Photooxygenation of Allylic Alcohols in Polymer Matrices - Synthesis of New Antimalarial Peroxides

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   Axel G. Griesbeck, Tamer T. El-Idreesy, and Anna Bartoschek.
   Pure & Applied Chem. **2005**, *77*, 1059-1074.
8. "A Concise Synthetic Route to 2,3,8-Trioxabicyclo[3.2.1]octanes, Ring-Contracted Analogues of the Artemisinin-Pharmacophore"
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   Axel G. Griesbeck, Tamer T. El-Idreesy, and Anna Bartoschek
   XXth IUPAC Conference on Photochemistry, June 17-22, **2004**, Granada, Spain.
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Abbreviations

abs.	Absolute
Ac	Acetyl
Acc.	Acceptor
b.p.	Boiling point (°C)
BET	Back Electron Transfer
br.	Broad
n-Bu	*n*-Butyl
i-Bu	Isobutyl
sec-Bu	*sec*-Butyl
t-Bu	*tert*-Butyl
calcd	Calculated
cat.	Catalytic amount
Cq	Quaternary carbon
Cq_{arom}	Quaternary carbon in an aromatic ring
d	Doublet
dd	Doublet of doublet
dq	Doublet of quartet
dt	Doublet of triplet
d.e.	Diastereomeric excess
DEPT	Distortionless Enhancement by Polarization Transfer
DMAP	N,N-Dimethylaminopyridine
DMF	N,N-Dimethyformamide
DMSO	Dimethylsulfoxide
Do.	Donor
d.r.	Diastereomeric ratio
DVB	Divinylbenzene
EA	Ethylacetate
elid	Code for NMR spectra
equiv.	Equivalent
Et	Ethyl

GP	General procedure
h	Hour
H_{arom}	Aromatic protons
c-Hex	cyclo-Hexyl
n-hex	*n*-Hexane
HMQC	Heteronuclear Multiple-Quantum Coherence Experiment
HOMO	Highest Occupied Molecular Orbital
HRMS	High Resolution Mass Spectrometry
IC	Internal Conversion
IC-50	The drug concentration that produces a 50 % inhibition of *plasmodium falciparum* growth *in vitro*.
IR	Infrared spectrum
ISC	Intersystem Crossing
J	Coupling constant (Hz)
LUMO	Lowest Unoccupied Molecular Orbital
M	Molar concentration
m	Multiplet
Me	Methyl
min	Minute
mmol.	Milli mole
M.p.	Melting Point
MS	Mass spectrometry
NMO	N-Methylmorpholine N-Oxide
NMR	Nuclear Magnetic Resonance
NOE	Nuclear Overhauser Enhancement
NOESY	Nuclear Overhuser Enhancement Spctrocopy
$^3O_2$	Ground state molecular oxygen ($^3\sum_g$-O_2)
$^1O_2$	Singlet oxygen ($^1\Delta_g$-O_2)
PET	Photoinduced Electron Transfer
Ph	Phenyl
PP	Protoporphyrine-IX
n-Pr	*n*-Propyl
i-Pr	Isopropyl
c-Pr	Cyclo-propyl

PS	Polystyrene
Q	Quencher
q	Quartet
rac.	Racemic mixture
RB	Rose Bengal
R_f	Rate of flow (retention Factor)
r.t.	Room Temperature
s	Second or Singlet (in NMR)
S_0	Singlet ground state
S_1	First excited singlet state
sat.	Saturated solution
Sens.	Sensitizer
T_1	First excited triplet state
t	Triplet
TBHP	*tert*-Butylhydroperoxide
TEA	Triethylamine
THF	Tetrahydrofuran
TLC	Thin-layer Chromatography
TPP	Tetraphenylporphyrine
PPTS	Pyridinium-*p*-toluenesulfonate
PTSA	*p*-Toluenesulfonic acid
TSP	Tetrastyrylporphyrine
TTP	Tetratolylporphrine
UV	Ultraviolet
λ	Wavelength
ε	Molar extinction coefficient
$^1\sum_g$-O_2	Second excited singlet state of molecular oxygen
τ	Lifetime
*	Excited state
Φ_Δ	Quantum yield of $^1O_2$ formation

Contents

Abstract **I**

Kurzzusammenfassung **II**

1. Introduction **1**

1.1 Photochemical *versus* thermal reactions 1

1.2 Electronic states of molecular oxygen 2

1.3 Singlet oxygen 3

1.3.1 Generation of singlet oxygen 3

1.3.2 Quenching of singlet oxygen 4

1.3.3 Chemical reactivity of singlet oxygen 6

1.3.4 Ene reaction of singlet oxygen 7

1.3.4.1 History and definition of the reaction 7

1.3.4.2 Mechanism of the ene reaction 7

1.3.4.3 Regioselectivity of the ene reaction 8

1.3.4.4 Stereoselectivity of the ene reaction 9

1.4 Type-II photooxygenation: Experimental scope and limitations 11

1.5 Malaria 13

1.5.1 Introduction and facts about the disease 13

1.5.2 Types of malaria 13

1.5.3 Drugs for malaria treatment 14

1.5.4 Mechanism of action of antimalarial 1,2,4-trioxanes like artemisinin 16

1.5.5 Selected routes to 1,2,4-trioxane and peroxidic antimalarial compounds 19

1.5.5.1 Semi synthetic routes stemming from the parent artemisinin 19

1.5.5.2 Synthesis of antimalarial 1,2,4-trioxanes and peroxidic compounds 21

2. Aim of the Work **27**

3. Results and Discussion **28**

3.1 Polystyrene matrix with covalently linked singlet oxygen sensitizers 28

3.1.1 Synthesis of 5,10,15,20-tetrakis(4-ethenylphenyl)-21*H*,23*H*-porphine 28

3.1.2 Polymerization, morphology and characterization of the sensitizer-bound resins 29

3.1.3 Determination of the sensitizer percentage in the resins 32

3.1.4 Solvent-free photooxygenation reactions using covalently-bound sensitizers 32

3.1.4.1 Diastereoselectivity of the ene and [4+2]-cycloaddition reactions using TSP-S-DVB and PP-S-DVB 33

3.1.4.2 Regioselectivity of the ene reaction using TSP-S-DVB and PP-S-DVB 35
3.1.4.3 Sorbinol and ethyl tiglate photooxygenations using TSP-S-DVB and PP-S-DVB 36
3.1.4.4 Photooxygenation of 5-methoxyoxazoles using TSP-S-DVB and PP-S-DVB 37
3.2 Homogeneous *versus* heterogeneous photooxygenation conditions 39
3.3 Polystyrene matrix with adsorbed singlet oxygen sensitizers 41
3.4 Synthesis of the allylic alcohols starting materials 41
3.5 Solvent-free photooxygenation reactions of allylic alcohols 46
3.6 Deuterium isotope effects on the diastereoselectivity of $^1O_2$ ene reaction with allylic alcohols 52
3.7 Synthesis of 1,2,4-trioxanes 54
3.7.1 Derived from 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol 55
3.7.1.1 By peroxyacetalization reaction with symmetric ketones 55
3.7.1.2 By peroxyacetalization reaction with asymmetric ketones 58
3.7.1.3 By peroxyacetalization reaction with aldehydes 59
3.7.1.4 By peroxyacetalization reaction with acetals 59
3.7.2 Derived from 1-cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol 61
3.7.2.1 By peroxyacetalization reaction with aldehydes 61
3.7.2.2 By peroxyacetalization reaction with symmetric ketones 62
3.7.3 Derived from 3-hydroperoxy-2-methyloct-1-en-4-ol 63
3.7.3.1 By peroxyacetalization reaction with aldehydes 63
3.7.3.2 By peroxyacetalization reaction with ketones 65
3.7.3.3 By peroxyacetalization reaction with acetals 65
3.7.4 Derived from 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol 66
3.7.4.1 By peroxyacetalization reaction with aldehydes 66
3.7.4.2 By peroxyacetalization reaction with symmetric ketones 70
3.7.4.3 By peroxyacetalization reaction with asymmetric ketones 74
3.7.4.4 By peroxyacetalization reaction with acetals 75
3.7.5 Derived from 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol 75
3.7.5.1 By peroxyacetalization reaction with ketones 75
3.7.6 Derived from 3-hydroperoxy-2,5-dimethylhept-1-en-4-ol 78
3.7.6.1 By peroxyacetalization reaction with ketones 78
3.7.6.2 By peroxyacetalization reaction with aldehydes 79
3.7.7 Derived from 3-hydroperoxy-2-methylhept-1-en-4-ol 80

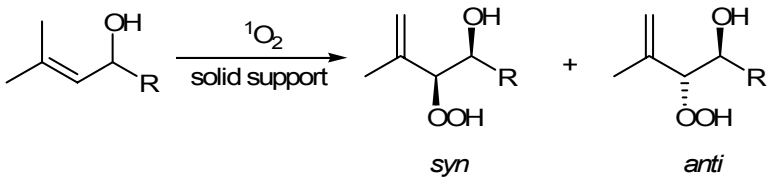
3.7.7.1 By peroxyacetalization reaction with ketones 80
3.7.7.2 By peroxyacetalization reaction with aldehydes 81
3.7.7.3 By peroxyacetalization reaction with acetals 84
3.7.8 Derived from 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol 84
3.7.8.1 By peroxyacetalization reaction with symmetric ketones 84
3.7.8.2 By peroxyacetalization reaction with asymmetric ketones 86
3.7.8.3 By peroxyacetalization reaction with aldehydes 86
3.7.8.4 By peroxyacetalization reaction with acetals 88
3.7.9 Derived from 4-hydroperoxy-5-methylhex-5-en-3-ol 88
3.7.9.1 By peroxyacetalization reaction with aldehydes 88
3.7.9.2 By peroxyacetalization reaction with symmetric ketones 90
3.7.9.3 By peroxyacetalization reaction with asymmetric ketones 91
3.7.9.4 By peroxyacetalization reaction with acetals 91
3.7.10 Derived from 3-hydroperoxy-4-methylpent-4-en-2-ol 92
3.7.10.1 By peroxyacetalization reaction with symmetric ketones 92
3.7.10.2 By peroxyacetalization reaction with asymmetric ketones 97
3.7.10.3 By peroxyacetalization reaction with aromatic aldehydes 99
3.7.10.4 By peroxyacetalization reaction with aliphatic aldehydes 100
3.7.10.5 By peroxyacetalization reaction with orthoesters 101
3.7.11 Derived from 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol 102
3.7.11.1 By peroxyacetalization reaction with aldehydes 102
3.7.11.2 By peroxyacetalization reaction with ketones 103
3.7.11.3 By Peroxyacetalization reaction with acetals 103
3.7.11.4 By peroxyacetalization reaction with orthoesters 105
3.7.12 Derived from 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol 107
3.7.12.1 By peroxyacetalization reaction with aldehydes 107
3.7.12.2 By peroxyacetalization reaction with ketones 108
3.7.13 Derived from 3-hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol 109
3.7.13.1 By peroxyacetalization reaction with ketones 109
3.8 Lewis-acid catalyzed cleavage of β-hydroperoxy alcohols and subsequent cross-peroxyacetalization reaction 111
3.9 Bis spiro-1,2,4-trioxanes synthesis 116
3.10 Intramolecular 1,2,4-trioxanes synthesis 120
3.11 Hydroperoxides as oxygen donor in dihydroxylation reaction 125

3.12 Antimalarial activity of some synthesized 1,2,4-trioxane compounds 130
4. Experimental Part 132
4.1 General remarks 132
4.2 General procedures 135
4.3 Synthesis of tetrastyrylporphyrin 143
4.4 Synthesis of substrates for $^1O_2$ photooxygenation reaction 146
4.5 Singlet oxygen photooxygenation reactions of different substrates 170
4.6 Synthesis of 1,2,4-trioxanes 191
4.6.1 Derived from 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol 191
4.6.2 Derived from 1-cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol 199
4.6.3 Derived from 3-hydroperoxy-2-methyloct-1-en-4-ol 201
4.6.4 Derived from 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol 206
4.6.5 Derived from 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol 217
4.6.6 Derived from 3-hydroperoxy-2,5-dimethylhept-1-en-4-ol 220
4.6.7 Derived from 3-hydroperoxy-2-methylhept-1-en-4-ol 222
4.6.8 Derived from 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol 230
4.6.9 Derived from 4-hydroperoxy-5-methylhex-5-en-3-ol 237
4.6.10 Derived from 3-hydroperoxy-4-methylpent-4-en-2-ol 245
4.6.11 Derived from 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol 264
4.6.12 Derived from 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol 269
4.6.13 Derived from 3-hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol 272
4.7 Lewis-acid catalyzed cleavage of β-hydroperoxy alcohols and subsequent cross-peroxyacetalization reaction 274
4.8 Bis spiro-1,2,4-trioxanes synthesis 284
4.9 Intramolecular 1,2,4-trioxanes synthesis 289
4.10 Hydroperoxides as oxygen donor in dihydroxylation reaction 299
5. Appendix 302
6. Summary 307
7. Zusammenfassung 313
8. References 320

Abstract

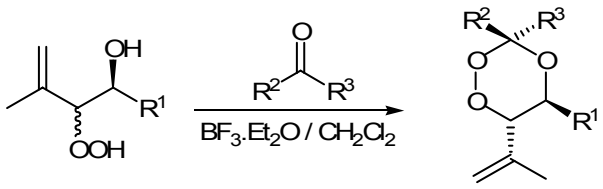
In this thesis the photooxygenation of several substrates in polymer matrix as solid support using a solvent-free protocol was investigated. Two microreactor systems were used: (1) the commercially available polystyrene beads (PS) crosslinked with divinylbenzene (DVB) and loaded with adsorbed tetraarylporphyrine dye sensitizers; (2) synthesized polymers covalently bound to porphyrin sensitizers. The solvent-free approach using both polymer matrices was found to be suitable for a broad variety of photooxygenation reactions resulting in sensitizer-free peroxidic products.

A two-step route for the synthesis of the 1,2,4-trioxane subunit (the pharmacophore of the naturally occurring antimalarial drug artemisinin) was developed. The first step is based on the conversion of different chiral allylic alcohols to sensitizer-free unsaturated β-hydroperoxy alcohols in (*syn*) diastereoselectivities by the ene reaction of singlet oxygen with allylic alcohols using the solvent-free photooxygenation approach (***Scheme I.1***).



Scheme I.1

Secondly, BF_3-catalyzed inter- and intramolecular peroxyacetalization reaction with different carbonyl compounds, resulted in a wide variety of mono-, polycyclic-, and spiro-1,2,4-trioxanes (***Scheme I.2***). Furthermore, the reaction was adapted to yield spiroannelated 1,2,4-trioxane dimers, a literature-unknown class of compounds.

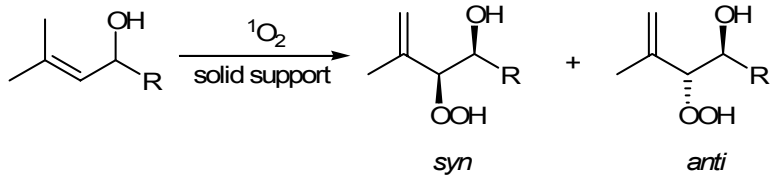


Scheme I.2

Kurzzusammenfassung

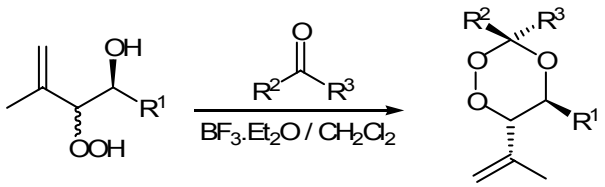
Im Rahmen dieser Arbeit wurden eine Reihe von Substraten mit Hilfe von Polymer-Matrix-Systemen als Träger lösungsmittelfrei photooxygeniert. Hierzu wurden zwei verschiedene Mikroreaktorsysteme verwendet.: (1) kommerziell erhältliche, mit Divinylbenzol (DVB) quervernetzte, Polystyrolkügelchen (PS) welche mit Tetraarylphorphyrin-Sensibilisator-Farbstoffen beladen wurden; (2) synthetisierte Polymere mit kovalent gebundenem Porphyrin-Sensibilisator. Die lösungsmittelfreien Verfahren lieferten unter Verwendung der oben beschriebenen Polymer-Träger für ein weites Spektrum von Photooxygenierungsreaktionen gute Ergebnisse. Außerdem waren die erhaltenen Peroxide farbstofffrei.

Es wurde eine zweistufige Syntheseroute zur Darstellung des 1,2,4-Trioxan-Grundgerüstes entwickelt, welches als pharmakophore Grundstruktur im natürlich vorkommenden Antimalaria Mittel Artemisinin enthalten ist. Der erste Schritt dieser Synthese besteht in der Umwandlung von verschiedenen Allylalkoholen durch die *syn*-diastereoselektive Reaktion mit Singulett-Sauerstoff zu (farbstofffreien) *vic*-Hydroperoxyallylhydroperoxiden unter Verwendung der lösungsmittelfreien Methode (***Schema I.1***).



Schema I.1

Im zweiten Schritt lieferte die BF_3-katalysierte inter- und intramolekulare Peroxy-acetalisierung mit verschiedenen Carbonyl-Verbindungen ein weites Spektrum von mono-, polycyclischen- und spirocyclischen 1,2,4-Trioxanen (***Schema I.2***). Darüberhinaus wurde die Reaktion auf die Synthese von spiroanellierten 1,2,4-Trioxan-Dimeren, eine noch literaturunbekannte Verbindungsklasse, erweitert.



Schema I.2

1. Introduction

1.1 Photochemical *versus* Thermal Reactions

Thermal reactions take place between molecules in the electronic ground singlet state (S_o) (electronic configuration having minimum energy where the electrons in the highest occupied molecular orbital, HOMO, have an antiparallel spin). On the other hand, in photochemical reactions one of the molecules is raised from its electronic ground state (S_o) to a higher electronic state. Absorption of electromagnetic radiation (mostly ultraviolet or visible light) promotes an electron from the HOMO to the lowest unoccupied molecular orbital (LUMO) where the total spin of the electrons remains zero and the molecule exists in the first excited singlet state (S_1). This excitation corresponds to the most prominent transition band in the absorption spectrum of many organic molecules.

An electronically excited molecule in the S_1 state can loose its excitation energy either by chemical change (chemical deactivation) or by one of different physical processes which may be radiative or non-radiative (***Figure 1.1***).

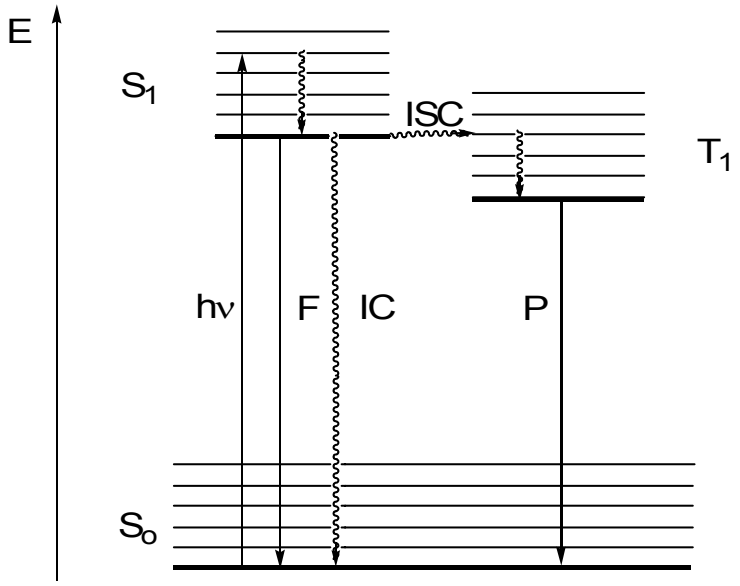


***Figure 1.1*:** Simplified Jablonski diagram: hν = excitation (10^{-15}s), IC = internal conversion, ISC = intersystem crossing F = fluorescence (10^{-9}-10^{-5}s), P = phosphorescence (10^{-5}-10^{-3}s)

1.2 Electronic States of Molecular Oxygen[1]

The ground state of all organic molecules having a closed-shell electronic configuration is S_o. Molecular oxygen represents an exception and exists in its electronic ground state in a triplet state.

The electronic configuration of ground state oxygen ($^3O_2$) has the two highest energy electrons unpaired and with parallel spins in π_x^* and π_y^* molecular orbitals (***Figure 1.2***). These orbitals are energetically degenerate and the electrons have identical spins in order to produce the maximum multiplicity and hence the lowest electronic energy state (Hund´s rule). The ground state of oxygen is thus a triplet state and because of the unpaired electrons paramagnetic state having a diradical character. This state has the spectroscopic notation $^3\Sigma^-_g$ or T_o.

Two relevant excited states are known for molecular oxygen (***Figure 1.2***), the first excited electronic state ($^1\Delta_g$) lying 22.4 kcal mol^{-1} above the triplet ground state, having both electrons paired in a single orbital leaving the other vacant; hence this state might be expected to undergo two electrons reactions. The second excited electronic singlet state ($^1\Sigma_g^+$) lying 37 kcal mol^{-1} above the ground state comes from spin pairing of electrons in different orbitals and hence is expected to undergo one-electron free radical reactions. This state is also characterized by shorter lifetime in solution (10^{-12} sec) due to the rapid spin-allowed transition to the longer lived first excited state $^1\Delta_g$ (10^{-3}–10^{-6} sec).

The more stable singlet oxygen species ($^1\Delta_g$) is considered to be one of the most active intermediates involved in chemical and biochemical oxidation processes. I shall refer to the $^1\Delta_g$ form of oxygen as “singlet oxygen” or even simpler as $^1O_2$.

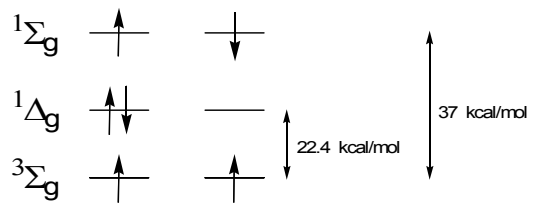


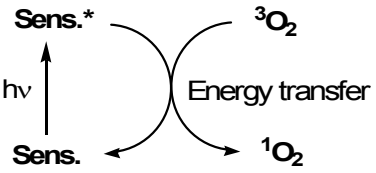
***Figure 1.2*:** Electron distribution in the HOMO of O_2 in its three different electronic states.

1.3 Singlet Oxygen

1.3.1 Generation of singlet oxygen

Singlet oxygen ($^1O_2$) can be generated in solution by a variety of processes[1] including the reaction of hydrogen peroxide with sodium hypochlorite,[2] the decomposition of 9,10-diphenylanthracene endoperoxide,[3] the thermolysis of triarylphosphite ozonides,[4] exciting gaseous oxygen by electrodeless discharge,[5] and the photochemical energy transfer from an excited dye sensitizer to triplet oxygen[6]. The latter technique is not only the most efficient but also it circumvents the separation of the byproducts such as 9,10-diphenylanthracene and triphenyl phosphate produced in the chemical pathways. This accounts for the utility of energy transfer approach in the vast majority of $^1O_2$ reactions in organic synthesis.

The energy transfer sensitization mechanism to generate $^1O_2$ involves the excitation of an appropriate dye with visible light from the ground state (^{1}Sens) to its excited singlet state (^{1}Sens*), after which rapid ISC takes place and the excited triplet state of the dye (^{3}Sens*) is formed. Although both singlet and triplet excited states of the sensitizer can transfer energy to $^3O_2$, the triplet state of the sensitizer has a longer lifetime (since deactivation needs spin inversion) and with very few exceptions energy transfer takes place from the triplet excited state of the sensitizer. A prerequisite for this energy transfer to occur is that the triplet energy of the sensitizer must exceed the excitation energy of triplet oxygen which is 22.4 kcal mol^{-1}. After this energy transfer to the triplet state of molecular oxygen, $^1O_2$ is formed with concomitant regeneration of the ground state of the sensitizer molecule (***Scheme 1.1***). Some common sensitizers for generation of singlet oxygen and their triplet energies are given in ***Table 1.1***.[7]



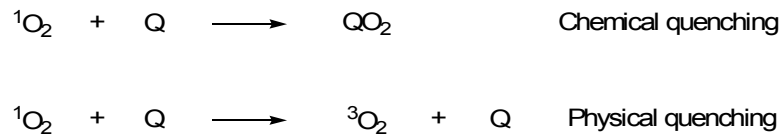
***Scheme 1.1*:** Photosensitized generation of singlet oxygen.

Sensitizer	Triplet energy (kcal mol^{-1})
Tetraphenylporphyrin (TPP)	34.0
Methylene blue	33.5-34.0
Rose Bengal	39.2-42.2
Eosin	43.2-46.0
Hematoporphyrin	37.2

***Table 1.1*:** Singlet oxygen photosensitizers and their triplet energies.

1.3.2 Quenching of singlet oxygen[1]

The term "quenching of singlet oxygen" can be used to refer to both "chemical" and "physical" quenching. In the former case, singlet oxygen reacts with the quencher (Q) to give a new product (QO_2). In the latter case, the interaction with the quencher (which can be the solvent, substrate, or sensitizer molecule) leads only to deactivation of singlet oxygen to its triplet ground state with neither oxygen consumption nor product formation (***Scheme 1.2***).

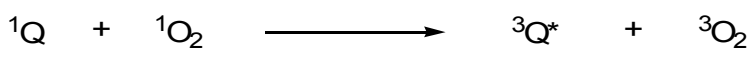


***Scheme 1.2*:** Chemical versus physical quenching of singlet oxygen

Two major mechanisms of physical singlet oxygen quenching have been established, energy transfer and charge transfer quenching.

(a) Energy-Transfer Quenching:[1]

The electronic-electronic energy transfer mechanism is rare and was first suggested for quenchers as β-carotene. It is the reverse of the reaction by which singlet oxygen is formed (***Scheme 1.3***). For this mechanism to be efficient the triplet state energy of the quencher must be very near or lower in energy of $^1O_2$ (22.4 kcal mol^{-1}).



***Scheme 1.3*:** Energy-transfer quenching of singlet oxygen.

The observation that the rate of quenching of $^1O_2$ is related to vibrational frequencies of the quencher led to the theory that the rate of $^1O_2$ quenching is determined by the ease with which the electronic transition energy (produced by $^1O_2$ quenching) is distributed as vibrational and rotational energy to the quencher. This affects the rate of $^1O_2$ quenching since as the quencher has higher vibrational frequency, the electronic energy produced by $^1O_2$ quenching will lead to excitation of the quencher to the first or second vibrational energy level. These are rapid processes when they are almost resonant (i.e. all the electronic energy of $^1O_2$ quenching can be taken up causing easily excited vibrational modes and allowed rotational transitions in the quencher).

Since the highest vibrational frequencies are found in molecules which contain hydrogen atoms strongly bound to another atom as in O-H, S-H, N-H, C-H bonds, so it is not surprising

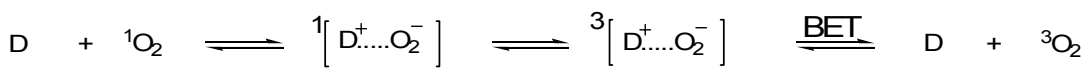
to find H_2O, alcohols, amines and alkanes to be good $^1O_2$ quenchers. These compounds are excited to higher vibrational states often to the second vibrational level which is an easy accessible vibrational mode. On the other hand, the fact that CCl_4 is considered as a suitable solvent for $^1O_2$ reactions is explained by the low vibrational frequency (800-900 cm^{-1}) of the C-Cl bond whereby $^1O_2$ deactivation excites CCl_4 to a high vibrational energy level which is a less probable transition. In a similar manner, since deuteration results in lowering of the vibrational frequency, $^1O_2$ quenching rates in deuterated solvents are lower than in the nondeuterated.[8] As seen in ***Table 1.2***, the singlet oxygen lifetime is increased by a factor of about 20 in deuterated solvents compared to the protonated compounds and by a factor of about 700 by exchanging CH with CF.

Solvent	**$^1O_2$-Lifetime (µs)**	**Solvent**	**$^1O_2$-Lifetime (µs)**
H_2O	3.1	D_2O	68
CH_3OH	9.1	CD_3OD	270[9]
C_6H_6	30	C_6D_6	681
C_6F_{14}	68000	C_6F_6	21000
$(CH_3)_2CO$	51	$(CD_3)_2CO$	992
$CHCl_3$	229	$CDCl_3$	7000
$C_6H_5CH_3$	29[10]	air	86000[11]
CH_3CN	30[7], 61[12]	$CFCl_3$	1000[13]
CCl_4	59000	-	-

***Table 1.2*:** Singlet-oxygen lifetimes in different solvents.

(b) Charge-Transfer Quenching:

In this mechanism singlet oxygen as an electron-poor compound interacts with an electron donor to give a charge-transfer complex in the singlet state (in some cases, complete electron transfer takes place) which subsequently undergoes ISC to the triplet state. Dissociation and back electron transfer (BET) results in the donor molecule and deactivation of singlet oxygen to the ground state triplet oxygen (***Scheme 1.4***).



***Scheme 1.4*:** Charge-transfer quenching of singlet oxygen.

The rate of this reaction can be estimated from the Rehm-Weller equation using the oxidation potential of the donor (E_D^{ox}), reduction potential of the acceptor (E_A^{red}), coulombic energy (E_{coul}) and the excitation energy of the excited component (E*).[14]

$$\Delta G^{\circ} = E_D^{ox} - E_A^{red} - E_{oo}^{*} + E_{Coul.}$$

Compounds with low oxidation potential (low ionization energy) such as amines and phenols or electron rich compounds as azides, iodide and superoxide ions are good $^1O_2$ quenchers that operate by this mechanism. It is also noteworthy to say that compounds with low triplet energies and low oxidation potentials can quench $^1O_2$ by both mechanisms.

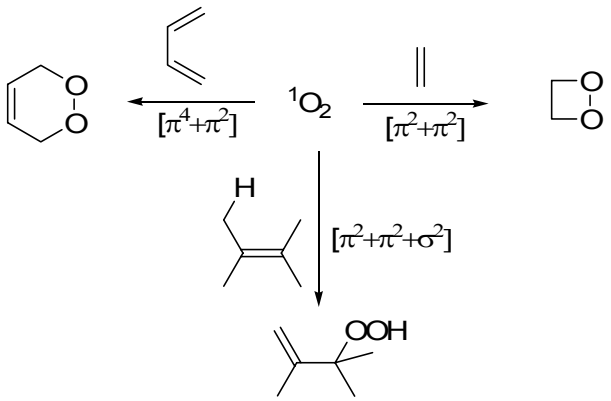
1.3.3 Chemical reactivity of singlet oxygen

In contrast to the paramagnetic triplet oxygen ($^3O_2$), which is mostly involved in free radical reactions (Type-I photooxygenation reactions) and Type-III photooxygenation reactions (electron transfer induced photooxygenation) involving the superoxide radical anion or the reaction of the substrate radical cation with triplet oxygen, singlet oxygen ($^1O_2$) is an electrophilic species that undergoes two-electron reactions analogous to electron-poor ethylenes. Reactions involving $^1O_2$ are called Type-II photooxygenation reactions. Singlet oxygen can undergo heteroatom oxidation (e.g. sulfides to sulfoxides[15]) or chemically react with olefins in different modes, the most important are as follows: (***Scheme 1.5***)

(a) Conjugated dienes react preferentially by [4+2]-cycloaddition (Diels-Alder type) resulting in endoperoxides.[16,17]

(b) Electron rich activated olefins react by [2+2]-cycloaddition to give 1,2-dioxetanes.[1,16,18,19]

(c) Not-activated olefins with allylic hydrogens react by an ene reaction to give allylic hydroperoxides.[1,20]

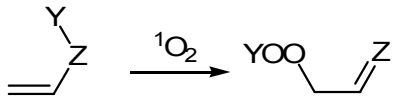


***Scheme 1.5*:** Reaction modes of $^1O_2$ with alkenes and dienes.

1.3.4 Ene reaction of singlet oxygen

1.3.4.1 History and definition of the reaction

In 1943, G. O. Schenck was the first to describe in a patent the singlet oxygen ene reaction[21] (therefore often termed Schenck reaction). In the course of this reaction, $^1O_2$ attacks one center of a CC double bond with abstraction of an allylic hydrogen atom or an allylic silyl group (bound to oxygen, in case of the silyl-ene reaction) with simultaneous allylic shift of the double bond. As a result of this reaction, allylic hydroperoxides or O-silylated α-hydroperoxy carbonyl compounds are formed (***Scheme 1.6***). Since the first report, the $^1O_2$ ene reaction has attracted major interest not only in the mechanistic photochemistry but also in modern organic synthesis.[20]



***Scheme 1.6*:** Ene reaction (Z=C, Y=H)
versus silyl-ene reaction (Z=O, Y=SiR_3)

1.3.4.2 Mechanism of the ene reaction

Several mechanisms have been postulated for this reaction with concerted or "concerted two-stage" mechanisms,[22] as well as 1,4-biradicals,[23] 1,4-zwitterions,[24] perepoxide, dioxetane[25] or exciplex intermediates. (***Figure 1.3***).

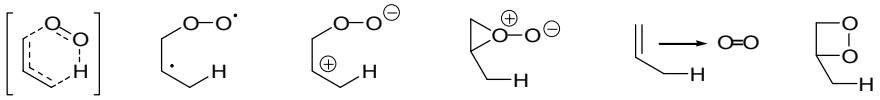
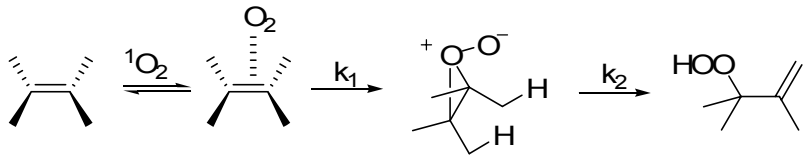


Figure 1.3

The dioxetane suggestion (F) was excluded after the isolation of dioxetanes, showing that they decompose to carbonyl fragments rather than rearrange to the hydroperoxides. Also the diradical (B) and the zwitterionic (C) mechanisms have been dismissed due to the absence of *cis-trans* isomerization of the substrates[24] and the lack of Markovnikov directing effects in the photooxygenation of trisubstituted olefins,[20d] that radical scavengers have no effect on the reaction and since only minor solvent effects have been observed for the reaction.[26] The

results of Stephenson's inter- and intramolecular isotope effect experiment[27a] with isotopically labeled tetramethylethylenes provide an evidence for the perepoxide intermediate and not the concerted pathway. Also, the small negative activation enthalpies and highly negative activation entropies observed for the singlet oxygen ene reaction and kinetic measurements[26b,c] have shown that the reaction of $^1O_2$ with electron-rich olefins proceed 10^3 times slower than the diffusion rate of $^1O_2$ which proves the presence of non-productive encounters between $^1O_2$ and the olefin[27a] favoring the participation of a reversibly formed exciplex as intermediate.[28] As a result a three-step mechanism involving an exciplex and perepoxide can be assumed for the ene reaction (***Scheme 1.7***)



***Scheme 1.7*:** Mechanism of ene reaction of singlet oxygen.

1.3.4.3 Regioselectivity of the ene reaction

The ene reaction of singlet oxygen with substrates possessing different allylic hydrogen atoms often results in a complex mixture of products. The regiochemistry of the reaction was extensively studied and some general effects were found useful to predict the regioselective introduction of the hydroperoxy group:

(a) *cis*-effect[29] (*syn*-effect)

In the reaction of $^1O_2$ with trisubstituted alkenes[30] or enol ethers[31], the allylic hydrogen atoms on the more substituted side of the double bond are more reactive for H-abstraction by $^1O_2$ (***Figure 1.4***).

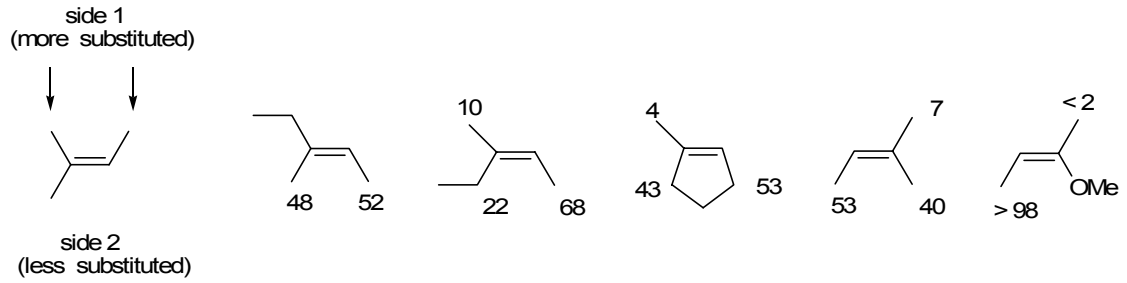


***Figure 1.4*:** *cis*-effect of different substrates.
The numbers indicate % hydrogen abstraction.

(b) *gem*-effect[32]

Leads to highly selective abstraction of an allylic hydrogen atom from a substituent at the α position of an α,β-unsaturated carbonyl compound (***Figure 1.5***).

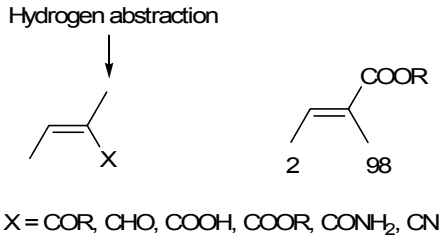


***Figure 1.5*: *gem*-effect.**

(c) large-group effect[33]

Leads to selective (moderate) abstraction of an allylic hydrogen from the substituent geminal to a large group (***Figure 1.6***).

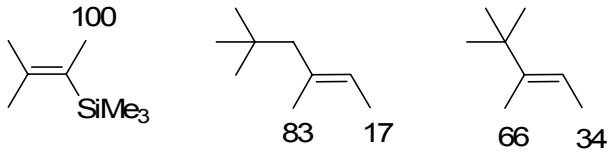
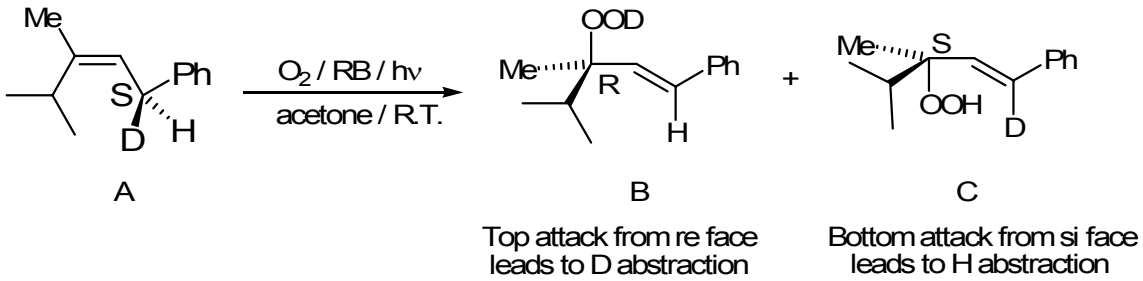


***Figure 1.6*:** Large-group effect. The numbers indicate % hydrogen abstraction.

1.3.4.4 Stereoselectivity of the ene reaction

Stereochemistry of the reaction

The singlet oxygen ene reaction is a suprafacial process where the addition of oxygen and abstraction of hydrogen occurs from the same face of the olefinic π-system. This was elegantly demonstrated by Stephenson[34] in the ene reaction of the optically active monodeuterated olefin A. This olefin has two diastereotopic faces, and its photooxygenation results in 82 % of the regioisomer formed by H/D-abstraction from the benzylic group with exclusive formation of the *trans* allylic hydroperoxide rather than the *cis* isomer (***Scheme 1.8***). In the model reaction, no isotope discrimination was observed and only the allylic hydroperoxides from the suprafacial hydrogen / deuterium abstraction by singlet oxygen from both faces (B and C) are obtained.



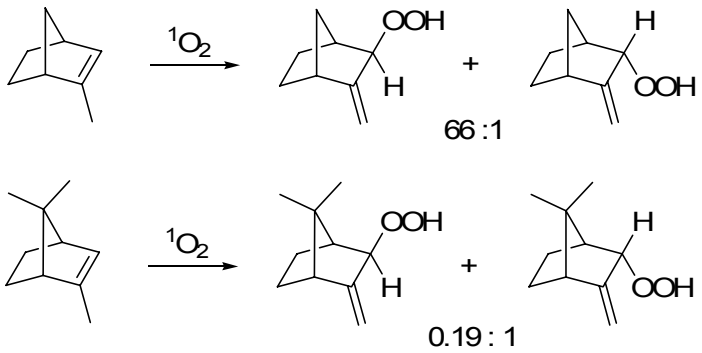
***Scheme 1.8*:** Stephenson's experiment showing the suprafacial character of the ene reaction.

Diastereoselectivity of the reaction

Many factors that control the π-facial selectivity of singlet oxygen ene reaction are known and can be summarized as follows:

(1) Steric factors

In view of the small size of the reactive molecule singlet oxygen, steric interactions are expected to be less important in directing the facial approach. However, in rigid (cyclic and polycyclic) substrates where changes in conformation to minimize such steric factors are impossible this effect is more pronounced and steric factors on one face of the double bond may bias $^1O_2$ attack to occur predominantly on the other face of the π-system (***Scheme 1.9***).[35]



***Scheme 1.9*:** Steric effects in the ene reaction.

(2) Conformational effects

For an efficient hydrogen abstraction to occur, the reactive allylic hydrogen atoms must adopt a low energy conformation which places them perpendicular to the olefinic plane.[36] This factor is often highly effective in rigid compounds in which allylic hydrogen atoms are conformationally blocked at one face of the double bond.

(3) Electronic effects and hydrogen bonding

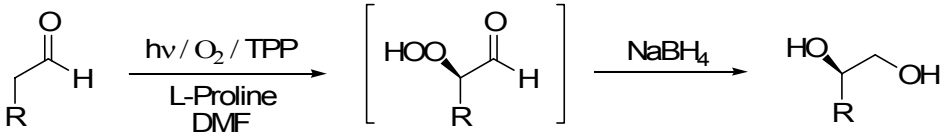
The electronic factors can be simply demonstrated by the fact that the tetrasubstituted alkene, 2,3,-dimethyl-2-butene with the more nucleophilic double bond reacts more than 30 times

faster than the corresponding trisubstituted alkene, 2-methyl-2-butene, and the latter reacts about 15 times faster than the disubstituted olefin Z-2-butene.[27a]

Adam et al. elegantly used hydrogen bonding interactions between the substrate and the incoming singlet oxygen for dictating the diastereoselectivity in the photooxygenation of allylic alcohols and other substrates.[37,141] The coordination of the conformationally fixed hydroxyl group (by 1,3-allylic strain) to the incoming singlet oxygen preferentially directs the incoming enophile to one face of the double bond.

Enantioselectivity of the reaction

In contrast to the high diastereoselective control of singlet oxygen ene reaction, enantioselective reactions are still rare. Several attempts to control the enantioselectivity were reported. The use of β-cyclodextrins covalently bound to porphyrin sensitizers in the photooxygenation of linoleic acid resulted in low ee values (10-20 %).[38] The photooxygenation of 2-methyl-4-phenyl-2-butene in NaY zeolite in presence of (+)-ephedrine as chiral inductor also resulted in 15 % ee hydroperoxide product.[39] Recently, Córdova et al.[40] reported the unprecedented amino acid-catalyzed asymmetric incorporation of molecular oxygen into the α position of a series of aldehydes and ketones. The mechanism is assumed to proceed through an ene reaction of singlet oxygen with the intermediate enamine to give the corresponding hydroperoxide which is in situ reduced to afford the vicinal diol in high ee values (***Scheme 1.10***).



***Scheme 1.10*:** Enantioselectivity in the ene reaction.

1.4 Type-II Photooxygenation: Experimental Scope and Limitations

Since the discovery of singlet oxygen by Kautsky,[41] most of the reactions involving molecular oxygen activation by triplet-triplet sensitization from dye sensitizers were conducted in solution phase. For each sensitizer used, a series of appropriate solvents are relevant in which the sensitizer's photophysical properties and chemical stability as well as singlet oxygen

quantum yields are known.[42] However, these condensed phase photooxygenation conditions suffer from at least five major drawbacks:

(a) Since the sensitizer must be soluble in the solvent, only a limited number of dye-solvent combinations can be used.

(b) Separation of the dye from the product after the reaction either by chromatography or distillation is an elaborate process.

(c) Singlet oxygen has longer lifetimes in environmentally problematic solvents (carbon tetrachloride, freons, etc.) and much shorter lifetime in benign solvents (water and methanol).[43]

(d) Irreversible photobleaching of the dye is often observed in halogenated solvents due to the formation of acid or is induced by singlet oxygen itself or the formed oxygenated products.[44]

(e) Solution purging with oxygen or even air is hazardous for industrial purposes and sometimes even for lab scale reactions.

In the last decade, the area of polymer-supported organic reactions[45] and polymer-supported catalysts[46] has blossomed. This is exemplified in solid phase synthetic chemistry where reactions carried out in resins and reactions that are catalyzed by polymer-supported catalysts. Photooxygenation in solution using insoluble polymer-bound sensitizers may solve the problem of dye recovery. The first polymer-bound sensitizer was the commercially available polystyrene-bound Rose Bengal discovered by Schaap,[47] followed by a series of immobilized sensitizers, e.g. immobilized fullerene (C_{60}) sensitizers,[48] ionic porphyrins immobilized on cationically functionalized polystyrene,[49] tetrakis(4-hydroxyphenyl)porphyrin supported to polyethylene glycol,[50] aluminum(III) tetracarboxyphthalocyanine bound to poly(styrene-*co*-chloromethylstyrene),[51] polystyrene-bound benzophenones,[52] immobilized pyrylium salts on Merrifield resins,[53] sensitizer-incorporated nafion membranes,[54] and ion-exchange resins ionically bound to photosensitizers.[55] Other heterogeneous catalysts using clay,[56] silica[57] and zeolites[58] were also recently developed as solid supports. However, the use of the non-polar solvents enhances dye oxidation and bleeding especially if long reaction times are needed which decreases the singlet oxygen quantum yield and hence the reaction efficiency. On the other hand, photooxygenation reactions carried out in aqueous solutions are also not favored due to low solubility of most organic substrates, low singlet oxygen lifetime and hydrophobic aggregations for nonpolar sensitizers (porphyrin-porphyrin self quenching) and as a consequence show marked reduction of the triplet life time.[59,60]

An unprecedented solution to circumvent the above problems was lately reported by Griesbeck and Bartoschek.[61] A sustainable solvent-free photooxygenation reaction conditions,

in which the substrates are embedded in a porphyrin-loaded polystyrene polymer matrix, irradiated and the product (sensitizer-free) is simply extracted by ethanol offers a shortcut to green photooxygenation reactions.

1.5 Malaria

1.5.1 Introduction and facts about the disease

As early as 6000 B.C., the malaria disease has tormented humankind.[62] In 400 B.C., the greek physician Hippocrates was the first to describe an intermittent and often relapsing fever which is followed by sweating, dizziness and shaking chills (known symptoms of malaria nowadays). Later, the Romans described malaria as "a horrid disease that comes every summer and kills".[62,63] Today, malaria is the third-most cause of death by infectious diseases, after tuberculosis and AIDS. The annual mortality estimations range between 1 and 2.5 million deaths,[64] and according to the World Health Organisation (WHO) at least 240 million people are chronically affected and there are 120 million new cases reported every year.[65] This number is expected to double by the year 2010 if no new antimalaria strategies were developed.[66]

1.5.2 Types of malaria

The female *Anopheles* mosquito (***Figure 1.7***) is the vector responsible for transmitting the parasite. The life cycle of the protozoa is complex occurring both in the mosquito (sexual cycle) and in man (asexual cycle). *Plasmodium* is the class of the parasites causing malaria.[67] According to the plasmodium class different types of malaria are known.

Figure 1.7*: *Anopheles mosquito

Plasmodium Vivax causing *Malaria Tertiana*.
Plasmodium Ovale causing *Malaria Tertiana*.
Plasmodium Malariae causing *Malaria Quartana*.
Plasmodium Falciparum causing *Malaria Tropica*.

The last type is the most lethal causing most of malaria infections and death of millions of people in the parts of world where malaria is endemic.

1.5.3 Drugs for malaria treatment

In 1820, a revolution in malaria treatment was achieved by isolation of the efficient antimalarial alkaloid quinine[68] from the bark *Cinchona* "Peruvian fever tree" (***Figure 1.8***). Quinine was the main treatment for malaria until 1930s, the date of development of several synthetic quinoline-based antimalaria drugs (as chloroquine, mefloquine and amodiaquine). Now quinine is considered as toxic for prophylaxis or treatment of malaria. Chloroquine was the gold standard for treating malaria for several decades until many parasite strains have developed now high resistance to it and nearly to all quinoline drugs.[69]

Combination chemotherapy, where a mixture of different drugs such as mefloquine combined with sulfadoxine or pyrimethamine is also used to enhance the antimalarial efficacy. However, parasite resistance to such combinations has also emerged.[70]

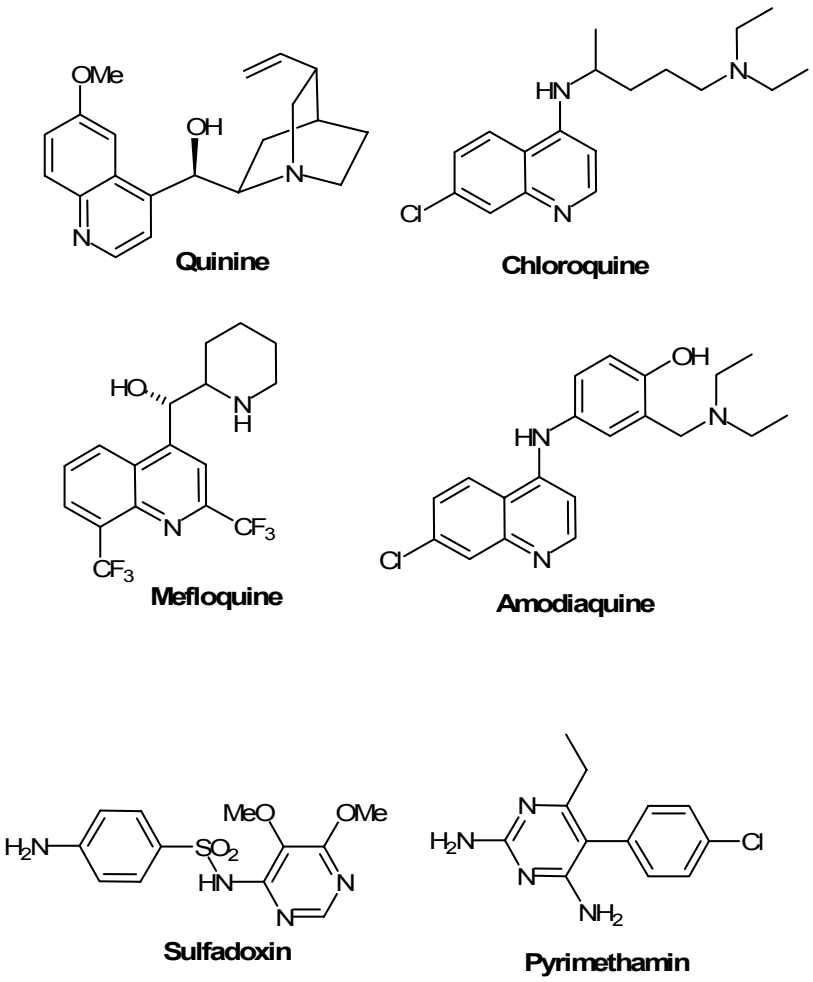


***Figure 1.8*:** Antimalaria drugs.

Artemisinin (also known as qinghaosu, ***Figure 1.9***) is an enantiomerically pure tetracyclic sesquiterpene lactone, the first natural 1,2,4-trioxane reported. In 1972, artemisinin was firstly isolated in China by low-temperature extraction from the leaves of *Artemisia annua*, and due to its remarkable antimalarial activity at the nanomolar concentration scale, artemisinin and its derivatives have been important as antimalarial drugs with the most effective activity against multidrug-resistant forms of *Plasmodium falciparum*.[83] The high pharmacological potential of artemisinin combined with its synthetically challenging structure have prompted Hofheinz,[71] Zho,[72] Avery,[73] Liu,[74] Yadav[75] and many others to carry out total syntheses of such structure. Consequently, another combination therapy was developed in which one of the 1,2,4-trioxane-containing artemisinin drugs is used in the drug mixture (artemisinin combination therapy, ACT). This is due to the fast antiparasitic action of such moieties[76]. However, high prices and shortage in amounts of such drugs have limited their use on patients of the developed countries, which is very problematic for under-developed countries in Africa or South-Asia.

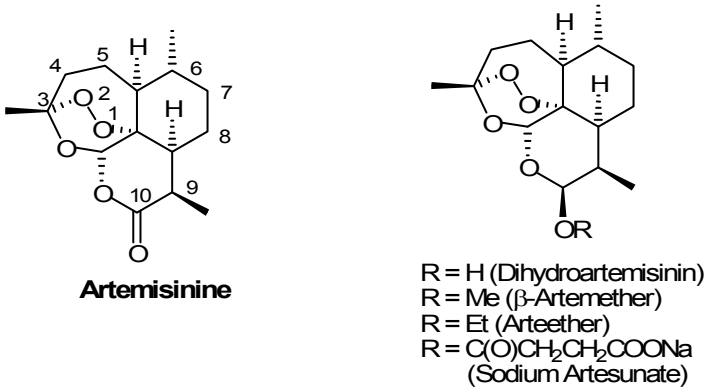
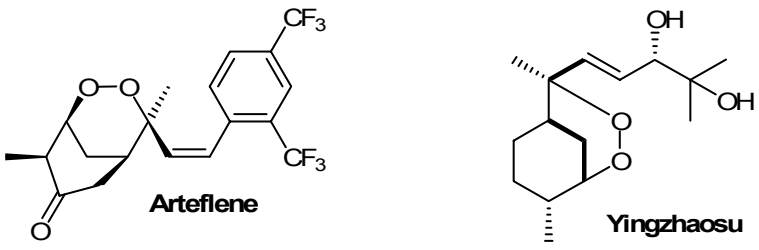


Figure 1.9

It is also noteworthy to mention here that many antimalaria-active compounds with different functionalities such as endoperoxide,[72a,77] isonitrile:[78] and naphthylisoquinoline[79] and many others were discovered (***Figure 1.10***)



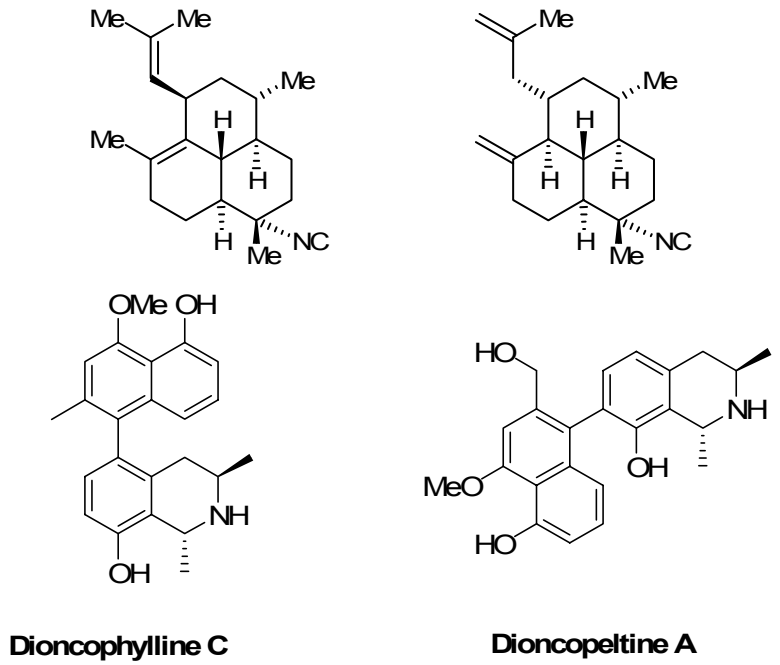
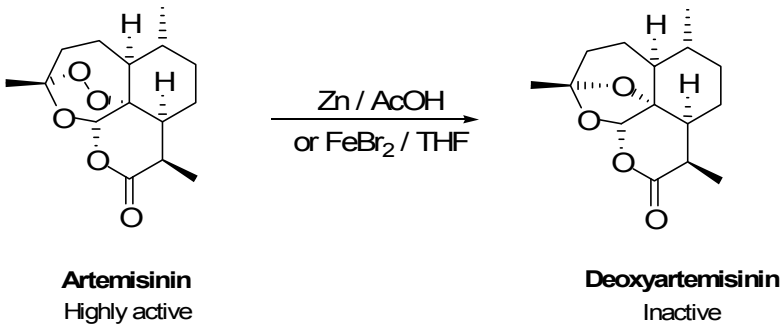


***Figure 1.10*:** Antimalaria drugs with different functionalities.

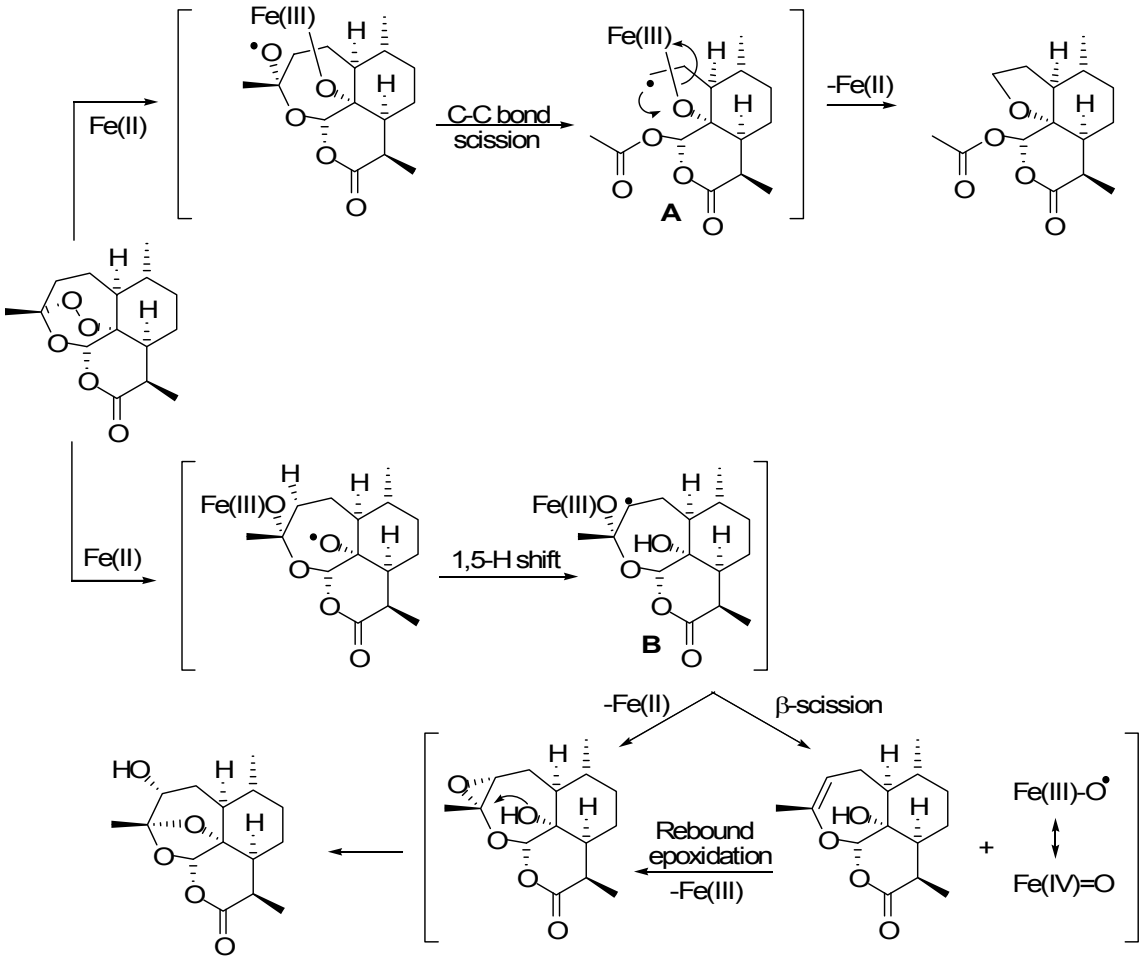
1.5.4 Mechanism of action of antimalarial 1,2,4-trioxanes like artemisinin

The mode of action of antimalarial 1,2,4- trioxanes exemplified by the natural sesquiterpene-endoperoxide artemisinin and its derivatives has been an enduring subject of research.[80,74] The mechanism is different from that of the traditional alkaloid quinoline-based drugs such as quinine and chloroquine.[81] The fact that deoxyartemisinin (an artemisinin derivative lacking the endoperoxide bridge and obtained by reduction of artemisinin) is devoid of antimalarial activity compared to artemisinin indicating that the peroxide functionality in the 1,2,4-trioxane ring is the key factor for the pharmacological activity of these trioxane drugs.[82] (***Scheme 1.11***).



