123.7 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 165.3 (s, C-3), 168.6 (s, COO).

***exo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-61b)** (sbo-582c)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.50 g of a yellow oil. Preparative chromatography on silica gel yielded 0.7 g of the *exo*-isomer (and 0.38 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.35 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.6 Hz, 3H, CH_3), 0.97 (d, J = 6.8 Hz, 3H, CH_3), 1.12 (t, J = 7.2 Hz, 3H, CH_3), 1.43 (q, J = 7.2 Hz, 2H, CH_2), 2.09 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 5.02 (septet, J = 6.6 Hz, 1H, OCH), 7.25-7.71 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

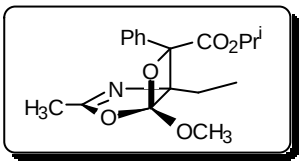
δ_{ppm} = 9.8 (q, CH_3), 14.1 (q, CH_3), 21.4 (q, CH_3), 21.8 (q, CH_3), 29.4 (t, CH_2), 51.7 (q, OCH_3), 71.0 (d, OCH), 82.2 (s, C-1), 86.5 (s, C-7), 123.6 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 165.4 (s, C-3), 167.4 (s, COO).

HRMS: ($C_{18}H_{23}NO_5$, M = 333.16 g/mol)

Calcd: 333.1639

Found: 333.1638

***endo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-61b)** (sbo-582d)



Yield: 23 %

TLC: R_f = 0.58 (ethyl acetate/n-hexane 1:4).

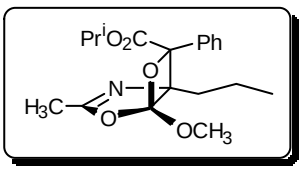
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.5 Hz, 3H, CH_3), 1.20 (d, J = 6.2 Hz, 3H, CH_3), 1.28 (d, J = 6.2 Hz, 3H, CH_3), 1.67 (m, 2H, CH_2), 1.72 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 5.28 (septet, J = 6.2 Hz, 1H, OCH), 7.27-7.31 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 14.3 (q, CH_3), 21.4 (q, CH_3), 21.8 (q, CH_3), 22.6 (t, CH_2), 51.9 (q, OCH_3), 70.4 (d, OCH), 81.9 (s, C-1), 90.9 (s, C-7), 123.8 (s, C-5), 126.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 129.0 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 165.4 (s, C-3), 169.3 (s, COO).

***exo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-61c)** (sbo-584b)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.56 g of a yellow oil. Preparative chromatography on silica

gel yielded 0.73 g of the *exo*-isomer (and 0.43 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 43 %

TLC: R_f = 0.42 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2990, 2893, 1745, 1610, 1600, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (t, J = 7.5 Hz, 3H, CH_3), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.47 (m, 2H, CH_2), 2.06 (s, 3H, CH_3), 2.33 (m, 2H, CH_2), 3.64 (s, 3H, OCH_3), 5.20 (septet, J = 6.2 Hz, 1H, OCH), 7.25-7.67 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 14.1 (q, CH_3), 16.4 (t, CH_2), 22.3 (q, CH_3), 22.6 (q, CH_3), 30.7 (t, CH_2), 51.6 (q, OCH_3), 71.5 (t, OCH), 86.4 (s, C-1), 92.5 (s, C-7), 123.4 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 165.3 (s, C-3), 168.2 (s, COO).

MS: (EI, 70 eV)

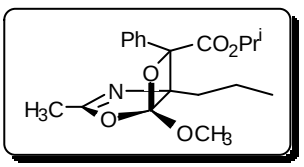
m/z (%) = 347 (M^+, 10), 305 (15), 262 (8), 260 (38), 173 (28), 155 (78), 130 (40), 105 (100), 102 (38), 91 (10), 77 (25), 71 (28), 57 (60).

HRMS: ($C_{19}H_{25}NO_5$, M = 347.17 g/mol)

Calcd: 347.1726

Found: 347.1721

***endo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-61c)** (sbo-584)



Yield: 25 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

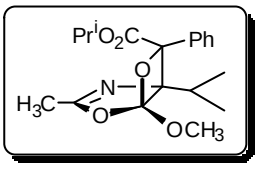
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (t, J = 6.9 Hz, 3H, CH_3), 1.23 (d, J = 6.2 Hz, 3H, CH_3), 1.28 (d, J = 6.2 Hz, 3H, CH_3), 1.49 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 1.73 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 5.15 (septet, J = 6.2 Hz, 1H, OCH), 7.27-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 14.9 (q, CH_3), 16.5 (t, CH_2), 22.4 (q, CH_3), 22.6 (q, CH_3), 31.2 (t, CH_2), 51.7 (q, OCH_3), 71.2 (d, OCH), 84.3 (s, C-1), 91.7 (s, C-7), 123.7 (s, C-5), 127.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 166.0 (s, C-3), 169.1 (s, COO).

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-61d)** (sbo-577a)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.49 g of a yellow oil. Preparative chromatography on silica gel yielded 0.7 g of the *exo*-isomer (and 0.4 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 41 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

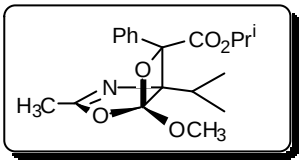
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.66 (d, J = 6.8 Hz, 3H, CH_3), 0.86 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.2 Hz, 3H, CH_3), 0.98 (d, J = 6.2 Hz, 3H, CH_3), 1.16 (septet, J = 6.8 Hz, 1H, CH), 2.08 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 5.25 (septet, J = 6.2 Hz, 1H, OCH), 7.33-7.82 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.7 (q, CH_3), 15.9 (q, CH_3), 16.5 (q, CH_3), 21.8 (q, CH_3), 22.0 (q, CH_3), 25.9 (d, CH), 51.6 (q, OCH_3), 71.0 (d, OCH), 86.0 (s, C-1), 92.9 (s, C-7), 123.6 (s, C-5), 127.2 (d, CH_{arom}), 128.0 (d, CH_{arom}), 128.7 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 166.0 (s, C-3), 168.3 (s, COO).

***endo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-61d)** (sbo-577b)



Yield: 23 %

TLC: R_f = 0.57 (ethyl acetate/n-hexane 1:4).

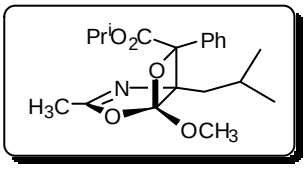
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 3H, CH_3), 1.13 (d, J = 6.2 Hz, 3H, CH_3), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.24 (d, J = 6.8 Hz, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.27 (septet, J = 6.6 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 5.22 (septet, J = 6.2 Hz, 1H, OCH), 7.25-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 17.4 (q, CH_3), 17.7 (q, CH_3), 22.8 (q, CH_3), 23.0 (q, CH_3), 27.8 (d, CH), 51.8 (q, OCH_3), 70.0 (d, OCH), 86.3 (s, C-1), 91.9 (s, C-7), 124.2 (s, C-5), 126.7 (d, CH_{arom}), 127.7 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.4 (s, Cq_{arom}), 165.4 (s, C-3), 169.6 (s, COO).

***exo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-61e)** (sbo-578a)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.62 g of a yellow oil. Preparative chromatography on silica gel yielded 0.76 g of the *exo*-isomer (and 0.43 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (d, J = 6.6 Hz, 3H, CH_3), 0.72 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.2 Hz, 3H, CH_3), 0.94 (d, J = 6.2 Hz, 3H, CH_3), 1.56 (m, 2H, CH_2), 1.58 (m, 1H, CH),

2.04 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 5.22 (septet, J = 6.2 Hz, 1H, OCH), 7.26-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

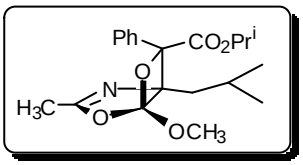
δ_{ppm} = 14.0 (q, CH_3), 21.4 (q, CH_3), 21.6 (q, CH_3), 22.6 (q, CH_3), 23.5 (q, CH_3), 25.7 (d, CH), 38.5 (t, CH_2), 51.6 (q, OCH_3), 70.1 (d, OCH), 81.7 (s, C-2), 91.5 (s, C-3), 123.3 (s, C-5), 126.3 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.2 (s, Cq_{arom}), 165.5 (s, C-3), 169.9 (s, COO).

HRMS: ($C_{20}H_{27}NO_5$, M = 361.19 g/mol)

Calcd: 361.1864

Found: 361.1860

***endo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-61e)** (sbo-578b)



Yield: 24 %

TLC: R_f = 0.58 (ethyl acetate/n-hexane 1:4).

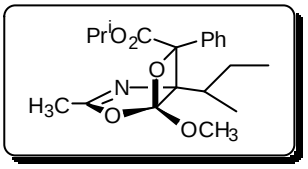
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (d, J = 6.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.18 (m, 1H, CH), 1.20 (d, J = 6.2 Hz, 3H, CH_3), 1.25 (d, J = 6.2 Hz, 3H, CH_3), 1.38 (m, 2H, CH_2), 1.72 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 5.32 (septet, J = 6.2 Hz, 1H, OCH), 7.26-7.80 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 22.9 (q, CH_3), 23.0 (q, CH_3), 24.1 (q, CH_3), 24.3 (q, CH_3), 25.2 (d, CH), 39.8 (t, CH_2), 52.0 (q, OCH_3), 71.0 (d, OCH), 81.8 (s, C-2), 90.8 (s, C-3), 123.8 (s, C-5), 126.4 (d, CH_{arom}), 127.8 (d, CH_{arom}), 129.9 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 164.7 (s, C-3), 169.3 (s, COO).

***exo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-61f)** (sbo-586g)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.65 g of a yellow oil. Preparative chromatography on silica gel yielded 0.74 g of the *exo*-isomer (and 0.39 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 41 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

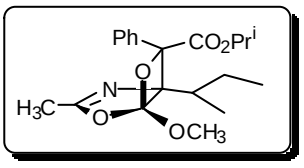
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.67 (t, J = 6.8 Hz, 3H, CH_3), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 0.93 (d, J = 6.2 Hz, 3H, CH_3), 1.12 (d, J = 6.2 Hz, 3H, CH_3), 1.31 (m, 2H, CH_2), 1.47 (m, 1H, CH), 2.08 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 5.25 (septet, J = 6.2 Hz, 1H, OCH), 7.22-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.2 (q, CH_3), 12.1 (q, CH_3), 14.2 (q, CH_3), 22.2 (q, CH_3), 22.8 (q, CH_3), 23.4 (d, CH), 32.6 (t, CH_2), 51.6 (q, OCH_3), 70.2 (d, OCH), 86.6 (s, C-1), 93.1 (s, C-7), 123.4 (s, C-5), 126.9 (d, CH_{arom}), 127.4 (d, CH_{arom}), 128.8 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 165.8 (s, C-3), 168.3 (s, COO).

***endo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-61f)** (sbo-586f)



Yield: 22 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.78 (d, J = 6.8 Hz, 3H, CH_3), 0.86 (t, J = 7.5 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.24 (d, J = 6.2 Hz, 3H, CH_3), 1.28 (m, 2H, CH_2), 1.69 (s, 3H, CH_3),

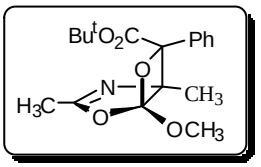
1.98 (m, 1H, CH), 3.64 (s, 3H, OCH_3), 5.24 (septet, J = 6.2 Hz, 1H, OCH), 7.17-7.45 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.6 (q, CH_3), 13.2 (q, CH_3), 14.2 (q, CH_3), 22.2 (q, CH_3), 22.6 (q, CH_3), 23.9 (d, CH), 34.5 (t, CH_2), 51.8 (q, OCH_3), 71.4 (d, OCH), 86.2 (s, C-1), 92.3 (s, C-7), 123.9 (s, C-5), 126.7 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.9 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 165.1 (s, C-3), 169.6 (s, COO).

Photolyses of *tert*-butyl phenylglyoxylate with 5-methoxyoxazoles 36a-f:

***exo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-62a)** (sbo-445d)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.4 g of a yellow oil. Preparative chromatography on silica gel yielded 0.76 g of the *exo*-isomer (and 0.37 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 46 %

TLC: R_f = 0.48 (ethyl acetate/n-hexane 1:4).

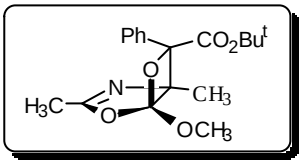
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.04 (s, 3H, CH_3), 1.46 (s, 9H, $3CH_3$), 2.07 (s, 3H, CH_3), 3.62 (s, 3H, OCH_3), 7.23-7.67 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 14.9 (q, CH_3), 27.9 (q, $3CH_3$), 51.8 (q, OCH_3), 78.8 (s, C-1), 82.9 (s, Cq), 91.1 (s, C-7), 123.4 (s, C-5), 126.2 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 166.2 (s, C-3), 167.4 (s, COO).

***endo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-62a)** (sbo-445c)



Yield: 22 %

TLC: R_f = 0.42 (ethyl acetate/n-hexane 1:4).

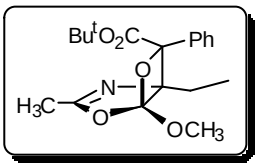
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.44 (s, 9H, $3CH_3$), 1.52 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 7.25-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 15.8 (q, CH_3), 27.9 (q, $3CH_3$), 51.9 (q, OCH_3), 78.2 (s, C-1), 83.1 (s, Cq), 90.5 (s, C-7), 123.7 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 165.2 (s, C-3), 168.0 (s, COO).

***exo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-62b)** (sbo-583c)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.62 g of a yellow oil. Preparative chromatography on silica gel yielded 0.72 g of the *exo*-isomer (and 0.38 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 41 %

TLC: R_f = 0.45 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{\nu}$ (cm^{-1}) = 2983, 2895, 1751, 1615, 1600, 1555, 1440, 1085, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.73 (t, J = 7.5 Hz, 3H, CH_3), 1.21 (m, 1H, CH), 1.46 (s, 9H, $3CH_3$), 1.60 (m, 1H, CH), 2.09 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 7.28-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.4 (q, CH_3), 14.8 (q, CH_3), 21.8 (t, CH_2), 27.9 (q, $3CH_3$), 51.6 (q, OCH_3), 81.9 (s, C-1), 82.9 (s, Cq), 91.4 (s, C-7), 123.4 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 166.5 (s, C-3), 167.4 (s, COO).

MS: (EI, 70 eV)

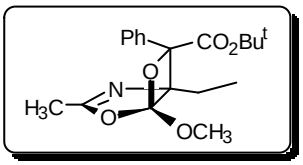
m/z (%) = 347 (M^+, 10), 310 (4), 264 (40), 222 (25), 159 (75), 127 (40), 116 (100), 105 (80), 102 (38), 91 (10), 77 (25), 71 (28), 57 (60).

HRMS: ($C_{19}H_{25}NO_5$, M = 347.17 g/mol)

Calcd: 347.1726

Found: 347.1722

***endo*-1-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-62b)** (sbo-583d)



Yield: 22 %

TLC: R_f = 0.50 (ethyl acetate/n-hexane 1:4).

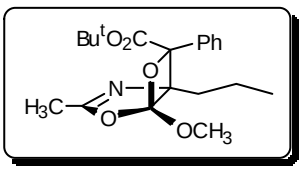
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.5 Hz, 3H, CH_3), 1.44 (s, 9H, $3CH_3$), 2.07 (s, 3H, CH_3), 2.14 (m, 1H, CH), 2.18 (m, 1H, CH), 3.69 (s, 3H, OCH_3), 7.27-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.2 (q, CH_3), 14.3 (q, CH_3), 22.6 (t, CH_2), 28.0 (q, $3CH_3$), 51.9 (q, OCH_3), 81.7 (s, C-1), 83.1 (s, Cq), 90.9 (s, C-7), 123.8 (s, C-5), 126.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 129.0 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 165.3 (s, C-3), 168.1 (s, COO).

***exo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-62c)** (sbo-585a)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.68 g of a yellow oil. Preparative chromatography on silica

gel yielded 0.84 g of the *exo*-isomer (and 0.41 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 47 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

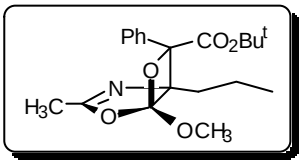
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (t, J = 6.8 Hz, 3H, CH_3), 0.92 (m, 2H, CH_2), 1.17 (m, 2H, CH_2), 1.46 (s, 9H, $3CH_3$), 2.08 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 7.25-7.69 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.8 (q, CH_3), 16.4 (t, CH_2), 27.9 (q, $3CH_3$), 30.9 (t, CH_2), 51.6 (q, OCH_3), 81.6 (s, C-1), 82.9 (s, Cq), 91.4 (s, C-7), 123.3 (s, C-5), 126.3 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 166.0 (s, C-3), 167.5 (s, COO).

***endo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-62c)** (sbo-585b)



Yield: 23 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

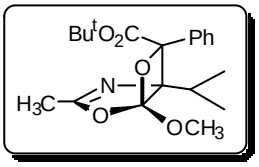
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.5 Hz, 3H, CH_3), 1.40 (m, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.77 (s, 3H, CH_3), 1.79-1.83 (m, 2H, CH_2), 3.69 (s, 3H, OCH_3), 7.27-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 14.4 (q, CH_3), 17.1 (t, CH_2), 27.9 (q, $3CH_3$), 31.9 (t, CH_2), 51.9 (q, OCH_3), 81.3 (s, C-1), 83.1 (s, Cq), 91.0 (s, C-7), 123.7 (s, C-5), 127.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 165.1 (s, C-3), 168.1 (s, COO).

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-62d)** (sbo-579a)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.65 g of a yellow oil. Preparative chromatography on silica gel yielded 0.74 g of the *exo*-isomer (and 0.46 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.39 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (d, J = 6.8 Hz, 3H, CH_3), 0.82 (d, J = 6.8 Hz, 3H, CH_3), 1.54 (s, 9H, $3CH_3$), 2.09 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 7.33-7.82 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 15.9 (q, CH_3), 16.7 (q, CH_3), 25.9 (d, CH), 28.1 (q, $3CH_3$), 51.5 (q, OCH_3), 82.9 (s, Cq), 85.8 (s, C-1), 92.6 (s, C-7), 123.2 (s, C-5), 127.2 (d, CH_{arom}), 128.0 (d, CH_{arom}), 128.7 (d, CH_{arom}), 134.8 (s, Cq), 166.0 (s, C-3), 168.3 (s, COO).

MS: (EI, 70 eV)

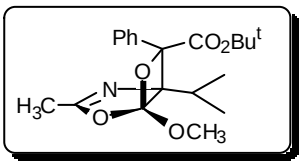
m/z (%) = 361 (M^+, 5), 348 (45), 334 (35), 278 (40), 236 (20), 218 (10), 173 (25), 130 (60), 105 (100), 102 (18), 91 (10), 77 (25), 71 (28), 57 (60).

HRMS: ($C_{20}H_{27}NO_5$, M = 361.19 g/mol)

Calcd: 361.1882

Found: 361.1876

***endo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-62d)** (sbo-579b)



Yield: 26 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

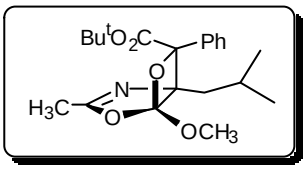
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 3H, CH_3), 1.24 (d, J = 6.8 Hz, 3H, CH_3), 1.45 (s, 9H, $3CH_3$), 1.75 (s, 3H, CH_3), 2.36 (septet, J = 6.6 Hz, 1H, CH), 3.72 (s, 3H, OCH_3), 7.25-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 17.4 (q, CH_3), 17.7 (q, CH_3), 27.5 (d, CH), 27.8 (s, 9H, $3CH_3$), 51.8 (q, OCH_3), 83.0 (s, Cq), 84.5 (s, C-1), 92.4 (s, C-7), 123.9 (s, C-5), 126.7 (d, CH_{arom}), 127.7 (d, CH_{arom}), 128.5 (d, CH_{arom}), 135.4 (s, Cq_{arom}), 165.2 (s, C-3), 168.5 (s, COO).

***exo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-62e)** (sbo-580c)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.69 g of a yellow oil. Preparative chromatography on silica gel yielded 0.75 g of the *exo*-isomer (and 0.39 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 40 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2983, 2895, 1755, 1610, 1607, 1558, 1440, 1075, 980, 778.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (d, J = 6.6 Hz, 3H, CH_3), 0.72 (d, J = 6.6 Hz, 3H, CH_3), 1.42 (s, 9H, $3CH_3$), 1.56 (m, 2H, CH_2), 1.58 (m, 1H, CH), 2.04 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 7.26-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 22.6 (q, CH_3), 23.5 (q, CH_3), 25.7 (d, CH), 27.9 (q, $3CH_3$), 36.5 (t, CH_2), 51.6 (q, OCH_3), 82.4 (s, Cq), 86.7 (s, C-2), 93.5 (s, C-3), 123.3 (s, C-

5), 126.3 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.2 (s, Cq_{arom}), 165.5 (s, C-3), 169.9 (s, COO).

MS: (EI, 70 eV)

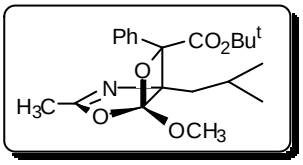
m/z (%) = 375 (M^+, 10), 348 (12), 320 (8), 292 (20), 274 (20), 187 (40), 168 (20), 144 (80), 105 (100), 102 (18), 91 (10), 77 (25), 71 (28), 57 (60).

HRMS: ($C_{21}H_{29}NO_5$, M = 375.20 g/mol)

Calcd: 375.2038

Found: 375.2034

***endo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-62e)** (sbo-580e)



Yield: 21 %

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

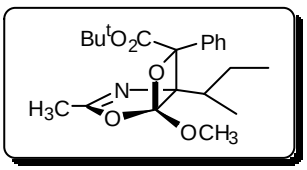
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (d, J = 6.5 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.18 (m, 1H, CH), 1.38 (m, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.72 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 7.26-7.80 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 22.9 (q, CH_3), 24.1 (q, CH_3), 24.2 (d, CH), 28.1 (q, $3CH_3$), 37.3 (t, CH_2), 51.9 (q, OCH_3), 83.0 (s, Cq), 85.8 (s, C-2), 92.8 (s, C-3), 123.8 (s, C-5), 126.4 (d, CH_{arom}), 127.8 (d, CH_{arom}), 129.9 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 164.7 (s, C-3), 169.3 (s, COO).

***exo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-62f)** (sbo-586c)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 2-*sec*-butyl4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the

above general procedure to give 1.72 g of a yellow oil. Preparative chromatography on silica gel yielded 0.76 g of the *exo*-isomer (and 0.4 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 41 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

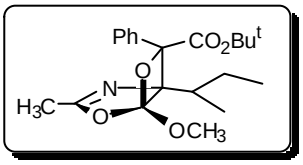
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.67 (t, J = 6.8 Hz, 3H, CH_3), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 1.44 (s, 9H, $3CH_3$), 1.31 (m, 2H, CH_2), 1.47 (m, 1H, CH), 2.08 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 7.22-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.7 (q, CH_3), 12.1 (q, CH_3), 13.8 (q, CH_3), 14.2 (q, CH_3), 23.4 (d, CH), 27.8 (q, $3CH_3$), 34.4 (t, CH_2), 51.7 (q, OCH_3), 82.9 (t, OCH_2), 86.0 (s, C-1), 92.5 (s, C-7), 123.9 (s, C-5), 126.9 (d, CH_{arom}), 127.4 (d, CH_{arom}), 128.8 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 164.9 (s, C-3), 168.5 (s, COO).

***endo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-62f)** (sbo-586b)



Yield: 21 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

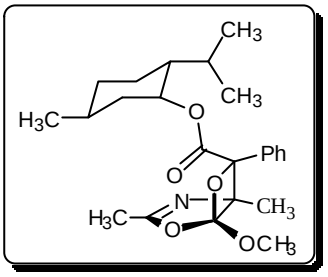
δ_{ppm} = 0.78 (d, J = 6.8 Hz, 3H, CH_3), 0.86 (t, J = 7.5 Hz, 3H, CH_3), 1.28 (m, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.69 (s, 3H, CH_3), 1.98 (m, 1H, CH), 3.64 (s, 3H, OCH_3), 7.17-7.45 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.3 (q, CH_3), 12.0 (q, CH_3), 12.9 (q, CH_3), 14.8 (q, CH_3), 23.4 (d, CH), 27.8 (q, $3CH_3$), 32.8 (t, CH_2), 51.6 (q, OCH_3), 82.9 (s, Cq), 86.2 (s, C-1), 92.7 (s, C-7), 123.3 (s, C-5), 126.7 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.9 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 165.4 (s, C-3), 167.2 (s, COO).

Photolyses of menthyl phenylglyoxylate with 5-methoxyoxazoles 36a-f:

***exo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*exo*-63a)** (sbo-373b)



A solution of menthyl phenylglyoxylate (1.44 g, 5 mmol) and 2,4-dimethyl-5-methoxyoxazole (0.64 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.87 g of a yellow oil. Preparative chromatography on silica gel yielded 0.95 g of the *exo*-isomer (and 0.45 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 46 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.65 (d, J = 6.9 Hz, 3H, CH_3), 0.81 (d, J = 7.1 Hz, 3H, CH_3), 0.82 (d, J = 6.5 Hz, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.45 (m, 3H), 1.63 (m, 3H), 1.85 (m, 1H, CH), 1.99 (m, 1H), 2.05 (s, 3H, CH_3), 3.63 (s, 3H, OCH_3), 4.74 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.31-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

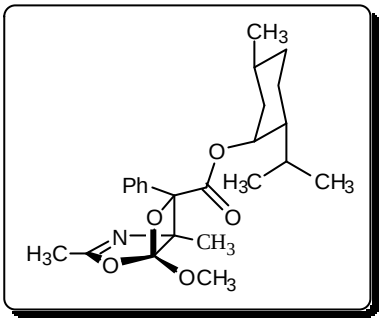
δ_{ppm} = 15.3 (q, CH_3), 15.4 (q, CH_3), 16.4 (q, CH_3), 21.1 (q, CH_3), 22.3 (q, CH_3), 23.6 (t, CH_2), 26.0 (d, CH), 31.8 (d, CH), 34.6 (t, CH_2), 41.1 (t, CH_2), 47.2 (d, CH), 52.3 (q, OCH_3), 76.6 (d, OCH), 79.4 (s, C-1), 91.9 (s, C-7), 123.7 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 166.3 (s, C-3), 168.7 (s, COO).

HRMS: ($C_{24}H_{33}NO_5$, M = 415.24 g/mol)

Calcd: 415.2425

Found: 415.2427

***endo*-5-Methoxy-1,3-dimethyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*endo*-63a)** (sbo-373)



Yield: 22 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

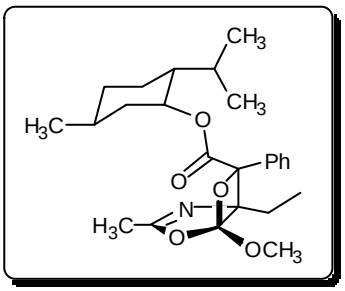
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (d, J = 6.9 Hz, 3H, CH_3), 0.83 (d, J = 7.2 Hz, 3H, CH_3), 0.84 (d, J = 6.5 Hz, 3H, CH_3), 1.02 (m, 2H, CH_2), 1.23 (m, 1H, CH), 1.37 (m, 2H, CH_2), 1.49 (s, 3H, CH_3), 1.54 (m, 2H, CH_2), 1.67 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 4.72 (ddd, J = 11.1, 4.6, 4.4 Hz, 1H, OCH), 7.32-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.2 (q, CH_3), 15.4 (q, CH_3), 16.5 (q, CH_3), 21.2 (q, CH_3), 22.5 (q, CH_3), 23.7 (t, CH_2), 26.2 (d, CH), 31.9 (d, CH), 34.8 (t, CH_2), 41.3 (t, CH_2), 47.4 (d, CH), 52.5 (q, OCH_3), 76.8 (d, OCH), 80.2 (s, C-1), 91.2 (s, C-7), 123.5 (s, C-5), 126.7 (d, CH_{arom}), 128.3 (d, CH_{arom}), 135.5 (s, Cq_{arom}), 165.6 (s, C-3), 168.1 (s, COO).

***exo*-5-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*exo*-63b)** (sbo-374b)



A solution of menthyl phenylglyoxylate (1.44 g, 5 mmol) and 4-ethyl-2-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.9 g of a yellow oil. Preparative chromatography on silica gel yielded 0.88 g of the *exo*-isomer (and 0.47 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 41 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

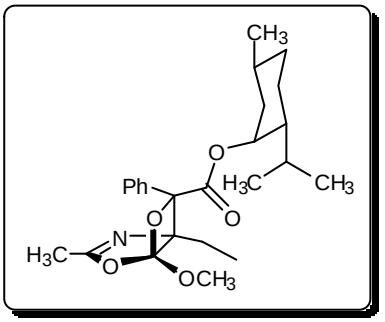
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (d, J = 6.9 Hz, 3H, CH_3), 0.72 (t, J = 7.5 Hz, 3H, CH_3), 0.78 (d, J = 7.1 Hz, 3H, CH_3), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 1.00 (m, 3H), 1.25 (m, 1H), 1.45 (m, 3H), 1.63 (m, 2H, CH_2), 1.92 (m, 2H, CH_2), 2.07 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.73 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.33-7.42 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.3 (q, CH_3), 14.8 (q, CH_3), 14.9 (q, CH_3), 16.0 (q, CH_3), 20.6 (q, CH_3), 21.7 (d, CH), 21.9 (t, CH_2), 23.2 (d, CH), 25.5 (t, CH_2), 31.4 (t, CH_2), 34.1 (t, CH_2), 40.8 (t, CH_2), 46.7 (d, CH), 51.7 (q, OCH_3), 76.0 (d, OCH), 82.2 (s, C-1), 91.8 (s, C-7), 123.2 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 165.6 (s, C-3), 168.3 (s, COO).

***endo*-5-Ethyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*endo*-63b)** (sbo-374)



Yield: 22 %

TLC: R_f = 0.58 (ethyl acetate/n-hexane 1:4).

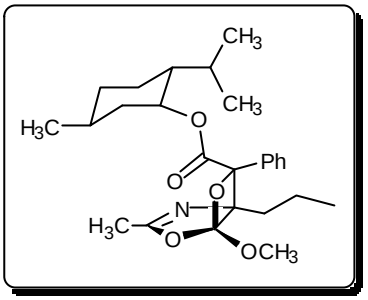
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.63 (d, J = 6.9 Hz, 3H, CH_3), 0.73 (t, J = 7.5 Hz, 3H, CH_3), 0.78 (d, J = 7.1 Hz, 3H, CH_3), 0.89 (d, J = 6.6 Hz, 3H, CH_3), 1.03 (m, 3H), 1.27 (m, 1H), 1.50 (m, 3H), 1.57 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.93 (m, 2H, CH_2), 3.70 (s, 3H, OCH_3), 4.75 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.35-7.78 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.4 (q, CH_3), 14.9 (q, CH_3), 15.2 (q, CH_3), 16.2 (q, CH_3), 20.9 (q, CH_3), 21.8 (d, CH), 22.0 (t, CH_2), 23.5 (d, CH), 25.7 (t, CH_2), 31.5 (t, CH_2), 34.7 (t, CH_2), 41.0 (t, CH_2), 47.0 (d, CH), 51.9 (q, OCH_3), 75.9 (d, OCH), 83.0 (s, C-1), 92.3 (s, C-7), 123.7 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 166.3 (s, C-3), 168.1 (s, COO).

***exo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*exo*-63c)** (sbo-375c)



A solution of menthyl phenylglyoxylate (1.44 g, 5 mmol) and 2-methyl-4-propyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.98 g of a yellow oil. Preparative chromatography on silica gel yielded 0.94 g of the *exo*-isomer (and 0.63 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 43 %

TLC: R_f = 0.37 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.61 (d, J = 6.9 Hz, 3H, CH_3), 0.71 (t, J = 7.2 Hz, 3H, CH_3), 0.78 (d, J = 7.1 Hz, 3H, CH_3), 0.85 (d, J = 6.5 Hz, 3H, CH_3), 1.14 (m, 2H, CH_2), 1.17 (m, 3H), 1.45 (m, 3H), 1.62 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 2.06 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.73 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.34-7.71 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

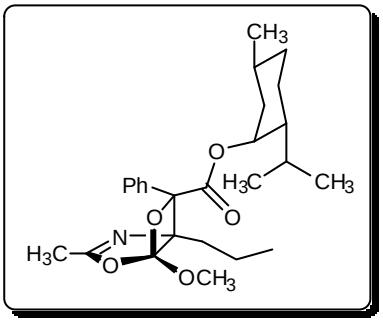
δ_{ppm} = 14.2 (q, CH_3), 14.9 (q, CH_3), 16.0 (q, CH_3), 16.4 (q, CH_3), 20.6 (q, CH_3), 21.9 (d, CH), 23.3 (t, CH_2), 25.6 (d, CH), 30.7 (t, CH_2), 31.4 (d, CH), 34.2 (t, CH_2), 40.8 (t, CH_2), 46.7 (d, CH), 51.7 (q, OCH_3), 76.0 (d, OCH), 81.9 (s, C-1), 91.8 (s, C-7), 123.2 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 165.4 (s, C-3), 168.4 (s, COO).

HRMS: ($C_{26}H_{37}NO_5$, M = 443.27 g/mol)

Calcd: 443.2659

Found: 443.2654

***endo*-5-Methoxy-3-methyl-7-phenyl-1-propyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*endo*-63c)** (sbo-375):



Yield: 28 %

TLC: R_f = 0.61 (ethyl acetate/n-hexane 1:4).

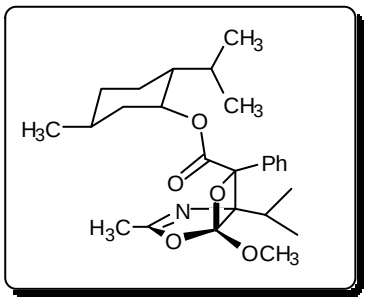
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.63 (d, J = 6.9 Hz, 3H, CH_3), 0.73 (t, J = 7.5 Hz, 3H, CH_3), 0.80 (d, J = 7.1 Hz, 3H, CH_3), 0.87 (d, J = 6.6 Hz, 3H, CH_3), 1.15 (m, 2H, CH_2), 1.18 (m, 3H), 1.49 (m, 3H), 1.65 (m, 2H, CH_2), 1.68 (s, 3H, CH_3), 1.83 (m, 2H, CH_2), 3.74 (s, 3H, OCH_3), 4.76 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.35-7.46 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 15.0 (q, CH_3), 16.2 (q, CH_3), 16.7 (q, CH_3), 20.9 (q, CH_3), 22.0 (d, CH), 23.5 (t, CH_2), 25.8 (d, CH), 30.9 (t, CH_2), 31.9 (t, CH_2), 34.6 (t, CH_2), 41.0 (t, CH_2), 47.0 (d, CH), 51.6 (q, OCH_3), 76.1 (d, OCH), 82.0 (s, C-1), 92.0 (s, C-7), 123.7 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 165.2 (s, C-3), 168.1 (s, COO).

***exo*-1-Isopropyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*exo*-63d)** (sbo-379d)



A solution of menthyl phenylglyoxylate (1.44 g, 5 mmol) and 4-isopropyl-2-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.95 g of a yellow oil. Preparative chromatography on silica gel yielded 0.98 g of the *exo*-isomer (and 0.53 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 45 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:4).

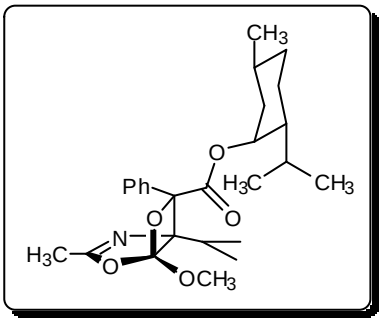
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.64 (d, J = 6.9 Hz, 3H, CH_3), 0.68 (t, J = 6.8 Hz, 3H, CH_3), 0.76 (d, J = 7.1 Hz, 3H, CH_3), 0.85 (d, J = 6.5 Hz, 3H, CH_3), 0.88 (d, J = 6.6 Hz, 3H, CH_3), 1.03 (m, 2H, CH_2), 1.22 (m, 1H, CH), 1.46 (m, 2H, CH_2), 1.62 (m, 2H, CH_2), 1.69 (m, 2H, CH_2), 1.79 (m, 2H, CH_2), 2.07 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.86 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.34-7.61 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.8 (q, CH_3), 15.8 (q, CH_3), 16.0 (q, CH_3), 16.5 (q, CH_3), 20.6 (q, CH_3), 21.9 (d, CH), 23.0 (d, CH), 25.2 (t, CH_2), 26.0 (t, CH_2), 31.4 (d, CH), 34.1 (d, CH), 40.9 (t, CH_2), 46.6 (d, CH), 51.6 (q, OCH_3), 75.7 (d, OCH), 85.9 (s, C-1), 92.9 (s, C-7), 123.2 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.2 (s, Cq_{arom}), 165.4 (s, C-3), 167.6 (s, COO).

***endo*-1-Isoproyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*endo*-63d)** (sbo-379)



Yield: 24 %

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

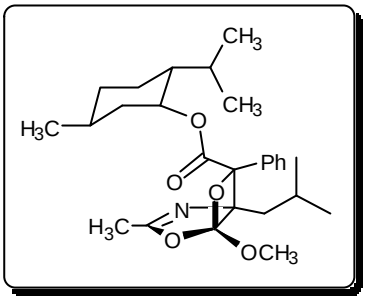
δ_{ppm} = 0.65 (d, J = 6.9 Hz, 3H, CH_3), 0.69 (t, J = 6.9 Hz, 3H, CH_3), 0.78 (d, J = 7.1 Hz, 3H, CH_3), 0.86 (d, J = 6.5 Hz, 3H, CH_3), 0.90 (d, J = 6.7 Hz, 3H, CH_2), 1.05 (m, 3H), 1.23 (m, 1H), 1.48 (m, 2H, CH_2), 1.64 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 1.75 (m, 2H, CH_2), 1.85 (m, 2H, CH_2), 3.74 (s, 3H, OCH_3), 4.78 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.35-7.61 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.6 (q, CH_3), 15.8 (q, CH_3), 16.2 (q, CH_3), 16.7 (q, CH_3), 21.7 (q, CH_3), 22.0 (d, CH), 22.6 (t, CH_2), 23.1 (d, CH), 26.1 (t, CH_2), 31.4 (t, CH_2), 35.5 (t, CH_2),

40.4 (t, CH_2), 47.0 (d, CH), 51.7 (q, OCH_3), 76.0 (d, OCH), 86.0 (s, C-1), 93.2 (s, C-7), 123.7 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.2 (s, Cq_{arom}), 164.7 (s, C-3), 168.2 (s, COO).

***exo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*exo*-63e)** (sbo-384c)



A solution of menthyl phenylglyoxylate (1.44 g, 5 mmol) and 4-isobutyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 2.0 g of a yellow oil. Preparative chromatography on silica gel yielded 0.95 g of the *exo*-isomer (and 0.48 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.34 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2983, 2895, 1745, 1610, 1600, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

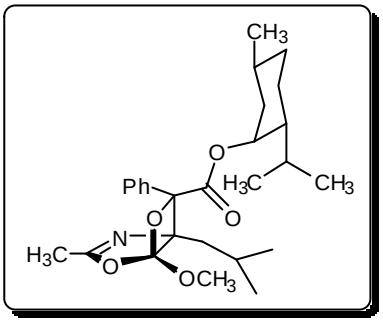
δ_{ppm} = 0.60 (d, J = 6.9 Hz, 3H, CH_3), 0.68 (d, J = 6.9 Hz, 3H, CH_3), 0.74 (d, J = 7.1 Hz, 3H, CH_3), 0.78 (d, J = 6.6 Hz, 3H, CH_3), 0.83 (d, J = 7.2 Hz, 3H, CH_3), 0.95 (m, 2H, CH_2), 1.00 (m, 1H, CH), 1.12 (m, 2H, CH_2), 1.24 (m, 2H, CH_2), 1.43 (m, 2H, CH_2), 1.53 (m, 2H, CH_2), 1.67 (m, 1H, CH), 1.83 (m, 2H, CH_2), 2.04 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.76 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.26-7.49 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.8 (q, CH_3), 16.0 (q, CH_3), 16.1 (q, CH_3), 20.6 (q, CH_3), 21.9 (q, CH_3), 22.3 (d, CH), 23.0 (d, CH), 23.2 (t, CH_2), 23.6 (d, CH), 24.1 (t, CH_2), 34.1 (d, CH), 40.8 (t, CH_2), 46.7 (d, CH), 51.7 (q, OCH_3), 75.9 (d, OCH), 81.9 (s, C-1), 91.9 (s,

C-7), 123.3 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 164.8 (s, C-3), 168.3 (s, COO).

***endo*-1-Isobutyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*endo*-63e)** (sbo-384)



Yield: 21 %

TLC: R_f = 0.58 (ethyl acetate/n-hexane 1:4).