Scheme 1.11

This mechanism of action is probably based firstly on a reductive cleavage of the peroxidic linkage in the 1,2,4-trioxane moiety by the ferrous ions of the hemoglobin leading to the formation of oxygen-centered radicals.[83] Subsequently, the oxy-radical intermediates undergo either bond scission or 1,5-hydrogen atom shift to form primary and secondary carbon-centered radicals (**A** and **B** in ***Scheme 1.12***).[84] The formation of the carbon centered radicals was proven by isotope labeling,[84] and spin trapping techniques.[85] The formation of the highly reactive ethyl radical **A** through bond scission is a spontaneous process driven by the formation of the thermodynamically stable acetate group. One (or more) of the formed reactive intermediates (e.g. oxy-radicals, carbon radicals and high valent iron-oxo species) is responsible for modification of the parasitic proteins causing the death of the malaria parasite.[86]



***Scheme 1.12*:** Mechanism of action of artemisinin.

The importance of the secondary carbon radical intermediates for the high antimalarial activity was demonstrated by a study of the activity of some simplified 4-methylated trioxanes [87] (***Figure 1.11***). From the antimalarial activities in ***Table 1.3*** it was deduced that 4-

β-methyl trioxane (entry 1) can undergo 1,5-hydrogen atom shift and is about 100 times more potent than the 4-α-methyl derivative (entry 2) that can not undergo such a hydrogen atom transfer. Likewise, 4-β-methyl trioxane (entry 1) is at least 100 times more potent than 4,4-dimethyl derivative (entry 3) that can not undergo such a hydrogen atom transfer.

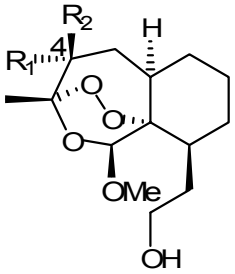


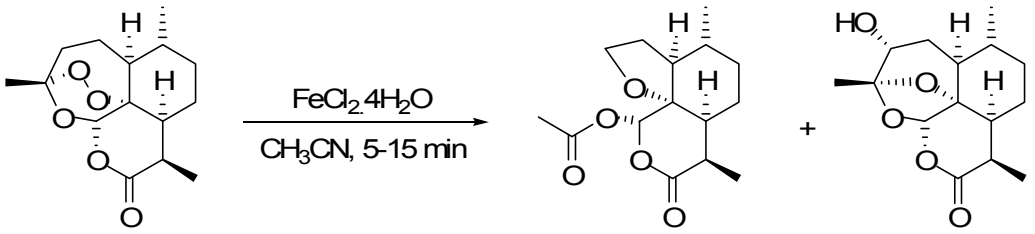
Figure 1.11

entry	R_1	R_2	IC_{50} (ng/mL)	
			W-Indochina clone	**D-6 African clone**
1	H	Me	4.5	3.5
2	Me	H	> 500	> 500
3	Me	Me	> 500	> 500

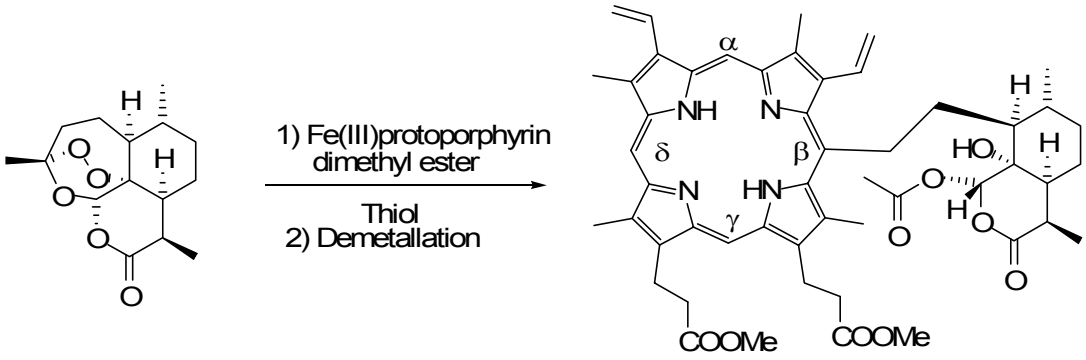
Table 1.3

Jefford et al.[88] also reported, that epiartemisinin (having an α-Me group in the lactone ring) shows drastically reduced antimalarial activity in comparison to the artemisinin (having the Me group in the lactone ring in the β–position). This was rationalized by a steric hindrance arising from the α-disposed methyl group which hinders or bias the complexation of epiartemisinin with the heme of the hemoglobin causing reduction of its activity.

Many reducing agents were used to mimic the heme role in the reduction of artemisinin including iron-(II) chloride in acetonitril[89] as well as the catalytic reaction in the presence of other reducing agents as ascorbic acid or cysteine.[90] Iron-(II) bromide in tetrahydrofuran was also efficiently used.[82a] The ring-contracted furano acetate was formed beside 3α-hydroxydeoxyartemisinin (***Scheme 1.13***). Meunier et al. also investigated the reaction of the artemisinin-derived radicals with manganese(II)-tetraphenylporphyrin[91] and the pharmacologically more relevant iron(II)-protoporphyrin-IX dimethyl ester as heme models, the reaction leads to a mixture of heme-artemisinin adducts resulting from alkylation alkylation at the α, β and δ carbon atoms (***Scheme 1.14***).[92]



***Scheme 1.13*:** Reduction of artemisinin with heme models.

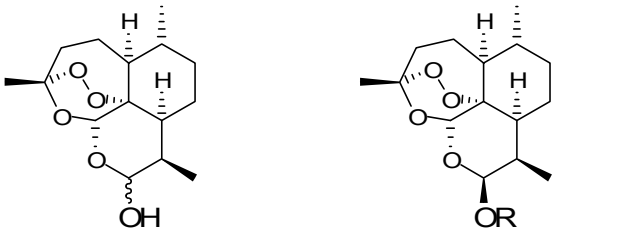


***Scheme 1.14**:* Reduction of artemisinin with heme models.
Adducts are also obtained from reaction at the α and δ carbon atoms.

1.5.5 Selected routes to 1,2,4-trioxane and peroxidic antimalarial compounds

1.5.5.1 Semi synthetic routes stemming from the parent artemisinin

One of the major drawbacks of artemisinin is its poor solubility in both water and oil.[93] To overcome this problem the Chinese researchers reduced artemisinin to dihydroartemisinin[93] which led to the preparation of a series of semisynthetic first-generation artemisinin analogues, including artemether, arteether, and artesunate which are used broadly in many areas of the world where malaria is endemic (***Figure 1.12***).[94]



Dihydroartemisinin

1) R = Me (artemether)
2) R = Et (arteether)
3) R = $COCH_2CH_2COO^-$ (artesunate)

Figure 1.12

Also, Venugopalan et al. synthesized various ethers and thioethers of dihydroartemisinin by treatment with alkyl, aryl, alkynyl and heteroalkyl alcohols or thiols in the presence of $BF_3.Et_2O$ (***Figure 1.13***). The products were tested *in vivo* and some show antimalarial activity comparable to arteether.[95]

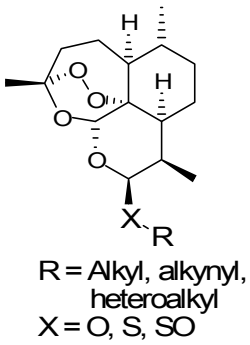


Figure 1.13

The poor bioavailability and rapid clearance (short pharmacological half-life) observed with these artemisinin-derived drugs are a major disadvantage. This results from the poor chemical and metabolic stability of the acetal function group present in such derivatives. To overcome this problem, many C-10 carba analogues and C-10-aryl analogues of dihydroartemisinin that are metabolically more robust were synthesized (***Figure 1.14***). Of relevance are the C-10 alkyl and the C-10-aryl or heteroaromatic derivatives prepared by Haynes et al.,[96] Posner et al.,[97] O'Neill et al.,[98] Jung et al.[99] and Ziffer et al.[100]

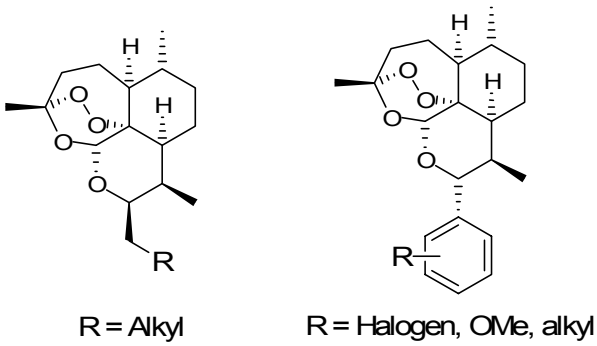


Figure 1.14

Recently, several groups reported the synthesis of C-10 carba artemisinin dimers lead compounds which are not only potent *in vitro* and *in vivo* antimalarials but also show anticancer properties (***Figure 1.15***) [101]

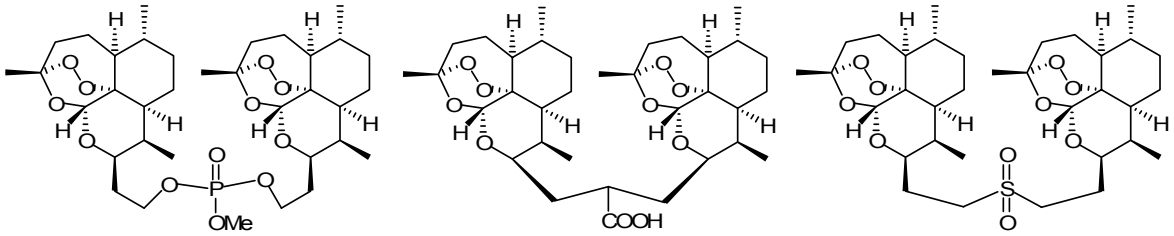


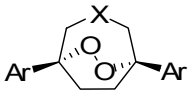
***Figure 1.15*:** Artemisinin dimers.

Despite the high efficacy of artemisinin and artemisinin-derived drugs, the synthesis of these analogues from the extracts of the original plant *Artemisia annua* with all its drawbacks and costs is highly problematic (the growing of *Artemisia annua* is possible only in limited geographic areas, namely in the South Chinese and Vietnamese uplands, and the yield of extraction is low, about 0.4 %.[102] Also, neurotoxicity has been reported for some of these derivatives as arteether at high doses in monkeys).[103] Under these circumstances, it will be difficult to extend the use of such artemisinin-derived drugs to a scale of billions of people. This has drawn the attention that design and full synthesis of analogues, structurally simple and easily accessible 1,2,4-trioxanes and peroxides as inexpensive antimalaria drugs that share the benefits of artemisinin high efficacy without its disadvantages. This is considered now by the WHO (world Health Organization) as a crucial matter.

1.5.5.2 Synthesis of antimalarial 1,2,4-trioxanes and peroxidic compounds

The danger accompanying the spreading of this infectious disease prompted many groups in the medicinal community to initiate synthetic studies for these biologically active compounds and develop new methodologies and design of alternative leading compounds that could be used as new efficious pharmaceuticals for malaria treatment. A Literature survey for the synthesis of peroxidic and 1,2,4-trioxane antimalarials results in thousands of candidates and the rate of synthesis of such compounds is increasing exponentially. Here, I will try to give a brief account on the research groups mostly siting in this area and some examples for their synthetic strategies to construct such units.

The Posner group applied the fundamental aspects of the artemisinin mechanism of action to the synthesis of some simple symmetrical endoperoxides that would undergo a mechanistic route similar to that of artemisinin (***Figure 1.16***)[104] The parent diphenyl endoperoxide (R = Ph) has considerable antimalarial activity (IC_{50} = 89 nM *versus* IC_{50} = 9-11 nM for artemisinin).



X = O, SO_2, NSO_2R

Figure 1.16

Nojima et al.[105] reported the synthesis of highly antimalaria active peroxides analogous to the antimalaria Yingzhaosu by the use of Co(II)-catalyzed peroxidation of dienes including (S)-limonene. The use of molecular oxygen and triethylsilane was elaborated by Isayama and Mukaiyama[106] with subsequent intramolecular cyclization of the unsaturated peroxy radical intermediates (***Figure 1.17***).

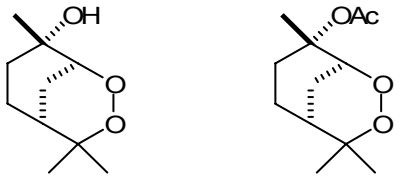
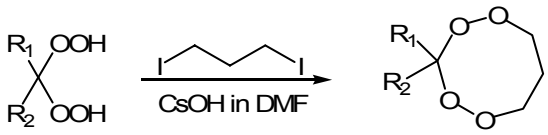


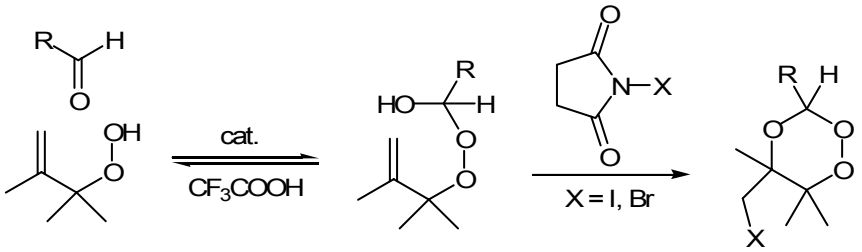
Figure 1.17

Wataya and coworkers[107] reported the synthesis of novel antimalaria-active 1,2,4,5-tetraoxacycloalkanes by cesium hydroxide or silver oxide mediated cycloalkylation of bishydroperoxides with dihaloalkanes (***Scheme 1.15***).



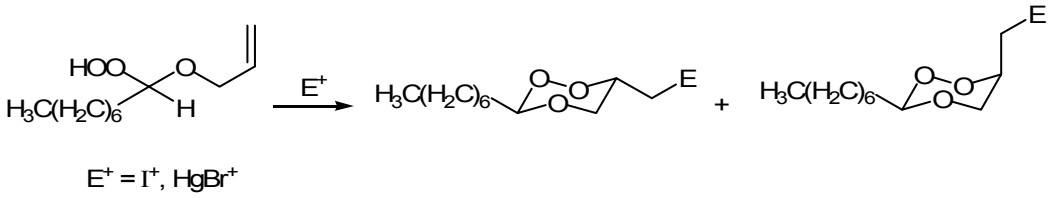
Scheme 1.15

Bloodworth et al. reported that the peroxyhemiacetals derived from reaction of aldehydes with allyllic hydroperoxides undergo cyclization with N-iodosuccinimide or NBS to afford 1,2,4-trioxanes (***Scheme 1.16***).[108]



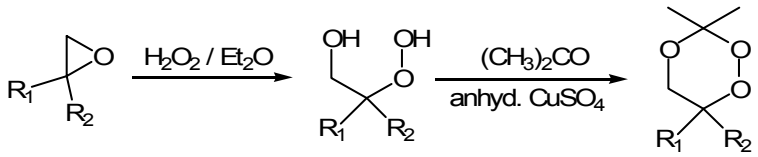
Scheme 1.16

In an analogous reaction, Dussault et al.[109] used the electrophilic cyclization of unsaturated hydroperoxy acetals or ketals with different electrophilic reagents for the synthesis of 1,2,4-trioxanes with moderate diastereoselectivity (***Scheme 1.17***). The unsaturated hydroperoxy acetals or ketals used in the reaction were prepared by trapping of ozonolysis-derived carbonyl oxides with allylic alcohol.



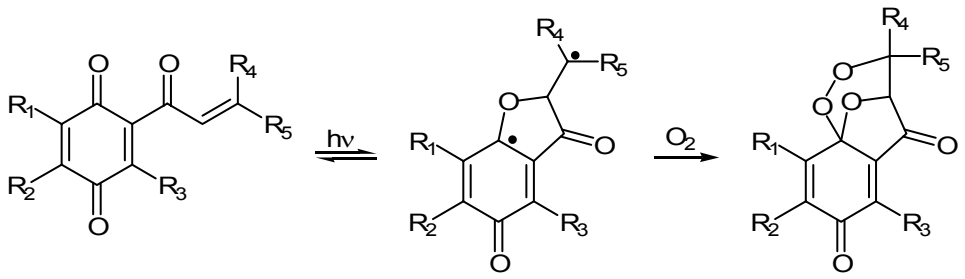
Scheme 1.17

1,2,4-Trioxanes were also synthesized by the condensation reaction of *vic*-hydroperoxy alcohols with carbonyl compounds using anhydrous $CuSO_4$ (***Scheme 1.18***). The *vic*-hydroperoxy alcohols used as starting materials in this reaction were obtained by acid-catalyzed perhydrolysis of epoxides with 98% H_2O_2.[110]



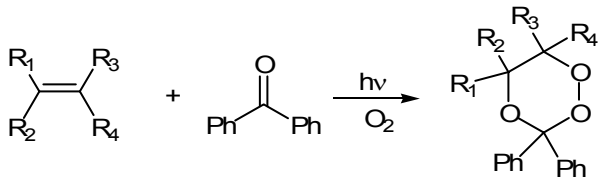
Scheme 1.18

Maruyama et al.[111] reported on the synthesis of different tricyclic 1,2,4-trioxanes upon irradiation of a series of alkenoyl-1,4-quinones in presence of oxygen. The reaction was assumed to proceed by trapping of the formed biradical by oxygen molecules (***Scheme 1.19***). The same concept was also utilized by Werbin[112] and Wilson.[113]



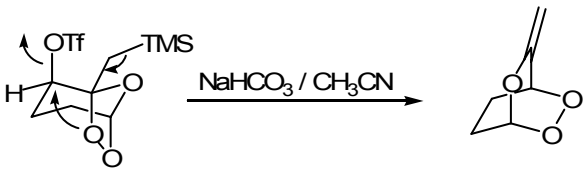
Scheme 1.19

Wilson et al.[114] were also able to trap the biradical formed in Paternò-Büchi reaction by molecular oxygen leading to formation of 1,2,4-trioxanes (***Scheme 1.20***).



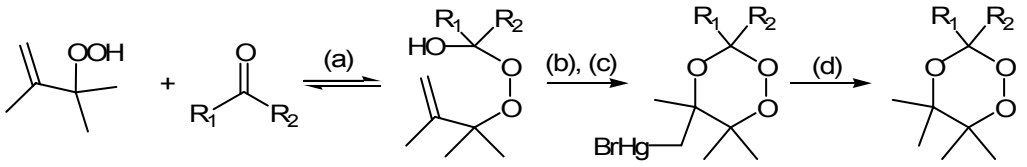
Scheme 1.20

Bunnelle et al.[115] used the cationic ring expansion of 1,2,4-trioxolanes (alkene ozonides) triggered by elimination of a good leaving group which leads to a 1,2-shift of the peroxide group and formation of 1,2,4-trioxanes (***Scheme 1.21***).



Scheme 1.21

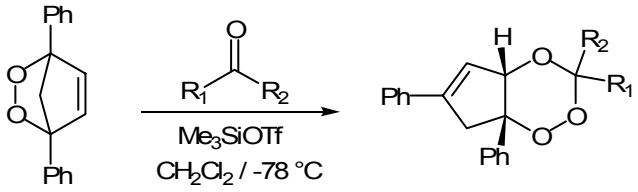
Bloodworth et al. used also the peroxyhemiacetals to undergo cyclization with mercury-(II) trifluoroacetate (modified cyclooxymercuriation) followed by reductive demercuriation with sodium borohydride to afford diasteriomeric mixtures of 1,2,4-trioxanes (***Scheme 1.22***).[116]



(a) cat. CF_3COOH (b) $Hg(OAc)_2$, 6 mol % $HClO_4$
(c) KBr (d) $NaBH_4$ / NaOH

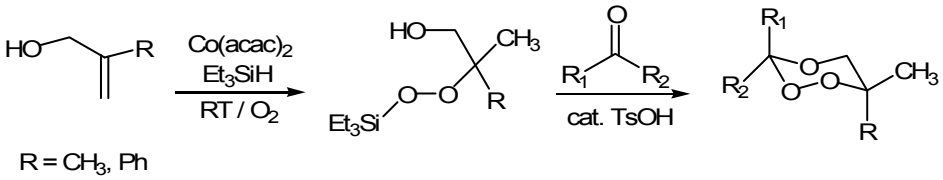
Scheme 1.22

Jefford et al.[117] used the reaction of endoperoxides or 1,2-dioxetanes with carbonyl compounds in presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) in methylene chloride at -78 °C to prepare a wide series of 1,2,4-trioxanes (***Scheme 1.23***)



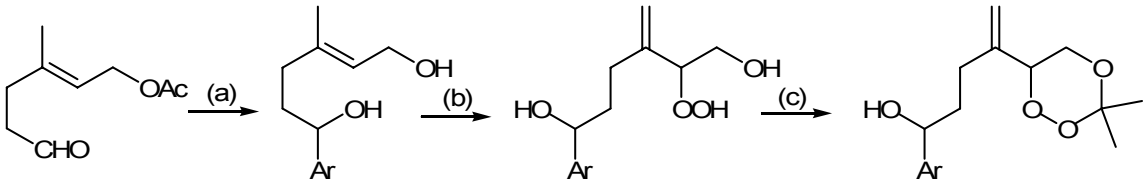
Scheme 1.23

O´Neill and coworkers[118] used the regioselective Co-(II)-mediated peroxysilylation reaction of allylic alcohols to give the corresponding β-peroxysilyl alcohol derivatives in good yields which condensed under acidic conditions with aldehydes and ketones to afford the 1,2,4-trioxanes. (***Scheme 1.24***).



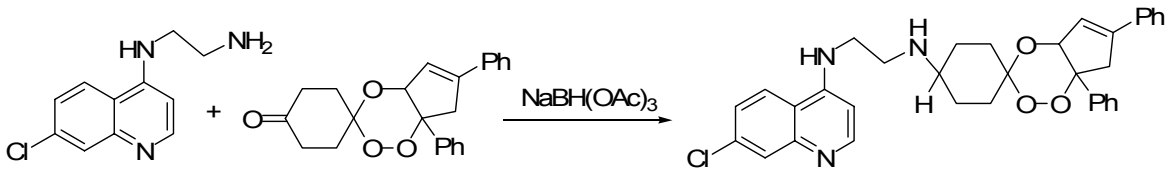
Scheme 1.24

Singh et al.[119] has also prepared a series of 1,2,4-trioxanes which showed good *in vitro* antimalarial activity by condensation of carbonyl compounds with β-hydroxy hydroperoxides, prepared by dye sensitized photooxygenation of different allylic alcohols (***Scheme 1.25***).



Scheme 1.25

The development of the artemisinin combination therapy concept was recently achieved by the synthesis of effective drugs that simultaneously contain the 1,2,4-trioxane moiety covalently bound with another active antimalarial pharmacophore, such as aminoquinolines[120] or aliphatic diamines[121]. The high activity of these molecules, termed trioxaquines (***Scheme 1.26***), is rationalized by the combination of a peroxidic entity that is a fast and potential alkylating agent, in the same molecule with the aminoquinoline unit which is characterized by easy penetration of the infected erythrocytes.[120b,c,122]



Scheme 1.26

2. Aim of the Work

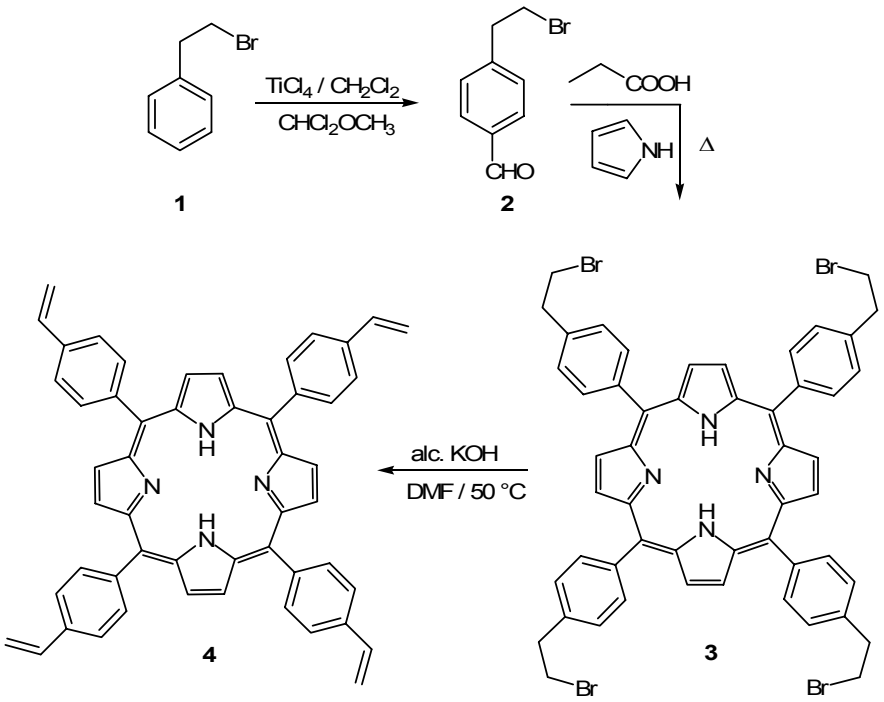
The 1,2,4-trioxane substructure is the pharmacophore in the naturally occurring antimalarial drug artemisinin. My research efforts have been primarily devoted to develop an efficient route to synthesize a broad series of mono-, polycyclic, and spiro-1,2,4-trioxanes using the photooxygenation ene reaction of singlet oxygen with different allylic alcohols.

Beside the previous synthetic aspect, the application of a new solvent-free photooxygenation reaction in polymer matrices will also be investigated. Commercially available polystyrene beads crosslinked with divinylbenzene and loaded with adsorbed tetraarylporphyrine dye sensitizers as well as synthesized polymers that are covalently bound to porphyrine sensitizers will be examined as reaction media for the photooxygention reaction of different substrates.

3. Results and Discussion

3.1 Polystyrene Matrix with Covalently Linked Singlet Oxygen Sensitizers

3.1.1 Synthesis of 5,10,15,20-tetrakis(4-ethenylphenyl)-21*H*,23*H*-porphine (tetrastyrylporphyrin,TSP)



***Scheme 3.1*:** TSP synthesis.

The synthesis of TSP **(4)** may be achieved either by Wittig reaction of 5,10,15,20-tetrakis(4-formylphenyl)porphyrin (prepared from terephthalaldehyde and pyrrole)[123] with methyltriphenylphosphonium bromide or by dehydrohalogenation of the porphyrin **3** ***(Scheme 3.1)***.[124] The latter method appeared advantageous because of higher yield and better reproducibility.

Formylation of 2-bromoethylbenzene **(1)** using dichloromethyl methyl ether in presence of Lewis acid as $TiCl_4$ gives the aldehyde **2** showing the aldehyde characteristic signal at 9.93, 191.8 ppm in ^1H and ^{13}C-NMR, respectively. Applying the usual Adler's procedure[125] used for porphyrin synthesis to the aldehyde **2** resulted in a deep violet crystals corresponding to **3**. The ^1H-NMR spectrum of **3** is characterized by the two triplet signals of the vicinal methylene groups at 3.50, 3.86 ppm as well as the olefinic singlet signal of pyrrole ring at δ =

8.82 ppm. Also and like all porphyrin systems, the highly shielded NH protons (due to anisotropic ring current effect) resonate highly up-field at δ = -2.80 ppm.

Treatment of **3** with alcoholic KOH in DMF resulted in dehydrobromination reaction with the formation of **4** in good yield. Similarly to **3**, the structure of TSP **(4)** was confirmed by NMR showing its characteristic vinylic proton signals at 5.48, 6.05 and 7.05 ppm (***Figure 3.1***).

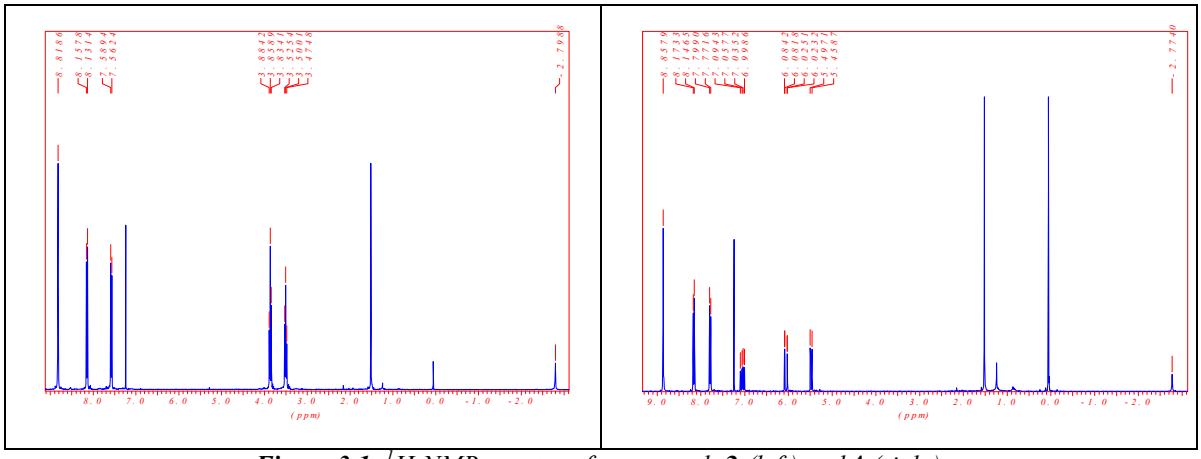
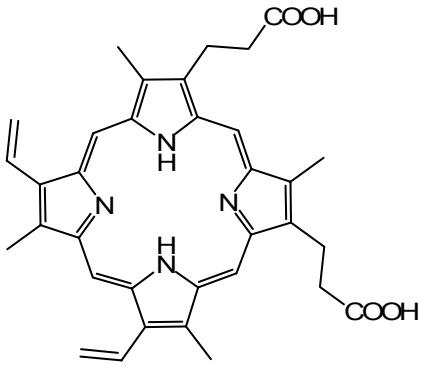


Figure 3.1: *^{1}H-NMR spectra of compounds* **3** *(left) and* **4** *(right).*

3.1.2 Polymerization, morphology and characterization of the sensitizer-bound resins

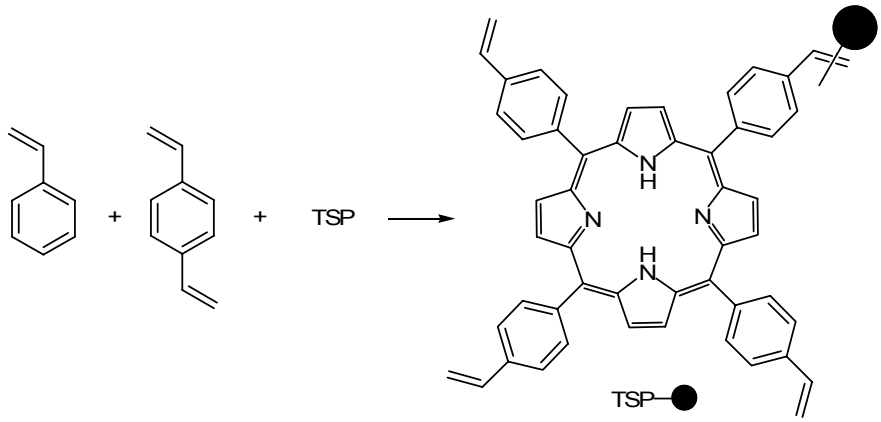
The synthetic TSP **(4)** and the natural protoporphyrin-IX **(5)** (PP), ***Figure 3.2***, are peripheral substituted porphyrins with unsaturated side chains and hence having crosslinking properties. PP **(5)** is the biological precursor for plant and animal pigments, it gained with its dimethyl ester derivative a considerable attention as efficient candidates in photodynamic therapy.[126]



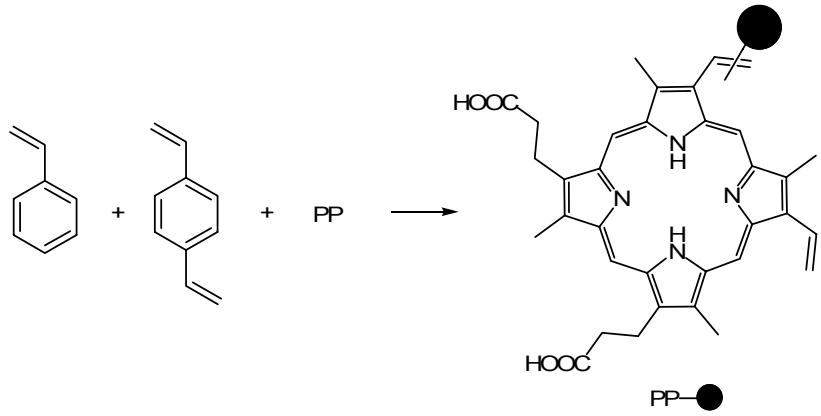
5

***Figure 3.2*: Protoporphyrin-IX (PP).**

Both singlet oxygen sensitizers **4** and **5** were copolymerized with styrene (S) and divinyl benzene (DVB) using an emulsifier-free emulsion polymerization. This technique was chosen for the copolymerization reaction since it allows the synthesis of the resin particles (TSP-S-DVB and PP-S-DVB copolymers) in a simple and reproducible way (***Scheme 3.2*** and ***3.3***). Styrene, DVB and the crosslinking sensitizer (TSP or PP) were suspended in an excess of an immiscible water phase (the continuous phase) that is maintained at pH = 2.3 and heated to 70 °C. On addition of a radical initiator (potassium peroxodisulfate) the polymerization starts and over a polymerization period of about 7 h, the monomer droplets are converted to polymer beads which are referred to as "resins".



***Scheme 3.2*:** Synthesis of the tetrastyrylporphyrin-loaded polymer (TSP-S-DVB).



***Scheme 3.3*:** Synthesis of the protoporphyrin-IX-loaded polymer (PP-S-DVB).

The TSP-S-DVB polymer particles are translucent in color, polyhedral in shape having size range from 200 to 500 nm. On the other hand, the PP-S-DVB resin is faint rose in color, spherical in shape having size range from 200 to 400 nm. (***Figure 3.3***). It is also noteworthy to mention that these resin nanoparticles are characterized by high surface area, accounting

for their high substrate loading capacity (up to 100 % by wt. for both catalysts, *vide infra*). SEM pictures of samples of each polymer (unswollen) is shown in ***Figure 3.3***.

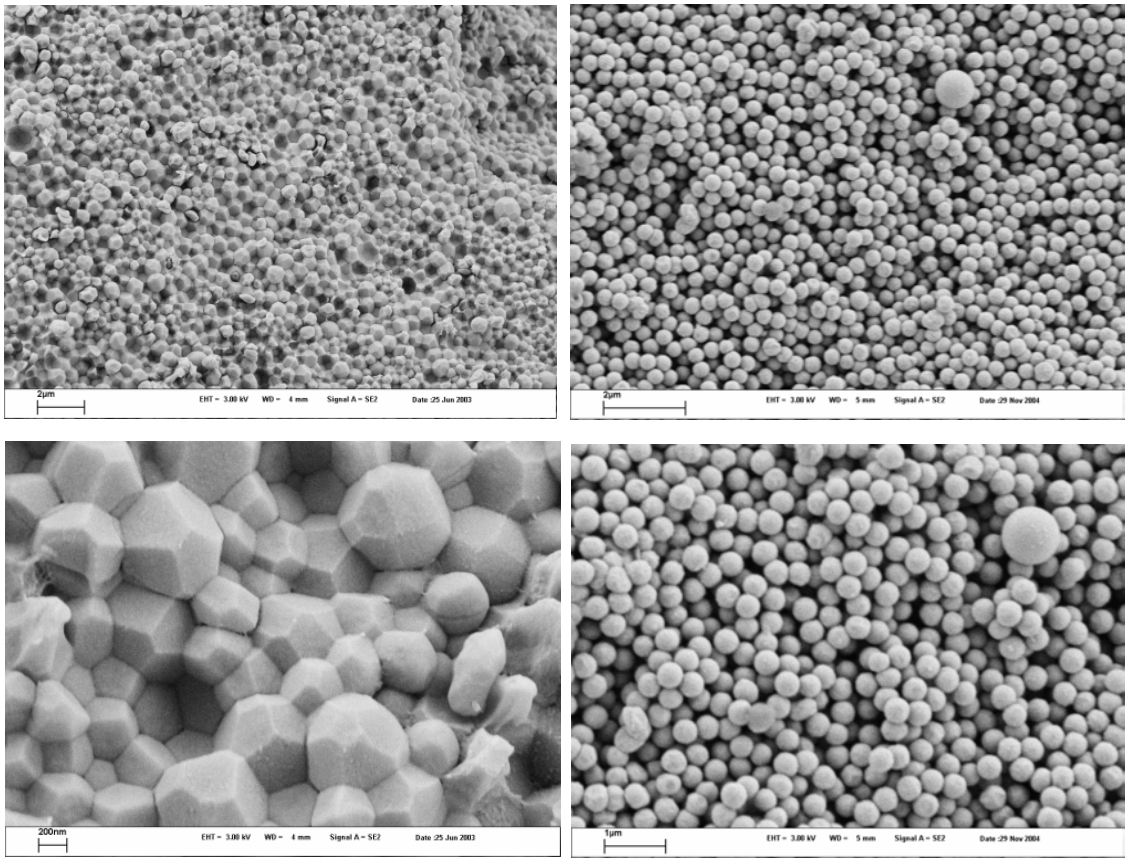
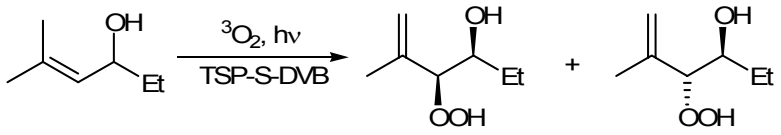


Figure 3.3*:*Scanning electron microscope (SEM) pictures of PP-S-DVB sample (right) and TSP-S-DVB sample (left).

Copolymerization of TSP and PP is expected to enhance the $^1O_2$ generation efficiency compared to the non-polymerized TSP and PP sensitizers due to saturation of the side-chain double bonds (styrene-type double bonds are oxidative labile).[127] Both macromolecular sensitizers, TSP-S-DVB and PP-S-DVB, have high photo and mechanical stability, efficiently generating $^1O_2$ and show good resistance toward bleeding and the irreversible photobleaching (oxidative degradation) by $^1O_2$ and/or the strong oxidizing peroxidic products (peroxides or hydroperoxides).[128] I also expect an enhancement of the porphyrin triplet lifetimes for the covalently-linked porphyrins in comparison with the free sensitizers in solution, because polymerization should prevent dye-aggregations that is known to cause self-quenching of the excited sensitizers and thereby reduces the triplet lifetimes.[129]

3.1.3 Determination of the sensitizer percentage in the resins

Estimation of the percentage of TSP (or PP) covalently bound in TSP-S-DVB (or PP-S-DVB) resins was achieved by running two parallel photooxygenation reactions using identical amounts of the synthesized TSP-S-DVP (or PP-S-DVB) resin and the commercially available PS-DVB copolymer (loaded with a given amount of the sensitizer). Both reactions were carried out under identical conditions using identical amount of the substrate **6b** (***Scheme 3.4***). From the comparison of the degree of conversion in both experiments, a loading degree of about 0.1 % of TSP in TSP-S-DVB resin (or PP in PP-S-DVB resin) was determined.



6b *syn*-**7b** *anti*-**7b**

Scheme 3.4

3.1.4 Solvent-free photooxygenation reactions using covalently-bound sensitizers

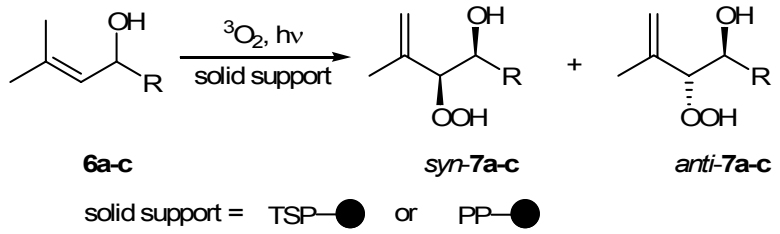
Motivated by developing an efficient, inexpensive, highly reproducible and reusable approach for $^1O_2$ photooxygenation reaction which can also avoid the aforementioned solution photochemistry drawbacks (and since filtration is one of the simplest and fastest methods for isolating a substance from a liquid, such as a solution of reactants), I developed a solvent-free pathway combining the use of visible light as a reagent in the presence of the polymer-fixed sensitizers microreactors as a reaction medium. This offers a new and convenient approach towards green singlet-oxygen photooxygenation reactions, where not only the production of side products is retarded due to enhanced selectivity but also the amount of expensive and environmentally problematic solvents is highly reduced (*vide infra*).

In this approach the polymer-bound sensitizer is placed in a small Petri-dish and swollen by a small amount of the substrate solution in dichloromethane followed by evaporation of excess solvent, gram scale reactions can be carried out applying a loading degree up to 100 % by wt. for both catalysts. The Petri-dish is irradiated with halogen lamp or sodium street lamp simply under atmospheric air needing no oxygen purging. In contrast to solid phase organic synthesis (SPOS)[130] in which the substrate is covalently attached to the solid support during a reaction sequence and the product has to be cleaved from the support at the end of the reaction, in the

solvent-free approach the substrate is only adsorbed to the solid support. This facilitates the product isolation by a simple routine of extraction with methanol or ethanol, filtration and evaporation. In order to explore the potential of the new TSP-S-DVB or PP-S-DVB solvent-free photooxygenation approach and identify its influence on the chemo-, regio-, and stereoselectivity patterns in type-II photooxygenation reaction, several substrates for both ene and [4+2]-cycloaddition reactions with singlet oxygen have been investigated.

3.1.4.1 Diastereoselectivity of the ene and [4+2]-cycloaddition reactions using TSP-S-DVB and PP-S-DVB

The diastereoselectivity of the ene reaction of $^1O_2$ was investigated using the chiral allylic alcohols **6a-c**.[37,141] The photooxygenation of **6a-c** (***Scheme 3.5***) yielded the *syn*-hydroxy allylic hydroperoxide as major diastereomers referring to the hydroxy-directing effect of $^1O_2$ in the conformationally fixed (by ^{1,3}A-strain) substrates (***Table 3.1***).



***Scheme 3.5*:**Photooxygenation of the allylic alcohols **6a-c**

compound	R	d.r. (*syn*:*anti*)[a] TSP-S-DVB	d.r. (*syn*:*anti*)[a] PP-S-DVB	d.r. (*syn*:*anti*)[a] TTP/TPP in CCl_4
7a	CH_3	81:19	80:20	93:7
7b	Et	78:22	-	93:7
7c	*i*-Pr	82:18	-	93:7

***Table 3.1*:** Diastereoselectivities of the photooxygenation of **6a-c** in different environments.
[a] d.r. values were calculated by ^{1}H NMR from the crude reaction mixture (5 % error).

As seen in ***Table 3.1***, both TSP-S-DVB and PP-S-DVB gave similar diastereoselectivities, however considerably lower than that obtained in the non-polar solvents as CCl_4. This can be rationalized by the intermolecular hydrogen-bonding between the the highly concentrated allylic alcohol molecules encapsulated in both nanocontainer beads (the hydrophobic nature of the beads interior also enhances aggregation of the highly polar substrate). This assumption was further supported by the fact that solvent-free photooxygenation of **6a** in a rose

bengal/cellulose acetate film (showing additional intermolecular hydrogen-bonding between the matrix and the substrate) results in even lower *syn* diastereoselectivity (d.r. 70:30).
The relative (*syn*) configuration of the major diastereoisomers has been confirmed by several chemical transformations of the β-hydroxy allylic hydroperoxides among them also the peroxyacetalization reaction to form 1,2,4-trioxanes (*vide infra*). The first unambiguous proof was achieved by successful crystallization of the homologous compound *syn*-**7j** prepared by identical procedure (***Figure 3.4***).

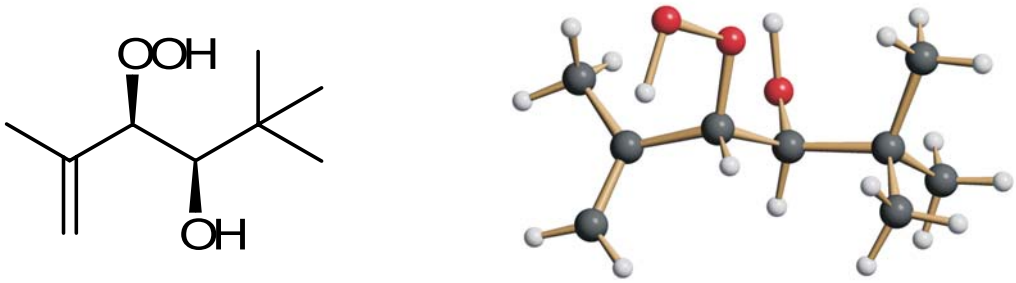


Figure 3.4**:** X-ray analysis for *syn*-**7j**.
(First X-ray of acyclic *vic*-hydroperoxy alcohol in literature).

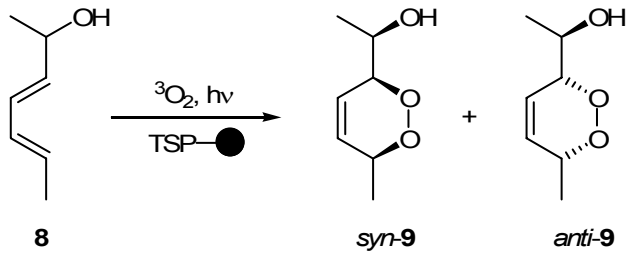
The formation of the 1,2-hydroperoxy alcohols was confirmed by the characteristic signals of the hydroperoxy carbons for both *syn*-**7a-c,j** and *anti*-**7a-c,j** diastereomers (***Table 3.2*****)**.

Compound	**R**	***syn*-diastereomer**		***anti*-diastereomer**	
		^{1}HNMR	**^{13}CNMR**	**^{1}HNMR**	**^{13}CNMR**
7a	CH_3	4.08	94.8	4.25	92.1
7b	Et	4.15	93.4	4.30	91.4
7c	*i*-Pr	4.28	92.0	4.34	89.9
7j	*t*-Bu	4.33	88.0	4.33	90.1

Table 3.2**:** ^{1}H- and ^{13}C-NMR chemical shifts (ppm) of the hydroperoxy carbon (**CH**-OOH) of *syn* and *anti* diastereomers of **7a-c,j** (in $CDCl_3$).

The chiral dienol **8** was used to probe the diastereoselectivity of the [4+2]-cycloaddition reaction of $^{1}O_2$.[131] The photooxygenation of **8** under solvent-free conditions using the sensitizer-bound polymer matrix gives a mixture of the endoperoxides *syn*- and *anti*-**9** in good yield but with low diastereoselectivity (d.r. 59:41) in pronounced opposition to monoalkenes reactions (***Scheme 3.6***). The poor facial selectivity in the formation of **9** is expected due to the negligible hydroxy-directing effect of $^{1}O_2$ since it is not conformationally fixed on one diastereotopic face of the diene **8**. The structure of the products was confirmed on the bases of

disappearance of a double bond and appearance of two peroxidic carbon atoms in ^{1}H as well as ^{13}C-NMR of both diastereomers.

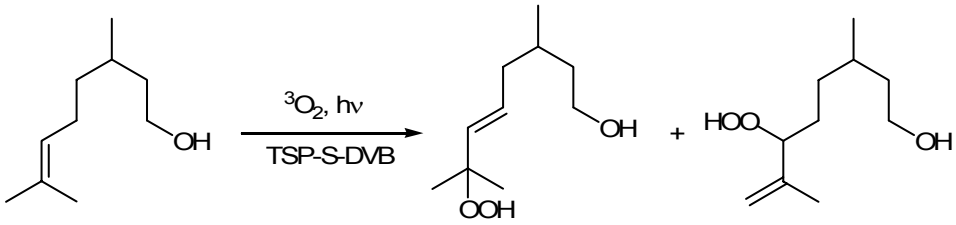


8 *syn*-**9** *anti*-**9**

***Scheme 3.6*:** Photooxygenation of the dienol **(8).**

3.1.4.2 Regioselectivity of the ene reaction using TSP-S-DVB and PP-S-DVB

In order to study the effect of this polymer environment on the regioselectivity of the ene reaction, I investigated the photooxygenation of citronellol **(10)**. Citronellol is the industrial precursor of the fragrant speciality rose oxide.[132] The photooxygenation reaction using the polymer-bound sensitizer yielded the regioisomers **11** and **12** in ratio 1.3:1, respectively (***Scheme 3.7***). Fortunately, compound **11** is the major regioisomer that is needed for rose oxide production. The regioisomer **12** is formed as 1:1 diastereomerc mixture (from ^{13}C-NMR). The structure of both compounds was confirmed by the characteristic signals of the hydroperoxy carbons in ^{1}H- and ^{13}C-NMR as shown in ***Table 3.3***.



10 **11** **12**

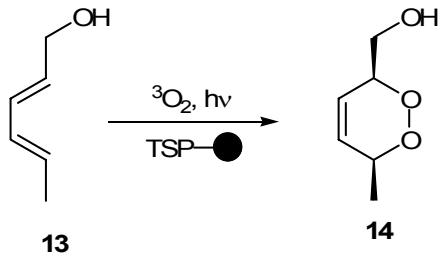
***Scheme 3.7*:** Photooxygenation of citronellol **(10).**

11		**12**	
^{1}HNMR	**^{13}CNMR**	**^{1}HNMR**	**^{13}CNMR**
-	81.6	4.14	89.1/89.5

***Table 3.3*:** Chemical shifts (ppm) of the hydroperoxy carbon (**CH**-OOH) of compounds **11, 12** (in $CDCl_3$).

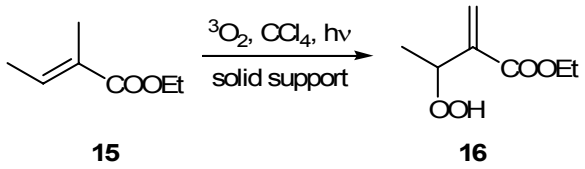
3.1.4.3 Sorbinol and ethyl tiglate photooxygenations using TSP-S-DVB and PP-S-DVB

The solvent-free photooxygenation reaction of the reactive alcohol derived from sorbic acid (sorbinol) **13** using the sensitizer-bound polymer proceeded in excellent yields forming the corresponding endoperoxide **14** (***Scheme 3.8***). The NMR of the product is consistent with **14** showing the two characteristic peroxidic carbons at 4.39, 4.77 ppm in ^{1}H-NMR and at 74.3 and 79.7 ppm in ^{13}C-NMR.



***Scheme 3.8*: Photooxygenation of sorbinol **(13)**.

Similarly, photooxygenation of the tiglate ester **15** affords in a clean reaction the corresponding hydroperoxide **16** (***Scheme 3.9***). The hydroperoxide is formed as one regioisomer as expected by the *gem*-effect (*vide supra*). The formation of **16** was unambiguously proved by the hydroperoxide carbon resonating as quartet at δ = 4.9 ppm in ^{1}H-NMR and at δ = 79 ppm in ^{13}C-NMR.

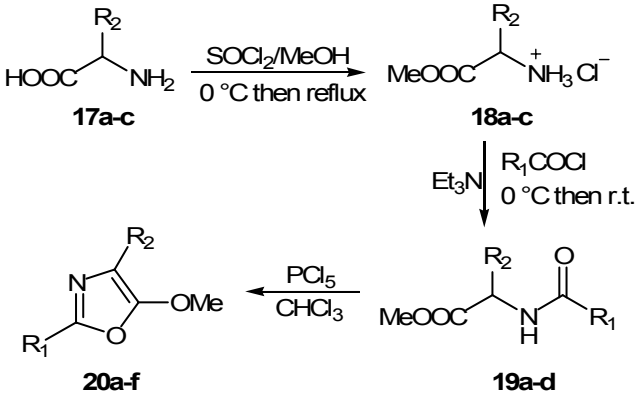


***Scheme 3.9*: Photooxygenation of ethyl tiglate **(15)**.

One of the major advantages of this solvent-free technique with the sensitizer-bound resins is the reusability. The recovered TSP-S-DVB and PP-S-DVB beads were recycled in three consecutive cycles simply by washing with methylene chloride (to remove any residual amount of the substrate or product) and reused again without any appreciable decrease in the catalytic efficiency. Minimum turn over number (TON) are 3000 for the TSP-S-DVB and slightly lower for the PP-S-DVB system.

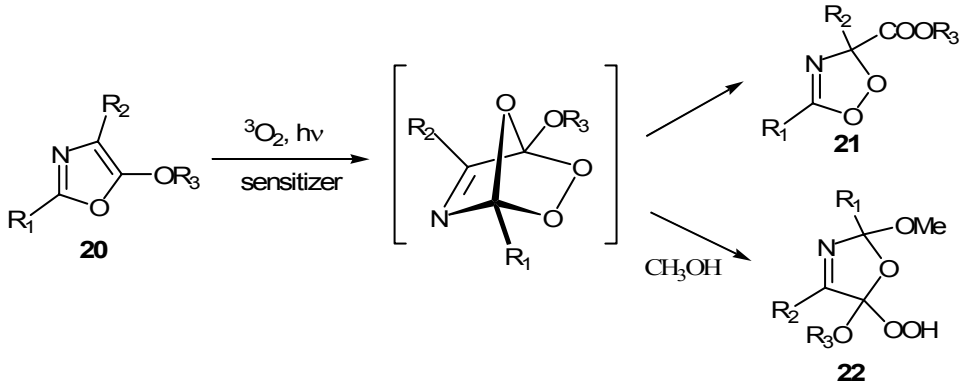
3.1.4.4 Photooxygenation of 5-methoxyoxazoles using TSP-S-DVB and PP-S-DVB

A set of the substrates 2,4-dialkylated-5-methoxyoxazoles were synthesized from the amino acids in a three-step procedure (***Scheme 3.10***). Firstly the amino acid was converted to the ester of its hydrochloride salt by treatment with thionylchloride in dry methanol, followed by acylation of the amino group with acid chloride in presence of triethylamine. The oxazole synthesis is completed by dehydration of the acylated amino acid ester with phosphorous pentachloride in chloroform. The oxazoles **20a-f** were obtained in high purity and their chemical structures were proven by NMR spectroscopy. For example in ^{1}H-NMR, the methoxy group resonates at about 3.7 ppm, in ^{13}C-NMR the two characteristic signals of C-5 and C-2 resonate for the different oxazoles between 152-155 and 154-161 ppm, respectively.



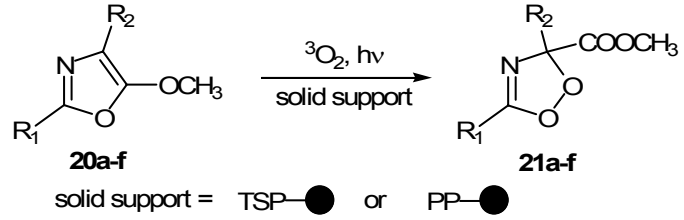
***Scheme 3.10*:** Synthesis of 2,4-dialkylated-5-methoxyoxazoles.

Oxazoles in general show high reactivity as electron-rich dienes in thermal 1,4-cycloaddition reactions[133] as well as in the type-II photooxygenation reaction.[134] The cycloaddition of singlet oxygen to 5-alkoxy-oxazoles involves an endoperoxide intermediate which could be trapped by nucleophiles such as methanol or rearranges to a peroxyimide, the 1,2,4-dioxazole (***Scheme 3.11***).[135,136]



***Scheme 3.11*:** Photooxygenation of 5-alkoxy-oxazoles: products.

The $^1O_2$ photooxygenation reaction of **20a-f** using the sensitizer-bound polymers TSP-S-DVB and PP-S-DVB resulted in 100 % conversion of the starting materials with the formation of the 1,2,4-dioxazoles **21a-f** (***Scheme 3.12***). The structure determination of the compounds **21a-f** was based on the characteristic chemical shifts of quaternary, peroxyimide, and the carbonyl carbon atoms in ^{13}C-NMR (***Table 3.4***).



***Scheme 3.12*:** Photooxygenation of 5-methoxyoxazoles **20a-f** on solid support.

Compound	R_1	R_2	Yield (%)[a]	Yield (%)[b]	Cq (ppm)	C=N (ppm)	C=O (ppm)
21a	Me	Me	60	44	106.1	160.7	168.4
21b	Et	Me	86	90	106.0	164.9	168.6
21c	*t*-Bu	Me	-	84	105.9	170.0	168.6
21d	Me	*i*-Pr	-	79	111.3	160.3	168.8
21e	Et	*i*-Pr	90	86	111.0	164.3	168.6
21f	Et	*i*-Bu	89	79	108.3	164.4	168.7

***Table 3.4*:** 1,2,4-dioxazoles **21a-f** using [a]TSP-S-DVB and [b]PP-S-DVB support systems, the characteristic signals in ^{13}C-NMR ($CDCl_3$) are also shown.

The peroxides are unstable and decompose slowly to give the corresponding amides and dicarbonyl fragments.[136] The amide formation was unambiguously confirmed by X-ray analysis of pivaloylamide derived from the decomposition of **21c** (***Figure 3.5***).

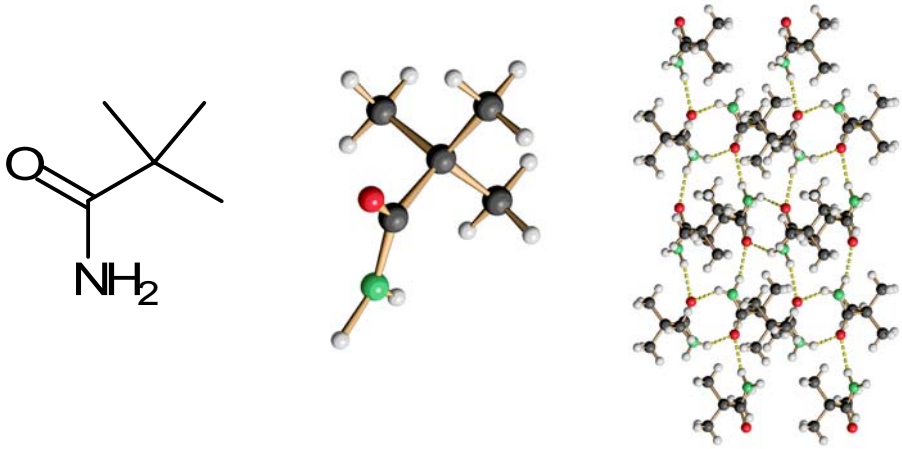


Figure 3.5**:** X-ray analysis of pivaloylamide (with and without showing the hydrogen bonding) obtained from decomposition of **21c.**

3.2 Homogeneous versus heterogeneous photooxygenation conditions

The photooxygenation reactions in solution can be performed either homogeneously or heterogeneously. In the former case, the dye sensitizer is completely soluble in the reaction mixture forming one phase reaction. In the latter case, one of the ingredients of the reaction (here the sensitizer) exist in a different phase (***Figure 3.6***).[137] Both PP-S-DVB and TSP-S-DVB sensitizers were also applied in a heterogeneous photooxygenation reaction.

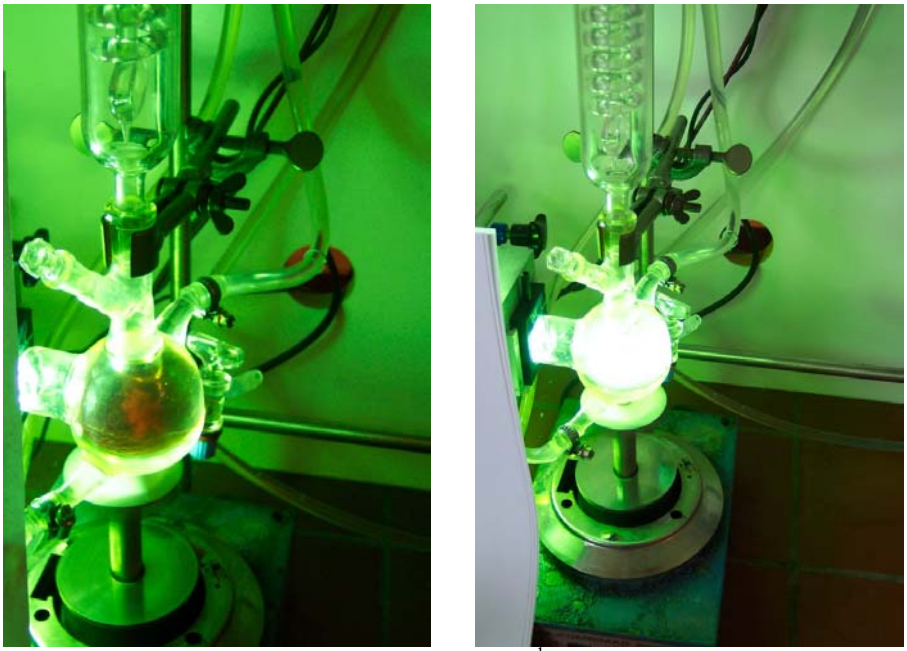


Figure 3.6**:** Homogeneous (left) and heterogeneous (right) $^1O_2$ photooxygenation reactions in solution.

Comparison of the efficiency of both the homogeneous and heterogeneous photooxygenation conditions was accomplished by studying the oxygen uptake in the $^1O_2$ photooxygenation reaction of the reactive model substrate 2,3-dimethyl-2-butene **(23)** (***Scheme 3.13***). All reactions were carried out in CCl_4 and under pseudo-first order conditions using large excess of substrate concentration (> 0.1 M alkene concentration) in order to make sure that the reaction rate is only dependent on the $^1O_2$ concentration that is produced by the sensitizer molecules.

***Scheme 3.13*:** Photooxygenation reaction of **23**.

Two concentrations of tetraphenylporphyrin (TPP) in CCl_4 were used for the homogeneous reaction condition (1.6 x 10^{-5} and 1.6 x 10^{-6} M). On the other hand, suspensions of the TSP-S-DVB and PP-S-DVB resins in CCl_4 were used for the heterogeneous reactions. The amount of sensitizer covalently bound in the polymer beads corresponds to a homogeneous solution of 2 x 10^{-6} M porphyrin (assuming 100 % integration of the sensitizer in the network during polymerization).

From the (linear) oxygen uptake it is concluded that the pseudo first-order conditions exist for a longer period of time without bleaching or degradation of the polymer-bound dyestuff.[127,138] From ***Figure 3.7***, it can be seen that the sensitizer activity is nearly identical comparing homogeneous conditions (1.6 x 10^{-6} M TPP) with the polymer bound tetrastyrylporphyrin (TSP-S-DVB) and only slightly lower for the polymer-bound protoporphyrin-IX (PP-S-DVB).

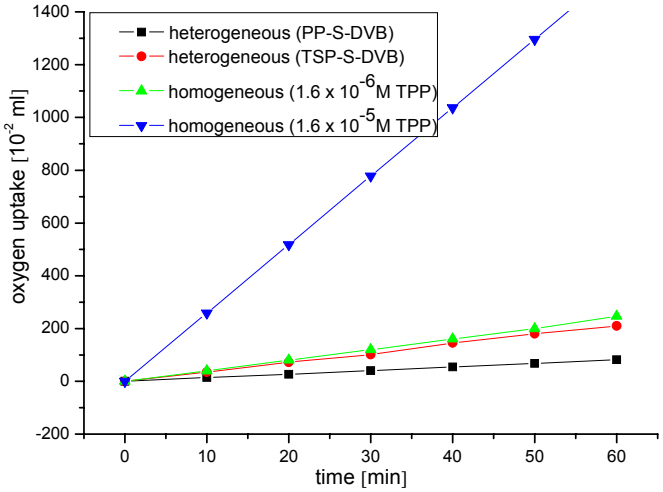


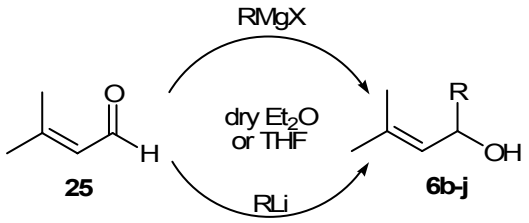
***Figure 3.7*:** Oxygen-gas uptake under homogeneous and heterogeneous conditions using the model compound 2,3-dimethyl-2-butene **23** (0.15 M in CCl_4).

3.3 Polystyrene Matrix with Adsorbed Singlet Oxygen Sensitizers

In this approach the non-polar dye sensitizer (*para*-substituted tetraaraylporphyrins or the parent *meso*-tetraphenylporphyrin TPP) for the generation of singlet oxygen was transferred in a catalytic amounts into the beads of the commercially available PS-DVB (polystyrene resin crosslinked with 1 % DVB) by swelling the resin with a solution of the sensitizer in dichloromethane with subsequent evaporation of the solvent. Then the substrate was transferred into the polymer by similar procedure where the molar ratio of the sensitizer to the substrate in the polymer matrix is about 1:1000. After evaporation of the solvent, the obtained sandy layer is irradiated under atmospheric oxygen. Based on the polarity difference between nonpolar sensitizer and polar reaction products as well as the extreme low solubility of the *meso*-tetraarylporphyrins in more polar solvents, the product is extracted after irradiation by repeated washing with methanol or ethanol. By this way the dye sensitizer stays nearly completely in the solid support and the reloading process can repeated.
The solvent-free approach of $^1O_2$ photooxygenation reactions is the basic reaction applied for a wide variety of substrates among them the allylic alcohols that are considered as the parent precursors for the antimalarial 1,2,4-trioxanes prepared in this thesis.

3.4 Synthesis of the Allylic Alcohols Starting Materials

A series of allylic alcohols **6b-j** was prepared in good yields from 3-methyl-2-butenal **(25)** by reaction either with Grignard reagents (method A) or with organolithium compounds (method B) in dry ether or THF as solvent. (***Scheme 3.14***).



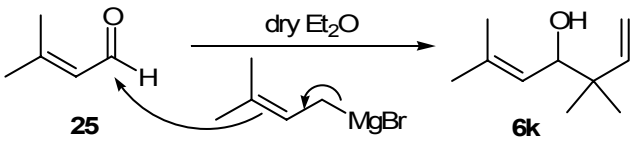
***Scheme 3.14*:** Synthesis of the allylic alcohols **6b-j** from 3-methyl-2-butenal.

All allylic alcohols prepared showed ^{1}H- and ^{13}C-NMR data that are consistent with the data in literature. The allylic alcohols prepared by these two methods and their characteristic signals of the carbinol carbons are summarized in ***Table 3.5***.

Compound	R	Synthesis method[a]	^{1}H-NMR (ppm)[b]	^{13}C-NMR (ppm)[b]	Yield (%)
6b	Et	(A)	4.20	70.0	52
6c	*i*-Pr	(A)	3.96	73.5	67
6d	*n*-Pr	(A)	4.28	68.3	83
6e	$CH_2CH=CH_2$	(A)	4.32	67.6	76
6f	$CH(Me)CH=CH_2$	(A)	4.17/4.03[c]	71.6/71.5[c]	57[c]
6g	*n*-Bu	(B)	4.26	68.6	81
6h	*i*-Bu	(A)	4.32	66.6	70
6i	*sec*-Bu	(B)	4.19[d]	68.8[d]	60[d]
6j	*t*-Bu	(B)	3.93	75.9	20

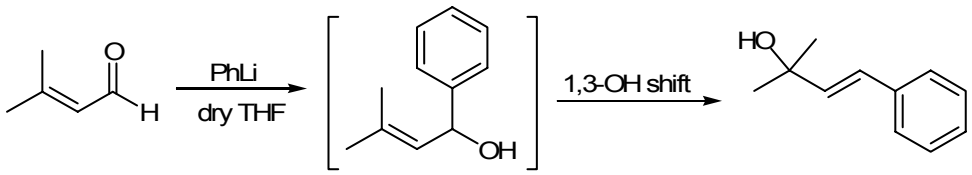
***Table 3.5*:** Synthesis of allylic alcohols **6b-j**: [a] Method (A) correspond to the use of Grignard reagent, while method (B) correspond to the use of organolithium compounds in synthesis. [b] The values correspond to the carbinol carbon (**C**H-OH) in $CDCl_3$. [c] Two diastereomers in ratio 53:47 are formed. [d] Two diastereomers in ratio 1:1 are formed.

The reaction of prenylmagnesium bromide (the potential reagent used for "isoprene unit" synthesis) with **25** in dry ether proceeds through a S_N2' mechanism to afford the natural C-10 terpene *artemesia alcohol* **6k** (***Scheme 3.15***). Confirmation of the structure of **6k** was achieved by comparison with literature data as well as NMR analyses. [139]



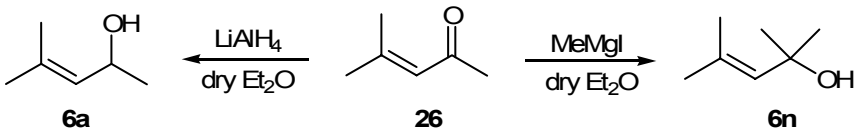
***Scheme 3.15*:** Synthesis of *artemesia alcohol* **6k**.

Unexpectedly, treatment of **25** with phenyllithium in dry THF afforded the conjugated tertiary allylic alcohol **6m** rather than the desired secondary allylic alcohol **6l** (***Scheme 3.16***). The formation of **6m** is explained in terms of the acid-catalyzed 1,3-hydroxy group shift, in the work-up step or induced by the acidic nature of the silica gel during purification.[140] The driving force for the rearrangement is the formation of the more conjugated (and hence more stable) tertiary allylic alcohol **6m**. The chemical structure of **6l** is established by the two olefinic signals resonating at δ = 6.22, 6.45 ppm with a coupling constant of 16.1 Hz indicating *trans* configuration. The two methyl groups are magnetically equivalent and appear as singlet at δ = 1.29 Hz, the absence of both the carbinol proton in ^{1}H-NMR and the carbinol carbon in DEPT also supports this structure.

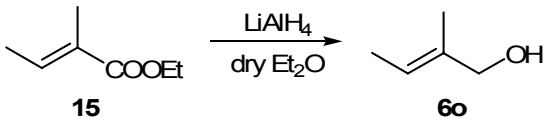


Scheme 3.16

Another two allylic alcohols were prepared from the commercially available mesityl oxide **26**. Reduction of **26** with lithium aluminum hydride in ether results in the formation of mesitylol **(6a)**; on the other hand, treatment of **26** with methyl magnesium iodide gives the tertiary allylic alcohol **6n** (***Schemes 3.17***). Similarly, the reduction of ethyl tiglate **(15)** affords the alcohol **6o** in good yield (***Schemes 3.18***). All compounds show identical analytical data consistent with that reported in literature.

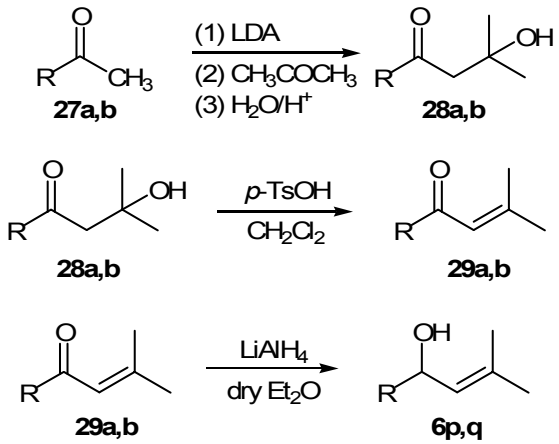


***Scheme 3.17*:** Syntheses of **6a** and **6n** from mesityl oxide **(26)**.



***Scheme 3.18*:** Synthesis of **6o** from ethyl tiglate **15**.

Starting from methyl ketones, another approach was optimized for the synthesis of allylic alcohols in three steps. Firstly, the methyl ketones are converted to an aldol by treatment with LDA and acetone, followed by dehydration of the aldol by *p*-toluenesulfonic acid in methylene chloride to give the corresponding α,β-unsaturaed carbonyl compound which is finally reduced with lithium aluminum hydride in dry ether to afford the allylic alcohol (***Scheme 3.19***).



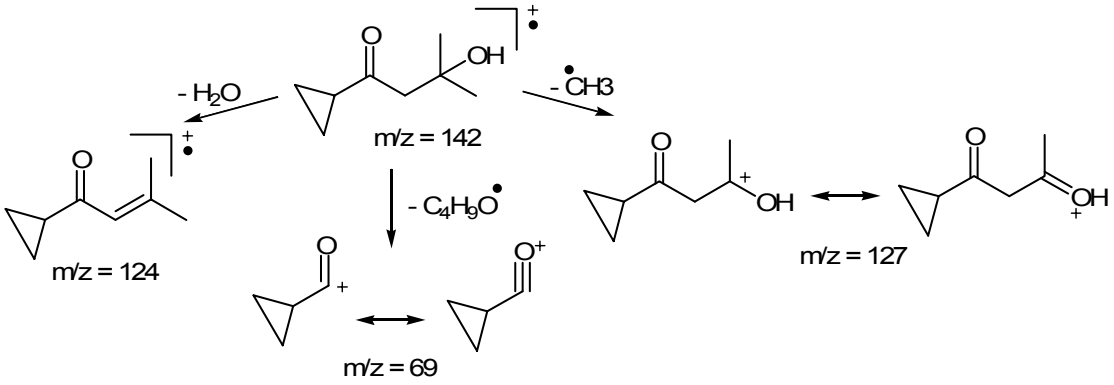
***Scheme 3.19*:** Synthesis of allylic alcohols **6p,q**.

The two aldol compounds **28a,b** were synthesized from the first step by addition of the methyl ketones **27a,b** to acetone. The constitution of the aldol products was based on spectroscopic methods (NMR, IR and mass spectra) as well as elemental analysis. The most characteristic signal in ^{1}H-NMR for **28a,b** is the signal of the methylene group (α to the carbonyl group) appearing as singlet. ***Table 3.6*** shows the most significant signals in ^{1}H- as well as in ^{13}C-NMR.

Compound	R	Cq-OH (ppm)	C=O (ppm)	$\underline{CH_2}CO$ (ppm)		Yield (%)
				^{1}HNMR	^{13}C-NMR	
28a	*c*-Pr	69.3	212.4	2.59	53.6	56
28b	*c*-Hex	69.5	216.4	2.55	50.7	55

***Table 3.6*:** Characteristic signals of **28a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

As a representative example, compound **28a** shows in the IR spectrum the characteristic band stretching at 3600-3200 cm^{-1} corresponding to the hydrogen-bonded OH group and the band corresponding to the carbonyl group at 1687 cm^{-1}. Its mass spectrum fragmentation pattern is also consistent with the structure (***Scheme 3.20***).



***Scheme 3.20*:** Fragmentation pattern of **28a.**

The dehydration of the aldol products **28a,b** led to the formation of the corresponding α,β-unsaturated carbonyl compounds (Michael systems) **29a,b** in good yield and high purity. The structure of the products is confirmed by NMR. The characteristic olefinic carbons as well as the carbonyl carbon chemical shifts in the ^{1}H- and ^{13}C-NMR are shown in ***Table 3.7***.

Compound	R	C=O (ppm)	Cq= (ppm)	CH= (ppm)		Yield (%)
				^{1}HNMR	^{13}C-NMR	
29a	*c*-Pr	200.5	153.9	6.13	124.2	82
29b	*c*-Hex	204.0	155.1	6.06	122.9	81

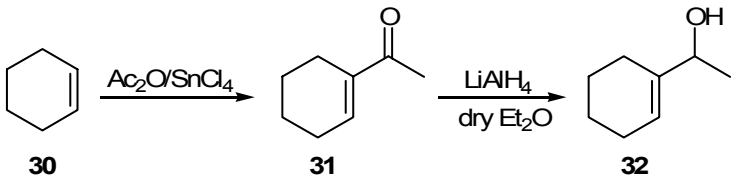
***Table 3.7*:** Characteristic signals in ^{1}H- and ^{13}C-NMR of **29a,b** (in $CDCl_3$).

Reduction of the enones **29a,b** with $LiAlH_4$ in ether afforded the corresponding allylic alcohols **6p,q** in good purity. Confirmation of the structure was based on NMR. The chemical shifts of the characteristic olefinic carbons as well as the carbinol carbon (**CH**-OH) in the ^{1}H- and ^{13}C-NMR are shown in ***Table 3.8***.

Compound	R	CH= (ppm)	Cq= (ppm)	CH-OH (ppm)		Yield (%)
				^{1}HNMR	^{13}C-NMR	
6p	*c*-Pr	126.5	135.0	3.76	72.5	67
6q	*c*-Hex	126.7	135.2	4.0	72.9	79

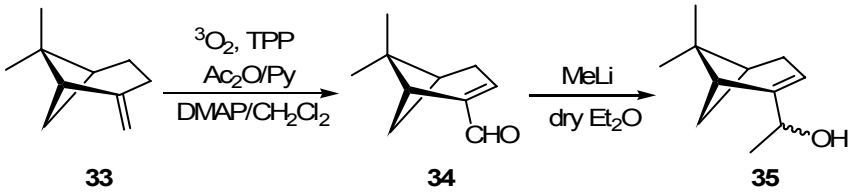
***Table 3.8*:** Characteristic signals in ^{1}H- and ^{13}C-NMR of **6p,q** (in $CDCl_3$).

The acetylation of cyclohexene **(30)** with acetic anhydride in presence of stannic chloride results in the formation of 1-acetylcyclohexene **(31)**, which was reduced with lithium aluminum hydride in dry ether to afford the allylic alcohol **32** in high purity showing spectroscopic data identical to the reported in literature (***Scheme 3.21***).



Scheme 3.21

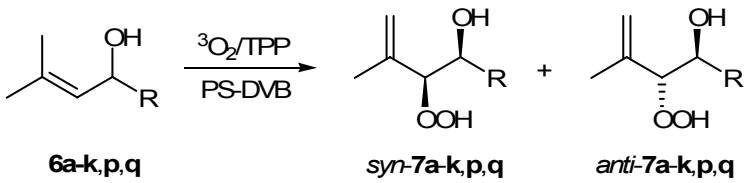
The terpene myrtenal **(34)** was synthesized by singlet-oxygen photooxygenation of β-pinene **(33)** in presence of acetic anhydride and pyridine / DMAP as bases. The reaction proceeds through the formation of the acetylated allylic hydroperoxide which eliminates acetic acid under the basic conditions to give **34**. The reaction of **34** with methyl lithium results in the formation of the allylic alcohol **35** in 2:3 diastereomeric mixture (***Scheme 3.22***). The allylic alcohol **35** shows in ^{1}H-NMR the characteristic signal corresponding to the proton of the carbinol carbon (**CH**-OH) at δ = 4.05 and in ^{13}C-NMR at 69.7/70.2 ppm.



Scheme 3.22

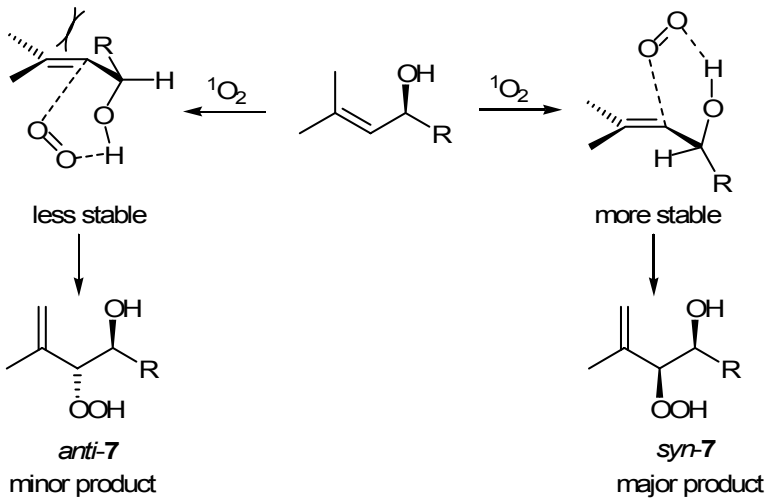
3.5 Solvent-Free Photooxygenation Reactions of Allylic Alcohols

The photooxygenation of a series of allylic alcohols **6a-k**,**p**,**q** using PS-DVB polymer matrix doped with adsorbed porphyrin sensitizer (TPP or TTP) resulted in the formation of a *syn* (or *threo*) and *anti* (or *erythro*) diastereomeric mixture of the *vic*-hydroperoxy alcohols in good yields (***Scheme 3.23***). The β-hydroperoxy alcohols are stable at r.t. and can be kept in the refrigerator for weeks without decomposition.



***Scheme 3.23*:** Solvent-free photooxygenation of the allylic alcohols **6a-k,p,q** using TPP embedded in PS-DVB matrix.

It is found that the diastereoselectivity of the ene reaction using the commercial PS-DVB with physically adsorbed sensitizer (***Table 3.9***) showed similar values to that obtained with the polymer-bound sensitizers, TSP-S-DVB or PP-S-DVB (somewhat higher with the polymer-bound sensitizers, ***Table 3.1***), accounting for the aforementioned intermolecular hydrogen-bonding between the highly concentrated substrate molecules in both polymer systems. The reaction diastereoselectivity as well as regiochemistry is dictated by the steering effect of the hydroxy group discovered by Adam and coworkers.[37,141] The 1,3-allylic strain with the stereogenic center provides stereodifferentiation between the two π-faces. This 1,3-allylic strain constrains the hydroxy group to be conformationally fixed on one face of the double bond and hence capable of directing the incoming enophile ($^1O_2$) by hydrogen bonding leading to preferential formation of the major *syn*-diastereomer (***Scheme 3.24***). Comparison of the chemical yields and the diastereoselectivities in the solvent-free photooxygenation reaction of the allylic alcohols **6a-k**,**p**,**q** is shown in ***Table 3.9***.



***Scheme 3.24*:** Hydroxy group directing the diastereoselectivity of $^1O_2$ attack.

Compund	R	d.r.[a] *syn*:*anti*	Yield (%)
7a	Me	75 : 25	83
7b	Et	77 : 23	72
7c	*i*-Pr	81 : 19	72
7d	*n*-Pr	79 : 21	78
7e	$CH_2CH{=}CH_2$	75 : 25	69
7f	$CH(Me)CH{=}CH_2$	d.l.	63
7g	*n*-Bu	79 : 21	78
7h	*i*-Bu	80 : 20	77
7i	*sec*-Bu	d.l.	73
7j	*t*-Bu	78 : 22	59
7k	$C(Me)_2CH{=}CH_2$	72 : 28	73
7p	*c*-Pr	62 : 38	80
7q	*c*-Hex	88 : 12	65

***Table 3.9*:** The photooxygenation of the allylic alcohols **6a-k,p,q** using solvent-free approach with PS-DVB copolymer. [a] The diastereoselectivity is determined from the integration of the characteristic signals in the NMR of the crude reaction mixture. d.l.: Four diastereomers are obtained which are discussed later.

The chemical constitution of these hydroxy allylic hydroperoxides was based on ^1H- and ^{13}C-NMR analysis. The literature-known hydroperoxide **7a** was confirmed by comparison with literature data.[37a] Both *syn* and *anti* diastereomers show mostly a pronounced difference in the chemical shifts of their characteristic signals (***Table 3.10***). The proton of the hydroperoxy carbon (C**H**-OOH) resonates in the range from 4.0 to 4.40 ppm and always appears as doublet

due to vicinal coupling with the adjacent carbinol proton (C**H**-OH). The latter resonates more up-field between 3.0 and 4.0 ppm and its multiplicity is variable depending on each compound. The shift of the double bond as a result of the ene reaction leads also to the formation of a vinylic methyl group resonating between 1.60 and 1.80 ppm and appearing as singlet (in some cases appears as multiplet with very small coupling constant (^4J) due to the allylic coupling with the two olefinic protons).
Assignment of the relative configuration of the major diastereomer (*syn*) was based on X-ray analysis achieved by compound **7j** (*vide supra*), as well as by chemical correlation to 1,2,4-trioxanes derived from the BF_3-peroxyacetalization reaction of the β-hydroperoxy alcohols with carbonyl compounds (*vide infra*).

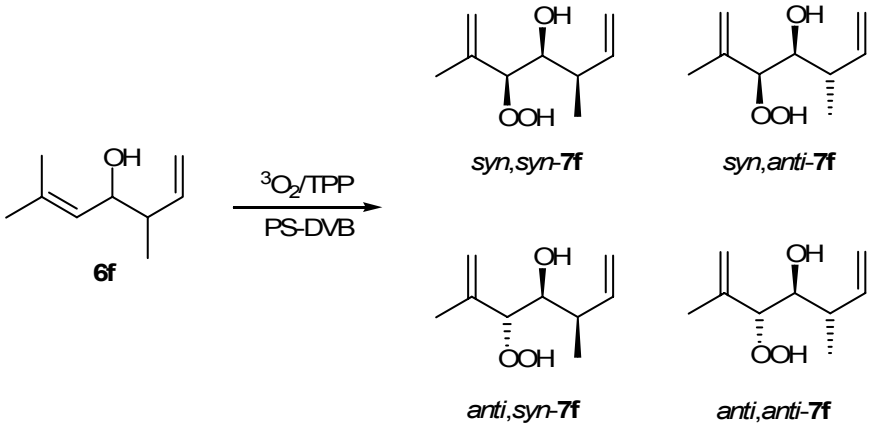
An interesting trend is observed on comparing the chemical shifts of the protons attached to both the hydroperoxy carbon (C**H**-OOH) and the carbinol carbon (C**H**-OH) for each diastereomeric pair, where these protons resonate always more up-field in the *syn*-diastereomer than in the *anti*-isomer (exception is **7k** where the *syn*-diastereomer resonate more down-field probably due to more the effective deshielding for both protons in *syn*-**7k** rather than the *anti*-isomer by the bulky tertiary alkyl groups attached to the stereogenic center).

Compound	**R**	**CH-OOH**		**CH-OH**	
		^{1}H-NMR	**^{13}C-NMR**	**^{1}H-NMR**	**^{13}C-NMR**
***syn*-7a**	Me	4.08	94.8	3.80	67.1
***anti*-7a**	Me	4.25	92.1	3.94	67.0
***syn*-7b**	Et	4.15	93.4	3.55	71.8
***anti*-7b**	Et	4.30	91.4	3.69	72.2
***syn*-7c**	*i*-Pr	4.28	92.0	3.49	74.5
***anti*-7c**	*i*-Pr	4.34	89.9	3.51	74.2
***syn*-7d**	*n*-Pr	4.13	93.8	3.63	70.3
***anti*-7d**	*n*-Pr	4.29	91.6	3.78	70.5
***syn*-7e**	$CH_2CH=CH_2$	4.17	92.8	3.71	70.0
***anti*-7e**	$CH_2CH=CH_2$	4.31	91.0	3.82	69.9
***syn*-7f**	$CH(Me)CH=CH_2$	4.12/4.22	90.8/91.3	3.50/3.52	73.1/73.4
***anti*-7f**	$CH(Me)CH=CH_2$	n.s.	89.2/89.5	n.s.	72.5/72.5
***syn*-7g**	*n*-Bu	4.15	93.7	3.64	70.6

Compound	R	CH-OOH		CH-OH	
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR
***anti*-7g**	*n*-Bu	4.30	91.7	3.75	70.7
***syn*-7h**	*i*-Bu	4.09	94.2	3.68	68.7
***anti*-7h**	*i*-Bu	4.26	92.0	3.83	68.9
***syn*-7i**	*sec*-Bu	4.15[a]	93.4/93.5	3.60[a]	70.8/70.6
***anti*-7i**	*sec*-Bu	4.29[a]	92.3/92.4	3.73[a]	70.9/71.1
***syn*-7j**	*t*-Bu	4.33	88.0	3.28	78.6
***anti*-7j**	*t*-Bu	4.33	90.1	3.28	76.1
***syn*-7k**	$C(Me)_2CH=CH_2$	4.28	87.5	3.34	77.8
***anti*-7k**	$C(Me)_2CH=CH_2$	4.27	89.8	3.26	75.1
***syn*-7p**	*c*-Pr	4.29	93.3	3.07	75.0
***anti*-7p**	*c*-Pr	4.41	91.2	3.14	75.6
***syn*-7q**	*c*-Hex	4.24	91.0	3.43	74.3
***anti*-7q**	*c*-Hex	4.29	89.2	n.s.	n.s.

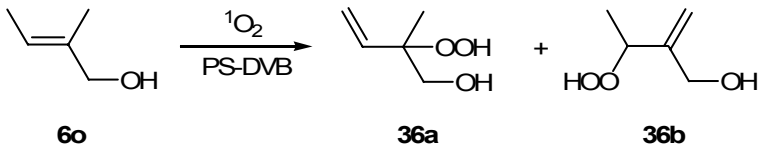
***Table 3.10*:** Characteristic signals of the hydroxy allylic hydroperoxides **7a-k**,**p**,**q** (in $CDCl_3$).
[a] Both diastereomers have the same chemical shift.
n.s.: Not seen due to overlap with other signals.

The photooxygenation of the allylic alcohols **6f**,**i** (possessing two stereogenic centers) afforded four diastereomers of the β-hydroxy allylic hydroperoxides, two correspond to the major products (assigned as *syn*,*syn*-**7f,i** and *syn*,*anti*-**7f,i**) and two to the minors (assigned as *anti*,*syn*-**7f/i** and *anti*,*anti*-**7f/i**). As a representative example, the photooxygenation of **6f** is depicted in ***Scheme 3.25***. The diastereomeric ratio of both major products *syn*,*syn*-**7f** and *syn*,*anti*-**7f** is about 1:1 and that of the *anti*,*syn*-**7f** and *anti*,*anti*-**7f** minor isomers is also about 1:1. However, both major diastereomers constitute around 85 % of the product mixture (determined from ^{13}C-NMR). Similar behavior is also found in the photooxygenation of **6i** that results in the formation of both diastereomeric major products *syn*,*syn*-**7i** and *syn*,*anti*-**7i** in about 83 % from the product mixture.



***Scheme 3.25*:** Solvent-free photooxygenation reaction of **6f**.

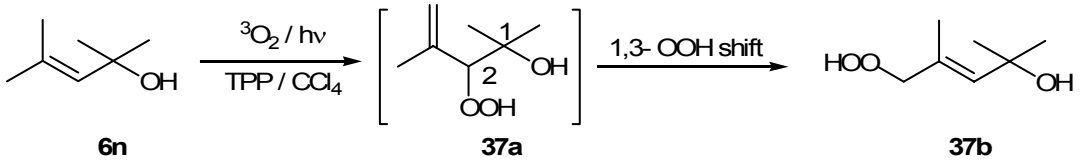
Unlike the photooxygenation reaction of ethyl tiglate **15** proceeding with excellent regioselectivity (due to the geminal effect), the solvent-free photooxygenation of the allylic alcohol derived from it **6o** proceeds with very poor regioselectivity giving the allylic hydroperoxy alcohols **36a**,**b** in a ratio about 53:47, respectively (***Scheme 3.26***). This poor regioselectivity as well as the inactivity of the carbinol protons (C**H**$_2$-OH) towards abstraction by $^1O_2$ derives from the previously discussed *cis*-effect. The chemical constitution of both isomers was evaluated by NMR analysis. Compound **36b** shows a doublet signal at 1.25 ppm having integration of three protons which correspond to the methyl group adjacent to a methine carbon, the proton on the hydroperoxy carbon (C**H**-OOH) resonates as quartet at 4.59 ppm. Also, in ^{13}C-NMR the hydrperoxy carbon appears at 82.9 ppm. Compound **36a** shows two diastereomeric methylene protons on the carbinol carbon that resonate at different chemical shifts (3.57 and 3.70 ppm), showing geminal coupling of 12 Hz and appearing as doublet of doublet (due to another long-range coupling with the CH of the double bond, J = 1.62 Hz) and doublet, respectively. The hydroperoxy carbon resonates at 84.6 ppm in ^{13}C-NMR.



***Scheme 3.26*:** Solvent-free photooxygenation reaction of **6o**.

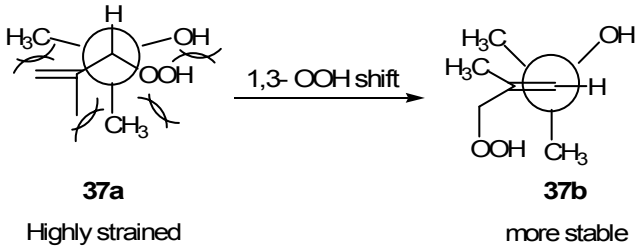
In contrast to the photooxygenation of **6a** affording the *vic*-hydroperoxy alcohol **7a** (*vide supra*), the photooxygenation of the allylic alcohol **6n** in tetrachloromethane gives the 1,4-hydroperoxy alcohol **37b** (***Scheme 3.27***). The formation of **37b** is explained by 1,3-allyic shift of the hydroperoxy group.[142] It is well known that allylic hydroperoxides rearrange by a free-

radical mechanism in dilute, non-polar solutions and produce an equilibrium mixture of allylic isomers.[143] That the photooxygenation reaction afforded no **37a** shows that steric effects strongly influence the relative stabilities of the hydroperoxides. The presence of the steric strain on the C_1-C_2 bond in **37a** (five substituents) is the driving force favoring rearrangement of **37a** to **37b** where this steric strain is released (***Scheme 3.28***). Another argument for the higher stability of **37b** stem from the presence of a trisubstituted double bond in **37b** compared to the disubstituted double bond in **37a**.



6n **37a** **37b**

***Scheme 3.27*:** Photooxygenation of **6n**.

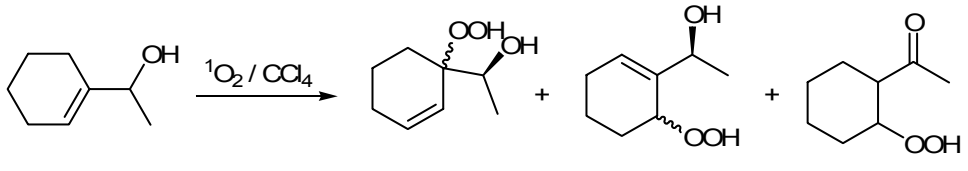


37a **37b**

Highly strained more stable

***Scheme 3.28*:** Newmann projections of **37a** and **37b**.

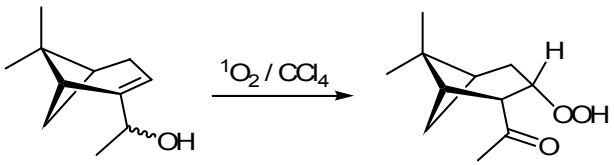
In order to examine the reactivity of the allylic alcohols **32,35** towards $^1O_2$ and identify the product pattern, an analytical scale photooxygenation reaction in CCl_4 was performed in the oxygen-uptake apparatus. The allylic alcohol **32** reacts with $^1O_2$ to afford a complex product mixture (***Scheme 3.29***). From the ^{13}C-NMR of the reaction product one can assume the presence of two diastereomeric mixtures (*syn* and *anti*) of both the *vic*-hydroperoxy alcohols **32a** as well as the 1,3-hydroxy hydroperoxide **32b** as indicated by the presence of eight signals in the region from 69-85 ppm corresponding to four carbinol carbons and four hydroperoxy carbons. This is further supported by the eight signals in the region 122-138 ppm that correspond to the four double bonds in these compounds. The presence of another small signal resonating at 209 ppm may be also related to the hydroperoxy ketone **32c** existing in minor amount in the product mixture.



32 **32a** **32b** **32c**

***Scheme 3.29*:** Photooxygenation of **32**.

The allylic alcohol **35** reacts slowly with singlet oxygen in CCl_4 where the oxygen-gas uptake by **35** is about 20 times slower than that of **6b** under the same photooxygenation conditions accounting for the steric effects in $^1O_2$ reactions. The reaction is assumed to furnish **35a** as indicated by a small signal at 207.2 ppm corresponding to the carbonyl group, and the signal at 75.7 ppm indicating the hydroperoxy carbon. The singlet oxygen is expected to attack from the less hindered side due to the steric factors with the bulky bridge having the two geminal methyl groups (***Scheme 3.30***).



35 **35a**

***Scheme 3.30*:** Photooxygenation of **35**.

3.6 Deuterium Isotope Effects on the Diastereoselectivity of $^1O_2$ Ene Reaction with Allylic Alcohols

In order to explore the role of hydrogen bonding between the attacking singlet oxygen and the hydroxy group in dictating the facial selectivity of the ene reaction with allylic alcohols, I also studied the effect of exchanging the OH group by an OD group in the allylic alcohols. Different photooxygenation runs were carried out in the oxygen-uptake apparatus using identical concentrations of the substrate **6a** in pure tetrachloromethane as well as tetrachloromethane with increasing amounts of methanol or methanol-D_4, and the differences in the oxygen-gas uptake rates as well as the diastereoselectivities of the reaction were compared (***Figure 3.8***). Three points can be addressed:

(a) For identical methanol percentages, the initial rates of the oxygen-gas uptake are always higher in case of methanol-D_4 / CCl_4 than in the methanol / CCl_4 solvent mixtures. This is expected due to the higher singlet oxygen lifetimes in presence of the deuterated *versus* non-deuterated solvents (the solvent-quenching rate constant of singlet oxygen increases by more than 25 folds on changing from methanol-D_4 to methanol).[144] Also, the initial rates of the oxygen-gas uptake are always decreasing with increasing the percent of methanol-D_4 or methanol in CCl_4, since both solvents are more effective $^1O_2$-quenchers than CCl_4.

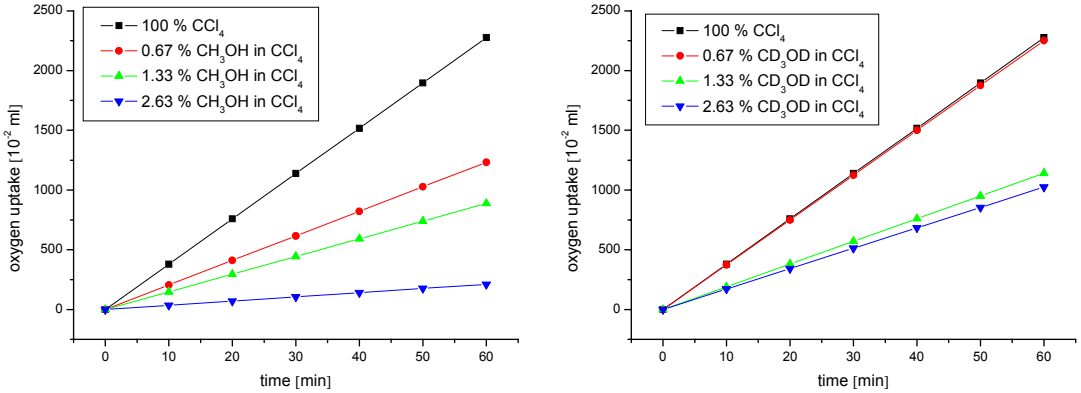


***Figure 3.8*:** Oxygen-uptake rates by **6a** in CCl_4 with increasing amount of CH_3OH (left), CD_3OD (right).

(b) Since the addition of methanol or methanol-D_4 (hydrogen bond acceptors and donors) decrease the steering effect of the substrate hydroxy group by intermolecular hydrogen bonding, lower diastereoselectivities were observed with increasing the amount of these solvents.

(c) Since the hydrogen bonding is expected to play a decisive factor in controlling the diastereoselectivity, we expect that it can be influenced by H- versus D-bonding interactions. From the ***Figure 3.9*** we can see that the diastereoselectivities in the presence of deuterated methanol is always lower than in the presence of non-deuterated methanol, this is also indicated by comparison of the diastereoselectivities in pure tetrachloromethan *versus* CH_3OH and CD_3OD (***Scheme 3.31***). This derives from competitive solvent-induced deactivation of the hydrogen bonding of the allylic hydroxy group with $^1O_2$ by the more effective OD *versus* OH bonding.[145]

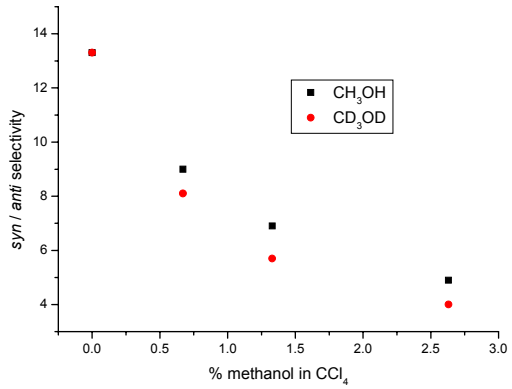
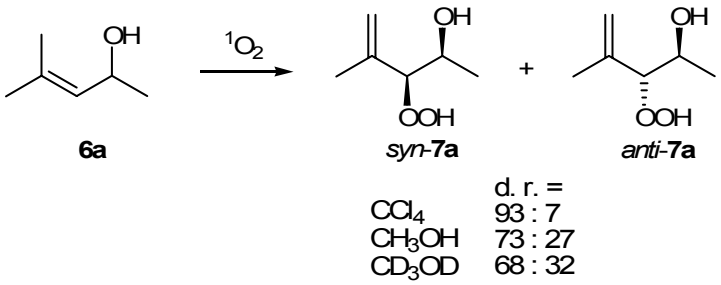


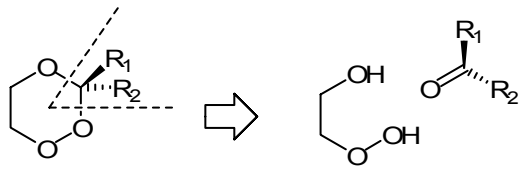
***Figure 3.9*:** Solvent dependence of the *syn*/*anti* ratio in the singlet oxygen ene reaction with **6a.**



***Scheme 3.31*:** Ene reaction of **6a**: solvent effect on *syn*/*anti*-diastereoselectivity.

3.7 Synthesis of 1,2,4-Trioxanes

For the synthesis of the 1,2,4-trioxane skeleton, a Lewis-acid catalyzed peroxyacetalization reaction of β-hydroperoxy alcohols with carbonyl compounds was developed (***Scheme 3.32***).



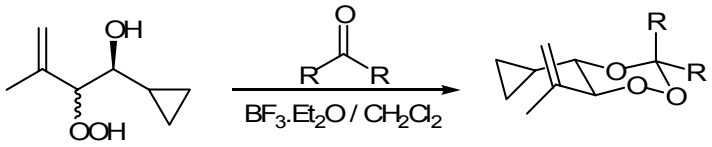
Scheme 3.32

This approach is especially attractive since sensitizer-free β-hydroperoxy alcohols are available by our convenient solvent-free $^1O_2$-photooxygenation reaction of the easily accessible allylic alcohols as substrates. Furthermore, this way enables the introduction of different functional groups at the level of the nonperoxidic starting materials. Catalytic amounts of borontrifluoride etherate in dry CH_2Cl_2 or dry Et_2O as solvent turned out to be the optimal condition for efficient condensation reaction of the *vic*-hydroxy hydroperoxides with aldehydes, ketones, acetals and orthoesters resulting in the formation of wide variety of the target 1,2,4-trioxanes. BF_3 is not only advantageous by its catalytic efficiency but also it can be easily removed in the work-up step and it tolerates the labile peroxidic linkage. Using the intermolecular peroxyacetalization reaction we were able to vary the substituents at C-3 and C-5 in the 1,2,4-trioxane unit. Since all the β-hydroxy hydroperoxides are synthesized as racemic mixtures, all the 1,2,4-trioxanes derived from them are also racemic mixtures.

3.7.1 Derived from 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol

3.7.1.1 By peroxyacetalization reaction with symmetric ketones

The BF_3-catalyzed peroxyacetalization reaction of the *vic*-hydroperoxy alcohol **7p** with different symmetric ketones in CH_2Cl_2 resulted in the formation of the corresponding 1,2,4-trioxanes **38-41** (***Scheme 3.33, Table 3.11***). Thin layer chromatography revealed the disappearance of the spot corresponding to the hydroperoxy alcohol starting material and the appearance of a new spot with higher R_f-value (indicating a less polar product). The products were chromatographically purified and their chemical structures were confirmed by ^{1}H- as well as ^{13}C-NMR, elemental analysis, IR, mass spectrometry and X-ray analysis.



7p **38-41**

Scheme 3.33

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
38	adamantane		3.33	73.0	4.38	87.9	105.0	7
39	$(CH_2)_2CO(CH_2)_2$		3.30	74.6	4.43	87.6	101.1	17
40	CH_3	CH_3	3.24	74.8	4.35	87.4	102.6	41
41	Et	Et	3.28	73.4	4.33	87.2	105.8	10

***Table 3.11*:** Characteristic signals of **38-41** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

As representative example, compound **38** shows in ^{1}H-NMR two highly up-field multiplets (δ = 0.40, 0.78 ppm) corresponding to the two methylene and the methine protons of the cyclopropyl group, respectively. The signals related to the adamantane protons are found as broad multiplet at δ = 1.50-2.19 ppm. Surprisingly, one of the protons of the adamantane residue is more deshielded by the effect of the ring oxygen atoms and consequently resonates more downfield as a broad signal (at about 2.82 ppm). The previous behavior was observed for all synthesized 1,2,4-trioxanes possessing adamantane subunit (***Figure 3.10***). A multiplet with small coupling constants absorbs at 1.79 ppm that corresponds to the methyl of the

isopropenyl group. The splitting of this methyl group is ascribed to the allylic coupling ($^4J_{HH}$) with the protons of the olefinic methylene group (a behavior often seen in the prepared trioxanes). The proton of the peroxy carbon (H-6) resonates at 4.38 ppm with doublet multiplicity ($^3J_{HH}$ = 9.40 Hz) due to vicinal coupling with the neighbouring H-5. The doublet of doublet at 3.33 ppm is related to H-5 that couples with H-6 ($^3J_{HH}$ = 9.40 Hz) and with the CH proton of the cyclopropyl group ($^3J_{HH}$ = 7.35 Hz). The olefinic signal is absorbing at 5.04 ppm as multiplet due to the small olefinic geminal coupling as well as the allylic coupling ($^4J_{HH}$) with the methyl group. In ^{13}C-NMR the peroxyacetal carbon (OO**C**O or C-3) represent the most characteristic signal used to confirm the formation of the 1,2,4-trioxane unit (***Figure 3.10***). Complete assignment of the carbon atoms and their multiplicity was confirmed by DEPT as well as 2D-NMR experiments. The most characteristic signals of the products **38**-**41** in ^{1}H- and ^{13}C-NMR are summarized in ***Table 3.11***.

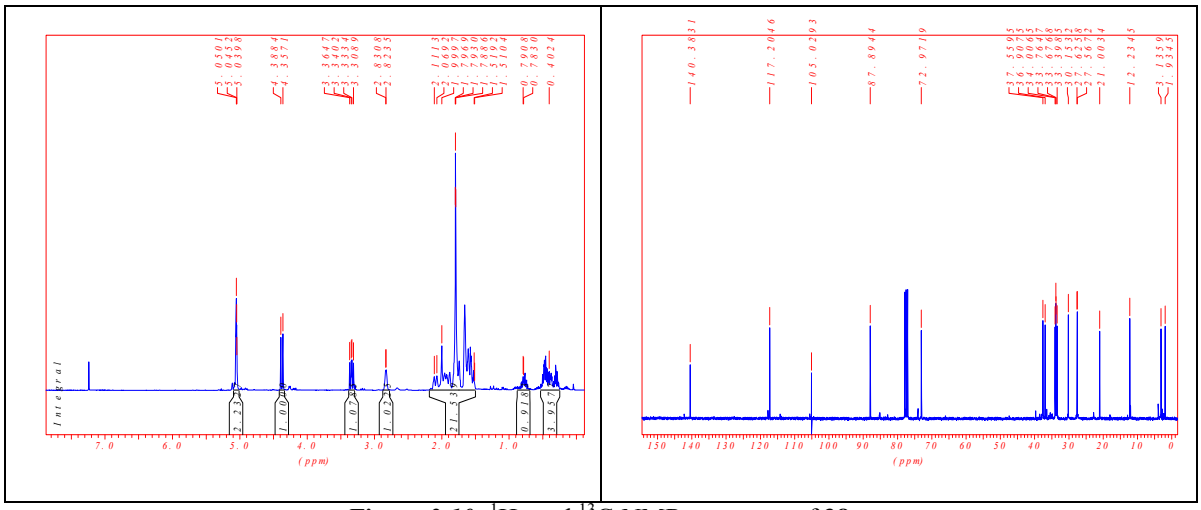
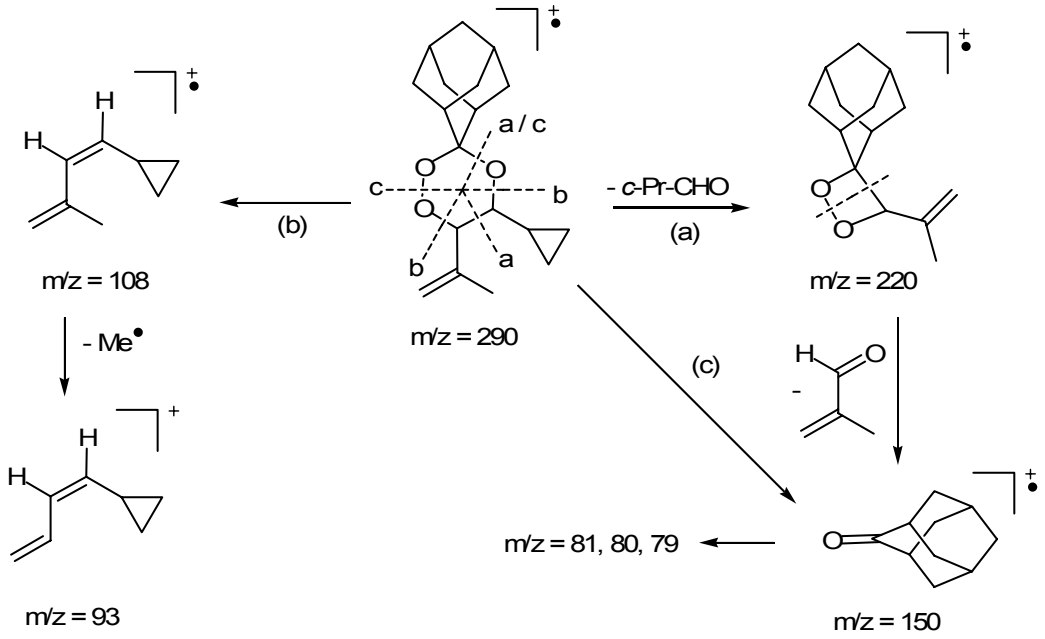


***Figure 3.10*:** ^{1}H- and ^{13}C-NMR spectrum of **38**.

From the IR spectrum, the absence of the broad band corresponding to the OH groups (between 3200 and 3600 cm^{-1}) is an indication for the peroxyacetalization reaction and disappearance of the *vic*-hydroperoxy alcohol starting material. Some of the characteristic IR bands (in cm^{-1}) of the 1,2,4-trioxane **38** are at 3079 (olefinic CH), 2931 (aliphatic CH), 1653 (isolated C=C), 1112, 1079, 1025 (C-O) and 926, 910 (O-O). The peaks obtained in the mass spectrum of compound **38** are depicted in ***Scheme 3.34***.



***Scheme 3.34*:** Fragmentation pattern of **38**.

The relative configuration of compound **38** was unambiguously established by X-ray analysis (***Figure 3.11***).

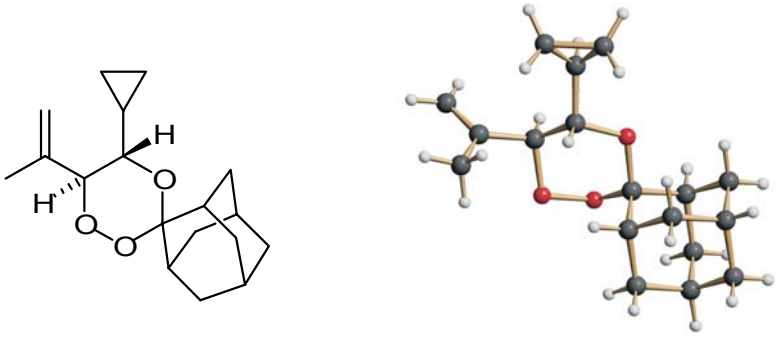


***Figure 3.11*:** X-ray structure of **38**.

The Karplus equation[146] was also used to deduce the relative configurations of the synthesized 1,2,4-trioxanes. According to Karplus, the vicinal coupling constant (^3J) between two *trans*-diaxial vicinal protons (having a dihedral angle in the vicinity of 180°) is expected to be in the range 9-12 Hz (***Figure 3.12***). Obviously, the two protons on C-5 and C-6 in **38** have a *trans*-diaxial orientation with calculated coupling constant of 9.4 Hz. By analogy, since the other 1,2,4-trioxanes show similar coupling constants, they must adopt the same configuration at the C-5,C-6 bond i.e. *trans*-diaxial configuration. It is also noteworthy to mention that that formation of the *trans* configuration is also expected since it comes from the major *syn*-hydroperoxy alcohol. In all cases, no *cis*-1,2,4-trioxanes (that may arise from the reaction with the minor *anti*-hydroxy allylic hydroperoxide) were observed in the purified product.

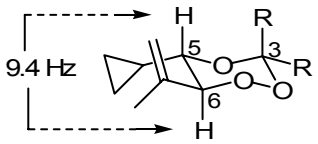
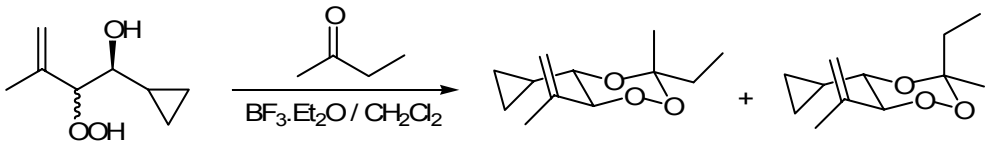


Figure 3.12

3.7.1.2 By peroxyacetalization reaction with asymmetric ketones

The use of asymmetric ketones for the condensation reaction with hydroperoxy alcohols leads to the formation of a third stereogenic center at C-3. As an example, the peroxyacetalization of **7p** with 2-butanone resulted in a 72:28 mixture of diastereomeric 1,2,4-trioxanes **42a** and **42b**, respectively (***Scheme 3.35***). The formation of **42a** and **42b** was proven by the presence of the peroxyacetal carbon resonating at 103.9, 104.9 ppm in ^{13}C-NMR. ***Table 3.12*** summarizes the main differences in ^{1}H- and ^{13}C-NMR characteristic signals for **42a** and **42b**. Both 1,2,4-trioxanes have a 5,6-*trans* configuration since the coupling constant between the protons on C-5 and C-6 in both cases is 9.4 Hz, which is consistent value with a dihedral angle near to 180°. The major diastereomer is assumed to be **42a** since it is the more thermodynamically stable isomer having the ethyl group in equatorial position.



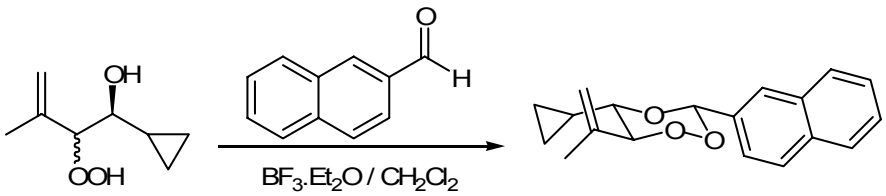
7p **42a** **42b**

Scheme 3.35

No.	OCH		OOCH		OCOO	Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
42a	3.34	73.6	4.31	87.6	103.9	62
42b	3.16	74.5	4.34	87.1	104.9	

***Table 3.12*:** Characteristic signals of **42a** and **42b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$)

3.7.1.3 By peroxyacetalization reaction with aldehydes



7p **43**

Scheme 3.36

The peroxyacetalization reaction of **7p** with 2-naphthaldehyde afforded the 1,2,4-trioxane **43** in moderate yield (***Scheme 3.36***). The chemical structure of **43** is based on NMR, IR, elemental analyses and HRMS. The IR spectrum shows the absorption bands at 3088 cm^{-1} (vinylic CH), 2968 cm^{-1} (aliphatic CH), 1647 cm^{-1} (isolated C=C), 1603 cm^{-1} (aromatic C=C); 1126, 1071 cm^{-1} (C-O), 904, 859 cm^{-1} (O-O). The proton of the peroxyacetal carbon appears in ^{1}H-NMR as singlet at 6.31 ppm, whereas this carbon appears in ^{13}C-NMR at 104.0 ppm. The all-equatorial relative configuration of **43** at C-3, C-5 and C-6 was undoubtedly assigned by X-ray analysis (***Figure 3.13***). The protons H-5 and H-6 show a *trans* diaxial-configuration ($^{3}J_{HH}$ = 9.1 Hz) and the 2-naphthyl substituent is located as expected in an equatorial position (thermodynamically favored) *cis* to the cyclopropyl group.

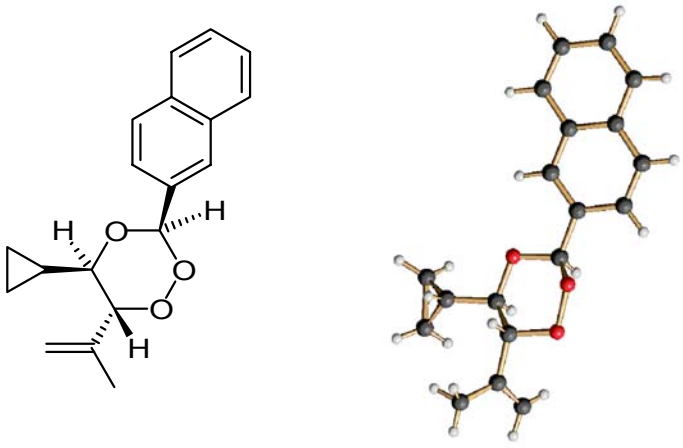
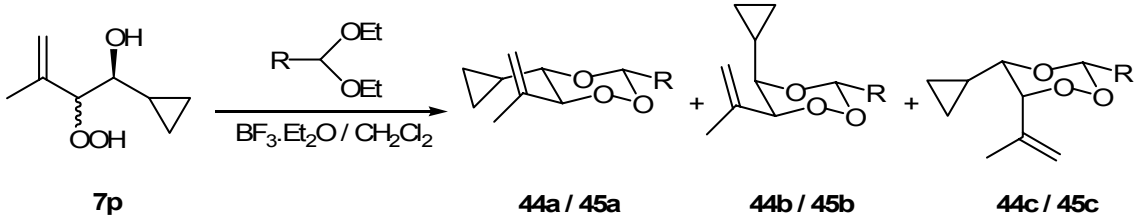


***Figure 3.13*:** X-ray structure of **43**.

3.7.1.4 By peroxyacetalization reaction with acetals

The peroxyacetalization reaction with acetals is highly advantageous over using the corresponding aliphatic aldehydes since in the latter case trimerization of the aldehydes to 1,3,5-trioxanes is a competing reaction (*vide infra*).

Treatment of **7p** with acetaldehyde diethylacetal or propionaldehyde diethylacetal afforded in each case three 1,2,4-trioxanes as estimated by the presence of sets of three signals in ^{13}C-NMR for almost all characteristic carbons in both reaction (***Scheme 3.37***, ***Table 3.13***).



7p **44a / 45a** **44b / 45b** **44c / 45c**

Scheme 3.37

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
44a	CH_3	3.03	80.6	4.39	87.3	5.26	101.1	26
44b,c	CH_3	3.10[a]	78.7/81.4	4.05[a]	83.5/84.0	5.67[a]	95.9/101.4	
45a	Et	3.08	80.3	4.41	87.6	5.08	105.1	21
45b,c	Et	3.10[a]	78.6/81.4	4.07[a]	83.8/84.3	5.48[a]	99.9/105.4	

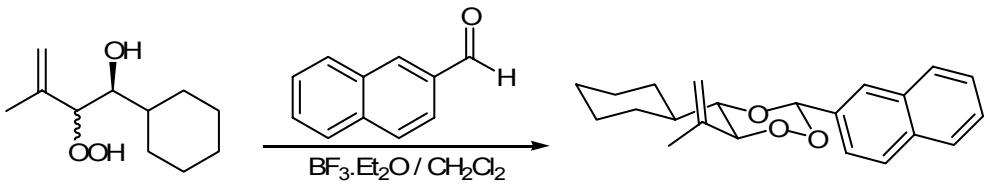
***Table 3.13*:** Characteristic signals of **44a-c** and **45a-c** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] Both diasetereomers have the same chemical shift.