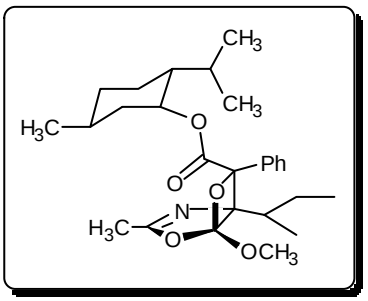
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (d, J = 6.9 Hz, 3H, CH_3), 0.70 (d, J = 6.9 Hz, 3H, CH_3), 75 (d, J = 6.9 Hz, 3H, CH_3), 0.79 (d, J = 6.6 Hz, 3H, CH_3), 0.85 (d, J = 7.2 Hz, 3H, CH_3), 0.97 (m, 2H,CH_2), 1.12 (m, 2H), 1.17 (m, 1H), 1.45 (m, 2H, CH_2), 1.55 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 1.87 (m, 2H, CH_2), 3.74 (s, 3H, OCH_3), 4.75 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.27-7.45 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.9 (q, CH_3), 15.9 (q, CH_3), 16.5 (q, CH_3), 21.0 (q, CH_3), 21.7 (q, CH_3), 23.1 (q, CH_3), 23.8 (d, CH), 24.1 (t, CH_2), 32.5 (t, CH_2), 37.2 (t, CH_2), 40.1 (t, CH_2), 47.1 (d, CH), 52.7 (q, OCH_3), 76.1 (d, OCH), 84.1 (s, C-1), 92.8 (s, C-7), 123.7 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 165.1 (s, C-3), 168.1 (s, COO).

***exo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*exo*-63f)** (sbo-385f)



A solution of menthyl phenylglyoxylate (1.44 g, 5 mmol) and 4-*sec*-butyl-2-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.98 g of a yellow oil. Preparative chromatography on silica gel yielded 0.9 g of the *exo*-isomer (and 0.5 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 39 %

TLC: R_f = 0.35 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.65 (d, J = 6.9 Hz, 3H, CH_3), 0.70 (d, J = 7.2 Hz, 3H, CH_3), 0.76 (d, J = 7.1 Hz, 3H, CH_3), 0.87 (d, J = 6.5 Hz, 3H, CH_3), 0.90 (d, J = 7.2 Hz, 3H, CH_3), 0.97 (m, 1H, CH), 1.10 (m, 2H, CH_2), 1.38 (m, 2H, CH_2), 1.40 (m, 2H, CH_2), 1.43 (m, 1H, CH), 1.47 (m, 2H, CH_2), 1.64 (m, 1H, CH), 2.05 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.87 (ddd, J = 11.0, 4.4, 4.5 Hz, 1H, OCH), 7.35-7.79 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

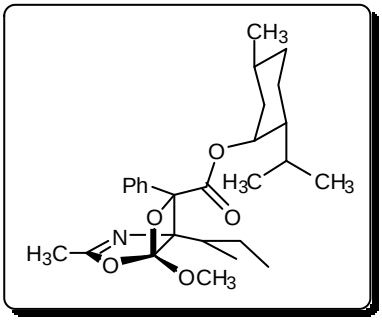
δ_{ppm} = 11.2 (q, CH_3), 12.1 (q, CH_3), 14.8 (q, CH_3), 15.8 (q, CH_3), 20.6 (q, CH_3), 22.0 (q, CH_3), 23.1 (d, CH), 23.3 (t, CH_2), 25.3 (d, CH), 31.4 (t, CH_2), 32.7 (d, CH), 34.1 (t, CH_2), 40.9 (t, CH_2), 46.6 (d, CH), 51.7 (q, OCH_3), 75.7 (d, OCH), 86.5 (s, C-1), 93.1 (s, C-7), 123.3 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 165.1 (s, C-3), 167.8 (s, COO).

HRMS: ($C_{27}H_{39}NO_5$, M = 457.28 g/mol)

Calcd: 457.2764

Found: 457.2760

***endo*-1-*sec*-Butyl-5-methoxy-3-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid 2-isopropyl-5-methyl-cyclohexyl ester (*endo*-63f)** (sbo-385):



Yield: 39 %

TLC: R_f = 0.35 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

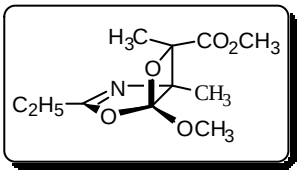
δ_{ppm} = 0.85 (d, J = 6.9 Hz, 3H, CH_3), 0.87 (d, J = 7.4 Hz, 3H, CH_3), 0.90 (d, J = 7.1 Hz, 3H, CH_3), 0.93 (t, J = 6.5 Hz, 3H, CH_3), 0.97 (d, J = 7.2 Hz, 3H, CH_3), 1.00 (m, 1H,CH), 1.07 (m, 2H), 1.18 (m, 2H), 1.27 (m, 2H, CH_2), 1.39 (m, 2H, CH_2), 1.47 (m, 2H, CH_2), 1.53 (m, 1H, CH), 1.67 (m, 2H, CH_2), 1.70 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 4.83 (ddd, J = 11.0, 4.4, 4.6 Hz, 1H, OCH), 7.36-7.80 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.3 (q, CH_3), 12.3 (q, CH_3), 15.0 (q, CH_3), 15.9 (q, CH_3), 20.9 (q, CH_3), 22.3 (q, CH_3), 23.2 (q, CH_3), 23.7 (t, CH_2), 25.7 (d, CH), 31.7 (t, CH_2), 32.9 (d, CH), 34.3 (t, CH_2), 41.0 (t, CH_2), 47.0 (d, CH), 52.8 (q, OCH_3), 76.0 (d, OCH), 85.7 (s, C-1), 92.5 (s, C-7), 123.7 (s, C-5), 126.6 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.7 (s, Cq_{arom}), 166.1 (s, C-3), 168.2 (s, COO).

Photolyses of a -keto esters with 2-ethyl-4-methyl-5-methoxyoxazole 49a:

***exo*-3-Ethyl-5-methoxy-1,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-64a)** (sbo-442b)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 2-ethyl-4-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 0.98 g of a yellow oil. Preparative chromatography on silica gel yielded 0.87 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 70 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2998, 2895, 1715, 1605, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.01 (t, J = 7.5 Hz, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.75 (q, J = 7.5 Hz, 2H, CH_2), 1.90 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

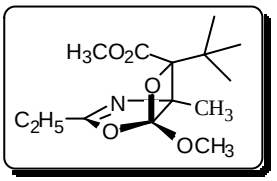
δ_{ppm} = 7.5 (q, CH_3), 17.8 (q, CH_3), 22.2 (q, CH_3), 31.6 (t, CH_2), 52.6 (q, OCH_3), 53.1 (q, OCH_3), 72.5 (s, C-1), 87.5 (s, C-7), 118.7 (s, C-5), 170.5 (s, C-3), 175.9 (s, COO).

HRMS: ($C_{11}H_{17}NO_5$, M = 243.11 g/mol)

Calcd: 243.1126

Found: 243.1122

***exo*-7-*tert*-Butyl-3-ethyl-5-methoxy-1-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-64b)** (sbo-442b)



A solution of methyl trimethylpyruvate (0.36 g, 5 mmol) and 2-ethyl-4-methyl-5-methoxyoxazole (0.35 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.53 g of a yellow oil. Preparative chromatography on silica gel yielded 0.58 g of the oxetane as a colorless oil. The product was thermally unstable and was subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy ester (see later).

Yield: 60 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

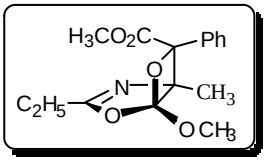
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.01 (t, J = 7.5 Hz, 3H, CH_3), 1.12 (s, 9H, $3CH_3$), 1.47 (s, 3H, CH_3), 1.75 (q, J = 7.5 Hz, 2H, CH_2), 3.56 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.5 (q, CH_3), 17.8 (q, CH_3), 27.9 (q, $3CH_3$), 31.4 (t, CH_2), 51.6 (q, OCH_3), 52.6 (q, OCH_3), 78.5 (s, C-1), 97.5 (s, C-7), 120.7 (s, C-5), 170.5 (s, C-3), 175.9 (s, COO).

***exo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-64c)** (sbo-441d)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 2-ethyl-4-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.39 g of a yellow oil. Preparative chromatography on silica gel yielded 0.72 g of the *exo*-isomer (and 0.38 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 47 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (s, 3H, CH_3), 1.29 (t, J = 7.4 Hz, 3H, CH_3), 2.60 (q, J = 7.4 Hz, 2H, CH_2), 3.03 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 7.31-7.59 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

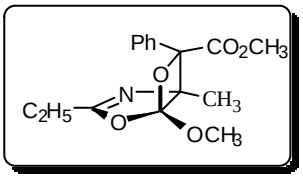
δ_{ppm} = 8.2 (q, CH_3), 17.3 (q, CH_3), 31.8 (t, CH_2), 52.2 (q, OCH_3), 52.3 (q, OCH_3), 74.8 (s, C-1), 80.4 (s, C-7), 121.3 (s, C-5), 126.3 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 168.9 (s, C-3), 173.1 (s, COO).

HRMS: ($C_{16}H_{19}NO_5$, M = 305.13 g/mol)

Calcd: 305.1258

Found: 305.1254

***endo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-64c)** (sbo-441d)



Yield: 24 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 1:4).

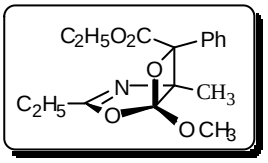
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.14 (t, J = 7.4 Hz, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.40 (q, J = 7.4 Hz, 2H, CH_2), 3.25 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.32-7.60 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.99 (q, CH_3), 16.9 (q, CH_3), 33.6 (t, CH_2), 52.7 (q, OCH_3), 53.2 (q, OCH_3), 75.7 (s, C-1), 91.6 (s, C-7), 123.4 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 169.7 (s, C-3), 174.8 (s, COO).

***exo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-64d)** (sbo-465)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 2-ethyl-4-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.42 g of a yellow oil. Preparative chromatography on silica gel yielded 0.70 g of the *exo*-isomer (and 0.35 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 43 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

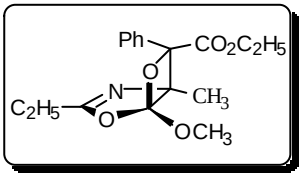
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (s, 3H, CH_3), 1.26 (t, J = 7.4 Hz, 3H, CH_3), 1.27 (t, J = 7.5 Hz, 3H, CH_3), 2.53 (q, J = 7.5 Hz, 2H, CH_2), 3.60 (s, 3H, OCH_3), 4.16 (q, J = 7.5 Hz, 2H, OCH_2), 7.28-7.63 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.5 (q, CH_3), 9.9 (q, CH_3), 13.6 (q, CH_3), 21.4 (t, CH_2), 52.3 (q, OCH_3), 61.6 (t, OCH_2), 78.4 (s, C-1), 90.2 (s, C-7), 123.0 (s, C-5), 126.3 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 169.6 (s, C-3), 170.4 (s, COO).

***endo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-64c)** (sbo-465)



Yield: 22 %

TLC: R_f = 0.57 (ethyl acetate/n-hexane 1:4).

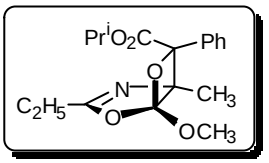
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (t, J = 7.5 Hz, 3H, CH_3), 1.23 (t, J = 7.5 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.36 (q, J = 7.5 Hz, 2H, CH_2), 3.62 (s, 3H, OCH_3), 4.21 (q, J = 7.5 Hz, 2H, OCH_2), 7.26-7.53 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ = 9.3 (q, CH_3), 9.6 (q, CH_3), 13.7 (q, CH_3), 22.0 (t, CH_2), 51.6 (q, OCH_3), 61.7 (t, OCH_2), 80.2 (s, C-1), 92.1 (s, C-7), 123.4 (s, C-5), 126.4 (d, CH), 127.7 (d, CH), 135.6 (s, C_q), 168.4 (s, C-3), 170.1 (s, COO).

***exo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-64e)** (sbo-463)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 2-ethyl-4-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.52 g of a yellow oil. Preparative chromatography on silica gel yielded 0.73 g of the *exo*-isomer (and 0.41 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 43 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

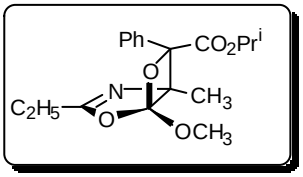
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (s, 3H, CH_3), 1.12 (t, J=7.5 Hz, 3H, CH_3), 1.17 (t, J=6.3 Hz, 3H, CH_3), 1.19 (d, J=6.3 Hz, 3H, CH_3), 2.13 (q, J=7.5 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 5.12 (septet, J= 6.3 Hz, 1H, OCH), 7.28-7.63 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.8 (q, CH_3), 15.9 (q, CH_3), 21.7 (q, CH_3), 21.8 (q, CH_3), 21.9 (t, CH_2), 52.3 (q, OCH_3), 70.1 (d, OCH), 79.2 (s, C-1), 91.2 (s, C-7), 123.5 (s, C-5), 126.4 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 168.1 (s, C-3), 169.8 (s, COO).

***endo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-64e)** (sbo-463a)



Yield: 24 %

TLC: R_f = 0.55 (ethyl acetate/n-hexane 1:4).

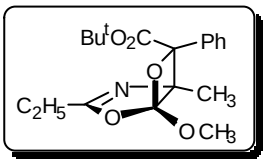
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (t, J = 7.5 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.26 (d, J = 6.2 Hz, 3H, CH_3), 1.53 (s, 3H, CH_3), 2.26 (q, J = 7.5 Hz, 2H, CH_2), 3.66 (s, 3H, OCH_3), 5.07 (septet, J = 6.2 Hz, 1H, OCH), 7.26-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.7 (q, CH_3), 15.7 (q, CH_3), 21.6 (q, CH_3), 21.7 (t, CH_2), 21.9 (q, CH_3), 52.1 (q, OCH_3), 69.9 (d, OCH), 78.1 (s, C-1), 90.3 (s, C-7), 123.6 (s, C-5), 126.7 (d, CH_{arom}), 127.4 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 168.6 (s, C-3), 169.6 (s, COO).

***exo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid tert-butyl ester (*exo*-64f)** (sbo-450c)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 2-ethyl-4-methyl-5-methoxyoxazole (0.71 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.60 g of a yellow oil. Preparative chromatography on silica gel yielded 0.74 g of the *exo*-isomer (and 0.36 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 42 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.06 (s, 3H, CH_3), 1.28 (s, 9H, $3CH_3$), 1.32 (q, J = 7.5 Hz, 3H, CH_3), 2.52 (q, J = 7.5 Hz, 2H, CH_2), 3.62 (s, 3H, OCH_3), 2.13 (q, J = 7.5 Hz, 2H, CH_2), 3.62 (s, 3H, OCH_3), 7.26-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

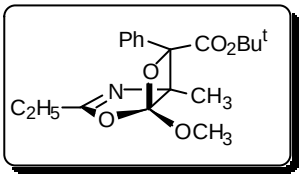
δ_{ppm} = 9.7 (q, CH_3), 15.0 (q, CH_3), 22.4 (t, CH_2), 28.0 (q, $3CH_3$), 52.4 (q, OCH_3), 78.4 (s, C-1), 83.1 (s, C_q), 91.1 (s, C-7), 123.1 (s, C-5), 125.9 (d, CH_{arom}), 127.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 170.1 (s, C-3), 170.3 (s, COO).

HRMS: ($C_{19}H_{25}NO_5$, M = 347.17 g/mol)

Calcd: 347.1739

Found: 347.1734

***endo*-3-Ethyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid tert-butyl ester (endo-64f)** (sbo-450d)



Yield: 21 %

TLC: R_f = 0.53 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

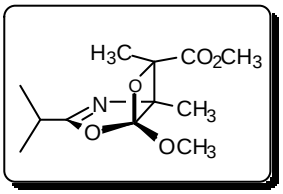
δ_{ppm} = 0.69 (t, J = 7.5 Hz, 3H, CH_3), 1.44 (s, 9H, $3CH_3$), 1.54 (s, 3H, CH_3), 2.16 (q, J = 7.5 Hz, 2H, CH_2), 3.66 (s, 3H, OCH_3), 7.29-7.63 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.7 (q, CH_3), 15.8 (q, CH_3), 21.9 (t, CH_2), 27.9 (q, $3CH_3$), 52.0 (q, OCH_3), 77.9 (s, C-1), 83.1 (s, C-1), 90.4 (s, C-7), 123.5 (s, C-5), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 167.9 (s, C-3), 169.5 (s, COO).

<u>Photolyses of α-keto esters with 2-isopropyl-4-methyl-5-methoxyoxazole 49b:</u>

***exo*-3-Isopropyl-5-methoxy-1,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-65a)** (sbo-460)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.13 g of a yellow oil. Preparative chromatography on silica gel yielded 0.58 g of the *exo*-isomer (and 0.42 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 46 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

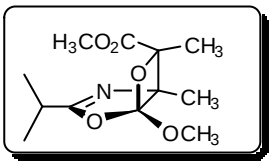
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.95 (d, J = 6.9 Hz, 3H, CH_3), 1.10 (d, J = 6.7 Hz, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.87 (septet, J = 6.7 Hz, 1H, CH), 1.91 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.6 (q, CH_3), 16.3 (q, CH_3), 18.6 (q, CH_3), 22.5 (q, CH_3), 37.8 (d, CH), 52.5 (q, OCH_3), 53.0 (q, OCH_3), 72.4 (s, C-1), 87.4 (s, C-7), 124.3 (s, C-5), 170.4 (s, COO), 176.2 (s, C-3).

***endo*-3-Isopropyl-5-methoxy-1,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-65a)** (sbo-460a)



Yield: 33 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

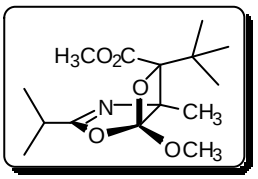
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.08 (d, J = 6.6 Hz, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.87 (septet, J = 6.7 Hz, 1H, CH), 1.91 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 16.3 (q, CH_3), 18.6 (q, CH_3), 22.5 (q, CH_3), 37.8 (d, CH), 52.5 (q, OCH_3), 53.1 (q, OCH_3), 72.4 (s, C-1), 87.2 (s, C-7), 120.3 (s, C-5), 170.4 (s, COO), 176.2 (s, C-3).

***exo*-7-*tert*-Butyl-3-isopropyl-5-methoxy-1-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-65b)** (sbo-483b)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.38 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.71 g of a yellow oil. Preparative chromatography on silica gel yielded 0.34 g of the *exo*-isomer (and 0.21 g of the *endo*-isomer) as a colorless oil.

Yield: 46 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.12 (s, 9H, $3CH_3$), 1.16 (d, J = 6.2 Hz, 6H, $2CH_3$), 1.51 (s, 3H, CH_3), 2.53 (septet, J = 6.2 Hz, 1H, CH), 3.57 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

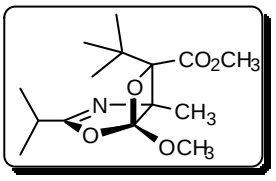
δ_{ppm} = 15.7 (q, CH_3), 19.2 (q, CH_3), 19.3 (q, CH_3), 26.3 (q, $3CH_3$), 28.6 (d, CH), 37.0 (s, Cq), 51.4 (q, OCH_3), 51.6 (q, OCH_3), 76.7 (s, C-1), 97.3 (s, C-7), 122.6 (s, C-5), 170.7 (s, COO), 172.3 (s, C-3).

HRMS: ($C_{15}H_{25}NO_5$, M = 299.17 g/mol)

Calcd: 299.1685

Found: 299.1681

***endo*-7-*tert*-Butyl-3-isopropyl-5-methoxy-1-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-65b)** (sbo-483)



Yield: 28 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:4).

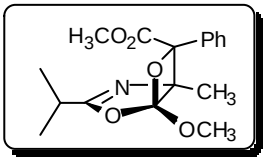
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (s, 9H, $3CH_3$), 1.18 (d, J = 6.3 Hz, 6H, $2CH_3$), 1.45 (s, 3H, CH_3), 1.87 (septet, J = 6.3 Hz, 1H, CH), 3.56 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 19.3 (q, CH_3), 19.6 (q, CH_3), 26.5 (q, $3CH_3$), 27.8 (d, CH), 38.1 (s, Cq), 51.5 (q, OCH_3), 52.1 (q, OCH_3), 75.4 (s, C-1), 97.2 (s, C-7), 123.3 (s, C-5), 170.7 (s, COO), 179.2 (s, C-3).

***exo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-65c)** (sbo-458)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.43 g of a yellow oil. Preparative chromatography on silica

gel yielded 0.76 g of the *exo*-isomer (and 0.39 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 47 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

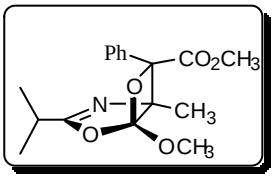
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.23 (d, J = 6.8 Hz, 3H, CH_3), 1.27 (d, J = 6.8 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.79 (septet, J = 6.8 Hz, 1H, CH), 3.54 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 7.35-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.2 (q, CH_3), 17.9 (q, CH_3), 18.6 (q, CH_3), 37.5 (d, CH), 52.3 (q, OCH_3), 52.7 (q, OCH_3), 78.2 (s, C-1), 90.2 (s, C-7), 123.7 (s, C-5), 126.3 (d, CH_{arom}), 128.2 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 170.1 (s, C-3), 172.1 (s, COO).

***endo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-65c)** (sbo-458d)



Yield: 25 %

TLC: R_f = 0.37 (ethyl acetate/n-hexane 1:4).

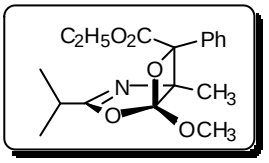
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.19 (d, J=6.8 Hz, 3H, CH_3), 1.43 (d, J = 6.8 Hz, 3H, CH_3), 1.96 (s, 3H, CH_3), 2.84 (septet, J = 6.8 Hz, 1H, CH), 3.11 (s, 3H, OCH_3), 3.30 (s, 3H, OCH_3), 7.30-7.64 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.4 (q, CH_3), 17.2 (q, CH_3), 18.0 (q, CH_3), 38.4 (d, CH), 52.7 (q, OCH_3), 53.2 (q, OCH_3), 74.5 (s, C-1), 81.4 (s, C-7), 123.4 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 169.1 (s, C-3), 173.4 (s, COO).

***exo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-65d)** (sbo-459e)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.46 g of a yellow oil. Preparative chromatography on silica gel yielded 0.67 g of the *exo*-isomer (and 0.33 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 39 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.96 (t, J = 7.5 Hz, 3H, CH_3), 1.20 (d, J = 6.9 Hz, 3H, CH_3), 1.36 (d, J = 6.8 Hz, 3H, CH_3), 2.00 (s, 3H, CH_3), 2.86 (septet, J = 6.8 Hz, 1H, CH), 3.12 (s, 3H, OCH_3), 4.28 (q, J = 7.5 Hz, 2H, OCH_2), 7.30-7.63 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

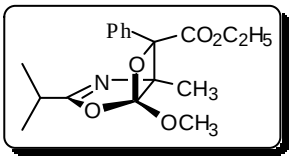
δ_{ppm} = 13.7 (q, CH_3), 16.1 (q, CH_3), 17.3 (q, CH_3), 17.4 (q, CH_3), 38.4 (d, CH), 52.2 (q, OCH_3), 62.4 (t, OCH_2), 74.5 (s, C-1), 81.7 (s, C-7), 123.2 (s, C-5), 126.3 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 168.7 (s, C-3), 169.2 (s, COO).

HRMS: ($C_{18}H_{23}NO_5$, M = 333.16 g/mol)

Calcd: 333.1587

Found: 333.1581

***endo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-65d)** (sbo-459)



Yield: 19 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2988, 2892, 1755, 1614, 1600, 1550, 1440, 1075, 980, 770.

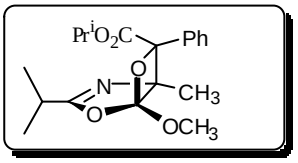
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.78 (d, J = 6.8 Hz, 3H, CH_3), 0.98 (d, J = 6.9 Hz, 3H, CH_3), 1.23 (t, J = 7.5 Hz, 3H, CH_3), 1.69 (s, 3H, CH_3), 2.24 (septet, J = 6.8 Hz, 1H, CH), 3.65 (s, 3H, OCH_3), 4.23 (q, J = 7.5 Hz, 2H, OCH_2), 7.32-7.47 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 17.6 (q, CH_3), 17.8 (q, CH_3), 18.5 (q, CH_3), 36.2 (d, CH), 52.7 (q, OCH_3), 62.1 (t, OCH_2), 82.1 (s, C-1), 92.1 (s, C-7), 123.4 (s, C-5), 126.4 (d, CH_{arom}), 127.7 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 166.2 (s, C-3), 170.2 (s, COO).

***exo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-65e)** (sbo-456d)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.52 g of a yellow oil. Preparative chromatography on silica gel yielded 0.43 g of the *exo*-isomer (and 0.72 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 25 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

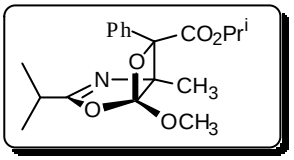
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.07 (s, 3H, CH_3), 1.20 (d, J = 6.2 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.26 (d, J = 6.9 Hz, 3H, CH_3), 1.32 (d, J = 6.9 Hz, 3H, CH_3), 2.68 (septet, J = 6.9 Hz, 1H, CH), 3.62 (s, 3H, OCH_3), 5.07 (septet, J = 6.2 Hz, 1H, OCH), 7.25-7.51 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.0 (q, CH_3), 18.8 (q, CH_3), 18.9 (q, CH_3), 21.7 (q, CH_3), 21.8 (q, CH_3), 28.8 (d, CH), 51.8 (q, OCH_3), 70.0 (d, OCH), 78.3 (s, C-1), 90.2 (s, C-7), 123.5 (s, C-5), 126.4 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 168.0 (s, C-3), 173.2 (s, COO).

***endo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-65e)** (sbo-456d)



Yield: 42 %

TLC: R_f = 0.57 (ethyl acetate/n-hexane 1:4).

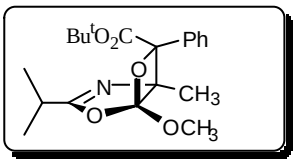
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (d, J = 6.9 Hz, 3H, CH_3), 0.81 (d, J = 6.9 Hz, 3H, CH_3), 1.20 (d, J = 6.2 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.24 (septet, J = 6.9 Hz, 1H, CH), 3.66 (s, 3H, OCH_3), 5.02 (septet, J = 6.2 Hz, 1H, OCH), 7.32-7.62 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.8 (q, CH_3), 19.0 (q, CH_3), 19.2 (q, CH_3), 21.5 (q, CH_3), 21.6 (q, CH_3), 28.5 (d, CH), 52.1 (q, OCH_3), 69.8 (d, OCH), 77.8 (s, C-1), 91.2 (s, C-7), 123.0 (s, C-5), 126.7 (d, CH_{arom}), 127.4 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 168.6 (s, C-3), 169.6 (s, COO).

***exo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-65f)** (sbo-453d)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 2-isopropyl-4-methyl-5-methoxyoxazole (0.75 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.62 g of a yellow oil. Preparative chromatography on silica gel yielded 0.46 g of the *exo*-isomer (and 0.74 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 26 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.06 (s, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.25 (d, J = 6.2 Hz, 3H, CH_3), 1.45 (s, 9H, $3CH_3$), 2.58 (septet, J = 6.2 Hz, 1H, CH), 3.61 (s, 3H, OCH_3), CH_2), 7.26-7.66 (m, 5H, H_{arom}).

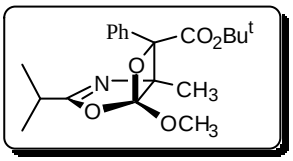
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 19.1 (q, CH_3), 19.2 (q, CH_3), 29.0 (d, CH), 28.0 (q, $3CH_3$), 51.8 (q, OCH_3), 78.2 (s, C-1), 82.8 (s, C_q), 90.3 (s, C-7), 123.0 (s, C-5), 125.9 (d, CH_{arom}), 127.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 167.1 (s, C-3), 173.2 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 332 (10), 278 (8), 260 (15), 105 (35), 86 (65), 84 (100), 77 (10), 57 (38).

***endo*-3-Isopropyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-65f)** (sbo-453d)



Yield: 42 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (d, J = 6.2 Hz, 3H, CH_3), 0.78 (d, J = 6.2 Hz, 3H, CH_3), 1.44 (s, 9H, $3CH_3$), 1.56 (s, 3H, CH_3), 2.23 (septet, J = 6.2 Hz, 1H, CH), 3.65 (s, 3H, OCH_3), 7.29-7.66 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.1 (q, CH_3), 18.8 (q, CH_3), 18.9 (q, CH_3), 27.9 (q, $3CH_3$), 52.0 (q, OCH_3), 77.6 (s, C-1), 83.1 (s, C_q), 91.1 (s, C-7), 123.5 (s, C-5), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 167.9 (s, C-3), 172.6 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 346 (M^+-Me, 10), 324 (45), 306 (15), 278 (20), 260 (18), 254 (25), 154 (28), 105 (100), 102 (38), 91 (10), 77 (25), 71 (28), 57 (60).

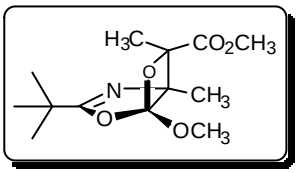
HRMS: ($C_{20}H_{27}NO_5$, M = 361.19 g/mol)

Calcd: 361.1882

Found: 361.1874

Photolyses of a -keto esters with 2-*tert*-butyl-4-methyl-5-methoxyoxazole 49c:

***exo*-3-*tert*-butyl-5-methoxy-1,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-66a)** (sbo-436c)



A solution of methyl pyruvate (0.51 g, 5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.21 g of a yellow oil. Preparative chromatography on silica gel yielded 0.37 g of the *exo*-isomer (and 0.38 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 28 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.95 (s, 9H, $3CH_3$), 1.43 (s, 3H, CH_3), 1.83 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

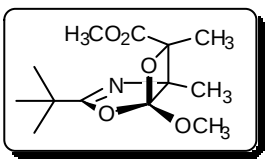
δ_{ppm} = 16.8 (q, CH_3), 18.3 (q, CH_3), 25.3 (q, $3CH_3$), 42.4 (s, Cq), 52.8 (q, OCH_3), 53.4 (q, OCH_3), 75.6 (s, C-1), 87.2 (s, C-7), 122.7 (s, C-5), 171.2 (s, COO), 179.6 (s, C-3).

HRMS: ($C_{13}H_{21}NO_5$, M = 271.14 g/mol)

Calcd: 271.1435

Found: 271.1433

***endo*-3-*tert*-Butyl-5-methoxy-1,7-dimethyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-65f)** (sbo-436c)



Yield: 29 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

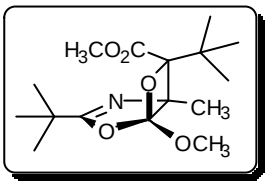
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (s, 9H, $3CH_3$), 1.36 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.2 (q, CH_3), 23.8 (q, CH_3), 25.1 (q, $3CH_3$), 40.6 (s, C_q), 52.8 (q, OCH_3), 53.4 (q, OCH_3), 74.7 (s, C-1), 86.7 (s, C-7), 124.6 (s, C-5), 171.4 (s, COO), 179.2 (s, C-3).

***exo*-3,7-Di-*tert*-butyl-5-methoxy-1-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-66b)** (sbo-484c)



A solution of methyl trimethylpyruvate (0.36 g, 2.5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.42 g, 2.5 mmol) in benzene (20 mL) was irradiated for 24 h according to the above general procedure to give 0.69 g of a yellow oil. Preparative chromatography on silica gel yielded 0.33 g of the *exo*-isomer (and 0.25 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 40 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.12 (s, 9H, $3CH_3$), 1.18 (s, 9H, $3CH_3$), 1.50 (s, 3H, CH_3), 3.56 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

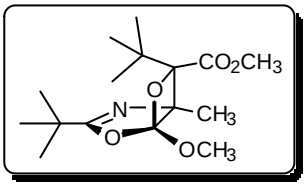
δ_{ppm} = 15.7 (q, CH_3), 24.1 (q, $3CH_3$), 27.3 (q, $3CH_3$), 33.5 (s, Cq), 33.7 (s, Cq), 51.8 (q, OCH_3), 52.4 (q, OCH_3), 76.8 (s, C-1), 97.3 (s, C-7), 122.7 (s, C-5), 170.4 (s, COO), 174.4 (s, C-3).

HRMS: ($C_{16}H_{27}NO_5$, M = 313.19 g/mol)

Calcd: 313.1886

Found: 313.1882

***endo*-3,7-Di-*tert*-Butyl-5-methoxy-1-methyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-66b)** (sbo-484)



Yield: 32 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

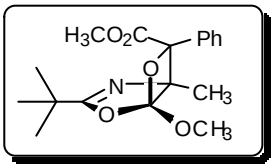
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.10 (s, 9H, $3CH_3$), 1.20 (s, 9H, $3CH_3$), 1.47 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.2 (q, CH_3), 23.8 (q, $3CH_3$), 28.1 (q, $3CH_3$), 33.6 (s, Cq), 33.9 (s, Cq), 51.3 (q, OCH_3), 52.4 (q, OCH_3), 77.0 (s, C-1), 96.7 (s, C-7), 124.0 (s, C-5), 171.4 (s, COO), 179.2 (s, C-3).

***exo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*exo*-66c)** (sbo-432c)



A solution of methyl phenylglyoxylate (0.82 g, 5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.47 g of a yellow oil. Preparative chromatography on silica gel yielded 0.69 g of the *exo*-isomer (and 0.41 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 39 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2993, 2885, 1725, 1608, 1600, 1558, 1440, 1085, 980, 775.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.09 (s, 3H, CH_3), 1.25 (s, 9H, $3CH_3$), 3.63 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 7.26-7.70 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

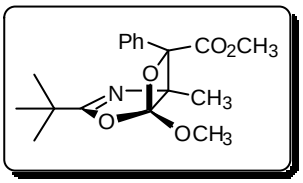
δ_{ppm} = 14.9 (q, CH_3), 27.4 (q, $3CH_3$), 33.8 (s, Cq), 51.9 (q, OCH_3), 52.5 (q, OCH_3), 78.6 (s, C-1), 91.6 (s, C-7), 123.2 (s, C-5), 126.1 (d, CH_{arom}), 127.2 (d, CH_{arom}), 135.0 (s, Cq_{arom}), 169.0 (s, COO), 175.6 (s, C-3).

HRMS: ($C_{18}H_{23}NO_5$, M = 333.16 g/mol)

Calcd: 333.1576

Found: 333.1580

***endo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid methyl ester (*endo*-66c)** (sbo-432)



Yield: 25 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

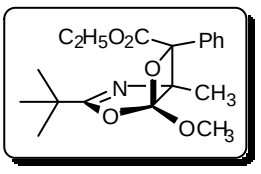
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.27 (s, 9H, $3CH_3$), 1.56 (s, 3H, CH_3), 3.62 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.30-7.64 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.3 (q, CH_3), 27.0 (q, $3CH_3$), 33.3 (s, Cq), 51.5 (q, OCH_3), 52.7 (q, OCH_3), 83.7 (s, C-1), 92.8 (s, C-7), 124.5 (s, C-5), 126.2 (d, CH_{arom}), 128.4 (d, CH_{arom}), 136.5 (s, Cq_{arom}), 170.2 (s, Coo), 175.9 (s, C-3).

***exo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*exo*-66d)** (sbo-451d)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.57 g of a yellow oil. Preparative chromatography on silica gel yielded 0.72 g of the *exo*-isomer (and 0.36 g of the *endo*-isomer) as a colorless oil. The

products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 40 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

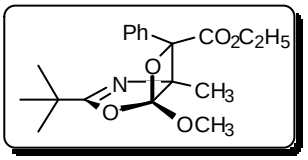
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.98 (s, 3H, CH_3), 1.21 (t, J = 7.5 Hz, 3H, CH_3), 1.27 (s, 9H, $3CH_3$), 3.75 (s, 3H, OCH_3), 4.17 (q, J = 7.5 Hz, 2H, OCH_2), 7.26-7.59 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 23.7 (q, CH_3), 27.5 (q, $3CH_3$), 33.5 (s, Cq), 52.6 (q, OCH_3), 62.1 (t, OCH_2), 80.9 (s, C-1), 92.1 (s, C-7), 124.1 (s, C-5), 126.4 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 169.9 (s, COO), 172.9 (s, C-3).

***endo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid ethyl ester (*endo*-66d)** (sbo-451)



A solution of ethyl phenylglyoxylate (0.89 g, 5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.57 g of a yellow oil. Preparative chromatography on silica gel yielded 0.72 g of the *exo*-isomer (and 0.36 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 40 %

TLC: R_f = 0.55 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 2983, 2895, 1745, 1610, 1600, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.12 (s, 9H, $3CH_3$), 1.23 (t, J = 7.5 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 4.21 (q, J = 7.5 Hz, 2H, OCH_2), 7.31-7.72 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

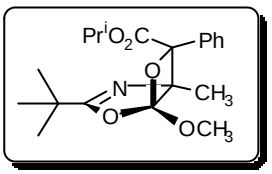
δ_{ppm} = 14.3 (q, CH_3), 23.2 (q, CH_3), 27.9 (q, $3CH_3$), 34.1 (s, Cq), 52.3 (q, OCH_3), 62.1 (t, OCH_2), 81.3 (s, C-1), 93.7 (s, C-7), 124.7 (s, C-5), 127.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 169.3 (s, COO), 172.8 (s, C-3).

HRMS: ($C_{19}H_{25}NO_5$, M = 347.17 g/mol)

Calcd: 347.1698

Found: 347.1694

***exo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*exo*-66e)** (sbo-457c)



A solution of isopropyl phenylglyoxylate (0.96 g, 5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.64 g of a yellow oil. Preparative chromatography on silica gel yielded 0.42 g of the *exo*-isomer (and 0.74 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 23 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

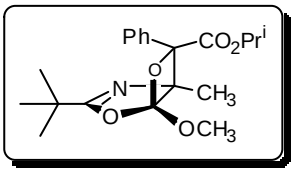
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.97 (s, 3H, CH_3), 1.16 (d, J = 6.2 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.35 (s, 9H, $3CH_3$), 3.76 (s, 3H, OCH_3), 5.00 (septet, J = 6.2 Hz, 1H, OCH), 7.26-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.5 (q, CH_3), 22.6 (q, CH_3), 24.0 (q, CH_3), 27.5 (q, $3CH_3$), 33.4 (s, Cq), 52.5 (q, OCH_3), 70.0 (d, OCH), 80.9 (s, C-1), 91.9 (s, C-7), 124.7 (s, C-5), 126.1 (d, CH_{arom}), 127.2 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 169.4 (s, COO), 172.9 (s, C-3).

***endo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid isopropyl ester (*endo*-66e)** (sbo-457)



Yield: 40 %

TLC: R_f = 0.57 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.02 (s, 9H, $3CH_3$), 1.18 (d, J = 6.2 Hz, 3H, CH_3), 1.21 (d, J = 6.2 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 5.02 (septet, J = 6.2 Hz, 1H, OCH), 7.28-7.62 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

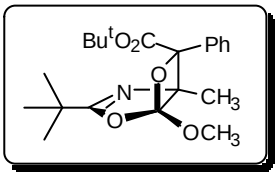
δ = 20.9 (q, CH_3), 21.3 (q, CH_3), 23.7 (q, CH_3), 28.1 (q, $3CH_3$), 33.5 (s, Cq), 52.7 (q, OCH_3), 71.2 (d, OCH), 82.3 (s, C-1), 92.3 (s, C-7), 124.3 (s, C-5), 126.1 (d, CH_{arom}), 128.5 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 165.7 (s, COO), 179.1 (s, C-3).

HRMS: ($C_{20}H_{27}NO_5$, M = 361.20 g/mol)

Calcd: 361.1946

Found: 361.1941

***exo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*exo*-66f)** (sbo-444e)



A solution of *tert*-butyl phenylglyoxylate (1.0 g, 5 mmol) and 2-*tert*-butyl-4-methyl-5-methoxyoxazole (0.84 g, 5 mmol) in benzene (50 mL) was irradiated for 24 h according to the above general procedure to give 1.69 g of a yellow oil. Preparative chromatography on silica gel yielded 0.73 g of the *exo*-isomer (and 0.74 g of the *endo*-isomer) as a colorless oil. The products were thermally unstable and were subsequently hydrolyzed to give the corresponding α-amino-β-hydroxy esters (see later).

Yield: 37 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

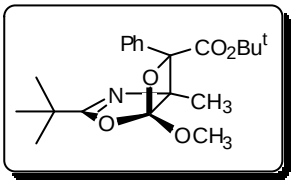
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.07 (s, 3H, CH_3), 1.26 (s, 9H, $3CH_3$), 1.43 (s, 9H, $3CH_3$), 3.60 (s, 3H, OCH_3), 7.22-7.36 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.2 (q, CH_3), 27.0 (q, $3CH_3$), 27.3 (q, $3CH_3$), 33.4 (s, Cq), 51.8 (q, OCH_3), 78.3 (s, C-1), 82.8 (s, C_q), 90.2 (s, C-7), 123.0 (s, C-5), 126.2 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 167.1 (s, COO), 175.2 (s, C-3).

***endo*-3-*tert*-Butyl-5-methoxy-1-methyl-7-phenyl-4,6-dioxa-2-aza-bicyclo[3.2.0]hept-2-ene-7-carboxylic acid *tert*-butyl ester (*endo*-66f)** (sbo-444e)



Yield: 42 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.82 (s, 9H, $3CH_3$), 1.45 (s, 9H, $3CH_3$), 1.58 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 7.48-7.67 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 27.9 (q, $3CH_3$), 28.1 (q, $3CH_3$), 33.8 (s, Cq), 52.1 (q, OCH_3), 77.7 (s, C-1), 83.1 (s, Cq), 91.1 (s, C-7), 123.6 (s, C-5), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.4 (s, Cq_{arom}), 167.9 (s, COO), 172.6 (s, C-3).

HRMS: ($C_{21}H_{29}NO_5$, M = 375.20 g/mol)

Calcd: 375.1849

Found: 375.1847

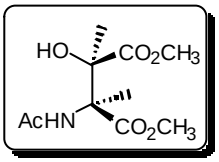
4.20 Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-amino-b-hydroxy succinic acid derivatives

Ring-opening of the bicyclic oxetanes; (Typical hydrolysis procedure):

To a stirred solution of the bicyclic oxetane (2 mmol) in chloroform (10 mL) was added 1N HCl (0.5 mL). After to 2h at room temperature, the course of reaction was monitored by TLC. Upon complete conversion, the reaction mixture was diluted with chloroform, washed with saturated sodium bicarbonate, water, and brine, dried ($MgSO_4$), and concentrated in *vacuo*. The crude product was purified by preparative thick-layer chromatography over silica gel using a mixture of ethylacetate/n-hexane as an eluent.

Synthesis of *erythro* (S*,R*) a-acetamido-b-hydroxy succinic acid derivatives 67a-f:

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2,3-dimethyl-succinic acid dimethyl ester (*erythro*-67a)** (sbo-394c)



According to the typical hydrolysis procedure, the bicyclic oxetane **55a** (0.5 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.4 g of the product as a colorless oil.

Yield: 81 %

TLC: R_f = 0.40 (ethyl acetate/n-hexane 1:4).

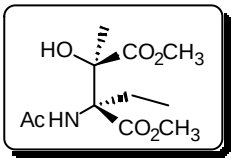
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.29 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 2.26 (s, 3H, $\underline{CH_3}CO$), 3.52 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 6.06 (s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 18.4 (q, CH_3), 21.4 (q, CH_3), 52.4 (q, OCH_3), 52.9 (q, OCH_3), 79.1 (s, C-2), 89.1 (s, C-3), 169.6 (s, CON), 171.2 (COO), 171.9 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-ethyl-3-hydroxy-3-methyl-succinic acid dimethyl ester (*erythro*-67b)** (sbo-399d)



According to the typical hydrolysis procedure, the bicyclic oxetane **55b** (0.51 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.45 g of the product as a colorless oil. A crystalline sample for X-ray crystal structure analysis could be obtained by crystallization of the product from pentane at –10 °C.

Yield: 86 %

M.p: 67-69 °C.

TLC: R_f = 0.39 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (t, J = 7.2 Hz, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.55 (m, 1H, CH), 1.63 (m, 1H, CH), 2.13 (s, 3H, $\underline{CH_3}CO$), 3.61 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

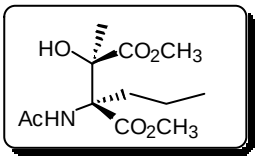
δ_{ppm} = 7.8 (q, CH_3), 14.9 (q, CH_3), 19.2 (q, CH_3), 21.6 (t, CH_2), 51.7 (q, OCH_3), 52.4 (q, OCH_3), 81.2 (s, C-2), 89.1 (s, C-3), 169.5 (s, CON), 170.1 (COO), 171.3 (s, COO).

HRMS: ($C_{11}H_{19}NO_6$, M = 261.12 g/mol)

Calcd: 261.1207

Found: 261.1204

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-3-methyl-2-propyl-succinic acid dimethyl ester (*erythro*-67c)** (sbo-405b)



According to the typical hydrolysis procedure, the bicyclic oxetane **55c** (0.5 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.47 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 1.21 (m, 2H, CH_2), 1.85 (dt, J = 11.0, 6.2 Hz, 1H, CH), 1.53 (s, 3H, CH_3), 2.04 (s, 3H, $\underline{CH_3}CO$), 2.42 (dt, J = 10.8, 6.2 Hz, 1H, CH), 3.21 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 6.39 (s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

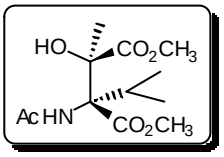
δ_{ppm} = 13.8 (q, CH_3), 14.1 (q, CH_3), 16.9 (q, CH_3), 23.8 (t, CH_2), 37.4 (t, CH_2), 51.5 (q, OCH_3), 53.1 (q, OCH_3), 74.1 (s, C-2), 81.9 (s, C-3), 169.3 (s, CON), 177.4 (COO), 178.3 (s, COO).

HRMS: ($C_{12}H_{21}NO_6$, M = 275.14 g/mol)

Calcd: 275.1363

Found: 275.1359

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-methyl-succinic acid dimethyl ester (*erythro*-67d)** (sbo-406b)



According to the typical hydrolysis procedure, the bicyclic oxetane **55d** (0.5 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.42 g of the product as a colorless oil.

Yield: 78 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3510, 3340, 2988, 2896, 1745, 1735, 1685, 1445, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (d, J = 6.9 Hz, 3H, CH_3), 1.23 (d, J = 6.8 Hz, 3H, CH_3), 1.51 (s, 1H, OH), 1.61 (s, 3H, CH_3), 2.02 (s, 3H, $\underline{CH_3}CO$), 2.98 (septet, J = 6.8 Hz, 1H, CH), 3.67 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 7.04 (s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

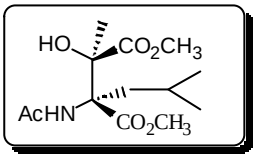
δ_{ppm} = 18.5 (q, CH_3), 18.8 (q, CH_3), 24.1 (q, CH_3), 25.1 (q, CH_3), 30.8 (d, CH), 52.3 (q, OCH_3), 52.9 (q, OCH_3), 73.6 (s, C-2), 82.4 (s, C-3), 171.1 (s, CON), 171.7 (COO), 174.9 (s, COO).

Anal: ($C_{12}H_{21}NO_6$, M = 275.3 g/mol)

Calcd: C 52.35 H 7.69 N 5.09

Found: C 52.52 H 7.89 N 5.12

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-methyl-succinic acid dimethyl ester (*erythro*-67e)** (sbo-407c)



According to the typical hydrolysis procedure, the bicyclic oxetane **55e** (0.54 g, 2 mmol) was cleaved hydrolytically in 2.5h. Preparative chromatography yielded 0.5 g of the product as a colorless oil.

Yield: 86 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

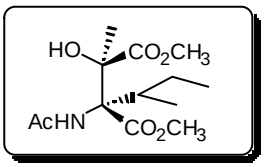
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.41 (m, 1H, CH), 1.56 (s, 3H, CH_3), 1.89 (m, 2H, CH_2), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.66 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 6.53 (s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 17.9 (q, CH_3), 23.4 (q, CH_3), 24.5 (q, CH_3), 24.8 (d, CH), 43.3 (t, CH_2), 52.4 (q, OCH_3), 52.7 (q, OCH_3), 82.4 (s, C-2), 89.7 (s, C-3), 164.7 (s, CON), 171.3 (COO), 172.5 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-methyl-succinic acid dimethyl ester (*erythro*-67f)** (sbo-408a)



According to the typical hydrolysis procedure, the bicyclic oxetane **55f** (0.54 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.46 g of the product as a colorless oil.

Yield: 80 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (t, J = 7.5 Hz, 3H, CH_3), 0.86 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.57 (s, 3H, CH_3), 1.89 (m, 1H, CH), 1.96 (s, 3H, $\underline{CH_3}CO$), 3.61 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.60 (s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.9 (q, CH_3), 11.1 (q, CH_3), 15.1 (q, CH_3), 23.3 (q, CH_3), 25.6 (t, CH_2), 34.4 (d, CH), 51.6 (q, OCH_3), 52.6 (q, OCH_3), 78.2 (s, C-2), 82.0 (s, C-3), 170.7 (s, CON), 170.9 (COO), 173.2 (s, COO).

MS: (EI, 70 eV)

m/z (%) = 273 (M^+-O, 5), 272 (M^+-OH, 7), 246 (M^+-MeCO, 15), 232 (5), 188 (55), 144 (15), 141 (100), 113 (90), 83 (27), 57 (25), 55 (30).

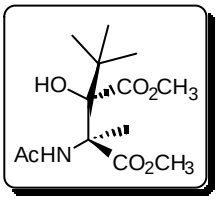
HRMS: ($C_{13}H_{23}NO_6$, M = 289.15 g/mol)

Calcd: 289.1519

Found: 289.1515

Synthesis of *threo* (S*,S*) a -acetamido-b -hydroxy succinic acid derivatives 68a-f:

***threo* (2S*,3S*) 2-Acetylamino-3-*tert*-butyl-3-hydroxy-2-methyl-succinic acid dimethyl ester (*threo*-68a)** (sbo-387a)



According to the typical hydrolysis procedure, the bicyclic oxetane **56a** (0.27 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 73 %

TLC: R_f = 0.45 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3490, 3360, 2994, 2934, 1740, 1735, 1685, 1443, 1065, 985, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.02 (s, 3H, CH_3), 1.12 (s, 9H, $3CH_3$), 1.50 (s, 3H, CH_3), 1.98 (s, 3H, $\underline{CH_3}CO$), 3.55 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

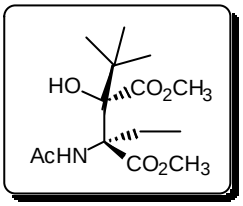
δ_{ppm} = 14.6 (q, CH_3), 15.6 (q, CH_3), 25.7 (q, CH_3), 41.3 (s, Cq), 51.4 (q, OCH_3), 51.7 (q, OCH_3), 92.2 (s, C-2), 97.3 (s, C-3), 167.1 (s, CON), 171.3 (COO), 174.5 (s, COO).

HRMS: ($C_{13}H_{23}NO_6$, M = 289.15 g/mol)

Calcd: 289.1519

Found: 289.1512

***threo* (2S*,3S*) 2-Acetylamino-3-*tert*-butyl-2-ethyl-3-hydroxy-succinic acid dimethyl ester (*threo*-68b)** (sbo-390a)



According to the typical hydrolysis procedure, the bicyclic oxetane **56b** (0.30 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.27 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:4).

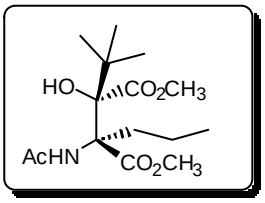
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (t, J = 7.4 Hz, 3H, CH_3), 1.12 (s, 9H, $3CH_3$), 1.92 (m, 1H, CH), 2.00 (s, 3H, $\underline{CH_3}CO$), 2.13 (s, 1H, CH), 3.56 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.0 (q, CH_3), 14.6 (q, CH_3), 21.8 (q, CH_3), 26.4 (t, CH_2), 37.9 (s, C_q), 51.2 (q, OCH_3), 52.0 (q, OCH_3), 80.7 (s, C-2), 81.3 (s, C-3), 169.8 (s, CON), 177.5 (COO), 180.9 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-*tert*-butyl-3-hydroxy-2-propyl-succinic acid dimethyl ester (*threo*-68c)** (sbo-389d)



According to the typical hydrolysis procedure, the bicyclic oxetane **56c** (0.31 g, 1 mmol) was cleaved hydrolytically in 3.5h. Preparative chromatography yielded 0.25 g of the product as a colorless oil.

Yield: 80 %

TLC: R_f = 0.42 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (t, J = 7.5 Hz, 3H, CH_3), 1.06 (s, 9H, $3CH_3$), 1.23 (m, 2H, CH_2), 1.53 (m, 2H, CH_2), 2.02 (s, 3H, $\underline{CH_3}CO$), 3.58 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

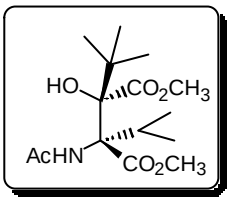
δ_{ppm} =13.6 (q, CH_3), 14.3 (q, CH_3), 14.8 (q, CH_3), 21.6 (q, CH_3), 25.4 (q, $3CH_3$), 32.9 (t, CH_2), 37.5 (t, CH_2), 39.9 (s, C_q), 52.4 (q, OCH_3), 53.4 (q, OCH_3), 80.5 (s, C-2), 81.0 (s, C-3), 165.5 (s, CON), 171.4 (COO), 175.4 (s, COO).

HRMS: ($C_{15}H_{27}NO_6$, M = 317.18 g/mol)

Calcd: 317.1786

Found: 317.1782

***threo* (2S*,3S*) 2-Acetylamino-3-*tert*-butyl-3-hydroxy-2-isopropyl-succinic acid dimethyl ester (*threo*-68d)** (sbo-574b)



According to the typical hydrolysis procedure, the bicyclic oxetane **56d** (0.31 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 67 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

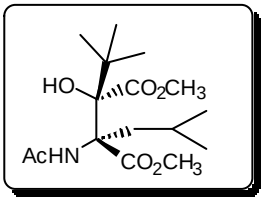
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.89 (d, J = 6.8 Hz, 3H, CH_3), 0.94 (d, J = 6.6 Hz, 3H, CH_3), 1.05 (s, 9H, $3CH_3$), 1.23 (m, 1H, CH), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.64 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 17.2 (q, CH_3), 17.5 (q, CH_3), 24.6 (d, CH), 38.7 (s, C_q), 52.3 (q, OCH_3), 53.6 (q, OCH_3), 83.5 (s, C-2), 85.0 (s, C-3), 165.3 (s, CON), 171.4 (COO), 175.7 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-*tert*-butyl-3-hydroxy-2-isobutyl-succinic acid dimethyl ester (*threo*-68e)** (sbo-575c)



According to the typical hydrolysis procedure, the bicyclic oxetane **56e** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 73 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

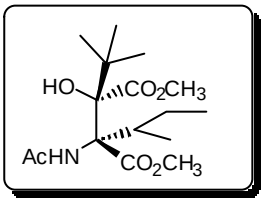
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.05 (s, 9H, $3CH_3$), 1.23 (m, 1H, CH), 1.53 (m, 2H, CH_2), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.63 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ =13.8 (q, CH_3), 19.3 (q, CH_3), 19.5 (q, CH_3), 26.4 (q, $3CH_3$), 27.5 (d, CH), 39.5 (t, CH_2), 40.2 (s, Cq), 52.2 (q, OCH_3), 53.2 (q, OCH_3), 82.5 (s, C-2), 84.0 (s, C-3), 165.6 (s, CON), 171.8 (COO), 175.9 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-2-*sec*-butyl-3-*tert*-butyl-3-hydroxy-succinic acid dimethyl ester (*threo*-68f)** (sbo-576b)



According to the typical hydrolysis procedure, the bicyclic oxetane **56f** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.50 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

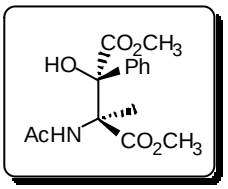
δ_{ppm} = 0.87 (t, J = 7.5 Hz, 3H, CH_3), 0.94 (d, J = 6.8 Hz, 3H, CH_3), 1.02 (s, 9H, $3CH_3$), 1.23 (m, 1H, CH), 1.59 (m, 2H, CH_2), 2.02 (s, 3H, $\underline{CH_3}CO$), 3.58 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} =13.8 (q, CH_3), 14.2 (q, CH_3), 14.8 (q, CH_3), 21.6 (d, CH), 27.4 (q, $3CH_3$), 32.9 (t, CH_2), 39.9 (s, C_q), 52.2 (q, OCH_3), 53.6 (q, OCH_3), 87.5 (s, C-2), 89.3 (s, C-3), 167.2 (s, CON), 173.4 (COO), 176.4 (s, COO).

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 69a-f:

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid dimethyl ester (*threo*-69a)** (sbo-359e)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-58a** (0.58 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.51 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.29 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.06 (s, 3H, CH_3), 2.11 (s, 3H, $\underline{CH_3}CO$), 3.09 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 7.32-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

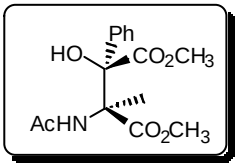
δ_{ppm} = 16.3 (q, CH_3), 28.1 (q, CH_3), 52.2 (q, OCH_3), 53.2 (q, OCH_3), 80.4 (s, C-2), 90.9 (s, C-3), 125.9 (d, CH_{arom}), 126.1 (d, CH_{arom}), 128.6 (d, CH_{arom}), 135.2 (s, Cq_{arom}), 168.7 (s, CON), 169.6 (s, COO), 174.7 (COO).

HRMS: ($C_{15}H_{19}NO_6$, M = 309.12 g/mol)

Calcd: 309.1176

Found: 309.1172

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid dimethyl (*erythro*-69a)** (sbo-359c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-58a** (0.29 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 91 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3500, 3346, 2983, 2890, 1745, 1735, 1670, 1600, 1550, 1440, 1075, 980, 770.

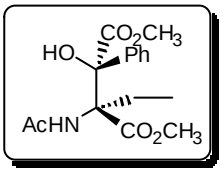
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.97 (s, 3H, CH_3), 2.27 (s, 3H, CH_3CO), 3.65 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 7.23-7.31 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.2 (q, CH_3), 27.9 (q, CH_3), 52.3 (q, OCH_3), 52.7 (q, OCH_3), 74.6 (s, C-2), 83.6 (s, C-3), 126.1 (d, CH_{arom}), 127.0 (d, CH_{arom}), 135.5 (s, Cq_{arom}), 168.8 (s, CON), 169.0 (s, COO), 172.0 (COO).

***threo* (2S*,3S*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid dimethyl ester (*threo*-69b)** (sbo-368a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-58b** (0.61 g 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.54 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.24 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3540, 3446, 2993, 2898, 1748, 1739, 1678, 1605, 1554, 1435, 1085, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.10 (t, J = 7.2 Hz, 3H, CH_3), 1.55 (m, 1H, CH), 2.25 (s, 3H, $\underline{CH_3}CO$), 2.45 (m, 1H, CH), 3.05 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.27-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

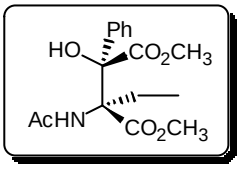
δ_{ppm} = 9.8 (q, CH_3), 14.2 (q, CH_3), 28.9 (t, CH_2), 51.8 (q, OCH_3), 52.9 (q, OCH_3), 87.1 (s, C-2), 92.6 (s, C-3), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 165.4 (s, CON), 168.7 (s, COO), 169.4 (s, COO).

HRMS: ($C_{16}H_{21}NO_6$, M = 333.14 g/mol)

Calcd: 333.1363

Found: 333.1356

***erythro* (2S*,3R*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid dimethyl ester (*erythro*-69b)** (sbo-368c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-58b** (0.31 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 90 %

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

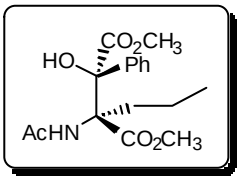
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.96 (t, J = 7.4 Hz, 3H, CH_3), 1.73 (s, 3H, $\underline{CH_3}CO$), 1.85 (m, 1H, CH), 2.07 (m, 1H, CH), 3.69 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 7.29-7.47 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.0 (q, CH_3), 14.3 (q, CH_3), 22.6 (t, CH_2), 51.9 (q, OCH_3), 52.7 (q, OCH_3), 77.2 (s, C-2), 82.0 (s, C-3), 126.4 (d, CH_{arom}), 127.9 (d, CH_{arom}), 128.8 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 164.9 (s, CON), 165.5 (s, COO), 169.9 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid dimethyl ester (*threo*-69c)** (sbo-361b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-58c** (0.63 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.51 g of the product as a colorless oil.

Yield: 79 %

TLC: R_f = 0.23 (ethyl acetate/n-hexane 1:4).

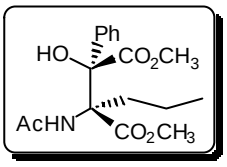
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (t, J = 7.5 Hz, 3H, CH_3), 1.44 (m, 2H, CH_2), 2.26 (s, 3H, $\underline{CH_3}CO$), 2.34 (m, 2H, CH_2), 3.04 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.27-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.4 (q, CH_3), 18.7 (t, CH_2), 37.9 (t, CH_2), 51.8 (q, OCH_3), 52.9 (q, OCH_3), 86.6 (s, C-2), 92.6 (s, C-3), 126.5 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 165.2 (s, CON), 168.7 (COO), 169.5 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid dimethyl ester (*erythro*-69c)** (sbo-361a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-58c** (0.31 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

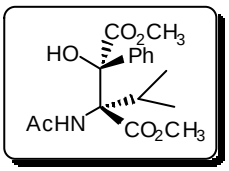
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.2 Hz, 3H, CH_3), 1.18 (m, 2H, CH_2), 1.53 (m, 2H, CH_2), 1.78 (s, 3H, $\underline{CH_3}CO$), 3.71 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 7.26-7.36 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.8 (q, CH_3), 17.9 (t, CH_2), 32.7 (t, CH_2), 52.8 (q, OCH_3), 53.3 (q, OCH_3), 72.7 (s, C-2), 81.7 (s, C-3), 126.3 (d, CH_{arom}), 128.1 (d, CH_{arom}), 138.3 (s, Cq_{arom}), 166.4 (s, CON), 170.7 (COO), 172.4 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid dimethyl ester (*threo*-69d)** (sbo-362g)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-58d** (0.63 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.58 g of the product as a colorless oil.

Yield: 86 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

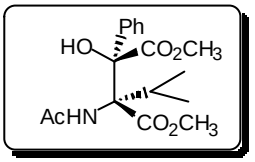
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.9 Hz, 3H, CH_3), 0.98 (d, J = 6.9 Hz, 3H, CH_3), 1.21 (m, 1H, CH), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.28 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 7.24-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.2 (q, CH_3), 18.0 (q, CH_3), 23.6 (q, CH_3), 34.7 (d, CH), 52.4 (q, OCH_3), 52.8 (q, OCH_3), 90.3 (s, C-2), 91.2 (s, C-3), 125.6 (d, CH_{arom}), 127.9 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 169.6 (s, CON), 170.1 (s, COO), 172.1 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid dimethyl ester (*erythro*-69d)** (sbo-362g)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-58d** (0.31 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.22 g of the product as a colorless oil.

Yield: 75 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

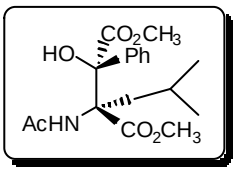
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.91 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (d, J = 6.9 Hz, 3H, CH_3), 1.68 (s, 3H, $\underline{CH_3}CO$), 1.85 (septet, J = 6.8 Hz, 1H, CH), 3.67 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 7.23-7.46 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 15.8 (q, CH_3), 19.1 (q, CH_3), 32.6 (d, CH), 51.6 (q, OCH_3), 53.1 (q, OCH_3), 83.1 (s, C-2), 90.4 (s, C-3), 126.7 (d, CH_{arom}), 127.4 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 168.1 (s, CON), 170.2 (s, COO), 171.4 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid dimethyl ester (*threo*-69e)** (sbo-366b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-58e** (0.67 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.59 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.28 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.6Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.35 (dd, J = 13.3, 5.7 Hz, 1H, CH), 1.80 (septet, J = 6.6 Hz, 1H, CH), 2.27 (s, 3H, $\underline{CH_3}CO$), 2.37 (dd, J = 13.3, 6.1 Hz, 1H, CH), 3.05 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.25-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

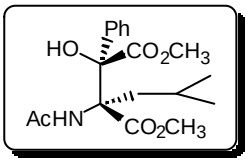
δ_{ppm} = 14.2 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 43.9 (t, CH_2), 51.8 (q, OCH_3), 52.8 (q, OCH_3), 86.5 (s, C-2), 93.0 (s, C-3), 125.6 (d, CH), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 164.6 (s, CON), 168.6 (s, COO), 170.0 (s, COO).

HRMS: ($C_{18}H_{25}NO_6$, M = 351.17 g/mol)

Calcd: 351.1657

Found: 351.1652

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid dimethyl ester (*erythro*-69e)** (sbo-366b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-58e** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.3 g of the product as a colorless oil.

Yield: 85 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

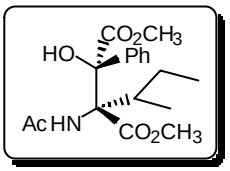
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.61 (dd, J = 13.4, 5.8 Hz, 1H, CH), 1.72 (s, 3H, $\underline{CH_3}CO$), 1.83 (m, 1H, CH), 2.02 (dd, J = 13.4, 6.1 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 7.26-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.4 (q, CH_3), 23.1 (q, CH_3), 24.1 (q, CH_3), 25.6 (d, CH), 37.1 (t, CH_2), 51.7 (q, OCH_3), 52.3 (q, OCH_3), 83.1 (s, C-2), 93.1 (s, C-3), 126.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.7 (s, Cq_{arom}), 165.1 (s, CON), 168.6 (s, COO), 171.0 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid dimethyl ester (*threo*-69f)** (sbo-367)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-58f** (0.67 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.62 g of the product as a colorless oil.

Yield: 92 %

TLC: R_f = 0.26 (ethyl acetate/n-hexane 1:4).

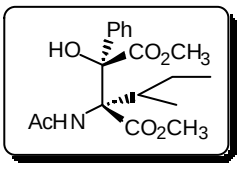
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.35 (m, 1H, CH), 2.26 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.27-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.5 (q, CH_3), 13.5 (q, CH_3), 14.2 (q, CH_3), 18.7 (d, CH), 37.9 (t, CH_2), 51.8 (q, OCH_3), 52.9 (q, OCH_3), 86.6 (s, C-2), 92.6 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.6 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 165.2 (s, CON), 168.8 (s, COO), 169.5 (COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-sec-butyl-3-hydroxy-3-phenyl- succinic acid dimethyl ester (*erythro*-69f)** (sbo-367)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-58f** (0.33 g, 1 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 80 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

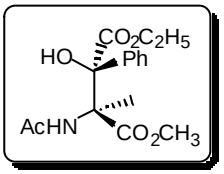
δ_{ppm} = 0.91 (t, J = 7.2 Hz, 3H, CH_3), 0.97 (d, J = 6.6 Hz, 3H, CH_3), 1.47-1.55 (m, 2H, CH_2), 1.69 (m, 1H, CH), 2.21 (s, 3H, $\underline{CH_3}CO$), 3.67 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.28-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.3 (q, CH_3), 14.1 (q, CH_3), 14.7 (q, CH_3), 19.2 (d, CH), 39.1 (t, CH_2), 51.6 (q, OCH_3), 52.3 (q, OCH_3), 86.2 (s, C-2), 93.5 (s, C-3), 126.7 (d, CH_{arom}), 129.1 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 166.1 (s, CON), 169.3 (s, COO), 172.1 (COO).

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 70a-f:

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*threo*-70a)** (sbo-351b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-60a** (0.61 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.58 g of the product as a colorless oil.

Yield: 90 %

TLC: R_f = 0.29 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.27 (t, J = 6.6 Hz, 3H, CH_3), 1.66 (s, 3H, CH_3), 2.23 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 4.22 (q, J = 6.6 Hz, 2H, OCH_2), 7.25-7.35 (m, 5H, H_{arom}).

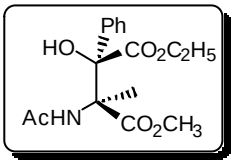
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 21.7 (q, CH_3), 51.8 (q, OCH_3), 62.3 (t, OCH_2), 82.2 (s, C-2), 92.6 (s, C-3), 126.06 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 135.2 (s, Cq_{arom}), 168.3 (s, CON), 169.2 (s, COO), 170.2 (COO).

Anal: ($C_{16}H_{21}NO_6$, M = 323.34 g/mol)

Calcd:	C 59.43	H 6.55	N 4.33
Found:	C 59.73	H 6.42	N 4.33

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*erythro*-70a)** (sbo-351a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-60a** (0.31 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.26 g of the product as a colorless oil.

Yield: 80 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

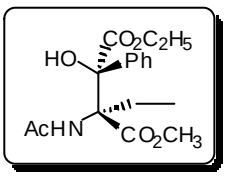
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25 (t, J = 7.2 Hz, 3H, CH_3), 1.50 (s, 3H, CH_3), 2.07 (s, 3H, $\underline{CH_3}CO$), 3.66 (s, 3H, OCH_3), 4.23 (q, J = 7.2 Hz, 2H, OCH_2), 7.25-7.34 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.8 (q, CH_3), 15.7 (q, CH_3), 51.9 (q, OCH_3), 61.8 (t, OCH_2), 78.5 (s, C-2), 91.3 (s, C-3), 126.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 135.2 (s, Cq_{arom}), 165.3 (s, CON), 168.3 (s, COO), 169.2 (COO).

***threo* (2S*,3S*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*threo*-70b)** (sbo-371a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-60b** (0.64 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.55 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.23 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.72 (t, J = 7.5 Hz, 3H, CH_3), 1.04 (t, J = 7.5 Hz, 3H, CH_3), 1.52 (sextet, J = 7.5 Hz, 1H, CH), 2.26 (s, 3H, $\underline{CH_3}CO$), 2.41 (sextet, J = 7.5 Hz, 1H, CH), 3.04 (s, 3H, OCH_3), 4.23 (q, J = 7.5 Hz, 2H, OCH_2), 7.25-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.0 (q, CH_3), 14.0 (q, CH_3), 21.7 (q, CH_3), 22.5 (t, CH_2), 51.7 (q, OCH_3), 62.2 (t, OCH_2), 91.6 (s, C-2), 92.4 (s, C-3), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 168.2 (s, CON), 168.7 (s, COO), 169.4 (s, COO).

MS: (EI, 70 eV)

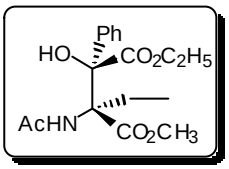
m/z (%) = 320 (M^+-OH, 5), 309 (M^+-CH_2=CH_2, 10), 294 (M^+-COMe, 15), 277 (7), 264 (25), 260 (12), 244 (5), 159 (53), 127 (26), 105 (100), 91 (20), 77 (30), 51 (45).

HRMS: ($C_{17}H_{23}NO_6$, M = 337.15 g/mol)

Calcd: 337.1519

Found: 337.1511

***erythro* (2S*,3R*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*erythro*-70b)** (sbo-371c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-60b** (0.32 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 83 %

TLC: R_f = 0.53 (ethyl acetate/n-hexane 1:4).

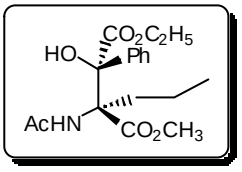
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.71 (t, J = 7.5 Hz, 3H, CH_3), 1.23 (t, J = 7.5 Hz, 3H, CH_3), 1.51 (sextet, J = 7.5 Hz, 1H, CH), 1.82 (sextet, J = 7.5 Hz, 1H, CH), 2.16 (s, 3H, $\underline{CH_3}CO$), 3.76 (s, 3H, OCH_3), 4.20 (q, J = 7.5 Hz, 2H, OCH_2), 7.23-7.32 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.9 (q, CH_3), 8.2 (q, CH_3), 14.6 (q, CH3), 22.4 (t, CH_2), 51.6 (q, OCH_3), 61.7 (t, OCH_2), 90.8 (s, C-2), 92.3 (s, C-3), 126.2 (d, CH), 127.9 (d, CH), 128.8 (d, CH), 134.8 (s, C_q), 167.9 (s, CON), 169.1 (s, COO), 171.2 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-ethyl ester 1-methyl ester (*threo*-70c)** (sbo-354b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-60c** (0.66 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.57 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.53 (ethyl acetate/n-hexane 1:4).

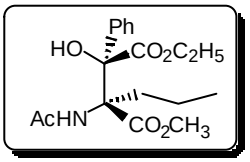
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.23 (t, J = 7.4 Hz, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3), 1.51 (m, 2H, CH_2), 2.23 (s, 3H, $\underline{CH_3}CO$), 2.33 (m, 2H, CH_2), 3.02 (s, 3H, OCH_3), 4.21 (q, J = 7.4 Hz, 2H, OCH_2), 6.39 (s, 1H, NH), 7.25-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 14.2 (q, CH_3), 14.8 (q, CH_3), 18.7 (t, CH_2), 37.9 (t, CH_2), 51.8 (q, OCH_3), 62.2 (t, OCH_2), 81.8 (s, C-2), 91.6 (s, C-3), 126.5 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 166.2 (s, CON), 168.1 (COO), 169.6 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-ethyl ester 1-methyl ester (*erythro*-70c)** (sbo-354)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-60c** (0.33 g, 1 mmol) was cleaved hydrolytically in 3.5h. Preparative chromatography yielded 0.26 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

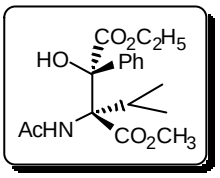
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25 (t, J = 7.4 Hz, 3H, CH_3), 1.27 (t, J = 7.2 Hz, 3H, CH_3), 1.53 (m, 2H, CH_2), 2.17 (s, 3H, CH_3CO), 2.45 (m, 2H, CH_2), 3.76 (s, 3H, OCH_3), 4.27 (q, J=7.4 Hz, 2H, OCH_2), 6.21 (s, 1H, NH), 7.27-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 14.2 (q, CH_3), 15.0 (q, CH_3), 19.0 (t, CH_2), 36.9 (t, CH_2), 51.9 (q, OCH_3), 61.9 (t, OCH_2), 82.1 (s, C-2), 91.7 (s, C-3), 127.1 (d, CH_{arom}), 128.9 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 169.1 (s, CON), 170.1 (COO), 171.3 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*threo*-70d)** (sbo-352)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-60d** (0.66 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.6 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.26 (ethyl acetate/n-hexane 1:4).

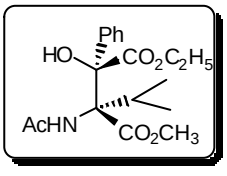
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.74 (d, J = 6.6 Hz, 3H, CH_3), 0.90 (d, J = 6.8 Hz, 3H, CH_3), 1.31 (t, J = 7.2 Hz, 3H, CH_3), 2.29 (s, 3H, $\underline{CH_3}CO$), 2.96 (septet, J = 6.6 Hz, 1H, CH), 3.11 (s, 3H, OCH_3), 4.28 (q, J = 7.2 Hz, 2H, OCH_2), 7.25-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.8 (q, CH_3), 13.9 (q, CH_3), 15.9 (q, CH_3), 19.1 (q, CH_3), 32.5 (d, CH), 51.5 (q, OCH_3), 62.1 (t, OCH_2), 90.3 (s, C-2), 91.2 (s, C-3), 125.6 (d, CH_{arom}), 127.9 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 163.4 (s, CON), 167.5 (s, COO), 170.2 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*erythro*-70d)** (sbo-352a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-60d** (0.33 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 90 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.65 (d, J = 6.8 Hz, 3H, CH_3), 0.82 (d, J = 6.8 Hz, 3H, CH_3), 0.98 (t, J = 7.4 Hz, 3H, CH_3), 2.12 (s, 3H, $\underline{CH_3}CO$), 2.71 (septet, J = 6.8 Hz, 1H, CH), 3.74 (s, 3H, OCH_3), 4.28 (q, J = 7.4 Hz, 2H, OCH_2), 7.26-7.79 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

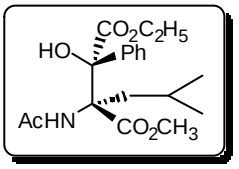
δ_{ppm} = 13.7 (q, CH_3), 14.0 (q, CH_3), 17.2 (q, CH_3), 18.9 (q, CH_3), 32.4 (d, CH), 51.4 (q, OCH_3), 61.4 (t, OCH_2), 85.9 (s, C-2), 92.7 (s, C-3), 126.7 (d, CH_{arom}), 127.4 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 169.2 (s, CON), 170.2 (s, COO), 172.8 (s, COO).

Anal: ($C_{18}H_{25}NO_6$, M = 351.2 g/mol)

Calcd: C 61.52 H 7.17 N 3.99

Found: C 61.98 H 7.11 N 4.31

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*threo*-70e)** (sbo-355b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-60e** (0.69 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.61 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.29 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3490, 3360, 2993, 2967, 1755, 1729, 1680, 1604, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

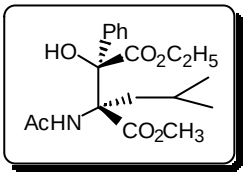
δ_{ppm} = 0.86 (d, J = 6.8Hz, 3H, CH_3), 0.97 (d, J = 6.6 Hz, 3H, CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_3), 1.39 (dd, J = 13.4, 5.9 Hz, 1H, CH), 1.80 (septet, J = 6.6 Hz, 1H, CH), 2.26 (s, 3H, $\underline{CH_3}CO$), 2.38 (dd, J = 13.4, 6.0 Hz, 1H, CH), 3.05 (s, 3H, OCH_3), 4.25 (q, J = 7.2 Hz, 2H, OCH_2), 7.25-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 14.2 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 43.9 (t, CH_2), 51.7 (q, OCH_3), 62.2 (t, OCH_2), 86.4 (s, C-2), 92.9 (s, C-3), 125.6 (d,

CH_{arom}), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 164.7 (s, CON), 168.1 (s, COO), 170.1 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*erythro*-70e)** (sbo-355)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-60e** (0.35 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

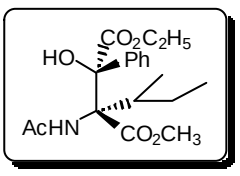
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (d, J = 6.6 Hz, 3H, CH_3), 0.90 (d, J = 6.8 Hz, 3H, CH_3), 1.27 (t, J = 7.5 Hz, 3H, CH_3), 1.41 (septet, J = 6.6 Hz, 1H, CH), 1.60 (m, 2H, CH_2), 2.10 (s, 3H, $\underline{CH_3}CO$), 3.78 (s, 3H, OCH_3), 4.25 (q, J = 7.5 Hz, 2H, CH_2), 7.26-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 14.2 (q, CH_3), 22.6 (q, CH_3), 23.7 (q, CH_3), 25.7 (d, CH), 37.1 (t, CH_2), 51.8 (q, OCH_3), 61.7 (t, OCH_2), 83.5 (s, C-2), 91.6 (s, C-3), 126.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.7 (s, Cq_{arom}), 165.7 (s, CON), 169.2 (s, COO), 171.3 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*threo*-70f)** (sbo-356a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-60f** (0.69 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.61 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.23 (ethyl acetate/n-hexane 1:4).

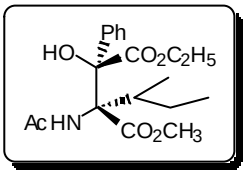
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.74 (d, J = 6.3 Hz, 3H, CH_3), 0.88 (t, J = 6.6 Hz, 3H, CH_3), 1.23 (t, J = 7.5 Hz, 3H, CH_3), 1.25 (m, 1H, CH), 1.54 (m, 2H, CH_2), 2.23 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 4.26 (q, J = 7.5 Hz, 2H, OCH_2), 7.27-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.2 (q, CH_3), 12.2 (q, CH_3), 13.9 (q, CH_3), 14.7 (q, CH_3), 22.1 (d, CH), 37.8 (t, CH_2), 51.5 (q, OCH_3), 62.2 (t, OCH_2), 86.5 (s, C-2), 92.9 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.6 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 167.3 (s, CON), 169.1 (s, COO), 172.3 (COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-ethyl ester 1-methyl ester (*erythro*-70f)** (sbo-356b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-60f** (0.35 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.3 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.59 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.84 (d, J = 6.6 Hz, 3H, CH_3), 0.94 (t, J = 7.4 Hz, 3H, CH_3), 1.26 (m, 1H, CH), 1.27 (t, J = 7.2 Hz, 3H, CH_3), 1.62 (m, 2H, CH_2), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.69 (s, 3H, OCH_3), 4.25 (q, J = 7.2 Hz, 2H, OCH_2), 7.28-7.36 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.3 (q, CH_3), 12.3 (q, CH_3), 14.0 (q, CH_3), 14.9 (q, CH_3), 22.7 (d, CH), 39.1 (t, CH_2), 51.6 (q, OCH_3), 62.3 (t, OCH_2), 84.1 (s, C-2), 91.5 (s, C-3), 126.7 (d, CH_{arom}), 129.1 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 169.1 (s, CON), 169.9 (s, COO), 172.3 (COO).

MS: (EI, 70 eV)

m/z (%) = 354 (4), 316 (10), 277 (18), 169 (50), 141 (45), 140 (100), 105 (43), 91 (20), 77 (30), 59 (10).

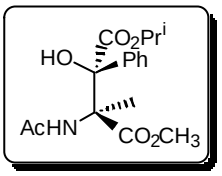
HRMS: ($C_{19}H_{27}NO_6$, M = 365.18 g/mol)

Calcd: 365.1831

Found: 365.1827

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 71a-f:

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*threo*-71a)** (sbo-562c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-61a** (0.64 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.6 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.31 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.6 Hz, 3H, CH_3), 0.94 (d, J = 6.6 Hz, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.11 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 5.07 (septet, J = 6.6 Hz, 1H, OCH), 7.32-7.38 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.3 (q, CH_3), 21.5 (q, CH_3), 23.1 (q, CH_3), 52.2 (q, OCH_3), 70.2 (d, OCH), 83.4 (s, C-2), 91.9 (s, C-3), 125.9 (d, CH_{arom}), 126.1 (d, CH_{arom}), 128.6 (d, CH_{arom}), 135.2 (s, Cq_{arom}), 165.7 (s, CON), 170.2 (s, COO), 174.7 (COO).

MS: (EI, 70 eV)

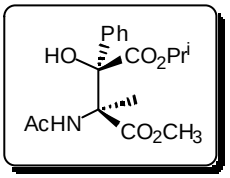
m/z (%) = 279 (M^+-MeCONH, 4), 260 (M^+-Ph, 5), 246 (8), 191 (71), 150 (10), 144 (10), 127 (60), 105 (100), 105 (50), 87 (6), 86 (50), 77 (60), 51 (45).