Elucidation of the relative configuration of the representative example **45a,b,c** by ^{1}H-NMR revealed the presence of two characteristic doublets related to H-6 due to vicinal coupling with H-5. The doublet corresponding to the major product has a coupling constant of 9.1 Hz indicating a *trans*-diaxial orientation of the H-5, H-6 protons, hence assigning **45a** as the major product. Clearly, the most stable conformation of **45a** has all substituents in equatorial positions. On the other hand, the doublet corresponding to the minor isomer has a coupling constant of 3.84 Hz indicating *cis*-relationship with dihedral angle of about 60°. Two configurations of the minor products (*cis*-1,2,4-trioxanes) are possible, **45b** and **45c**. Both show identical chemical shifts in ^{1}H-NMR and can be only distinguished in the ^{13}C-NMR. In both cases, the most stable conformation of this configuration should have the alkyl group on C-3 in the equatorial position. It is also noteworthy to mention that due to the presence of the oxygen atoms in the ring, compounds **44c** / **45c** with no 1,3-diaxial interaction are expected to be more stable than **44b** / **45b** with one destabilizing 1,3-diaxial interaction. Compound **44a** represents about 92 % and **45a** represents about 87 % of the product mixtures.

3.7.2 Derived from 1-cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol

3.7.2.1 By peroxyacetalization reaction with aldehydes

Combination of 2-naphthaldehyde with the hydroperoxy alcohol **7q** in CH_2Cl_2 and in the presence of catalytic amount of BF_3 led to the formation of the 1,2,4-trioxane **46** (***Scheme 3.38***). Assignment of structure of **46** was proven by ^{1}H- as well as ^{13}C-NMR, IR, elemental analyses and HRMS.



7q **46**

Scheme 3.38

The IR spectrum shows the characteristic signals of the aliphatic CH at 2933 cm^{-1}, isolated C=C at 1653 cm^{-1}, aromatic C=C at 1605 cm^{-1}, C-O stretching at 1112, 1074 cm^{-1}, O-O at 906, 822 cm^{-1}. The ^{1}H-NMR shows the characteristic singlet at 6.38 ppm corresponding to the peroxyacetal proton (H-3) and the doublet at 4.87 ppm related to the peroxy proton (H-6) due to coupling with H-5 ($^3J_{HH}$ = 9.5 Hz) indicating *trans* configuration. Surprisingly, H-5 appears also as doublet (and not doublet of doublet as expected) this can be ascribed to a dihedral angle in the vicinity of 90° between this proton and the CH proton of the cyclohexyl group leading to no coupling between them (***Figure 3.14***). The 2-naphthyl group is located in equatorial position as confirmed by X-ray for the analogous examples. The mass fragmentation pattern of **46** is depicted in ***Scheme 3.39***.

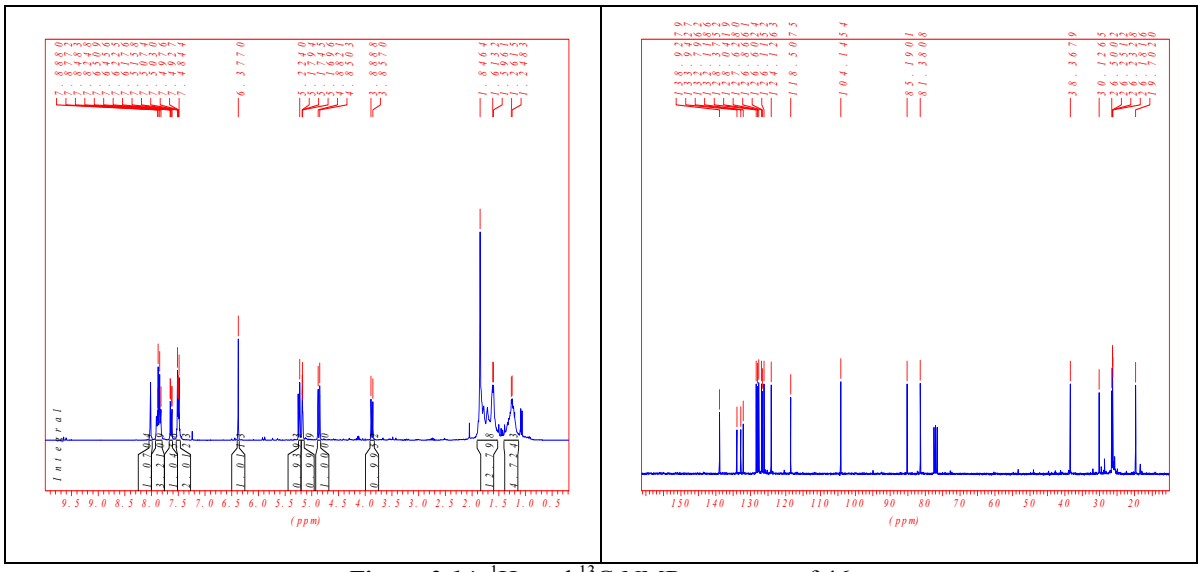
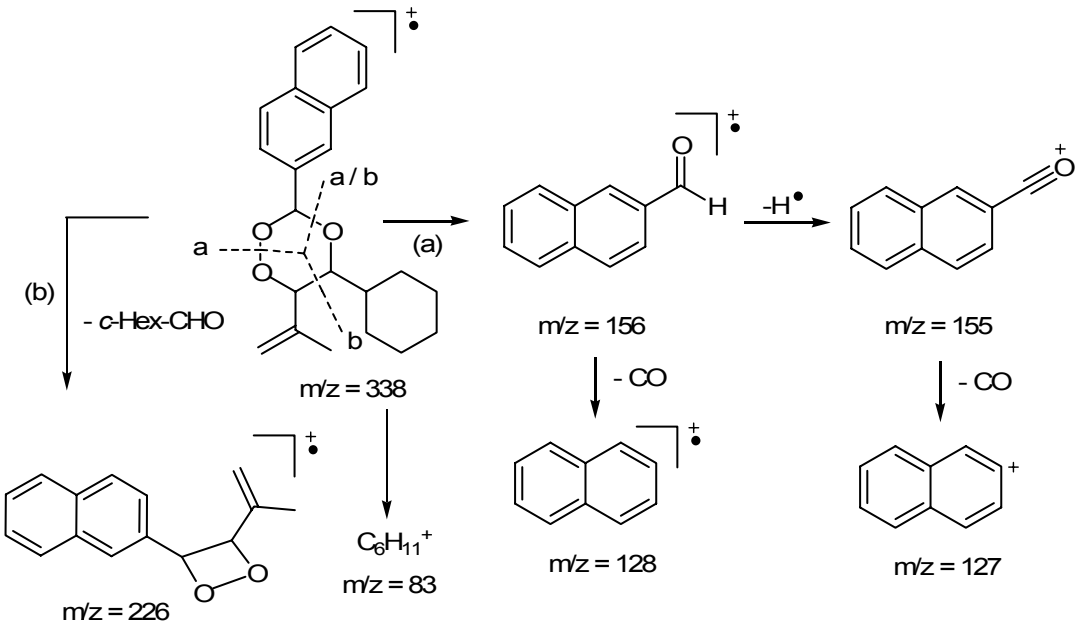
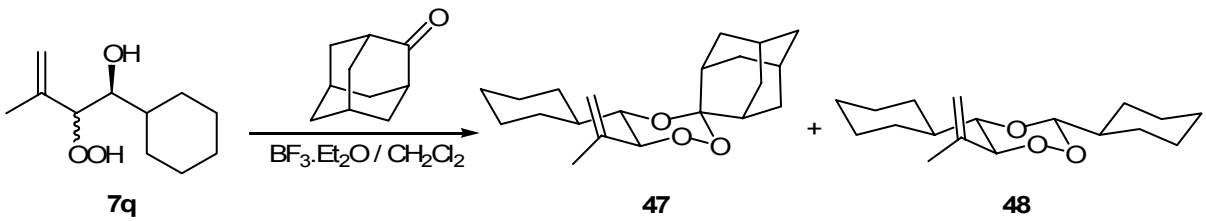


***Figure 3.14*:** ^{1}H- and ^{13}C-NMR spectrum of **46**.



***Scheme 3.39*:** Fragmentation pattern of **46**.

3.7.2.2 By peroxyacetalization reaction with symmetric ketones



7q **47** **48**

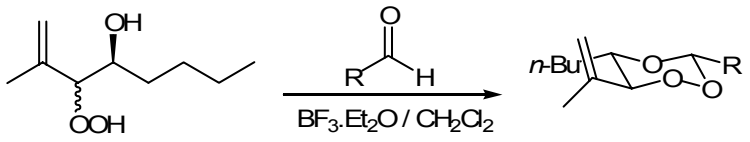
Scheme 3.40

Using adamantanone instead of 2-naphthaldehyde afforded two different 1,2,4-trioxanes (***Scheme 3.40***). The expected product **47** is formed by the usual condensation reaction whereas the product **48** is formed by another mechanism and does not involve the adamantanone moiety. Both 1,2,4-trioxanes show a *trans* configuration as estimated from the $^{3}J_{HH}$ coupling constant between H-5 and H-6 (9.9, 9.5 Hz for **47**, **48**, respectively). Again, for both trioxanes, H-5 exhibits no coupling with the neighboring CH group of the cyclohexyl group and hence appears as doublet. The formation of compound **48** is ascribed to Lewis-acid catalyzed partial fragmentation reaction of the *vic*-hydroxy allylic hydroperoxides **7p** resulting in the corresponding carbonyl components which subsequently condense with the rest of **7p** to yield **48**. This behavior of the hydroperoxy alcohols will be discussed separately in details using different substrates.

3.7.3 Derived from 3-hydroperoxy-2-methyloct-1-en-4-ol

3.7.3.1 By peroxyacetalization reaction with aldehydes

Different 1,2,4-trioxanes were synthesized in yields between 29-48 % from the condensation reaction of the β-hydroxy allylic hydroperoxide **7g** with aldehydes (***Scheme 3.41***). In all cases, only the 5,6-*trans* isomer having the aryl group on C-3 in equatorial position is formed. Full characterization of all the synthesized compounds **49-51** was achieved by IR, NMR, elemental analyses, mass spectrometry and HRMS. The significant signals observed in ^{1}H- and ^{13}C-NMR are summarized in ***Table 3.14***.



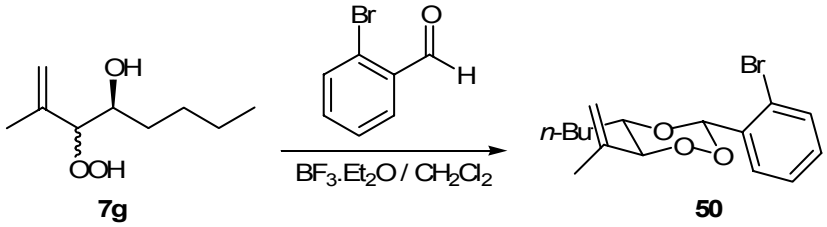
7g **49- 51**

Scheme 3.41

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
49	β-naphthyl	4.01	77.4	4.64	87.7	6.41	104.1	43
50	2-Br-C_6H_4	3.88	77.5	4.48	87.7	6.42	103.1	29
51	Ph	3.92	77.3	4.54	87.6	6.22	104.0	48

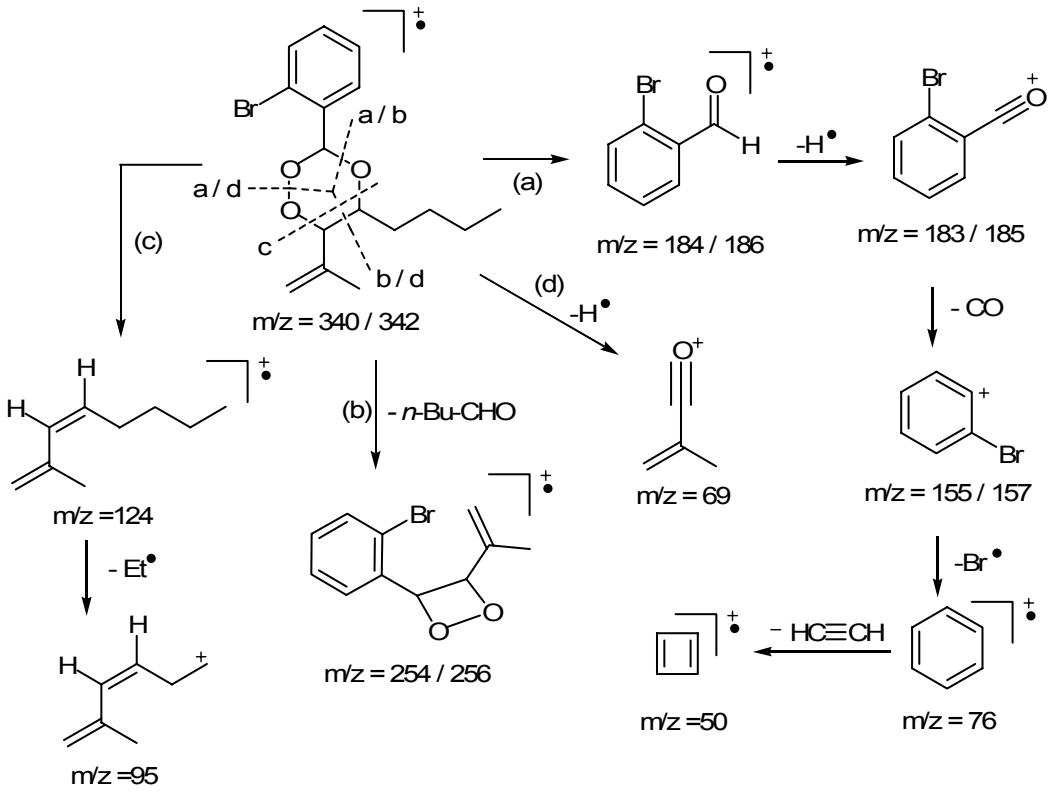
***Table 3.14*:** Characteristic signals of **49-51** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

As an example (***Scheme 3.42***), compound **50** shows the characteristic singlet signal at 6.42 ppm in ^{1}H-NMR which is related to the proton on the peroxyacetal carbon (H-3). The peroxyacetal carbon (C-3) absorbs at 103.1 ppm confirming the formation of the 1,2,4-trioxane structure. The IR spectrum is also consistent with the structure of **50**, the most significant absorption bands are found at 3078 cm^{-1} (aromatic CH), 2955 cm^{-1} (aliphatic CH), 1651 cm^{-1} (isolated C=C), 1570 cm^{-1} (conjugated C=C), 1125, 1081, 1025, 1000 cm^{-1} (C-O) and 948, 911 cm^{-1} (O-O).



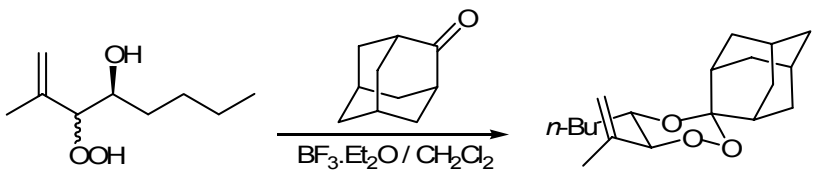
Scheme 3.42

The molecular ion peak in the mass spectrum of the 1,2,4-trioxane **50** is not observed and fragments spontaneously to smaller fragments. A plausible fragmentation pattern of **50** showing the isotopic effect of the bromine atom is depicted in ***Scheme 3.43***.



***Scheme 3.43*:** Mass fragmentation pattern of **50**.

3.7.3.2 By peroxyacetalization reaction with ketones



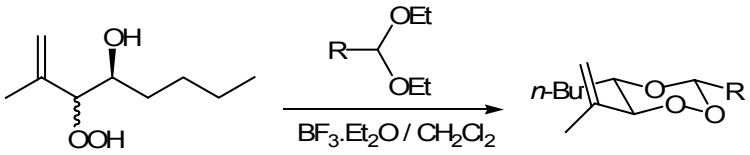
7g **52**

Scheme 3.44

The 1,2,4-trioxane **52** with *trans* configuration is formed on treating **7g** with adamantanone (***Scheme 3.44***). Elucidation of the structure was based on ^{1}H- and ^{13}C-NMR analyses. The relative configuration is based on the vicinal coupling constant between H-5 and H-6 (*vide supra*).

3.7.3.3 By peroxyacetalization reaction with acetals

Treatment of the hydroperoxy homoallylic alcohol **7g** with acetals affords the corresponding all-equatorial 1,2,4-trioxanes stereoisomers **53**, **54** (***Scheme 3.45***). Elucidation of the structure is based as before on spectroscopic data (IR, ^{1}H- and ^{13}C-NMR). The chemical shifts of the three CH groups of the trioxane ring are depicted in ***Table 3.15***. The NMR of **53** is represented in ***Figure 3.15***.



7g **53 / 54**

Scheme 3.45

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
53	CH_3	3.65	76.8	4.33	87.4	5.36	101.5	26
54	Et	3.65	76.7	4.32	87.7	5.16	105.5	26

***Table 3.15*: Characteristic signals of **53** and **54** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).**

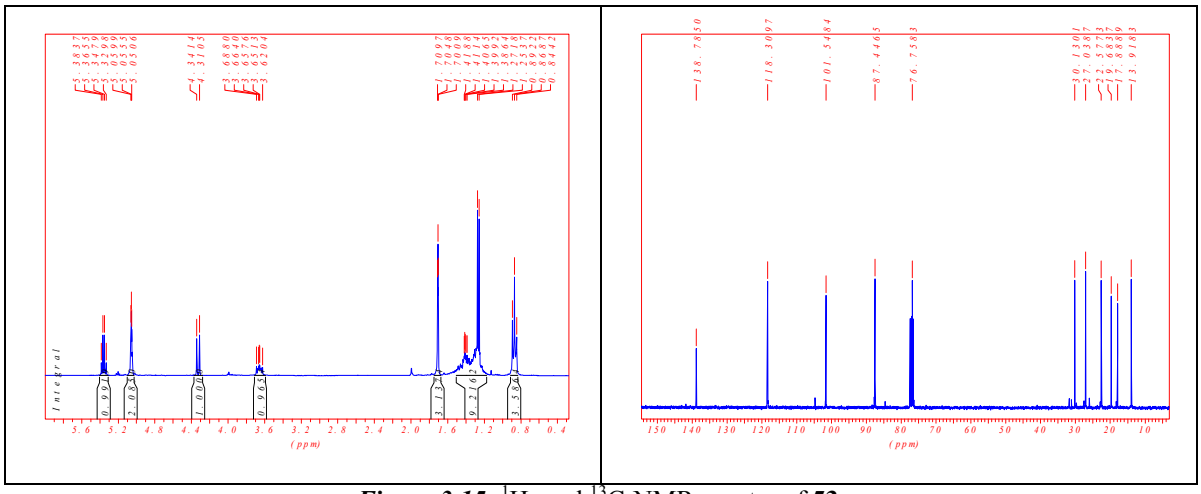
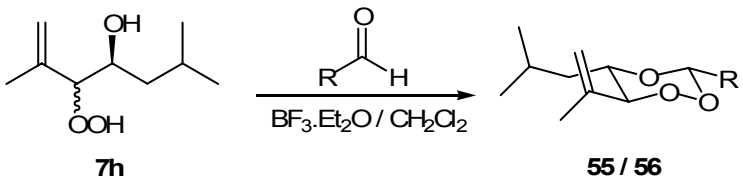


***Figure 3.15*:** ^{1}H- and ^{13}C-NMR spectra of **53**.

3.7.4 Derived from 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol

3.7.4.1 By peroxyacetalization reaction with aldehydes

The BF_3-catalyzed peroxyacetalization reaction of the *vic*-hydroxy allylic hydroperoxide **7h** with benzaldehydes or 2-naphthaldehyde affords the 1,2,4-trioxanes **55** and **56**, respectively (***Scheme 3.46***). Both compounds are fully characterized by ^{1}H-, ^{13}C-NMR, IR, elemental analyses as well as mass spectrometry. The introduction of the naphthyl group in the trioxane moiety is of special relevance since it is the carbocyclic analogue of quinoline which is the effective antimalaria pharmacophore in the quinoline drugs (as chloroquine, mefloquine and amodiaquine).



7h **55 / 56**

Scheme 3.46

As a representative example, compound **55** shows in ^{1}H-NMR a signal (ddd) at 4.0 ppm corresponding to H-5 that couples with the two diastereotopic methylene protons of the *i*-Bu group ($^{3}J_{HH}$ = 2.34, 12.04 Hz) as well as with H-6. The two diastereotopic methylene protons absorb expectedly as multiplets at different chemical shifts (1.25, 1.57 ppm). The proton H-6 couples only with H-5 and appears as doublet at 4.51 ppm. The coupling constant between H-5 and H-6 was found to be 9.24 Hz accounting for the *trans* configuration of the trioxane.

Both the singlet signal at 6.22 ppm in ^{1}H-NMR (attributed to H-3) and that corresponding to the C-3 in ^{13}C-NMR (absorbing at 103.9 ppm) undoubtedly confirm the formation of the 1,2,4-trioxane. Interestingly, in all the 1,2,4-trioxanes possessing *i*-Bu group the methylene carbons are shifted more downfield (at about 39 ppm) with respect to the methine carbons (at about 23 ppm) of the *i*-Bu group. For both compounds **55** and **56** only one diastereomer was detected with the substituents on C-3 and C-5 are *cis* to each other. The NMR characteristic signals for **55** and **56** and the spectra corresponding to **55** are shown in ***Table 3.16*** and ***Figure 3.16***.

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
55	Ph	4.0	75.6	4.51	88.1	6.22	103.9	20
56	β-naphthyl	4.12	75.6	4.65	88.0	6.45	104.0	21

***Table 3.16*:** Characteristic signals of **55** and **56** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

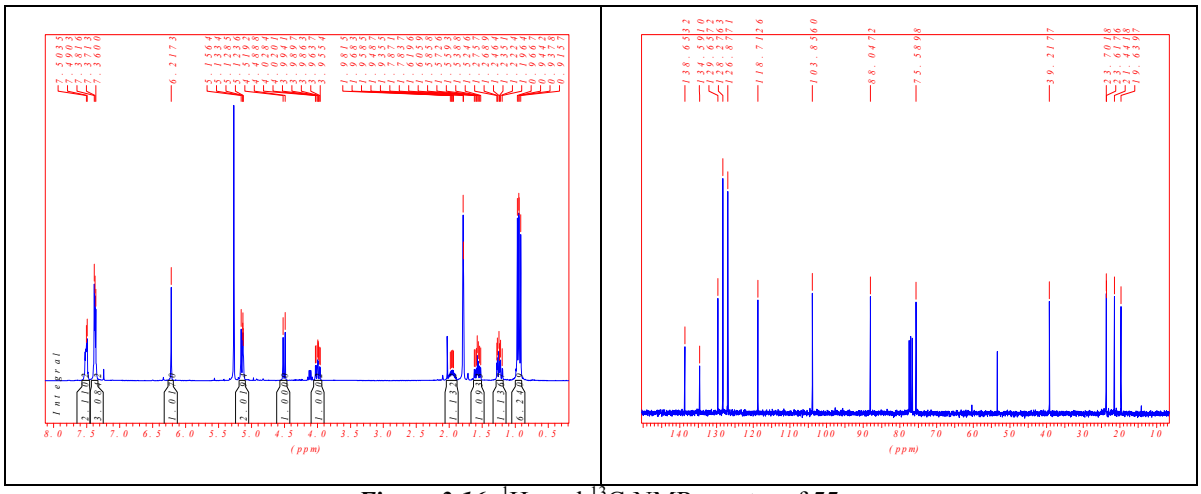
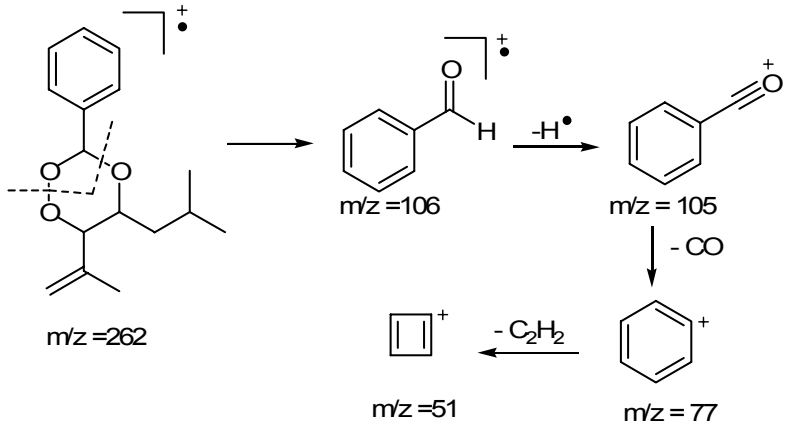
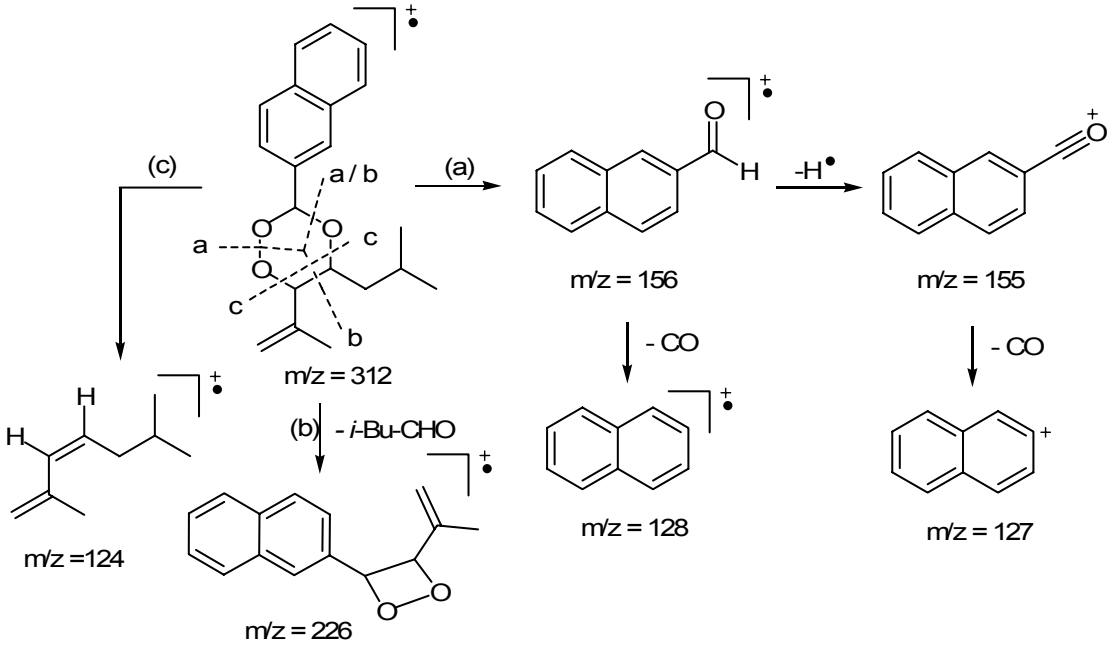


***Figure 3.16*:** ^{1}H- and ^{13}C-NMR spectra of **55**.

The mass spectrum of **55** shows no molecular ion peak, with the formation of the fragment at m/z 105 as the base peak. Plausible fragmentation patterns for the peaks obtained from **55** and **56** are depicted in ***Schemes 3.47***, ***3.48***, respectively.

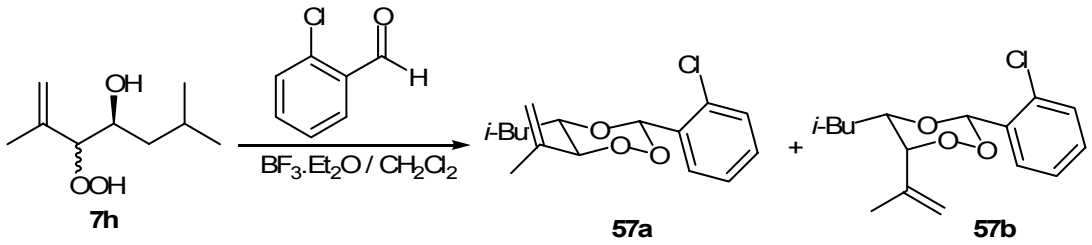


***Scheme 3.47*:** Fragmentation pattern of **55**.



***Scheme 3.48*:** Fragmentation pattern of **56**.

Using 2-chlorobenzaldehyde as the carbonyl component afforded a diastereomeric mixture of the two 1,2,4-trioxanes **57a** and **57b** in a 88:12 ratio, respectively (***Scheme 3.49***). The major isomer was assigned as explained before. Surprisingly, the ^{1}H-NMR of the minor diastereomer shows a strong upfield shift of the doublet signal corresponding to H-6 with respect to the multiplet signal corresponding to H-5 which is be attributed to the ring current effect of the aryl group on this proton in this configuration (***Table 3.17***).



Scheme 3.49

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
57a	2-Cl-C_6H_4	3.96	75.9	4.44	88.2	6.46	101.0	19
57b	2-Cl-C_6H_4	4.30	75.6	**4.06**	85.1	6.50	101.4	

***Table 3.17*:** Characteristic signals of **57a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

The fact that the coupling constant between H-5 and H-6 in the minor diastereoisomer is 3.8 Hz indicates according to Karplus curve a dihedral angle in the vicinity of 60° and consequently a *cis* relationship between these protons. However, two configurations **A** and **B** may fulfill this arrangement (***Figure 3.17***).

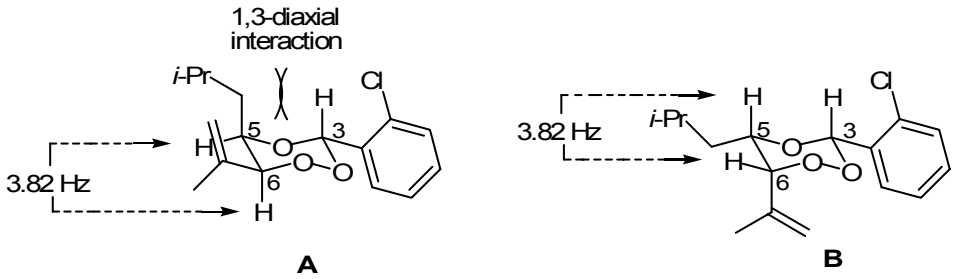


Figure 3.17

Based on NOE measurements (***Figure 3.19***), saturation of H-5 results in clear enhancement in the signal intensity of peroxyacetal proton (H-3) indicating a spatial proximity (*cis* relationship) between them, hence the configuration of the minor diastereomer is **B** (having the isopropenyl group axial, *i*-Bu and 2-chlorophenyl groups in equatorial positions as the most stable conformation of this configuration) and not **A**. This is further supported by the fact that configuration **B** exhibits no 1,3-diaxial interactions (due to the presence of the oxygen atoms in the ring) and thus is expected to be more stable than **A** which suffers from this destabilizing interaction. The destabilization effect due to 1,3-diaxial interaction in **A** is expected to be even more pronounced (i.e. the compound is less stable) than in the

corresponding carbocyclic analogue **C** (***Figure 3.18***) due to the shorter C-O bond length (about 1.42 Å) compared to the C-C bond (about 1.53 Å).[147,149]

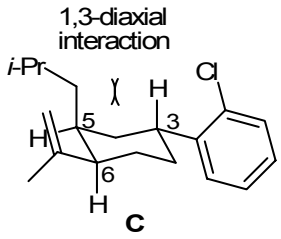


Figure 3.18

Also, the significant down-field shift of the signal corresponding to the isopropenyl methyl group in the minor diastereomer (δ = 2.02 ppm) indicates that this group is located in a spatial proximity to the ring proxidic oxygen atoms which is also consistent with the configuration **B** rather than **A**.

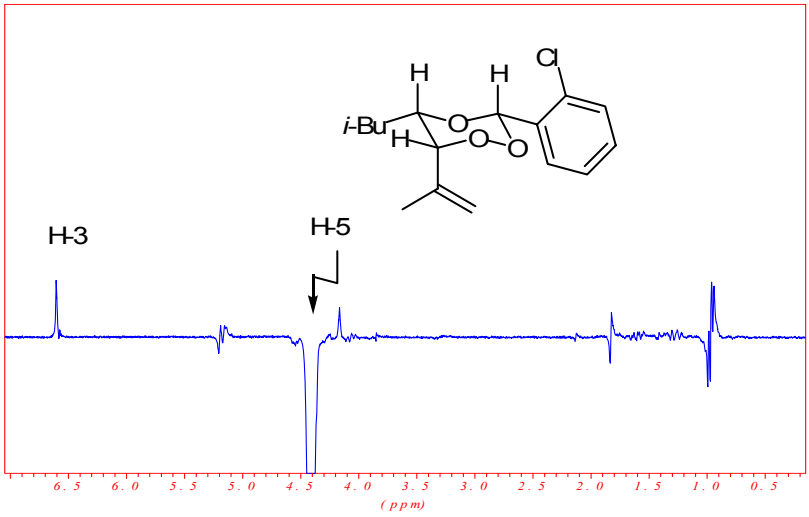
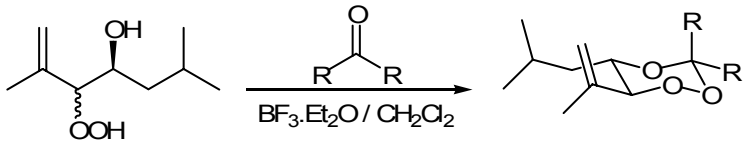


Figure 3.19**:** 1D-NOE experiment of **57b**.

3.7.4.2 By peroxyacetalization reaction with symmetric ketones

The Lewis-acid catalyzed condensation of **7h** with adamantanone, cyclohexanone, cyclopentanone, acetone and 4-heptanone in CH_2Cl_2 furnished the 1,2,4-trioxanes **58-62** in 10-48 % yields (***Scheme 3.50***, ***Table 3.18***).



7h **58-62**

Scheme 3.50

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
58	adamantane		3.99	66.6	4.20	87.8	104.7	10
59	$(CH_2)_5$		3.98	67.2	4.22	88.0	102.8	48
60	$(CH_2)_4$		3.85	70.1	4.29	87.9	**114.7**	11
61	CH_3	CH_3	3.93	68.0	4.17	87.8	102.6	33
62	*n*-Pr	*n*-Pr	3.95	67.4	4.17	87.8	105.6	18

***Table 3.18*:** Characteristic signals of **58-62** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

All the trioxanes **58-62** showed a vicinal coupling constant between C-5 and C-6 in the range of 9.4-9.6 Hz which confirms the *trans* configuration. As a representative example, the chemical structure of compound **58** was confirmed by ^{1}H,^{1}H-COSY and HMQC (***Figure 3.20, 3.21***). Clearly, the broad downfield signal at 2.91 ppm belongs to the adamantane subunit. Three off diagonal cross peaks correspond to H-5 due to coupling with the two diastereotopic methylene protons of the isobutyl group and with H-6. The proton H-6 has only one off diagonal cross peak due to coupling with H-5. The allylic coupling between the olefinic methylene protons with the methyl of the isopropenyl group can be also seen. The cross peaks in HMQC correlates the proton signals with the signals of the carbons directly attached to them (^{1}J coupling).

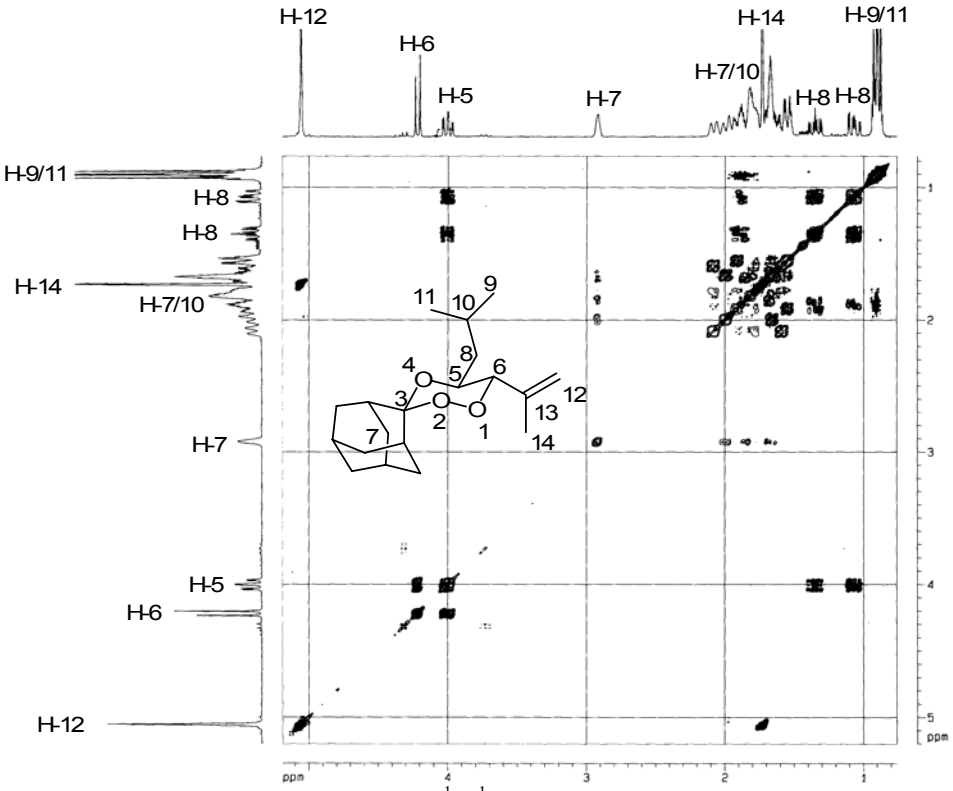


***Figure 3.20*:** $^{1}H,^{1}H$-COSY of **58**.

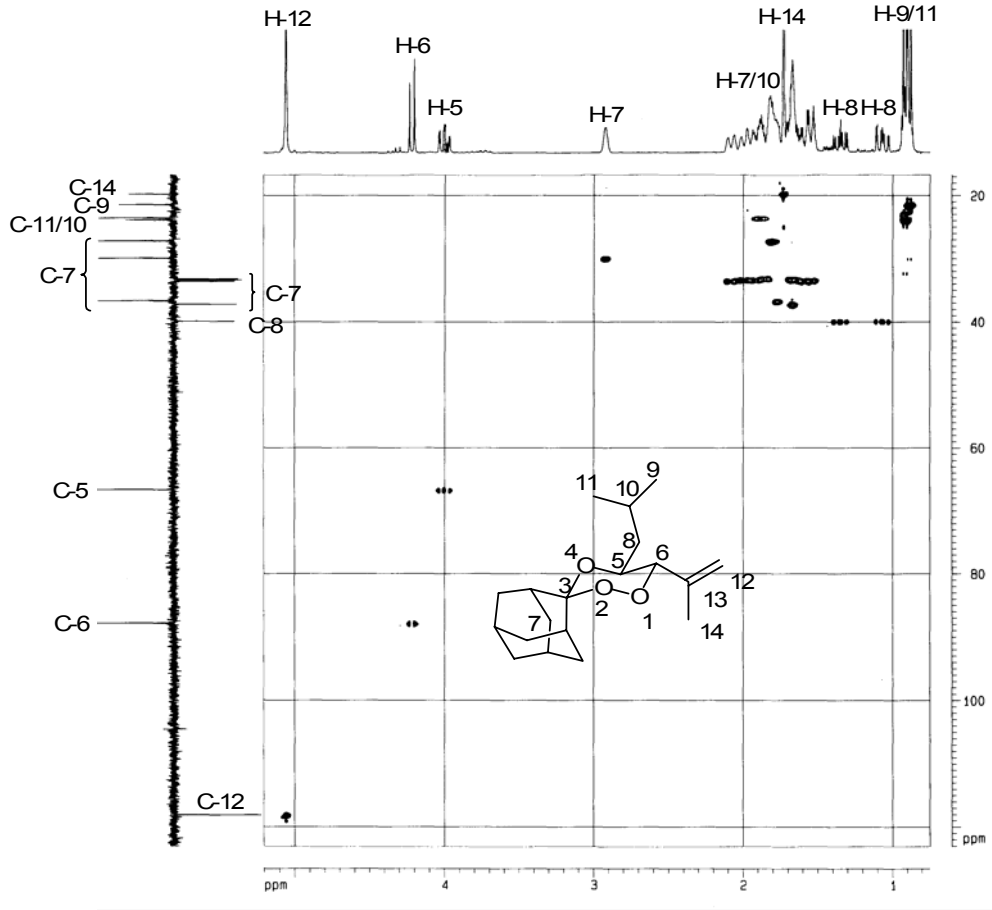


***Figure 3.21*:** HMQC of **58**.

The stereochemical assignment for **58** is further supported by a NOESY experiment showing off diagonal cross peaks between protons of spatial proximity. The key NOEs are indicated by double headed arrows (***Figure 3.22***). The X-ray analysis is a definite proof of the relative configuration of this compound (***Figure 3.23***).

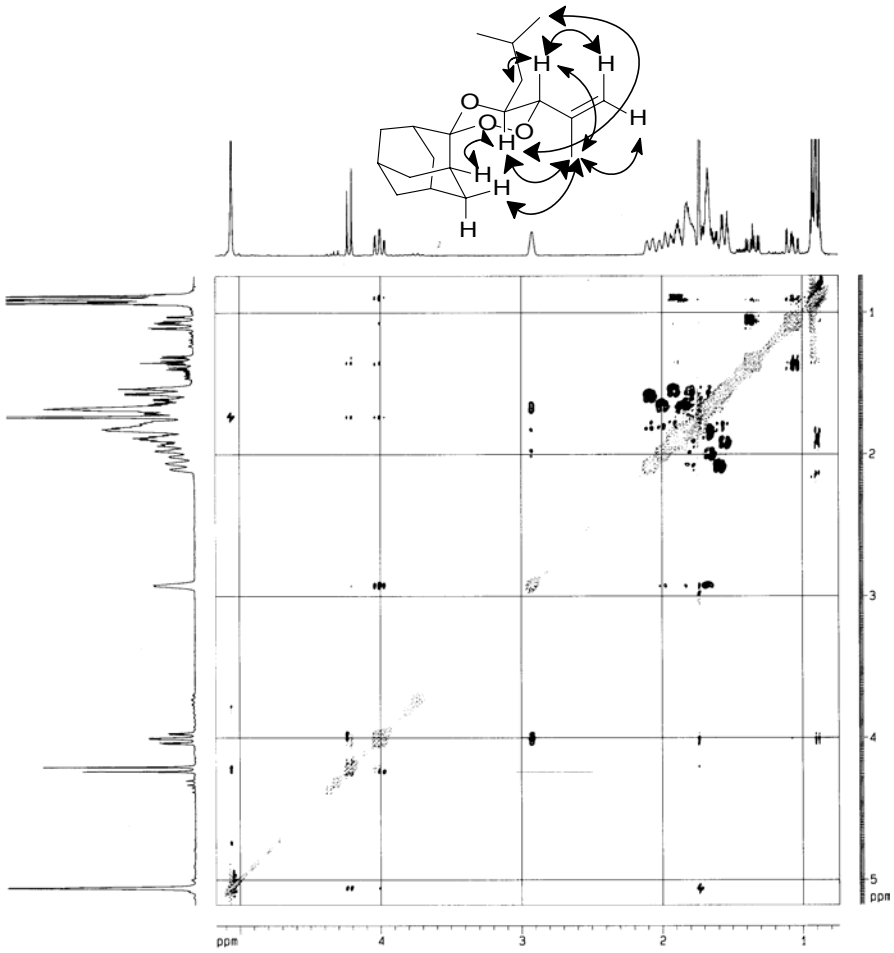


***Figure 3.22*: NOESY of **58**.**

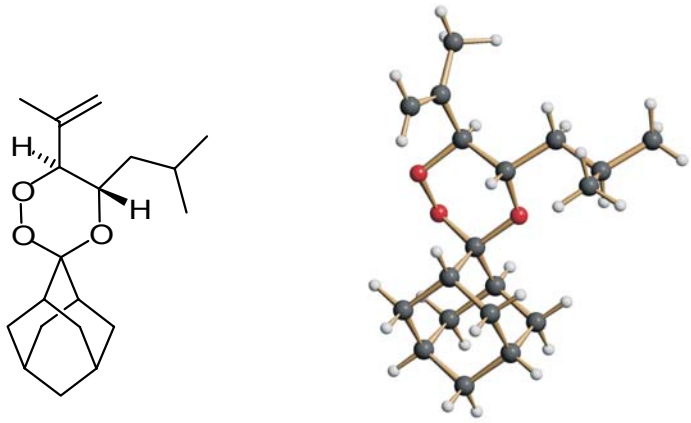
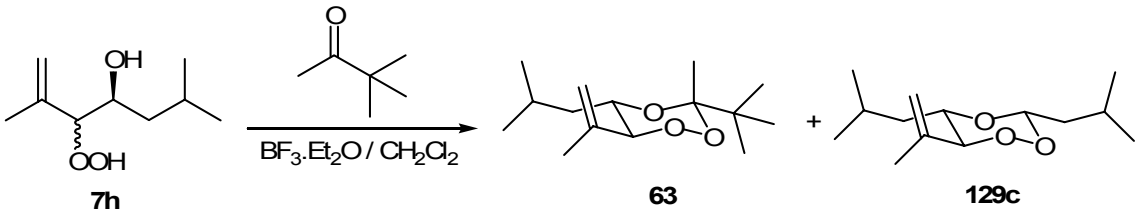


***Figure 3.23*: X-ray structure of **58**.**

3.7.4.3 By peroxyacetalization reaction with asymmetric ketones

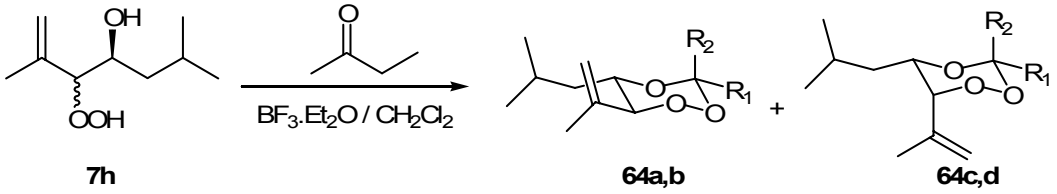
Two asymmetric ketones were used in this study, 3,3-dimethyl-2-butanone and 2-butanone. In the former case (***Scheme 3.51***), the trioxanes **63** and **129c** were obtained in 89:11 ratio. Compound **63** was proven to have the *trans* configuration as discussed before with the anchoring *t*-Bu group is in an equatorial position. The formation of compound **129c** is attributed to the observed Lewis-acid catalyzed fragmentation of β-hydroperoxy alcohols / cross-peroxyacetalization sequence (*vide infra*).



7h **63** **129c**

Scheme 3.51

In the second reaction using 2-butanone a complex mixture of products was obtained in 52 % yield (***Scheme 3.52***). The formation of the trioxanes **64a-d** was estimated from the presence of four signals corresponding to the peroxycarbon (C-6) and four signals corresponding to C-5. in the ^{13}C-NMR of the product mixture (***Table 3.19***). Coupling constant measurements revealed that the thermodynamically most stable trioxane **64a** with *trans* configuration and having an equatorial ethyl group at C-3 is the major product constituting about 85 % of the product mixture.



7h **64a,b** **64c,d**

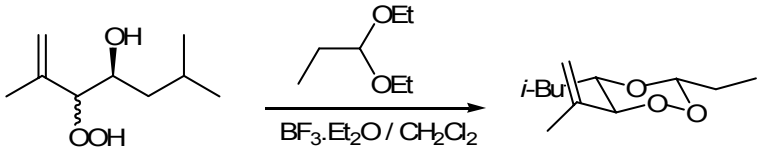
Scheme 3.52

No.	R_1	R_2	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
64a	Et	CH_3	3.96	67.9	4.17	88.0	104.0	52
64b	CH_3	Et	3.89	67.6	4.10	87.6	105.0	
64c	Et	CH_3	3.83	68.8	4.24	94.1	[a]	
64d	CH_3	Et	[a]	68.6	[a]	92.1	[a]	

***Table 3.19*:** Characteristic signals of **64a-d** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] The signal is overlapping.

The diminished tendency for a *t*-Bu group to adopt an axial position in the 1,2,4-trioxane moiety (due to severe 1,3-diaxial interaction) led to the fact that no products analogous to **64b,d** in case of using pinacolone as the carbonyl component were formed.

3.7.4.4 By peroxyacetalization reaction with acetals



7g **65**

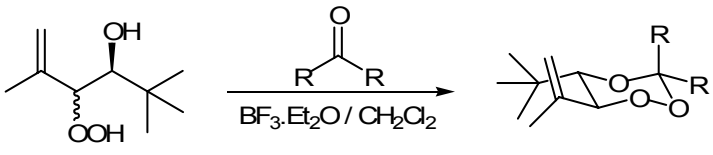
Scheme 3.53

Using propionaldehyde diethylacetal for the condensation reaction furnished the trioxane **65** in 50 % (***Scheme 3.53***). The characteristic signal of proton of the peroxyacetal carbon resonates in ^{1}H-NMR at 5.14 ppm as triplet (actually doublet of doublet with identical coupling constants of 5.58 Hz) due to coupling with the two diastereotopic protons of the ethyl group. This carbon is also absorbing in the ^{13}C-NMR at 105.5 ppm confirming the formation of **65**. Similar to the products obtained from the condensation reaction with aldehydes, the trioxane **65** has a *trans* configuration with equatorial ethyl group at the peroxyacetal carbon.

3.7.5 Derived from 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol

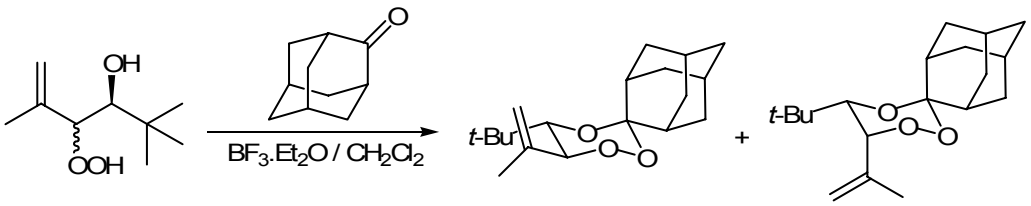
3.7.5.1 By Peroxyacetalization Reaction with Ketones

In contrast to the peroxyacetalization reaction of the hydroperoxy homoallylic alcohol **7j** with cyclopentanone or cyclohexanone furnishing in each case only one 1,2,4-trioxane diastereomer **66**, **67**, respectively (***Scheme 3.54***, ***Table 3.20***), carrying out the condensation reaction with 2-adamantanone results in a 84:16 mixture of two trioxane diastereomers **68a,b** (***Scheme 3.55***).



7j **66 / 67**

Scheme 3.54



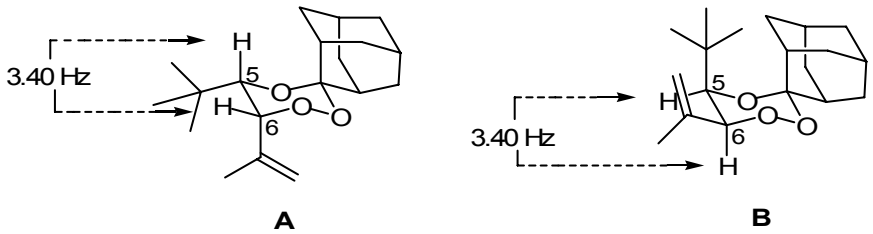
7j **68a** **68b**

Scheme 3.55

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
66	$(CH_2)_4$		3.57	77.7	4.90	85.8	**114.3**	8
67	$(CH_2)_5$		3.67	74.9	4.43	85.8	102.4	11
68a	2-adamantan		3.70	74.4	4.43	85.5	104.3	12
68b			3.63	63.4	4.83	89.0	102.4	

***Table 3.20*:** Characteristic signals of **66-68** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

Compounds **66**, **67**, **68a** showed coupling constants between H-5 and H-6 of 9.7 Hz which, according to the Karplus curve, is consistent with a dihedral angle around 180° supporting that these compounds have the *trans* configuration. On the other hand, the coupling constant between H-5 and H-6 in the minor diastereoisomer **68b** is about 3.40 Hz which is indicative of a dihedral angle in the vicinity of 60° and consequently a *cis* relationship between these protons. Two conformations **A** and **B** can be suggested for the minor configuration (***Figure 3.24***).



A **B**

***Figure 3.24*:** Two suggested conformations for the minor diastereomer **68b**.

Based on NOE measurements, double irradiation of H-5 of the minor diastereomer resulted in enhancement in the signals corresponding to H-6, the adamantane residue and the *t*-Bu group indicating a spatial proximity between the protons of these groups with H-5 (***Figure 3.25***). Hence, the minor diastereomer adopts the **A** conformation (having the isopropenyl group in axial and the *t*-Bu group in equatorial positions) and not **B**. Also, the absence of any

enhancement in the adamantane signals under saturation of the protons of the *t*-Bu group of the minor diastereomer clearly excludes the conformation **B**. This result is in agreement with the expectation since the conformation **B** is highly disfavored by a severe 1,3-diaxial interaction between the bulky *t*-Bu group with the adamantane residue. Also, the high propensity of the *t*-Bu group to anchor in an equatorial position prefers the formation of **A** rather than **B**.

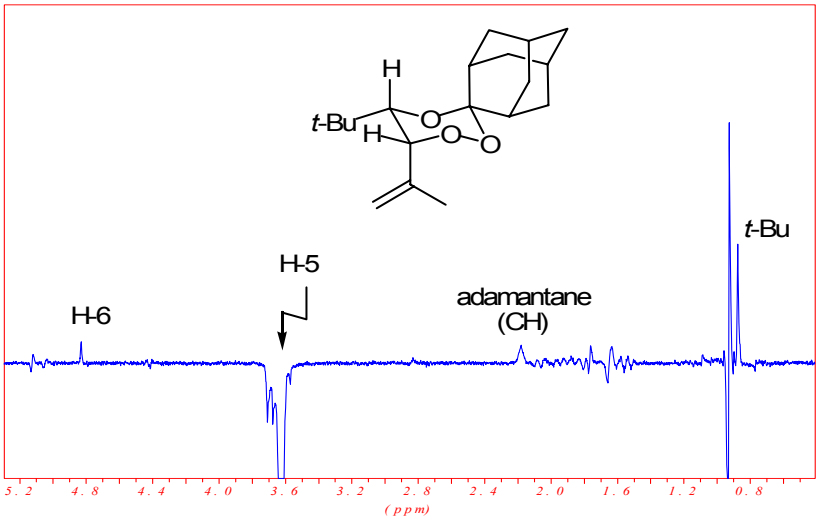


***Figure 3.25*:** 1D-NOE experiment of **68b**.

The relative configuration of **66** was also established by NOESY experiment showing off diagonal cross peaks for the protons in spatial proximity. The key NOEs are represented by double headed arrows (***Figure 3.26***).

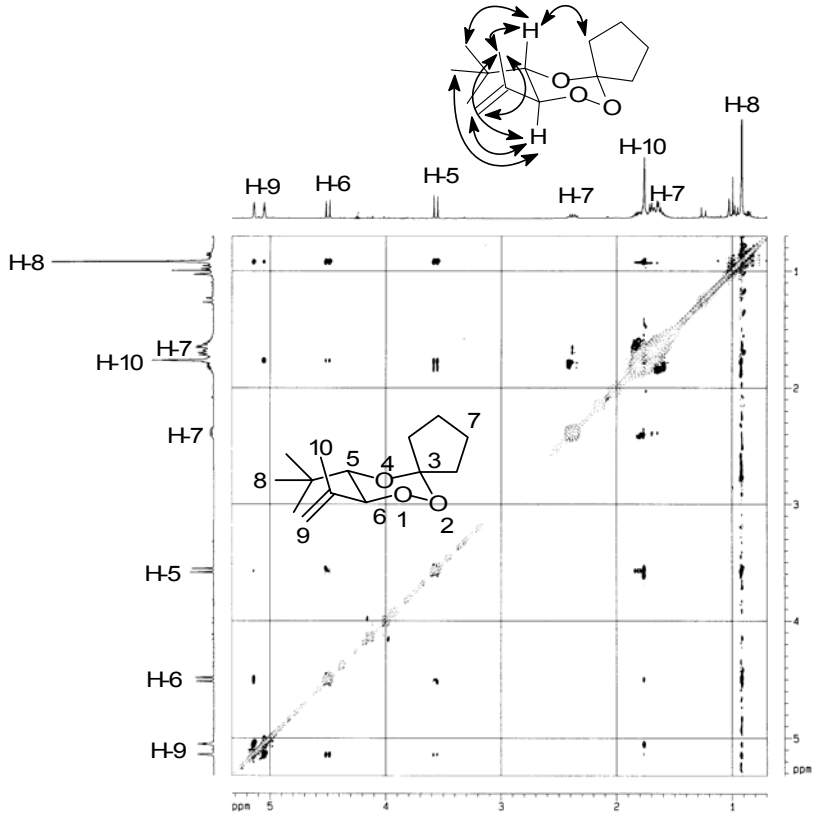
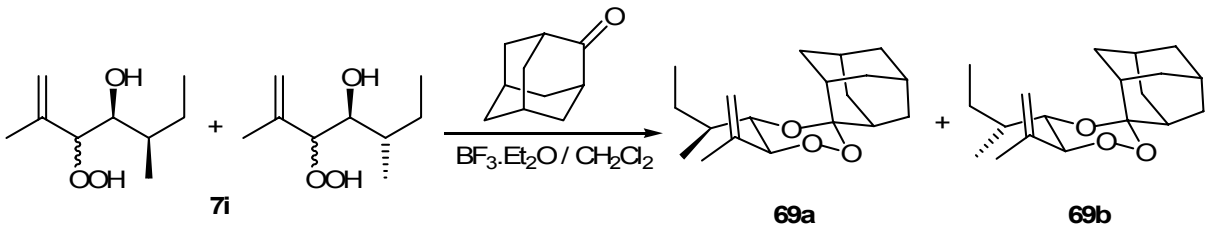


***Figure 3.26*:** NOESY experiment of **66**.

3.7.6 Derived from 3-hydroperoxy-2,5-dimethylhept-1-en-4-ol

3.7.6.1 By peroxyacetalization reaction with ketones

Condensation of adamantanone with the two diastereomeric mixtures of the β-hydroperoxy alcohol **7i** furnished a 1:1 diastereomeric mixture of the spiro-fused 1,2,4-trioxanes **69a,b** (***Scheme 3.56***). Both products are undistinguishable by ^{1}H-NMR. In ^{13}C-NMR sets of twin signals for most of the carbon atoms could be observed. For example the two signals corresponding to C-5 and C-6 for each diastereomer are shown in ***Table 3.21***. The chemical structure of the trioxanes was based on NMR, IR and elemental analyses. The characteristic absorption bands in the IR spectrum are stretching at 3081; 2914; 1648; 1109, 1096, 1024; 925, 908 cm^{-1} corresponding to the vinylic CH, aliphatic CH, nonconjugated C=C, C-O and O-O, respectively. The relative configuration was assigned as *trans* by the vicinal coupling constant between H-5 and H-6 which was found to be 9.54 Hz indicating a dihedral angle of 180°.



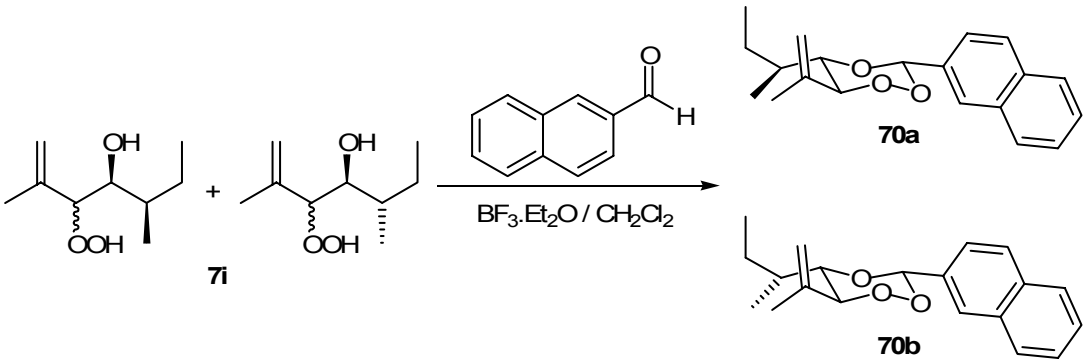
Scheme 3.56

No.	OCH		OOCH		OCOO	Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
69a,b	3.83[a]	68.6/69.1	4.22[a]	87.6/87.7	104.7[a]	20

***Table 3.21*:** Characteristic signals of **69a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] Both diastereomers have the same chemical shift.