HRMS: ($C_{17}H_{23}NO_6$, M = 337.15 g/mol)

Calcd: 337.1519

Found: 337.1514

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*erythro*-71a)** (sbo-562)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-61a** (0.32 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

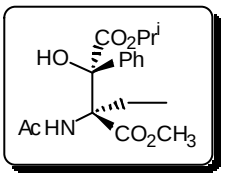
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.96 (d, J = 6.6 Hz, 3H, CH_3), 0.98 (d, J = 6.6 Hz, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.00 (s, 3H, $\underline{CH_3}CO$), 3.65 (s, 3H, OCH_3), 5.23 (septet, J = 6.6 Hz, 1H, OCH), 7.32-7.42 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.5 (q, CH_3), 21.8 (q, CH_3), 23.5 (q, CH_3), 52.3 (q, OCH_3), 70.1 (d, OCH), 79.4 (s, C-2), 87.9 (s, C-3), 126.4 (d, CH_{arom}), 127.4 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.2 (s, Cq_{arom}), 168.7 (s, CON), 171.2 (s, COO), 173.6 (COO).

***threo* (2S*,3S*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*threo*-71b)** (sbo-582a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-61b** (0.67 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.62 g of the product as a colorless oil.

Yield: 85 %

TLC: R_f = 0.24 (ethyl acetate/n-hexane 1:4).

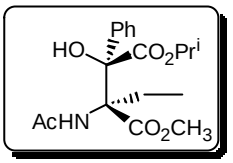
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (d, J = 6.2 Hz, 3H, CH_3), 0.95 (d, J = 6.2 Hz, 3H, CH_3), 1.10 (t, J = 7.2 Hz, 3H, CH_3), 1.55 (m, 1H, CH), 2.25 (s, 3H, $\underline{CH_3}CO$), 2.45 (m, 1H, CH), 3.05 (s, 3H, OCH_3), 5.08 (septet, J = 6.2 Hz, 1H, OCH), 7.27-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.8 (q, CH_3), 14.2 (q, CH_3), 22.2 (q, CH_3), 22.6 (q, CH_3), 28.9 (t, CH_2), 51.5 (q, OCH_3), 70.9 (d, OCH), 86.4 (s, C-2), 91.6 (s, C-3), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 168.4 (s, CON), 169.7 (s, COO), 169.4 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*erythro*-71b)** (sbo-582c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-61b** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.26 g of the product as a colorless oil.

Yield: 74 %

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

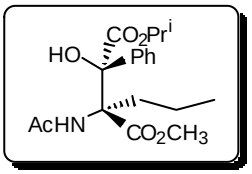
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.96 (t, J = 7.4 Hz, 3H, CH_3), 1.21 (d, J = 6.2 Hz, 3H, CH), 1.26 (d, J = 6.2 Hz, 3H, CH_3), 1.85 (m, 1H, CH), 1.93 (s, 3H, $\underline{CH_3}CO$), 2.07 (m, 1H, CH), 3.69 (s, 3H, OCH_3), 5.07 (septet, J = 6.2 Hz, 1H, OCH), 7.29-7.47 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.4 (q, CH_3), 14.7 (q, CH_3), 22.6 (t, CH_2), 22.8 (q, CH_3), 22.9 (q, CH_3), 51.8 (q, OCH_3), 70.3 (d, OCH), 79.2 (s, C-2), 84.0 (s, C-3), 126.4 (d, CH_{arom}), 127.9 (d, CH_{arom}), 128.8 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 167.8 (s, CON), 169.5 (s, COO), 170.2 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-isopropyl ester 1-methyl ester (*threo*-71c)** (sbo-584b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-61c** (0.68 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.58 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.23 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (t, J = 6.8 Hz, 3H, CH_3), 1.25 (d, J = 6.2 Hz, 3H, CH_3), 1.30 (d, J = 6.2 Hz, 3H, CH_3), 1.51 (m, 2H, CH_2), 2.26 (s, 3H, $\underline{CH_3}CO$), 2.34 (m, 2H, CH_2), 3.04 (s, 3H, OCH_3), 5.06 (septet, J = 6.2 Hz, 1H, OCH), 7.27-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

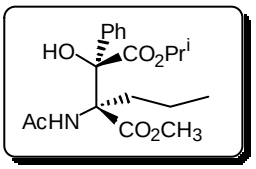
δ_{ppm} = 14.2 (q, CH_3), 14.4 (q, CH_3), 18.4 (t, CH_2), 21.5 (q, CH_3), 21.6 (q, CH_3), 37.9 (t, CH_2), 51.7 (q, OCH_3), 70.5 (d, OCH), 86.3 (s, C-2), 92.5 (s, C-3), 126.4 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 165.4 (s, CON), 167.6 (COO), 169.7 (s, COO).

HRMS: ($C_{19}H_{27}NO_6$, M = 365.18 g/mol)

Calcd: 365.1784

Found: 365.1781

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-isopropyl ester 1-methyl ester (*erythro*-71c)** (sbo-584d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-61c** (0.34 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

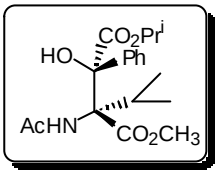
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.2 Hz, 3H, CH_3), 1.18 (m, 2H, CH_2), 1.23 (d, J = 6.2 Hz, 3H, CH_3), 1.26 (d, J = 6.2 Hz, 3H, CH_3), 1.53 (m, 2H, CH_2), 2.02 (s, 3H, $\underline{CH_3}CO$), 3.65 (s, 3H, OCH_3), 5.07 (septet, J = 6.2 Hz, 1H, OCH), 7.26-7.36 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.8 (q, CH_3), 17.9 (t, CH_2), 21.5 (q, CH_3), 21.9 (q, CH_3), 32.7 (t, CH_2), 52.8 (q, OCH_3), 70.3 (d, OCH), 76.7 (s, C-2), 82.7 (s, C-3), 126.3 (d, CH_{arom}), 128.1 (d, CH_{arom}), 138.3 (s, Cq_{arom}), 169.4 (s, CON), 170.7 (COO), 172.4 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*threo*-71d)** (sbo-577e)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-61d** (0.68 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.36 g of the product as a colorless oil.

Yield: 62 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

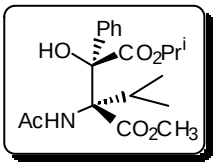
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.9 Hz, 3H, CH_3), 0.98 (d, J = 6.9 Hz, 3H, CH_3), 1.17 (d, J = 6.2 Hz, 3H, CH_3), 1.19 (d, J = 6.2 Hz, 3H, CH_3), 1.21 (m, 1H, CH), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.08 (s, 3H, OCH_3), 5.07 (septet, J = 6.2 Hz, 1H, OCH), 7.24-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.2 (q, CH_3), 18.0 (q, CH_3), 21.8 (q, CH_3), 22.0 (q, CH_3), 23.6 (q, CH_3), 34.7 (d, CH), 52.4 (q, OCH_3), 70.8 (d, OCH), 88.3 (s, C-2), 91.2 (s, C-3), 125.6 (d, CH_{arom}), 127.9 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 169.6 (s, CON), 170.1 (s, COO), 172.1 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*erythro*-71d)** (sbo-577d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-61d** (0.34 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 62 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

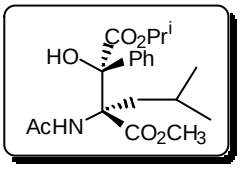
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.91 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (d, J = 6.9 Hz, 3H, CH_3), 1.25 (d, J = 6.2 Hz, 3H, CH_3), 1.85 (septet, J = 6.8 Hz, 1H, CH), 2.18 (s, 3H, $\underline{CH_3}CO$), 3.67 (s, 3H, OCH_3), 5.05 (septet, J = 6.2 Hz, 1H, OCH), 7.23-7.46 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 15.8 (q, CH_3), 19.1 (q, CH_3), 22.2 (q, CH_3), 22.6 (q, CH_3), 32.6 (d, CH), 51.6 (q, OCH_3), 70.1 (d, OCH), 83.1 (s, C-2), 90.4 (s, C-3), 126.7 (d, CH_{arom}), 127.4 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 165.1 (s, CON), 170.2 (s, COO), 171.4 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*threo*-71e)** (sbo-578c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-61e** (0.72 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.45 g of the product as a colorless oil.

Yield: 67 %

TLC: R_f = 0.28 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3500, 3370, 2993, 2898, 1745, 1728, 1670, 1600, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.6Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.12 (m, 1H, CH), 1.27 (d, J = 6.2 Hz, 3H, CH_3), 1.38 (d, J = 6.2 Hz, 3H, CH_3), 1.79 (dd, J = 13.3, 5.7 Hz, 1H, CH), 1.80 (septet, J = 6.6 Hz, 1H, CH), 2.27 (s, 3H, $\underline{CH_3}CO$), 2.37 (dd, J = 13.3, 6.1 Hz, 1H, CH), 3.05 (s, 3H, OCH_3), 5.10 (septet, J = 6.2 Hz, 1H, OCH), 3.67 (s, 3H, OCH_3), 7.25-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

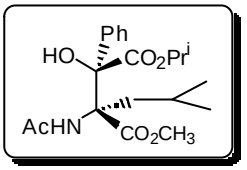
δ_{ppm} = 14.2 (q, CH_3), 22.1 (q, CH_3), 22.3 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 43.9 (t, CH_2), 51.8 (q, OCH_3), 70.8 (d, OCH), 86.5 (s, C-2), 93.0 (s, C-3), 125.6 (d, CH_{arom}), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 164.6 (s, CON), 168.6 (s, COO), 170.0 (s, COO).

HRMS: ($C_{20}H_{29}NO_6$, M = 379.20 g/mol)

Calcd: 379.2018

Found: 379.2014

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*erythro*-71e)** (sbo-578b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-61e** (0.36 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.13 g of the product as a colorless oil.

Yield: 58 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

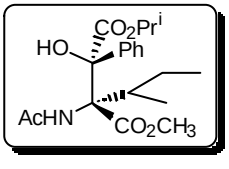
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.24 (d, J = 6.2 Hz, 3H, CH_3), 1.26 (d, J = 6.2 Hz, 3H, CH_3), 1.61 (dd, J = 13.4, 5.8 Hz, 1H, CH), 1.72 (s, 3H, $\underline{CH_3}CO$), 1.83 (m, 1H, CH), 2.02 (dd, J=13.4, 6.1 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 5.06 (septet, J = 6.2 Hz, 1H, OCH), 7.26-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.4 (q, CH_3), 22.7 (q, CH_3), 22.9 (q, CH_3), 23.1 (q, CH_3), 24.1 (q, CH_3), 25.6 (d, CH), 37.1 (t, CH_2), 51.7 (q, OCH_3), 70.3 (d, OCH), 83.1 (s, C-2), 93.1 (s, C-3), 126.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.7 (s, Cq_{arom}), 165.1 (s, CON), 168.6 (s, COO), 171.0 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*threo*-71f)** (sbo-586h)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-61f** (0.72 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.38 g of the product as a colorless oil.

Yield: 58 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

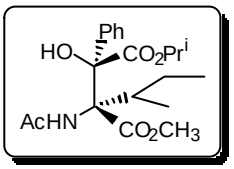
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.20 (d, J = 6.2 Hz, 3H, CH_3), 1.22 (d, J = 6.2 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.35 (m, 1H, CH), 2.26 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 5.18 (septet, J = 6.2 Hz, 1H, OCH), 7.27-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.5 (q, CH_3), 13.5 (q, CH_3), 14.2 (q, CH_3), 18.7 (d, CH), 21.4 (q, CH_3), 21.6 (q, CH_3), 37.9 (t, CH_2), 51.8 (q, OCH_3), 70.9 (d, OCH), 86.6 (s, C-2), 92.6 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.6 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 165.2 (s, CON), 168.8 (s, COO), 169.5 (COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-isopropyl ester 1-methyl ester (*erythro*-71f)** (sbo-586i)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-61f** (0.36 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 65 %

TLC: R_f = 0.55 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

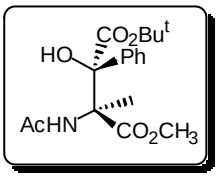
δ_{ppm} = 0.91 (t, J = 7.2 Hz, 3H, CH_3), 0.97 (d, J = 6.6 Hz, 3H, CH_3), 1.47-1.55 (m, 2H, CH_2), 1.69 (m, 1H, CH), 2.21 (s, 3H, $\underline{CH_3}CO$), 3.67 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.28-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.3 (q, CH_3), 14.1 (q, CH_3), 14.7 (q, CH_3), 19.2 (d, CH), 22.4 (q, CH_3), 22.7 (q, CH_3), 39.1 (t, CH_2), 51.6 (q, OCH_3), 70.3 (d, OCH), 86.2 (s, C-2), 93.5 (s, C-3), 126.7 (d, CH_{arom}), 129.1 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 166.1 (s, CON), 169.3 (s, COO), 172.1 (COO).

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-acetamido-b-hydroxy succinic acid derivatives 72a-f:

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-*tert*-butyl ester 1-methyl ester (*threo*-72a)** (sbo-455b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-62a** (0.67 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.57 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.29 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.49 (s, 9H, $3CH_3$), 1.71 (s, 3H, CH_3), 2.13 (s, 3H, $\underline{CH_3}CO$), 3.79 (s, 3H, OCH_3), 7.33-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.4 (q, CH_3), 24.2 (q, CH_3), 27.8 (q, $3CH_3$), 52.7 (q, OCH_3), 83.4 (s, Cq), 96.9 (s, C-2), 107.9 (s, C-3), 125.5 (d, CH_{arom}), 126.2 (d, CH_{arom}), 128.7 (d, CH_{arom}), 136.0 (s, Cq), 168.4 (s, CON), 169.9 (s, COO), 170.3 (COO).

MS: (EI, 70 eV)

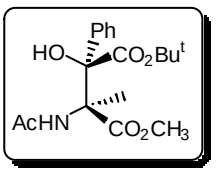
m/z (%) = 334 (M^+-OH, 40), 318 (100), 296 (12), 278 (72), 250 (8), 145 (10), 105 (80), 91 (20), 77 (30), 51 (10).

HRMS: ($C_{18}H_{25}NO_6$, M = 351.17 g/mol)

Calcd: 351.1675

Found: 351.1669

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-*tert*-butyl ester 1-methyl ester (*erythro*-72a)** (sbo-455a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-62a** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 80 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3500, 3346, 2983, 2890, 1745, 1738, 1662, 1605, 1558, 1441, 1085, 980, 778.

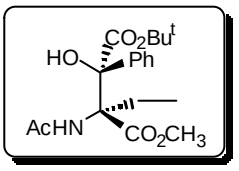
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.50 (s, 3H, CH_3), 1.53 (s, 9H, $3CH_3$), 1.95 (s, 3H, $\underline{CH_3}CO$), 3.65 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 7.23-7.31 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.6 (q, CH_3), 23.9 (q, CH_3), 27.8 (q, CH_3), 52.4 (q, OCH_3), 66.5 (s, C-2), 79.6 (s, C-3), 126.9 (d, CH_{arom}), 127.9 (d, CH_{arom}), 137.2 (s, Cq_{arom}), 169.7 (s, CON), 171.3 (s, COO), 172.0 (COO).

***threo* (2S*,3S*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-*tert*-butyl ester 1-methyl ester (*threo*-72b)** (sbo-583b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-62b** (0.69 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.65 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.24 (ethyl acetate/n-hexane 1:4).

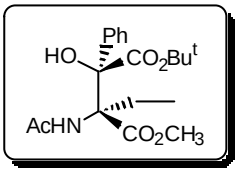
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.04 (t, J = 7.5 Hz, 3H, CH_3), 1.47 (s, 9H, $3CH_3$), 1.56 (m, 1H, CH), 2.10 (s, 3H, $\underline{CH_3}CO$), 2.25 (m, 1H, CH), 3.00 (s, 3H, OCH_3), 7.27-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.9 (q, CH_3), 14.2 (q, CH_3), 21.8 (t, CH_2), 27.8 (q, $3CH_3$), 51.6 (q, OCH_3), 82.9 (s, Cq), 86.7 (s, C-2), 92.6 (s, C-3), 126.5 (d, CH_{arom}), 127.5 (d, CH_{arom}), 128.0 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 165.6 (s, CON), 166.9 (s, COO), 169.6 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-*tert*-butyl ester 1-methyl ester (*erythro*-72b)** (sbo-368c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-62b** (0.35 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 79 %

TLC: R_f = 0.54 (ethyl acetate/n-hexane 1:4).

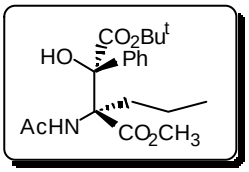
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.96 (t, J = 7.4 Hz, 3H, CH_3), 1.49 (s, 9H, $3CH_3$), 1.73 (s, 3H, $\underline{CH_3}CO$), 1.85 (m, 1H, CH), 2.07 (m, 1H, CH), 3.69 (s, 3H, OCH_3), 7.29-7.47 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.0 (q, CH_3), 14.3 (q, CH_3), 22.6 (t, CH_2), 27.9 (q, $3CH_3$), 51.9 (q, OCH_3), 77.2 (s, C-2), 82.0 (s, C-3), 83.4 (s, Cq), 126.4 (d, CH_{arom}), 127.9 (d, CH_{arom}), 128.8 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 164.9 (s, CON), 165.5 (s, COO), 169.9 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-*tert*-butyl-1-methyl ester (*threo*-72c)** (sbo-585c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-62c** (0.71 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.59 g of the product as a colorless oil.

Yield: 79 %

TLC: R_f = 0.23 (ethyl acetate/n-hexane 1:4).

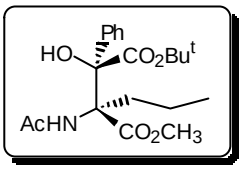
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92 (t, J = 7.5 Hz, 3H, CH_3), 1.44 (m, 2H, CH_2), 1.48 (s, 9H, $3CH_3$), 2.26 (s, 3H, $\underline{CH_3}CO$), 2.34 (m, 2H, CH_2), 3.04 (s, 3H, OCH_3), 7.27-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.4 (q, CH_3), 18.7 (t, CH_2), 28.2 (q, $3CH_3$), 37.9 (t, CH_2), 51.8 (q, OCH_3), 82.9 (s, Cq), 86.6 (s, C-2), 92.6 (s, C-3), 126.5 (d, CH_{arom}), 128.4 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 165.2 (s, CON), 168.7 (COO), 169.5 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-*tert*-butyl-1-methyl ester (*erythro*-72c)** (sbo-585d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-62c** (0.36 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

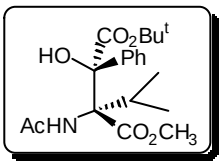
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.93 (t, J = 7.2 Hz, 3H, CH_3), 1.18 (m, 2H, CH_2), 1.53 (m, 2H, CH_2), 1.56 (s, 9H, $3CH_3$), 1.78 (s, 3H, $\underline{CH_3}CO$), 3.71 (s, 3H, OCH_3), 7.26-7.36 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.1 (q, CH_3), 14.8 (q, CH_3), 17.9 (t, CH_2), 27.8 (q, $3CH_3$), 32.7 (t, CH_2), 52.8 (q, OCH_3), 72.7 (s, C-2), 81.7 (s, C-3), 83.3 (s, Cq), 126.3 (d, CH_{arom}), 128.1 (d, CH_{arom}), 138.3 (s, Cq_{arom}), 166.4 (s, CON), 170.7 (COO), 172.4 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-*tert*-butyl 1-methyl ester (*threo*-72d)** (sbo-579c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-62d** (0.71 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.65 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3543, 3349, 2993, 2899, 1740, 1735, 1670, 1608, 1559, 1448, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (d, J = 6.9 Hz, 3H, CH_3), 0.98 (d, J = 6.9 Hz, 3H, CH_3), 1.21 (m, 1H, CH), 1.47 (s, 9H, $3CH_3$), 2.04 (s, 3H, $\underline{CH_3}CO$), 3.08 (s, 3H, OCH_3), 7.24-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

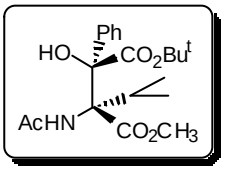
δ_{ppm} = 16.2 (q, CH_3), 18.0 (q, CH_3), 23.6 (q, CH_3), 27.9 (q, $3CH_3$), 34.7 (d, CH), 52.4 (q, OCH_3), 83.2 (s, Cq), 90.3 (s, C-2), 91.2 (s, C-3), 125.6 (d, CH_{arom}), 127.9 (d, CH_{arom}), 135.8 (s, Cq_{arom}), 169.6 (s, CON), 170.1 (s, COO), 172.1 (s, COO).

HRMS: ($C_{20}H_{29}NO_6$, M = 379.20 g/mol)

Calcd: 379.2039

Found: 379.2034

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-*tert*-butyl-1-methyl ester (*erythro*-72d)** (sbo-579d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-62d** (0.36 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.32 g of the product as a colorless oil.

Yield: 86 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

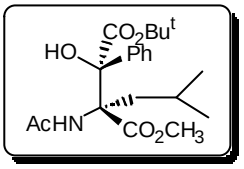
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.91 (d, J = 6.8 Hz, 3H, CH_3), 1.23 (d, J = 6.9 Hz, 3H, CH_3), 1.52 (s, 9H, $3CH_3$), 1.68 (s, 3H, $\underline{CH_3}CO$), 1.85 (septet, J = 6.8 Hz, 1H, CH), 3.67 (s, 3H, OCH_3), 7.23-7.46 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 15.8 (q, CH_3), 19.1 (q, CH_3), 32.6 (d, CH), 51.6 (q, OCH_3), 82.9 (s, Cq), 83.1 (s, C-2), 90.4 (s, C-3), 126.7 (d, CH_{arom}), 127.4 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 168.1 (s, CON), 170.2 (s, COO), 171.4 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-*tert*-butyl ester 1-methyl ester (*threo*-72e)** (sbo-580c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-62e** (0.75 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.45 g of the product as a colorless oil.

Yield: 63 %

TLC: R_f = 0.32 (ethyl acetate/n-hexane 1:4).

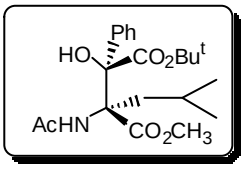
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (d, J = 6.6Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.35 (dd, J = 13.3, 5.7 Hz, 1H, CH), 1.49 (s, 9H, $3CH_3$), 1.81 (septet, J = 6.6 Hz, 1H, CH), 2.13 (s, 3H, $\underline{CH_3}CO$), 2.37 (dd, J = 13.3, 6.1 Hz, 1H, CH), 3.05 (s, 3H, OCH_3), 7.25-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 23.3 (q, CH_3), 24.5 (q, CH_3), 25.8 (d, CH), 27.9 (q, $3CH_3$), 43.9 (t, CH_2), 51.8 (q, OCH_3), 83.7 (s, Cq), 86.1 (s, C-2), 93.2 (s, C-3), 125.6 (d, CH_{arom}), 126.4 (d, CH_{arom}), 127.5 (d, CH_{arom}), 134.8 (s, Cq_{arom}), 163.7 (s, CON), 164.9 (s, COO), 166.8 (s, COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-*tert*-butyl ester 1-methyl ester (*erythro*-72e)** (sbo-580d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-62e** (0.38 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.22 g of the product as a colorless oil.

Yield: 65 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

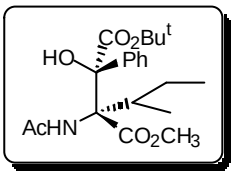
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.81 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.6 Hz, 3H, CH_3), 1.47 (s, 9H, $3CH_3$), 1.61 (dd, J = 13.4, 5.8 Hz, 1H, CH), 1.72 (s, 3H, $\underline{CH_3}CO$), 1.83 (m, 1H, CH), 2.02 (dd, J = 13.4, 6.1 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 7.26-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.4 (q, CH_3), 23.1 (q, CH_3), 24.1 (q, CH_3), 25.6 (d, CH), 28.3 (q, $3CH_3$), 37.1 (t, CH_2), 51.7 (q, OCH_3), 82.9 (s, Cq), 83.1 (s, C-2), 93.1 (s, C-3), 126.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 135.7 (s, Cq_{arom}), 165.1 (s, CON), 168.6 (s, COO), 171.0 (s, COO).

***threo* (2S*,3S*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl- succinic acid 4-*tert*-butyl ester 1-methyl ester (*threo*-72f)** (sbo-586a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-62f** (0.75 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.6 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.26 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 0.95 (d, J = 6.6 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.35 (m, 1H, CH), 1.47 (s, 9H, $3CH_3$), 2.26 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 7.27-7.56 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

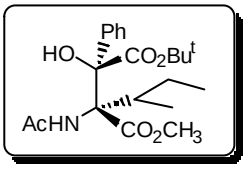
δ_{ppm} = 11.5 (q, CH_3), 13.5 (q, CH_3), 14.2 (q, CH_3), 18.7 (d, CH), 27.8 (q, $3CH_3$), 37.9 (t, CH_2), 51.8 (q, OCH_3), 83.2 (s, Cq), 86.6 (s, C-2), 92.6 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.6 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 165.2 (s, CON), 168.8 (s, COO), 169.5 (COO).

HRMS: ($C_{21}H_{31}NO_6$, M = 399.22 g/mol)

Calcd: 399.2236

Found: 399.2233

***erythro* (2S*,3R*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-*tert*-butyl 1-methyl ester (*erythro*-72f)** (sbo-586d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-62f** (0.38 g, 1 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 72 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

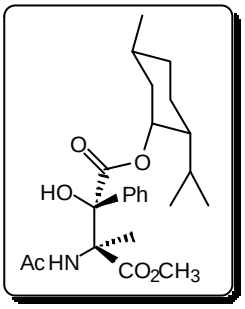
δ_{ppm} = 0.91 (t, J = 7.2 Hz, 3H, CH_3), 0.97 (d, J = 6.6 Hz, 3H, CH_3), 1.42 (s, 9H, $3CH_3$), 1.47-1.55 (m, 2H, CH_2), 1.69 (m, 1H, CH), 2.21 (s, 3H, $\underline{CH_3}CO$), 3.67 (s, 3H, OCH_3), 7.28-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 12.3 (q, CH_3), 14.1 (q, CH_3), 14.7 (q, CH_3), 19.2 (d, CH), 28.2 (q, $3CH_3$), 39.1 (t, CH_2), 51.6 (q, OCH_3), 86.2 (s, Cq), 87.6 (s, C-2), 93.6 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.6 (d, CH_{arom}), 134.5 (s, Cq_{arom}), 166.2 (s, CON), 169.3 (s, COO), 172.1 (COO).

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a -acetamido-b -hydroxy succinic acid derivatives 73a-f:

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*threo*-73a)** (sbo-373d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-63a** (0.83 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.62 g of the product as a colorless oil.

Yield: 75 %

TLC: R_f = 0.29 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3540, 3370, 2983, 2890, 1736, 1725, 1670, 1595, 1550, 1440, 1075, 980, 770.

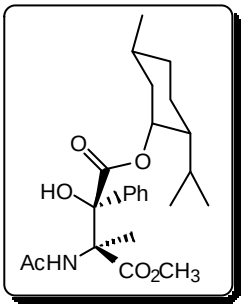
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.65 (d, J = 6.9 Hz, 3H, CH_3), 0.85 (d, J = 6.9 Hz, 3H, CH_3), 0.86 (d, J = 7.0 Hz, 3H, CH_3), 0.95 (m, 2H, CH_2), 1.03 (m, 2H, CH_2), 1.45 (m, 2H, CH_2), 1.68 (s, 3H, CH_3), 1.74 (m, 2H, CH_2), 1.84 (m, 2H, CH_2), 1.84 (m, 2H, CH_2), 2.23 (s, 3H, $\underline{CH_3}CO$), 3.05 (s, 3H, OCH_3), 4.66 (ddd, J = 11.0 , 4.6, 4.4 Hz, 1H, OCH), 7.25-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 15.6 (q, CH_3), 16.1 (q, CH_3), 20.6 (q, CH_3), 21.5 (q, CH_3), 21.9 (q, CH_3), 22.9 (d, CH), 23.3 (d, CH), 25.5 (t, CH_2), 26.1 (d, CH), 31.4 (d, CH), 33.9 (t, CH_2), 40.2 (t, CH_2), 46.9 (d, CH), 51.8 (q, OCH_3), 77.2 (t, OCH), 82.1 (s, C-2), 92.7 (s, C-3), 126.06 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 135.3 (s, Cq_{arom}), 166.2 (s, CON), 167.9 (s, COO), 170.2 (COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*erythro*-73a)** (sbo-373a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-63a** (0.41 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 68 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

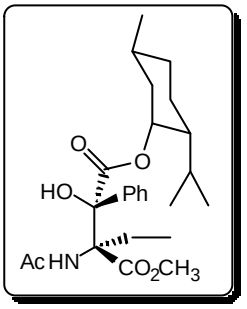
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.67 (d, J = 6.9 Hz, 3H, CH_3), 0.80 (d, J = 6.9 Hz, 3H, CH_3), 0.82 (d, J = 6.5 Hz, 3H, CH_3), 0.87 (m, 2H, CH_2), 1.00 (m, 2H, CH_2), 1.34 (m, 2H, CH_2), 1.47 (m, 2H, CH_2), 1.53 (s, 3H, CH_3), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.74 (s, 3H, OCH_3), 4.74 (ddd, J = 11.0 , 4.6, 4.4 Hz, 1H, OCH), 7.32-7.50 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.7 (q, CH_3), 15.8 (q, CH_3), 16.2 (q, CH_3), 20.7 (q, CH_3), 21.9 (q, CH_3), 22.0 (q, CH_3), 23.2 (q, CH_3), 25.6 (d, CH), 25.8 (d, CH), 31.4 (d, CH), 34.2 (t, CH_2), 40.3 (t, CH_2), 47.1 (d, CH), 52.2 (q, OCH_3), 74.9 (t, OCH), 75.9 (d, OCH), 109.9 (s, C-3), 127.3(d, CH_{arom}), 128.2 (d, CH_{arom}), 134.1 (s, Cq_{arom}), 164.9 (s, CON), 169.0 (s, COO), 169.2 (COO).

***threo* (2S*,3S*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*threo*-73b)** (sbo-374a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-63b** (0.86 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.52 g of the product as a colorless oil.

Yield: 60 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.59 (d, J = 6.9 Hz, 3H, CH_3), 0.76 (d, J = 7.1 Hz, 3H, CH_3), 0.86 (d, J = 6.6 Hz, 3H, CH_3), 1.02 (t, J = 7.2 Hz, 3H, CH_3), 1.12 (m, 2H, CH_2), 1.25 (m, 1H, CH), 1.35 (m, 2H, CH_2), 1.43 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.67 (m, 1H, CH), 1.83 (m, 2H, CH_2), 2.22 (s, 3H, $\underline{CH_3}CO$), 2.46 (m, 1H, CH), 3.03 (s, 3H, OCH_3), 4.67 (ddd, J = 11.0, 4.5, 4.4 Hz, 1H, OCH), 7.26-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.9 (q, CH_3), 14.1 (q, CH_3), 15.5 (q, CH_3), 20.7 (q, CH_3), 21.9 (q, CH_3), 22.9 (q, CH_3), 25.5 (d, CH), 28.9 (t, CH_2), 31.4 (d, CH), 33.9 (t, CH_2), 40.3 (t, CH_2), 46.9 (d, CH), 51.7 (q, OCH_3), 81.9 (d, OCH), 86.8 (s, C-2), 92.7 (s, C-3), 126.4 (d, CH_{arom}), 127.4 (d, CH_{arom}), 128.3 (d, CH), 134.9 (s, Cq_{arom}), 165.5 (s, CON), 167.8 (s, COO), 169.5 (COO).

MS: (EI, 70 eV)

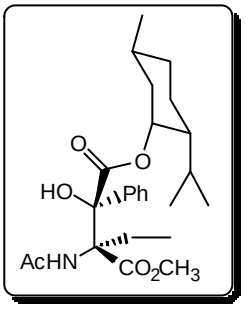
m/z (%) = 430 (M^+ – OH), 392 (4), 388 (M^+-CO_2Me, 6), 288 (30), 353 (7), 244 (8), 159 (30), 127 (15), 105 (40), 83 (100), 57 (43), 55 (62).

HRMS: ($C_{25}H_{37}NO_6$, M = 447.26 g/mol)

Calcd: 447.2611

Found: 447.2605

***erythro* (2S*,3R*) 2-Acetylamino-2-ethyl-3-hydroxy-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*erythro*-73b)** (sbo-374b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-63b** (0.43 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.25 g of the product as a colorless oil.

Yield: 53 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

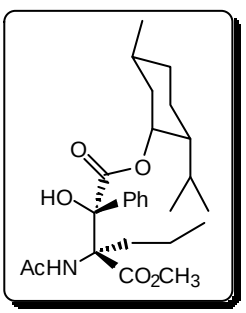
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.62 (d, J = 6.9 Hz, 3H, CH_3), 0.78 (d, J = 7.2 Hz, 3H, CH_3), 0.88 (d, J = 6.6 Hz, 3H, CH_3), 1.03 (t,J = 7.2 Hz, 3H, CH_3), 1.14 (m, 2H, CH_2), 1.27 (m, 2H, CH_2), 1.37 (m, 1H, CH), 1.45 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 1.68 (m, 1H, CH), 1.89 (m, 2H, CH_2), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.67 (s, 3H, OCH_3), 4.67 (ddd, J = 11.0 , 4.5, 4.4 Hz, 1H, OCH), 7.26-7.53 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.7 (q, CH_3), 14.2 (q, CH_3), 15.7 (q, CH_3), 20.9 (q, CH_3), 22.0 (q, CH_3), 22.8 (q, CH_3), 25.7 (q, CH_3), 29.0 (t, CH_2), 31.7 (d, CH), 33.5 (t, CH_2), 40.7 (t, CH_2), 47.0 (d, CH), 52.3 (q, OCH_3), 76.0 (d, OCH), 82.7 (s, C-2), 93.2 (s, C-3), 126.1 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH), 134.7 (s, Cq_{arom}), 169.1 (s, CON), 170.1 (s, COO), 171.3 (COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*threo*-73c)** (sbo-375a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-63c** (0.87 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.54 g of the product as a colorless oil.

Yield: 64 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.74 (d, J = 6.9 Hz, 3H, CH_3), 0.82 (d, J = 6.9 Hz, 3H, CH_3), 0.84 (t, J = 7.2 Hz, 3H, CH_3), 0.88 (d, J = 6.5 Hz, 3H, CH_3), 0.98 (m, 2H, CH_2), 1.24 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 1.43 (m, 1H, CH), 1.47 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 2.20 (s, 3H, CH_3CO), 3.00 (s, 3H, OCH_3), 4.68 (ddd, J = 11.1, 4.6, 4.4 Hz, 1H, OCH), 7.20-7.52 (m, 5H, H_{arom}).

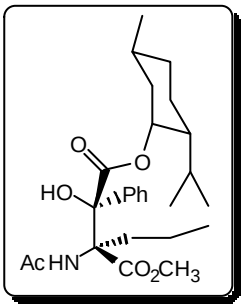
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.4 (q, CH_3), 15.7 (q, CH_3), 18.8 (q, CH_3), 20.8 (q, CH_3), 21.9 (d, CH), 22.9 (t, CH_2), 25.6 (d, CH), 31.4 (t, CH_2), 34.0 (t, CH_2), 38.2 (t, CH_2), 40.4 (t, CH_2), 46.9 (d, CH), 51.8 (q, OCH_3), 73.2 (d, OCH), 86.2 (s, C-2), 92.7 (s, C-3), 126.2 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.9 (s, Cq_{arom}), 165.5 (s, CON), 167.8 (s, COO), 168.6 (COO).

Anal: ($C_{21}H_{37}NO_6$, M = 339.3 g/mol)

Calcd:	C 63.32	H 9.33	N 3.51
Found:	C 64.00	H 9.12	N 3.59

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-3-phenyl-2-propyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*erythro*-73c)** (sbo-375b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-63c** (0.44 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.28 g of the product as a colorless oil.

Yield: 74 %

TLC: R_f = 0.59 (ethyl acetate/n-hexane 1:4).

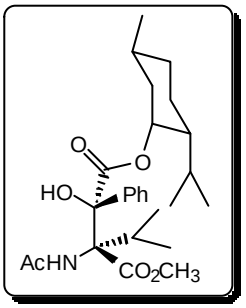
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (d, J = 6.9 Hz, 3H, CH_3), 0.82 (d, J = 6.9 Hz, 3H, CH_3), 0.83 (d, J = 7.0 Hz, 3H, CH_3), 0.85 (d, J = 6.5 Hz, 3H, CH_3), 0.95 (m, 2H, CH_2), 1.05 (m, 2H, CH_2), 1.25 (m, 1H, CH), 1.29 (m, 2H, CH_2), 1.34 (m, 2H, CH_2), 1.45 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 2.06 (s, 3H, CH_3CO), 3.46 (s, 3H, OCH_3), 4.72 (ddd, J = 11.1 , 4.5, 4.4 Hz, 1H, OCH), 7.26-7.68 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 16.1 (q, CH_3), 17.2 (q, CH_3), 17.3 (q, CH_3), 20.7 (q, CH_3), 21.9 (q, CH_3), 23.9 (t, CH_2), 25.9 (d, CH), 29.9 (d, CH), 31.5 (t, CH_2), 34.1 (t, CH_2), 39.8 (t, CH_2), 42.6 (t, CH_2), 46.4 (d, CH), 52.5 (q, OCH_3), 72.8 (d, OCH), 80.4 (s, C-2), 86.1 (s, C-3), 126.2 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 137.9 (s, Cq_{arom}), 171.5 (s, CON), 172.3 (s, COO), 175.8 (COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*threo*-73d)** (sbo-379a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-63d** (0.87 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.69 g of the product as a colorless oil.

Yield: 72 %

TLC: R_f = 0.29 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3500, 3346, 2956, 2873, 1738, 1732, 1683, 1600, 1550, 1494, 1055, 942, 640.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (d, J = 6.6 Hz, 3H, CH_3), 0.72 (d, J = 6.9 Hz, 3H, CH_3), 0.78 (d, J = 6.6 Hz, 3H, CH_3), 0.88 (d, J = 6.6 Hz, 3H, CH_3), 0.92 (d, J = 6.8 Hz, 3H, CH_3), 1.10 (m, 2H, CH_2), 1.23 (m, 2H, CH_2), 1.29 (m, 1H, CH), 1.34 (m, 2H, CH_2), 1.44 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 2.29 (s, 3H, $\underline{CH_3}CO$), 3.15 (s, 3H, OCH_3), 4.80 (ddd, J = 11.0, 4.5 , 4.4Hz, 1H, OCH), 7.23-7.31 (m, 5H, H_{arom}).

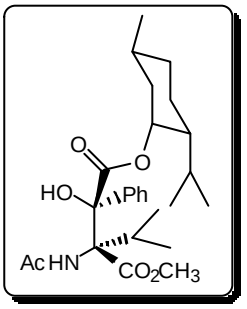
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 15.8 (q, CH_3), 16.3 (q, CH_3), 18.9 (q, CH_3), 20.4 (q, CH_3), 21.9 (q, CH_3), 23.2 (d, CH), 25.6 (d, CH), 31.4 (t, CH_2), 31.5 (d, CH), 23.4 (t, CH_2), 34.1 (t, CH_2), 40.1 (t, CH_2), 46.8 (d, CH), 51.6 (q, OCH_3), 76.2 (d, OCH), 89.9 (s, C-2), 91.3 (s, C-3), 126.6 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 136.0 (s, Cq_{arom}), 163.4 (s, CON), 167.1 (s, COO), 170.4 (COO).

Anal: ($C_{26}H_{39}NO_6$, M = 461.59 g/mol)

Calcd:	C 67.65	H 8.52	N 3.03
Found:	C 66.98	H 8.22	N 3.14

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isopropyl-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*erythro*-73d)** (sbo-379b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-63d** (0.44 g, 1 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.4 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

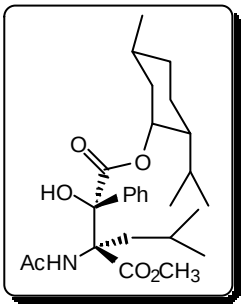
δ_{ppm} = 0.54 (d, J = 6.5 Hz, 3H, CH_3), 0.62 (d, J = 6.9 Hz, 3H, CH_3), 0.80 (d, J = 6.9 Hz, 3H, CH_3), 0.82 (d, J = 6.8 Hz, 3H, CH_3), 0.85 (d, J = 6.5 Hz, 3H, CH_3), 1.23 (m, 2H, CH_2), 1.34 (m, 2H, CH_2), 1.37 (m, 1H, CH), 1.53 (m, 2H, CH_2), 1.57 (m, 2H,

CH_2), 1.60 (m, 2H, CH_2), 1.83 (m, 2H, CH_2), 2.18 (s, 3H, $\underline{CH_3}CO$), 3.81 (s, 3H, OCH_3), 4.48 (ddd, J = 11.0 , 4.6, 4.4 Hz, 1H, OCH), 7.25-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 15.9 (q, CH_3), 18.7 (q, CH_3), 20.7 (q, CH_3), 21.8 (q, CH_3), 21.9 (q, CH_3), 22.9 (d, CH), 23.0 (t, CH_2), 25.6 (d, CH), 31.2 (t, CH_2), 34.0 (d, CH), 34.2 (d, CH), 40.1 (t, CH_2), 46.8 (d, CH), 52.4 (q, OCH_3), 77.0 (t, OCH), 82.1 (s, C-2), 92.7 (s, C-3), 126.3 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.1 (s, Cq_{arom}), 163.4 (s, CON), 169.8 (s, COO), 173.4 (COO).