3.7.6.2 By peroxyacetalization reaction with aldehydes

Similarly, the reaction with 2-naphthaldehyde afforded the two diastereomeric 1,2,4-trioxanes **70a,b** in 17 % yield. Also, both compounds show a *trans* configuration having the substituents at C-3 and C-5 *cis* to each other (***Scheme 3.57***). The most characteristic signals for both diastereomers are summarized in ***Table 3.22***.



Scheme 3.57

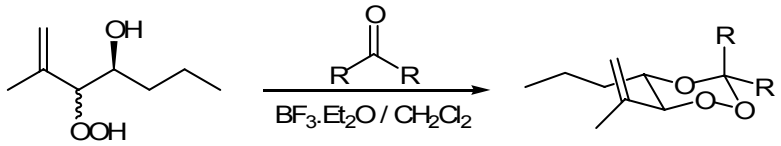
No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
70a,b	3.98	77.6	4.62	87.7	6.39	104.1	17

***Table 3.22*:** Characteristic signals of **70a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

3.7.7 Derived from 3-hydroperoxy-2-methylhept-1-en-4-ol

3.7.7.1 By peroxyacetalization reaction with ketones

The 1,2,4-trioxanes **71-75** were synthesized in 14-49 % yields by BF_3-catalyzed condensation reaction of adamantanone, cycloheptanone, cyclohexanone, cyclopentanone and 3-pentanone with **7d** (***Scheme 3.58***). The characteristic signals for each product are summarized in ***Table 3.23***. All the isolated products were formed as one diastereomer (*trans* at C-5 and C-6) that were fully characterized by spectroscopic and analytical methods as well as mass spectrometry. Compound **74** showed a remarkable downfield shift of the peroxyacetal carbon in ^{13}C-NMR (this behavior was also observed for all 1,2,4-trioxanes involving cyclopentanone subunit). Also, for all the synthesized monocyclic and polycyclic spiro-1,2,4-trioxanes (synthesized by condensation with cyclopentanone, cyclohexanone, cycloheptanone and adamantanone) a common behavior was observed: one (sometimes two) of the carbocyclic ring protons is absorbing down-field from the rest of the ring protons. This is ascribed to through-space electronic effects of the oxygen atoms in the trioxane ring causing more deshielding of this proton (***Figure 3.27***). Comparison of the antimalarial activity of the series **71-74** might be helpful to study the effect of the lipophilicity in these spiro compounds on the activity. Comparing the activity of **74** and **75**, having the same number of carbons, may be also informative about the spiroannelation effect on the antimalarial activity.



7d **71-75**

Scheme 3.58

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
71	adamantane		3.88	68.3	4.22	87.6	104.7	30
72	$(CH_2)_6$		3.85	69.1	4.22	87.6	107.2	18
73	$(CH_2)_5$		3.87	68.8	4.21	87.7	102.7	49
74	$(CH_2)_4$		3.77	71.6	4.30	87.5	**114.7**	19
75	Et	Et	3.86	69.1	4.21	87.3	106.0	14

***Table 3.23*:** Characteristic signals of **71-75** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

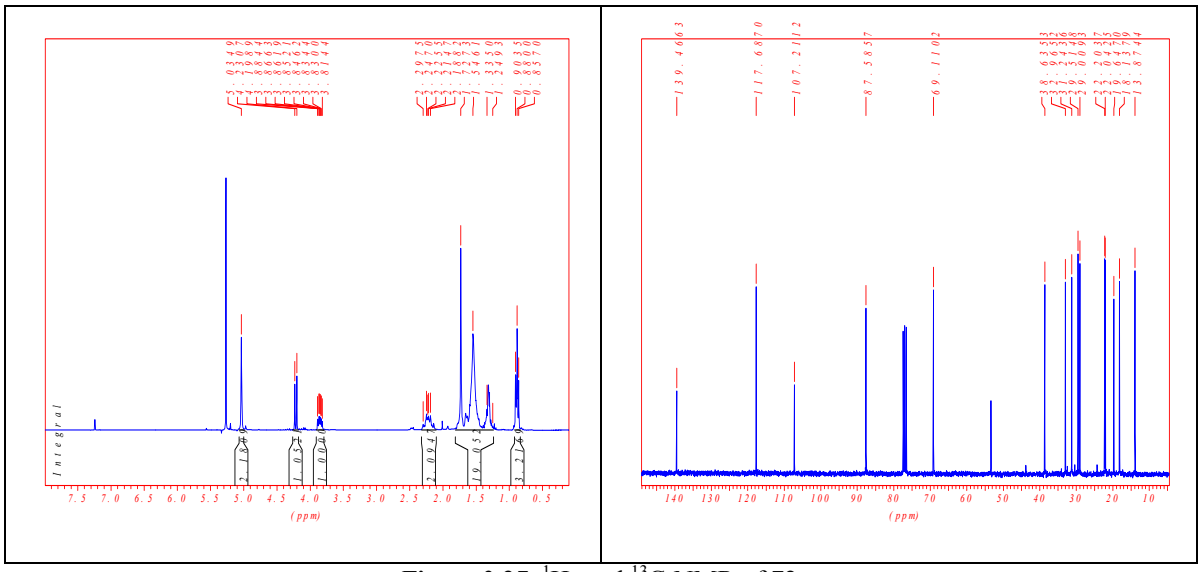
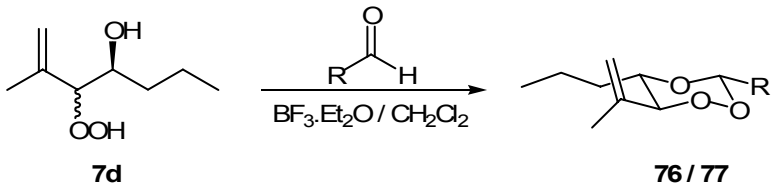


***Figure 3.27*:** ^{1}H- and ^{13}C-NMR of **72**.

3.7.7.2 By peroxyacetalization reaction with aldehydes

Similar to the reaction of **7h** with aldehydes, the peroxyacetalization reaction of the 1,2-hydroperoxy alcohol **7d** with 2-naphthaldehyde and benzaldehyde afforded only the *trans* 1,2,4-trioxanes **76**, **77**, respectively, with the aryl groups in equatorial position as the more stable configuration (***Scheme 3.59***). The structures of the products were proven by ^{1}H-, ^{13}C-NMR, IR, elemental analyses, mass spectrometry and HRMS. The characteristic signals in NMR are summarized in ***Table 3.24***. An indisputable assignment of the relative configuration of **76** was based on X-ray analysis (***Figure 3.28***).



7d **76 / 77**

Scheme 3.59

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
76	2-naphthyl	4.04	77.1	4.67	87.7	6.43	104.0	40
77	Ph	3.95	77.0	4.56	87.6	6.24	103.9	36

***Table 3.24*:** Characteristic signals of **76** and **77** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

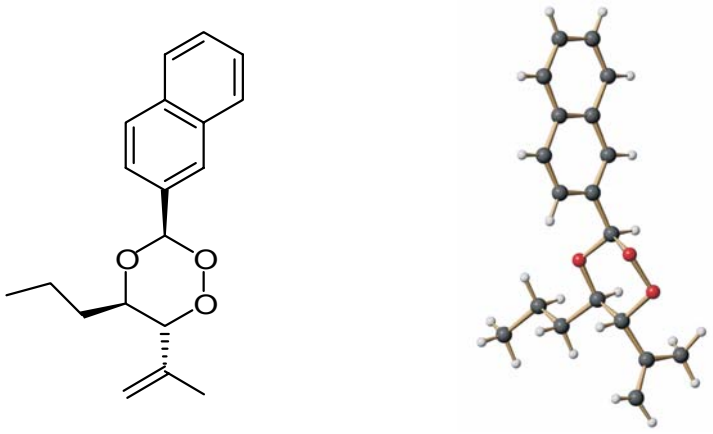
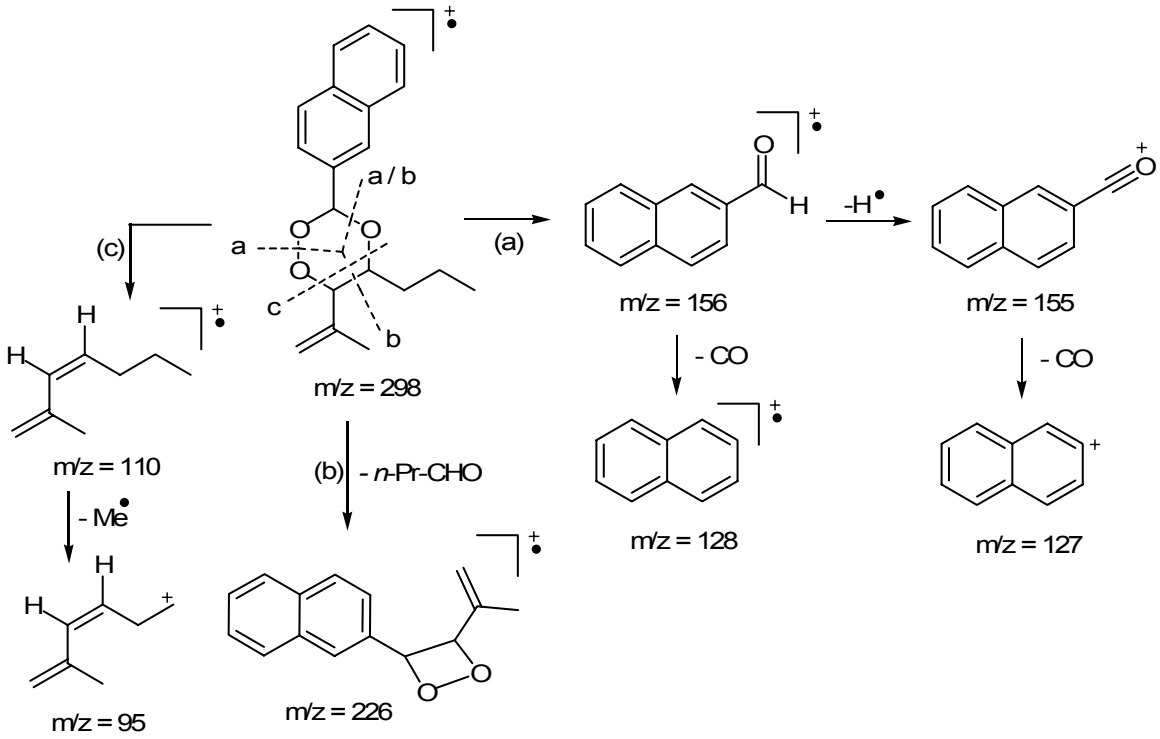


***Figure 3.28*:** X-ray structure of **76**.

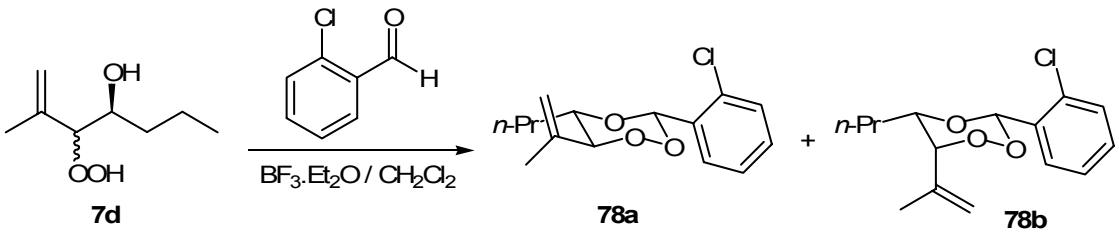
The mass fragmentation pattern of the representative example **76** is summarized in ***Scheme 3.60***.



Scheme 3.60.

Also similar to the reaction of **7h** with 2-chlorobenzaldehyde, treatment of **7d** with this aldehyde furnished a 88:12 mixture of diastreomers **78a,b**, respectively. The major product is expected to have the *trans* configuration **(78a)** since it exhibits a coupling constant between H-5 and H-6 of 9.26 Hz. On the other hand, the coupling constant between H-5 and H-6 in the minor product is 3.82 Hz indicating a *cis* configuration (**78b**). Again, in both compounds the aromatic residues are located in equatorial position (***Scheme 3.61***). Saturation of H-5 of the

minor product in an NOE experiment resulted in clear enhancement in the intensity of H-3 (***Figure 3.29***). Compound **78b** is expected to be stable since it is free of any 1,3-diaxial interactions (due to the presence of the oxygen atoms in the ring). A strong upfield shift in the doublet signal of H-6 in the minor product **78b** was also observed. Also, the methyl of the isopropenyl group of the minor diastereomer is located near to the peroxidic oxygen atoms and hence absorbs downfield at 2.03 ppm. The characteristic signals of **78a,b** are summarized in ***Table 3.25***.



Scheme 3.61

No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
78a	3.90	77.3	4.48	87.7	6.47	101.0	40
78b	3.62	77.1	**4.09**	85.0	6.49	101.4	

***Table 3.25*:** Characteristic signals of **78a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

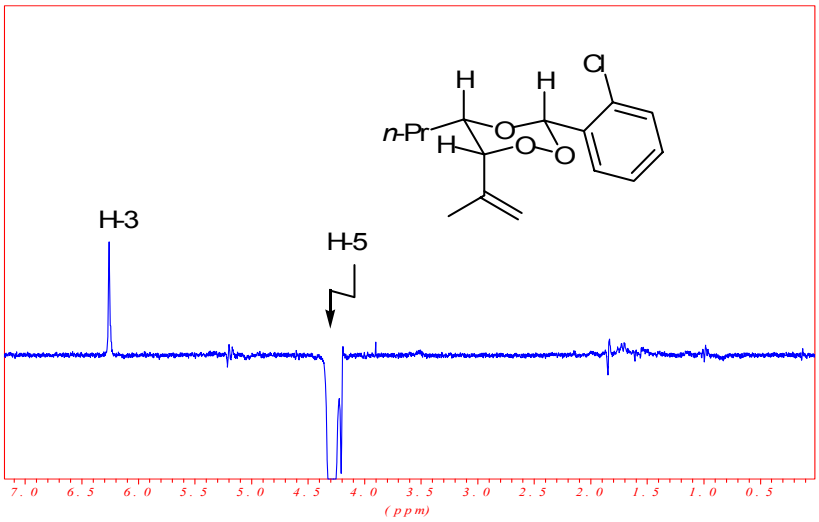
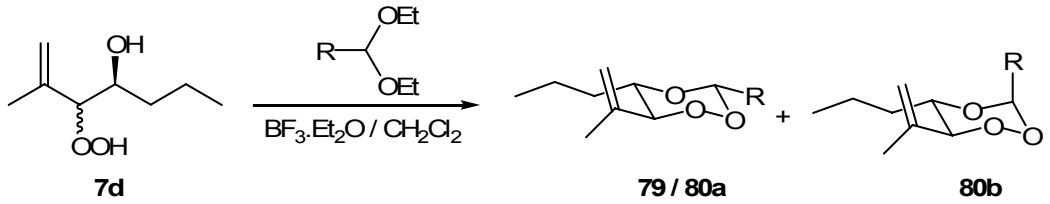


***Figure 3.29*:** 1D-NOE experiment of **78b**.

3.7.7.3 By peroxyacetalization reaction with acetals

Whereas only one 1,2,4-trioxane diastereoemer **79** was isolated in case of condensing **7d** with propionaldehyde diethylacetal, a 90:10 mixture of two 1,2,4-trioxane diastereomers **80a,b** were isolated on using acetaldehyde dimethylacetal (***Scheme 3.62***). The less propensity of the ethyl compared to the methyl group to adopt an axial position may account for that. All the three products have a *trans* configuration confirmed by spectroscopic methods as mentioned before. The characteristic NMR signals are summarized in ***Table 3.26***.



7d **79 / 80a** **80b**

Scheme 3.62

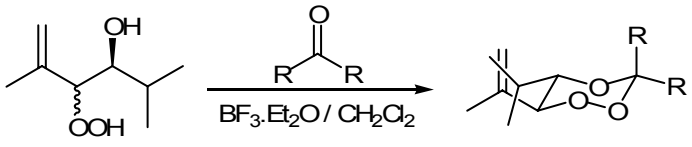
No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
79	Et	3.66	76.5	4.33	87.7	5.15	105.5	41
80a	CH_3	3.66	76.4	4.32	87.4	5.35	101.4	48
80b	CH_3	3.75	75.9	4.38	84.5	[a]	101.6	

***Table 3.26*:** Characteristic signals of **79** and **80** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] The signal is overlapping.

3.7.8 Derived from 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol

3.7.8.1 By peroxyacetalization reaction with symmetric ketones

The BF_3-catalyzed reaction of **7c** with different symmetric ketones resulted in the formation the 1,2,4-trioxanes **81-84** in yields 15-50 %. Due to the symmetry at C-3, the stereochemistry of the products is controlled by substituents at C-5 and C-6. Coupling constant measurements (9.8-9.9 Hz) revealed that in all products the protons H-5 and H-6 are in *trans*-diaxial conformation (***Scheme 3.63***). As an example, compound **81** is characterized by NMR, IR, elemental analyses, mass spectrometry and HRMS. The characteristic signals in ^{1}H-, ^{13}C-NMR for all compounds are shown in ***Table 3.27***.



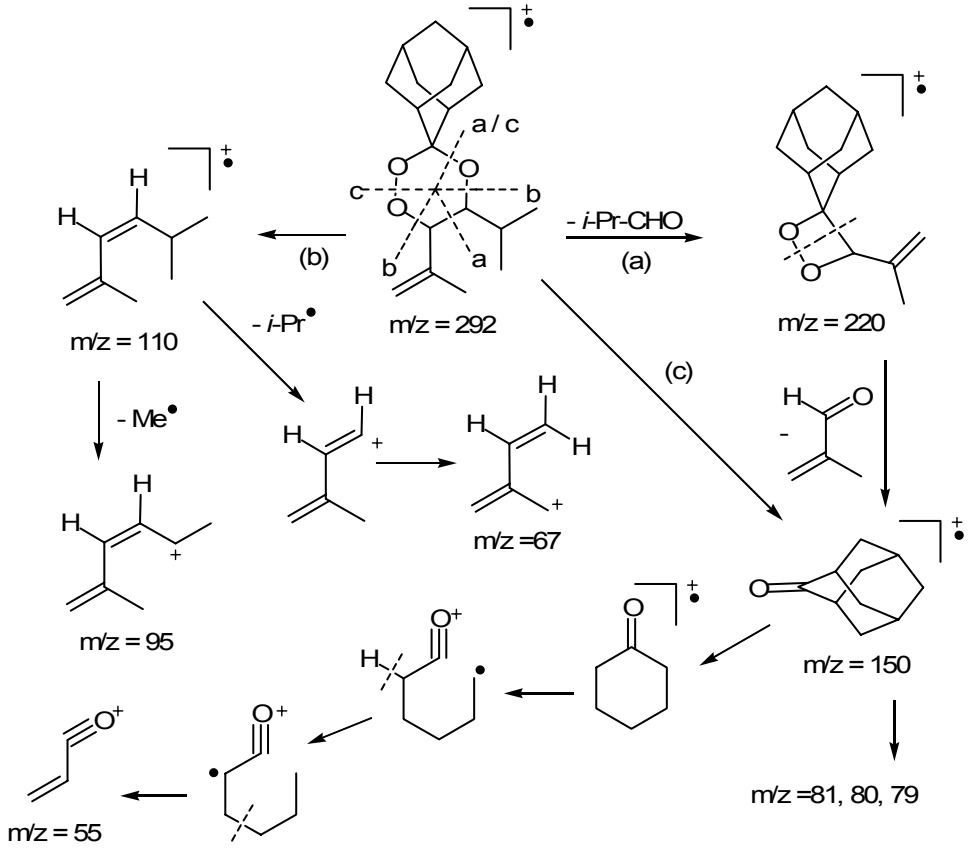
7c **81-84**

Scheme 3.63

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
81	adamantane		3.78	72.1	4.41	85.4	104.4	28
82	$(CH_2)_4$		3.67	75.6	4.49	85.6	**114.7**	15
83	CH_3	CH_3	3.79	73.6	4.41	85.5	102.6	43
84	Et	Et	3.72	72.8	4.37	85.2	105.6	50

***Table 3.27*:** Characteristic signals of **81-84** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

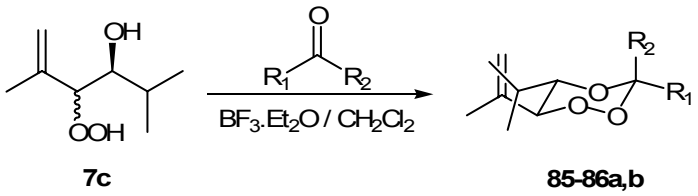
The characteristic IR bands for compound **81** are stretching at 3081 cm^{-1} (olefinic CH), 2913 cm^{-1} (aliphatic CH), 1649 cm^{-1} (nonconjugated C=C), 1110, 1097, 1077, 1025 cm^{-1} (C-O), 925, 908 cm^{-1} (O-O). The mass spectrum of **81** shows the fragments depicted in ***Scheme 3.64***.



***Scheme 3.64*:** Fragmentation pattern of **81**.

3.7.8.2 By peroxyacetalization reaction with asymmetric ketones

Incorporation of a new stereogenic center at C-3 by condensing **7c** with asymmetric ketones such as 2-pentanone and 3,3-dimethyl-2-butanone affords a 87:13 of **85a,b** and 83:17 of **86a,b** diastereomeric mixtures, respectively. The fact that all 1,2,4-trioxane products have vicinal coupling constants between H-5 and H-6 in the range from 8.22-9.99 Hz is indicative that all have the *trans* configuration at these centers. Consequently, the difference between the diastereomers is at the third chiral center C-3. The major product in both reactions is assumed to have the more bulky substituent at C-3 (*n*-Pr or *t*-Bu) *cis* to the isopropyl group at C-5 (***Scheme 3.65***). Signals characteristic to the diastereomers as well as the chemical yields are summarized in ***Table 3.28***.



7c **85-86a,b**

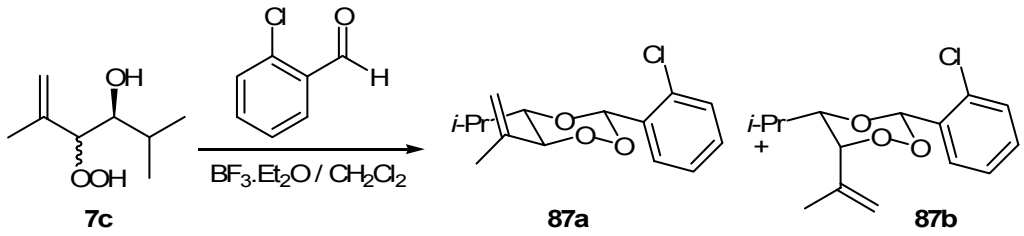
Scheme 3.65

No.	R_1	R_2	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
85a	*n*-Pr	CH_3	3.80	73.4	4.41	85.6	103.8	17
85b	CH_3	*n*-Pr	3.74	73.0	[a]	85.1	104.3	
86a	*t*-Bu	CH_3	3.78	73.1	4.37	85.3	106.3	36
86b	CH_3	*t*-Bu	3.50	74.7	4.29	91.7	104.8	

***Table 3.28*:** Characteristic signals of **85a,b** and **86a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] Signal is overlapping

3.7.8.3 By peroxyacetalization reaction with aldehydes

As discussed previously for the condensation reaction of **7h**, **7d** with 2-chlorobenzaldehyde, the *vic*-hydroxy allylic hydroperoxide **7c** reacts in similar way affording a mixture of the *trans*-1,2,4-trioxane **87a** as the major product as well as the *cis*-1,2,4-trioxane **87b** as the minor product in 91:9 ratio and 33 % yield (***Scheme 3.66***, ***Table 3.29***).



7c **87a** **87b**

Scheme 3.66

No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
87a	3.78	81.2	4.64	85.8	6.46	101.0	33
87b	3.74	83.1	**4.15**	83.7	6.44	101.5	

***Table 3.29*:** Characteristic signals of 87a,b in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

Confirmation of the relative configuration at C-3 for the major product **87a** was also based on an NOE experiment (***Figure 3.30***). Saturation of H-5 resulted in a clear positive enhancement in the singlet signal corresponding to H-3 proving that they are in spatial proximity and hence *cis* to each other. Other enhancements were also observed for the olefinic signal, the methyl of the isopropenyl group, the methyl and the methine of the isopropyl group. Compound **87b** represents the most stable conformation of the configuration corresponding to the minor diastereomer showing no 1,3-diaxial interactions (*vide supra*).

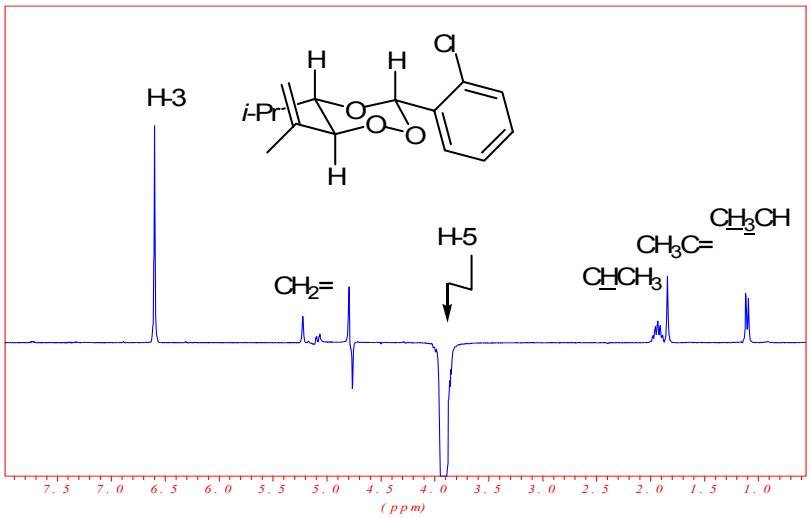
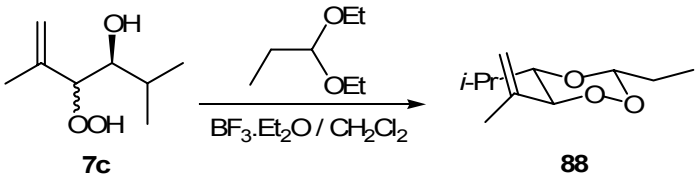


***Figure 3.30*:** 1D-NOE experiment of **87a**.

3.7.8.4 By peroxyacetalization reaction with acetals

Similar to the peroxyacetlization reaction of **7d** with propionaldehyde diethylacetal, carrying out the reaction using the with **7c** results in the all-equatorial 1,2,4-trioxane **88** in 44 % yield. The stereochemical assignment at the three stereogenic centers was confirmed by NMR as before (***Scheme 3.67***).



7c **88**

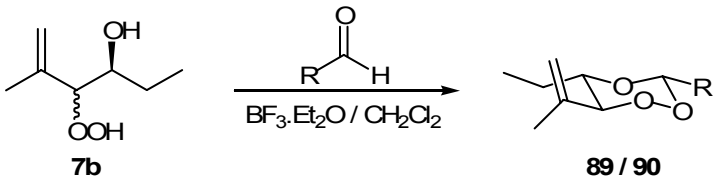
Scheme 3.67

3.7.9 Derived from 4-hydroperoxy-5-methylhex-5-en-3-ol

3.7.9.1 By peroxyacetalization reaction with aldehydes

Treatment of the hydroperoxy homoallylic alcohol **7b** with 2-naphthaldehyde or 2-chlorobenzaldehyde in presence of catalytic amount of BF_3 furnished the peroxyacetals **89** and **90**, respectively, in moderate yields (***Scheme 3.68***). As confirmed by X-ray analysis of **89** (***Figure 3.31***), these trioxanes have also the *trans* configuration with the aryl groups in equatorial position. Both products were fully characterized by spectral data (IR, NMR), elemental analysis and low resolution as well as high resolution mass spectrometry. The significant NMR signals are summarized in ***Table 3.30***. For ^{1}H-NMR of compound **90**, H-5 appears as ddd at 3.82 ppm due to coupling with H-6 (appearing as doublet at 4.48 ppm with $^3J_{HH}$ = 9.24 Hz) and with the two diastereotopic methylene protons of the ethyl group (appearing as multiplet at 1.42-1.62 ppm). The vicinal coupling constant between H-5 and H-6 is therefore 9.24 Hz (*trans* diaxial protons) while that between H-5 and the methylene protons is 3.54 and 8.10 Hz. The characteristic peroxyacetal proton (H-3) absorb as singlet at 5.48 ppm. As a result of the allylic coupling, the two olefinic protons (showing small geminal coupling) and the methyl protons of the isopropenyl group appear as multiplets. The methyl protons in the ethyl group couple with the two diastereotopic methylene protons with identical coupling constants of 7.41 Hz and hence the doublet of doublet appears triplet. The multiplet at 7.21-7.65 ppm corresponds to the aromatic protons. The IR spectrum of **90** shows the characteristic absorption bands at 3079 cm^{-1} (vinylic and aromatic CH), 2971 cm^{-1} (aliphatic CH), 1647 cm^{-1} (isolated C=C), 1597 cm^{-1} (aromatic C=C), 1086, 1053, 1003 cm^{-1} (C-O) and

960, 916 cm^{-1} (O-O). The mass fragmentation patterns for both compounds are depicted in ***Scheme 3.69*** and ***3.70***.

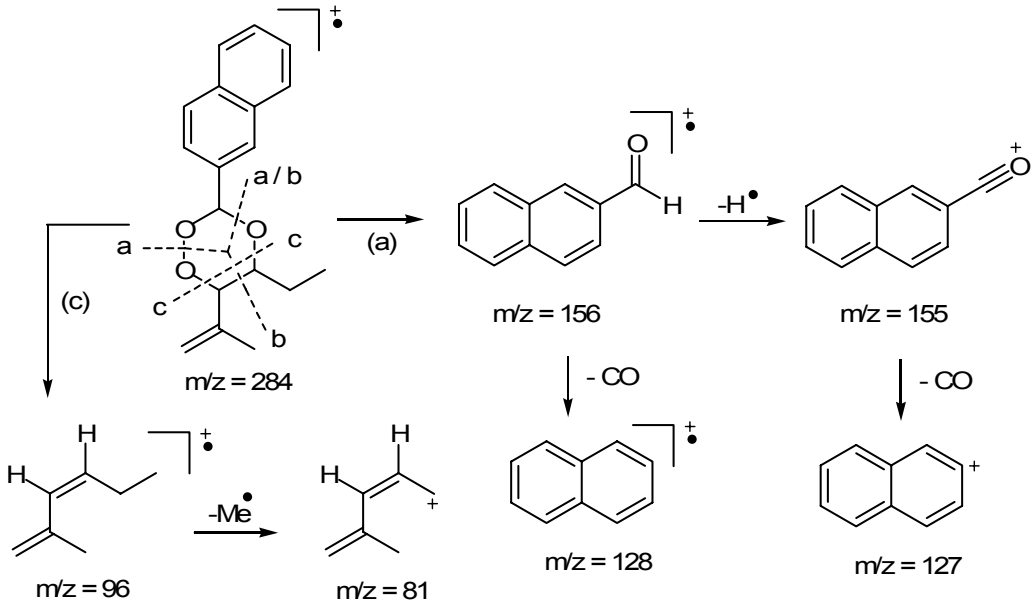


7b **89 / 90**

Scheme 3.68

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
89	2-naphthyl	3.96	78.5	4.67	87.4	6.43	104.0	24
90	2-Cl-C_6H_4	3.82	78.7	4.48	87.4	5.48	101.0	22

***Table 3.30*:** Characteristic signals of **89** and **90** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).



Scheme 3.69: Fragmentation pattern of **89**.

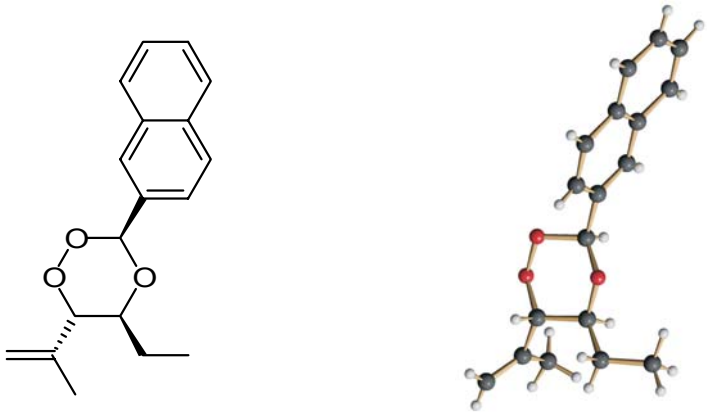
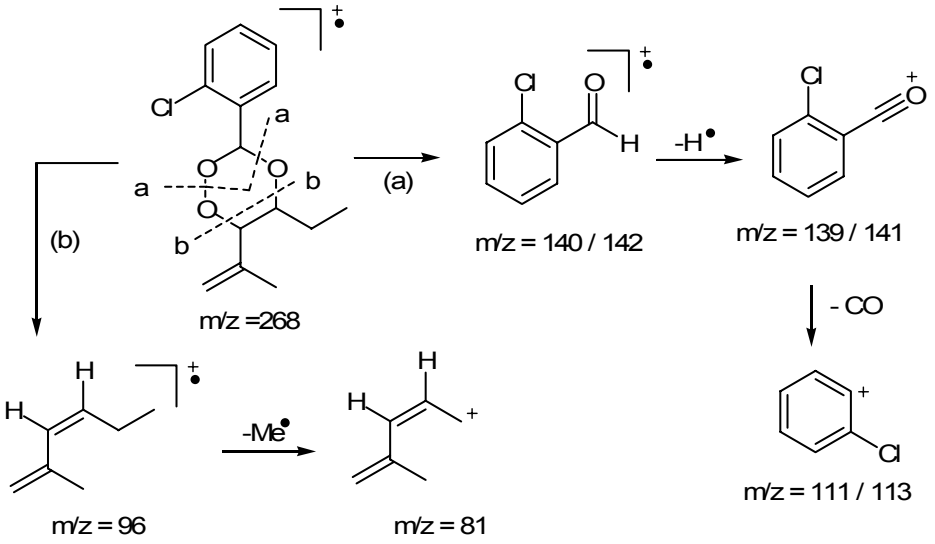


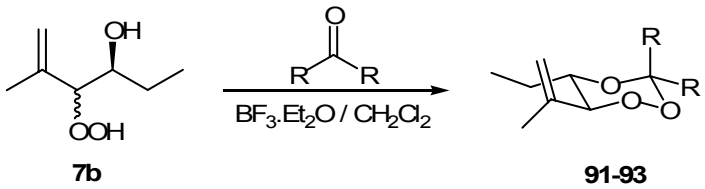
***Figure 3.31*:** X-ray structure of **89**.



Scheme 3.70: Fragmentation pattern of **90**.

3.7.9.2 By peroxyacetalization reaction with symmetric ketones

As the previous hydroperoxy alcohols, condensation of **7b** with symmetric ketones gives the corresponding *trans*-1,2,4-trioxane as sole product (***Scheme 3.71***). The products were assigned as reported previously. Examples for the significant signals of each compound in NMR are summarized in ***Table 3.31***.



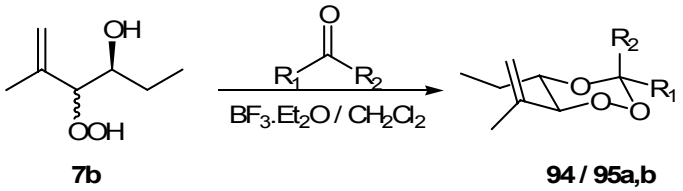
Scheme 3.71

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
91	adamantane		3.80	70.0	4.24	87.5	104.8	5
92	CH_3	CH_3	3.81	71.2	4.24	87.2	102.7	32
93	Et	Et	3.78	70.5	4.21	87.0	106.0	22

***Table 3.31*:** Characteristic signals of **91-93** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

3.7.9.3 By peroxyacetalization reaction with asymmetric ketones

Whereas condensation of **7b** with pinacolone resulted in one trioxane diastereomer, using 2-pentanone afforded a 83:17 trioxane diastereomeric mixture (***Scheme 3.72***). All trioxanes were formed as *trans* configuration (from the coupling constant between H-5 and H-6) with the more bulky group in equatorial position for the major product. ^{1}H- and ^{13}C-NMR characteristic signal are shown in ***Table 3.32***.



7b **94 / 95a,b**

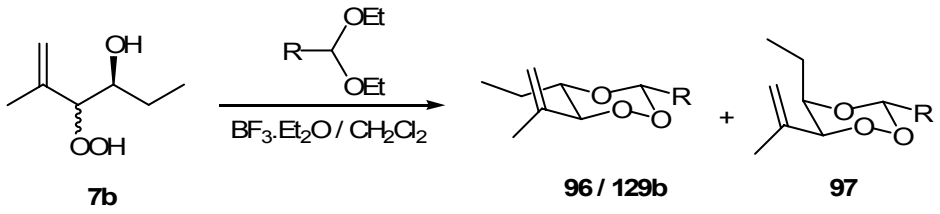
Scheme 3.72

No.	R_1	R_2	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
94	*t*-Bu	CH_3	3.82	70.6	4.20	87.1	106.4	39
95a	*n*-Pr	CH_3	3.82	70.9	4.23	87.3	104.0	38
95b	CH_3	*n*-Pr	3.76	70.1	[a]	87.0	104.6	

***Table 3.32*:** Characteristic signals of **94** and **95** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] Signal is overlapping.

3.7.9.4 By peroxyacetalization reaction with acetals

Reaction of **7b** with acetals such as acetaldehyde dieethylacetal or propionaldehyde diethylacetal afforded the corresponding 1,2,4-trioxanes in 37 and 49 % yields, respectively (***Scheme 3.73***). Whereas in the condensation with acetaldehyde diethylacetal only the *trans* isomer was isolated, in the condensation with propionaldehyde diethylacetal both *cis* (minor) and *trans* (major) isomers were detected. The most significant signals in NMR of all compounds are summarized in ***Table 3.33***. Notably is the downfield shift of the signal corresponding to H-5 in the *cis* isomer **97** (located in equatorial position) which is ascribed to the deshielding effect by the ring oxygen atoms on this equatorial proton.



7b **96 / 129b** **97**

Scheme 3.73

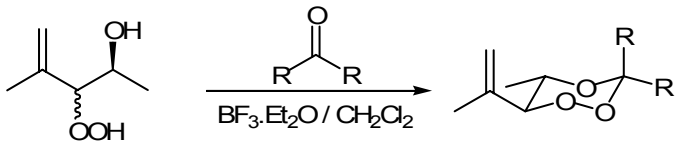
No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
96	CH_3	3.57	77.9	4.30	87.2	5.33	101.5	37
129b	Et	3.57	77.9	4.32	87.5	5.16	105.5	49
97	Et	**3.88**	77.7	4.02	84.6	5.16	105.6	

***Table 3.33*:** Characteristic signals of **96,97** and **129b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

3.7.10 Derived from 3-hydroperoxy-4-methylpent-4-en-2-ol

3.7.10.1 By peroxyacetalization reaction with symmetric ketones

The Lewis-acid catalyzed peroxyacetalization reaction of the hydroperoxy homoallylic alcohol **7a** with a series of symmetric ketones furnished the corresponding 1,2,4-trioxanes **98-103** (***Scheme 3.74***). Full characterization of the products through spectral data (NMR, IR) as well as elemental analysis, mass spectrometry and X-ray analysis revealed the formation of 5,6-*trans* isomer as sole product in all cases (the vicinal coupling constant between H-5 and H-6 is found to be in all products about 9.5 Hz). The chemical shifts of some significant signals in ^{1}H and ^{13}C-NMR of the products were summarized in ***Table 3.34***.



7a **98-103**

Scheme 3.74

No.	R	R	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
98	adamantane		4.04	65.0	4.17	88.7	104.8	12
99	$(CH_2)_6$		4.01	65.9	4.17	88.7	107.5	16
100	$(CH_2)_5$		4.07	65.6	4.18	88.8	102.8	26
101	$(CH_2)_4$		3.29	68.4	4.24	88.6	114.7	73
102	*n*-Pr	*n*-Pr	4.01	65.9	4.14	88.5	105.6	14
103	CH_3	CH_3	3.91	66.2	4.03	88.4	102.3	65

***Table 3.34*:** Characteristic signals of **98-103** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

The ^{1}H,^{1}H-COSY of **99** shows that the two down-field multiplet signals at 2.15, 2.33 ppm belong to the cycloheptanone moiety. Two off diagonal cross peaks are observed for H-5 due to coupling with the methyl group and H-6. The proton H-6 couples only with H-5 and hence has only one cross peak. The allylic coupling between the methyl protons of the isopropenyl group with the olefinic methylene group can be also clearly seen (***Figure 3.32***).

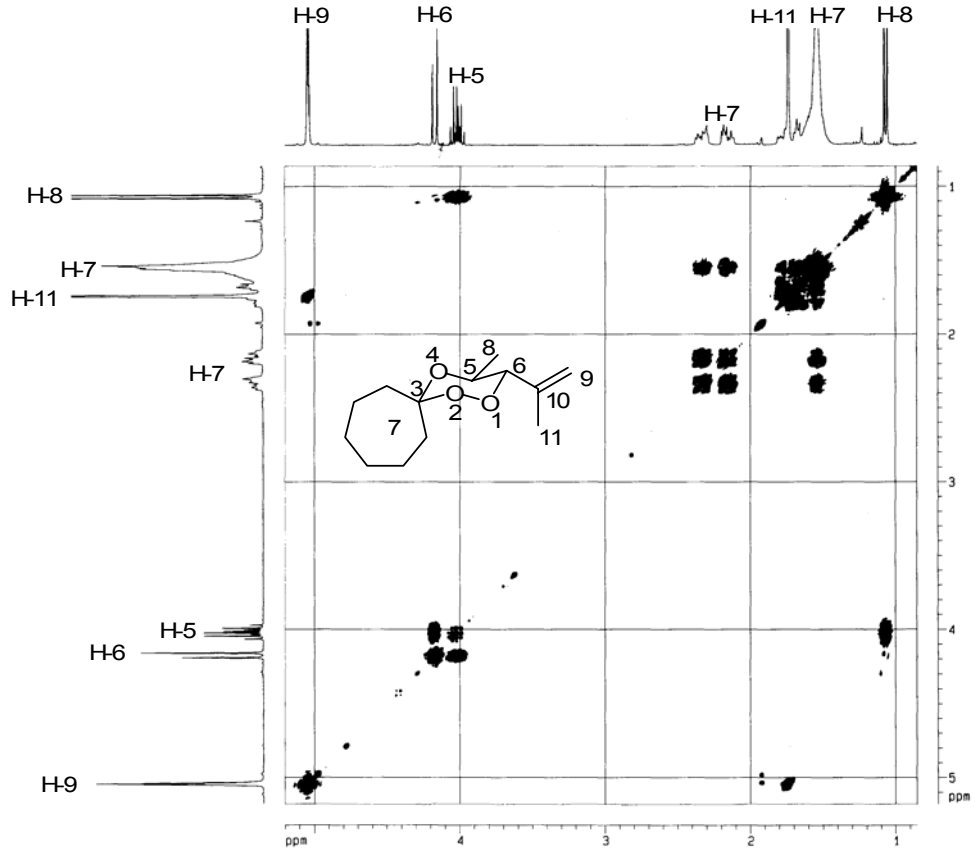


***Figure 3.32*:** ^{1}H,^{1}H-COSY of **99**.

The protons of spatial proximity could be assigned by the off diagonal cross peaks in NOESY experiment (***Figure 3.33***). The key NOEs are indicated by the double headed arrows.

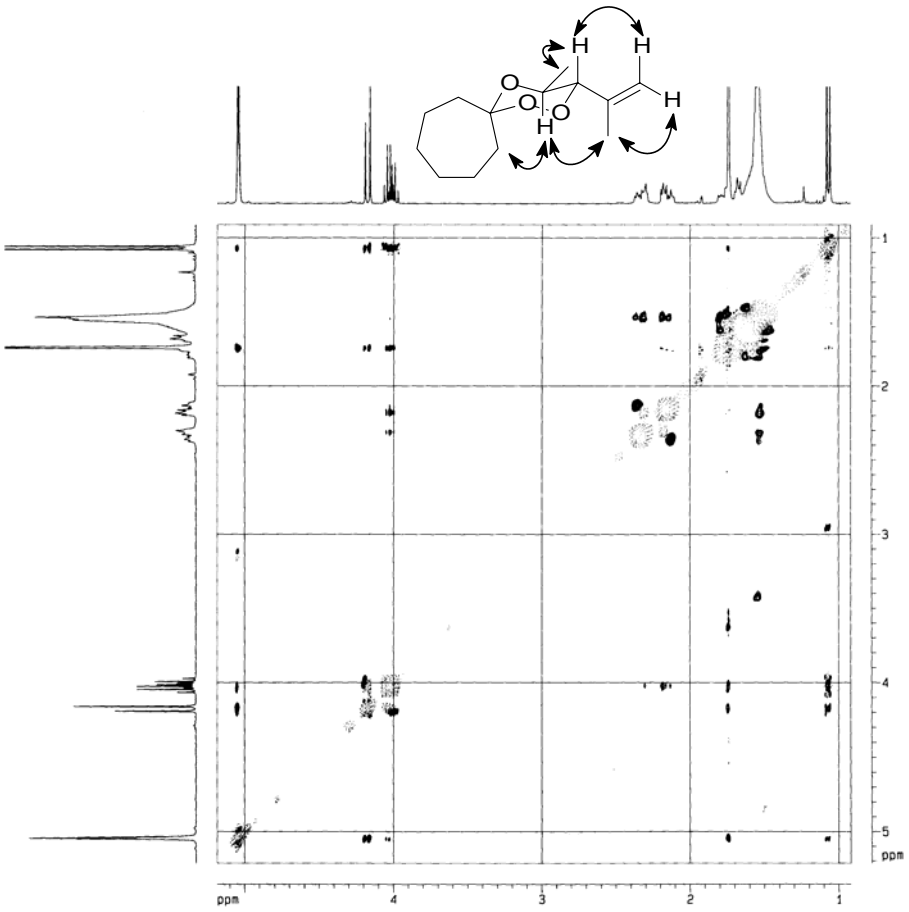


***Figure 3.33*:** NOESY of **99**.

Unambiguous confirmation of the relative configuration was achieved by X-ray analysis for compound **98** (***Figure 3.34***).

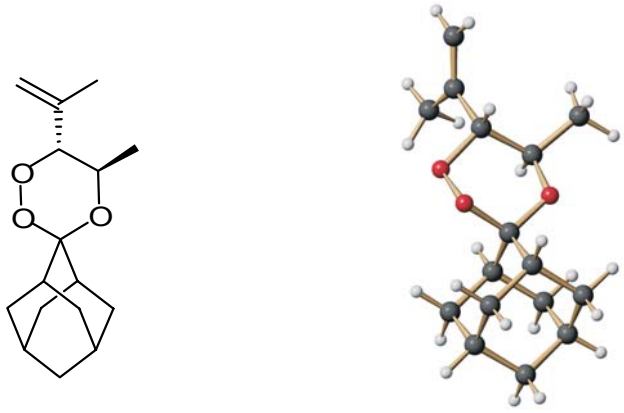
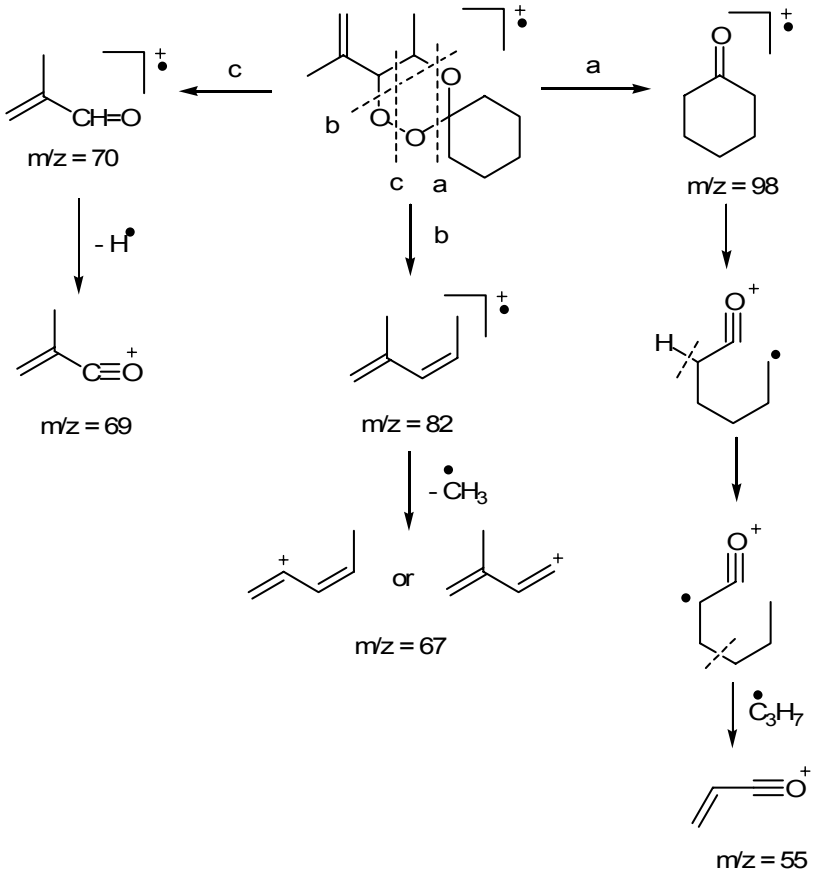


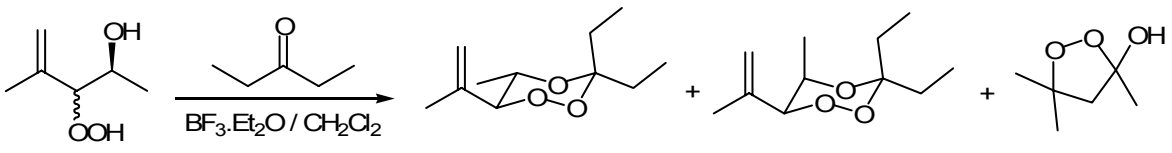
***Figure 3.34*:** X-ray structure of **98**.

The IR spectrum of **98** shows absorption bands at 2912 cm^{-1} (aliphatic CH), 1648 cm^{-1} (isolated C=C), 1222, 1109, 1023, 999 cm^{-1} (C-O), 926 cm^{-1} (O-O). The mass fragmentation pattern of **100** is depicted in ***Scheme 3.75***.



***Scheme 3.75*:** Mass fragmentation pattern of **100**.

Condensing a 73:27 *syn*/*anti* diastereomeric mixture of the *vic*-hydroperoxy alcohol **7a** (synthesized by photooxygenation reaction of **6a** in MeOH as solvent) with 3-pentanone furnished a 78:22 mixture of two 1,2,4-trioxne products **104a,b** beside the minor 1,2-dioxolane derivative **104c** (***Scheme 3.76***). The coupling constants ($^3J_{HH}$) clearly indicate that the major diastereomer ($^3J_{HH}$ = 9.5 Hz) has the *trans* configuration (also expected since it is derived from the major *syn*-hydrperoxy alcohol), and the minor diastereomer ($^3J_{HH}$ = 5.4 Hz) has the *cis* configuration (also expected since it is derived from the minor *anti*-isomer). The most significant signals in ^{1}H-NMR corresponding to **124a,b** are shown in ***Figure 3.35***.



7a **104a** **104b** **104c**

Scheme 3.76

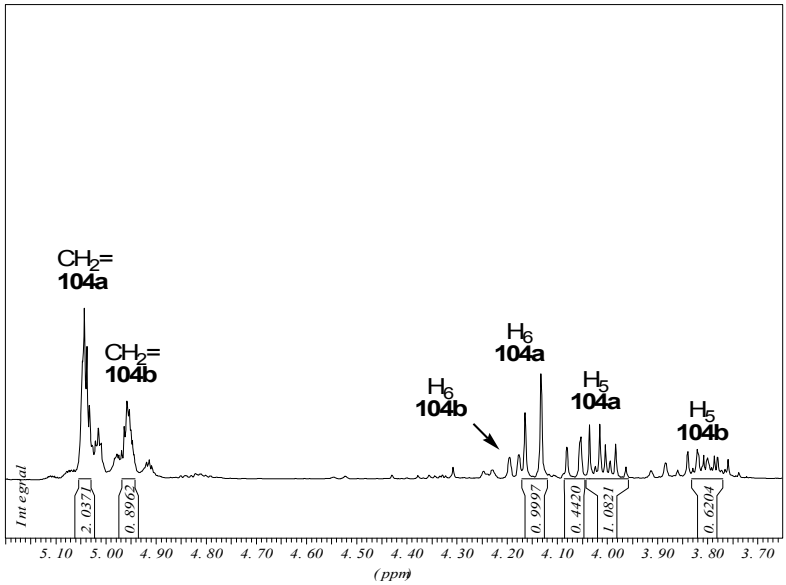


***Figure 3.35*:** Part of the ^{1}H-NMR spectrum showing signals of **104a,b**.

Dual display parts of the ^{1}H-NMR spectra for **124a** isolated as sole product as well as that of a diastereomeric mixture of **124a,b** are shown in ***Figure 3.36*** and ***3.37***. The spectral data of the minor products **124b** and **124c** can be determined by spectral substraction.

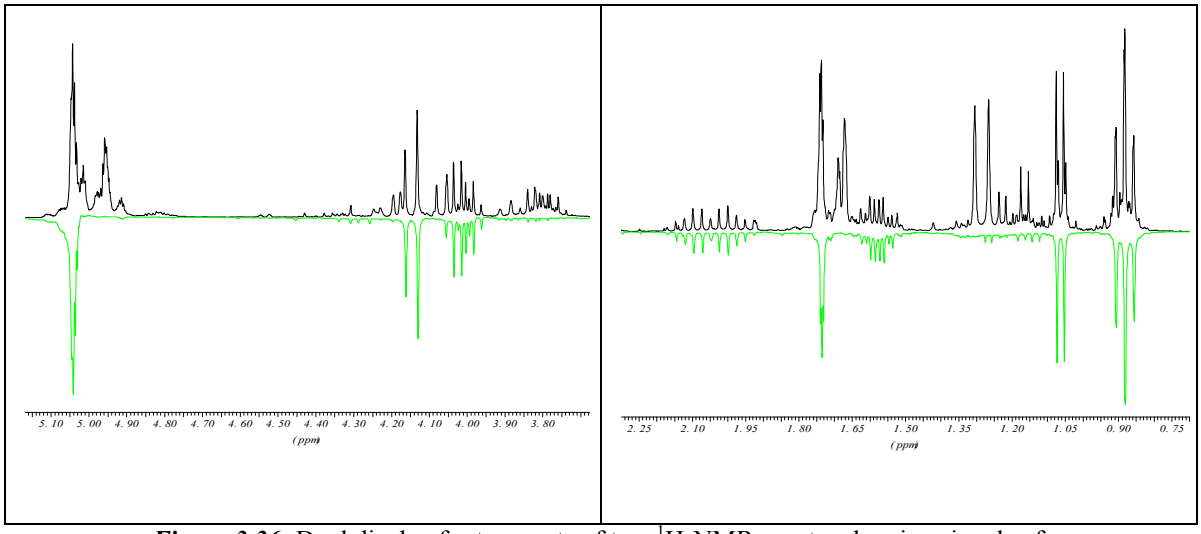


***Figure 3.36*:** Dual display for two parts of two ^{1}H-NMR spectra showing signals of:
1) *trans*-1,2,4-trioxane **104a** as sole product (down).
2) Diastereomeric mixture of *trans* and *cis* 1,2,4-trioxanes **104a,b** (up).

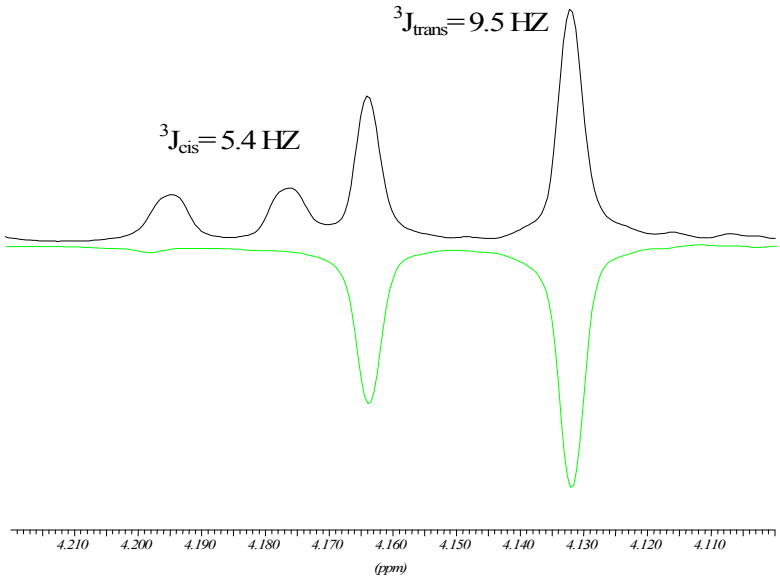
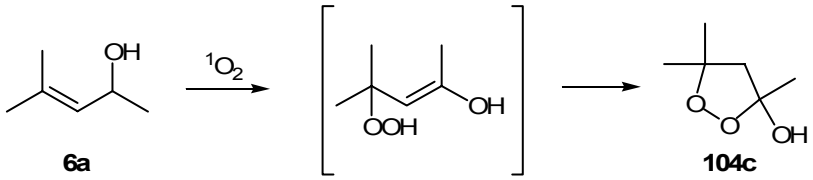


***Figure 3.37*:** Dual display for part of the ^{1}H-NMR spectra showing H-6 signals in:
1) *trans*-1,2,4-trioxane **104a** as sole product (down).
2) Diastereomeric mure of *trans*- and *cis*-1,2,4-trioxanes **104a,b** (up).

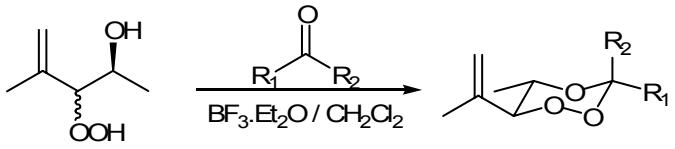
The byproduct **104c** proceeds is formed by cyclization of the other hydroperoxy alcohol regioisomer (***Scheme 3.77***).



***Scheme 3.77*:** Formation of the byproduct **104c**.

3.7.10.2 By peroxyacetalization reaction with asymmetric ketones

Using 1,5-diphenylpentan-1,5-dione as the carbonyl compound afforded only the *trans*-1,2,4-trioxne diastereomer **105** having the phenyl group at C-3 in axial position (as proved by the NOE experiment in ***Figure 3.38***, where on saturation of H-5 a characteristic enhancement of the phenyl group at C-3 is observed and hence *cis* relationship between them is predicted). In contrast, both acetophenone and 2-butnone afforded dastereomeric mixtures of two trans-1,2,4-trioxanes **106a,b** and **107a,b**, respectively. Assignment of the structures was based on NMR and IR data. The characteristic NMR signals for the products are shown in ***Table 3.35***.



7a **105 / 106-107a,b**

Scheme 3.78

No.	R_1	R_2	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
105	$(CH_2)_3COPh$	Ph	3.74	67.2	4.27	88.6	106.4	4
106a	Ph	CH_3	3.99	76.0	**3.84**	86.3	108.4	30
106b	CH_3	Ph	**3.71**	75.0	4.05	87.4	108.3	
107a	Et	CH_3	4.06	66.3	4.16	88.8	104.1	77
107b	CH_3	Et	4.0	66.1	4.18	88.4	105.0	

***Table 3.35*:** Characteristic signals of **105-107** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

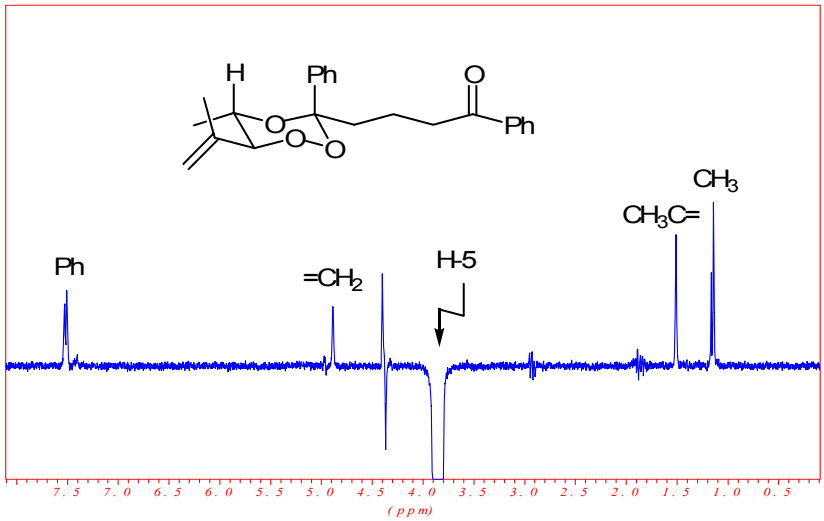


Figure 3.38: 1D-NOE experiment of **105**.