***threo* (2S*,3S*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*threo*-73e)** (sbo-384b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-63e** (0.9 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.85 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.26 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

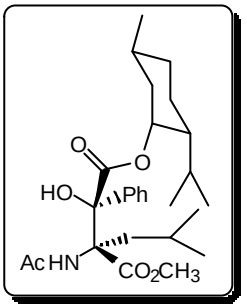
δ_{ppm} = 0.64 (d, J = 6.9 Hz, 3H, CH_3), 0.82 (d, J = 6.9 Hz, 3H, CH_3), 0.83 (d, J = 6.8 Hz, 3H, CH_3), 0.85 (d, J = 6.6 Hz, 3H, CH_3), 0.96 (d, J = 6.6 Hz, 3H, CH_3), 1.02 (m, 1H, CH), 1.23 (m, 2H, CH_2), 1.34 (m, 2H, CH_2), 1.43 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.67 (m, 2H, CH_2),1.83 (m, 2H, CH_2), 2.12 (s, 3H, $\underline{CH_3}CO$), 3.03 (s, 3H, OCH_3), 4.74 (ddd, J = 11.0, 4.6 , 4.5Hz, 1H, OCH), 7.23-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.2 (q, CH_3), 14.3 (q, CH_3), 15.8 (q, CH_3), 15.9 (q, CH_3), 20.8 (q, CH_3), 21.8 (q, CH_3), 23.0 (d, CH), 23.4 (t, CH_2), 24.1 (d, CH), 25.9 (d, CH), 31.2 (t, CH_2), 33.9 (t, CH_2), 40.1 (t, CH), 46.8 (d, CH), 52.3 (q, OCH_3), 76.8 (d, OCH), 86.2 (s, C-

2), 93.3 (s, C-3), 126.7 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 165.1 (s, CON), 170.4 (s, COO), 172.9 (COO).

***erythro* (2S*,3R*) 2-Acetylamino-3-hydroxy-2-isobutyl-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*erythro*-73e)** (sbo-384)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-63e** (0.46 g, 1 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.4 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.36 (ethyl acetate/n-hexane 1:4).

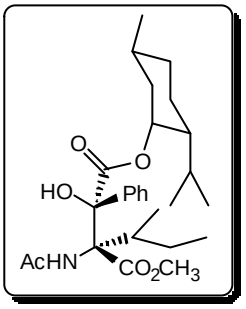
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.65 (d, J = 6.9 Hz, 3H, CH_3), 0.83 (d, J = 6.9 Hz, 3H, CH_3), 0.85 (d, J = 6.8 Hz, 3H, CH_3), 0.87 (d, J = 6.6 Hz, 3H, CH_3), 0.98 (d, J = 6.6 Hz, 3H, CH_3), 1.19 (m, 1H, CH), 1.23 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 1.47 (m, 2H, CH_2), 1.58 (m, 2H, CH_2), 1.69 (m, 2H, CH_2),1.87 (m, 2H, CH_2), 2.13 (s, 3H, $\underline{CH_3}CO$), 3.69 (s, 3H, OCH_3), 4.78 (ddd, J = 11.0, 4.6 , 4.5Hz, 1H, OCH), 7.28-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.3 (q, CH_3), 14.6 (q, CH_3), 15.6 (q, CH_3), 16.0 (q, CH_3), 21.0 (q, CH_3), 21.8 (q, CH_3), 23.2 (d, CH), 23.4 (t, CH_2), 24.3 (d, CH), 25.8 (d, CH), 31.3 (t, CH_2), 34.5 (t, CH_2), 42.1 (t, CH), 47.0 (d, CH), 52.7 (q, OCH_3), 76.9 (d, OCH), 87.3 (s, C-2), 94.1 (s, C-3), 126.9 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.2 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 169.1 (s, CON), 170.1 (s, COO), 172.1 (COO).

***threo* (2S*,3S*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*threo*-73f)** (sbo-385c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-63f** (0.9 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.82 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.27 (ethyl acetate/n-hexane 1:4).

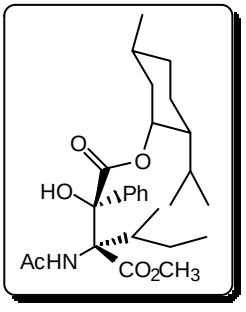
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.53 (d, J = 6.8 Hz, 3H, CH_3), 0.65 (d, J = 6.8 Hz, 3H, CH_3), 0.75 (d, J = 6.5 Hz, 3H, CH_3), 0.83 (d, J = 6.9 Hz, 3H, CH_3), 0.90 (t, J = 7.2 Hz, 3H, CH_3), 1.03 (m, 2H, CH_2), 1.15 (m, 1H, CH), 1.23 (m, 2H, CH_2), 1.25 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 1.45 (m, 1H, CH), 1.89 (m, 2H, CH_2), 2.29 (s, 3H, $\underline{CH_3}CO$), 3.14 (s, 3H, OCH_3), 4.84 (ddd, J = 11.0, 4.6, 4.4 Hz, 1H, OCH), 7.25-7.37 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 11.8 (q, CH_3), 12.3 (q, CH_3), 12.7 (q, CH_3), 13.9 (q, CH_3), 15.8 (q, CH_3), 20.4 (q, CH_3), 20.8 (t, CH_2), 21.9 (d, CH), 23.2 (d, CH), 25.6 (t, CH_2), 26.3 (d, CH), 31.5 (t, CH_2), 34.0 (d, CH), 39.3 (t, CH_2), 40.1 (t, CH_2), 46.8 (d, CH), 51.6 (q, OCH_3), 76.3 (d, OCH), 88.5 (s, C-2), 90.8 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.1 (d, CH_{arom}), 135.9 (s, Cq_{arom}), 163.4 (s, CON), 167.1 (s, COO), 170.5 (COO).

***erythro* (2S*,3R*) 2-Acetylamino-2-*sec*-butyl-3-hydroxy-3-phenyl-succinic acid 4-(2-isopropyl-5-methyl-cyclohexyl) ester 1-methyl ester (*erythro*-73f)** (sbo-385)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-63f** (0.46 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.42 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

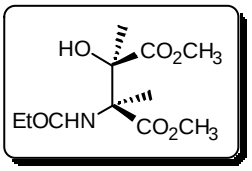
δ_{ppm} = 0.55 (d, J = 6.9 Hz, 3H, CH_3), 0.67 (d, J = 6.8 Hz, 3H, CH_3), 0.77 (d, J = 6.5 Hz, 3H, CH_3), 0.85 (d, J = 7.2 Hz, 3H, CH_3), 0.93 (t, J = 7.2 Hz, 3H, CH_3), 1.17 (m, 2H, CH_2), 1.27 (m, 1H, CH), 1.30 (m, 2H, CH_2), 1.34 (m, 2H, CH_2), 1.43 (m, 2H, CH_2), 1.49 (m, 1H, CH), 1.93 (m, 2H, CH_2), 2.17 (s, 3H, $\underline{CH_3}CO$), 3.74 (s, 3H, OCH_3), 4.76 (ddd, J = 11.0, 4.6, 4.4 Hz, 1H, OCH), 7.26-7.35 (m, 5H, H_{arom}).

^{13}C-NMR: ($CDCl_3$)

δ_{ppm} = 11.3 (q, CH_3), 12.7 (q, CH_3), 12.9 (q, CH_3), 13.5 (q, CH_3), 15.9 (q, CH_3), 20.5 (q, CH_3), 20.9 (t, CH_2), 22.3 (d, CH), 27.4 (d, CH), 29.3 (t, CH_2), 30.1 (d, CH), 34.1 (t, CH_2), 37.2 (d, CH), 40.1 (t, CH_2), 42.3 (t, CH_2), 47.0 (d, CH), 52.7 (q, OCH_3), 76.0 (d, OCH), 89.1 (s, C-2), 92.3 (s, C-3), 125.7 (d, CH_{arom}), 127.3 (d, CH_{arom}), 128.1 (d, CH_{arom}), 136.5 (s, Cq_{arom}), 165.4 (s, CON), 169.1 (s, COO), 173.1 (COO).

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-propionylamino-b-hydroxy succinic acid derivatives 74a-f:

***erythro* (2S*,3R*) 2,3-Dimethyl-3-hydroxy-2-propionylamino-succinic acid dimethyl ester (*erythro*-74a)** (sbo-442)



According to the typical hydrolysis procedure, the bicyclic oxetane **64a** (0.49 g, 2 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.48 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.45 (ethyl acetate/n-hexane 1:4).

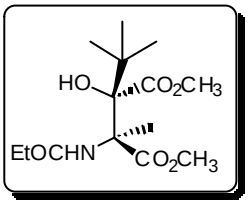
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.12 (t, J = 7.2 Hz, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 1.98 (q, J = 7.2 Hz, 2H, CH_2), 3.67 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.9 (q, CH_3), 19.2 (q, CH_3), 25.7 (q, CH_3), 35.2.4 (t, CH_2), 52.9 (q, OCH_3), 53.2 (q, OCH_3), 78.3 (s, C-2), 87.2 (s, C-3), 169.2 (s, CON), 172.1 (COO), 174.3 (s, COO).

***threo* (2S*,3S*) 3-*tert*-Butyl-2-propionylamino-3-hydroxy-2-methyl-succinic acid dimethyl ester (*threo*-74b)** (sbo-442c)



According to the typical hydrolysis procedure, the bicyclic oxetane **64b** (0.3 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.23 g of the product as a colorless oil.

Yield: 81 %

TLC: R_f = 0.45 (ethyl acetate/n-hexane 1:4).

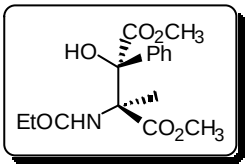
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.14 (t, J = 7.2 Hz, 3H, CH_3), 1.42 (s, 9H, $3CH_3$), 1.65 (s, 3H, CH_3), 1.98 (q, J = 7.2 Hz, 2H, CH_2), 3.69 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.7 (q, CH_3), 20.2 (q, CH_3), 28.7 (q, $3CH_3$), 35.2.4 (t, CH_2), 37.8 (s, Cq), 52.9 (q, OCH_3), 53.2 (q, OCH_3), 82.3 (s, C-2), 89.2 (s, C-3), 169.2 (s, CON), 172.1 (COO), 175.3 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid dimethyl ester (*threo*-74c)** (sbo-441c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-64c** (0.61 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.52 g of the product as a colorless oil.

Yield: 85 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

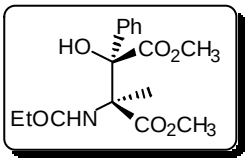
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.04 (t, J = 7.5 Hz, 3H, CH_3), 1.60 (s, 3H, CH_3), 2.14 (q, J = 7.5 Hz, 2H, CH_2), 3.12 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 7.28-7.62 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.4 (q, CH_3), 16.0 (q, CH_3), 29.9 (t, CH_2), 52.8 (q, OCH_3), 53.9 (q, OCH_3), 80.9 (s, C-2), 83.2 (s, C-3), 126.3 (d, CH_{arom}), 128.2 (d, CH_{arom}), 137.2 (s, Cq_{arom}), 168.4 (s, CON), 172.2 (s, COO), 173.9 (s, COO).

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid dimethyl ester (*erythro*-74c)** (sbo-441d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-64c** (0.31 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.27 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 1:4).

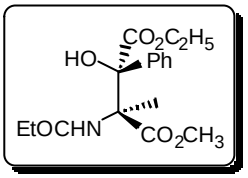
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.30 (t, J = 7.5 Hz, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.53 (q, J = 7.5 Hz, 2H, CH_2), 3.68 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.28-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.6 (q, CH_3), 16.1 (q, CH_3), 30.1 (t, CH_2), 52.8 (q, OCH_3), 53.4 (q, OCH_3), 66.6 (s, C-2), 82.1 (s, C-3), 126.2 (d, CH_{arom}), 128.2 (d, CH_{arom}), 136.5 (s, Cq_{arom}), 170.3 (s, CON), 172.6 (s, COO), 174.9 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid 1-ethyl ester-4-methyl ester (*threo*-74d)** (sbo-465b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-64d** (0.64 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.44 g of the product as a colorless oil.

Yield: 76 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3490, 3365, 2983, 2890, 1743, 1720, 1650, 1600, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.08 (t, J = 7.5 Hz, 3H, CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.56 (q, J = 7.5 Hz, 2H, CH_2), 3.03 (s, 3H, OCH_3), 4.26 (q, J = 7.5 Hz, 2H, OCH_2), 7.26-7.32 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

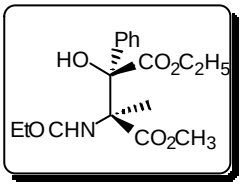
δ_{ppm} = 9.5 (q, CH_3), 14.0 (q, CH_3), 21.7 (q, CH_3), 30.1 (t, CH_2), 51.8 (q, OCH_3), 62.3 (t, OCH_2), 82.3 (s, C-2), 84.5 (s, C-3), 126.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 136.9 (s, Cq_{arom}), 168.4 (s, CON), 170.1 (s, COO), 172.5 (s, COO).

HRMS: ($C_{17}H_{23}NO_6$, M = 337.15 g/mol)

Calcd: 337.1468

Found: 351.1463

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid 1-ethyl ester-4-methyl ester (*erythro*-74d)** (sbo-465d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-64d** (0.32 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 76 %

TLC: R_f = 0.53 (ethyl acetate/n-hexane 1:4).

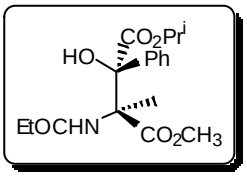
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.11 (t, J = 7.5 Hz, 3H, CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_3), 1.57 (s, 3H, CH_3), 2.19 (q, J = 7.5 Hz, 2H, CH_2), 3.61 (s, 3H, OCH_3), 4.22 (q, J = 7.2 Hz, 2H, OCH_2), 6.38 (s, 1H, NH), 7.31-7.66 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.6 (q, CH_3), 13.9 (q, CH_3), 19.9 (q, CH_3), 30.0 (t, CH_2), 52.7 (q, OCH_3), 62.2 (t, OCH_2), 66.7 (s, C-2), 82.9 (s, C-3), 126.5 (d, CH_{arom}), 128.5 (d, CH_{arom}), 136.7 (s, Cq_{arom}), 172.1 (s, CON), 172.4 (s, COO), 174.7 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid 1-isopropyl ester-4-methyl ester (*threo*-74e)** (sbo-463)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-64e** (0.67 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.51 g of the product as a colorless oil.

Yield: 74 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.07 (t, J = 7.5 Hz, 3H, CH_3), 1.24 (d, J = 6.2 Hz, 3H, CH_3), 1.27 (d, J = 6.2 Hz, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.32 (q, J = 7.5 Hz, 2H, CH_2), 3.05 (s, 3H, OCH_3), 5.17 (septet, J = 6.2 Hz, 1H, OCH), 7.28-7.39 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

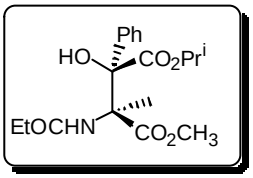
δ_{ppm} = 9.7 (q, CH_3), 15.7 (q, CH_3), 21.6 (q, CH_3), 21.7 (q, CH_3), 28.3 (t, CH_2), 52.8 (q, OCH_3), 70.3 (t, OCH_2), 85.6 (s, C-2), 92.3 (s, C-3), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 165.1 (s, CON), 170.1 (s, COO), 171.3 (s, COO).

Anal: ($C_{18}H_{25}NO_6$, M = 351.17 g/mol)

Calcd: C 61.52 H 7.17 N 3.99

Found: C 61.72 H 7.14 N 4.03

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid 1-isopropyl ester-4-methyl ester (*erythro*-74e)** (sbo-463a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-64e** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.2 g of the product as a colorless oil.

Yield: 74 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

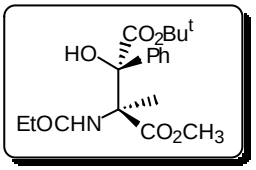
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.04 (t, J = 7.5 Hz, 3H, CH_3), 1.23 (d, J = 6.2 Hz, 3H, CH_3), 1.25 (d, J = 6.2 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.13 (q, J = 7.5 Hz, 2H, CH_2), 3.76 (s, 3H, OCH_3), 5.12 (septet, J = 6.2 Hz, 1H, OCH), 7.28-7.39 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.8 (q, CH_3), 15.9 (q, CH_3), 21.7 (q, CH_3), 21.9 (q, CH_3), 27.2 (t, CH_2), 52.7 (q, OCH_3), 70.1 (d, OCH), 82.7 (s, C-2), 87.3 (s, C-3), 126.2 (d, CH_{arom}), 128.3 (d, CH), 135.6 (s, Cq_{arom}), 169.2 (s, CON), 172.1 (s, COO), 173.1 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid 1-*tert*-butyl ester-4-methyl ester (*threo*-74f)** (sbo-450c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-64f** (0.69 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.64 g of the product as a colorless oil.

Yield: 79 %

TLC: R_f = 0.42 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.22 (t, J = 7.5 Hz, 3H, CH_3), 1.44 (s, 9H, $3CH_3$), 1.72 (s, 3H, CH_3), 2.37 (q, J = 7.5 Hz, 2H, CH_2), 3.02 (s, 3H, OCH_3), 7.28-7.67 (m, 5H, H_{arom}).

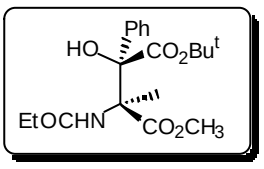
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.1 (q, CH_3), 21.6 (t, CH_2), 21.7 (q, CH_3), 27.9 (q, $3CH_3$), 52.8 (q, OCH_3), 82.0 (s, C-2), 83.8 (s, C_q), 92.3 (s, C-3), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 167.1 (s, CON), 170.1 (s, COO), 170.2 (s, COO).

Anal: ($C_{19}H_{27}NO_6$, M = 365.2 g/mol)

Calcd:	C 62.45	H 7.45	N 3.83
Found:	C 62.92	H 7.38	N 3.96

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-propionylamino-succinic acid 1-*tert*-butyl ester-4-methyl ester (*erythro*-74f)** (sbo-450a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-64f** (0.35 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.31 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

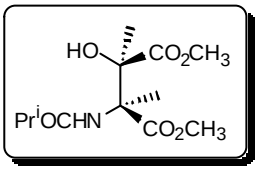
δ_{ppm} = 1.09 (t, J = 7.5 Hz, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.55 (s, 9H, $3CH_3$), 2.19 (q, J = 7.5 Hz, 2H, CH_2), 3.67 (s, 3H, OCH_3), 7.35-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 9.5 (q, CH_3), 18.7 (q, CH_3), 27.8 (q, $3CH_3$), 30.1 (t, CH_2), 52.4 (q, OCH_3), 66.4 (s, C-2), 79.7 (s, C-3), 85.3 (s, Cq), 126.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 171.3 (s, CON), 172.1 (s, COO), 173.4 (s, COO).

Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a-isobutyrylamino-b-hydroxy succinic acid derivatives 75a-f:

***erythro* (2R*,3S*) 2-Hydroxy-3-isobutyrylamino-2,3-dimethyl-succinic acid dimethyl ester (*erythro*-75a)** (sbo-460)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-65a** (0.25 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.21 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:3).

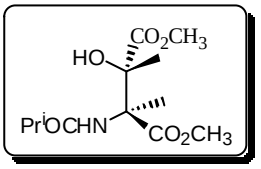
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (d, J = 6.8 Hz, 3H, CH_3), 1.13 (d, J = 6.9 Hz, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.45 (septet, J = 6.8 Hz, 1H, CH), 3.64 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 18.3 (q, CH_3), 18.5 (q, CH_3), 23.5 (q, CH_3), 42.1 (d, CH), 52.7 (q, OCH_3), 53.5 (q, OCH_3), 75.6 (s, C-2), 89.1 (s, C-3), 169.1 (s, CON), 171.1 (COO), 176.2 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-isobutyrylamino-2,3-dimethyl-succinic acid dimethyl ester (*threo*-75a)** (sbo-460a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-65a** (0.5 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.42 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:3).

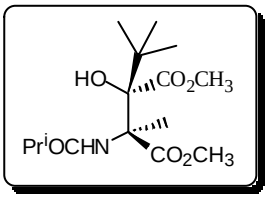
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.08 (d, J = 6.8 Hz, 3H, CH_3), 1.19 (d, J = 6.9 Hz, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 2.49 (septet, J = 6.8 Hz, 1H, CH), 3.67 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.6 (q, CH_3), 18.8 (q, CH_3), 18.9 (q, CH_3), 23.5 (q, CH_3), 42.1 (d, CH), 52.7 (q, OCH_3), 53.5 (q, OCH_3), 75.6 (s, C-2), 89.1 (s, C-3), 169.1 (s, CON), 174.1 (COO), 175.2 (s, COO).

***threo* (2S*,3S*) 2-*tert*-Butyl-2-hydroxy-3-isobutyrylamino-3-methyl-succinic acid dimethyl ester (*threo*-75b)** (sbo-461)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-65b** (0.31 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.29 g of the product as a colorless oil.

Yield: 86 %

TLC: R_f = 0.52 (ethyl acetate/n-hexane 1:4).

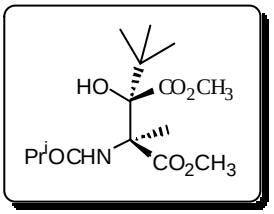
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.0 (d, J = 6.8 Hz, 3H, CH_3), 1.12 (d, J = 6.9 Hz, 3H, CH_3), 1.45 (s, 9H, $3CH_3$), 1.95 (s, 3H, CH_3), 2.45 (septet, J = 6.8 Hz, 1H, CH), 3.54 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.9 (q, CH_3), 18.3 (q, CH_3), 18.5 (q, CH_3), 27.5 (q, $3CH_3$), 38.1 (s, Cq), 42.1 (d, CH), 52.7 (q, OCH_3), 53.5 (q, OCH_3), 75.6 (s, C-2), 89.1 (s, C-3), 169.1 (s, CON), 171.1 (COO), 176.2 (s, COO).

***erythro* (2R*,3S*) 2-*tert*-Butyl-2-hydroxy-3-isobutyrylamino-3-methyl-succinic acid dimethyl ester (*erythro*-75b)** (sbo-461a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-65b** (0.21 g, 0.8 mmol) was cleaved hydrolytically in 2h. Preparative chromatography yielded 0.15 g of the product as a colorless oil.

Yield: 76 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:4).

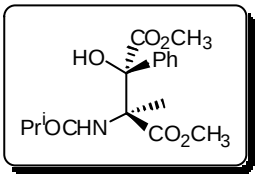
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.03 (d, J = 6.8 Hz, 3H, CH_3), 1.15 (d, J = 6.9 Hz, 3H, CH_3), 1.49 (s, 9H, $3CH_3$), 1.98 (s, 3H, CH_3), 2.49 (septet, J = 6.8 Hz, 1H, CH), 3.57 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 15.6 (q, CH_3), 18.8 (q, CH_3), 18.9 (q, CH_3), 28.5 (q, $3CH_3$), 39.2 (s, Cq), 42.1 (d, CH), 52.7 (q, OCH_3), 53.5 (q, OCH_3), 75.6 (s, C-2), 89.1 (s, C-3), 169.1 (s, CON), 174.1 (COO), 175.2 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid dimethyl ester (*threo*-75c)** (sbo-458c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-65c** (0.63 g, 2 mmol) was cleaved hydrolytically in 5h. Preparative chromatography yielded 0.52 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.38 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.13 (d, J = 6.6 Hz, 3H, CH_3), 1.27 (d, J = 6.9 Hz, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.54 (septet, J = 6.6 Hz, 1H, CH), 3.00 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 7.28-7.47 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

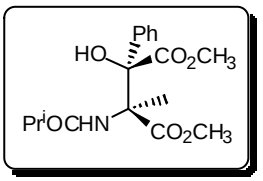
δ_{ppm} = 15.9 (q, CH_3), 17.9 (q, CH_3), 18.1 (q, CH_3), 36.7 (d, CH), 52.1 (q, OCH_3), 52.9 (q, OCH_3), 78.1 (s, C-2), 83.1 (s, C-3), 126.7 (d, CH_{arom}), 128.4 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 170.1 (s, CON), 173.1 (s, COO), 175.1 (s, COO).

HRMS: ($C_{17}H_{23}NO_6$, M = 337.15 g/mol)

Calcd: 337.1474

Found: 337.1470

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid dimethyl ester (*erythro*-75c)** (sbo-458d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-65c** (0.31 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.22 g of the product as a colorless oil.

Yield: 73 %

TLC: R_f = 0.53 (ethyl acetate/n-hexane 1:4).

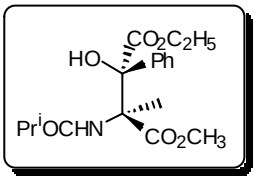
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.10 (d, J = 6.6 Hz, 3H, CH_3), 1.30 (d, J = 6.9 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.79 (septet, J = 6.6 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.32-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 16.1 (q, CH_3), 18.2 (q, CH_3), 18.5 (q, CH_3), 37.2 (d, CH), 52.3 (q, OCH_3), 52.7 (q, OCH_3), 75.5 (s, C-2), 79.7 (s, C-3), 126.2 (d, CH_{arom}), 128.2 (d, CH_{arom}), 136.5 (s, Cq_{arom}), 169.1 (s, CON), 172.1 (s, COO), 175.1 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid 1-ethyl ester-4-methyl ester (*threo*-75d)** (sbo-459e)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-65d** (0.66 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.51 g of the product as a colorless oil.

Yield: 79 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

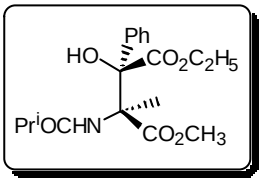
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (d, J = 6.8 Hz, 3H, CH_3), 1.30 (t, J = 7.5 Hz, 3H, CH_3), 1.35 (d, J = 6.9 Hz, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.54 (septet, J = 6.8 Hz, 1H, CH), 3.13 (s, 3H, OCH_3), 4.26 (q, J = 7.5 Hz, 2H, OCH_2), 7.35-7.53 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 16.5 (q, CH_3), 17.6 (q, CH_3), 17.9 (q, CH_3), 37.3 (d, CH), 52.3 (q, OCH_3), 62.8 (t, OCH_2), 79.7 (s, C-2), 91.9 (s, C-3), 126.2 (d, CH_{arom}), 127.5 (d, CH_{arom}), 136.9 (s, Cq_{arom}), 168.8 (s, CON), 169.2 (s, COO), 173.3 (s, COO).

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid 1-ethyl ester-4-methyl ester (*erythro*-75d)** (sbo-459a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-65d** (0.33 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 4:1).

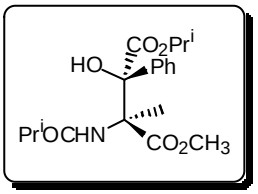
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (d, J = 6.9 Hz, 3H, CH_3), 1.08 (d, J = 6.8 Hz, 3H, CH_3), 1.28 (t, J = 7.5 Hz, 3H, CH_3), 1.58 (s, 3H, CH_3), 2.36 (septet, J = 6.8 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 4.31 (q, J = 7.5 Hz, 2H, OCH_2), 7.31-7.67 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 18.9 (q, CH_3), 19.3 (q, CH_3), 19.8 (q, CH_3), 35.9 (d, CH), 52.7 (q, OCH_3), 62.2 (t, OCH_2), 80.6 (s, C-2), 83.0 (s, C-3), 126.5 (d, CH_{arom}), 128.5 (d, CH_{arom}), 136.7 (s, Cq_{arom}), 172.1 (s, CON), 172.2 (s, COO), 172.4 (s, COO).

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid 1-isopropyl ester-4-methyl ester (*threo*-75e)** (sbo-456c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-65e** (0.34 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.22 g of the product as a colorless oil.

Yield: 78 %

TLC: R_f = 0.43 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3525, 3370, 2983, 2890, 1756, 1730, 1645, 1605, 1550, 1440, 1075, 980, 770.

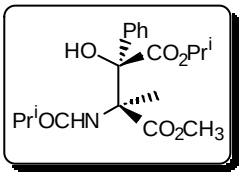
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.22 (d, J = 6.5 Hz, 3H, CH_3), 1.24 (d, J = 6.3 Hz, 3H, CH_3), 1.33 (d, J = 6.9 Hz, 3H, CH_3), 1.36 (d, J = 6.9 Hz, 3H, CH_3), 1.68 (s, 3H, CH_3), 2.83 (septet, J = 6.9 Hz, 1H, CH), 3.00 (s, 3H, OCH_3), 5.03 (septet, J = 6.5 Hz, 1H, OCH), 7.26-7.45 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.5 (q, CH_3), 21.6 (q, CH_3), 21.7 (q, CH_3), 19.3 (q, CH_3), 19.5 (q, CH_3), 28.5 (d, CH), 51.8 (q, OCH_3), 70.4 (d, OCH), 82.1 (s, C-2), 91.8 (s, C-3), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 167.9 (s, CON), 170.4 (s, COO), 173.1 (s, COO).

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid 1-isopropyl ester-4-methyl ester (*erythro*-75e)** (sbo-456a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-65e** (0.66 g, 2 mmol) was cleaved hydrolytically in 8h. Preparative chromatography yielded 0.53 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.05 (d, J = 6.9 Hz, 3H, CH_3), 1.10 (d, J = 6.8 Hz, 3H, CH_3), 1.14 (d, J = 6.2 Hz, 3H, CH_3), 1.19 (d, J = 6.2 Hz, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.35 (septet, J = 6.2 Hz, 1H, CH), 3.68 (s, 3H, OCH_3), 5.13 (septet, J = 6.2 Hz, 1H, OCH), 7.28-7.59 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.7 (q, CH_3), 18.8 (q, CH_3), 19.2 (q, CH_3), 19.3 (q, CH_3), 21.6 (q, CH_3), 36.0 (d, CH), 52.5 (q, OCH_3), 66.6 (d, OCH), 71.6 (s, C-2), 80.1 (s, C-3), 126.2 (d,

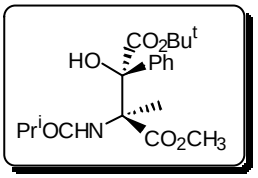
CH_{arom}), 128.3 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 171.8 (s, CON), 172.4 (s, COO), 176.8 (s, COO).

Anal: ($C_{19}H_{27}N\,O_6$, M = 365.2 g/mol)

Calcd: C 62.45 H 7.45 N 3.83

Found: C 62.10 H 7.52 N 4.00

***threo* (2S*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid 1-*tert*-butyl ester-4-methyl ester (*threo*-75f)** (sbo-453c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-65f** (0.36 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.26 g of the product as a colorless oil.

Yield: 78 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

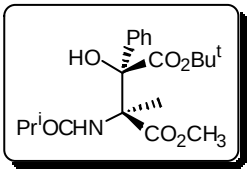
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.34 (d, J = 6.2 Hz, 3H, CH_3), 1.36 (d, J = 6.2 Hz, 3H, CH_3), 1.44 (s, 9H, $3CH_3$), 1.72 (s, 3H, CH_3), 2.18 (septet, J=6.2 Hz, 1H, CH), 3.00 (s, 3H, OCH_3), 7.28-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.4 (q, CH_3), 19.5 (q, CH_3), 21.6 (q, CH_3), 27.9 (q, $3CH_3$), 28.4 (d, CH), 51.8 (q, OCH_3), 82.1 (s, C_q), 83.7 (s, C-2), 91.9 (s, C-3), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 167.3 (s, CON), 170.5 (s, COO), 173.0 (s, COO).

***erythro* (2R*,3S*) 2-Hydroxy-3-methyl-2-phenyl-3-isobutyrylamino-succinic acid 1-*tert*-butyl ester-4-methyl ester (*erythro*-75f)** (sbo-453a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-65f** (0.71 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.68 g of the product as a colorless oil.

Yield: 90 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.97 (d, J = 6.2 Hz, 6H, $2CH_3$), 1.50 (s, 3H, CH_3), 1.52 (s, 9H, $3CH_3$), 2.32 (septet, J = 6.2 Hz, 1H, CH), 3.66 (s, 3H, OCH_3), 7.28-7.60 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

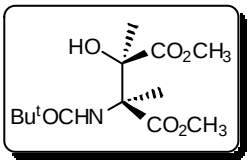
δ_{ppm} = 18.5 (q, CH_3), 19.2 (q, $2CH_3$), 27.8 (q, $3CH_3$), 36.0 (d, CH), 52.5 (q, OCH_3), 66.4 (s, C-2), 79.9 (s, C-3), 83.9 (s, C_q), 126.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 170.9 (s, CON), 174.1 (s, COO), 174.6 (s, COO).

Anal: ($C_{20}H_{29}NO_6$, M = 379.45 g/mol)

Calcd:	C 63.31	H 7.70	N 3.69
Found:	C 63.51	H 7.65	N 4.05

<u>Synthesis of *erythro* (S*,R*) & *threo* (S*,S*) a -(2,2-dimethyl-propionylamino)-b -hydroxy succinic acid derivatives 76a-f:</u>

***erythro* (2S*,3R*) 2-(2,2-Dimethyl-propionylamino)-3-hydroxy-2,3-dimethyl-succinic acid dimethyl ester (*erythro*-76a)** (sbo-436b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-66a** (0.25 g, 1 mmol) was cleaved hydrolytically in 2h. Preparative chromatography yielded 0.23 g of the product as a colorless oil.

Yield: 81 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

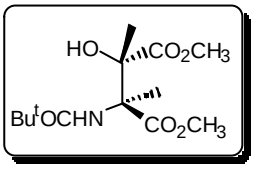
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.36 (s, 9H, $3CH_3$),1.43 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.3 (q, CH_3), 19.3 (q, CH_3), 23.1 (q, CH_3), 52.1 (q, OCH_3), 52.7 (q, OCH_3), 74.9 (s, C-2), 82.1 (s, C-3), 169.1 (s, CON), 172.1 (COO), 173.2 (s, COO).

***threo* (2S*,3S*) 2-(2,2-Dimethyl-propionylamino)-3-hydroxy-2,3-dimethyl-succinic acid dimethyl ester (*threo*-76a)** (sbo-436)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-66a** (0.25 g, 1 mmol) was cleaved hydrolytically in 2h. Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 83 %

TLC: R_f = 0.47 (ethyl acetate/n-hexane 1:4).

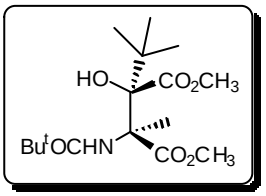
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.33 (s, 9H, $3CH_3$), 1.44 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.2 (q, CH_3), 18.7 (q, CH_3), 22.9 (q, CH_3), 52.3 (q, OCH_3), 53.2 (q, OCH_3), 78.2 (s, C-2), 87.2 (s, C-3), 165.1 (s, CON), 170.1 (COO), 172.1 (s, COO).

***erythro* (2R*,3S*) 2-*tert*-Butyl-3-(2,2-dimethyl-propionylamino)-2-hydroxy-3-methyl-succinic acid dimethyl ester (*erythro*-76b)** (sbo-484a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-66b** (0.25 g, 0.8 mmol) was cleaved hydrolytically in 2h. Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.44 (ethyl acetate/n-hexane 1:4).

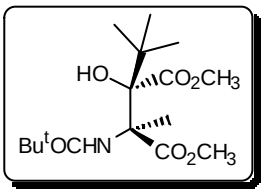
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.36 (s, 9H, $3CH_3$),1.43 (s, 9H, $3CH_3$), 1.56 (s, 3H, CH_3), 3.54 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.3 (q, CH_3), 28.3 (q, $3CH_3$), 28.6 (q, $3CH_3$), 33.8 (s, Cq), 52.1 (q, OCH_3), 52.7 (q, OCH_3), 78.2 (s, C-2), 84.1 (s, C-3), 169.1 (s, CON), 172.1 (COO), 173.2 (s, COO).

***threo* (2S*,3S*) 2-*tert*-Butyl-3-(2,2-dimethyl-propionylamino)-2-hydroxy-3-methyl-succinic acid dimethyl ester (*threo*-76b)** (sbo-484b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-66b** (0.33 g, 1 mmol) was cleaved hydrolytically in 2h. Preparative chromatography yielded 0.27 g of the product as a colorless oil.

Yield: 85 %

TLC: R_f = 0.49 (ethyl acetate/n-hexane 1:4).

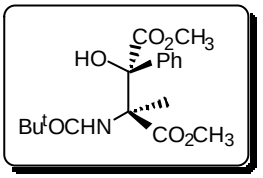
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.33 (s, 9H, $3CH_3$), 1.44 (s, 9H, $3CH_3$), 1.67 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.2 (q, CH_3), 27.8 (q, $3CH_3$), 28.3 (q, $3CH_3$), 33.6 (s, Cq), 52.3 (q, OCH_3), 53.2 (q, OCH_3), 78.2 (s, C-2), 87.2 (s, C-3), 165.1 (s, CON), 170.1 (COO), 172.1 (s, COO).

***threo* (2S*,3S*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid dimethyl ester (*threo*-76c)** (sbo-432a)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-66c** (0.67 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.55 g of the product as a colorless oil.

Yield: 82 %

TLC: R_f = 0.39 (ethyl acetate/n-hexane 1:4).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.47 (s, 9H, $3CH_3$), 1.54 (s, 3H, CH_3), 3.05 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 7.28-7.48 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

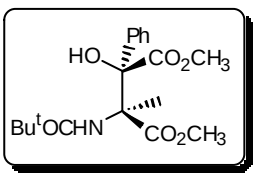
δ_{ppm} = 18.1 (q, CH_3), 27.9 (q, CH_3), 38.1 (s, Cq), 52.1 (q, OCH_3), 53.2 (q, OCH_3), 78.2 (s, C-2), 83.5 (s, C-3), 126.2 (d, CH_{arom}), 128.3 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 169.1 (s, CON), 170.1 (s, COO), 171.3 (s, COO).

HRMS: ($C_{18}H_{25}NO_6$, M = 351.17 g/mol)

Calcd: 351.1689

Found: 351.1683

***erythro* (2S*,3R*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid dimethyl ester (*erythro*-76c)** (sbo-432b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-66c** (0.33 g, 1 mmol) was cleaved hydrolytically in 2h. Preparative chromatography yielded 0.35 g of the product as a colorless oil.

Yield: 87 %

TLC: R_f = 0.53 (ethyl acetate/n-hexane 1:4).

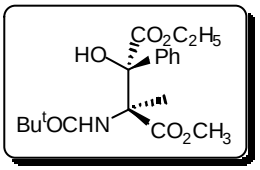
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.27 (s, 9H, $3CH_3$), 1.67 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 7.32-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 18.3 (q, CH_3), 28.0 (q, $3CH_3$), 40.1 (s, Cq), 52.3 (q, OCH_3), 53.2 (q, OCH_3), 79.2 (s, C-2), 84.1 (s, C-3), 126.8 (d, CH_{arom}), 129.1 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 169.2 (s, CON), 172.1 (s, COO), 173.1 (s, COO).

***threo* (2S*,3S*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-ethyl ester-1-methyl ester (*threo*-76d)** (sbo-451e)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-66d** (0.69 g, 2 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.64 g of the product as a colorless oil.

Yield: 89 %

TLC: R_f = 0.46 (ethyl acetate/n-hexane 1:4).

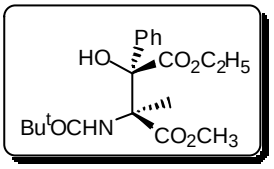
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25 (t, J = 7.5 Hz, 3H, CH_3), 1.38 (s, 9H, $3CH_3$), 1.67 (s, 3H, CH_3), 3.00 (s, 3H, OCH_3), 4.20 (q, J = 7.5 Hz, 2H, OCH_2), 7.27-7.53 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 13.9 (q, CH_3), 21.4 (q, CH_3), 27.4 (q, $3CH_3$), 33.5 (s, Cq), 51.8 (q, OCH_3), 62.1 (t, OCH_2), 82.3 (s, C-2), 91.9 (s, C-3), 126.2 (d, CH_{arom}), 127.5 (d, CH_{arom}), 135.1 (s, Cq_{arom}), 168.6 (s, CON), 168.6 (s, COO), 175.1 (s, COO).

***erythro* (2S*,3R*) 2(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-ethyl ester-1-methyl ester (*erythro*-76d)** (sbo-451b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-66d** (0.35 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.25 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3530, 3420, 2993, 2898, 1755, 1724, 1675, 1600, 1558, 1440, 1078, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.11 (s, 9H, $3CH_3$), 1.32 (t, J = 7.5 Hz, 3H, CH_3), 1.55 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 4.29 (q, J = 7.5 Hz, 2H, OCH_2), 7.32-7.69 (m, 5H, H_{arom}).

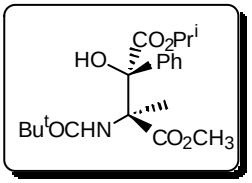
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 14.0 (q, CH_3), 18.5 (q, CH_3), 27.2 (q, $3CH_3$), 39.0 (s, Cq), 52.6 (q, OCH_3), 63.1 (t, OCH_2), 66.6 (s, C-2), 80.5 (s, C-3), 126.2 (d, CH_{arom}), 127.1 (d, CH_{arom}), 134.6 (s, Cq), 172.1 (s, CON), 172.7 (s, COO), 178.5 (s, COO).

Anal: ($C_{19}H_{27}NO_6$, M = 365.42 g/mol)

Calcd:	C 62.45	H 7.45	N 3.83
Found:	C 62.67	H 7.27	N 3.91

***threo* (2S*,3S*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-isopropyl ester-1-methyl ester (*threo*-76e)** (sbo-457d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-66e** (0.36 g, 1 mmol) was cleaved hydrolytically in 3h. Preparative chromatography yielded 0.24 g of the product as a colorless oil.