The trioxanes **106a**,**b** are formed in 1:1 ratio. Interestingly, the ring current effect causes an up-field shift of H-5 signal in **106b** and of H-6 signal in **106a**, as shown by NOE experiment (***Figure 3.39***).

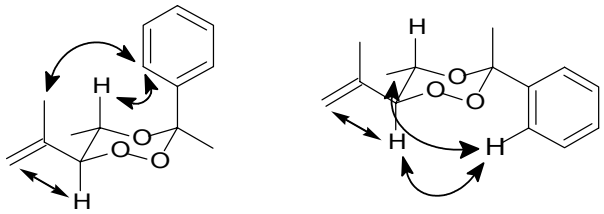
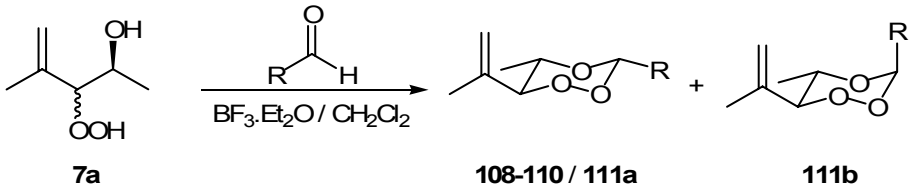


***Figure 3.39*:** NOE experiment of **106a,b**.

3.7.10.3 By peroxyacetalization reaction with aromatic aldehydes

Condensation of **7a** with aromatic aldehydes such as furfural, 1-naphthaldehyde, 2-bromobenzaldehyde afforded only the more stable trioxane diastereomer with all substituents equatorial. In case of using benzaldehyde as the carbonyl component, a 97:3 diastereomeric mixture of two *trans* 1,2,4-trioxanes **111a,b** was formed. The diastereomer **111a** having the phenyl group equatorial is also the major product (***Scheme 3.79***). The chemical constitution as well as the relative configuration were unequivocally confirmed by a full characterization with ^{1}H-, ^{13}C-NMR, IR, elemental analyses, mass spectrometry and X-ray analysis. The most significant signals in NMR are summarized in ***Table 3.36***.



Scheme 3.79

No.	R	OCH		OOCH		OCHOO		Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
108	2-furyl	4.0	74.1	4.45	88.7	6.25	**98.4**	34
109	1-naphthyl	4.20	74.2	4.61	88.9	6.84	102.6	46
110	2-Br-C_6H_4	4.08	73.8	4.47	88.7	6.52	102.9	53
111a	Ph	4.05	73.8	4.46	88.8	6.21	104.1	33
111b	Ph	3.90	79.7	[a]	84.2	6.40	[a]	

***Table 3.36*: Characteristic signals of **108-111** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).**
[a] Signal is overlapping.

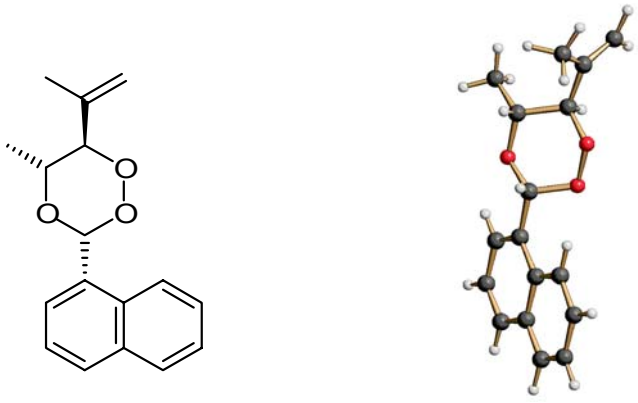
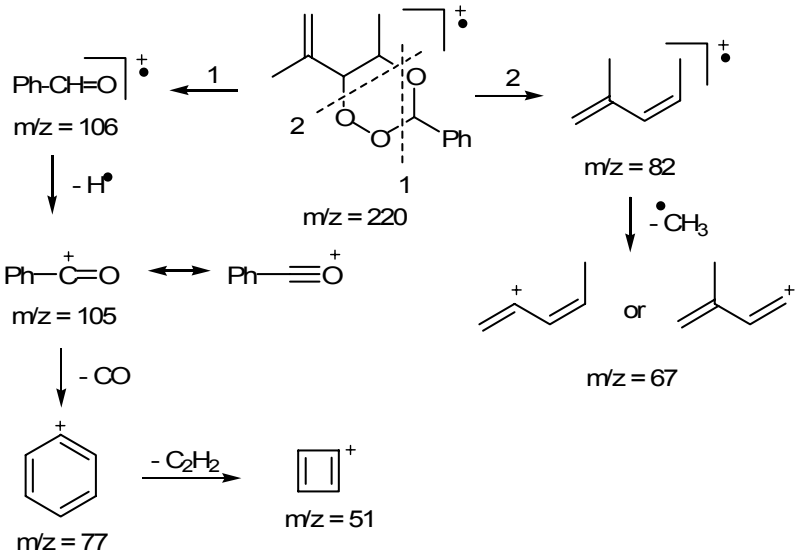


***Figure 3.40*: X-ray structure of **109**.**

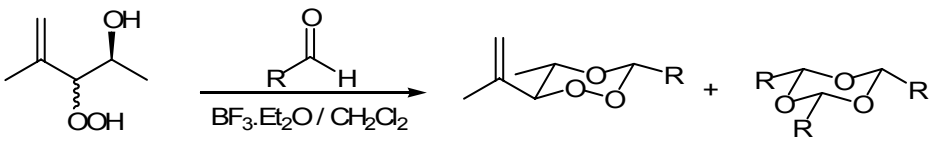
The mass fragmentation pattern of the trioxane **111** is depicted in ***Scheme 3.80***.



***Scheme 3.80*:** Fragmentation pattern of **111**.

3.7.10.4 By peroxyacetalization reaction with aliphatic aldehydes

In contrast to aromatic aldehydes, the BF_3-catalyzed peroxyacetalization of **7a** with aliphatic aldehydes afforded inseparable mixtures of 1,2,4-trioxanes as well as 1,3,5-trioxanes (***Scheme 3.81***). The latter products are formed by the competing Lewis-acid catalyzed trimerization reaction of the aldehydes. Only one diastereomer was detected for the 1,2,4-trioxanes **129e**, **113**, **115** having all substituents equatorial. The characteristic signals corresponding to the 1,2,4-trioxanes and 1,3,5-trioxanes are summarized in ***Table 3.37*** and ***3.38***, respectively. The trimerization problem in case of using aliphatic aldehydes was overcome by using the corresponding acetals for the peroxyacetalization reaction, by this way only the desired 1,2,4-trioxanes are formed (*vide supra*).



7a **129e / 113/ 115** **112 / 114 / 116**

Scheme 3.81

No.	R	OCH		OOCH		OCHOO	
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR
129e	CH_3	3.79	73.2	4.25	88.5	5.36	101
113	Et	3.78	73.0	4.24	88.7	5.15	105
115	*i*-Pr	3.76	73.1	4.24	88.8	4.96	108

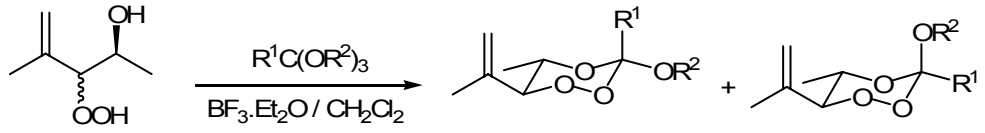
***Table 3.37*:** Characteristic signals of **129e,113** and **115** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

No.	R	OCHO	
		^{1}H-NMR	^{13}C-NMR
112	CH_3	5.0	98
114	Et	4.73	102
116	*i*-Pr	4.45	105

***Table 3.38*:** Characteristic signals of **112,114** and **116** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

3.7.10.5 By peroxyacetalization reaction with orthoesters

Previously we discussed many condensation reactions of the hydroperoxy homoallylic alcohols with aldehydes or acetals were two *trans*-1,2,4-trioxanes are formed. In these reactions we found a high diastereomeric preference for the formation of the diastereomer having an equatorial alkyl substituent at C-3. This was explained by the less tendency for such substituents to adopt the axial position due to the 1,3-diaxial interaction found in the minor diastereomer. In contrast to this behavior we found that treatment of the *vic*-hydroperoxy allylic hydroperoxide **7a** with different orthoesters resulted in two 5,6-*trans*-1,2,4-trioxanes mostly with very poor stereoselectivities (***Scheme 3.82***). The diastereomeric ratios are 57:43 for **117a,b**; 72:28 for **118a,b** and about 1:1 for **119a,b**. Unequivocally, strong anomeric effect of the axial alkoxy group is responsible for the extra stability of these diastereomers. This extra stability was not found in the previous examples with C-3 alkyl-substituted analogues and hence the participation of the minor diastereomers with an axial C-3 alkyl-substituted trioxanes in the product mixture was significantly lower. The *trans* configuration was confirmed by the coupling constant as described before and all products were characterized by ^{1}H- and ^{13}C-NMR analyses (***Table 3.39***). The most characteristic signal is that corresponding to the peroxyortho ester carbon resonating at 110-115 ppm in ^{13}C-NMR. To the best of my knowledge, compounds **117-119a,b** are the first perortho esters with 1,2,4-trioxane substructure described in literature.



7a **117a-119a** **117b-119b**

Scheme 3.82

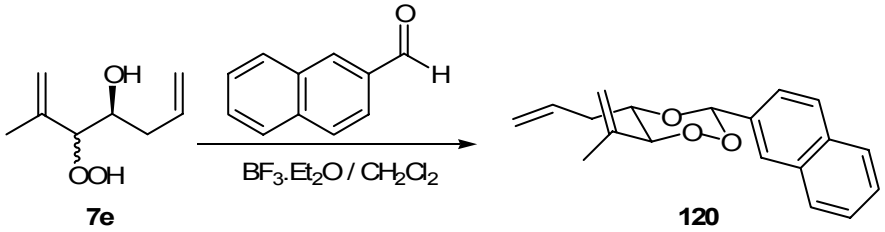
No.	R^1	R^2	OCH		OOCH		OCHOO	
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR
117a,b	H	Me	4.02 (4.30)	74.2 (65.9)	4.20 (4.36)	87.5 (88.9)	5.72 (5.48)	113.6 (111.0)
118a,b	H	Et	4.02 (3.60)	63.8 (65.8)	4.20[a]	87.5 (88.9)	5.77 (5.58)	113.3 (110.0)
119a,b	Me	Et	4.14[a]	66.1[a]	4.24[a]	87.8[a]	-	113.8 (114.3)

***Table 3.39*:** Characteristic signals of **117-119a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$). The chemical shifts between parentheses correspond to minor diastereomer.

3.7.11 Derived from 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol

3.7.11.1 By peroxyacetalization reaction with aldehydes

Compound **120** was obtained in low yield on treatment of a solution of **7e** with 2-naphthaldehyde in dichloromethane with BF_3 as catalyst (***Scheme 3.83***). The chemical structure as well as the stereochemical assignment were based on NMR data (as before), elemental analysis, mass spectrometry and HRMS. Some significant NMR signals are summarized in ***Table 3.40***.



7e **120**

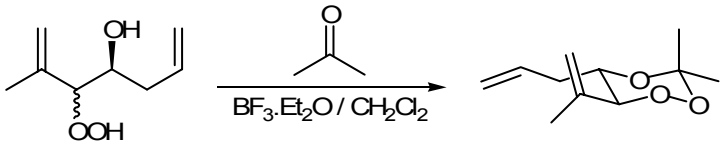
Scheme 3.83

No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
120	4.06	76.8	4.64	87.1	6.37	104.1	4

***Table 3.40*:** Characteristic signals of **120** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

3.7.11.2 By peroxyacetalization reaction with ketones

Similarly, the trioxane **121** was isolated from the reaction of **7e** with acetone (***Scheme 3.84***). The product was assigned on the basis of NMR (***Table 3.41***).



7e **121**

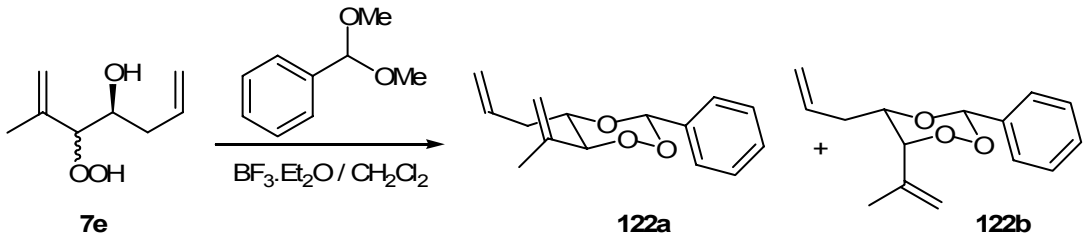
Scheme 3.84

No.	OCH		OOCH		OCOO	Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
121	3.98	69.6	4.28	86.7	102.7	17

***Table 3.41*:** Characteristic signals of **121** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

3.7.11.3 By peroxyacetalization reaction with acetals

The peroxyacetalization reaction of **7e** with benzaldehyde dimethylacetal furnished the 1,2,4-trioxane diastereomeric mixture **122a,b** in 93:7 diastereomeric ratio and 26 % chemical yield (***Scheme 3.85***). Based on the coupling constant between H-5 and H-6 it was found that the major product has a 5,6-*trans* configuration **122a** and the minor isomer has 5,6-*cis* configuration **122b**. In both compounds the phenyl group is in equatorial position to circumvent any destabilizing 1,3-diaxial interaction. Characteristic signals in NMR are shown in ***Table 3.42***.



Scheme 3.85

No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
122a	4.03	76.6	4.61	86.9	6.23	103.9	26
122b	**4.31**	76.4	**4.22**	84.1	6.38	104.4	

***Table 3.42*:** Characteristic signals of **122a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

The configuration of the minor diastereomer was also based on NOE experiment. Saturation of H-5 resulted in clear enhancement in the singlet signal corresponding to H-3. This indicates that the allyl group is equatorial and hence the isopropenyl group should be in axial position (***Figure 3.41***).

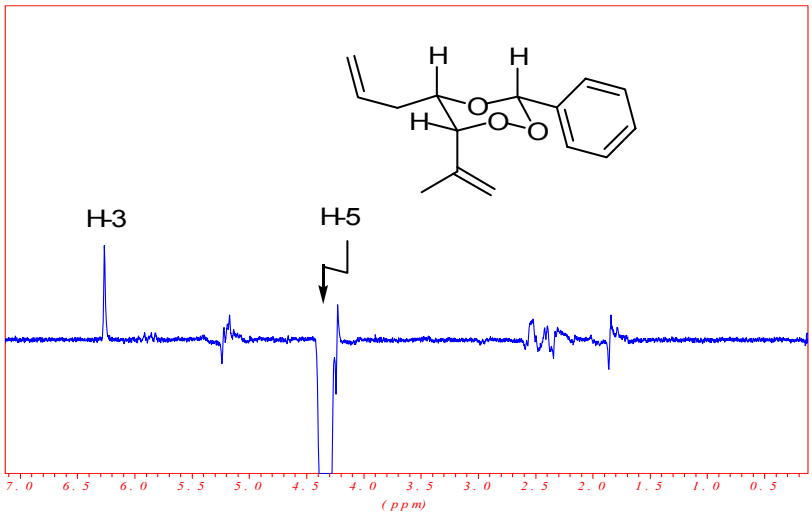
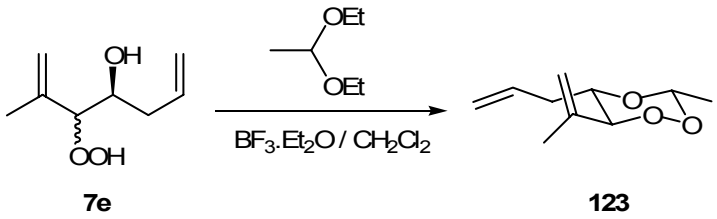


***Figure 3.41*:** 1D-NOE experiment of **122b**.

Changing the acetal component to acetaldehyde diethylacetal led only to the more stable 1,2,4-trioxane diastereomer **123**, having all the substituents in equatorial positions.

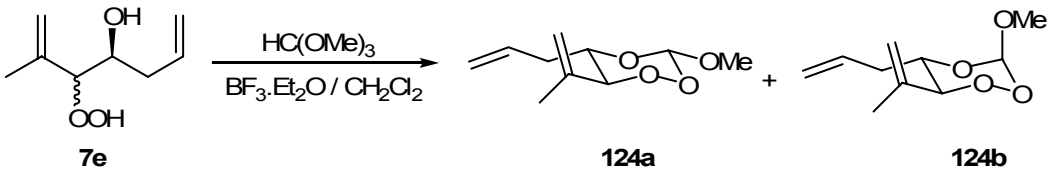


7e **123**

Scheme 3.86

3.7.11.4 By peroxyacetalization reaction with orthoesters

The peroxyacetalization of the *vic*-hydroperoxy allylic hydroperoxide **7e** with orthoesters such as trimethyl orthoformate resulted in two 5,6-*trans*-1,2,4-trioxanes with very low stereoselctivity, about 45:55 (***Scheme 3.87***). Unequivocally, the strong anomeric effect of the axial methoxy group in **124b** is responsible for the extra stability of this diastereomer.



7e **124a** **124b**

Scheme 3.87

No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
124a	4.25	**68.8**	4.45	87.0	5.48	**111.0**	21
124b	3.94	**76.9**	4.28	85.5	5.69	**113.5**	

***Table 3.43*:** Characteristic signals of **124a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

Confirmation of the chemical structure was based on NMR analysis. The most characteristic signal is that corresponding to the peroxyortho ester carbons resonating as singlet at 5.69, 5.48 ppm in ^{1}H-NMR and at 113.5, 111.0 ppm in ^{13}C-NMR. Interestingly, a large difference in the chemical shifts for C-5 in both diastereomers ($\Delta\delta$ = 8.1 ppm). Clearly, C-5 in **124b** is more deshielded by the effect of the axial methoxy group than in case of **124a**. Other significant signals corresponding to C-6 were also shown in ***Table 3.43***. Fortunately, the major diastereomer (**124b**) could be separated from the diastereomeric mixture by chromatography, the NMR of the separated major diastereomer and that of the diastereomeric mixture **124a,b** are shown in ***Figure 3.42.***

Consistent with the NMR, PM3 calculations (***Figure 3.43***) revealed that the heat of formation (ΔH_f) of **124a** is -78.86 kcal/mol while that for **124b** is -80.68 kcal/mol. Clearly, the diastereomer **124b** with an axial methoxy group at C-3 is more stable by about 1.8 kcal/mol. The anomeric effect of alkoxydioxanes and 2-alkoxytetrahydropyrans has also been reported and an alkoxide group preferentially favors an axial position by approximately 0.2-0.8 kcal/mol.[148,149]

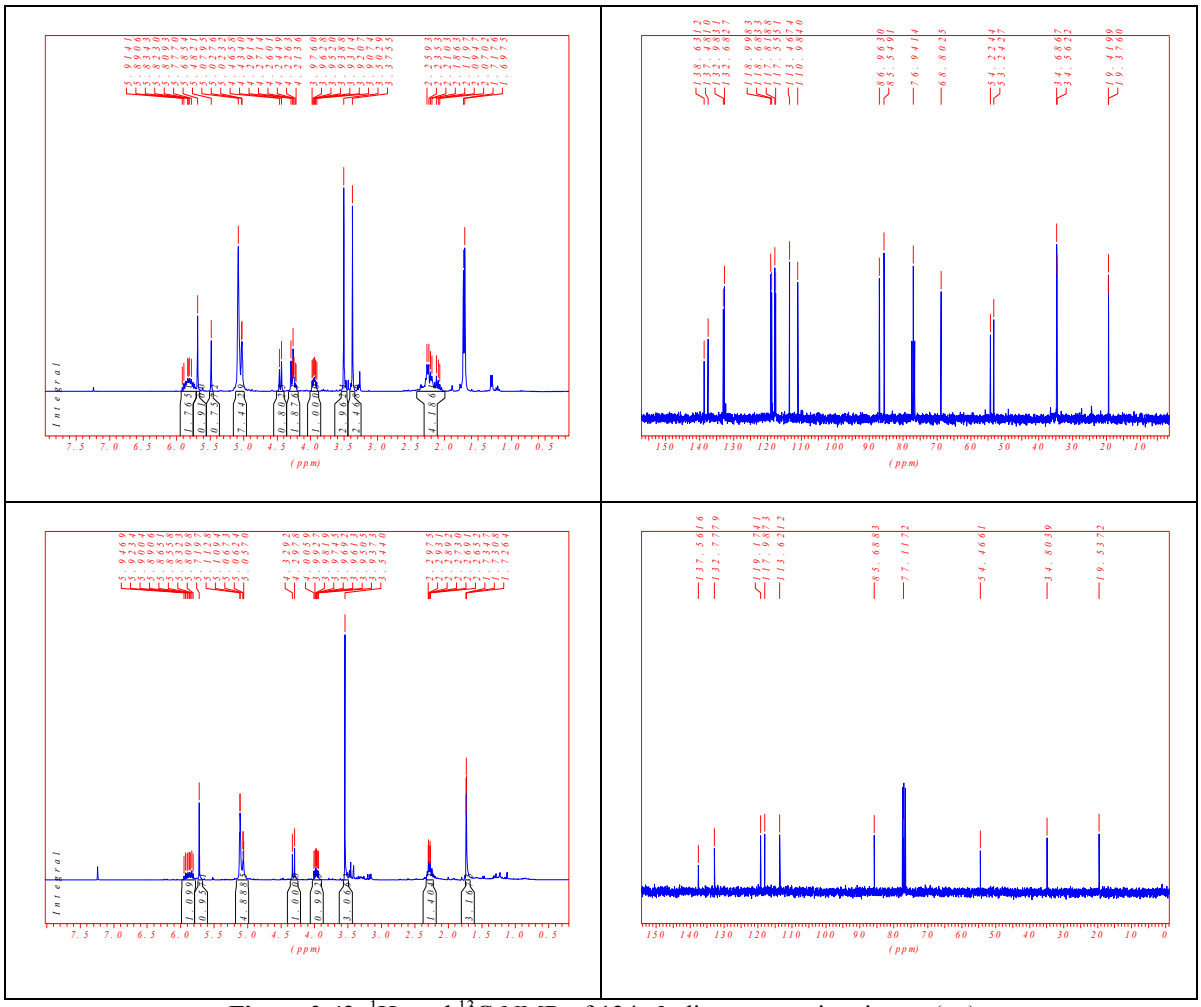


***Figure 3.42*: ^{1}H- and ^{13}C-NMR of **124a,b** diastereomeric mixture (up) and ^{1}H- and ^{13}C-NMR of the major diastereomer **124b** (down).**

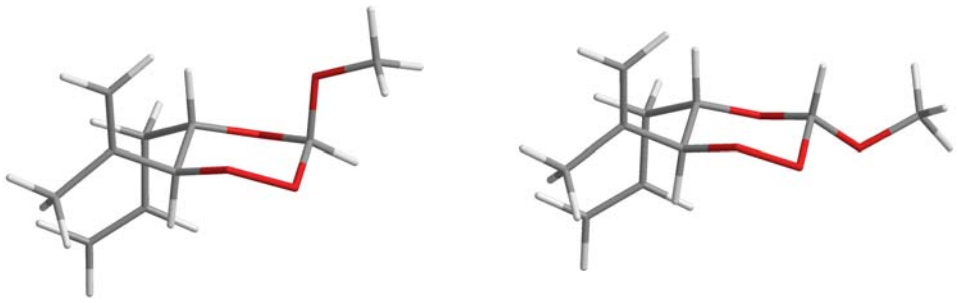
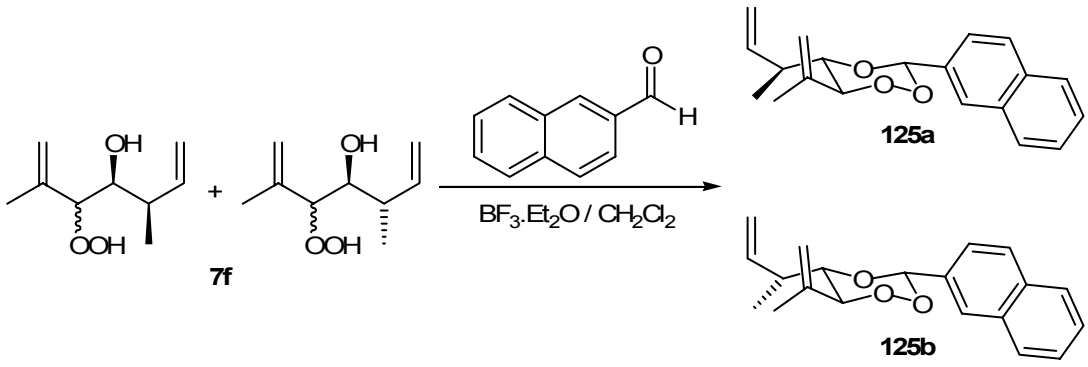


***Figure3.43*: Model of 1,2,4-trioxane **124a,b** in a minimum energy conformations. The model was generated using PM3.**

3.7.12 Derived from 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol

3.7.12.1 By peroxyacetalization reaction with aldehydes

The condensation reaction of 2-naphthaldehyde with the two diastereomeric mixtures of the *vic*-hydroxy allylic hydroperoxide **7f** furnished a 1:1 diastereomeric mixture of the 1,2,4-trioxanes **125a,b** (***Scheme 3.88***). In both ^{1}H- and ^{13}C-NMR, many sets of twin signals could be observed (***Figure 3.44***, ***Table 3.44***). The chemical structure of the trioxanes was based on NMR, IR and elemental analyses as well as low and high resolution mass spectrometry. The characteristic absorption bands in the IR spectrum are stretching at 3078 cm^{-1} (aromatic or vinylic CH), 2978, 2923 cm^{-1} (aliphatic CH), 1653, 1647 cm^{-1} (isolated C=C), 1605 cm^{-1} (aromatic C=C), 1127, 1076, 999 cm^{-1} (C-O) and at 904, 866 cm^{-1} (O-O). Proton H-6 appears as doublet (with coupling constant about $^{3}J_{HH}$ = 9.5 Hz for both diastereomers) while H-5 appears as doublet of doublet ($^{3}J_{HH}$ = 1.9, 9.54 Hz for one diastereomer and 2.51, 9.57 Hz for the other). Clearly, the vicinal coupling constant between H-5 and H-6 is assigned to be about 9.5 Hz indicating a dihedral angle of 180° (and hence the relative configuration of both trioxane diastereomers is *trans*), while the small coupling constants correspond to the coupling of H-5 with the allylic proton. As confirmed before, the 2-naphthyl group in both diastereomers is located *cis* to the substituent on C-5. Notoriously, both isolated 1,2,4-trioxanes result from the two major diastereomers of the *vic*-hydroxy allylic hydroperoxide *syn*,*syn*-**7f** and *syn*,*anti*-**7f** (*vide supra*). The NMR of **125a**,**b** is shown in ***Figure 3.44***.



Scheme 3.88

No.	OCH		OOCH		OCHOO		Yield (%)
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	
125a,b	4.02/ 4.12	79.9/ 80.0	4.83/ 4.89	85.4/ 85.6	6.40/ 6.41	103.9/ 104.0	15

Table 3.44: Characteristic signals of **125a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

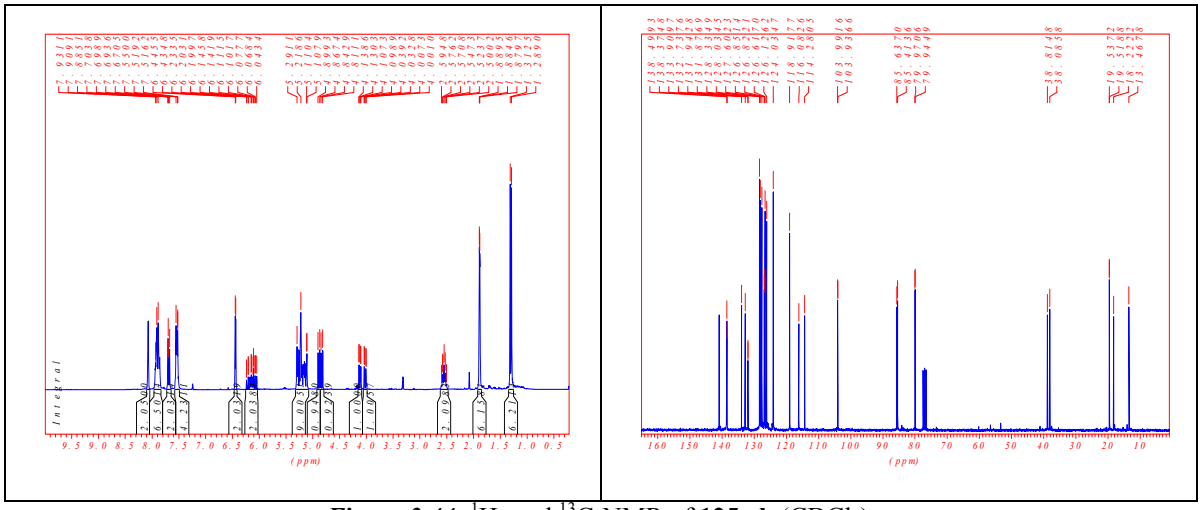
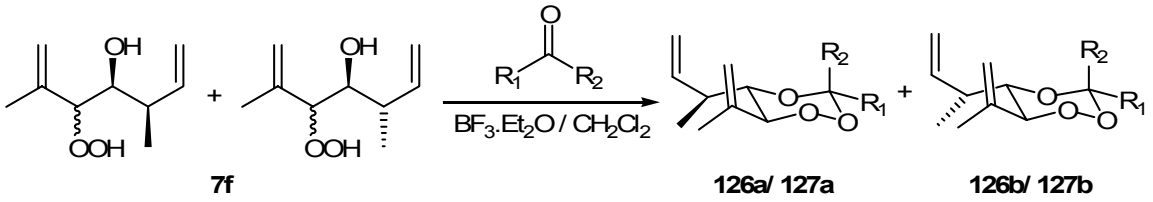


Figure 3.44: ^{1}H- and ^{13}C-NMR of **125a,b** ($CDCl_3$).

3.7.12.2 By Peroxyacetalization Reaction with Ketones

Similarly, the reaction with symmetric ketones as adamantanone or acetone afforded the diastereomeric 1,2,4-trioxanes **126a,b** and **127a,b** in 4 and 14 % yield, respectively. Also, all compounds show a *trans* configuration of H-5 and H-6 (***Scheme 3.89***). Surprisingly, whereas about 1:1 diastereomeric mixture of **127a,b** is formed, higher stereoselectivity was observed for the two diastereomers **126a,b** (about 31:69). The most characteristic signals for both diastereomers are summarized in ***Table 3.45***.



7f **126a/ 127a** **126b/ 127b**

Scheme 3.89

No.	R_1	R_2	OCH		OOCH		OCOO	Yield (%)
			^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
126a,b	adamantane		3.86/ 3.93	71.5/ 71.5	4.39/ 4.44	85.3/ 85.2	104.6/ 103.5	4
127a,b	CH_3	CH_3	3.84/ 3.94	72.8/ 72.7	4.36/ 4.43	85.3/ 85.1	102.6[a]	14

***Table 3.45*:** Characteristic signals of **126a,b** and **127a,b** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] Both diastereomers have the same chemical shift.

Interestingly, for each pair of the trioxane diastereomers (**125a**,**b**; **126a**,**b** and **127a**,**b**) a large difference in the chemical shift of the allylic methyl group (**CH_3**CH) between each pair of the trioxane diastereomers was observed (in ^{13}C-NMR of **125a,b**, **126a,b** and **127a,b** $\Delta\delta$ = 5.0 ±0.3 ppm where one methyl resonate at about 13 ppm and the other at 18 ppm) and (in ^{1}H-NMR of **126a,b** and **127a,b** $\Delta\delta$ = 0.4 ppm). This can be interpreted by drawing the Newmann projection of the most stable conformer (possessing only two gauche interactions) for each diastereomer (***Figure 3.45***). Clearly, the methyl group in conformer **B** is located in spatial vicinity to the oxygen atom of the ring and hence is expected to be more deshielded and absorb more down-field than the shielded methyl group in the conformer **A**.

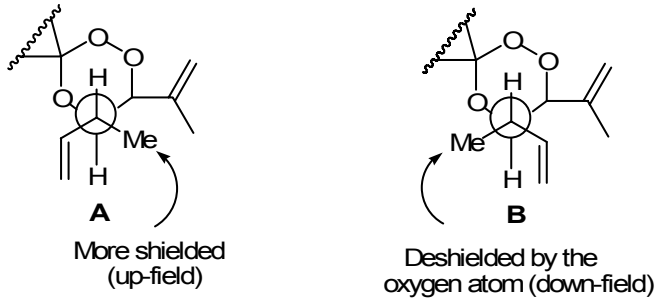
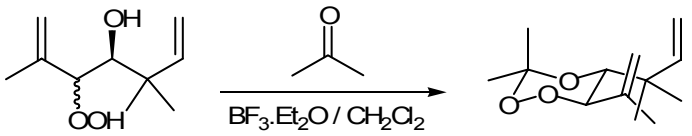


***Figure 3.45*:** The most stable conformation of each 1,2,4-trioxane diastereomer.

3.7.13 Derived from 3-hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol

3.7.13.1 By peroxyacetalization reaction with ketones

Condensing the β-hydroperoxy alcohol **7k** (derived from the natural terpene *artemisia alcohol*) with acetone in dichloromethane and in presence of a catalytic amount of BF_3 furnished a single isomeric 1,2,4-trioxane product **128** (***Scheme 3.90***).



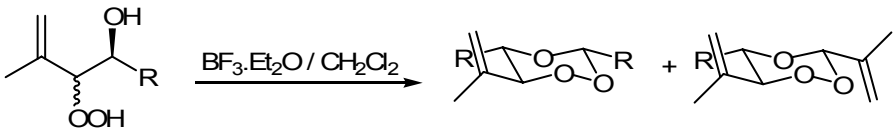
7k **128**

Scheme 3.90

The ^{1}H-NMR of **128** shows four singlet signals corresponding to the protons of the four methyl groups on saturated carbons, and a multiplet (due to allylic coupling) corresponds to the methyl group on the unsaturated carbon. Both H-5 (at 3.74 ppm) and H-6 (at 4.34 ppm) absorb as doublet due to vicinal coupling between them (with coupling constant of 9.7 Hz indicating 180° dihedral angle between them and hence *trans* diaxial-configuration of the trioxane). The two isopropenyl olefinic protons couple to each other with small olefinic geminal coupling and also to the allylic methyl group with small allylic coupling and hence appearing as multiplet. Whereas the signals of both olefinic methylene groups overlap at 4.90-5.10 ppm, the signal corresponding to the CH of the vinyl group shows at 5.92 ppm a characteristic doublet of doublet pattern with coupling constants 17.5 and 10.9 Hz corresponding to the olefinic vicinal coupling with the *trans* and *cis* protons respectively. The most significant signal in ^{13}C-NMR is that related to the peroxyacetal carbon (C-3) resonating at 102.4 ppm.

3.8 Lewis-Acid Catalyzed Cleavage of β-Hydroperoxy Alcohols and Subsequent Cross-Peroxyacetalization Reaction

A series of 1,2,4-trioxanes was synthesized by treating the β-hydroxy hydroperoxides with catalytic amount of BF_3 in absence of any external carbonyl compounds (***Scheme 3.91***).[150] The reaction is chemoselective with the formation of the 1,2,4-trioxanes **129a-h** as the major components in all cases (***Table 3.46***).



7a-e,g,h,p **129a-h** **130a-h**

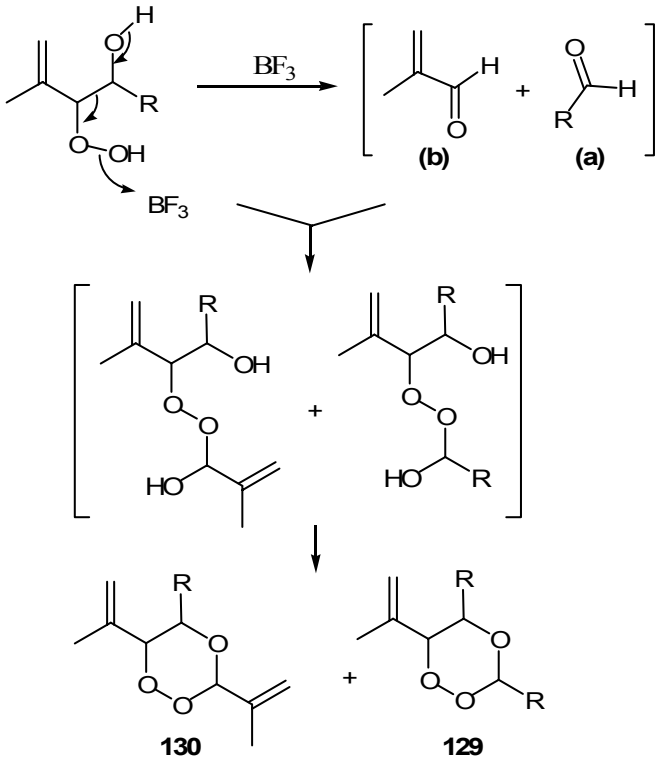
Scheme 3.91

Entry	R	129 : 130[a]	Yield[c] (%)
1	*c*-Pr	61 : 39	33
2	Et	63 : 37	41
3	*i*-Bu	83 : 17	59
4	*n*-Bu	68 : 32	60
5	Me	79 : 21	62
6	*n*-Pr	95 : 5[b]	24
7	allyl	80 : 20	52
8	*i*-Pr	91 : 9	50

***Table 3.46*: Chemoselectivity of the BF_3-catalyzed cleavage and peroxyacetalization of β-hydroxy hydroperoxides **7a-e,g,h,p**. [a] Calculated from the characteristic signals in the ^{1}H-NMR of the crude reaction mixture. [b] Calculated from the characteristic signals in the ^{1}H-NMR of the pure reaction mixture. [c] Total yield of the crude 1,2,4-trioxanes mixture.**

The reaction is entropically favored and is assumed to proceed through a slow cleavage (Hock-type cleavage) of the β-hydroperoxy alcohols, catalyzed by the Lewis acid, leading to the corresponding carbonyl fragments that subsequently reacts with the excess β-hydroperoxy alcohols to give the mixed trioxanes **129a-h**, **130a-h**, respectively (***Scheme 3.92***). β-Hydroperoxy alcohols are known to undergo decomposition with the formation of carbonyl compounds.[110a,b] The fact that the 1,2,4-trioxanes **129** were always formed as the major product is expected since the non-conjugated carbonyl fragments **(a)** show more electrophilic

carbonyl carbon than the carbonyl carbon of the α-methylacrolein fragment **(b)**. Consequently, the nucleophilic attack of the hydroperoxy group on the former carbon is expected to be faster leading to the formation of **129** as the major product (kinetic control of product formation).



***Scheme 3.92*:** BF_3-catalyzed fragmentation of β-hydroperoxy alcohols and subsequent peroxyacetalization reaction.

Confirmation of the chemical structures and the relative configuration was based on ^{1}H- and ^{13}C-NMR (***Table 3.47***). For all the synthesized trioxanes, the coupling constant between the two protons H-5 and H-6 was found in the range $^{3}J_{HH}$ = 9.0-9.6 Hz indicating a dihedral angle of 180° and consequently, a *trans* diaxial-configuration. The substituents at the peroxyacetal carbon (C-3) in **129** and **130** are always located *cis* to the substituents at C-5.

The 1,2,4-trioxanes **130** are characterized in ^{1}H-NMR by a singlet signal absorbing at about 5.50-5.60 ppm corresponding to H-3 (the downfield shift of this signal is due to the double bond anisotropic effect of the geminal isopropenyl group). Another broad singlet signal resonating at about 5.20 ppm corresponds to the olefinic proton of the isopropenyl group on C-3 is also characteristic of this series. Beside the peroxyacetal carbon in ^{13}C-NMR, the appearance of another signal at about 116 ppm corresponding to the methylene carbon of the isopropenyl group at C-3 is very indicative of **130** trioxanes. The 1,2,4-trioxanes **129** are confirmed in ^{1}H-NMR by the characteristic H-3 appearing with a very significant multiplicity.

No.	R	O<u>CH</u>		OO<u>CH</u>		O<u>CH</u>OO	
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR
129a	*c*-Pr	3.06	80.8	4.45	87.4	4.73	106.4
130a	*c*-Pr	3.21	79.8	4.43	87.5	5.45	104.5
129b	Et	3.57	77.9	4.32	87.5	5.16	105.5
130b	Et	3.77	76.8	4.38	86.8	5.60	104.1
129c	*i*-Bu	3.72	75.0	4.30	88.1	5.26	103.8
130c	*i*-Bu	3.80	75.2	4.34	88.0	5.54	104.6
129d	*n*-Bu	3.65	76.8	4.33	87.7	5.21	104.8
130d	*n*-Bu	3.74	76.8	4.38	87.6	5.55	104.7
129e	Me	3.79	73.2	4.25	88.5	5.36	101.4
130e	Me	3.88	73.2	4.32	88.7	5.56	104.8
129f	*n*-Pr	3.65	76.5	4.32	87.7	5.21	104.5
130f	*n*-Pr	3.76	76.6	4.39	87.6	5.56	104.7
129g	allyl	3.77	76.3	4.40	87.0	5.27	103.7
130g	allyl	3.85	76.2	4.45	86.9	5.57	104.7
129h	*i*-Pr	3.54	80.3	4.49	85.7	4.95	107.6
130h	*i*-Pr	3.65	80.5	4.56	85.7	5.55	104.8

***Table 3.47*:** Characteristic signals in ^{1}H- and ^{13}C-NMR of **129a-h** and **130a-h** (in $CDCl_3$).

In most cases the major trioxane products could be separated by chromatography as shown in ***Figure 3.46*** for the **129d** and **130d**.

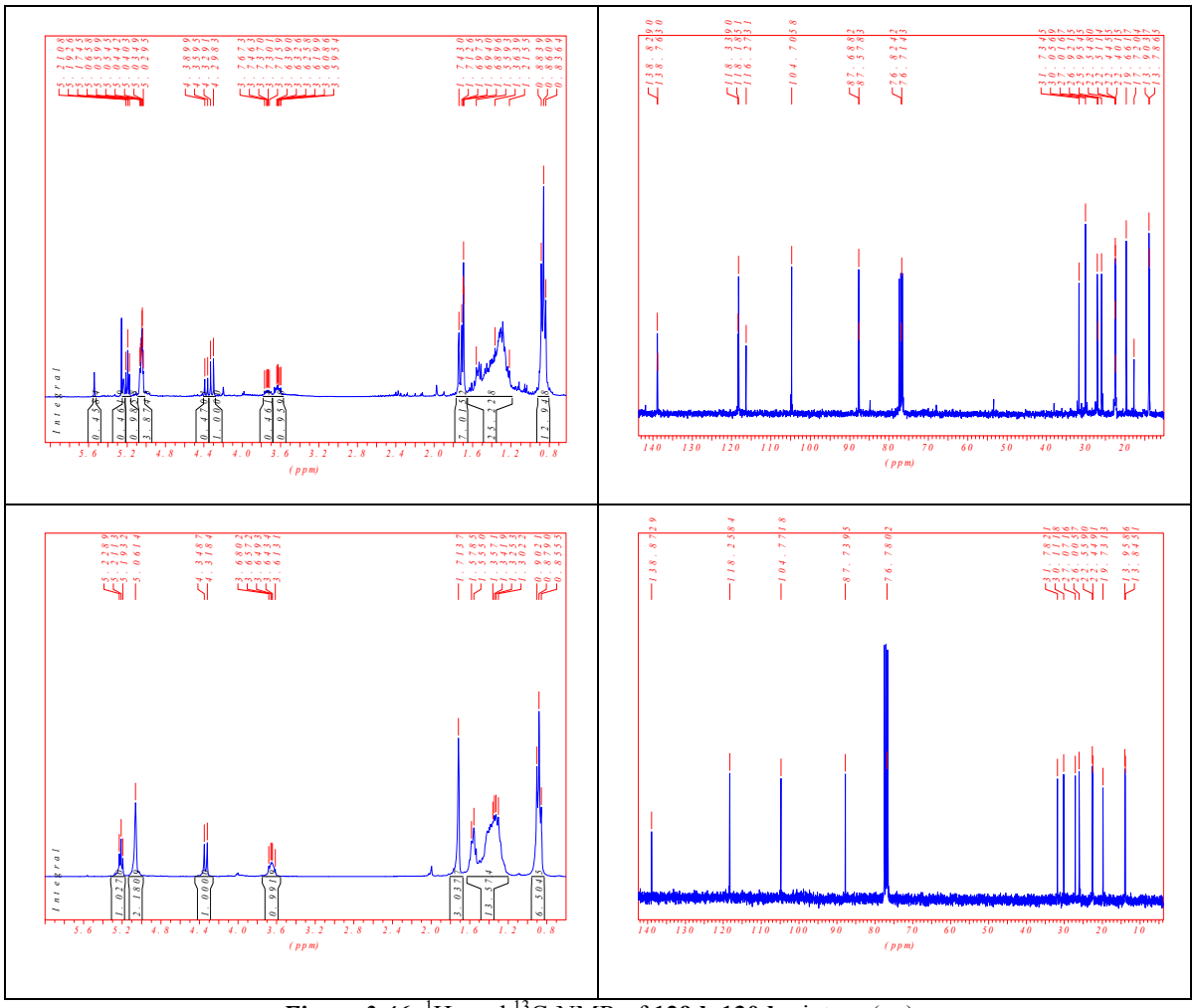
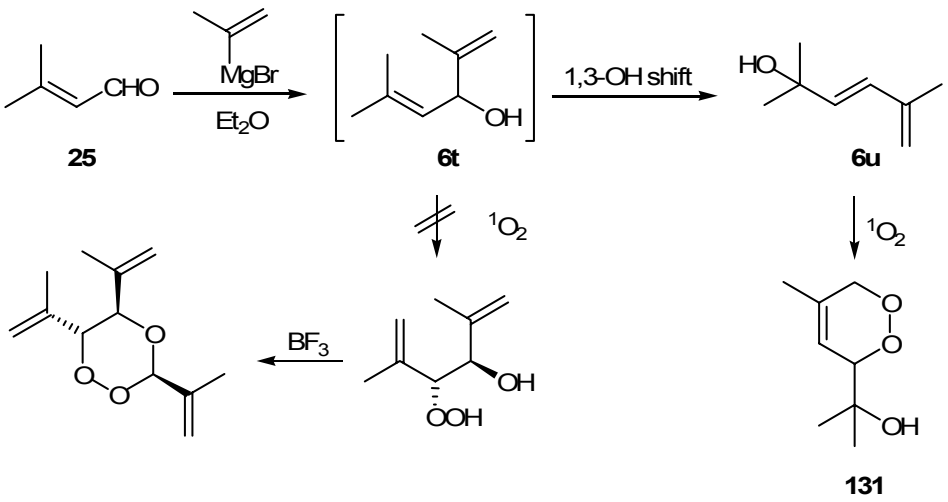


***Figure 3.46*:** ^{1}H- and ^{13}C-NMR of **129d, 130d** mixture (up) and ^{1}H- and ^{13}C-NMR of **129d** (down).

It is also worth mentioning that the formation of the 1,2,4-trioxanes **129** and **130** is sometimes a competitive side reaction to the previously used condensation reaction of *vic*-hydroxy allylic hydroperoxides with carbonyl compounds, acetals and orthoesters where it becomes more pronounced for reactions involving less reactive condensing reagents (e.g. due to steric effects) especially those which are less volatile (cannot be added in large excess). Also, it was found that the *vic*-hydroxy allylic hydroperoxides with bulky alkyl group on the carbinol carbon are more susceptible to this fragmentation-condensation reaction since as the size of the alkyl group increases, the stability of the β-hydroperoxy alcohols becomes lower due to steric strains. The driving force of this fragmentation to the carbonyl compounds by C(OOH)-C(OH) bond fission is sterically assisted by releasing this steric strain.

I have also tried to synthesize an allylic alcohol which, after photooxgenation, yields β-hydroperoxy alcohols that when treated with BF_3 fragments slowly into only one carbonyl component, by this way only one 1,2,4-trioxane can be isolated. The allylic alcohol **6t**

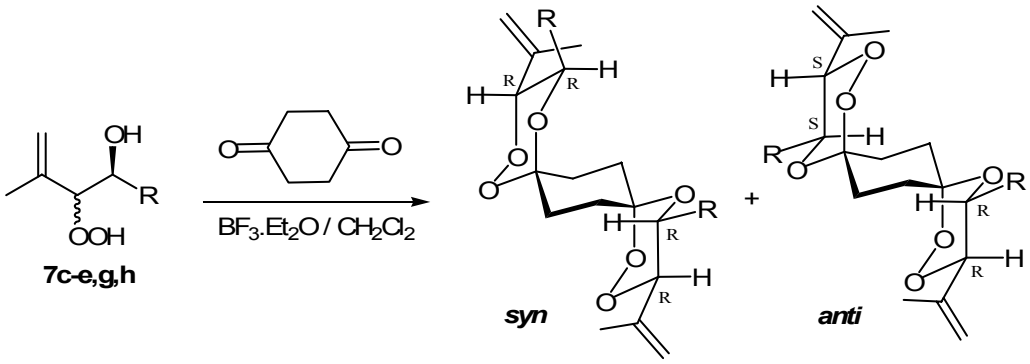
represents a simple candidate that fulfills the previous conditions. However, on treatment of **25** with isopropenyl magnesium bromide the allylic alcohol **6t** was not isolated. Instead, an acid-catalyzed 1,3-allylic shift of the hydroxy group in **6t** took place leading to the formation of the dieneol **6u**. The formation of **6u** was further supported by [4+2]-cycloaddition reaction with $^1O_2$ resulting in the formation of the endoperoxide **131** which was characterized by NMR analysis (***Scheme 3.93***). Compound **131** shows only one olefinic proton in ^{1}H-NMR appearing as multiplet (due to vicinal and allylic coupling) at 5.65 ppm, the methine proton appearing as multiplet at 4.20 ppm while the methylene is appearing as singlet at 4.28 ppm. In an APT experiment, the most characteristic signals are the olefinic carbons at 117.1 and 133.5 ppm, the quaternary carbinol carbon at 72.8 ppm as well as the peroxidic methylene and methine carbons resonating at 72.6 and 84.3 ppm, respectively.



Scheme 3.93

3.9 Bis Spiro-1,2,4-Trioxanes Synthesis

In the light of combinational chemotherapy in fighting malaria (*vide supra*) and the semisynthetic artemisinin dimers mentioned before, I used similar concept to enhance the antimalarial activity of the prepared 1,2,4-trioxanes by integration of two trioxane pharmacophoric moieties in the same molecule. The idea is based on condensing two hydroperoxy alcohols to a central dicarbonyl component (as cyclohexane-1,4-dione) resulting in bis spiro-1,2,4-trioxanes, a literature-unknown class of compounds (***Scheme 3.94***).



***Scheme 3.94*: *syn* and *anti* bis spiro-1,2,4-trioxanes.**

The crude product mixture of the reaction seemed to be a complex mixture of products involving in some cases the trioxanes obtained by the Lewis acid catalyzed fragmentation-peroxyacetalization reaction of the 1,2-hydroperoxy alcohols as side products. However, on chromatographic purification it was efficiently feasible to separate the monocyclic 1,2,4-trioxanes from the 1,2,4-trioxane dimers.

Based on ^{1}H-NMR of all the synthesized bis spiro-1,2,4-trioxane dimers, the two vicinal methine protons in each 1,2,4-trioxane ring adopt a *trans* diaxial-orientation with coupling constant in the range of 9.55-9.84 Hz. This means that, both 1,2,4-trioxane rings in all the synthesized bis spiro-1,2,4-trioxanes are derived only from the major diastereomer of the *vic*-hydroxy allylic hydroperoxide (*syn*-isomer). The bis spiro-1,2,4-trioxanes were formed as mixtures of two diastereomers that can be referred to as *syn* (the peroxidic bond on the same side) and *anti* (the peroxidic bonds in opposite sides). Both diastereomers were formed in the most stable configuration showing all substituents in equatorial positions (RS,RS/RS,RS for the *syn* isomer and RS,RS/SR,SR for the *anti* isomer)

The chemical constitution of the bis spiro-1,2,4-trioxanes dimers was confirmed by ^{1}H-, ^{13}C-NMR and in some cases also by IR and elemental analyses. The high volatility and low thermal stability was problematic for any mass analysis technique. In contrast to ^{1}H-NMR where both *syn* and *anti* isomers of the synthesized bis spiro-1,2,4-trioxanes dimers show identical spectra (exception is **135** were some signals of the *syn* and *anti* isomers showing different chemical shifts), ^{13}C-NMR was more advantageous showing mostly different signals corresponding to the *syn* and *anti* isomers (***Table 3.48***). A multiplet with integration of three protons and a small coupling constant (allylic coupling) is absorbing at 1.60 ppm and is related to the isopropenyl methyl group.

No.	R	OCH		OOCH		OCOO	Yield (%)
		^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{13}C-NMR	
132	*n*-Bu	3.86[a]	69.8/ 69.8	4.25[a]	87.7/ 87.7	102.4/ 102.3	4
133	*i*-Pr	3.76[a]	73.4[a]	4.45[a]	85.7[a]	102.2[a]	18
134	*n*-Pr	3.89[a]	69.5/ 69.5	4.25[a]	87.6/ 87.6	102.3/ 102.3	19
135	allyl	3.97/ 3.35	69.5/ 69.5	4.31/ 4.30	86.9/ 87.1	102.4/ 102.4	8
136	*i*-Bu	3.97[a]	67.8[a]	4.24[a]	88.1/ 88.1	102.3/ 102.3	15

***Table 3.48**:* Characteristic signals of *syn*- and *anti*-**132-136** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).
[a] Both diastereomers have identical chemical shifts for this signal.

It is clear that while the *anti* bis-1,2,4-trioxane diastereomer possesses a center of symmetry, the *syn* diastereomer has a twofold axis of symmetry. This symmetry tends to produce NMR spectral and magnetic equivalence of pairs of the groups located on both sides of each diastereomer (e.g. at position 5 and 5`, or 6 and 6` of the trioxane rings, or the two vicinal methylene groups of the central cyclohexane ring). Compound **132**, as a representative example (***Figure 3.47***), shows in ^{1}H-NMR a triplet signal at 0.86 ppm related to the methyl group vicinal to a methylene group, a multiplet at 1.05-1.72 correspond to four methylene groups (three of the *n*-butyl and one of the central cyclohexane ring). The multiplet signal at about 2.20 ppm is consistent with the other methylene group of the cyclohexane ring (two diastereotopic protons). At 3.86 ppm a multiplet with integration of one proton correspond to

H-5 of the trioxane ring which couples with the vicinal two diastereotopic methylene protons of the *n*-butyl group as well as the vicinal H-6 (appearing as doublet at 4.25 ppm). Finally, the signal at 5.04 ppm is related to the olefinic methylene protons. For all bis spirotrioxane dimers, the most characteristic signal in ^{13}C-NMR is the peroxyacetal carbon appearing more up-field (at about δ = 102 ppm) than the previously synthesized monocyclic-1,2,4-trioxanes probably due to more shielding effect by the electronic cloud generated by the lone pairs of the six oxygen atoms in the molecule. The ^{13}C-NMR of **132** shows two signals at 102.3 and 102.4 ppm corresponding to the peroxyacetal carbons of the *syn* and *anti* diastereomers. The two methylene carbons of the central cyclohexane ring are resonating at 25.2, 30.8 ppm for one isomer and at 24.9, 31.2 ppm for the other. The isopropenyl methyl group is resonating at 19.7 and 19.8 ppm for the *syn* and *anti* isomers. Also each isomer shows two distinct signals corresponding to C-5 and C-6. While the olefinic methylene carbon in both isomers have identical chemical shift, the olefinic quaternary carbon is absorbing at 139.1 and 139.2 ppm for both diastereomers.

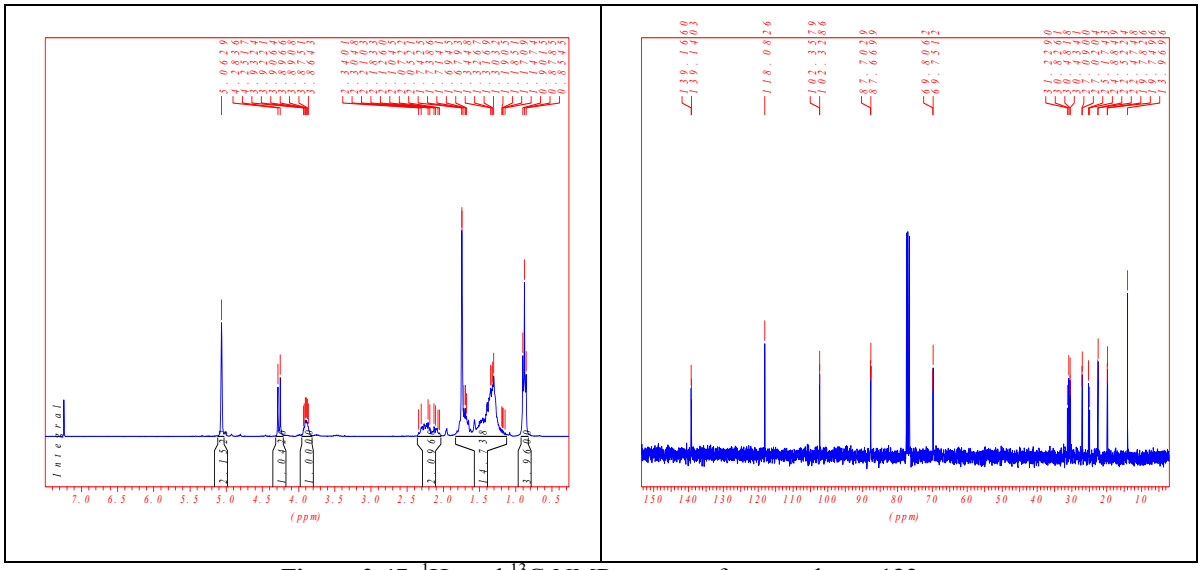


***Figure 3.47*:** ^{1}H- and ^{13}C-NMR spectra of *syn*- and *anti*-**132**.

The IR spectrum of compound **132** shows the following characteristic bands: 3083 cm^{-1} (vinylic CH), 2957 cm^{-1} (aliphatic CH), 1648 cm^{-1} (isolated C=C), 1253, 1105, 1007 cm^{-1} (C-O) and 928, 911 cm^{-1} (O-O). The relative configuration of the synthesized bis spiro-1,2,4-trioxane dimers was unambiguously assigned by means of X-ray analysis (***Figure 3.48***).