Yield: 84 %

TLC: R_f = 0.42 (ethyl acetate/n-hexane 1:4).

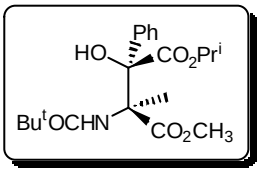
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.24 (d, J = 6.3 Hz, 3H, CH_3), 1.25 (d, J = 6.3 Hz, 3H, CH_3), 1.38 (s, 9H, $3CH_3$), 1.69 (s, 3H, CH_3), 3.00 (s, 3H, OCH_3), 5.03 (septet, J = 6.3 Hz, 1H, OCH), 7.26-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.4 (q, CH_3), 21.6 (q, CH_3), 21.7 (q, CH_3), 27.5 (q, $3CH_3$), 33.5 (s, Cq), 51.7 (q, OCH_3), 70.3 (d, OCH), 82.3 (s, C-2), 91.7 (s, C-3), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 168.1 (s, CON), 170.3 (s, COO), 175.1 (s, COO).

***erythro* (2S*,3R*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-isopropyl ester-1-methyl ester (*erythro*-76e)** (sbo-457b)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-66e** (0.72 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.56 g of the product as a colorless oil.

Yield: 88 %

TLC: R_f = 0.56 (ethyl acetate/n-hexane 1:4).

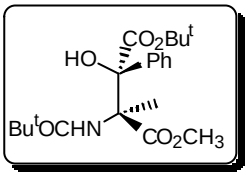
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.15 (s, 3H, CH_3), 1.16 (d, J = 6.2 Hz, 3H, CH_3), 1.18 (d, J = 6.3 Hz, 3H, CH_3), 1.36 (s, 9H, $3CH_3$), 3.76 (s, 3H, OCH_3), 5.00 (septet, J = 6.2 Hz, 1H, OCH), 7.28-7.59 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.5 (q, CH_3), 21.7 (q, CH_3), 21.8 (q, CH_3), 27.8 (q, $3CH_3$), 33.4 (s, Cq), 51.3 (q, OCH_3), 70.1 (d, OCH), 83.5 (s, C-2), 92.8 (s, C-3), 126.3 (d, CH_{arom}), 128.3 (d, CH_{arom}), 134.7 (s, Cq), 169.1 (s, CON), 171.2 (s, COO), 176.2 (s, COO).

***threo* (2S*,3S*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-*tert*-butyl ester-1-methyl ester (*threo*-76f)** (sbo-444d)



According to the typical hydrolysis procedure, the bicyclic oxetane ***exo*-66f** (0.38 g, 1 mmol) was cleaved hydrolytically in 4h. Preparative chromatography yielded 0.22 g of the product as a colorless oil.

Yield: 70 %

TLC: R_f = 0.41 (ethyl acetate/n-hexane 1:4).

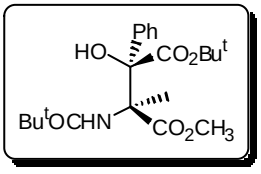
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.38 (s, 9H, $3CH_3$), 1.45 (s, 9H, $3CH_3$), 1.73 (s, 3H, CH_3), 3.00 (s, 3H, OCH_3), 7.28-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.6 (q, CH_3), 27.6 (q, $3CH_3$), 28.0 (q, $3CH_3$), 33.4 (s, Cq), 51.7 (q, OCH_3), 82.4 (s, C-2), 83.6 (s, Cq), 91.8 (s, C-3), 126.3 (d, CH_{arom}), 129.2 (d, CH_{arom}), 134.7 (s, Cq_{arom}), 167.4 (s, CON), 170.6 (s, COO), 174.9 (s, COO).

***erythro* (2S*,3R*) 2-(2,2-Dimethylpropionylamino)-3-hydroxy-2-methyl-3-phenyl-succinic acid 4-*tert*-butyl ester-1-methyl ester (*erythro*-76f)** (sbo-444c)



According to the typical hydrolysis procedure, the bicyclic oxetane ***endo*-66f** (0.75 g, 2 mmol) was cleaved hydrolytically in 6h. Preparative chromatography yielded 0.58 g of the product as a colorless oil.

Yield: 69 %

TLC: R_f = 0.51 (ethyl acetate/n-hexane 1:4).

IR: (Film)

$\tilde{n}$ (cm^{-1}) = 3510, 3450, 2989, 2897, 1740, 1735, 1670, 1600, 1550, 1440, 1075, 980, 770.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.96 (s, 3H, CH_3), 1.38 (s, 9H, $3CH_3$), 1.39 (s, 9H, $3CH_3$), 3.78 (s, 3H, OCH_3), 7.31-7.58 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 24.5 (q, CH_3), 27.7 (q, $3CH_3$), 27.8 (q, $3CH_3$), 33.4 (s, Cq), 52.5 (q, OCH_3), 80.8 (s, C-2), 83.0 (s, Cq), 92.3 (s, C-3), 126.3 (d, CH_{arom}), 128.3 (d, CH_{arom}), 135.6 (s, Cq_{arom}), 168.8 (s, CON), 172.6 (s, COO), 173.4 (s, COO).

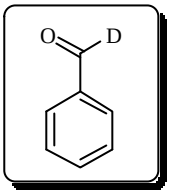
HRMS: ($C_{21}H_{31}NO_6$, M = 399.22 g/mol)

Calcd: 399.2175

Found: 399.2171

4.21 Synthesis of starting materials

4.21.1 Preparation of benzaldehyde-1-d (77)[138] (sbo-461d)



To a stirred solution of benzil (13.9 g, 66.1 mmol) in p-dioxane (30 mL) was added deuterium oxide (14.4 g, 0.719 mol) and then potassium cyanide (4.68 g, 71.9 mmol) in five portions over 0.5 h. The mixture was stirred for another 0.5 h and then diluted with water (120 mL). The mixture was extracted with ether (3 x 50 mL) and the ether solution washed with saturated sodium bicarbonate (2 x 50 mL) and saturated sodium chloride (2 x 50 mL). After evaporation of the dried ($MgSO_4$) ether solution, distillation gave pure 4.32 g of the product as a pale yellow oil.

Yield: 61 %

B.p: 74-76 °C, 22 mmHg (Lit.[138], 76-78 °C, 22 mmHg).

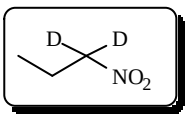
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 7.45-7.51 (m, 2H, H_{arom}), 7.55-7.61 (m, 1H, H_{arom}), 7.81-7.85 (m, 1H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 126.5 (d, CH_{arom}), 128.9 (d, CH_{arom}), 129.6 (d, CH_{arom}), 136.2 (s, Cq_{arom}), 192.0 (t, COD).

Preparation of nitropropane-1,1-d_2 (78)[139] (sbo-589)



A mixture of nitropropane (50 mL) and deuterium oxide (50 mL) containing 3 drops of NaOD (40 wt. % solution in D_2O) was refluxed for two days. Then the layer of deuterated nitropropane was separated and distilled off. The yield of colorless liquid was 26 mL. The product was 85 % deuterated by ^{1}H-NMR analysis.

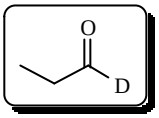
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.88 (t, J = 7.5 Hz, 3H, CH_3), 1.89 (q, J = 7.5 Hz, 2H, CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 10.7 (q, CH_3), 20.9 (t, CH_2), 76.4 (t, CD_2).

4.21.2 Preparation of propanal-1-d (79)[139] (sbo-589a)



Nitropropane-1,1-d_2 (26 mL) was dissolved in 290 mL of ice-cold aqueous 15 % sodium hydroxide in a separatory funnel. The solution was added slowly dropwise to a beaker containing 53.2 mL of conc. sulfuric acid dissolved in 355 mL water. The sulfuric acid solution was cooled in an ice-bath and stirred continuously while the solution of nitropropane-1,1-d_2 was added. After the addition was completed, the reaction was stirred an additional 30 min. The product, propanal-1-d (96 % D) was purified by distillation to give 2.5 g as a colorless liquid.

Yield: 35 %

B.p: 43-45°C.

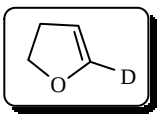
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.87 (t, J = 7.5 Hz, 3H, CH_3), 2.25 (q, J = 7.5 Hz, 2H, CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 6.0 (q, CH_3), 37.0 (t, CH_2), 202.8 (t, COD).

4.21.3 Preparation of 5-deuterio-2,3-dihydrofuran (80)[140] (sbo-566c)



To a stirred solution of a freshly distilled 2,3-dihydrofuran (0.9 g, 13 mmol) and TMEDA (0.3 g, 25 mmol) was added rapidly a solution of 1.6 M butyllithium (6.0 mL, 13 mmol) until the precipitation of a solid began. The reaction mixture was cooled with an ice-bath and then the addition of butyllithium was completed. The resulting solid was washed with hexane (3 x 4 mL) and then suspended in 1 mL of hexane. To this suspension was added 1 mL of D_2O. The hexane layer was isolated and dried over $MgSO_4$ and kept under N_2.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.55 (dt, J = 2.5, 9.5 Hz, 2H, 3-H), 4.29 (t, J = 9.5 Hz, 2H, 2-H), 4.93 (t, J = 2.5, 1H, 4-H).

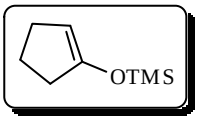
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 28.4 (t, C-3), 69.5 (t, C-2), 99.2 (d, C-2), 145.6 (t, C-5).

4.21.4 Preparation of 1-trimethylsilyoxycycloalkenes (81-83); General procedure:[141]

Sodium iodide (9.3 g, 62 mmol) in acetonitrile (62 mL) was added dropwise (15 min), at room temperature to a solution of the ketone (50 mmol); triethyl amine (6.26 g, 62 mmol) and trimethylchlorosilane (6.72 g, 62 mmol) successively introduced in the reaction flask. An exothermic reaction generally occured with concomitant formation of a white precipitation ($Et_3NH^+I^-$), while the acetonitrile solution become brownish. The stirring was continued for 4 h. The reaction was quenched by adding cold pentane (50 mL) and then ice water (50 mL). After decantation, the aqueous layer was extracted with pentane (2 x 50 mL) and the collected organic layers were washed with ice water (2 x 50 mL) or with aqueous solution of NH_4Cl until neutrality, dried over $MgSO_4$ and evaporation under vacum gave the crude product. Purification was carried out by Büchi distillation.

1-Trimethylsilyoxycyclopentene (81)[142] (sbo-482)



The reaction was carried out following the above general procedure using cyclopentanone (4.2 g, 50 mmol). Distillation of the crude product under vacum afforded 5.8 g of the pure product as a colorless liquid.

Yield: 75 %

B.p: 55-57°C, 10 torr (Lit.,[142] 99°C, 40 torr)

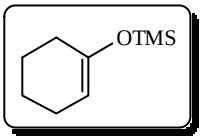
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.17 (s, 9H, $3CH_3$), 1.77-1.87 (m, 2H, CH_2), 2.19-2.26 (m, 4H, $2CH_2$), 4.58 (dd, J = 2.7, 1.6 Hz, 1H, CH=) .

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = -0.06 (q, $3CH_3$), 21.3 (t, C-4), 28.7 (t, C-3), 33.5 (t, C-5), 102.0 (s, C-1), 154.9 (d, C-2).

1-Trimethylsilyoxycyclohexene (82)[143] (sbo-481)



The reaction was carried out following the above general procedure using cyclohexanone (4.9 g, 50 mmol). Distillation of the crude product under vacum afforded 7.0 g of the pure product as a colorless liquid.

Yield: 82 %

B.p: 78-80°C, 10 torr (Lit.,[143] 60-62°C, 8 torr)

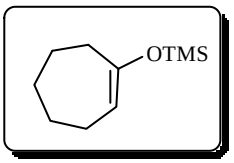
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.14 (s, 9H, $3CH_3$), 1.45-1.49 (m, 2H, CH_2), 1.60-1.64 (m, 2H, CH_2), 1.93-1.99 (m, 4H, $2CH_2$), 4.82 (dd, J = 1.3, 1.3 Hz, 1H, CH=) .

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.24 (q, $3CH_3$), 22.3 (t, CH_2), 23.1 (t, CH_2), 23.8 (t, CH_2), 29.9 (t, CH_2), 104.1 (s, C-2), 150.3 (d, C-2).

1-Trimethylsilyoxycyclopentene (83)[144] (sbo-497)



The reaction was carried out following the above general procedure using cycloheptanone (5.6 g, 50 mmol). Distillation of the crude product under vacum afforded 7.8 g of the pure product as a colorless liquid.

Yield: 85 %

B.p: 78-81°C, 10 torr (Lit.,[144] 73-74°C, 8 torr).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.13 (s, 9H, $3CH_3$), 1.48-1.65 (m, 8H, $4CH_2$), 1.92-1.98 (m, 2H, CH_2), 2.17-2.22 (m, 2H, CH_2), 4.98 (t, J = 6.6 Hz, 1H, CH=) .

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.13 (q, $3CH_3$), 25.2 (t, CH_2), 25.3 (t, CH_2), 27.8 (t, CH_2), 31.5 (t, CH_2), 35.5 (t, CH_2), 108.6 (s, C-1), 155.9 (d, C-2).

4.22 General procedure for photolyses of benzaldehyde and benzaldehyde-1d with cycloalkenes:

Under a nitrogen atmosphere, a solution of either benzaldehyde or benzaldehyde-1d (0.3 g, 3 mmol) and cyclic alkene (3 mmol) in 25 mL benzene was irradiated in a Rayonet photoreactor (λ = 300 nm) for 24 h. After removal of the solvent under vacum, the crude photolysate was subjected to ^{1}H-NMR analysis to determine the diastereoselectivity. Purification was carried out by Büchi distillation.

Irradiation of benzaldehyde with 2,3-dihydrofuran (sbo-542)

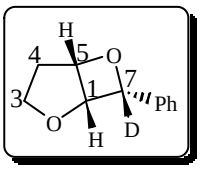
A solution of benzaldehyde (0.3 g, 3 mmol) and 2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.42 g (80 %) of inseparable mixture of oxetanes as a colorless oil.

Both ^{1}H-NMR and ^{13}C-NMR data was reported earlier (*endo*- & *exo*- **3a**).

Irradiation of benzaldehyde-1-d with 2,3-dihydrofuran (sbo-464)

A solution of benzaldehyde-1d (0.3 g, 3 mmol) and 2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.47 g (89 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-7-Deuterio-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-84b)**



IR: (Film, mixture of *endo* & *exo*)

$\tilde{n}$ (cm^{-1}) = 3020, 2928, 1600, 1505, 1470, 1400, 1050, 835, 778.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.62-1.70 (m, 2H, 4-H), 3.72-3.80 (m, 2H, 3-H), 5.00 (d, J = 3.8 Hz, 1H, 1-H), 5.48 (dd, J = 4.1, 3.8 Hz, 1H, 5-H), 7.15-7.35 (m, 5H, $H_{arom.}$).

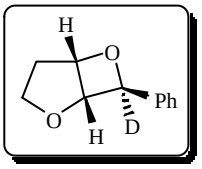
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.7 (t, C-4), 68.8 (t, C-3), 79.4 (d, C-1), 84.6 (d, C-5), 85.1 (t, C-7), 124.4 (d, $CH_{arom.}$), 127.0 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 137.1 (s, $Cq_{arom.}$).

GC-MS: (EI, 70 eV, *endo* & *exo*)

m/z (%) = 177 (M^+, 15), 121 (20), 105 (20), 92 (50), 77 (10), 70 (100), 65 (4), 51 (10).

***exo*-7-Deuterio-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-84b)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 2.08-2.15 (m, 2H, 4-H), 3.97 (t, J = 8.4 Hz, 2H, 3-H), 4.57 (d, J = 4.3 Hz, 1H, 1-H), 5.44 (dd, J = 4.3, 4.4 Hz, 1H, 5-H), 7.20-7.50 (m, 5H, $H_{arom.}$).

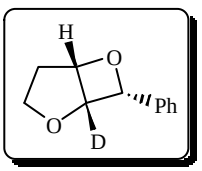
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.1 (t, C-4), 67.3 (t, C-3), 82.9 (d, C-1), 84.7 (d, C-5), 85.8 (d, C-7), 125.2 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 135.8 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde with 5-deuterio-2,3-dihydrofuran (sbo-567)

A solution of benzaldehyde (0.3 g, 3 mmol) and 5-deuterio-2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.51 g (94 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-1-Deuterio-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-84c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.48-1.75 (m, 2H, 4-H), 3.55-3.86 (t, J = 6.5 Hz, 2H, 3-H), 5.49 (d, J = 4.3 Hz, 1H, 5-H), 5.77 (s,1H, 7-H), 7.26-7.35 (m, 5H, $H_{arom.}$).

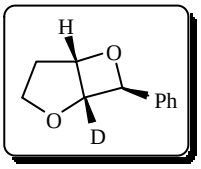
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.7 (t, C-4), 68.8 (t, C-3), 78.9 (t, C-1), 84.9 (d, C-5), 85.0 (d, C-7), 124.5 (d, $CH_{arom.}$), 127.9 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 134.3 (s, $Cq_{arom.}$).

GC-MS: (EI, 70 eV, *endo* & *exo*)

m/z (%) = 177 (M^+, 10), 121 (17), 105 (14), 91 (30), 77 (10), 71 (100), 65 (4), 51 (10).

***exo*-1-Deuterio-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-84c)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.78-2.12 (m, 2H, 4-H), 3.94 (t, J = 7.8 Hz, 2H, 3-H), 5.37 (s, 1H, 7-H), 5.44 (d, J = 4.4 Hz, 1H, 5-H), 7.26-7.42 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.1 (t, C-4), 67.2 (t, C-3), 79.5 (t, C-1), 85.1 (d, C-5), 85.2 (d, C-7), 126.2 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.9 (d, $CH_{arom.}$), 133.8 (s, $Cq_{arom.}$).

HRMS: ($C_{11}H_{11}DO_2$, M = 177.1 g/mol)

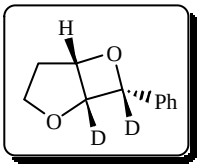
Calcd: 177.0918

Found: 177.0913

Irradiation of benzaldehyde-1-d with 5-deuterio-2,3-dihydrofuran (sbo-568)

A solution of benzaldehyde-1-d (0.3 g, 3 mmol) and 5-deuterio-2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.49 g (92 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-1,7-Dideuterio-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-84d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.52-1.72 (m, 2H, 4-H), 3.57 (t, J = 6.8 Hz, 2H, 3-H), 5.44 (d, J = 4.3 Hz, 1H, 5-H), 7.28-7.39 (m, 5H, $H_{arom.}$).

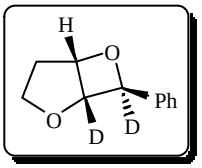
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 32.7 (t, C-4), 68.7 (t, C-3), 78.9 (t, C-1), 84.9 (d, C-5), 85.6 (t, C-7), 124.4 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 134.2 (s, $Cq_{arom.}$).

GC-MS: (EI, 70 eV, *endo* & *exo*)

m/z (%) = 178 (M^+, 10), 122 (20), 105 (21), 92 (20), 77 (10), 71 (100), 65 (4), 51 (12).

***exo*-1,7-Dideuterio-7-phenyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-84d)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.81-2.14 (m, 2H, 4-H), 3.91 (t, J = 7.8 Hz, 2H, 3-H), 5.40 (d, J = 4.3 Hz, 1H, 5-H), 7.26-7.38 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 31.3 (t, C-4), 67.3 (t, C-3), 79.0 (t, C-1), 85.2 (d, C-5), 87.1 (t, C-7), 124.4 (d, $CH_{arom.}$), 124.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 134.2 (s, $Cq_{arom.}$).

HRMS: ($C_{11}H_{10}D_2O_2$, M = 178.1 g/mol)

Calcd: 178.1348

Found: 178.1343

Irradiation of benzaldehyde with 5-methyl-2,3-dihydrofuran (sbo-474a)

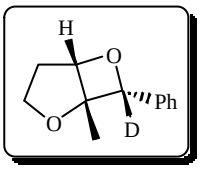
A solution of benzaldehyde (0.3 g, 3 mmol) and 5-methyl-2,3-dihydrofuran (0.25 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure.

Distillation of the crude photolysate yielded 0.48 g (84 %) of inseparable mixture of oxetanes as a colorless oil. Both ^{1}H-NMR and ^{13}C-NMR data was reported earlier.

Irradiation of benzaldehyde-1-d with 5-methyl-2,3-dihydrofuran (sbo-474)

A solution of benzaldehyde-1-d (0.3 g, 3 mmol) and 5-methyl-2,3-dihydrofuran (0.25 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.5 g (87 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-7-Deuterio-7-phenyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-84f)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.60 (s, 3H, CH_3), 1.69-2.14 (m, 2H, 4-H), 3.71-3.82 (m, 2H, 3-H), 5.17 (d, J = 4.0 Hz, 1H, 5-H), 7.23-7.39 (m, 5H, $H_{arom.}$).

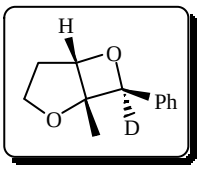
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 21.7 (q, CH_3), 33.8 (t, C-4), 68.9 (t, C-3), 75.1 (s, C-1), 89.0 (d, C-5), 91.1 (t, C-7), 124.4 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 134.2 (s, $Cq_{arom.}$).

GC-MS: (EI, 70 eV, *endo* & *exo*)

m/z (%) = 191 (M^+, 10), 135 (155), 105 (30), 92 (12), 84 (100), 77 (30), 69 (10), 63 (4), 52 (12).

***exo*-7-Deuterio-7-phenyl-1-methyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-84f)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.00 (s, 3H, CH_3), 1.82-2.28 (m, 2H, 4-H), 4.21-4.38 (m, 2H, 3-H), 5.06 (d, J = 4.1 Hz, 1H, 5-H), 7.20-7.35 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 17.5 (q, CH_3), 33.7 (t, C-4), 67.8 (t, C-3), 79.1 (s, C-1), 89.2 (d, C-5), 90.7 (t, C-7), 125.6 (d, $CH_{arom.}$), 127.3 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 137.2 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde with cyclopentene (sbo-474a)

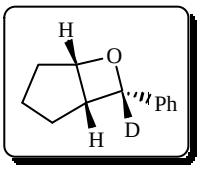
A solution of benzaldehyde (0.3 g, 3 mmol) and cyclopentene (0.2 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.45 g (86 %) of inseparable mixture of oxetanes as a colorless oil.

Both ^{1}H-NMR and ^{13}C-NMR data was reported earlier in literature.[37]

Irradiation of benzaldehyde-1-d with cyclopentene (sbo-474)

A solution of benzaldehyde-1d (0.3 g, 3 mmol) and cyclopentene (0.2 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.47 g (90 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-7-Deuterio-7-phenyl-6-oxa-bicyclo[3.2.0]heptane (*endo*-84h)**



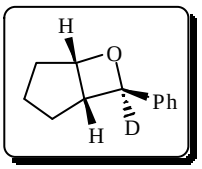
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25-2.38 (m, 6H), 3.31 (dd, J = 7.2 Hz, 5.6 Hz, 1H, 1-H), 5.39 (dd, J = 5.6, 3.4 Hz, 1H, 5-H), 7.20-7.50 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 24.7 (t), 25.1 (t), 34.6 (t), 42.8 (d, C-1), 83.7 (d, C-5), 85.4 (t, C-6), 124.4 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 139.2 (s, $Cq_{arom.}$).

***exo*-7-Deuterio-7-phenyl-6-oxa-bicyclo[3.2.0]heptane (*exo*-84h)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.25-2.40 (m, 6H), 2.98 (dd, J = 6.2, 6.2 Hz, 1H, 1-H), 5.30 (dd, J = 4.0, 6.2 Hz, 1H, 5-H), 7.25-7.48 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 23.8 (t), 30.3 (t), 34.1 (t), 46.8 (d, C-1), 83.6 (d, C-5), 85.3 (t, C-6), 125.6 (d, $CH_{arom.}$), 127.3 (d, $CH_{arom.}$), 129.2 (d, $CH_{arom.}$), 139.2 (s, $Cq_{arom.}$).

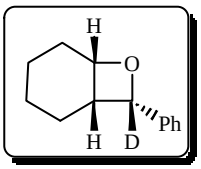
Irradiation of benzaldehyde with cyclohexene (sbo-472a)

A solution of benzaldehyde (0.3 g, 3 mmol) and cyclohexene (0.25 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.49 g (87 %) of inseparable mixture of oxetanes as a colorless oil. Both ^{1}H-NMR and ^{13}C-NMR data was reported earlier in literature.[37]

Irradiation of benzaldehyde-1-d with cyclohexene (sbo-472)

A solution of benzaldehyde-1-d (0.3 g, 3 mmol) and cyclohexene (0.25 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.51 g (89 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-8-Deuterio-8-phenyl-7-oxa-bicyclo[4.2.0]octane (*endo*-84j)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92-1.49 (m, 8H), 2.99 (m, 2H, 1-H), 5.00 (m, 1H, 6-H), 7.22-7.48 (m, 5H, $H_{arom.}$).

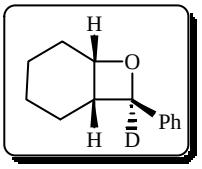
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.9 (t), 21.1 (t), 28.7 (t), 37.0 (d, C-7), 75.6 (d, C-6), 81.0 (t, C-8), 125.0 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 139.7 (s, $Cq_{arom.}$).

GC-MS: (EI, 70 eV, *endo* & *exo*)

m/z (%) = 189 (M^+, 5), 178 (10), 120 (15), 108 (27), 105 (100), 91 (15), 80 (30), 77 (60), 50 (27).

***exo*-8-Deuterio-8-phenyl-7-oxa-bicyclo[4.2.0]octane (*exo*-84j)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.92-1.49 (m, 8H), 2.92 (m, 1H, 1-H), 4.95 (m, 1H, 6-H), 7.22-7.48 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.8 (t), 20.9 (t), 29.0 (t), 40.3 (d, C-1), 76.7 (d, C-6), 85.6 (t, C-8), 126.6 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 143.1 (s, $Cq_{arom.}$).

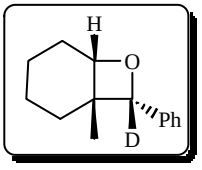
Irradiation of benzaldehyde with 1-methylcyclohexene (sbo-473a)

A solution of benzaldehyde (0.3 g, 3 mmol) and 1-methylcyclohexene (0.29 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.54 g (89 %) of inseparable mixture of oxetanes as a colorless oil. Both ^{1}H-NMR and ^{13}C-NMR data was reported earlier in literature.[37]

Irradiation of benzaldehyde-1-d with 1-methylcyclohexene (sbo-473)

A solution of benzaldehyde-1-d (0.3 g, 3 mmol) and 1-methylcyclohexene (0.29 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.53 g (87 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-8-Deuterio-8-phenyl-1-methyl-7-oxa-bicyclo[4.2.0]octane (*endo*-84l)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 1.60 (s, 3H, CH_3), 0.93-2.05 (m, 8H), 4.61 (m, 1H, 6-H), 7.18-7.48 (m, 5H, $H_{arom.}$).

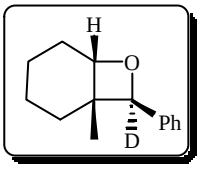
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.5 (t), 20.2 (t), 21.0 (q), 28.3 (t), 35.0 (t), 42.0 (s, C-1), 84.1 (d, C-6), 88.6 (t, C-7), 124.8 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 139.7 (s, $Cq_{arom.}$).

GC-MS: (EI, 70 eV, *endo* & *exo*)

m/z (%) = 203 (M^+, 5), 202 (M^+-1, 9), 181 (21), 166 (30), 109 (53), 108 (75), 105 (24), 90 (11), 80 (100), 50 (20).

***exo*-8-Deuterio-8-phenyl-1-methyl-7-oxa-bicyclo[4.2.0]octane (*exo*-84l)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.68 (s, 3H, CH_3), 0.93-2.05 (m, 8H), 4.55 (m, 1H, 6-H), 7.18-7.48 (m, 5H, $H_{arom.}$).

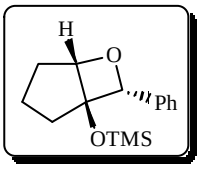
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 19.7 (t), 20.2 (t), 23.9 (t), 27.8 (q, CH_3), 28.9 (t), 42.4 (s, C-1), 81.5 (d, C-6), 87.3 (t, C-8), 126.5 (d, $CH_{arom.}$), 128.5 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 140.5 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde with 1-trimethylsilyoxycyclopentene (sbo-493)

A solution of benzaldehyde (0.3 g, 3 mmol) and 1-trimethylsilyoxycyclopentene (0.47 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.69 g (88 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-7-Phenyl-1-trimethylsilyoxy-6-oxa-bicyclo[3.2.0]heptane (*endo*-84m)**



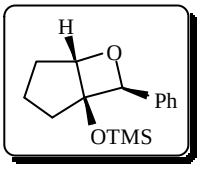
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.15 (s, 9H, $3CH_3$), 1.25-2.38 (m, 6H), 5.18 (d, J = 3.5 Hz, 1H, 5-H), 5.92 (s, 1H, 7-H), 7.20-7.45 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 1.2 (q, $3CH_3$), 24.7 (t), 24.9 (t), 34.3 (t), 81.0 (d, C-5), 85.4 (s, C-1), 98.1 (d, C-7), 124.9 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 129.2 (d, $CH_{arom.}$), 135.2 (s, $Cq_{arom.}$).

***exo*-7-Phenyl-1-trimethylsilyoxy-6-oxa-bicyclo[3.2.0]heptane (*exo*-84m)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = - 0.12 (s, 9H, $3CH_3$), 1.25-2.42 (m, 6H), 5.05 (s, 1H, 7-H), 5.15 (d, J = 2.6 Hz, 1H, 7.20-7.45 (m, 5H, $H_{arom.}$).

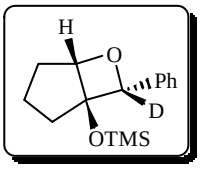
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 1.3 (q, $3CH_3$), 24.1 (t), 30.6 (t), 34.8 (t), 85.6 (d, C-5), 86.3 (d, C-1), 90.1 (t, C-7), 126.4(d, $CH_{arom.}$), 127.3 (d, $CH_{arom.}$), 129.2 (d, $CH_{arom.}$), 134.2 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde-1-d with 1-trimethylsilyoxycyclopentene (sbo-494)

A solution of benzaldehyde-1-d (0.3 g, 3 mmol) and 1-trimethylsilyoxycyclopentene (0.47 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.62 g (79 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-7-Deuterio-7-phenyl-1-trimethylsilyloxy-6-oxa-bicyclo[3.2.0]heptane (*endo*-84n)**



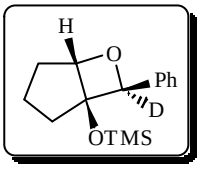
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.17 (s, 9H, $3CH_3$), 1.26-2.43 (m, 6H), 5.14 (d, J = 3.4 Hz, 1H, 5-H), 7.25-7.45 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 1.6 (q, $3CH_3$), 21.2 (t), 23.3 (t), 28.6 (t), 84.4 (d, C-5), 90.5 (s, C-1), 101.2 (t, C-7), 125.41(d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 129.1 (d, $CH_{arom.}$), 139.3 (s, $Cq_{arom.}$).

***exo*-7-Deuterio-7-phenyl-1-trimethylsilyoxy-6-oxa-bicyclo[3.2.0]heptane (*exo*-84n)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = - 0.13 (s, 9H, $3CH_3$), 1.26-2.43 (m, 6H), 5.18 (d, J = 2.5 Hz, 1H, 5-H), 7.25-7.48 (m, 5H, $H_{arom.}$).

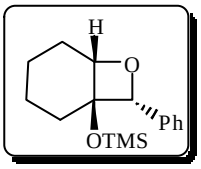
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 1.2 (q, $3CH_3$), 23.9 (t), 32.3 (t), 38.2 (t), 85.8 (d, C-5), 92.4 (s, C-1), 102.3 (t, C-7), 125.6 (d, $CH_{arom.}$), 127.3 (d, $CH_{arom.}$), 129.2 (d, $CH_{arom.}$), 140.1 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde with 1-trimethylsilyoxycyclohexene (sbo-495)

A solution of benzaldehyde (0.3 g, 3 mmol) and 1-trimethylsilyoxycyclohexene (0.51 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.75 g (90 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-8-Phenyl-1-trimethylsilyoxy-7-oxa-bicyclo[4.2.0]octane (*endo*-84o)**



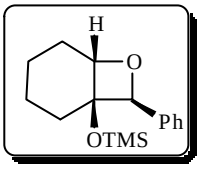
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.17 (s, 9H, $3CH_3$), 0.92-1.99 (m, 8H), 5.00 (m, 1H, 6-H), 5.93 (s, 1H, 8-H), 7.23-7.48 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.14 (q, $3CH_3$), 20.1 (t), 21.2 (t), 24.2 (t), 30.1 (t), 74.4 (d, C-6), 86.1 (s, C-1), 90.6 (s, C-8), 125.0 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 135.1 (s, $Cq_{arom.}$).

***exo*-8-Phenyl-1-trimethylsilyoxy-7-oxa-bicyclo[4.2.0]octane (*exo*-84o)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = -0.12 (s, 9H, $3CH_3$), 0.90-1.99 (m, 8H), 5.10 (m, 1H, 6-H), 5.85 (s, 1H, 8H), 7.23-7.49 (m, 5H, $H_{arom.}$).

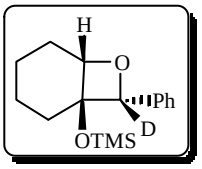
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.21 (q, $3CH_3$), 19.2 (t), 23.8 (t), 29.7 (t), 83.7 (d, C-6), 85.7 (d, C-8), 90.6 (s, C-1), 126.6 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 137.2 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde-1d with 1-trimethylsilyoxycyclohexene (sbo-496)

A solution of benzaldehyde-1d (0.3 g, 3 mmol) and 1-trimethylsilyoxycyclohexene (0.51 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.72 g (87 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-8-Deuterio-8-phenyl-1-trimethylsilyoxy-7-oxa-bicyclo[4.2.0]octane (*endo*-84p)**



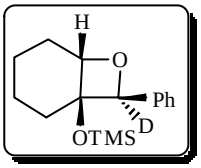
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.14 (s, 9H, $3CH_3$), 0.93-1.99 (m, 8H), 4.93 (m, 1H, 6-H), 7.19-7.38 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.13 (q, $3CH_3$), 19.1 (t), 22.2 (t), 29.7 (t), 35.1(t), 74.4 (d, C-6), 86.9 (s, C-1), 104.1 (t, C-8), 124.8 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 139.7 (s, $Cq_{arom.}$).

***exo*-8-Deuterio-8-phenyl-1-trimethylsilyoxy-7-oxa-bicyclo[4.2.0]octane (*exo*-84p)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = -0.17 (s, 9H, $3CH_3$), 0.92-1.99 (m, 8H), 4.98 (m, 1H, 6-H), 7.19-7.38 (m, 5H, $H_{arom.}$).

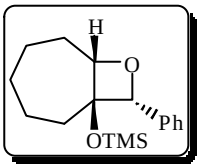
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.20 (q, $3CH_3$), 21.2 (t), 23.9 (t), 26.0 (t), 29.7 (t), 76.9 (d, C-6), 83.9 (t, C-7), 107.8 (s, C-1), 126.6 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 134.6 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde with 1-trimethylsilyoxycycloheptene (sbo-503)

A solution of benzaldehyde (0.3 g, 3 mmol) and 1-trimethylsilyoxycycloheptene (0.55 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.8 g (92 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-9-Phenyl-1-trimethylsilyoxy-8-oxa-bicyclo[5.2.0]nonane (*endo*-84q)**



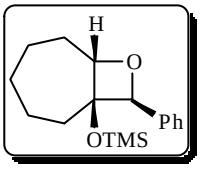
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.13 (s, 9H, $3CH_3$), 1.12-2.44 (m, 10H), 4.75 (t, J = 8.4 Hz, 1H, 7-H), 5.22 (s, 1H, 9-H), 7.18-7.36 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.14 (q, $3CH_3$), 24.6 (t), 25.0 (t), 27.1 (t), 41.7 (t), 83.8 (d, C-7), 91.1 (d, C-9), 93.4 (d, C-9), 125.0 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 134.6 (s, $Cq_{arom.}$).

***exo*-9-Phenyl-1-trimethylsilyoxy-8-oxa-bicyclo[5.2.0]nonane (*exo*-84p)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = -0.26 (s, 9H, $3CH_3$), 1.12-2.45 (m, 10H), 4.80 (t, J = 8.2 Hz, 1H, 7-H), 5.07 (s, 1H, 9-H), 7.18-7.36 (m, 5H, $H_{arom.}$).

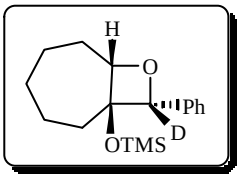
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 0.21 (q, 3 CH_3), 23.7 (t), 25.7 (t), 28.1 (t), 42.1 (t), 81.6 (d, C-7), 90.3 (s, C-1), 92.4 (d, C-9), 126.6 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 134.1 (s, $Cq_{arom.}$).

Irradiation of benzaldehyde-1d with 1-trimethylsilyoxycycloheptene (sbo-504)

A solution of benzaldehyde1-d (0.3 g, 3 mmol) and 1-trimethylsilyoxycycloheptene (0.55 g, 3 mmol) in 25 mL benzene was irradiated for 24 h according to the above general procedure. Distillation of the crude photolysate yielded 0.75 g (86 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-9-Deuterio-9-phenyl-1-trimethylsilyoxy-8-oxa-bicyclo[5.2.0]nonane (*endo*-84r)**



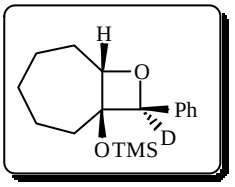
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.19 (s, 9H, 3 CH_3), 1.12-2.44 (m, 10H), 4.83 (t, J = 8.4 Hz, 1H, 7-H), 7.26-7.52 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 1.8 (q, 3 CH_3), 24.1 (t), 25.2 (t), 26.9 (t), 30.4 (t), 41.6 (t), 81.3 (d, C-7), 90.3 (s, C-1), 93.4 (t, C-9), 124.7 (d, $CH_{arom.}$), 126.8 (d, $CH_{arom.}$), 128.1 (d, $CH_{arom.}$), 134.7 (s, $Cq_{arom.}$).

***exo*-9-Deuterio-9-phenyl-1-trimethylsilyoxy-8-oxa-bicyclo[5.2.0]nonane (*exo*-86r)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = -0.18 (s, 9H, 3 CH_3), 1.12-2.44 (m, 10H), 4.76 (t, J = 8.2 Hz, 1H, 7-H), 7.26-7.52 (m, 5H, $H_{arom.}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 2.1 (q, $3CH_3$), 24.1 (t), 25.2 (t), 26.9 (t), 30.4 (t), 34.4 (t), 42.3 (t), 81.0 (d, C-7), 90.7 (s, C-1), 92.3 (t, C-9), 126.6 (d, $CH_{arom.}$), 127.8 (d, $CH_{arom.}$), 129.3 (d, $CH_{arom.}$), 134.7 (s, $Cq_{arom.}$).

4.23 Photolyses of propanal & propanal-1-d with 2,3-dihydrofuran & 5-deuterio-2,3-dihydrofuran

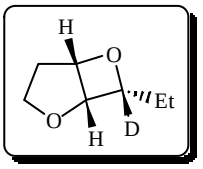
Irradiation of propanal with 2,3-dihydrofuran (sbo-596)

Under a nitrogen atmosphere, a solution of propanal (0.17 g, 3 mmol) and 2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL hexane was irradiated in a Rayonet photoreactor (λ = 300 nm) for 24 h. Distillation of the residue after removal of the solvent afforded 0.37 g (96 %) of inseparable mixture of oxetanes as a colorless oil. Both ^{1}H-NMR and ^{13}C-NMR data was reported earlier (*endo*- & *exo*- **3c**).

Irradiation of propanal-1-d with 2,3-dihydrofuran (sbo-596)

Under a nitrogen atmosphere, a solution of propanal-1-d (0.17 g, 3 mmol) and 2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL hexane was irradiated in a Rayonet photoreactor (λ = 300 nm) for 24 h. Distillation of the residue after removal of the solvent afforded 0.36 g (93 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-7-Deuterio-7-ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-85)**



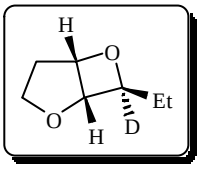
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.78 (t, J = 7.5 Hz, 3H, CH_3), 1.52 (m, 1H, 4-H), 1.54 (m, 2H, CH_2), 1.96 (m, 1H, 4-H), 4.08-4.17 (m, 2H, 3-H), 4.64 (d, J = 3.8 Hz, 1H, 1-H), 5.22 (dd, J = 3.8, 3.8 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.2 (q, CH_3), 22.1 (t, CH_2), 32.6 (t, C-4), 69.6 (t, C-3), 78.3 (d, C-1), 83.8 (d, C-5), 85.7 (t, C-7).

***exo*-7-Deuterio-7-ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-85)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.86 (t, J = 7.5 Hz, 3H, CH_3), 1.56 (m, 1H, 4-H), 1.62 (m, 2H, CH_2), 1.98 (m, 1H, 4-H), 4.08-4.16 (m, 2H, 3-H), 4.41 (d, J = 4.3 Hz, 1H, 1-H), 5.15 (dd, J = 4.3, 3.7 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.8 (q, CH_3), 26.7 (t, CH_2), 33.2 (t, C-4), 66.8 (t, C-3), 80.4 (d, C-1), 84.0 (d, C-5), 87.5 (t, C-7).