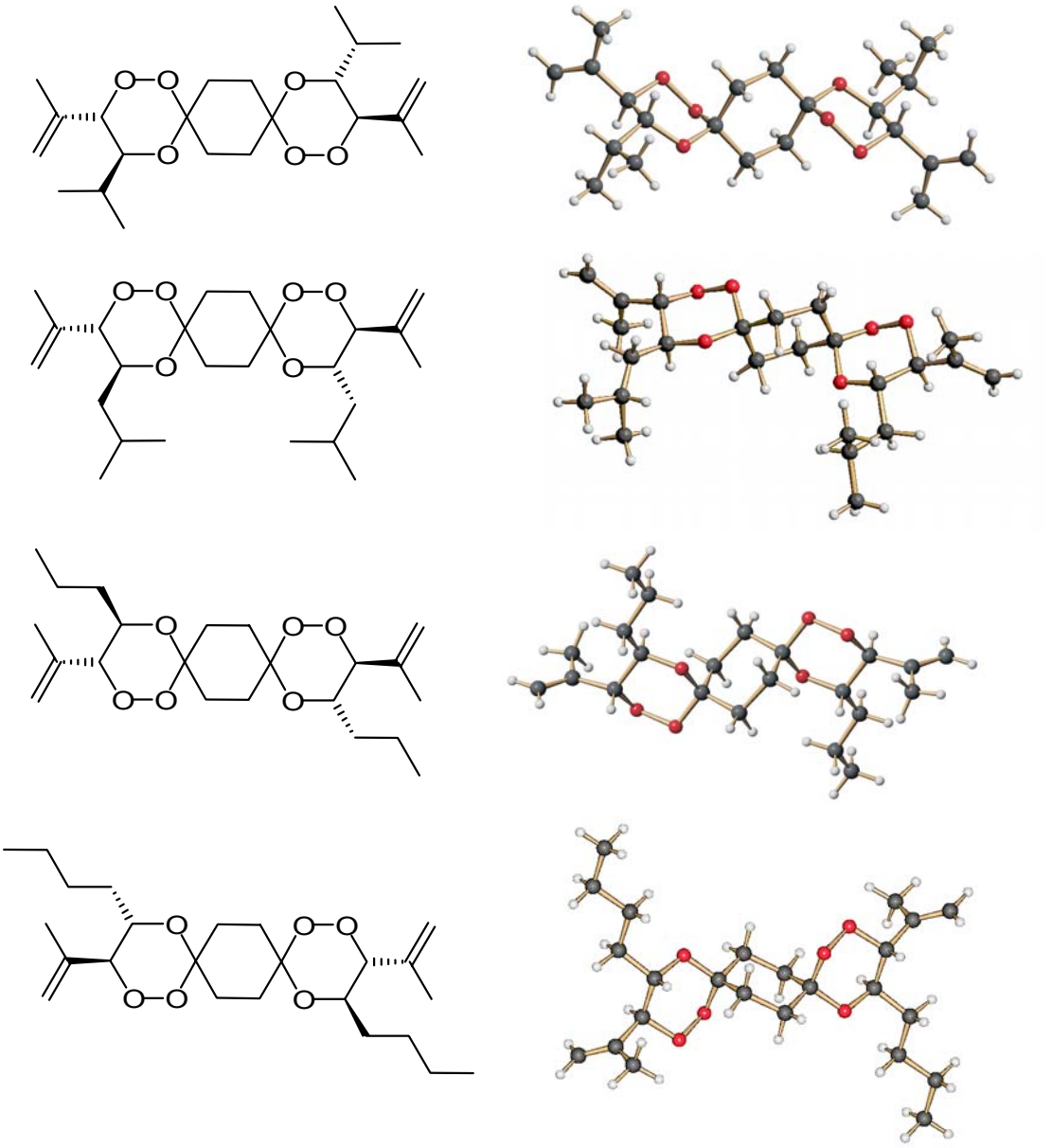


***Figure 3.48*:** X-ray structure of compounds **133**, **136**, **134**, **132**.

It can be anticipated that the antiparasitic activity of such compounds is higher than for mono-1,2,4-trioxanes since they might act twice as electron acceptors when reduced by Fe(II) of the hemoglobin and hence are expected to be more potent. Calculations revealed that in the *syn* spiro compounds the electron-accepting pharmacophoric peroxo-bridges are less shielded and thus better exposed to the reactive iron center than the corresponding *anti* isomers (***Figure 3.49***).

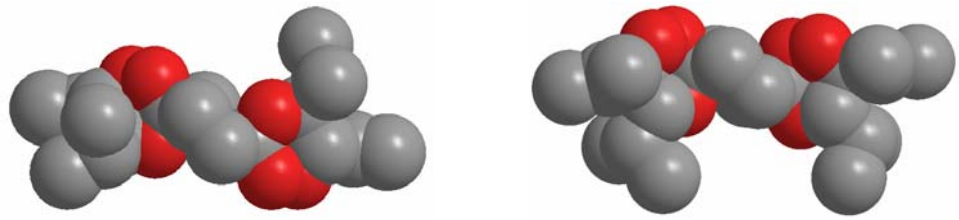


***Figure 3.49*:** Space-filling structures of *syn* (right) and *anti* (left) isomers of the bis 1,2,4-trioxanes **133**.

3.10 Intramolecular 1,2,4-Trioxanes Synthesis

The 1,2,4-trioxane pharmacophore in the natural occurring antimalarial drug artemisinin is a part of a bicyclo[3.2.2]nonane sekeleton (*vide supra*). In this part I tried to develop a new route for a simplification of this pharmacophore. Four possible isomers for the trioxabicyclo[3.2.1]octane peroxides are known (***Figure 3.50***). However, the 2,3,8-trioxa isomer **D** is the only isomer that has a 1,2,4-trioxane unit and hence can be considered as a ring-contracted analogue to the pharmacophore in artemisinin.

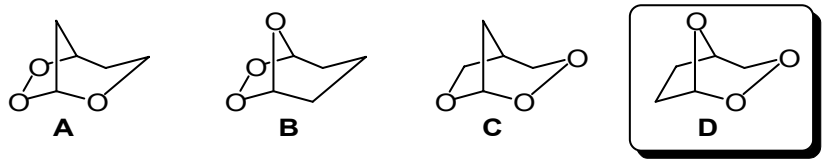
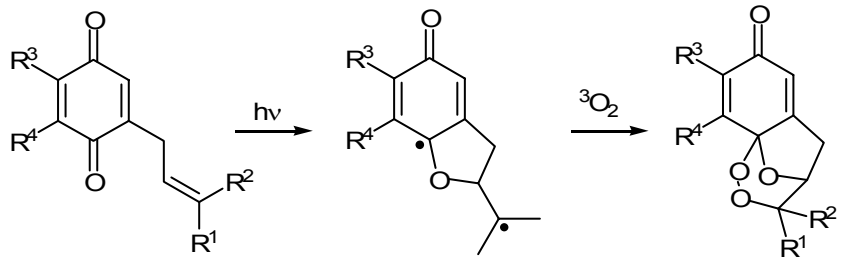


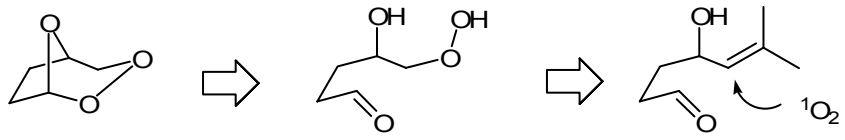
***Figure 3.50*:** All possible trioxabicyclo[3.2.1]octane peroxides.

There is only one route to the 2,3,8-trioxabicyclo-[3.2.1]octane skeleton that is known in literature which is based on trapping of the triplet biradicals formed in intramolecular photochemical quinone-alkene addition by molecular oxygen (***Scheme 3.95***).[151,111,113] However, the yields of this reaction are generally low due to competition with unimolecular radical reactions.



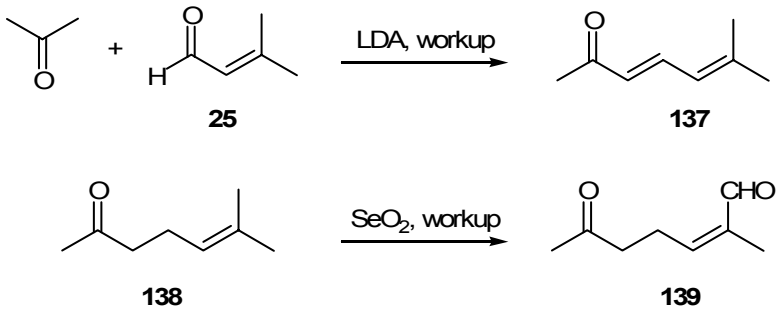
***Scheme 3.95*:** Synthesis if bicyclo[3.2.1]octanes by triplet biradicals trapping.

Retrosynthetic analysis of such skeleton assumes the involvement of an intramolecular peroxyacetalization reaction as the key step in synthesis (***Scheme 3.96***). Here, the carbonyl component and the allylic alcohol must be involved in the same substrate molecule.



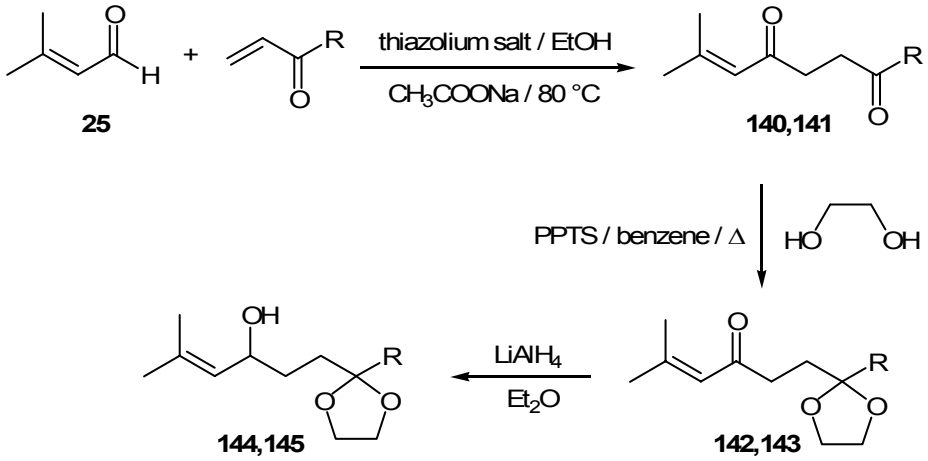
***Scheme 3.96*:** Retrosynthesis of the 2,3,8-trioxabicyclo[3.2.1]octane skeleton.

Two direct routes to such substrates were investigated (***Scheme 3.97***). However, secondary products were obtained in both cases. In the first route, the NMR spectra of the isolated product showed no carbinol signals, instead, four olefinic signals absorbing in ^{13}C-NMR at δ = 124.0, 127.9, 139.4, 147.4 ppm were observed. This is consistent with spontaneous dehydration of the primarily formed allylic alcohol giving the more conjugated dienol **137**. In the second route, the allylic hydroxylation of the non-conjugated enone **138** with SeO_2 took place at the methyl group leading to the formation of the 1,6-dicarbonyl compound **139**. The formation of **139** was confirmed by the aldehyde singlet signal resonating at δ = 9.32 ppm in ^{1}H-NMR and at δ = 195.0 ppm in ^{13}C-NMR as well as by the absence of the carbinol signals.



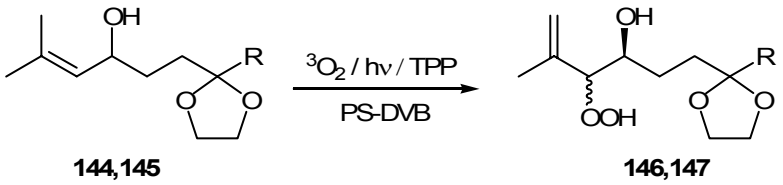
Scheme 3.97

An old publication by Stetter et al. reported on the synthesis of unsaturated 1,4-diketones by thiazolium salt catalyzed addition of unsaturated aliphatic aldehydes to vinyl ketones prompted me to follow this concept.[192] The addition of 3-methylcrotonaldehyde **25** to methyl vinyl ketone or ethyl vinyl ketone in presence thiazolium salt resulted in the corresponding 1,4-diketones **140** and **141** in good purity (***Scheme 3.98***). In order to reduce the conjugated carbonyl group to the corresponding allylic alcohol, protection of the isolated carbonyl group as acetal was carried out by the conventional acid catalyzed acetalization with ethylene glycol. Subsequent reduction of the enone acetal **142** and **143** with lithium aluminum hydride in ether followed by basic workup furnished the corresponding allylic alcohols **144** and **145** in 62 % yield.



Scheme 3.98

The $^1O_2$ photooxygenation reaction of **144** and **145** using the developed solvent-free approach afforded the 1,2-hydroperoxy alcohols **146** and **147** with moderate *syn* diastereoelectivity (***Scheme 3.99, Table 3.49***). The characteristic hydroperoxy signals corresponding to both diastereomers are summarized in ***Table 3.50***.



Scheme 3.99

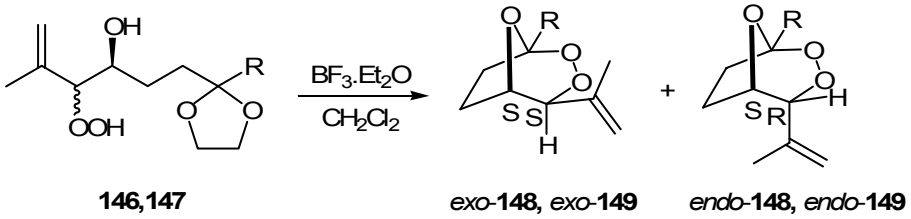
Compound	R	d.r.[a] *syn*:*anti*	Yield (%)
146	Me	77 : 23	84
147	Et	74 : 26	91

***Table 3.49*:** The photooxygenation of the allylic alcohols **144** and **145** using solvent-free approach with PS-DVB copolymer. [a] The diastereoselectivity is determined from the integration of the characteristic signals in the NMR of the crude reaction mixture.

Compound	R	*syn*-diastereomer		*anti*-diastereomer	
		^{1}HNMR	^{13}CNMR	^{1}HNMR	^{13}CNMR
146	CH_3	4.07	93.2	n.s.	91.5
147	Et	4.05	93.1	4.17	91.4

***Table 3.50*:** ^{1}H- and ^{13}C-NMR chemical shifts (ppm) of the hydroperoxy carbon (**CH**-OOH) of *syn* and *anti* diastereomers of **147** and **147** (in $CDCl_3$).
n.s. Not seen due to overlap with other signals.

Transperoxyacetalization reaction of **146** and **147** in methylene chloride using catalytic amount of BF_3 afforded in both cases a 77:23 diastereomeric mixture of 2,3,8-trioxabicyclo[3.2.1]octane derivatives (***Scheme 3.100***). Clearly, the *exo*-bicyclic derivatives (*exo*-**148** and *exo*-**149**, with the two hydrogen atoms of the vicinal stereogenic centers in the same direction) are the major products resulting from the major *syn*-hydroperoxy alcohols, while the *endo*-diastereomers (*endo*-**148** and *endo*-**149**) are the minor product that results from the minor *anti*-hydroperoxy alcohol.



Scheme 3.100

The constitution of both 2,3,8-trioxabicyclo[3.2.1]octane derivatives **148** and **149** was proven by 1D- and 2D-NMR data as well as IR and elemental analyses. As representative example, the IR spectrum of **148** showed the following characteristic absorption bands: at 3092 cm^{-1} (vinylic CH), 2993, 2954 cm^{-1} (aliphatic CH), 1650 cm^{-1} (nonconjugated C=C), 1189, 1147, 1055 cm^{-1} (C-O) and 900, 865 cm^{-1} (O-O). The most characteristic signals in ^{1}H- and ^{13}C-NMR are shown in ***Table 3.51***.

No.	**R**	**OCH**		**OOCH**		**OOCO**	**Yield (%)**
		^{1}H-NMR	**^{13}C-NMR**	**^{1}H-NMR**	**^{13}C-NMR**	**^{13}C-NMR**	
***exo*-148**	CH_3	**4.60**	75.0	**3.94**	85.8	**111.0**	19
***endo*-148**	CH_3	4.30	76.3	4.65	84.4	**110.0**	
***exo*-149**	Et	**4.54**	74.8	**3.89**	85.8	**113.1**	12
***endo*-149**	Et	4.35	76.3	4.70	84.8	**112.4**	

***Table 3.51*:** Characteristic signals of **148** and **149** in ^{1}H- and ^{13}C-NMR (in $CDCl_3$).

Fortunatly, it was possible to separate the major *exo*-**148** isomer from the diastereomeric mixture. Comparison of the NMR of the diastereomeric mixture and the separated *exo*-**148** isomer is shown in ***Figure 3.51***. Obviously, the peroxyacetal carbon atoms in the 2,3,8-trioxabicyclo[3.2.1]octanes are absorbing more downfield (δ = 110-113 ppm) since they represent the bridgehead of the bicyclic system.

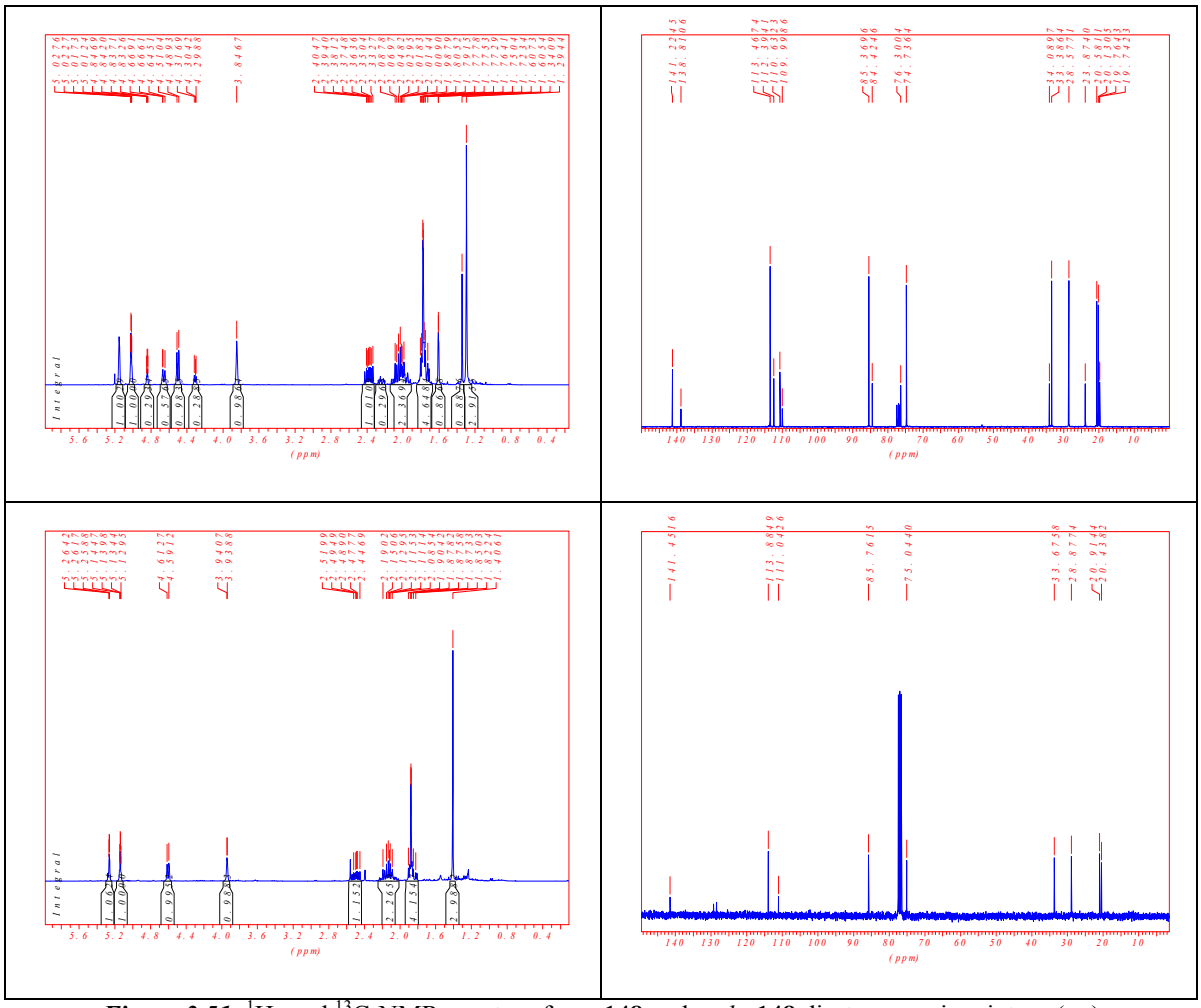


Figure 3.51: ^{1}H- and ^{13}C-NMR spectra of *exo*-**148** and *endo*-**148** diastereomeric mixture (up) and only *exo*-**148** isomer (down)

Consistent with the NMR data, PM3 calculations (***Figure 3.52***) revealed that the heat of formation (ΔH_f) of ***exo*-148** is -56.53 kcal/mol while that for ***endo*-148** is -52.87 kcal/mol. Clearly, the ***exo*-148** diastereomer is more stable by about 3.7 kcal/mol than the *endo* isomer (due to the steric interactions between the isopropenyl group and the the bicyclic bridge in the *endo* isomer).

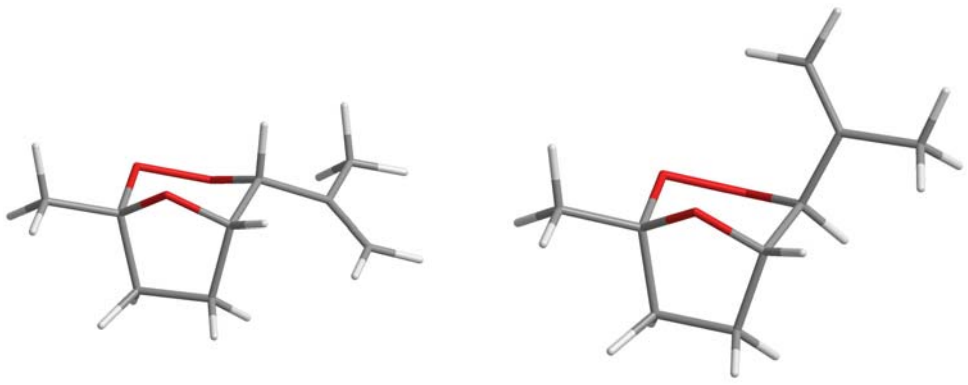
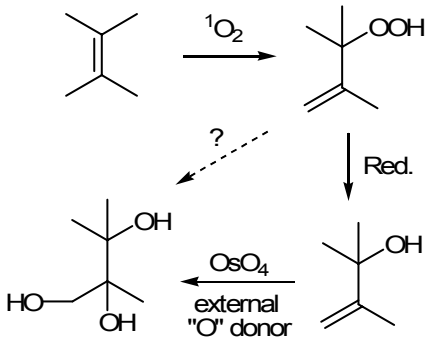


***Figure 3.52*:** Model of 1,2,4-trioxane *endo*-**148** (left) and *exo*-**149** (right) in a minimum energy conformations. The model was generated using PM3.

3.11 Hydroperoxides as Oxygen Donor in Dihydroxylation Reaction

The introduction of oxygen functionalities to double bonds is a valuable transformation in the synthesis of polyoxygenated natural products such as macrolides and carbohydrates. The dihydroxylation reaction (also termed bishydroxylation) is an efficient route to diols from olefins.[152] OsO_4 is the most efficient oxidant often used for such conversion. It may be applied either in stoichiometric or catalytic amounts. However, due to the high price and extreme toxicity of this oxidant catalytic reactions are favored. Catalytic dihydroxylation reactions require the presence of another external oxygen donor (used in excess) to reoxidize the reduced "Os" species and regenerate OsO_4 in the reaction mixture. Several cooxidants with variable efficiency such as alkali metal chlorates and hypochlorites,[153] H_2O_2,[154] *t*-BuOOH,[155] N-methylmorpholine N-oxide,[156] and potassium ferricyanide[157] were used.

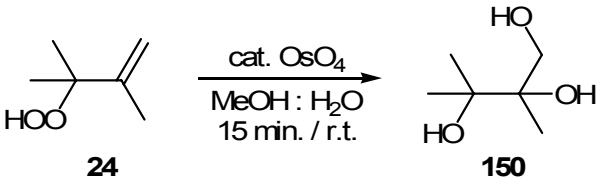
Using the allylic alcohols as substrates serves as template reaction in carbohydrate chemistry. One of the several routes to allylic alcohols is the reduction of the allylic hydroperoxides obtained by $^1O_2$-ene reaction with olefins (*vide supra*). While intensive work on the dihydroxylation reaction of allylic alcohols was performed, the dihydroxylation of the parent hydroperoxides is almost absent in literature. In this part, I examined the feasibility of transforming allylic hydroperoxides into triols using a catalytic dihydroxylation reaction not only in presence but also **in absence of the external cooxidant** (***Scheme 3.101***).



Scheme 3.101

Optimization of the reaction conditions for the catalytic dihydroxylation reaction of allylic hydroperoxides was performed for the substrate **24** (***Scheme 3.102***). As a reaction solvent I chose a polar solvent mixture to ensure the homogeneity of the reaction since osmium tetraoxide is soluble in polar solvents. Equivolume mixture of MeOH and water is the most convenient solvent not only for the reaction efficiency but also from the stand point of green

chemistry. By this way, no phase transfer conditions are needed making the reaction rate faster than heterogeneous conditions. Compared to the conventional bishydroxylation procedures that needs long reaction times, in our case, complete conversion to the corresponding triols proceeded smoothly at ambient temperature **in only 15 minutes**. No starting compounds could be identified in the product (by NMR). At the end of the reaction, the catalyst and any excess hydroperoxide reactant are decomposed by aqueous solution of an alkali metal sulfite with subsequent extraction of the triol by ethyl acetate. The reaction is simple, efficient, and cost effective procedure can lead to up to three chirality centers in a single step.



Scheme 3.102

The formation of **150** was unequivocally confirmed by the disappearance of the olefinic signals in ^{1}H- and ^{13}C-NMR. ^{1}H-NMR is characterized by two new doublets (having coupling constant of about 11.5 Hz) resonating at 3.45 and 3.86 ppm are corresponding to the two diastereotopic protons of the methylene group. The large coupling constant is expected since it is geminal coupling on a saturated carbon. In ^{13}C-NMR the two new methylene and quaternary carbinol carbons are absorbing at 68.3 and 75.3 (or 76.1) ppm respectively (***Figure 3.53***).

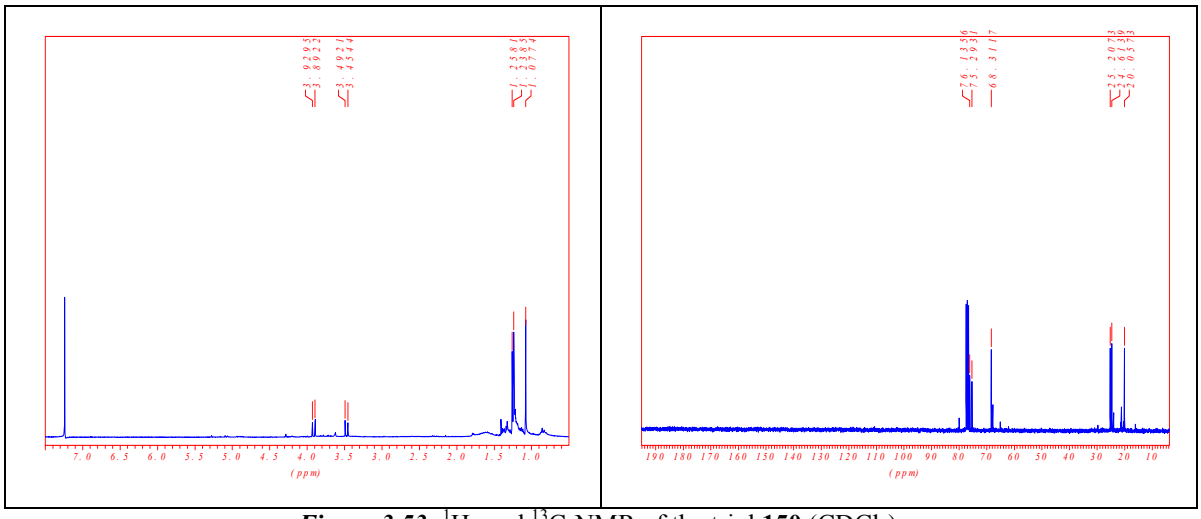
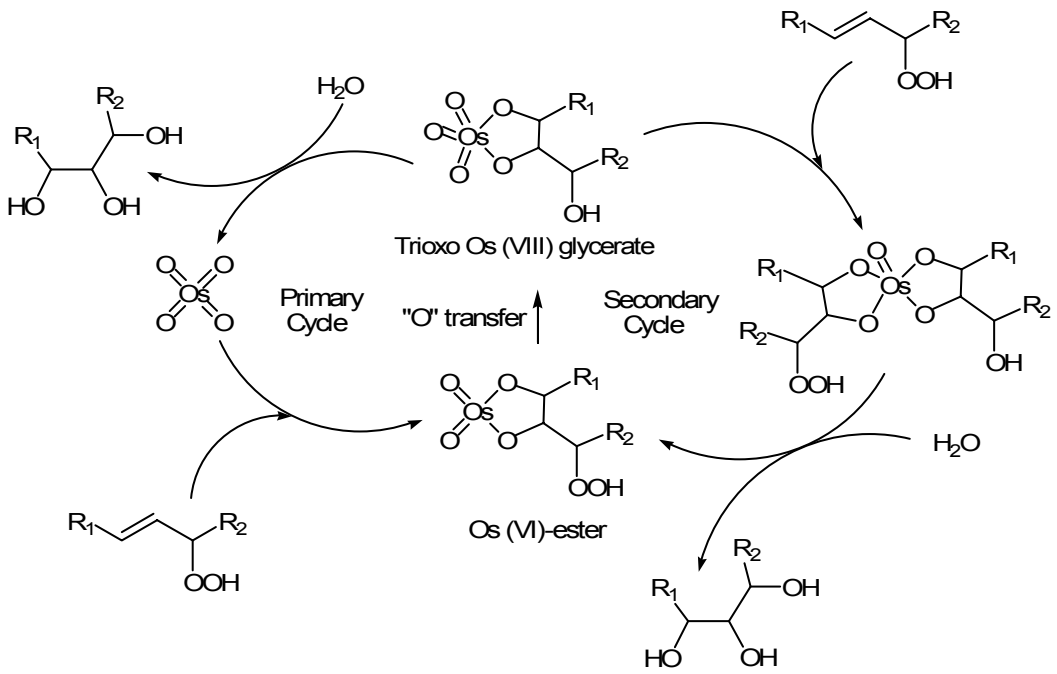


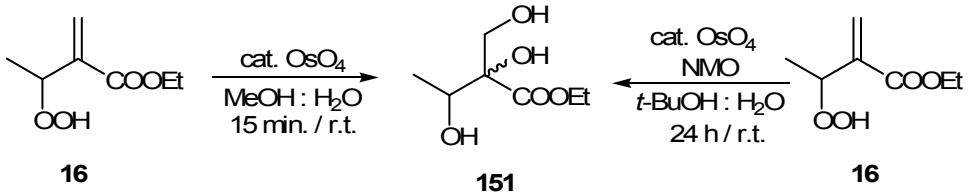
***Figure 3.53*:** ^{1}H- and ^{13}C-NMR of the triol **150** ($CDCl_3$).

Analogous to the titanium catalyzed direct hydroxy-epoxidation reaction of the allylic hydroperoxide,[158] in the catalytic bishydroxylation reaction in absence of external cooxidants, the allylic hydroperoxide plays a double role as the oxygen donor (for osmium tetraoxide regeneration) and after the oxygen transfer step, as the oxygen acceptor. A suggested mechanism for the reaction is depicted in ***Scheme 3.103***.



***Scheme 3.103*:** Mechanism of dihydroxylation of allylic hydroperoxides in absence of external cooxidant.

I compared also the catalytic dihydroxylation reaction of the less reactive allylic hydroperoxide of the acrylate derivative **16** (OsO_4 is electrophilic in nature) in presence of two equivalent of NMO as an external oxygen donor versus the no cooxidant conditions were the substrate itself is the cooxidant (***Scheme 3.104***). For the former reaction I used a substrate concentration of 0.31 M while in the latter reaction two fold this substrate concentration was used (0.6 M). In both reactions a diastereomeric mixture of the triol is obtained (about 85:15 for the former while 79:21 for the latter reaction as calculated from ^{13}C-NMR). However, the procedure where the substrate it self act simultaneously as an oxygen donor and acceptor is clearly advantageous since less reagents and shorter reaction times were needed even at a two-fold substrate concentration.



16 **151** **16**

Scheme 3.104

The chemical constitution of **151** was assigned on the basis of 1D-NMR as well as 2D-NMR analysis. In ^{1}H-NMR, the disappearance of the olefinic signal and the appearance of the characteristic signal corresponding to the two diastereotopic protons of the methylene group adjacent to the newly formed chiral center is indicative of the formation of **151**. Each proton from the two diastereotopic protons appear as doublet (e.g. for the major diastereomer they resonate at 3.65 and 3.78 ppm) with large coupling constant (about 11.5 Hz) due to the geminal coupling on a saturated carbon. In ^{13}C-NMR, the two signals corresponding to the double bond are no more detected, and the two new carbinol carbons absorbing at 64.8 and 81.5 for the methylene and the quaternary carbons, respectively, of the major diastereomer are observed. While in ^{1}H-NMR some signals of the minor diastereomer are partially overlapped with those of the major isomer, all signals of the minor diastereomer in ^{13}C-NMR could be identified.

To evaluate the effect of catalyst loading on the reaction efficiency, several runs of dihydroxylation reactions comprising different amounts of the oxidant catalyst (ranging from 0.1 to 0.001 equiv.) were run for **24** under identical conditions and the yield of the products as well as their purity were examined (***Table 3.52***). Neither longer reaction times nor any noticeable decrease in the reaction efficiency was observed even on going to catalyst concentration of 0.1 mol %. However, in all cases due to the high hydrophilicity of the products modest reaction yields were obtained.

Entry	mol % OsO_4	Reaction time (min)	% Yield[a]
1	10	15	37
2	5	15	25
3	1	15	37
4	0.5	15	19
5	0.1	15	31

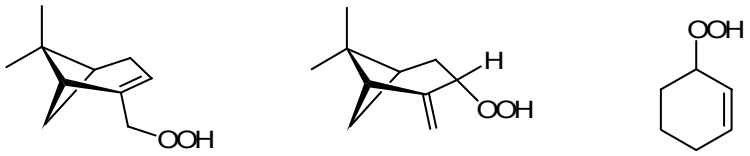
***Table 3.52*:** Effect of catalyst loading on the bishydroxylation reaction of **24**.
[a] Yields correspond to the isolated triol.

It is worth mentioning that this approach is advantageous over that with an external cooxidant where the reagents used in this reaction stem from renewable sources: One oxygen atom comes from water (since the reaction is highly catalytic) and the other two oxygen atoms come from air and they could be incorporated in the substrate with complete atom economy by activating molecular oxygen with visible light using a green photooxygenation approach

(solvent-free for the less volatile tiglate ester). This provides a simple and highly sustainable approach to triols from olefins.

Searching for other catalysts which may catalyze such reaction is also advantageous due to the high toxicity of osmium tetraoxide. A patent[159] concerning the synthesis of glycerol from allyl alcohol using catalytic amount of WO_3 stimulated my attention to this oxidant. Repeating the reaction using the more benign WO_3 for the hydroperoxide **24** led also to the corresponding triol. However, longer reaction time (3 days) was needed. This is attributed to the less solubility of WO_3 compared to OsO_4 in the reaction mixture and hence it's less reactivity as oxygen donor.

Whereas, acyclic terminal olefins could be efficiently converted to the corresponding triols in absence of external cooxidants, attempts to prepare the triols derived from cyclic allylic hydroperoxides such as **152-154** under similar conditions were not successful (***Figure 3.54***). A plausible explanation may be that due to the rigidity of such compounds, low energy conformational changes in the molecule in order to locate the hydroperoxy group in an optimum geometry for oxygen transfer reaction to the oxidant is not possible. It is known that these conformational effects in the cyclic substrates can retard the analogous oxygen-transfer epoxidation reaction.[160] Also, the attack of OsO_4 catalyst on the double bond may also be retarded by steric factors with the cyclic substrates.



152 **153** **154**

Figure 3.54

Studies directed toward the nature of the oxygen transfer step (intra- or intermolecular mechanism), regiochemistry of the reaction using diene hydroperoxides as well as effect of addition of chiral ligands on the reaction enantioselectivity should be accomplished in the future.

3.12 Antimalarial Activity of some Synthesized 1,2,4-Trioxane Compounds

In a cooperative work, many synthesized 1,2,4-trioxanes were submitted to the Swiss Tropical Institute for testing the antimalarial activity. The compounds were tested *in vitro* against *Plasmodium falciparum* strain. It seems that lipophilicity plays an important factor in determining the antimalarial activity of the 1,2,4-trioxanes probably by causing fast diffusion through membranes. The obtained IC-50 data of some compounds are summarized in ***Table 3.53***.

Compound	**P. *falciparum*. IC-50**	**Cytotoxicity IC-50**
Artemisinin	0.0008	1.9
Chloroquine	0.0638	1.9
38	0.00054	0.74
40	0.0055	4.3
42	0.118	9.2
43	0.1698	n.a.
52	0.0061	2.3
55	0.3656	4.1
58	0.0014	2.6
59	0.0078	2.6
60	0.0038	2.5
61	0.07975	6.8
64	0.1374	4.7
65	0.02475	1.8
66	0.0088	3.7
71	0.00053	1.4
72	0.0020	2.5
74	0.0053	1.7
82	0.0024	0.82
83	0.04825	n.a.
85	0.00965	9.4
86	0.0116	n.a.

88	0.3948	n.a.
90	0.1696	1.2
92	> 5	> 90
96	> 5	36.5
98	0.0013	1.7
99	0.0127	> 10.0
101	0.178	n.a.
102	0.00615	n.a.
103	0.225	n.a.
104a	0.276	n.a.
111	0.0895	3.0
117	0.160	3.0
118	1.495	7.1
129b	2.031	53.8

***Table 3.53*:** All data are in µg/mL.
n.a. Not applicable, data did not substantiate a cytotoxicity test.

4. Experimental Part

4.1 General Remarks

Chromatographic methods:

Column Chromatography (CC): Silica gel 60, 0.063-0.200 mm (70-230 mesh ASTM) purchased from Merck company or silica gel 60, 0.040-0.063 mm (230-240 mesh ASTM) purchased from Macherey-Nagel company was used as stationary phase. All solvents used for the mobile phase were predried.

TLC: Thin layer chromatography was performed on plastic sheets precoated with silica gel 60 F_{254} (Merck) or aluminum sheets precoated polygram® SIL-G/UV_{254} (Macherey-Nagel) spots were visualized by adsorption of iodine or under UV lamp (254 or 366 nm). Peroxidic compounds could be also visualized as yellow to brown spots by spraying with 10% KI solution and then subjecting the plate to hot air. R_f (rate of flow values) were used to characterize each compound.

Preparative thick layer chromatography: 20 x 20 cm glass plates precoated with silica gel G F_{254} purchased from Merck company were used. The sample is placed as a line about 1 cm from the plate's edge and the plate is eluted. The spots were visualized and the spot corresponding to the compound is scratched and collected. The pure product is extracted by adding dry CH_2Cl_2 to the silica gel, filtration and evaporation of the solvent.

Spectroscopic methods

IR: Infrared spectra were obtained using Perkin-Elmer 1600 series FTIR spectrometer and are given in cm^{-1} units. Solid samples are measured as CsI or KBr discs while liquids are measured as neat between two NaCl plates.

UV-Vis: Beckman Coulter DU 800 spectrophotometer was used for measurement of absorption spectra.

^{1}H-NMR: The ^{1}H-NMR spectra were recorded on Bruker AC 300, Bruker DPX 300 spectrometers operating at 300 MHz or on Bruker DRX 500 spectrometer instrument operating at 500 MHz. Chemical shifts are reported as δ in ppm and the coupling constant, *J*, in Hz units. In all spectra solvent peaks were used as internal standard. Solvent used are $CDCl_3$ (δ = 7.24 ppm), DMSO-d_6 (δ = 2.49 ppm), acetone-d_6 (δ = 2.04 ppm), and MeOH-d_4 (δ = 3.35, 4.78 ppm). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

^{13}C-NMR: The ^{13}C-NMR spectra were recorded either on a Bruker AC 300 spectrometer instrument operating at 75 MHz or on Bruker DRX 500 spectrometer instrument operating at 125 MHz.. In all spectra solvent peaks were used as internal standard. Solvent used are $CDCl_3$ (δ = 77 ppm), DMSO-d_6 (δ = 39.7 ppm), acetone-d_6 (δ = 29.8, 206.3 ppm), and MeOH-d_4 (δ = 49.2 ppm). Carbon multiplicities are determined either by DEPT experiment (distortionless enhancement by polarization transfer) or by APT experiment (attached proton test).

Ms: Mass spectra were recorded on Finnigan Incos 500 quadrupole mass spectrometer applying 20 or 70 eV as ionization potential. Fragments masses are designated as m/z followed by the intensity (%).

HRMS: High resolution mass spectra were recorded on Finnigan MAT 900 spectrometer and are measured for the molecular ion peak (M^+).

Analytical methods

Elemental analysis: CHN-combustion analyses were measured using Elementar Vario EL Instrument.

M.p: Melting points were measured using Büchi melting point apparatus type B-535 and they are uncorrected.

X-ray analysis: All X-ray measurements were Nonius KappaCCD diffractometer ($2\Theta_{max}$ = 54°, $Mo_{K\alpha}$ radiation, λ = 0.71073 Å), graphite monochromator, φ / ω-scans. The structures were solved using direct methods (SHELXS-97, SHELXL-97).

Conversion: The conversion of the reactions was determined using the integration of characteristic signals in the NMR spectra (± 5 % error).

Reagents and solvents: Solvents used are dried by distillation over the appropriate drying agent, THF and Et_2O (over Na / benzophenone), *n*-hexane, CH_2Cl_2, $CHCl_3$, ethyl acetate (over $CaCl_2$), methanol and ethanol (over Mg), Et_3N and pyridine (over KOH). All chlorinated hydrocarbons are also pretreated with potassium carbonate to remove HCl traces. Sensitizers as *meso*-tetraphenylporphyrin (TPP) and *meso*-tetratolylporphyrin (TTP) purchased from porphyrin-systems company and were used for chlorinated solvents or benzene while rose Bengal (RB) purchased from Fluka company was used for polar solvents.

Nomenclature: New compounds were named according to AutoNom program.[161]

Photolyses: Solvents used for irradiations are purchased from Fluka company (puriss. P.a.) and are used without further purification. Pyrex irradiation vessels purchased from Normag company were used for photooxygenation reaction in solutions.
Halogen lamps or sodium street lamps (150 W) are used as irradiation source for gram scale photooxygenation experiments while High-pressure mercury lamp (150 W) in combination with a 370-nm cutoff filter was used for O_2-uptake kinetic measurements in 30 mL irradiation unit.[162]

4.2 General Procedures

General procedure for synthesis of allylic alcohols by Grignard reaction (GP-1):

Under an inert atmosphere (note 1), a three-necked, round bottomed flask, fitted with a reflux condenser, pressure-equalized addition funnel and gas inlet, was charged with a suspension of magnesium turnings in dry Et_2O (20 mL)(note 2). Then a solution of alkyl halide in dry Et_2O (20 mL) was added dropwise at such a rate that the solvent refluxed smoothly. The reaction mixture was heated at reflux for 30 min and then left to come to r.t. and then a solution of 3-methyl-2-butenal in dry Et_2O (25 mL) was added dropwise. After complete addition, reflux was continued for 4 h, then the solution was cooled to r.t. and excess reagent was hydrolyzed by cold saturated NH_4Cl solution (50 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 x 30 mL), the combined organic phases were collected, washed with brine (2 x 50 mL) and dried over Na_2SO_4. Evaporation of the solvent by rotary evaporation (at ca. 20 °C, 15 torr) afforded the crude allylic alcohol which was further purified either by column chromatography or fractional distillation.

Notes

1. The reaction can be carried out either under Ar atmosphere, using a balloon, or under nitrogen, passing a continuous flow of nitrogen gas over the solution.
2. The magnesium turnings were preactivated by heating with some crystals of iodine.

General procedure for synthesis of allylic alcohols by organolithium compounds (GP-2):

A 250 mL, three-necked, round-bottomed flask equipped with a pressure-equalized dropping funnel, N_2 gas inlet and reflux condenser. The flask was charged with 3-methyl-2-butenal (4.41 g, 52.4 mmol) dissolved in dry THF or Et_2O (100 mL). The organolithium compound (62.5 mmol) was carefully added dropwise at 0 °C under an atmosphere of N_2. After complete addition the mixture was stirred at 0 °C for 4 h, and then the reaction was quenched with cold saturated NH_4Cl solution (50 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 30 mL), the combined organic layers were collected, washed with brine (3 x 50 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified either by fractional distillation or column chromatography.

General procedure for synthesis of aldol products (GP-3):

To a stirred cold (-78 °C using dry ice/acetone bath) solution of LDA (1.1 equiv.) (Note 1) in 30 mL dry Et_2O (or THF) was added dropwise under an inert atmosphere a solution of the

methyl ketone (1 equiv.) in Et_2O (or THF) (30 mL) over a period of 30 min. After complete addition the mixture was stirred for an additional 1 h at the same temperature. Then a solution of the appropriate carbonyl compound (1 equiv.) in 20 mL Et_2O (or THF) was added and stirring was continued for 30 min. The temperature of the reaction mixture was raised to r.t. then it was poured into aqueous 1M HCl. The phases were separated and the aqueous phase was successively extracted with Et_2O (3 x 50 mL). The combined organic phase was washed with aqueous $NaHCO_3$, brine and dried over Na_2SO_4. Evaporation of the solvent followed by fractional distillation or column chromatography afforded the pure aldol.

Notes

1. LDA was prepared by addition of *n*-BuLi (caution !) at 0 °C to an equivalent amount of diisopropyl amine in dry Et_2O (or THF) under an inert atmosphere.

General procedure for the dehydration of aldol products to α,β-unsaturated carbonyl compounds (GP-4):

To a solution of the β-hydroxy carbonyl compounds (1 equiv.) in CH_2Cl_2 (100 mL) was added 10 mol % solid *p*-toluenesulfonic acid (0.1 equiv.) and the mixture was stirred at r.t overnight. The mixture was partitioned between CH_2Cl_2 and aqueous $NaHCO_3$ then the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. Solvent evaporation under reduced pressure followed by fractional distillation or column chromatography afforded the pure α,β-unsaturated carbonyl compounds.

General procedure for the reduction of α,β-unsaturated carbonyl compounds to allylic alcohols (GP-5):

Under an inert atmosphere, an ether solution of the enone (1 equiv.) was added dropwise at r.t. to a suspension of $LiAlH_4$ (1 equiv.) in dry ether at such a rate as to maintain gentle reflux. After stirring at r.t. overnight the reaction mixture was treated slowly (caution, vigorous evolution of hydrogen gas !) with 1 mL water then 1 mL 15 % aqueous NaOH and at last with 3.5 mL water (For each gram of the reducing agent used unless otherwise mentioned). The precipitate was removed by filtration, digested with ether and the combined ether extracts were washed with water, brine and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure followed by fractional distillation or column chromatography afforded the pure allylic alcohol.

General procedure for the polymerization of sensitizers with styrene and divinylbenzene (GP-6):

Deionized water (200 ml), acidified to pH = 2.3 with sulfuric acid, was purged with nitrogen and heated to 70 °C for 20 min in a 500 ml three-necked flask equipped with stopper, reflux condenser and gas inlet. Subsequently, 10 g of styrene (S), 100 mg of divinylbenzene (DVB) and 10 mg of the polymerizable sensitizer were added rapidly and the system was sealed in order to prevent contamination with air. While the mixture was being vigorously stirred, 120 mg of potassium peroxodisulfate in 10 ml of water was added at once. As the polymerization proceeds, the color of the reaction mixture turns faint red and after a polymerization period of about 7-9 h, the reaction mixture was quenched with methanol (200 mL) and then cooled to room temperature. The polymer particles were separated by centrifugation at 3500 rpm, and any free (non-polymerized) sensitizer particles were removed by extraction with methylene chloride several times until the dye in the washing solvent is no more detected. The beads dried at 40 °C under vacuum to afford the polymer-bound sensitizer.

(a) Polymerization of tetrastyrylporphyrin (TSP) with styrene and divinylbenzene:

Following GP-6, using 10 mg of TSP, 4.2 g (42 %) of the polymer-bound sensitizer TSP-S-DVB was obtained as sandy solid.

(b) Polymerization of protoporphyrin-IX (PP) with styrene and divinylbenzene:

Following GP-6, using 10 mg of PP, 3.25 g (33 %) of the polymer-bound sensitizer PP-S-DVB was obtained as sandy solid.

General procedure for the homogeneous type-II photooxygenation reaction (GP-7):

The substrate (ca. 10 mmol) and the photosensitizer were dissolved in the appropriate solvent (100 mL) and irradiated with two external 150 W halogen lamps (sodium street lamps could be also used) while a stream of air (or oxygen) was passed through the reaction mixture. The course of the reaction was monitored over time by means of TLC. After complete consumption of the starting material, the solvent was distilled off under reduced pressure (caution, water bath temperature should not exceed 30 °C) and the composition of the crude reaction mixture was determined by ^{1}H- as well as ^{13}C-NMR.

(a) Using rose Bengal (RB) as sensitizer:

10^{-3} M solution of RB in dry MeOH (100 mL) was used as solvent.

(b) Using *meso*-tetraphenylporphyrin (TPP) as sensitizer:

5 x 10^{-4} M solution of TPP in dry CCl_4 (100 mL) was used as solvent. Other *p*-substituted *meso*-tetraarylporphyrin as *meso*-tetratolylporphyrin (TTP) and other halogenated solvents as CH_2Cl_2 or $CHCl_3$ can be also used.

General procedure for the heterogeneous type-II photooxygenation reaction (GP-8):

The substrate (ca. 5 mmol) was dissolved in CCl_4 (30 mL) and the polymer-bound sensitizer (ca. 35 mg) was suspended in the solution and the whole mixture is irradiated in the oxygen-uptake apparatus. The reaction progress was monitored against time. At the end of the reaction, the sensitizer-bound to polymer was filtered off (for regeneration and reuse) and the filtrate was distilled off under reduced pressure to afford the product (caution, water bath temperature should not exceed 30 °C).

General procedure for solvent-free type-II photooxygenation reaction in polymer matrices (GP-9):

(a) Using commercial PS-DVB copolymer:

The polymer particles (ca. 2-3 g) were introduced into a Petri dish (19 cm diameter) and were swollen by CH_2Cl_2 (20 mL). The substrate (ca. 10 mmol) and the nonpolar sensitizer (TPP or TTP, ca. 3-6 mg) in ethyl acetate (20 mL) were subsequently added and the excess solvent is evaporated by leaving the Petri dish in a well ventilated hood. The Petri dish is covered with a glass plate and the sandy solid is irradiated with halogen lamp or sodium street lamp. The polymer beads were subsequently rinsed with ethanol (3 x 30 mL) and filtered (the beads are kept for regeneration and reuse). The solvent was evaporated under reduced pressure (caution, water bath temperature should not exceed 30 °C) and the composition of the product was determined by ^{1}H- as well as ^{13}C-NMR.

(b) Using synthesized TSP-S-DVB or PP-S-DVB copolymers:

The dye-cross-linked polymer beads (TSP-S-DVB or PP-S-DVB, ca. 0.60 g) in a Petri dish (14 cm in diameter) were swollen by CH_2Cl_2 (20 mL) then the substrate (ca. 5 mmol) in ethyl acetate (20 mL) was added. Subsequent treatment as in protocol (a) affords the product.

General procedure for analytical-scale type-II photooxygenation reaction for kinetic measurements (GP10):

For kinetic runs, developed O_2-uptake measuring instrument with automatic oxygen-consumption recording system was used.[163] An irradiation unit with capacity up to 30 mL was used as reaction vessel (Duran glass with a quartz side window and cooling jacket). The

irradiation unit is connected to a graduated burette (having cooling jacket too) which in turn connected to a moving reservoir filled with water by means of tubing. Ethanol adapted at the required reaction temperature was circulated through the system by a pumping thermostat. The irradiation unit is filled with the solution of the sensitizer and substrate then the whole system is saturated with oxygen and closed.

The amount of oxygen consumed during the reaction results in a decrease in the internal pressure in the burette which is compensated by transfer of water from the reservoir into the burette. This change in pressure is detected by a small sponge in a U-shaped tube surrounded by a light beam. As a consequence of cutting this light beam during the sponge's movement the reservoir moves. The reservoir movement over time is recorded on a xt-writing instrument and from the curve obtained (cm/h) or from the recalculated oxygen volume per unit time (mL/h), photooxygenation reaction rate of different substrates can be compared.[164,162]

General procedure for synthesis of amino acids methyl ester hydrochloride (GP-11):

To a cold (NaCl/crushed ice bath) absolute methanol (50 mL) is added dropwise thionyl chloride (4.2 mL, 60 mmol) over a period of 5-10 min. The solution is stirred for 5 min then solid amino acid (30 mmol) is added in one portion. Stirring is continued for 30 min at the same temperature then the ice bath is removed and the solution is refluxed for 3 h. The solution is allowed to cool to r.t. and the excess solvent is removed under reduced pressure to afford the amino acid methyl ester hydrochloride as white solid which is used without further purification.

General procedure for synthesis of N-acylamino acids methyl ester (GP-12):

To a cold (0 °C, NaCl/crushed ice bath), suspension of the amino acid methyl ester hydrochloride (100 mmol) in dry $CHCl_3$ (150 mL), is added dropwise under stirring triethyl amine (20.20 g, 200 mmol). Stirring is completed 15 min followed by dropwise addition of the acid chloride (100 mmol) and the solution is allowed to warm to room temperature. After stirring for 1 h, the solvent is evaporated and the remaining solid is digested by ethyl acetate, filtered through a pad of silica gel. Evaporation of ethyl acetate under reduced pressure affords the corresponding amide in high purity which is used without further purification.

General procedure for synthesis of 2,4-disubstituted-5-methoxyoxazoles (GP-13):

To a solution of the N-acyl-L-amino acid methyl ester (100 mmol) in dry $CHCl_3$ (30 mL) is added phosphorous pentachloride (20.8 g, 100 mmol) and the flask is protected from moisture

by a reflux condenser having calcium chloride-filled drying tube. The solution is gently warmed in a water bath at about 60 °C (until no HCl gas is evolved). When the solution becomes yellow, Et_2O (50 mL) and ice were added followed by dropwise addition of 20 % aqueous KOH or saturated $NaCO_3$ solution until neutralization then the mixture is stirred at r.t. for 30 min. The layers are separated and the aqueous phase is extracted with Et_2O (3 x 100 mL). The combined organic phase is washed with water, brine and dried over Na_2SO_4. The solvent is evaporated under reduced pressure and the residue is fractionally distilled to give the product.

General procedure for solvent-free photooxygenation of oxazoles (GP-14):

The dye-crosslinked polymer beads, TSP-S-DVB or PP-S-DVB (0.50 g) were added into a Petri dish (14 cm diameter) and treated with 20 ml methylene chloride, subsequently the oxazole dissolved in 20 ml ethyl acetate and the excess solvent was evaporated. The Petri dish was covered with a glass plate and irradiated with a 150 W halogen or sodium street lamp. The product was extracted with 2 x 30 ml of methanol or ethyl acetate and filtrated. After evaporation of the solvent the corresponding 1,2,4-dioxazole was isolated as pure product. The peroxides are not infinitely stable and decompose slowly to give the corresponding amide and dicarbonyl fragments.[165]

General procedure for the peroxyacetalization reaction and 1,2,4-trioxanes synthesis (GP-15)

To a stirred solution of β-hydroxy hydroperoxides and the condensing reagent in dry CH_2Cl_2 (100 mL) was added at r.t. a catalytic amount of boron trifluoride etherate (ca. 0.2 mL) and the mixture was further stirred for about 12 h (overnight) at the same temperature. The reaction mixture was partitioned between CH_2Cl_2 and saturated $NaHCO_3$ solution then the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic phases were washed with brine, water, dried over Na_2SO_4. Solvent evaporation (caution, water bath temperature should not exceed 30 °C) followed by chromatographic purification afforded the 1,2,4-trioxane as pure product.

General procedure for Lewis-acid catalyzed cleavage of β-hydroxy hydroperoxides and their cross-peroxyacetalization reaction into 1,2,4-trioxanes (GP-16)

To a stirred solution of β-hydroxy hydroperoxides in dry CH_2Cl_2 (100 mL) was added at r.t. a catalytic amount of boron trifluoride etherate (ca. 0.2 mL) and the mixture was further stirred

for about 12 h (overnight) at the same temperature. The reaction mixture was partitioned between CH_2Cl_2 and saturated $NaHCO_3$ solution then the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic phases were washed with brine, water, dried over Na_2SO_4. Solvent evaporation (caution, water bath temperature should not exceed 30 °C) followed by chromatographic purification afforded the 1,2,4-trioxanes as pure products.

Note

All β-hydroxy allylic hydroperoxides used in 1,2,4-trioxane syntheses are prepared according to **GP-9a** unless otherwise is mentioned.

General procedure for synthesis of triols from allylic hydroperoxides or allylic alcohols using catalytic OsO_4 and N-methylmorpholine N-oxide as cooxidant (GP-17):

To a stirred solution of the allylic hydroperoxide or allylic alcohol (0.62 mmol) in *tert*-butanol (1 mL) and H_2O (1 mL) is added N-methylmorpholine N-oxide (145 mg, 1.24 mol, 2 equiv.) followed by 2.5 % solution of OsO_4 in *tert*-butanol (0.03 mmol, 0.05 equiv.) (caution, highly toxic !). The reaction mixture is stirred at r.t. for 24 h then quenched with aqueous sodium sulfite solution. The phases were separated and the aqueous phase is extracted with ethyl acetate (3 x 30 mL), then the combined organic layers are dried over $MgSO_4$. Evaporation of the solvent under reduced pressure affords the corresponding triol in good purity.

Synthesis of triols from allylic hydroperoxides using catalytic OsO_4 and in absence of external cooxidant (GP-18):

To a stirred solution of the allylic hydroperoxide (1.2 mmol) in H_2O (1 mL) and methanol (1 mL) is added 2.5 % solution of OsO_4 in *tert*-butanol (0.1-0.001 equiv.) (caution, highly toxic !). The reaction mixture is stirred for 15 min at r.t. then quenched with aqueous sodium sulfite solution. The phases were separated and the aqueous phase is extracted with ethyl acetate (3 x 30 mL), then the combined organic layers are dried over $MgSO_4$. Evaporation of the solvent under reduced pressure affords the corresponding triol in good purity.

Synthesis of triols from allylic hydroperoxides using catalytic WO_3 and in absence of external cooxidant (GP-19):

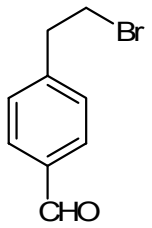
To a solution of the allylic hydroperoxide (1.2 mmol) in H_2O (1 mL) and methanol (1 mL) is added under stirring solid WO_3 (0.1-0.05 equiv.). The reaction mixture is stirred for 3-5 days at r.t. then quenched with aqueous sodium sulfite solution. The phases were separated and the

aqueous phase is extracted with ethyl acetate (3 x 30 mL), then the combined organic layers are dried over $MgSO_4$. Evaporation of the solvent under reduced pressure affords the corresponding triol in good purity.

4.3 Synthesis of tetrastyrylporphyrin (TSP)

4-(2-Bromoethyl)benzaldehyde (2)

(elid 296c)



To a cold (0°C using ice bath) solution of 2-bromoethylbenzene **(1)** (18.5 g, 100 mmol) in CH_2Cl_2 (100 mL) is added in one portion $TiCl_4$ (22 mL) followed by gradual addition of dichloromethyl methyl ether (11.5 g, 100 mol). The reaction mixture is stirred for 1 h then it is poured into ice cold water and the phases are separated. The aqueous phase is extracted with CH_2Cl_2 (2 x 30 mL), and the combined organic phases are washed with saturated $NaHCO_3$, water and brine. Solvent is evaporated under reduced pressure and the residue is purfied by fractional distillation (116-118 °C, 2.3 torr, Lit. 108-110 °C, 1 torr[166]) to give the pure aldehyde (5.58 g, 26.2 mmol).

Yield: 26 %

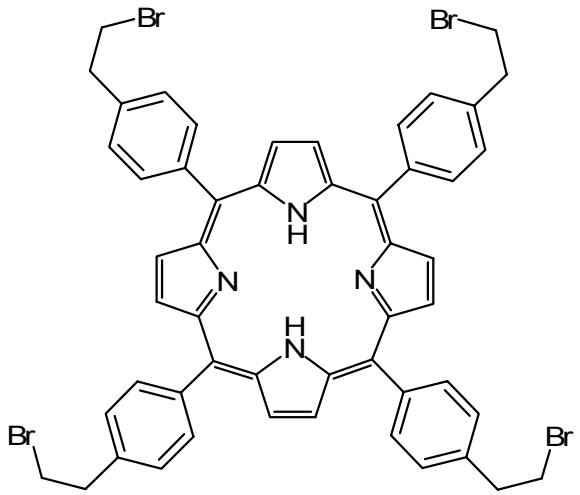
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 3.19 (t, 2H, *J* = 7.20 Hz, C$\underline{H}_2$), 3.54 (t, 2H, *J* = 7.20 Hz, C$\underline{H}_2$Br), 7.32 (d, 2H, *J* = 8.07 Hz, 2 x C$\underline{H}_{arom}$), 7.77 (d, 2H, *J* = 8.25 Hz, 2 x C$\underline{H}_{arom}$), 9.93 (s, 1H, C$\underline{H}$O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 31.9 (t, $\underline{C}H_2$Br), 39.1 (t, $\underline{C}H_2$C), 129.3 (d, 2 x $\underline{C}H_{arom}$), 130.0 (d, 2 x $\underline{C}H_{arom}$), 135.2 (s, $\underline{C}q_{arom}$), 145.7 (s, $\underline{C}q_{arom}$), 191.8 (d, CHO).