HRMS: ($C_7H_{11}DO_2$, M = 129.1 g/mol)

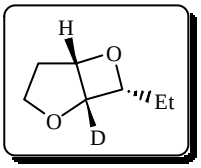
Calcd: 129.0947

Found: 129.0943

Irradiation of propanal with 5-deuterio-2,3-dihydrofuran (sbo-592)

Under a nitrogen atmosphere, a solution of propanal (0.17 g, 3 mmol) and 5-deuterio-2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL hexane was irradiated in a Rayonet photoreactor (λ = 300 nm) for 24 h. Distillation of the residue after removal of the solvent afforded 0.34 g (88 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-1-Deuterio-7-ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-86)**



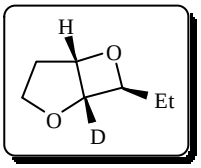
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.79 (t, J = 7.5 Hz, 3H, CH_3), 1.55 (m, 2H, CH_2), 1.58 (m, 1H, 4-H), 2.00 (m, 1H, 4-H), 4.12-4.20 (m, 2H, 3-H), 4.53 (t, J = 7.5 Hz, 1H, 7-H), 5.27 (d, J = 4.0 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.5 (q, CH_3), 22.4 (t, CH_2), 32.8 (t, C-4), 69.9 (t, C-3), 78.3 (d, C-1), 84.0 (d, C-5), 86.4 (t, C-7).

***exo*-1-Deuterio-7-ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-86)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.87 (t, J = 7.5 Hz, 3H, CH_3), 1.61 (m, 1H, 4-H), 1.66 (m, 2H, CH_2), 2.02 (m, 1H, 4-H), 4.12-4.19 (m, 2H, 3-H), 4.24 (t, J = 7.5 Hz, 1H, 7-H), 5.19 (d, J = 4.3 Hz, 1H, 5-H).

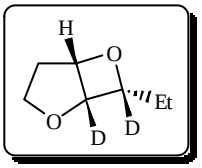
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.1 (q, CH_3), 27.0 (t, CH_2), 33.4 (t, C-4), 67.1 (t, C-3), 80.4 (t, C-1), 84.2 (d, C-5), 88.2 (t, C-7).

Irradiation of propanal-1-d with 5-deuterio-2,3-dihydrofuran (sbo-593)

Under a nitrogen atmosphere, a solution of propanal-1-d (0.17 g, 3 mmol) and 5-deuterio-2,3-dihydrofuran (0.21 g, 3 mmol) in 25 mL hexane was irradiated in a Rayonet photoreactor (λ = 300 nm) for 24 h. Distillation of the residue after removal of the solvent afforded 0.33 g (85 %) of inseparable mixture of oxetanes as a colorless oil.

***endo*-1,7-Dideuterio-7-ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*endo*-87)**



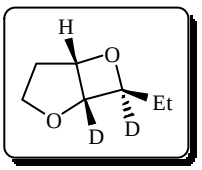
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.75 (t, J = 7.5 Hz, 3H, CH_3), 1.50 (m, 2H, CH_2), 1.53 (m, 1H, 4-H), 1.95 (m, 1H, 4-H), 4.06-4.15 (m, 2H, 3-H), 5.22 (d, J = 4.0 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 8.4 (q, CH_3), 22.2 (t, CH_2), 32.8 (t, C-4), 69.6 (t, C-3), 78.1 (t, C-1), 83.9 (d, C-5), 85.8 (t, C-7).

***exo*-1,7-Dideuterio-7-ethyl-2,6-dioxa-bicyclo[3.2.0]heptane (*exo*-87)**



^{1}H-NMR: (300 MHz, $CDCl_3$)

δ_{ppm} = 0.83 (t, J = 7.5 Hz, 3H, CH_3), 1.56 (m, 1H, 4-H), 1.60 (m, 2H, CH_2), 1.97 (m, 1H, 4-H), 4.06-4.14 (m, 2H, 3-H), 5.14 (dd, J = 4.0 Hz, 1H, 5-H).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ_{ppm} = 7.9 (q, CH_3), 26.8 (t, CH_2), 33.3 (t, C-4), 67.0 (t, C-3), 80.2 (t, C-1), 84.1 (d, C-5), 87.6 (t, C-7).

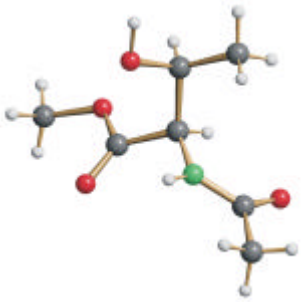
HRMS: ($C_7H_{10}D_2O_2$, M = 130.1 g/mol)

Calcd: 130.1345

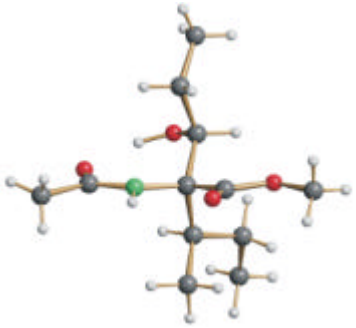
Found: 130.1340

5. Appendix

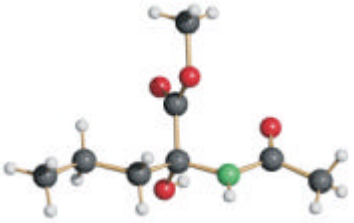
"Crystal growth is a science and an art. The scientists role in the crystal growth process is that of an assistant who helps molecules to crystallize."[177]



39g



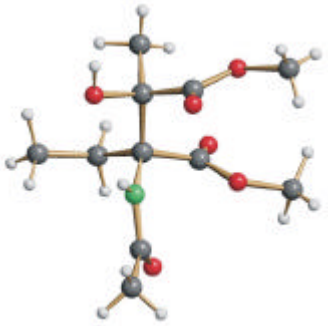
43df



45

Crystal data	**39g**	**43df**	**45**
Emperical formula	$C_7H_{13}NO_4$	$C_{12}H_{23}NO_4$	$C_8H_{15}NO_4$
Formula mass	175.18	245.31	189.21
Size [mm]	0.25 x 0.15 x 0.15	0.15 x 0.08 x 0.05	0.25 x 0.20 x 0.20
a [Å]	4.831 (10)	6.434 (1)	6.163 (1)
b [Å]	11.381 (10)	14.945 (1)	7.834 (1)
c [Å]	8.634 (10)	15.721 (1)	11.184 (1)
α [°]	90	90	95.93 (1)
β [°]	105.17	90	95.28 (1)
γ [°]	90	90	105.65 (1)
V [Å^3]	458.17 (12)	1511.7 (3)	513.11 (12)
Z	2	4	2
$d_{calcd.}$ [g/cm^3]	1.270	1.078	1.225
Crystal system	monoclinic	orthorhombic	triclinic
Space group[178]	P-2$_1$	P2$_1$2$_1$2$_1$	P-1
No. refl. meas.	1022	3219	4338
No. uni. Refl.	1022	3219	2223
No. obs. Refl.[a]	815	1762	1570
R	0.0373	0.0605	0.0438
R_w	0.0746	0.1396	0.0685
Largest diff. Peak / hole [e/Å^{-3}]	0.123/-0.111	0.116/-0.134	0.155/-0.197

[a] For I > 2σ (I)



67b

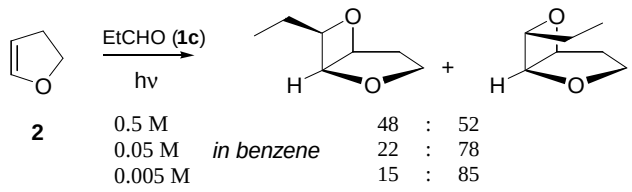
Crystal data	**67b**
Emperical formula	$C_{11}H_{19}NO_6$
Formula mass	261.27
Size [mm]	0.35 x 0.08 x 0.08
a [Å]	7.319 (1)
b [Å]	21.573 (1)
c [Å]	8.799 (1)
α [°]	90
β [°]	108.02 (1)
γ [°]	90
V [Å^3]	1321.2 (12)
Z	4
$d_{calcd.}$ [g/cm^3]	1.314
Crystal system	monoclinic
Space group[178]	P-2$_1$/c
No. refl. meas.	5302
No. uni. refl.	2722
No. obs. refl.[a]	1023
R	0.0559
R_w	0.0997
Largest diff. Peak / hole [e/Å^{-3}]	0.150/-0.230

[a] For I > 2σ (I)

6. Summary

This work was performed in order to study the mechanism and synthetic applications of the Paternò-Büchi reaction: Spin-mapping of the stereoselectivity of [2+2]-photocycloaddition *via* concentration, viscosity and temperature effects and, as a synthetic tool, the photo-aldol reaction of 5-methoxyoxazoles.

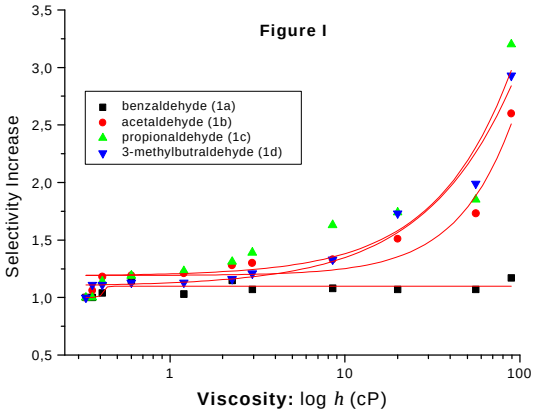
The difference between the simple diastereoselectivities in the photocycloaddition reactions following the singlet *versus* the triplet route were studied by determination of the concentration dependence of the Paternò-Büchi reaction. Carbonyl substrates which have both reactive singlet and triplet states, exhibit one characteristic substrate concentration where a 1:1 ratio of singlet and triplet reactivity, i.e *isospinselectivity* could be detected.[a]

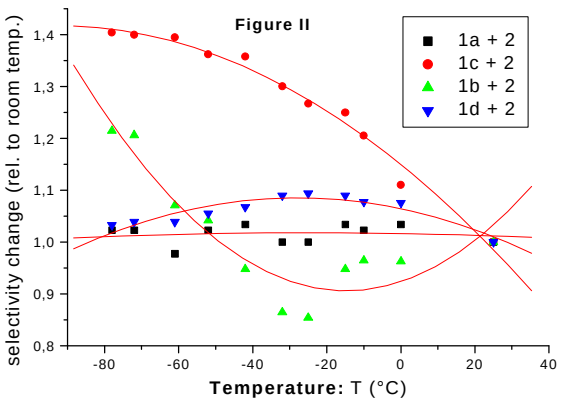


2	0.5 M		48	:	52
	0.05 M	*in benzene*	22	:	78
	0.005 M		15	:	85

Scheme I

The effect of solvent viscosity and temperature on the spin-directed stereoselectivity of the carbonyl-ene photocycloaddition was investigated. The variation of the solvent viscosity over a large effective range (η = 0.3 to 1500 cp) resulted in a weak but significant increase in the *endo*-selectivity of the (triplet) benzaldehyde cycloaddition to 2,3-dihydrofuran from 82 % to 91 %. For aliphatic aldehydes, the diastereoselectivity strongly increased with increasing

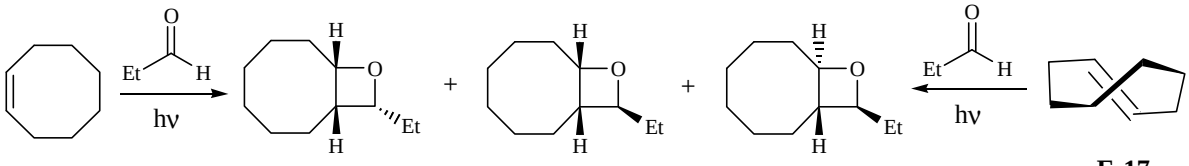




solvent viscosity. The temperature dependence of the *endo/exo* selectivity with aliphatic aldehydes **1b-d** showed characteristic non-linear curves with inversion points from which activation parameters for singlet as well as the triplet photocycloaddition were determined.[b]

The concentration dependence of the photocycloaddition of *cis*- and *trans*-cyclooctene with aliphatic aldehydes was studied.[c] The results showed that a moderate but still significant spin-

correlation effect. The *exo*-diastereoisomer **tc-18** was formed with similar probability as the *endo*-diastereoisomer **cc-18** in the singlet carbonyl manifold, whereas the triplet excited aldehydes preferred the formation of the *endo*-diastereoisomer and *trans* fused product, **tt-18**.

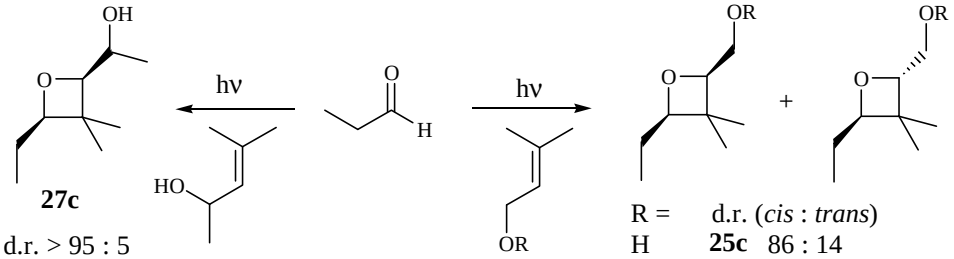


Z-17 **cc-18** **tc-18** **tt-18** **E-17**

5M 42 : 44 : 14
1M 28 : 34 : 36
0.01M 24 : 34 : 42

Scheme II

The effect of hydrogen bonding in the first excited singlet *versus* the first excited triplet state of aliphatic aldehydes in the photocycloaddition was compared for allylic alcohols and acetates. The simple diastereoselectivity for oxetanes was nearly the same, but the presence of hydrogen bonding interactions increased the rate of the Paternò-Büchi reaction. Moreover, the effect of hydrogen bonding for simple diastereoselectvity was completely different than that for the induced diastereoselectivity, what was confirmed by comparsion with the mesitylol photocycloaddition to aliphatic aldehydes.[d]



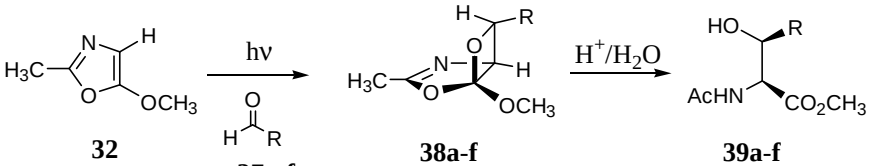
27c

d.r. > 95 : 5

R =	d.r. (*cis* : *trans*)	
H	**25c**	86 : 14
Ac	**26c**	81 : 19

Scheme III

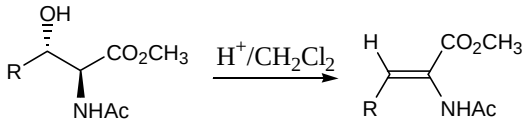
5-Methoxyoxazoles were prepared in three steps and evaluated with respect to their use as dienes in stereoselective Paternò-Büchi reaction. The photocycloaddition of 2-methyl-5-methoxyoxazole (glycine equivalent) with a series of aldehydes was investigated. In all cases only one regioisomeric bicyclic oxetane was detected in the crude photolysis mixture and in most cases also only one (*exo)*-diastereoisomer. Ring-opening of the bicyclic oxetanes proceeded with retention of configuration to give *erythro* (S*,S*) α-acetamido-β-hydroxy esters.[e]



R = Ph(**a**), 2-Nph(**b**), $BnCH_2$(**c**), Et(**d**), i-Pr(**e**), i-Bu(**f**)

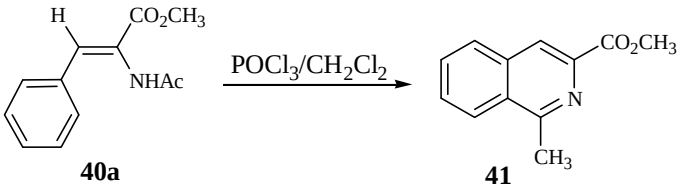
Scheme IV

Acid-catalyzed water elimination from α-acetamido-β-hydroxy esters gave the (Z)-α,β-didehydroamino acid preferentially.



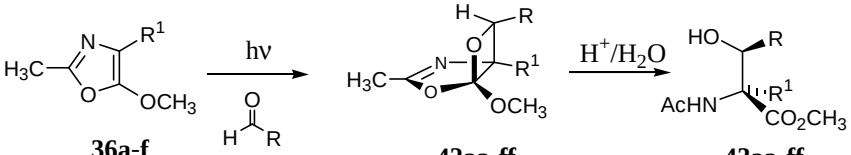
Scheme V

Compound **40a**, when treated with $POCl_3$ in methylene chloride afforded methyl 1-methylisoquinoline-3-carboxylate **41** in good yield via a Bischler-Napieralski cyclization.



Scheme VI

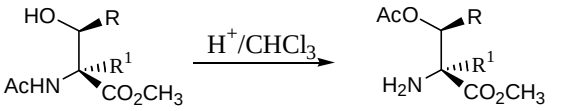
Furthermore, the photocycloaddition of a series of 5-methoxyoxazoles as substrate with an additional substituent at C-4 was studied. The primary photoadducts were formed with excellent *exo*-diastereoselectivities except for the benzaldehyde addition to oxazole substrates with bulky substituents R^1. The products were hydrolyzed to give the *erythro* (S*,S*) α-alkylated-α-acetamido-β-hydroxy esters.



R^1 = Me(**a**), Et(**b**), n-Pr(**c**), i-Pr(**d**), i-Bu(**e**), sec-Bu(**f**)

Scheme VII

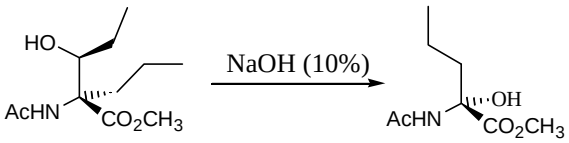
Treatment of the photo aldol adducts with a catalytic amount of conc. HCl in chloroform led to formation of transacylation products.



43da, 43dc & 43fc **44da, 44dc & 44fc**

Scheme VIII

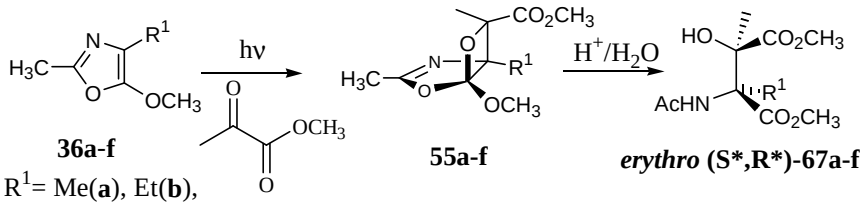
When compound **43c** was heated in aqueous NaOH (10%), the retro-aldol cleavage product **45** was obtained. The structure of compound **45** was established by means of an X-ray crystallographic analysis.



43dc **45**

Scheme IX

Following the semial work by Scharf *et al*., the photo aldol addition of 5-methoxyoxazoles to aliphatic and aromatic α-keto esters was investigated in detail. Photolysis of methylpyruvate with 5-methoxyoxazoles in benzene at 350 nm gave only one regio- and (*exo*)-diastereoisomer in high chemical yield. Acid treatment of the bicyclic oxetanes furnished *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives in quantitative chemical yield. The *erythro* configuration of compound **67b** was unambiguously established by means of an X-ray structure analysis.



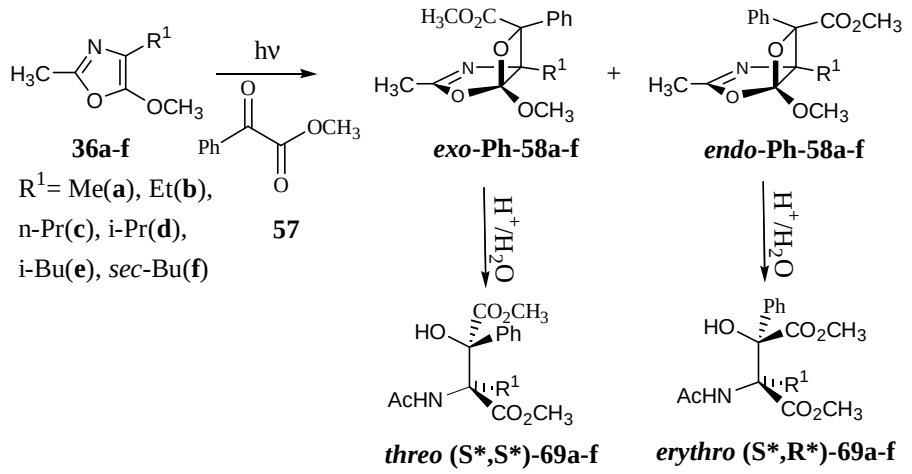
36a-f **55a-f** ***erythro* (S*,R*)-67a-f**

R^1= Me(**a**), Et(**b**), n-Pr(**c**), i-Pr(**d**), i-Bu(**e**), sec-Bu(**f**)

54

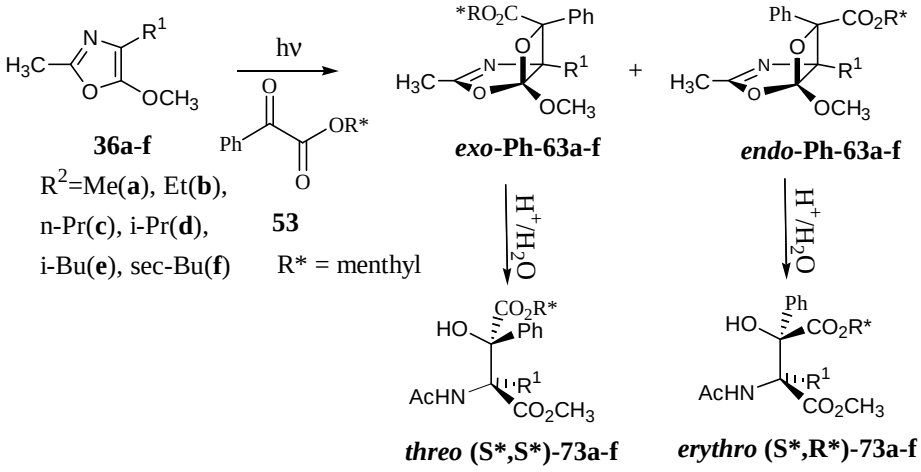
Scheme X

In contrast to aliphatic α-keto ester, irradiation of alkyl phenylglyoxylate in the presence of 5-methoxyoxazoles afforded two diastereoisomers with preferential formation of the *exo*-Ph diastereoisomer. The *exo/endo*-Ph diastereoselectivity decreased with increasing steric demand either at C-4 of oxazole and /or the alkyl group of the phenylglyoxylate. Acid hydrolysis of the chromatographically separated *exo*-Ph and *endo*-Ph bicyclic oxetanes afforded *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives in high chemical yield, respectively.



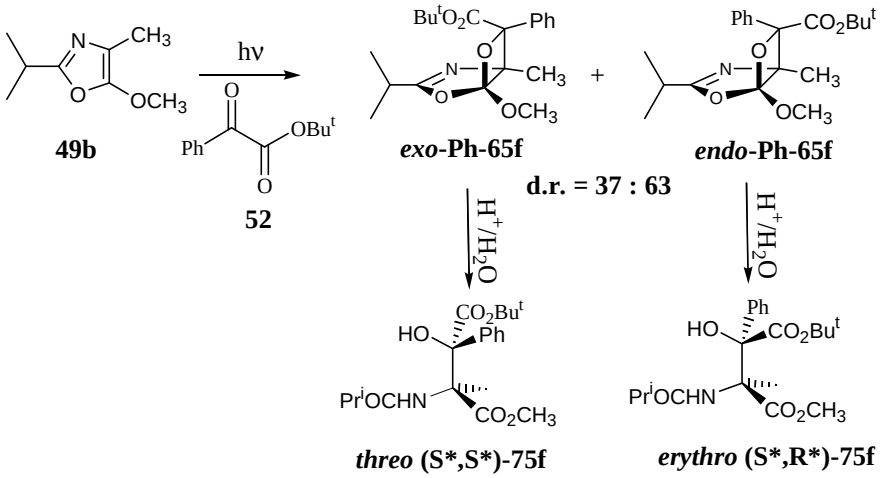
Scheme XI

Furthermore, the asymmetric induction in the Paternò-Büchi reaction of menthyl phenylglyoxylate with 5-methoxyoxazoles was investigated. The simple *exo/endo*-Ph diastereoselectivity was moderate, the facial selectivity for both *exo* and *endo* diastereoisomers was low. Hydrolysis of the chromatographically isolated *exo*-Ph and *endo*-Ph bicyclic oxetanes led to formation of *threo* (S*,S*) and *erythro* (S*,R*) α-acetamido-β-hydroxy succinic acid derivatives in high chemical yield, respectively.



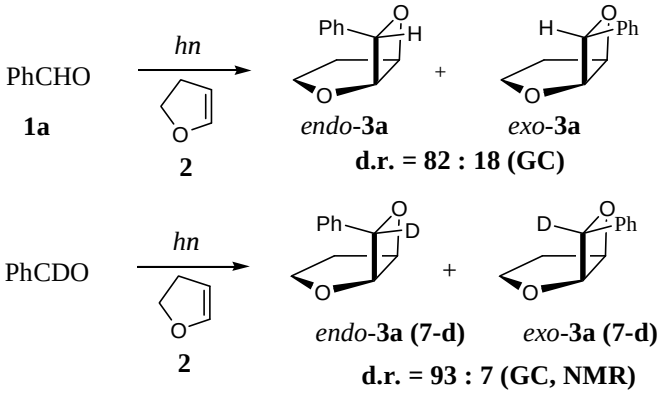
Scheme XII

The effect of the substituent at C-2 of the oxazole substrates on the diastereoselectivity of the triplet α-keto ester photocycloaddition was also studied. Surprisingly, the *exo/endo*-Ph diastereoselectivity of the photocycloaddition of *tert*-butyl phenylglyoxate to 2-isopropy-4-methyl-5-methoxyoxazole was inverted. This result indicated that secondary orbital interactions (SOI) may play an important role for determining the stereoselectvity in the triplet photocycloaddition reaction. Acid hydrolysis of the chromatographyically isolated *exo* and *endo*-Ph bicyclic oxetanes led to the formation of *threo* (S*,S*) and *erythro* (S*,R*) α-isobutyrylamino-β-hydroxy succinic acid derivatives in high chemical yields, respectively.



Scheme XIII

Finally, a substantial magnetic isotope effect on stereoselectivity in the triplet [2+2]-photocycloaddition of benzaldehyde-1-d to 2,3-dihydrofuran was measured. The results revealed that spin-orbit coupling (SOC) is not the only responsible interaction for intersystem crossing (ISC) as well as product distribution but also hyperfine coupling (HFC) plays an additional role for ISC even for 1,4-biradical intermediate.[f]



Scheme XIV

(a) "Spin-Directed Stereoselectivity of Carbonyl-Alkene Photocycloadditions" Axel G. Griesbeck, Maren Fiege, Samir Bondock and Murthy S.Gudipati, *Organic Letters* **2000**, *2*, 3623-3625.

(b) "Temperatur- und Viskositätsabhängigkeit der spingesteuerten Stereoselektivität von Carbonyl-Alken-Photocycloadditionen" Axel G. Griesbeck, Samir Bondock and Murthy S.Gudipati, *Angew. Chem.* **2001**, *113*, 4828-4832; *Angew. Chem. Int. Ed.* **2001**, *40*, 4684-4687.

(c) "Spin-Imposed Stereoselection in the Photocycloaddition of cis- and trans-Cyclooctene with Aliphatic Aldehydes" Axel G. Griesbeck and Samir Bondock, *Photochem. Photobiol. Sciences.* **2002**, *1*, 81-83.

(d) "Paternò-Büchi Reactions of Allylic Alcohols and Acetates with Aliphatic Aldehydes: Evidences for Hydrogen-Bond Activation in the Excited Singlet and Triplet States?" Axel G. Griesbeck and Samir Bondock *J. Am. Chem. Soc.* **2001**, *123*, 6191-6192.

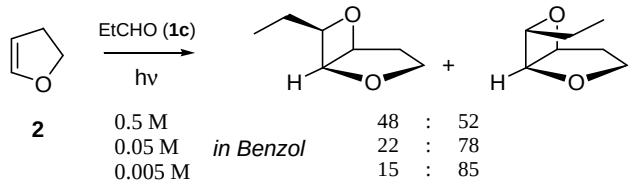
(e) "Photo Aldol Reactions with 5-Methoxyoxazoles: Highly Regio- and Diastereoselective Synthesis of α-Amino β-Hydroxy Carboxylic Acid Derivatives" Axel G. Griesbeck and Samir Bondock, *Can. J. Chem.* **2003**, *81*, 1-5.

(f) "Substantial ^{2}H-Magnetic Isotope Effects on the Diastereoselectivity of Triplet Photocycloaddition Reactions" Axel G. Griesbeck and Samir Bondock, *J. Am. Chem. Soc.*, **2003**, submitted.

7. Zusammenfassung

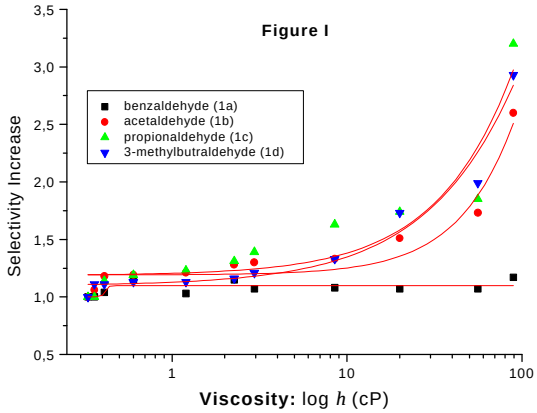
In dieser Arbeit wurden mechanistische Aspekte und Syntheseanwendungen von Paternò-Büchi-Reaktionen untersucht: „spin-mapping“ der Stereoselektivität von [2+2]-Cycloadditionen mittels Konzentrations-, Solvensviskositäts- und Temperaturvariation sowie, als eine synthetische Anwendung, die Photo-Aldolreaktion von 5-Methoxyoxazolen.

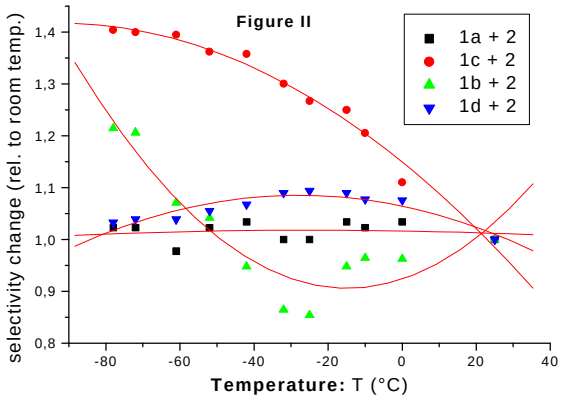
Der Unterschied zwischen den einfachen (nicht-induzierten) Diastereoselektivitäten bei Photocycloadditionreaktionen über die Singulett- und die Triplettroute wurden durch Bestimmung der Konzentrationsabhängigkeit der Paternò-Büchi-Reaktion bestimmt. Carbonylsubstrate, die sowohl aus dem Singulett- als auch dem Triplettzustand reagieren können, zeigen eine charakteristische Substratkonzentration, bei der ein 1:1-Verhältnis von Singulett- und Triplettreaktivität, d.h. *Isospinselektivität*, nachgewiesen werden konnte.[a]



Schema I

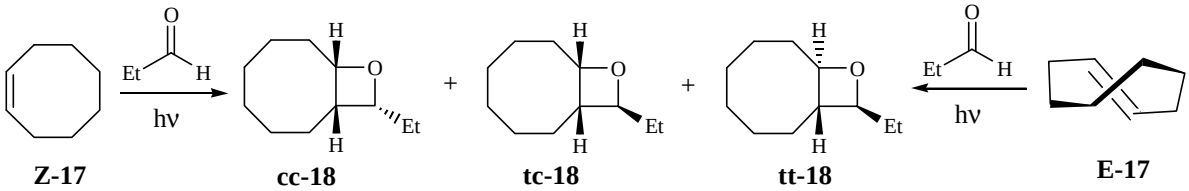
Der Effekt der Viskosität des Lösungsmittels und der Reaktionstemperatur auf die spin-gesteuerte Stereoselektivität der Carbonyl-En-Photocycloaddition wurde ebenfalls untersucht. Eine Erhöhung der Lösungsmittelviskosität über einen grossen Bereich (η = 0.3 bis 1500 cp) führte zu einem schwachen, aber signifikanten Anstieg der *endo*-Selektivität bei der Addition von (Triplett) Benzaldehyd an 2,3-Dihydrofuran von 82% auf 91%. Bei aliphatischen Aldehyden hingegen stieg die Diastereoselektivität stark mit der Lösungsmittelviskosität an.





Die Temperaturabhängigkeit der *endo*/*exo*-Selektivität mit den aliphatischen Aldehyden **1b-d** zeigte charakteristische nicht-lineare Korrelationen mit Inversionspunkten, aus denen die Aktivierungsparameter sowohl für die Singulett- als auch die Triplettphotocycloadditionen bestimmt wurden.[b]

Die Konzentrationsabhängigkeit der Photocycloaddition von *cis*- sowie *trans*-Cycloocten mit aliphatischen Aldehyden wurde untersucht.[c] Die Ergebnisse zeigten einen schwachen, aber aussagekräftigen Spin-Korrelationseffekt. Das *exo*-Diastereoisomer **tc-18** wurde im Singulett-bereich mit ähnlicher Wahrscheinlichkeit gebildet wie das *endo*-Diastereoisomer **cc-18**, hingegen bevorzugten Triplett-angeregte Aldehyde die Bildung des *endo*-Diastereoisomers **tt-18** mit *trans*-Konfiguration.

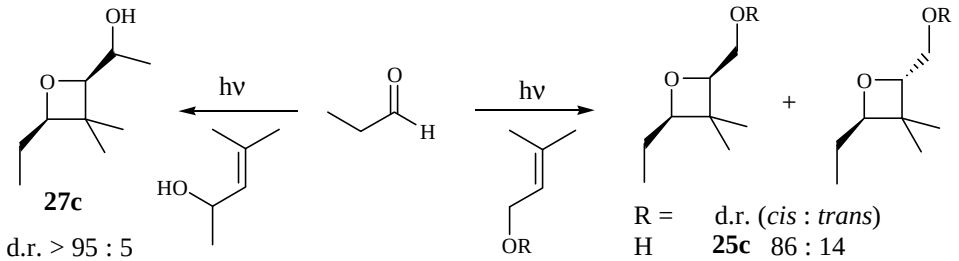


Z-17 **cc-18** **tc-18** **tt-18** **E-17**

5M	42 : 44 : 14
1M	28 : 34 : 36
0.01M	24 : 34 : 42

Schema II

Der Effekt von Wasserstoffbrückenbindungen auf die Reaktivität und Selektivität von Photo-cycloadditionen erster angeregter Singulettzustände im Vergleich zu den ersten angeregten Triplettzuständen wurde mit Allylalkoholen bzw. Acetaten untersucht. Die einfache, nicht-induzierte Diastereoselektivität für die Oxetanbildung war annähernd identisch, allerdings erhöhten Wasserstoffbrückenwechselwirkungen die Effizienz der Paternò-Büchi Reaktion. Darüberhinaus war der Effekt der Wasserstoffbrückenbindung auf die einfache Diastereoselektivität verschieden vom Einfluß auf die induzierte Diastereoselektivität. Dies wurde durch Vergleich von Photocycloadditionen mit Mesitylol und aliphatischen Aldehyden gezeigt.[d]



27c

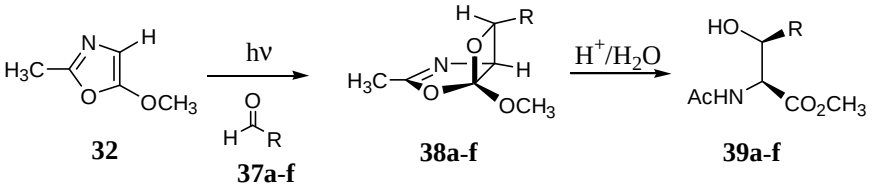
d.r. > 95 : 5

R =	d.r. (*cis* : *trans*)
H	**25c** 86 : 14
Ac	**26c** 81 : 19

Schema III

Verschiedene 5-Methoxyoxazole wurden in einer Dreistufenreaktion hergestellt und auf ihre Eignung als Diene in stereoselektiven Paternò-Büchi-Reaktionen getestet. Die Photocyclo-addition von 2-Methyl-5-methoxyoxazol (einem Glycinäquivalent) wurde mit einer Serie von Aldehyden untersucht. In allen Fällen wurde nur ein regioisomeres bicyclisches Oxetan mit hoher *exo*-Diastereoselektivität gebildet. Die Ringöffnung der bicyclischen Oxetane verlief

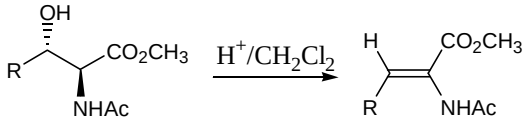
mit Retention der Konfiguration unter Bildung der *erythro* (S*,S*) α-Acetamido-β-hydroxy ester.[e]



R = Ph(**a**), 2-Nph(**b**), $BnCH_2$(**c**), Et(**d**), i-Pr(**e**), i-Bu(**f**)

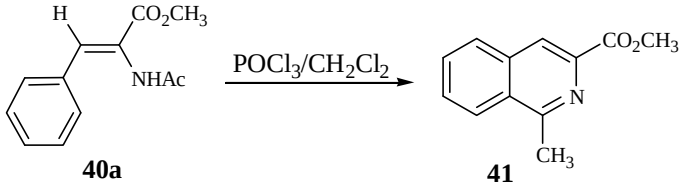
Schema IV

Die durch Brönsted-Säuren katalysierte Wassereliminierung ergab ausgehend von den α-Acetamido-β-hydroxyestern bevorzugt die (Z)-α,β-Didehydroaminosäuren.



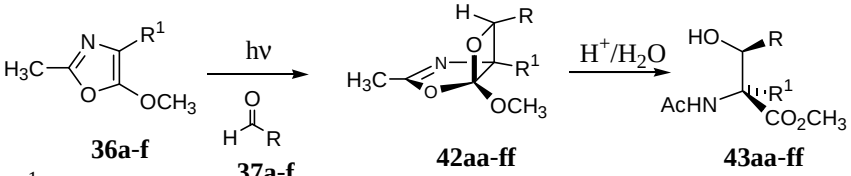
Schema V

Aus der Verbindung **40a** wurde durch Umsetzung mit $POCl_3$ in Methylenchlorid das Methylisoquinolin-3-carboxylat **41** in guten Ausbeuten über eine Bischler-Napieralski-Cyclisierung gebildet.



Schema VI

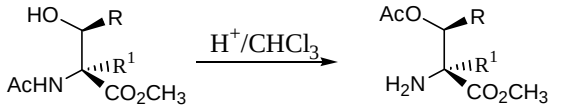
Weiterhin wurden Photocycloadditionen mit einer Serie von C-4-substituierten 5-Methoxyoxazolen als Dienkomponenten studiert. Die Photoaddukte wurden mit exzellenten *exo*-Diastereoselectivitäten gebildet. Eine Ausnahme stellten Benzaldehyd-Additionen an Oxazole mit sterisch anspruchsvollen Substituenten R^1 dar. Alle Produkte konnten leicht zu den entsprechenden *erythro* (S*,S*) α-alkylierten α-Acetamido-β-hydroxy estern hydrolisiert werden.



R^1 = Me(**a**), Et(**b**), n-Pr(**c**), i-Pr(**d**), i-Bu(**e**), sec-Bu(**f**)

Schema VII

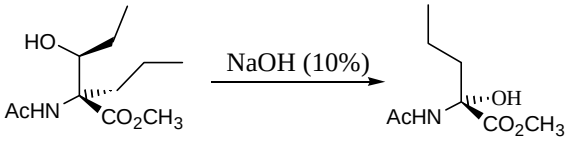
Die Umsetzung der Photo-Aldol-Produkte mit katalytischen Mengen conc. HCl führte zur quantitativen Bildung der Transacylierungsprodukte.



43da, 43dc & 43fc **44da, 44dc & 44fc**

Schema VIII

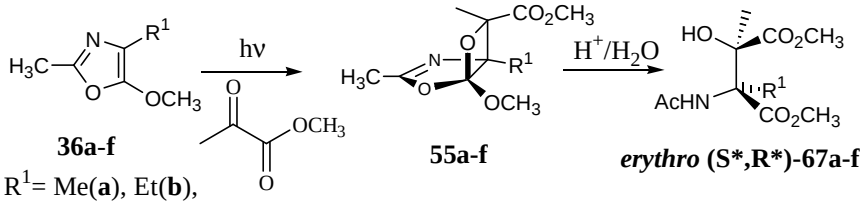
Bei der Umsetzung von Verbindung **43c** mit wässriger NaOH (10%) wurde das Retro-Aldol Spaltungsprodukt **45** erhalten. Die Struktur von Verbindung **45** wurde zusätzlich durch eine Kristallstrukturanalyse bestätigt.



43dc **45**

Schema IX

In Analogie zu den bahnbrechenden Arbeiten von Scharf und Mitarbeitern, wurde die Photoaldolreaktion von 5-Methoxyoxazolen auch mit aliphatischen und aromatischen α-Ketoestern untersucht. Die Belichtung von Methylpyruvat mit 5-Methoxyoxazol in Benzol bei 350 nm ergab lediglich ein regio- und (*exo*)-diastereoisomerenreines Oxetan in hohen Ausbeuten. Die Säurespaltung der bicyclischen Oxetane ergab quantitativ die *erythro* (S*,R*) α-Acetamido-β-hydroxybernsteinsäurederivate. Die *erythro*-Konfiguration von Verbindung **67b** wurde zusätzlich durch eine Kristallstrukturanalyse bestätigt.



36a-f

R^1= Me(**a**), Et(**b**), n-Pr(**c**), i-Pr(**d**), i-Bu(**e**), sec-Bu(**f**)

54

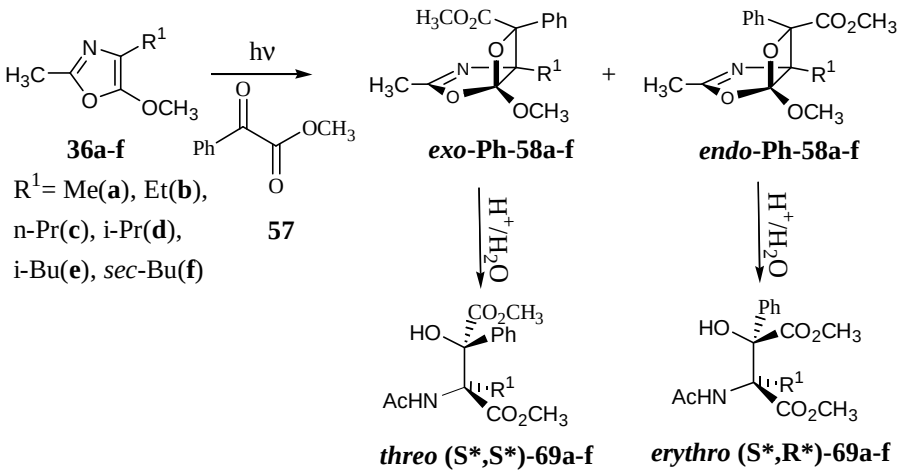
55a-f

***erythro* (S*,R*)-67a-f**

Schema X

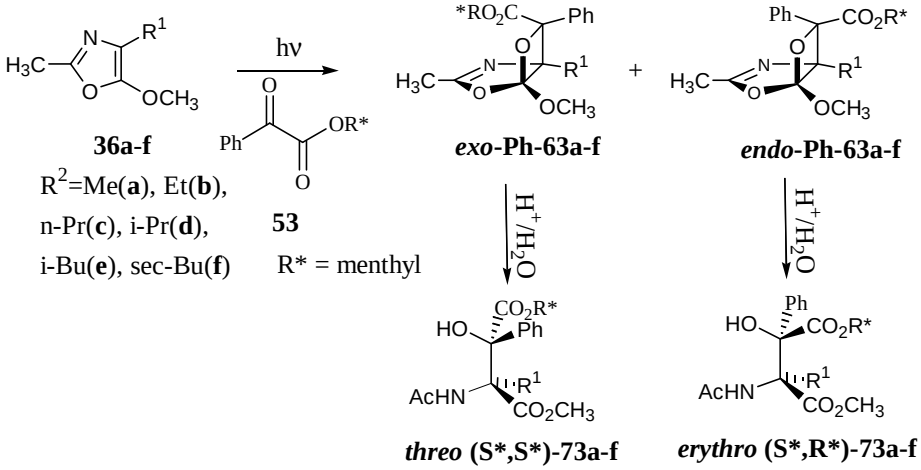
Im Gegensatz zu den aliphatischen α-Ketoestern, ergab die Belichtung von Alkylphenylglyoxylaten in Gegenwart von 5-Methoxyoxazolen zwei Diastereoisomere unter bevorzugter Bildung des *exo*-Phenyl-Stereoisomeren. Die *exo/endo*-Phenyl-Diastereoselektivität nahm mit zunehmenden Raumanspruch an C-4 der Oxazolkomponente und / oder der Alkylgruppe am Phenylglyoxylat ab. Die saure Hydrolyse der chromatographisch getrennten *exo*-Ph- und

endo-Ph-Oxetane lieferte die *threo* (S*,S*) und *erythro* (S*,R*) α-Acetamido-β-hydroxy-bernsteinsäurederivate in hohen Ausbeuten.



Schema XI

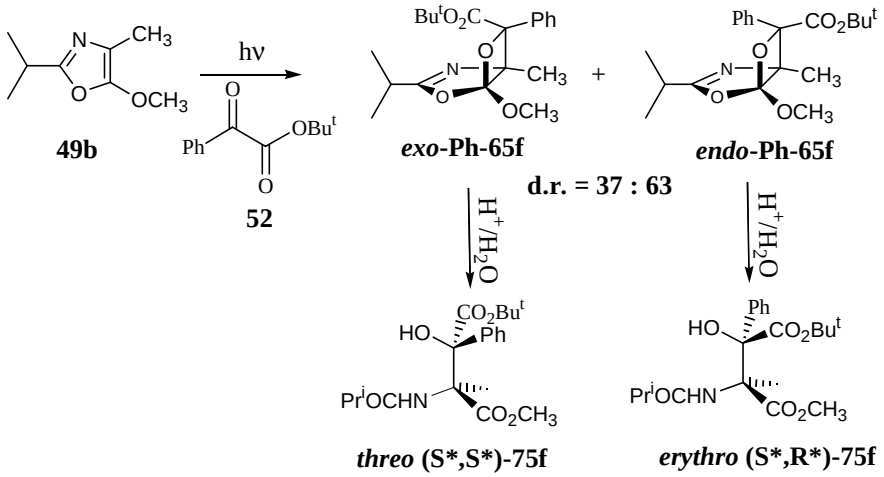
Weiterhin wurde die asymmetrische Induktion bei der Paternò-Büchi-Reaktion von Menthyl-phenylglyoxylat mit 5-Methoxyoxazolen untersucht. Die einfache *exo/endo*-Ph-Diastereo-selektivität war mässig, die induzierte Diastereoselektivtiät für beide *exo*- und *endo*-Diastereoisomere gering. Die Hydrolyse der chromatographisch getrennten *exo*-Ph- und *endo*-Ph-Oxetane ergab in sehr guten Ausbeuten die *threo* (S*,S*) und *erythro* (S*,R*) α-Acetamido-β-hydroxybernsteinsäurederivative.



Schema XII

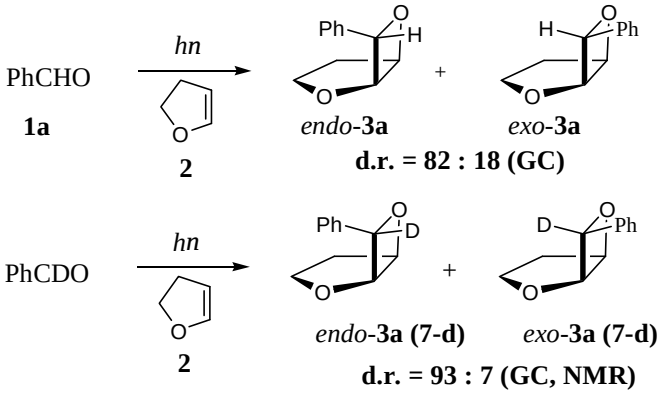
Der Einfluss eines Substituenten an C-2 der Oxazolkomponente auf die Diastereoselektivität bei der Photocycloaddition von Triplett-angeregten α-Ketoestern wurde untersucht. Überraschenderweise drehte sich die *exo/endo*-Ph-Diastereoselektivität bei der Cycloaddition von *tert*-Butylphenylglyoxat an 2-Isopropyl-4-methyl-5-methoxyoxazol um. Dieses Ergebnis lässt vermuten, dass sekundäre Orbitalwechselwirkungen (SOI) eine wichtige Rolle bei der Steuerung der Stereoselektivität von Triplett-Photocycloadditionen spielen. Die säurekatalysierte Hydrolyse der chromatographisch getrennten *exo* and *endo*-Ph-Oxetane

ergab die *threo* (S*,S*) and *erythro* (S*,R*) α-Isobutyrylamino-β-hydroxybernsteinsäure-derivate in guten Ausbeuten.



Schema XIII

Schliesslich wurde ein beachtlicher magnetischer Isotopeneffekt auf die Stereoselektivität der Triplett-[2+2]-Photocycloaddition von Benzaldehyd-1-d an 2,3-Dihydrofuran bestimmt. Diese Ergebnisse zeigten, dass die Spin-Bahn-Kopplung (SOC) nicht die einzige Wechselwirkung ist, die für das Intersystem-Crossing (ISC) und somit auch für die Produktverteilung verantwortlich ist, sondern dass auch die Hyperfeinkopplung (HFC) eine zusätzliche Rolle beim ISC, sogar bei 1,4-Biradikalen, spielt.[f]



Schema XIV

(a) "Spin-Directed Stereoselectivity of Carbonyl-Alkene Photocycloadditions" Axel G. Griesbeck, Maren Fiege, Samir Bondock und Murthy S.Gudipati, *Organic Letters* **2000**, *2*, 3623-3625.

(b) "Temperatur- und Viskositätsabhängigkeit der spingesteuerten Stereoselektivität von Carbonyl-Alken-Photocycloadditionen" Axel G. Griesbeck, Samir Bondock und Murthy S.Gudipati, *Angew. Chem.* **2001**, *113*, 4828-4832; *Angew. Chem. Int. Ed.* **2001**, *40*, 4684-4687.

(c) "Spin-Imposed Stereoselection in the Photocycloaddition of cis- and trans-Cyclooctene with Aliphatic Aldehydes" Axel G. Griesbeck und Samir Bondock, *Photochem. Photobiol. Sciences.* **2002**, *1*, 81-83.

(d) "Paternò-Büchi Reactions of Allylic Alcohols and Acetates with Aliphatic Aldehydes: Evidences for Hydrogen-Bond Activation in the Excited Singlet and Triplet States?" Axel G. Griesbeck und Samir Bondock *J. Am. Chem. Soc.* **2001**, *123*, 6191-6192.

(e) "Photo Aldol Reactions with 5-Methoxyoxazoles: Highly Regio- and Diastereoselective Synthesis of α-Amino β-Hydroxy Carboxylic Acid Derivatives" Axel G. Griesbeck und Samir Bondock, *Can. J. Chem.* **2003**, *81*, 1-5.

(f) "Substantial ^{2}H-Magnetic Isotope Effects on the Diastereoselectivity of Triplet Photocycloaddition Reactions" Axel G. Griesbeck und Samir Bondock, *J. Am. Chem. Soc.*, **2003**, eingereicht.

8. References

1. Zewail, A. H., *J. Phys. Chem. A*. **2000**, *104*, 5660-5694.
2. Buchachenko, A. L., *Pure Appl. Chem.* **2000**, *72*, 2243-2258.
3. Paternò, E., Chieffi, G., *Gazz. Chim. Ital.* **1909**, *39*, 431-436.
4. Büchi, G., Inman, C. G., Lipinski, E. S., *J. Am. Chem. Soc.* **1954**, *76*, 4327-4331.
5. Arnold, D. R., in *Advances in Photochemistry*, Noyes, W. A., Hammond, G. S., Pitts, J. N., Eds., Wiley Interscience, New York **1968**, *6*, 301.
6. Jones, G., *in Organic Photochemistry*, Padwa, A., Ed., Marcel Dekker, New York. **1981**, *5*, 1.
7. Mattay, J., Conrads, R., Hoffmann, R., in *Methods of Organic Chemistry (Houben-Weyl)* Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds., Thieme Verlag: Stuttgart **1995**, *E21c*, 3133.
8. Bach, T., *Synthesis* **1998**, 683-703.
9. a) Griesbeck, A. G., in *Handbook of Organic Photochemistry and Photobiology*, Horspool, W.M., Song, P.-S., Eds., CRC press: Boca Raton **1995**, 550.
   b) Griesbeck, A. G., in *Handbook of Organic Photochemistry and Photobiology*, Horspool, W.M., Song, P.-S., Eds., CRC press : Boca Raton **1995**, 755.
   c) Griesbeck, A. G., Fiege, M., In *Molecular and Supramolecular Photochemistry*, Hrsg.: Ramamurthy, V., Schanze, K. S., Marcel Dekker, New York **2000**, *6*, 33.
   d) Griesbeck, A. G., *Synlett* **2003**, 451-472.
10. Kopecky, J., in *Organic Photochemistry, A Visual Approach*, VCH Publishers, New York **1992**, 126.
11. Carless, H. A. J., *Carbonyl Compounds : Cycloaddition, in Photochemistry in Organic Synthesis*, Coyle, J. D. , Ed., The Royal Society of Chemistry, London **1986**, 96.
12. Freilich, S. C., Peters, K. S., *J. Am. Chem. Soc.* **1985**, *107*, 3819-3822.
13. Turro, N. J., *Modern Molecular Photochemistry*, Benjamin-Cummings, Menlo Park, **1978**.
14. Dauben, W. G., Salem, L., Turro, M. J., *Acc. Chem. Res.* **1975**, *8*, 41-44.
15. Berson, J. A., *Acc. Chem. Res.* **1978**, *11*, 446-453.
16. Michl, J., Bonacic`-Koutecky`, V., *Tetrahedron* **1988**, *44*, 7559-7585.
17. Wirz, J., *Pure Appl. Chem.* **1984**, *56*, 1289-1300.
18. a) Caldwell, R. A., in *Kinetics and Spectroscopy of Biradicals and Carbenes*, Platz, M. S., Ed., Plenum press, New York **1989**, 77-116.
    b) Johnston, L. J., Scaiano, J. C., *Chem. Rev.* **1989**, *89*, 521-547.

19. a) Zimmt, M. B., Doubleday Jr., C., Gould, I., Turro, N. J., *J. Am. Chem. Soc.* **1985**, *107*, 6724-6726.
b) Zimmt, M. B., Doubleday Jr., C., Gould, I., Turro, N. J., *J. Am. Chem. Soc.* **1985**, *107*, 6726-6727.
c) Closs, G. L., Redwine, O. D., *J. Am. Chem. Soc.* **1985**, *107*, 6131-6133.

20. a) Scaiano, J. C., Lissi, E. A., Encinas, M. V., *Rev. Chem. Intermed.* **1978**, *2*, 139.
b) Wagner, P. J., *Acc. Chem. Res.* **1971**, *4*, 168-177.
c) Wagner, P. J., *Acc. Chem. Res.* **1989**, *22*, 83-91.

21. a) Weiss, D. S., *Organic Photochemistry* **1981**, *5*, 347.
b) Roth, W. R., Langer, R., Bartmann, M., Stevermann, B., Maier, Reisenauer, H. P., Sustmann, R., Müller, W., *Angew. Chem.* **1987**, *99*, 271-272.
c) Barton, D. H. R., Charpiot, B., Ingold, K. U., Johnston, L. J., Motherwell, W. B., Scaiano, J. C., Stansforths, S., *J. Am. Chem. Soc.* **1985**, *107*, 3607-3611.

22. Adam, W., Grabowski, S., Wilson, R., M., Hannemann, K., Wirz, J., *J. Am. Chem. Soc.* **1987**, *109*, 7572-7573.

23. Freilich, S. C., Peters, K. S., *J. Am. Chem. Soc.* **1981**, *103*, 6255-6257.

24. Wilson, R. M., Wunderly, S. W., *J. Am. Chem. Soc.* **1974**, *96*, 7350-7351.

25. Scaiano, J. C., Wagner, P. J., *J. Am. Chem. Soc.* **1984**, *106*, 4626-4627.

26. Carlacci, L., Doubleday, C., Jr., Furlani, T. R., King, H. F., Mclver, J.W., Jr., *J. Am. Chem. Soc.* **1987**, *109*, 5323-5329.

27. a) Doubleday, C. Jr., Turro, N. J., Wang, J.-F., *Acc. Chem. Res.* **1989**, *22*, 199-205.
b) Closs, G. L., Miller, R. J., Redwine, O. D., *Acc. Chem. Res.* **1985**, *18*, 196-202.

28. Salem, L., Rowland, C., *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 92.

29. Adam, W., Hössel, P., Hümmer, W., Platsch, H., Wilson, R. M., *J. Am. Chem. Soc.* **1987**, *109*, 5323-5329.

30. Michl, J., *J. Am. Chem. Soc.* **1996**, *118*, 3568-3579.

31. Kita, F., Nau, W. M., Adam, W., Wirz, J., *J. Am. Chem. Soc.* **1995**, *117*, 8670-8671.

32. Kutateladze, A. G., *J. Am. Chem. Soc.* **2001**, *123*, 9279-9282.

33. Yang, N. C., Loeschen, R., Mitchell, D., *J. Am. Chem. Soc.* **1967**, *89*, 5465-5466.

34. Hansen, D. A., Lee, E. K. C., *J. Chem. Phys.* **1975**, *62*, 183.

35. Turro, N. J., Wriede, P. A., *J. Am. Chem. Soc.* **1970**, *92*, 320-329.

36. Griesbeck, A. G., Mauder, H., Peters, K., Peters, E.-M., von Schnering, H. G., *Chem. Ber.* **1991**, *124*, 407-410.

37. Griesbeck, A. G., Stadtmüller, S., *J. Am. Chem. Soc.* **1991**, *113*, 6923-6928.

38. Park, S.-K., Lee, S.-J., Baek, K., Yu, C.-M., *Bull. Korean. Chem. Soc.* **1998**, *19*, 35-36.

39. Abe, M., Shirodai, Y., Nojima, M., *J. Chem. Soc., Perkin Trans. 1* **1998**, 3253-3260.

40. a) Sun, D. L., Hubig, S. M., Kochi, J. K., *J. Org. Chem.* **1999**, *64*, 2250-2258.
b) Hubig, S. M., Sun, D. L., Kochi, J. K., *J. Chem. Soc., Perkin Trans. 2* **1999**, 781-788.
c) Bosch, E., Hubig, S. M., Kochi, J. K., *J. Am. Chem. Soc.* **1998**, *120*, 386-395.

41. a) Weller, A. Z., *Phys. Chem. N. F.* **1982**, *130*, 129.
b) Rehm, D., Weller, A., *Isr. J. Chem.* **1970**, *8*, 259.

42. Griesbeck, A. G., Buhr, S., Fiege, M., Schmickler, H., Lex, J., *J. Org. Chem.* **1998**, *63*, 3847-3854.

43. a) Eckert, G., Goez, M., *J. Am. Chem. Soc.* **1994**, *116*, 11999-12009.
b) Goez, M., Eckert, G., *J. Am. Chem. Soc.* **1996**, *118*, 140-154.

44. Abe, M., Masayuki, I., Nojima, M., *J. Chem. Soc., Perkin Trans. 1* **1998**, 3261-3266.

45. Thopate, S. R., Kulkarni, M. G., Puranik, V. G., *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 1110.

46. a) Arnold, D. R., Hinman, R. L., Glick, A. H., *Tetrahedron Lett.* **1964**, 1425-1430.
b) Caldwell, R. A., Sovocool, G. W., Gajewski, R. P., *J. Am. Chem. Soc.* **1973**, *95*, 2549-2557.

47. Barltrop, J. A., Carless, H. A. J., *J. Am. Chem. Soc.* **1972**, *94*, 1951-1959.

48. Turro, N. J., Dalton, J. C., Dawes, K., Farrington, G., Hautala, R. R., Morton, D., Niemczyk, N., Schore, N., *Acc. Chem. Res.* **1972**, *5*, 92.

49. Griesbeck, A. G., Stadtmüller, S., *J. Am. Chem. Soc.* **1990**, *112*, 1281-1283.

50. Griesbeck, A. G., Stadtmüller, S., *Chem. Ber.* **1990**, *123*, 357-362.

51. Griesbeck, A. G., Mauder, H., Stadtmüller, S., *Acc. Chem. Res.* **1994**, *27*, 70-75.

52. a) Bach, T., Schröder, J., *J. Org. Chem.* **1999**, *64*, 1265-1273.
b) Bach, T., *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 884-886.

53. Bach, T., Schröder, J., *Synthesis* **2001**, *8*, 1117-1124.

54. Bach, T., Jödicke, K., *Chem. Ber.* **1993**, *126*, 2457-2466.

55. Bach, T., *Liebigs Ann.* **1997**, 1627.

56. Abe, M., Fujimoto, K., Nojima, M., *J.Am.Chem. Soc.* **2000**, *122*, 4005-4010.

57. Jones II, G., Khalil, Z. H., Phan, X. T., Chen, T. J., Welankiwar, S., *Tetrahedron Lett.* **1981**, *22*, 3823-3826.

58. Bryce-Smith, D., Evans, E. H., Gilbert, A., McNeill, H. S., *J. Chem. Soc., Perkin Trans 1* **1992**, 485-489.

59. Bryce-Smith, D., Evans, E. H., Gilbert, A., McNeill, H. S., *J. Chem. Soc., Perkin Trans 1* **1991**, 1587-1593.

60. Shima, K., Sakai, Y., Sakurai, H., *Bull. Chem.Soc. Jpn.* **1971**, *4*, 215-218.

61. Gotthardt, H., Lenz, W., *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 868-869.

62. Oppenländer, T., Schönholzer, P., *Helv. Chim. Acta* **1989**, *72*, 1792-1800.

63. a) Buschmann, H., Scharf, H.-D., Hoffmann, N., Esser, P., *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 477-515.

b) Nehrings, A., Scharf, H.-D., Runsik, J., *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 877-878.

64. a) Bach, T., Jödicke, K., Kather, K., Fröhlich, R., *J. Am.Chem. Soc.* **1997**, *119*, 2437-2445.

b) Bach, T., Jödicke, K., Kather, K., Hecht, J., *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2271-2273.

c) Bach, T., Jödicke, K., Wibbeling, B., *Tetrahedron* **1996**, *52*, 10861-10878.

65. Hoffmann, R. W., *Chem. Rev.* **1989**, *89*, 1841-1860.

66. Bach, T., Schröder, J., Brandl, T., Hecht, J., Harms, K., *Tetrahedron* **1998**, *54*, 4507-4520.

67. Bach, T., Schröder, J., Harms, K., *Tetrahedron Lett.* **1990**, *40*, 9004-9005.

68. Buschmann, H., Scharf, H.-D., Hoffmann, N., Plath, M.W., Runsink, J., *J. Am. Chem. Soc.* **1989**, *111*, 5367-5373.

69. Giese, B., *Acc. Chem. Res.* **1984**, *17*, 438-442.

70. a) Adam, W., Stegmann, V.R., *J. Am. Chem. Soc.* **2002**, *124*, 3600-3607.

b) Adam, W., Stegmann, V.R., Weinkoetz, S., *J. Am. Chem. Soc.* **2001**, *123*, 2452-2453.

71. Sauers, R. R., Valenti, P. C., Tavss, E., *Tetrahedron Lett.* **1975**, 3129.

72. a) D`Auria, M., Racioppi, R., Romaniello, G., *Eur. J. Org. Chem.* **2000**, 3265-3272.

b) D`Auria, M., Emanuele, L., Poggi, G., Racioppi, R., Romaniello, G., *Tetrahedron* **2002**, *58*, 5054-5051.

73. a) Adam, W., Peters, K., Peters, E. M., Stegmann, V. R., *J. Am. Chem. Soc.* **2000**, *122*, 2958-2959.

b) Adam, W., Stegmann, V.R., *Synthesis* **2001**, 1203-1214.

74. a) Kubota, T., Shima, K., Toki, S., Sakurai, H., *Chem. Comm.* **1969**, 1462-1463.

b) Shima, K., Kubota, T., Sakurai, H., *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2567-2571.

75. Jones, G., Acquardo, M., Carmody, M. A., *J. Chem. Soc., Chem. Comm.* **1975**, 206-207.

76. a) Schreiber, S. L., *Science* **1985**, *227*, 857-863.
b) Schreiber, S. L., Hoveyda, A. H., Wu, H.-J., *J. Am. Chem. Soc.* **1983**, *105*, 660-661.
c) Porco, J. A., Schreiber, S. L., in *Comprehensive Organic Synthesis*, Pergamon, Oxford **1991**, *5*, chap. 2.4.

77. Schreiber, S. L., Hoveyda, A. H., *J. Am. Chem. Soc.* **1984**, *106*, 7200-7202.

78. Weuthen, M., Scharf, H.-D., Runsink, J., Vassen, R., *Chem. Ber.* **1988**, *121*, 971-976.

79. Bach, T., Schröder, J., *Tetrahedron Lett*. **1997**, *38*, 3707-3708.

80. a) Bach, T., Brummerhop, H., *Angew.Chem. Int. Ed.* **1998**, *37*, 3400-3402.
b) Bach, T., Brummerhop, H., Harms, K., *Chem. Eur. J.* **2000**, *6*, 3838-3848.

81. Griesbeck, A. G., Fiege, M., Lex, J., *Chem. Comm.* **2000**, 589-590.

82. Zagar, C., Scharf, H.-D., *Chem. Ber.* **1991**, *124*, 967-969.

83. Inoue, Y., Sugahara, N., Wada, T., *Pure Appl.Chem.* **2001**, *73*, 475-480.

84. a) Yokoyama, A., Mizuno, K., *Org. Lett*. **2000**, *2*, 3457-3459.
b) Bach, T., Bergmann, H., Harms, K., *J. Am. Chem. Soc.* **1999**, *121*, 10650-10651.
c) Sieburth, S. McN., McGee, Jr., K.F., *Org. Lett*. **1999**, *1*, 1775-1777.
d) Sydnes, L. K., Hansen, K. I., Oldroyd, D. L., Weedon, A., C., Jorgensen, E., *Acta Chem. Scan*. **1993**, *47*, 916-924.

85. Kossanyi, J., Sabbah, S., Chaquin, P., Ronfart-Haret, J. C., *Tetrahedron* **1981**, *37*, 3307-3315.

86. Huet, J., *Bull. Soc. Chim. Fr.* **1964**, *26*, 447.

87. Henry, R. H., Bruce, B. A., William, B. C., *J. Org. Chem.* **1942**, 326-335.

88. Shono, T., Ishifune, M., Kashimura, S., *Chem. Lett*. **1990**, 449-452.

89. Moses, F. G., Liu, R. S. H., Monroe, B. H., *Mol. Photochem.* **1969**, *1*, 245.

90. Wagner, P. J., Kemppainen, A. E., *J. Am. Chem. Soc.* **1972**, *94*, 7495-7499.

91. Yang, N. C., Loeschen, R., Mitchell, D., *J. Am. Chem. Soc.* **1967**, *89*, 5465-5466.

92. Engel, P. S., *Chem. Rev*. **1980**, *80*, 99-150.

93. Giese, B., Wettstein, P., Stahelin, C., Barbosa, F., Neuburger, M., Zehnder, M., Wessig, P., *Angew.Chem., Int. Ed.* **1999**, *38*, 2586.

94. Adam, W., Marti, V., Sahin, C., Trofimov, A. V., *J. Am. Chem. Soc.* **2000**, *122*, 5002-5003.

95. a) Debye, P., *Trans. Electrochem. Soc.* **1942**, *82*, 265.
b) Wagner, P. J., Kochevar, I., *J. Am. Chem. Soc.* **1968**, *90*, 2232-2238.

96. Palmer, I. J., Ragazos, I. N., Bernardi, F., Olivucci, M., Robb, M. A., *J. Am. Chem. Soc.* **1994**, *116*, 2121-2132.

97. Griesbeck, A. G., Fiege, M., Bondock, S., Gudipati, M. S., *Org. Lett.* **2000**, *2*, 3623-3625.

98. a) Chang, M. H., Dougherty, D.A., *J. Am. Chem. Soc.* **1982**, *104*, 2333-2334.
b) Turro, N. J., Renner, C.A., Waddell, W. H., Katz, T. J., *J. Am. Chem. Soc.* **1976**, *98*, 4320-4322.

99. Hale, K. J., Ridd, J. H., *J. Chem. Soc. Chem. Commun.* **1995**, 357-358.

100. Inoue, Y., Tsuneishi, H., Hakushi, T., Tai, A., In *Photochemical Key Steps in Organic Synthesis*, Experimental course book, Mattay, J., Griesbeck, A.G., Eds., VCH: Weinheim **1994**, 207.

101. Deyrup, J.A., Betkouski, M., *J. Org. Chem.* **1972**, *37*, 3561-3562.

102. Gau, A. H., Lin, G. L., Uang, B. J., Liao, F. L., Wang, S. L., *J. Org. Chem.* **1999**, *64*, 2194-2201.

103. Knights, J., Waight, E. S., *J. Chem. Soc.* **1955**, 2830-2833.

104. a) Bonazza, B. R., Lillya., P. C., Maggar, E. S., Scholes, G., *J. Am. Chem. Soc.* **1979**, *101*, 4100-4106.
b) Michejda, C. J., Comnik, R. W., *J. Org. Chem.* **1975**, *40*, 1046- 1050.

105. Arnold, D. A., Hinman, R. L., Glick, A. H., *Tetrahedron Lett*. **1964**, 1425-1430.

106. Beereboom, J., von Mittenau, M. S., *J. Org. Chem.* **1965**, *30*, 1231-1234.

107. Turro, N.J., *Modern Molecular Photochemistry*, University Science Books: Sausalito, **1991**.

108. Parenti, F., Cavalleri, B., *Drugs of the Future* **1990**, *15*, 17.

109. Rao, A. V. R., Gurjar, M. K., Reddy, K. L., Rao, A. S., *Chem. Rev*. **1995**, *95*, 2135-2167.

110. Schreiber, S. L., *Science* **1989**, *111*, 5367-5373.

111. Singh, R. S, Singh, R. M., *Ind. J. Chem. Sect. B.* **2000**, *39*, 688-693.

112. Kondrat`ewa, G. Y., *Chem. Abstr*. **1958**, *52*, 6345.

113. Karrer, P., Gränacher, C., *Helv. Chim. Acta* **1924**, *7*, 763.

114. Doktorora, N. D., Ionova, L. V., Karpeisky, M. Y. A., Padyukoua, N. S. , Turchin, K. F., and Florentiev, V. L., *Tetrahedron* **1969**, *25*, 3527-3553.

115. Tolstikov, A. G., Shul`ts, E. E., *J. Org. Chem. USSR.* **1984**, *20*, 2032-2036.

116. Pfister, K., Robinson, C. A., Shabica, A. C., Tishler, M., *J. Am. Chem. Soc.* **1949**, *71*, 1101-1103.

117. Chenevert, R., Letourneau, M., Thioboutot, S., *Can. J. Chem*. **1990**, *68*, 960-963.

118. Cardillo, G., Gentilucci, L., Gianotti, M., Tolomelli, A., *Tetrahedron Asymmetry* **2001**, *12*, 563-570.

119. a) Gross, E., *Adv. Exp. Med. Biol.* **1977**, *86B*, 131.
b) Schmidt, U., Lieberknecht, A., Wild, J., *Synthesis* **1988**, 159-172.

120. a) MacNeil, P. A., Roberts, N. K., Bosnich, B., *J. Am. Chem. Soc.* **1981**, *103*, 2273 2280.
b) Meyer, D., Poulin, J., Kagan, H. B., *J. Org. Chem.* **1980**, *45*, 4680-4682.

121. Hickey, D. M. B., Mackenzie, A. R., Moody, C. J., Ress, C. W., *J. Chem. Soc. Perkin Trans. 1* **1987**, 921-926.

122. a) Kumano, R., Ito, Y., *J. Am. Chem. Soc.* **1999**, *121*, 3236-3237.
b) Wessjohann, L., Gabriel, T., *J. Org. Chem.* **1997**, *62*, 3772-3774.

123. Heathcock, C. H., Pirrung, M. C., Sohn, J. E., *J. Am. Chem. Soc.* **1979**, *44*, 4294- 4299.

124. Hoffmann, R. W., Metternich, R., *Liebigs Ann. Chem.* **1985**, 2390-2402.

125. Heatchcock, C. H., Pirrung, M. C., Young, S. D., *J. Am. Chem. Soc.* **1984**, *106*, 8161-8174.

126. Karplus, M., *J. Chem. Phys.* **1959**, *30*, 11.

127. Heathcock, C. H., *Science* **1982**, *214*, 395-400.

128. Wagner, I., Musso, H., *Angew. Chem., Int. Engl*. **1983**, *22*, 816.

129. Kondrat`ewa, G. Y., Tschshi-Chen, K., *J. Gen. USSR Engl. Trans 1*. **1962**, *32*, 2315-2320.

130. Bauer, P., Dubois, J. E., *J. Am. Chem. Soc.* **1976**, *98*, 6999-7007.

131. a) Hu, S., Neckers, D. C., *J. Org. Chem.* **1996**, *61*, 6407-6415.
b) Huyser, E. S., Neckers, D. C., *J. Org. Chem.* **1964**, *29*, 276-278.

132. a) Stadler, P. A., *Helv. Chim. Acta* **1978**, *61*, 1675-1681.
b) Herzog, H., Scharf, H.-D., *Synthesis* **1986**, 420-422.
c) Buschmann, H., Scharf, H.-D., *Synthesis* **1988**, 827-830.

133. Sauer, J., Sustmann, R., *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779-807.

134. Singleton, D. A., Hang, C., *J. Am. Chem. Soc.* **1999**, *121*, 11885-11893.

135. Gajewski, J. J., Bocian, W., Brichford, N. L., Henderson, J. L., *J. Org. Chem.* **2002**, *67*, 4236-4240.

136. Turro, N. J., Kraeutler, B., *Acc. Chem. Res.* **1980**, *13*, 369-377.

137. Buchachenko, A. L., *J. Phys. Chem. A.* **2001**, *105*, 9995-10011.

138. a) Polavarapu, P. L., Fontana, L. P., Simth, H. E., *J. Am. Chem. Soc*. **1986**, *108*, 94-99.
b) Nguyen, M. T., Clarke, L. K., Hegarty, A. F., *J. Org. Chem.* **1990**, *55*, 6177-6183.
c) David, D. M., Kane-Maguire, L. A. P., Pyne, S. G., *J. Chem. Soc. Dalton Trans.* **1994**, 289-295.

139. a) Leitch, L. C., *Can. J. Chem.* **1955**, *33*, 400-404.
b) Cai, H., Fishbein, J. C., *Tetrahedron* **1997**, *53*, 1067-10676.

140. Oakes, F. T., Sebastian, J. F., *J. Org. Chem.* **1980**, *45*, 4959-4961.

141. Cazeau, P., Duboudin, F., Moulines, F., Babot, O., Dunogues, J., *Tetrahedron* **1987**, *43*, 2075-2088.

142. Nakamura, E., Murofushi, T., Shimizu, M., Kuwajima, I., *J. Am. Chem. Soc.* **1976**, *98*, 2346-2348.

143. Aizpurua, J. M., Palomo, C., Palomo, A. L., *Can. J. Chem.* **1984**, *62*, 336-340.

144. Blanco, L., Amice, P., Conia, J-M., *Synthesis* **1981**, 289-291.

145. Wilkinson, F., *Organic Molecular Photophysics*; Birks, J. B., Ed.; Wiley: New York **1975**.

146. Griesbeck, A.G., Bondock, S., Gudipati, M. S., *Angew. Chem. Int. Eng*. **2001**, *40*, 336-340.

147. Miller, R. C., and Lee, E. K. C., *Chem. Phys. Letters.* **1976**, *41*, 52.

148. a) Halpern, A. M., and Ware, W. R., *J. Chem. Phys.* **1971**, *154*, 1271.
b) Luntz, A. C., Maxson, V. T., *J. Chem. Phys.* **1974**, *26*, 553.

149. Longmire, M. L., Posey, L. A., Schuh, M. D., *J. Phys. Chem.* **1986**, *90*, 5700-5702.

150. Autonom 1.0, *Beilstein-Institut*, Beilstein Information System **1991**.

151. Pretsch, E., Seibl, J., Simon, W., Clerc, T., *Tables of Spectral Data for Strucutre Determination of Organic Compounds*, Springer-Verlag, Berlin 2nd edn. **1983**, 190.

152. Stadtmüller, S., *Dissertation*, Universität Würzburg **1991**.

153. Mauder, H., *Dissertation*, Universität Würzburg **1992**.

154. Mauder, H., *Diplomarbeit*, Universität Würzburg **1988**.

155. Fiege, M., *Dissertation*, Universität zu Köln **2000**.

156. Voelter, W., Altenburg, A., *Liebigs Ann. Chem.* **1983**, 1641-1655.

157. Prein, M., Manley, P. J., Padwa, A., *Tetrahedron* **1997**, *53*, 7777-7794.

158. Nakamura, J., Tagami, C., Nishida, K., Sasaki, H., *J. Pharm. Pharmacol.* **1992**, *44*, 295-299.

159. Afzali-Ardakami, A., Rapoport, H., *J. Org. Chem.* **1980**, *45*, 4817-4820.

160. Belokon, Y. N., Yashkina, L. V., Moscalenko, M. A., Chesnokov, A. A., Kublitsky, V. S., *Russ. Chem. B1*. **1997**, *46*, 1936-1938.

161. Aitali, M., Allaoud, S., Karim, A., Meliet, C., Mortreux, A., *Tetrahedron: Asymmetry* **2000**, *11*, 1367-1374.

162. Balajthy, Z., Aradi, J., Kiss, I. P., *J. Med. Chem.* **1992**, *35*, 3344-3349.

163. Lloyd-Williams, P., Monerris, P., Gonzalez, I., Jou, G., Giralt, E., *J. Chem. Soc. Perkin. Trans.1* **1994**, 1969-1974.

164. Kolar, A. J., Olsen, R. K., *Synthesis* **1971**, 457-459.

165. Paradisi, Z., *Tetrahedron* **1977**, *33*, 1729-1732.

166. Picur, B., Siemion, I. Z., *Org. Magn. Reson.* **1983**, *21*, 271-274.

167. Toniolo, C., Bonora, G. M., Sullivan, G. R., Bearden, W. H., Roberts, J. D., *J. Org. Chem.* **1980**, *45*, 288-290.

168. Smart, N. A., Young, G. T., Williams, M.W., *J. Chem. Soc.* **1960**, 3902-3912.

169. Applewhite, T. H., Waite, H., Niemann, C., *J. Am. Chem. Soc.* **1958**, *80*, 1465-1468.

170. Suga, H., Shi, X., Ibata, T., Kakehi, A., *Heterocycles* **2001**, *55*, 1711-1726.

171. Kuwano, R., Okuda, S., Ito, Y., *J. Org. Chem.* **1998**, *63*, 3499-3503.

172. Cook, A. H., Harris, G., Heilbron, S. I., Shaw, G., *J. Chem. Soc.* **1948**, 1056-1060.

173. Burk, M. J., Feaster, J. E., Nugent, W. A., Harlow, R. L., *J. Am. Chem. Soc.* **1993**, *115*, 10125-10138.

174. Poisel, H., Schmidt, U., *Chem. Ber.* **1975**, *108*, 2547-2553.

175. Kuwano, R., Sawamura, M., Ito, Y., *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2571-2578.

176. White, E. H., Jelinski, L. W., Politzer, I. R., Branchini, B. R., Roswell, D. F., *J. Am. Chem. Soc.* **1981**, *103*, 4231-4239.

177. Etter, M. C., *Preprints Int. Workshop Cryst. Growth Org. Matter*., Tokyo University, Tokyo, **1989**, 1; taken from: Hulliger, J., *Angew. Chem*. **1994**, *106*, 151-171.

178. Hahn, T., *International Tables for Crystallography, Vol. A: Space-Group Symmetry*, Riedel, D. Publishing company, Dordrecht, 2. Ed.**1987**.

Ich versichere, dass ich die von mir vorgelegte Dissertation selbständig angefertigt, die benutzten Quellen und Hilfsmittel vollständig angegeben und die Stellen der Arbeit – einschließlich Tabellen, Spektren und Abbildungen –, die anderen Werken im Wortlaut oder dem Sinn nach entnommen wurden, in jedem Einzelfall als Entlehnung kenntlich gemacht habe; dass diese Dissertation noch keiner anderen Fakultät oder Universität zur Prüfung vorgelegen hat; dass sie – abgesehen von unten angegebenen Teilpublikationen – noch nicht veröffentlicht worden ist, und dass ich eine solche Veröffentlichung vor Abschluss des Promotionsverfahrens nicht vornehmen werde. Die Bestimmungen dieser Promotionsordnung sind mir bekannt.

Die von mir vorgelegte Dissertation ist von Herrn Prof. Dr. Axel. G. Griesbeck betreut worden.

Samir Bondock

Lebenslauf

Persönliche Daten

Name	Samir Bahgat Abd El-Razek Bondock
Geburtsdatum	20.09.1970
Geburtsort	Mansoura/Ägypten
Familienstand	ledig
Staatsangehörigkeit	ägyptisch

Schulbildung

1976-1982	Grundschule Meet El-Sarem
1982-1985	Mittelschule Ameria
1985-1988	El-Malek El-Kamel-Gymnasium
07/1988	Abitur

Studium

1988-1992	Studium der Chemie an der Mansoura Univerisität
05/1992	B.Sc. in Chemie
1992-1993	Magister-Vorprüfung
1993-1995	Magisterarbeit an der Mansoura Universität im Arbeitskreis von Prof. Dr. Ahmed Fadda Thema: " Synthesis of Some New Azo Disperse Dyes for Dyeing Synthetic Fiberes"
09/1995	M.Sc. in Chemie
1995-2000	Forschungsarbeit im Arbeitskreis von Prof. Dr. M.A. Metwally
2000-2003	Promotionsstudium an der Universität zu Köln im Arbeitskreis von Prof. Dr. Axel G. Griesbeck Thema: "Mechanism and Synthetic Use of Paternò-Büchi Reactions: Spin-Mapping and Photo-Aldol Reactions"

Berufserfahrung

1992-1995	Assistent an der Mansoura Universität
1995-2003	Oberassistent an der Mansoura Universität
2002-2003	Wissenschaftlicher Assistent an der Universität zu Köln