5,10,15,20-Tetrakis-[4-(2-bromo-ethyl)-phenyl]-porphyrin (3)
(elid 299a)



4-(2-Bromoethyl)benzaldehyde **(2)** (5.58 g, 26.2 mmol) and pyrrole (1.75 g, 26.1 mmol) are heated in propionic acid for 20 min then cooled to r.t., filtered, washed with ethanol and water then dried. The residue is purified with column chromatography (SiO_2, $CCl_4/CHCl_3$, 1:1, R_f = 0.58) to give the product (5.73 g, 5.5 mmol) as violet solid.

Yield: 21 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = -2.80 (s, 2H, 2 x NH), 3.50 (t, 8H, *J* = 7.59 Hz, CH_2), 3.86 (t, 8H, *J* = 7.52 Hz, 4 x CH_2Br), 7.57 (d, 8H, *J* = 8.10 Hz, 8 x CH_{arom}), 8.15 (d, 8H, *J* = 7.92 Hz, 8 x CH_{arom}), 8.82 (s, 8H, 4 x CH=CH).

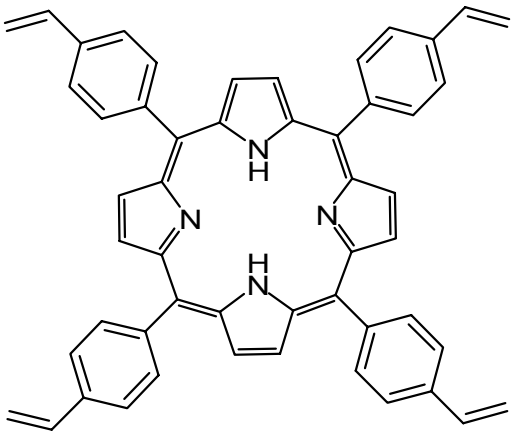
IR: (CsI)

ν (cm^{-1}) = 3471, 3419, 3386, 3316, 3023, 2963, 2925, 1603, 1349, 1261, 1095, 1021, 803, 661

UV: (CH_2Cl_2)

λ_{max} = 419 nm ($\varepsilon_{419\ nm}$ = 448990 M^{-1} cm^{-1}), C = 9.41 x 10^{-7} M.

5,10,15,20-Tetrakis-(4-vinyl-phenyl)-porphyrin (4)
(elid 301a, 491g, 369a)



A solution of **(3)** (90 mg, 0.086 mmol) in N,N-dimethylformamide and 25 % alcoholic potassium hydroxide were heated at 50 °C for 7 h. then cooled to r.t., filtered, washed with ethanol and water then dried. The residue is purified with column chromatography (SiO_2, $CCl_4/CHCl_3$, 3:1, $R_f = 0.71$) to give the pure product (58.7 mg, 0.082 mmol) as violet solid.

Yield: 95 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = -2.77 (s, 2H, 2 x NH), 5.48 (d, 4H, *J* = 11.52 Hz, 4 x C$\underline{H_2}$=CH), 6.05 (dd, 4H, *J* = 0.57, 17.58 Hz, 4 x C$\underline{H_2}$=CH), 7.05 (dd, 8H, *J* = 10.98, 17.73 Hz, 4 x C$\underline{H}$=CH_2), 7.79 (d, 8H, *J* = 8.22 Hz, 8 x C$\underline{H}_{arom}$), 8.16 (d, 8H, *J* = 8.04 Hz, 8 x C$\underline{H}_{arom}$), 8.86 (s, 8H, 4 x C$\underline{H}$=C$\underline{H}$).

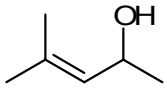
UV: (CH_2Cl_2)

λ_{max} = 421 nm ($\varepsilon_{421\ nm}$ = 483468 M^{-1} cm^{-1}), C = 1.73 x 10^{-6} M.

4.4 Synthesis of Substrates for $^1O_2$ Photooxygenation Reaction

4-Methylpent-3-en-2-ol[167] **(6a)**

(elid 84)



The preparation and work-up were carried out according to **GP-5** using mesityl oxide **(26)** (5.0 g, 50.9 mmol) and $LiAlH_4$ (1.0 g, 26.4 mmol). The crude product was fractionally distilled (b.p**.** 87-89 °C, 90 torr) to give the pure allylic alcohol (4.23 g, 42.3 mmol) as colorless oil.

Yield: 83 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

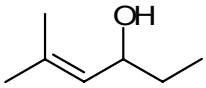
δ (ppm) = 1.16 (d, 3H, *J* = 6.3 Hz, C$\underline{H}_3$CH), 1.62 (d, 3H, *J* = 1.3 Hz, C$\underline{H}_3$C=), 1.65 (d, 3H, *J* = 1.3 Hz, C$\underline{H}_3$C=), 4.49 (dq, 1H, *J* = 6.3, 8.6 Hz, C$\underline{H}$-OH), 5.14 (d, 1H, *J* = 8.6 Hz, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, $\underline{C}H_3$CH), 23.5 (q, $\underline{C}H_3$C=), 25.6 (t, $\underline{C}H_2$), 64.7 (d, $\underline{C}$H-OH), 129.3 (d, $\underline{C}$H=C), 133.9 (s, $\underline{C}$=CH).

5-Methylhex-4-en-3-ol[168] **(6b)**

(elid 318d)



The preparation and work-up were carried out according to **GP-1** using ethyl bromide (6.13 g, 56.3 mmol), magnesium turnings (1.37 g, 56.3 mmol) and 3-methyl-2-butenal **(25)** (3.79 g, 45.0 mmol). Büchi distillation of the crude product at about 112 °C, 90 torr using water vacuum pump (Lit. 63 °C, 12 torr[168]) afforded 2.64 g (23.2 mmol) of the pure allylic alcohol as colorless oil.

Yield: 52 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

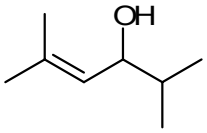
δ (ppm) = 0.83 (dd, 3H, *J* = 7.42, 7.42 Hz, C<u>H</u>$_3$CH$_2$), 1.32-1.63 (m, 2H, C<u>H</u>$_2$CH$_3$), 1.64 (d, 3H, *J* = 1.32 Hz, C<u>H</u>$_3$C=), 1.68 (d, 3H, *J* = 1.32 Hz, C<u>H</u>$_3$C=), 4.20 (ddd, 1H, *J* = 6.60, 6.60, 8.67 Hz, C<u>H</u>-OH), 5.08 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.7 (q, <u>C</u>H$_3$CH$_2$), 18.1 (q, <u>C</u>H$_3$C=), 25.7 (q, <u>C</u>H$_3$C=), 30.5 (t, <u>C</u>H$_2$CH$_3$), 70.0 (d, <u>C</u>H-OH), 128.0 (d, <u>C</u>H=C), 135.0 (s, <u>C</u>=CH).

2,5-Dimethylhex-4-en-3-ol[168] **(6c)**

(elid 476u)



The preparation and work-up were carried out according to **GP-1** using isopropyl bromide (9.23 g, 75.0 mmol), magnesium turnings (1.80 g, 75.0 mmol) and 3-methyl-2-butenal **(25)** (4.92 g, 58.6 mmol). Büchi distillation of the crude product at about 125 °C, 90 torr using water vacuum pump (Lit. 59 °C, 12 torr[168]) afforded the pure allylic alcohol (5.0 g, 39.0 mmol) as colorless oil.

Yield: 67 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

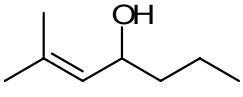
δ (ppm) = 0.77 (d, 3H, *J* = 6.78 Hz, C<u>H</u>$_3$CH), 0.87 (d, 3H, *J* = 6.75 Hz, C<u>H</u>$_3$CH), 1.58 (m, 1H, C<u>H</u>(CH$_3$)$_2$), 1.60 (d, 3H, *J* = 1.47 Hz, C<u>H</u>$_3$C=), 1.66 (d, 3H, *J* = 1.47 Hz, C<u>H</u>$_3$C=), 3.96 (dd, 1H, *J* = 6.75, 8.97 Hz, C<u>H</u>-OH), 5.12 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, <u>C</u>H$_3$CH), 18.2 (q, <u>C</u>H$_3$CH), 18.2 (q, <u>C</u>H$_3$C=), 25.7 (q, <u>C</u>H$_3$C=), 34.3 (d, <u>C</u>H(CH$_3$)$_2$), 73.5 (d, <u>C</u>H-OH), 126.4 (d, <u>C</u>H=C), 135.2 (s, <u>C</u>=CH).

2-Methylhept-2-en-4-ol (6d)

(elid 465c)



The preparation and work-up were carried out according to **GP-1** using *n*-propyl bromide (6.15 g, 50 mmol), magnesium turnings (1.20 g, 50 mmol) and 3-methyl-2-butenal **(25)** (3.36

g, 40 mmol). Büchi distillation of the crude product at about 137 °C, 90 torr using water vacuum pump gives the pure allylic alcohol (4.25 g, 33.2 mmol) as colorless oil.

Yield: 83 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

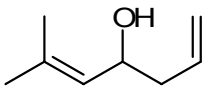
δ (ppm) = 0.86 (t, 3H, *J* = 7.20 Hz, C<u>H</u>$_3$CH$_2$), 1.18-1.57 (m, 4H, C<u>H</u>$_2$C<u>H</u>$_2$), 1.62 (d, 3H, *J* = 1.32 Hz, C<u>H</u>$_3$C=), 1.66 (d, 3H, *J* = 1.47 Hz, C<u>H</u>$_3$C=), 4.28 (ddd, 1H, *J* = 6.46, 6.46, 8.67 Hz, C<u>H</u>-OH), 5.08 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.0 (q, <u>C</u>H$_3$CH$_2$), 18.1 (q, <u>C</u>H$_3$C=), 18.6 (t, <u>C</u>H$_2$CH$_3$), 25.7 (q, <u>C</u>H$_3$C=), 39.8 (t, <u>C</u>H$_2$CH), 68.3 (d, <u>C</u>H-OH), 128.3 (d, <u>C</u>H=C), 134.6 (s, <u>C</u>=CH).

6-Methylhept-1,5-dien-4-ol[170] **(6e)**

(elid 481d)



The preparation and work-up were carried out according to **GP-1** using allyl bromide (6.05 g, 50 mmol), magnesium turnings (1.20 g, 50 mmol) and 3-methyl-2-butenal **(25)** (3.36 g, 40 mmol). The crude product was purified by column chromatography (SiO_2, EA/*n*-hex, 1:8, R_f = 0.48) to give the pure allylic alcohol (3.83 g, 30.4 mmol) as colorless oil.

Yield: 76 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.62 (s, 3H, C<u>H</u>$_3$C=), 1.66 (s, 3H, C<u>H</u>$_3$C=), 2.20 (m, 2H, C<u>H</u>$_2$CH=), 4.32 (ddd, 1H, *J* = 6.84, 6.84, 7.65 Hz, C<u>H</u>-OH), 5.01-5.15 (m, 3H, C<u>H</u>=C and C<u>H</u>$_2$=CH), 5.75 (m, 1H, C<u>H</u>=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.1 (q, <u>C</u>H$_3$C=), 25.6 (q, <u>C</u>H$_3$C=), 42.1 (t, <u>C</u>H$_2$CH=), 67.6 (d, <u>C</u>H-OH), 117.5 (t, CH$_2$=CH), 127.3 (d, <u>C</u>H=C), 134.5 (d, <u>C</u>H=CH$_2$), 135.0 (s, C=CH).

3,6-Dimethylhepta-1,5-dien-4-ol[169] **(6f)**

(elid 486j)

The preparation and work-up were carried out according to **GP-1** using 3-chlorobut-1-ene (9.05 g, 100 mmol), magnesium turnings (3.6 g, 150 mmol) and 3-methyl-2-butenal **(25)** (8.4 g, 100 mmol). The crude product was fractionally distilled **(**67-69 °C, 5 torr[169]) to give the pure allylic alcohol (8.0 g, 57.1 mmol, 57 %) as colorless oil in a 53:47 diastereomeric mixture a,b.

^{1}H-NMR: (300 MHz, $CDCl_3$, diastereomer a)

δ (ppm) = 0.97 (d, 3H, *J* = 6.93 Hz, C$\underline{H}_3$CH), 1.63 (d, 3H, *J* = 3.09 Hz, C$\underline{H}_3$C=), 1.69 (d, 3H, *J* = 4.56 Hz, C$\underline{H}_3$C=), 2.29 (m, 1H, C$\underline{H}$CH$_3$), 4.17 (dd, 1H, *J* = 5.73, 8.97 Hz, C$\underline{H}$-OH), 5.0-5.13 (m, 3H, C$\underline{H}$=C and C$\underline{H}_2$=CH), 5.74 (m, 1H, C$\underline{H}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, diastereomer a)

δ (ppm) = 14.8 (q, $\underline{C}$H$_3$CH), 18.3 (q, $\underline{C}$H$_3$C=), 25.8 (q, $\underline{C}$H$_3$C=), 43.8 (d, $\underline{C}$HCH$_3$), 71.6 (d, $\underline{C}$H-OH), 115.2 (t, $\underline{C}$H$_2$=CH), 125.8 (d, $\underline{C}$H=C), 135.8 (s, $\underline{C}$=CH), 140.1 (d, $\underline{C}$H=CH$_2$).

^{1}H-NMR: (300 MHz, $CDCl_3$, diastereomer b)

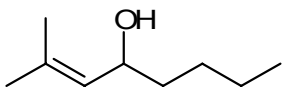
δ (ppm) = 0.91 (d, 3H, *J* = 6.90 Hz, C$\underline{H}_3$CH), 1.63 (d, 3H, *J* = 3.09 Hz, C$\underline{H}_3$C=), 1.69 (d, 3H, *J* = 4.56 Hz, C$\underline{H}_3$C=), 2.14 (m, 1H, C$\underline{H}$CH$_3$), 4.03 (dd, 1H, *J* = 8.29, 8.29 Hz, C$\underline{H}$-OH), 5.0-5.13 (m, 3H, C$\underline{H}$=C and C$\underline{H}_2$=CH), 5.74 (m, 1H, C$\underline{H}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, diastereomer b)

δ (ppm) = 16.0 (q, $\underline{C}$H$_3$CH), 18.4 (q, $\underline{C}$H$_3$C=), 25.8 (q, $\underline{C}$H$_3$C=), 45.1 (d, $\underline{C}$HCH$_3$), 71.5 (d, $\underline{C}$H-OH), 116.1 (t, $\underline{C}$H$_2$=CH), 125.4 (d, $\underline{C}$H=C), 136.1 (s, $\underline{C}$=CH), 140.9 (d, $\underline{C}$H=CH$_2$).

2-Methyloct-2-en-4-ol[170] **(6g)**

(elid 420b)



The preparation and work-up were carried out according to **GP-2** using *n*-BuLi (39 mL of 1.6 M solution, 62.4 mmol) and 3-methyl-2-butenal **(25)** (4.41 g, 52.5 mmol). The crude product

was purified by column chromatography (SiO_2, EA/*n*-hex, 1:8, R_f = 0.31) to give the pure allylic alcohol as colorless oil.

Yield: 6.0 g (81 %)

^{1}H-NMR: (300 MHz, $CDCl_3$)

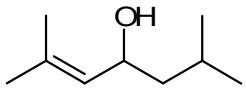
δ (ppm) = 0.84 (t, 3H, *J* = 6.91 Hz, C$\underline{H_3}$CH$_2$), 1.13-1.58 (m, 6H, C$\underline{H_2}$C$\underline{H_2}$C$\underline{H_2}$), 1.62 (d, 3H, *J* = 1.47 Hz, C$\underline{H_3}$C=), 1.67 (d, 3H, *J* = 1.32 Hz, C$\underline{H_3}$C=), 4.26 (ddd, 1H, *J* = 6.47, 6.47, 8.82 Hz, C$\underline{H}$-OH), 5.08 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.0 (q, $\underline{C}H_3CH_2$), 18.1 (q, $\underline{C}H_3C$=), 22.6 (t, $\underline{C}H_2CH_3$), 25.7 (q, $\underline{C}H_3C$=), 27.6 (t, $\underline{C}H_2CH_2$), 37.4 (t, $\underline{C}H_2CH$), 68.6 (d, $\underline{C}$H-OH), 128.3 (d, $\underline{C}$H=C), 134.7 (s, $\underline{C}$=CH).

2,6-Dimethylhept-2-en-4-ol (6h)

(elid 483g)



The preparation and work-up were carried out according to **GP-1** using isobutyl bromide (6.85 g, 50 mmol), magnesium turnings (1.20 g, 50 mmol) and 3-methyl-2-butenal **(25)** (3.36 g, 40 mmol). Büchi distillation of the crude product using water vacuum pump at about 150 °C, 90 torr (Lit. 74-76 °C, 12 torr[171]) afforded the pure allylic alcohol (3.87 g, 28.2 mmol) as colorless oil.

Yield: 70 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

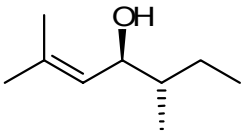
δ (ppm) = 0.83 (m, 6H, (C$\underline{H_3}$)$_2$CH), 1.16 (m, 1H, C$\underline{H_2}$CH), 1.40 (m, 1H, C$\underline{H_2}$CH), 1.55 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 1.60 (d, 3H, *J* = 3.39 Hz, C$\underline{H_3}$C=), 1.63 (d, 3H, *J* = 3.09 Hz, C$\underline{H_3}$C=), 4.32 (m, 1H, C$\underline{H}$-OH), 5.05 (m, 1H, C$\underline{H}$=C).

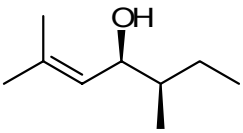
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, $\underline{C}H_3C$=), 22.5 (q, $\underline{C}H_3CH$), 22.8 (q, $\underline{C}H_3CH$), 24.4 (d, $\underline{C}$H(CH$_3$)$_2$), 25.5 (q, $\underline{C}H_3C$=), 46.7 (t, $\underline{C}H_2CH$), 66.6 (d, $\underline{C}$H-OH), 128.7 (d, $\underline{C}$H=C), 133.9 (s, $\underline{C}$=CH).

2,5-Dimethylhept-2-en-4-ol (6i)

(elid 500p, 496r, 465d)





The preparation and work-up were carried out according to **GP-2** using *sec*-butyl lithium (48.1 mL of 1.3 M solution, 62.5 mmol), and 3-methyl-2-butenal **(25)** (4.41 g, 52.5 mmol) in dry THF. The crude product was purified by column chromatography (SiO_2; EA/*n*-hex; 1:5, R_f = 0.67) to afford the pure allylic alcohol (4. 48 g, 31.5 mmol) as yellow oil.

Yield: 60 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.77 (m, 6H, C$\underline{H}_3$CH and C$\underline{H}_3$CH$_2$), 0.92-1.56 (m, 6H, C$\underline{H}_2$CH$_3$ and C$\underline{H}$CH$_3$), 1.59 (d, 3H, *J* = 1.46 Hz, C$\underline{H}_3$C=), 1.63 (d, 3H, *J* = 1.32 Hz, C$\underline{H}_3$C=), 4.19 (m, 1H, C$\underline{H}$-OH), 5.06 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major product)

δ (ppm) = 11.2 (q, $\underline{C}$H$_3$CH$_2$), 18.0 (q, $\underline{C}$H$_3$CH), 19.0 (q, $\underline{C}$H$_3$C=), 25.6 (q, $\underline{C}$H$_3$C=), 29.2 (t, $\underline{C}$H$_2$CH$_3$), 32.0 (t, $\underline{C}$H$_2$), 34.3 (d, $\underline{C}$HCH$_3$), 25.1 (t, $\underline{C}$H2), 68.8 (d, $\underline{C}$H-OH), 128.4 (d, $\underline{C}$H=C), 134.3 (s, $\underline{C}$=CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, significant additional signals of minor product)

δ (ppm) = 11.2 (q, $\underline{C}$H$_3$CH$_2$), 19.0 (q, $\underline{C}$H$_3$C=), 29.3 (t, $\underline{C}$H$_2$CH$_3$), 128.4 (d, $\underline{C}$H=C), 134.4 (s, $\underline{C}$=CH).

IR: (Film)

ν (cm^{-1}) = 3200-3600, 2962, 2929, 1677, 1376, 1017.

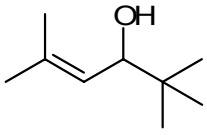
Elemental Analysis: ($C_9H_{18}O$, M =142.24)

Calcd: C 76.00 H 12.76

Found: C 76.21 H 12.76

2,2,5-Trimethylhex-4-en-3-ol[168] (6j)

(elid 449e)



The preparation and work-up were carried out according to **GP-2** using *tert*-BuLi (25 mL of 1.5 M solution, 37.5 mmol), and 3-methyl-2-butenal **(25)** (2.63 g, 31.3 mmol) in dry Et_2O (100 mL). The crude product was purified by column chromatography (SiO_2, EA/*n*-hex, 1:8, R_f = 0.49) to afford 0.90 g (6.3 mmol) of the pure allylic alcohol as yellow oil.

Yield: 20 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

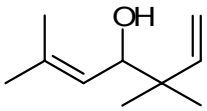
δ (ppm) = 0.83 (s, 9H, $(C\underline{H}_3)_3C$), 1.62 (d, 3H, *J* = 1.47 Hz, $C\underline{H}_3C$=), 1.68 (d, 3H, *J* = 1.47 Hz, $C\underline{H}_3C$=), 3.93 (d, 1H, *J* = 9.24 Hz, C<u>H</u>-OH), 5.15 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.3 (q, $\underline{C}H_3C$=), 25.4 (q, $(\underline{C}H_3)_3C$), 26.0 (q, $\underline{C}H_3C$=), 35.3 (s, $\underline{C}(CH_3)_3$), 75.9 (d, <u>C</u>H-OH), 124.9 (d, <u>C</u>H=C), 135.6 (s, <u>C</u>=CH).

3,3,6-Trimethylhepta-1,5-dien-4-ol (*artemesia alcohol*) (6k)

(elid 483l)



The preparation and work-up were carried out according to **GP-1** using prenyl magnesium bromide (12.37 g, 83 mmol), and 3-methyl-2-butenal **(25)** (5.0 g, 59.5 mmol). The crude product was purified by column chromatography (SiO_2, EA/*n*-hex, 1:8, R_f = 0.43) to give the pure allylic alcohol (1.50 g, 9.7 mmol) as faint yellow oil.

Yield: 16 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

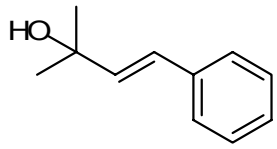
δ (ppm) = 0.94 (s, 3H, $(C\underline{H}_3)_2C$),0.96 (s, 3H, $(C\underline{H}_3)_2C$), 1.65 (s, 3H, $C\underline{H}_3C$=), 1.71 (s, 3H, $C\underline{H}_3C$=), 3.99 (d, 1H, *J* = 9.24 Hz, C<u>H</u>-OH), 4.99-5.16 (m, 3H, $C\underline{H}_2$=CH and C<u>H</u>=C), 5.85 (dd, 1H, *J* = 10.86, 17.34 Hz, C<u>H</u>=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.4 (q, $\underline{C}H_3C$=), 21.2 (q, $(\underline{C}H_3)_2C$), 23.9 (q, $(\underline{C}H_3)_2C$), 26.0 (q, $\underline{C}H_3C$=), 41.9 (s, $\underline{C}(CH_3)_2$), 74.5 (d, <u>C</u>H-OH), 113.2 (t, $\underline{C}H_2$=CH), 124.1 (d, <u>C</u>H=C), 136.3 (s, <u>C</u>=CH), 145.1 (d, <u>C</u>H=CH_2).

(E)-2-Methyl-4-phenylbut-3-en-2-ol[170] **(6m)**

(elid 422c)



The preparation and work-up were carried out according to **GP-2** using Phenyl lithium (34.7 mL of 1.8 M solution, 62.5 mmol), and 3-methyl-2-butenal **(25)** (4.41 g, 52.5 mmol) in dry THF. The crude product was purified by column chromatography (SiO_2; EA/*n*-hex; 1:8, R_f = 0.22) to afford the pure allylic alcohol (6.89 g, 42.5 mmol) as yellow oil.

Yield: 81%

^{1}H-NMR: (300 MHz, $CDCl_3$)

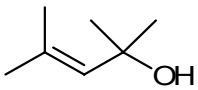
δ (ppm) = 1.29 (s, 6H, $(C\underline{H}_3)_2C$), 6.22 (d, 1H, *J* = 16.14 Hz, C<u>H</u>=CH), 6.45 (d, 1H, *J* = 16.14 Hz, C<u>H</u>=CH), 7.05-7.31 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 29.7 (q, $(\underline{C}H_3)_2C$), 70.8 (s, <u>C</u>-OH), 126.2 (d, $\underline{C}H_{arom}$), 126.3 (d, 2 x $\underline{C}H_{arom}$), 127.2 (d, <u>C</u>H=CH), 128.4 (d, 2 x $\underline{C}H_{arom}$), 136.9 (s, $\underline{C}q_{arom}$), 137.5 (d, <u>C</u>H=CH).

2,4-Dimethylpent-3-en-2-ol[172] **(6n)**

(elid 67)



Magnesium turnings (3.65 g, 150 mmol) in dry Et_2O (30 mL) are allowed to react with some methyl iodide [ca. 1/20 of 150 mmol (10.7 g)]. After the reaction has started, the rest of the methyl iodide in dry Et_2O is added dropwise at r.t. in a rate which sustains gentle boiling of the solvent. The reaction mixture is refluxed for 30 min and then cooled at 0 °C using ice bath. Freshly distilled mesityl oxide (11.8 g, 120 mmol) in dry Et_2O (30 mL) is added over a period of 3-4 h. The reaction mixture is stirred at 0 °C for 1 h and then left stirring overnight at r.t. then re-cooled to 0 °C and ice-cold water is added over 2-3 h (the temperature should be kept below 10 °C). As soon as the evolution of gas has ceased and the temperature does not rise further, the mixture is poured into saturated NH_4Cl solution, the phases were separated and the organic phase is washed with 10 % aqueous K_2CO_3, water, brine and dried over

$MgSO_4$. Evaporation of solvent under reduced pressure followed by Büchi-distillation of the residue using water vacuum pump at about 90 torr (temperature should not exceed 80 °C) gives the pure alcohol (9.5 g, 83.3 mmol) as yellow oil.

Yield: 69 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

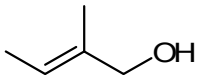
δ (ppm) = 1.30 (s, 6H, $(C\underline{H}_3)_2$)C), 1.64 (d, 3H, *J* = 1.47 Hz, $C\underline{H}_3C$=), 1.80 (d, 3H, *J* = 1.32 Hz, $C\underline{H}_3C$=), 5.28 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.6 (q, $\underline{C}H_3C$=), 27.1 (q, $\underline{C}H_3C$=), 31.2 (q, $(\underline{C}H_3)_2C$), 70.8 (s, <u>C</u>-OH), 132.1 (d, <u>C</u>H=C), 133.9 (s, <u>C</u>=CH).

(E)-2-Methylbut-2-en-1-ol[173] **(6o)**

(elid 258c)



According to **GP-5**, tiglic acid (1.50 g, 15 mmol) was reduced by $LiAlH_4$ (1.13 g, 30 mmol) to afford 0.93 g (10.8 mmol) of the allylic alcohol which was obtained as oil.

Yield: 72 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

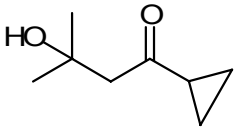
δ (ppm) = 1.56 (m, 3H, $C\underline{H}_3CH$=), 1.60 (m, 3H, $C\underline{H}_3C$=), 3.92 (s, 2H, $C\underline{H}_2$-OH), 5.42 (m., 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.0 (q, $\underline{C}H_3$), 13.2 (q, $\underline{C}H_3$), 68.7 (t, $\underline{C}H_2$-OH), 120.4 (d, <u>C</u>H=C), 135.3 (s, <u>C</u>=CH).

1-Cyclopropyl-3-hydroxy-3-methylbutan-1-one (28a)

(elid 498x)



The preparation and work-up were carried out according to **GP-3** using LDA (256.0 mmol) in THF, cyclopropyl methyl ketone (20 g, 238.1 mmol) and acetone (13.8 g, 238.1 mmol). The crude product (24.1 g, 169.7 mmol, 71 %) was fractionally distilled (b.p. 80 °C, 3.25 torr) to give the pure aldol (18.9 g, 133.1 mmol, 56 %) as faint yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.76 (m, 2H, C$\underline{H_2}$CH$_2$), 0.88 (m, 2H, C$\underline{H_2}$CH$_2$), 1.09 (s, 6H, (C$\underline{H_3}$)$_2$C), 1.79 (m, 1H, C$\underline{H}$), 2.59 (s, 2H, C$\underline{H_2}$CO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 10.9 (t, $\underline{C}H_2\underline{C}H_2$), 21.6 (d, $\underline{C}$H), 29.0 (q, 2 x $\underline{C}H_3$), 53.6 (t, $\underline{C}H_2CO$), 69.3 (s, $\underline{C}$-OH), 212.4 (s, $\underline{C}$=O).

IR: (Film)

ν (cm^{-1}) = 3200-3600, 3008, 2973, 2933, 1687, 1391, 1076.

MS: (EI, 70 eV)

m/z (%) = 142 (M^+, not observed), 127 (M^+-CH_3, 100), 124 (M^+-H_2O, 34), 69 ($C_4H_5O^+$, 17).

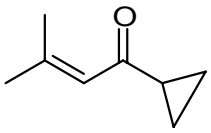
Elemental Analysis: ($C_8H_{14}O_2$, M = 142.20)

Calcd: C 67.57 H 9.92

Found: C 66.93 H 9.98

1-Cyclopropyl-3-methylbut-2-en-1-one[174] **(29a)**

(elid 494b)



The preparation and work-up were carried out according to **GP-4** using 1-cyclopropyl-3-hydroxy-3-methylbutan-1-one **(28a)** (35.0 g, 246.5 mmol) and *p*-toluenesulfonic acid (4.70 g, 24.7 mmol). The crude product was purified either by Büch-distillation (137.5 °C, at about 90 torr using water vacuum pump, Lit. 46-48 °C, 10 torr[174]) or by column chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.59) to afford the pure enone (25.0 g, 201.6 mmol) as colorless oil.

Yield: 82 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

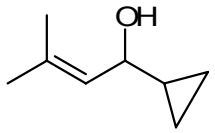
δ (ppm) = 0.74 (m, 2H, C<u>H</u>$_2$CH$_2$), 0.92 (m, 2H, C<u>H</u>$_2$CH$_2$), 1.80 (d, 3H, *J* = 0.75 Hz, C<u>H</u>$_3$C=), 1.82 (m, 1H, C<u>H</u>), 2.04 (s, 3H, C<u>H</u>$_3$C=), 6.13 (s, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 10.5 (t, 2 x <u>C</u>H$_2$), 20.5 (d, <u>C</u>H), 21.9 (q, <u>C</u>H$_3$C=), 27.4 (q, <u>C</u>H$_3$C=), 124.2 (d, <u>C</u>H=C), 153.9 (s, <u>C</u>=CH), 200.5 (s, <u>C</u>=O).

1-Cyclopropyl-3-methylbut-2-en-1-ol (6p)

(elid 379a)



The preparation and work-up were carried out according to **GP-5** using 1-cyclopropyl-3-methylbut-2-en-1-one **(29a)** (11.4 g, 91.9 mmol) and $LiAlH_4$ (3.65 g, 96.0 mmol). Büch-distillation (162.5 °C at about 90 torr using water vacuum pump) gives the pure allylic alcohol (7.70 g, 61.1 mmol) as colorless oil.

Yield: 67 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

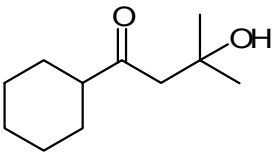
δ (ppm) = 0.22 (m, 2H, C<u>H</u>$_2$), 0.44 (m, 2H, C<u>H</u>$_2$), 0.93 (m, 1H, C<u>H</u>), 1.62 (d, 3H, *J* = 1.47 Hz, C<u>H</u>$_3$C=), 1.70 (d, 3H, *J* = 1.32 Hz, C<u>H</u>$_3$C=), 3.76 (dd, 1H, *J* = 8.22, 8.25 Hz, C<u>H</u>-OH), 5.22 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.6 (t, <u>C</u>H$_2$), 2.7 (t, <u>C</u>H$_2$), 17.8 (q, <u>C</u>H$_3$C=), 18.2 (d, <u>C</u>H), 25.7 (q, <u>C</u>H$_3$C=), 72.5 (d, <u>C</u>H-OH), 126.5 (d, <u>C</u>H=C), 135.0 (s, <u>C</u>=CH).

1-Cyclohexyl-3-hydroxy-3-methylbutan-1-one (28b)

(elid 482y)



The preparation and work-up were carried out according to **GP-3** using LDA (107.7 mmol), cyclohexylmethylketone (12.37 g, 98.2 mmol) and acetone (5.7 g, 98.2 mmol). The crude

product was fractionally distilled (b.p. 113-115 °C, 0.84 torr) to give the pure aldol (9.9 g, 53.8 mmol) as colorless oil.

Yield: 55 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

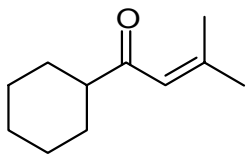
δ (ppm) = 1.15 (2 x s, 6H, $(C\underline{H}_3)_2C$), 1.20 (m, 4H, 2 x $C\underline{H}_2$), 1.59-1.85 (m, 6H, 3 x $C\underline{H}_2$), 2.22 (m, 1H, C<u>H</u>), 2.55 (s, 2H, $C\underline{H}_2CO$), 3.88 (br. s, 1H, OH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 25.4 (t, 2 x $\underline{C}H_2$), 25.6 (t, $\underline{C}H_2$), 27.9 (t, 2 x $\underline{C}H_2$), 29.2 (q, 2 x $\underline{C}H_3$), 50.7 (t, $\underline{C}H_2CO$), 51.9 (d, <u>C</u>H), 69.5 (s, <u>C</u>-OH), 216.4 (s, CO).

1-Cyclohexyl-3-methylbut-2-en-1-one (29b)

(elid 483n)



The preparation and work-up were carried out according to **GP-4** using 1-cyclohexyl-3-hydroxy-3-methylbutan-1-one **(28b)** (16.1 g, 87.5 mmol) and *p*-toluenesulfonic acid (1.7 g, 8.95 mmol). Distillation of the solvent gives the enone (11.82 g, 71.2 mmol) as yellow oil.

Yield: 81 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

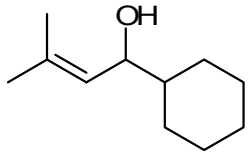
δ (ppm) = 1.10-1.30 (m, 6H, 3 x $C\underline{H}_2$), 1.60-1.80 (m, 4H, 2 x $C\underline{H}_2$), 1.83 (s, 3H, $C\underline{H}_3C$=), 2.07 (m, 3H, $C\underline{H}_3C$=), 2.24 (m, 1H, C<u>H</u>), 6.06 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.6 (q, $\underline{C}H_3$), 25.7 (t, 2 x $\underline{C}H_2$), 25.9 (t, $\underline{C}H_2$), 27.6 (q, $\underline{C}H_3$), 28.5 (t, 2 x $\underline{C}H_2$), 51.5 (d, <u>C</u>H), 122.9 (d, <u>C</u>H=C), 155.1 (s, <u>C</u>=CH), 204.0 (s, CO).

1-Cyclohexyl-3-methylbut-2-en-1-ol (6q)

(elid 483t)



The preparation and work-up were carried out according to **GP-5** using 1-cyclohexyl-3-methylbut-2-en-1-one **(29b)** (10.0 g, 60 mmol) and $LiAlH_4$ (2.27 g, 60 mmol). Distillation of the solvent gives the allylic alcohol (8.0 g, 47.6 mmol) as faint yellow oil.

Yield: 79 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

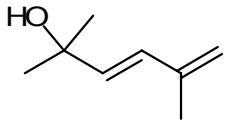
δ (ppm) = 0.80-1.89 (m, 11H, C<u>H</u> and 5 x C<u>H$_2$</u>), 1.62 (s, 3H, C<u>H$_3$</u>C=), 1.69 (s, 3H, C<u>H$_3$</u>C=), 4.0 (dd, 1H, *J* = 7.20, 8.97 Hz, C<u>H</u>-OH), 5.13 (d, 1H, *J* = 9.09 Hz, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.3 (q, <u>C</u>H$_3$C=), 25.8 (q, <u>C</u>H$_3$C=), 26.0 (t, <u>C</u>H$_2$), 26.1 (t, <u>C</u>H$_2$), 26.5 (t, <u>C</u>H$_2$), 28.5 (t, <u>C</u>H$_2$), 28.9 (t, <u>C</u>H$_2$), 44.2 (d, <u>C</u>H), 72.9 (d, <u>C</u>H-OH), 126.7 (d, <u>C</u>H=C), 135.2 (s, <u>C</u>=CH).

(E)-2,5-Dimethylhexa-3,5-dien-2-ol[175] **(6u)**

(elid 475f)



The preparation and work-up were carried out according to **GP-1** using Isopropenyl bromide (6.05 g, 50.0 mmol), magnesium turnings (1.20 g, 50.0 mmol) and 3-methyl-2-butenal **(25)** (3.36 g, 40.0 mmol). The crude product was purified either by fractional distillation or by column chromatography (SiO_2; EA/*n*-hex; 1:10, R_f = 0.08) to give the pure dienol (3.62 g, 28.7 mmol) as yellow oil.

Yield: 72%

^{1}H-NMR: (300 MHz, $CDCl_3$)

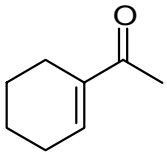
δ (ppm) = 1.31 (s, 6H, (C<u>H$_3$</u>)$_2$C), 1.80 (s, 3H, C<u>H$_3$</u>C=), 4.93 (s, 2H, C<u>H$_2$</u>=C), 5.75 (d, 1H, *J* = 16.02 Hz, C<u>H</u>=CH), 6.27 (d, 1H, *J* = 16.02 Hz, C<u>H</u>=CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.5 (q, <u>C</u>H$_3$C=), 29.8 (q, (<u>C</u>H$_3$)$_2$C), 70.7 (s, <u>C</u>-OH), 116.3 (t, CH$_2$=C), 129.2 (d, <u>C</u>H=CH), 137.4 (d, <u>C</u>H=CH), 141.4 (s, <u>C</u>=CH$_2$).

1-cyclohexenylethanone[176] **(31)**

(elid 474n)



A mixture of cyclohexene (26.16 g, 319 mmol) and stannic chloride (55.42 g, 212.7 mmol) was placed in half-liter, three-necked round-bottomed flask equipped with magnetic stirring bar, dropping funnel, reflux condenser having a $CaCl_2$ tube and a thermometer extending into the reaction mixture. The reaction mixture is cooled in ice bath and then acetic anhydride (21.7 g, 212.7 mmol) was added dropwise over a period of 30 min (during the addition, the temperature in the solution varied from 25-35 °C). After complete addition the mixture is stirred for 15 min in ice and then poured over cracked ice (100 g). The resulting mixture is extracted with ether (3 x 30 mL) and the combined ether extract was washed with aqueous $NaHCO_3$, water and brine then dried over Na_2SO_4. Evaporation of the solvent under reduced pressure followed by fractional distillation of the residue (b.p**.** 59-61 °C, 5 torr, Lit. 88-89 °C, 19.5 torr[177]) gives the pure enone (13.2 g, 106.5 mmol) as yellow oil.

Yield: 50 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

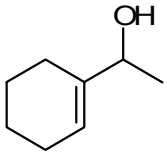
δ (ppm) = 1.50 (m, 4H, 2 x C$\underline{H}_2$), 2.05-2.25 (m, 4H, 2 x C$\underline{H}_2$), 2.16 (s, 3H, C$\underline{H}_3$), 6.79 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 21.3 (t, $\underline{C}H_2$), 21.7 (t, $\underline{C}H_2$), 22.7 (t, $\underline{C}H_2$), 24.9 (t, $\underline{C}H_2$), 25.9 (q, $\underline{C}H_3$), 139.4 (s, $\underline{C}$=CH), 140.7 (d, $\underline{C}$H=C), 199.0 (s, C=O).

1-Cyclohexenylethanol[177] (32)

(elid 474y)



The preparation and work-up were carried out according to **GP-5** using 1-cyclohexenylethanone **(31)** (7.55 g, 60.9 mmol) and $LiAlH_4$ (2.9 g, 76.3 mmol). Excess reducing reagent was hydrolyzed by cold 10% sulfuric acid. The crude product was fractionally distilled using Büchi-distillation apparatus connected to water vacuum pump at

about 165 °C, 90 torr (Lit. 87-88 °C, 14 torr[177]) to give the pure allylic alcohol (4.53 g, 36.0 mmol) as colorless oil.

Yield: 59 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

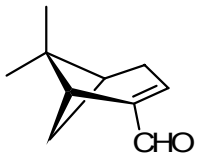
δ (ppm) = 1.18 (dd, 3H, *J* = 1.31, 6.45 Hz, C<u>H</u>$_3$CH), 1.52 (m, 4H, 2 x C<u>H</u>$_2$), 1.95 (m, 4H, 2 x C<u>H</u>$_2$), 4.08 (q, 1H, *J* = 6.45 Hz, C<u>H</u>-OH), 5.58 (m., 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 21.3 (q, <u>C</u>H$_3$), 22.5 (2 x t, 2 x <u>C</u>H$_2$), 23.5 (t, <u>C</u>H$_2$), 24.8 (t, <u>C</u>H$_2$), 71.9 (t, <u>C</u>H-OH), 121.2 (d, <u>C</u>H=C), 141.2 (s, <u>C</u>=CH).

(1R)-6,6-Dimethylbicyclo[3.1.1]hept-2-ene-2-carbaldehyde (myrtenal)[178] (34)

(elid 390c, 390e)



A solution of β-pinene (40 g, 294 mmol), acetic anhydride (29.1 mL, 303 mmol), pyridine (11.9 mL, 147 mmol), TPP (21 mg), and DMAP (716 mg, 6 mmol) in CH_2Cl_2 (270 mL) was irradiated at r.t. while a gentle stream of air was bubbled through the reaction mixture. The course of the reaction is monitored by TLC and after complete consumption of the starting material the solution was diluted with CH_2Cl_2 (250 mL) and extracted with sat. $NaHCO_3$ solution until it becomes basic (to remove the acetic acid by-product). The organic layer was then washed with 1N HCl solution until it turned mint green and the aqueous washes are acidic. Further extraction with saturated $CuSO_4$ (100 mL) and then with brine (2 x 100 mL) followed by drying over $MgSO_4$ and concentration under vacuum gives the crude product which was fractionally distilled (b.p. = 90-93 °C at 2 torr, Lit. 52-54 °C at 0.45 torr)[179] to afford the pure product (15 g, 100 mmol) as yellow oil.

Yield: 34 %

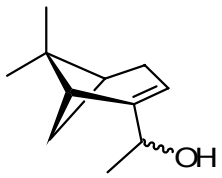
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.70 (s, 3H, C<u>H</u>$_3$), 1.01 (d, 1H, *J* = 9.27 Hz, CH_2), 1.29 (s, 3H, C<u>H</u>$_3$), 2.14 (m, 1H, CH), 2.41-2.54 (m, 3H, CH_2 and CH_2), 2.82 (dt, 1H, *J* = 1.20, 5.61 Hz, CH), 6.63 (m, 1H, C<u>H</u>=C), 9.36 (s, 1H, CHO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.8 (q, $\underline{C}H_3$), 25.5 (q, $\underline{C}H_3$), 30.9 (t, $\underline{C}H_2$), 32.8 (t, $\underline{C}H_2$), 37.4 (s, $\underline{C}q$), 37.9 (d, $\underline{C}H$), 40.5 (d, $\underline{C}H$), 147.6 (d, $\underline{C}H$=C), 151.3 (s, $\underline{C}$ =CH), 191.0 (d, $\underline{C}HO$).

1-((1R)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethanol [2-(1-hydroxyethyl)apopinene] (35) (elid 390d)



Under an inert atmosphere, a solution of myrtenal **(34)** (8 g, 53.3 mmol) in freshly distilled Et_2O (50 mL) was added slowly at 0 °C to a solution of methyllithium in Et_2O (160 mmol). After complete addition the reaction mixture is refluxed for 1 h. The reaction mixture is allowed to cool to r.t. and then poured into a cold solution of saturated NH_4Cl. The phases were separated and the aqueous phase is extracted with ether (3 x 50 mL). The organic phases were combined, washed with brine and dried over $MgSO_4$. The solvent is removed under reduced pressure and the residue is fractionally distilled (b.p. = 82-83 °C at 0.72 torr, Lit. 60-62 °C at 0.40 torr)[179] to give the product (7.61 g, 45.8 mmol) as colorless oil in a 2:3 diastereomeric mixture a and b.

Yield: 86 %

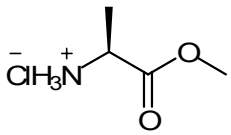
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.70 (s, 3H, C$\underline{H}_3$ of a), 0.73 (s, 3H, C$\underline{H}_3$ of b), 1.06 (m, 3H, 2 x C$\underline{H}_3$CH of a and b), 1.19 (s, 3H, C$\underline{H}_3$ of a and b), 1.98-2.34 (m, 6H, 2 x C$\underline{H}$ and 2 x C$\underline{H}_2$ of a and b), 4.05 (m, 1H, C$\underline{H}$-OH of a and b), 5.30 (m, 1H, C$\underline{H}$=C of a and b).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.7/20.8 (q, $\underline{C}H_3$ of a and b), 21.0/21.1 (q, $\underline{C}H_3$ of a and b), 26.0 (q, 2 x $\underline{C}H_3$ of a and b), 30.8 (2 x t, 2 x $\underline{C}H_2$ of b and a), 31.5 (2 x t, 2 x $\underline{C}H_2$ of a and b), 37.4/37.5 (s, $\underline{C}q$ of a and b), 40.8 (2 x d, $\underline{C}H$ of a and b), 41.4 (d, $\underline{C}H$ of a and b), 42.2 (d, $\underline{C}H$ of a and b), 69.7/70.2 (d, $\underline{C}H$-OH of b and a), 115.3/116.3 (d, $\underline{C}H$=C of b and a), 151.3/151.4 (s, $\underline{C}$ =CH of b and a).

L-Alanine methyl ester hydrochloride[180] **(18a)**



The preparation and work-up were carried out according to **GP-11** using L-alanine (2.67 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give the product (3.6 g, 25.8 mmol) as white solid.

Yield: 86 %

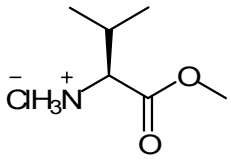
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.72 (d, 3H, *J* = 7.20 Hz, C$\underline{H}_3$), 3.79 (s, 3H, OC$\underline{H}_3$), 4.26 (m, 1H, C$\underline{H}$-N), 8.67 (br s, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.0 (q, $\underline{C}H_3$), 49.3 (d, $\underline{C}$H-N), 53.2 (q, O$\underline{C}H_3$), 170.5 (s, $\underline{C}OOCH_3$).

L-Valine methyl ester hydrochloride[181] **(18b)**



The preparation and work-up were carried out according to **GP-11** using L-valine (3.51 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give the product (4.60 g, 27.5 mmol) as white solid.

Yield: 92 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

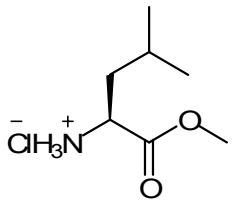
δ (ppm) = 0.85 (d, 6H, *J* = 7.50 Hz, ($C\underline{H}_3)_2$CH), 2.0 (m, 1H, C$\underline{H}$($CH_3)_2$), 3.70 (s, 3H, OC$\underline{H}_3$), 4.51 (m, 1H, C$\underline{H}$-N), 8.50 (br s, 3H, NH_3).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.7 (q, $\underline{C}H_3$), 18.7 (q, $\underline{C}H_3$), 30.0 (d, $\underline{C}$H), 51.9 (q, O$\underline{C}H_3$), 56.0 (d, $\underline{C}$H-N), 173.0 (s, $\underline{C}OOCH_3$).

L-Leucine methyl ester hydrochloride[182] **(18c)**

(elid 287a)



The preparation and work-up were carried out according to **GP-11** using L-leucine (3.93 g, 30 mmol) and thionyl chloride (4.2 mL, 60 mmol) to give the product (4.72 g, 26.0 mmol) as white solid.

Yield: 87 %

^{1}H-NMR: (300 MHz, D_2O/acetone-d_6)

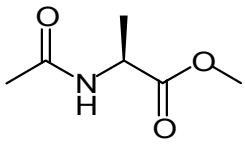
δ (ppm) = 0.88 (d, 3H, *J* = 6.33 Hz, (C$\underline{H}_3$)$_2$CH), 0.89 (d, 3H, *J* = 6.30 Hz, (C$\underline{H}_3$)$_2$CH), 1.75 (m, 3H, C$\underline{H}$C$\underline{H}_2$), 3.76 (s, 3H, OC$\underline{H}_3$), 4.10 (m, 1H, C$\underline{H}$-N).

^{13}C-NMR: (75.5 MHz, D_2O/acetone-d_6)

δ (ppm) = 22.0 (q, $\underline{C}H_3$), 22.0 (q, $\underline{C}H_3$), 24.7 (d, $\underline{C}$H), 39.6 (t, $\underline{C}H_2$), 51.8 (q, O$\underline{C}H_3$), 53.5 (d, $\underline{C}$H-N), 170.8 (s, $\underline{C}$OOCH$_3$).

(S)-Methyl 2-acetamidopropanoate[183] **(19a)**

(elid 276b)



The preparation and work-up were carried out according to **GP-12** using L- alanine methyl ester hydrochloride **18a** (11.80 g, 84.6 mmol), Et_3N (19.0 g, 188.1 mmol) and acetyl chloride (6.64 g, 84.6 mmol) to give the amide (9.0 g, 62.1 mmol) in good purity.

Yield: 73 %

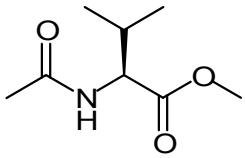
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.34 (d, 3H, *J* = 7.20 Hz, C$\underline{H}_3$), 1.98 (s, 3H, C$\underline{H}_3$CO), 3.70 (s, 3H, OC$\underline{H}_3$), 4.51 (m, 1H, C$\underline{H}$-NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.0 (q, $\underline{C}H_3$), 22.7 (q, $\underline{C}H_3CO$), 47.8 (d, $\underline{C}H$-NH), 52.2 (q, $O\underline{C}H_3$), 169.8 (s, $\underline{C}ONH$), 173.5 (s, $\underline{C}OOCH_3$).

(S)-Methyl 2-acetamido-3-methylbutanoate[184] **(19b)**



The preparation and work-up were carried out according to **GP-12** using L-valine methyl ester hydrochloride **18b** (12.54 g, 74.9 mmol), Et_3N (18.0 g, 178.2 mmol) and acetyl chloride (6.25 g, 79.6 mmol) to give the amide (12.0 g, 69.4 mmol) in good purity.

Yield: 93 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

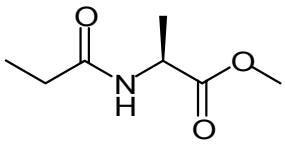
δ (ppm) = 0.83 (d, 3H, *J* = 9.40 Hz, $(C\underline{H}_3)_2CH$), 0.86 (d, 3H, *J* = 9.40 Hz, $(C\underline{H}_3)_2CH$), 1.97 (s, 3H, $C\underline{H}_3CO$), 2.06 (m, 1H, $C\underline{H}(CH_3)_2$), 3.67 (s, 3H, $OC\underline{H}_3$), 4.49 (dd, 1H, *J* = 2.5, 5.1 Hz, $C\underline{H}$-NH), 6.13 (d, 1H, *J* = 5.1 Hz, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.7 (q, $(\underline{C}H_3)_2CH$), 18.7 (q, $(\underline{C}H_3)_2CH$), 23.0 (q, $\underline{C}H_3CO$), 31.1 (d, $\underline{C}H(CH_3)_2$), 51.9 (q, $O\underline{C}H_3$), 56.9 (d, $\underline{C}H$-NH), 169.9 (s, $\underline{C}ONH$), 172.6 (s, $\underline{C}OOCH_3$).

(S)-Methyl 2-(propionamido)propanoate[185] **(19c)**

(elid 279a)



The preparation and work-up were carried out according to **GP-12** using L-alanine methyl ester hydrochloride **18a** (3.30 g, 23.7 mmol), Et_3N (6.7 mL, 53 mmol) and propionyl chloride (2.10 mL, 24 mmol) to give the amide (3.10 g, 19.5 mmol) in good purity.

Yield: 82 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

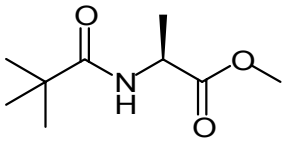
δ (ppm) = 1.03 (t, 3H, *J* = 7.64 Hz, C<u>H</u>$_3$CH$_2$), 1.27 (d, 3H, *J* = 7.20 Hz, C<u>H</u>$_3$CH), 2.13 (q, 2H, *J* = 7.64 Hz, C<u>H</u>$_2$CH$_3$), 3.62 (s, 3H, OC<u>H</u>$_3$), 4.46 (m, 1H, C<u>H</u>-NH), 6.37 (br. s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.4 (q, <u>C</u>H$_3$CH$_2$), 18.0 (q, <u>C</u>H$_3$CH), 29.1 (t, <u>C</u>H$_2$CH$_3$), 47.6 (d, <u>C</u>H-NH), 52.1, (q, O<u>C</u>H$_3$) 173.3 (s, <u>C</u>ONH), 173.5 (s, <u>C</u>OOCH$_3$)

(S)-Methyl 2-(pivalamido)propanoate (19d)

(elid 280a)



The preparation and work-up were carried out according to **GP-12** using L-alanine methyl ester hydrochloride **18a** (3.30 g, 23.7 mmol), Et_3N (6.7 mL, 53 mmol) and pivaloyl chloride (3.0 mL, 24.0 mmol) to give the amide (4.0 g, 21.4 mmol) in good purity

Yield: 90 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

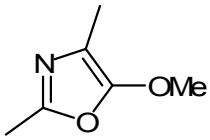
δ (ppm) = 1.13 (s, 9H, (C<u>H</u>$_3$)$_3$C), 1.31 (d, 3H, *J* = 7.21 Hz, C<u>H</u>$_3$CH), 3.67 (s, 3H, OC<u>H</u>$_3$), 4.48 (m, 1H, C<u>H</u>-NH), 6.16 (br. s, 1H, NH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = = 18.2 (q, <u>C</u>H$_3$CH), 27.3 (q, (<u>C</u>H$_3$)$_3$C), 38.4 (s, <u>C</u>(CH$_3$)$_3$), 47.8 (d, <u>C</u>H-NH), 52.2 (q, O<u>C</u>H$_3$), 173.7 (s, <u>C</u>ONH), 177.9 (s, <u>C</u>OOCH$_3$).

2,4-Dimethyl-5-methoxyoxazole[186] (20a)

(elid 497g)



The preparation and work-up were carried out according to **GP-13** using Methyl 2-acetamidopropanoate **(19a)** (9.0 g, 62.1 mmol) and PCl_5 (13.5 g, 62.1 mmol), the crude product is fractionally distilled using Büchi-distillation apparatus (112.5 °C at about 90 torr

using water-vacuum pump, Lit. 61-63 °C/10 torr[186]) to give the oxazole (4.0 g, 31.7 mmol) as yellow oil.

Yield: 51 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

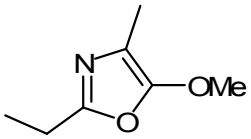
δ (ppm) = 1.90 (s, 3H, C$\underline{H}_3$), 2.21 (s, 3H, C$\underline{H}_3$), 3.77 (s, 3H, OC$\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.7 (q, $\underline{C}H_3C$=C), 14.0 (q, $\underline{C}H_3C$=N), 61.0 (q, O$\underline{C}H_3$), 111.1 (s, C-4), 151.7 (s, C-5), 154.5 (s, C-2).

2-Ethyl-5-methoxy-4-methyloxazole[185] (20b)

(elid 497u, 497v)



The preparation and work-up were carried out according to **GP-13** using Methyl 2-(propionamido)propanoate **(19c)** (13.28 g, 83.5 mmol) and PCl_5 (20.0 g, 92.0 mmol), the crude product is fractionally distilled using Büchi-distillation apparatus (137 °C at about 90 torr using water-vacuum pump, Lit. 83 °C/31 torr[185]) to give the oxazole (6.83 g, 48.4 mmol) as faint yellow oil.

Yield: 58 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

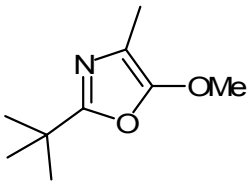
δ (ppm) = 1.15 (t, 3H, *J* = 7.56 Hz, C$\underline{H}_3$CH$_2$), 1.88 (s, 3H, C$\underline{H}_3$), 2.50 (q, 2H, J = 7.56 Hz, C$\underline{H}_2$CH$_3$), 3.74 (s, 3H, OC$\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.7 (q, $\underline{C}H_3$), 10.7 (q, $\underline{C}H_3CH_2$), 21.7 (t, $\underline{C}H_2$), 60.9 (q, O$\underline{C}H_3$), 110.6 (s, C-4), 154.3 (s, C-5), 156.0 (s, C-2).

2-*tert*-Butyl-5-methoxy-4-methyloxazole (20c)

(elid 497w, 497x)



The preparation and work-up were carried out according to **GP-13** using Methyl 2-(pivalamido)propanoate **(19d)** (15.0 g, 80.2 mmol) and PCl_5 (20.0 g, 92.0 mmol), the crude product is fractionally distilled using Büchi-distillation apparatus (187 °C at about 90 torr using water-vacuum pump) to give the oxazole (9.52 g, 56.3 mmol) as yellow oil.

Yield: 70 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

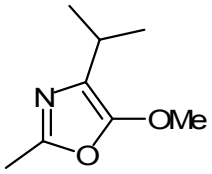
δ (ppm) = 1.24 (s, 9H, $(C\underline{H}_3)_3C$), 1.94 (s, 3H, $C\underline{H}_3$), 3.80 (s, 3H, $OC\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.8 (q, $\underline{C}H_3$), 28.2 (q, $\underline{C}H_3)_3C$), 33.5 (s, $\underline{C}(CH_3)_3$), 61.0 (q, $O\underline{C}H_3$), 110.6 (s, C-4), 154.2 (s, C-5), 161.4 (s, C-2).

4-Isopropyl-2-methyl-5-methoxyoxazole[187] **(20d)**

(elid 489p)



The preparation and work-up were carried out according to **GP-13** using Methyl 2-acetamido-3-methylbutanoate **(19b)** (15.40 g, 89.0 mmol) and PCl_5 (19.30 g, 89.0 mmol), the crude product is fractionally distilled using Büchi-distillation apparatus (150 °C at about 90 torr using water-vacuum pump, Lit. 72 °C/10 torr[187]) to give the oxazole (8.69 g, 56.1 mmol) as yellow oil.

Yield: 63 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

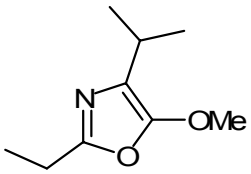
δ (ppm) = 1.01 (d, 6H, J = 6.93 Hz, $(C\underline{H}_3)_2CH$), 2.13 (s, 3H, $C\underline{H}_3$), 2.57 (septet, 1H, J = 6.93 Hz, $C\underline{H}(CH_3)_2$), 3.67 (s, 3H, $OC\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3$), 21.4 (2 x q, $(\underline{C}H_3)_2CH$), 24.6 (d, $\underline{C}H$), 61.1 (q, $O\underline{C}H_3$), 121.0 (s, C-4), 151.7 (s, C-5), 153.1 (s, C-2).

2-Ethyl-4-isopropyl-5-ethoxyoxazole (20e)

(elid 489n)



The preparation and work-up were carried out according to **GP-13** using Methyl 3-methyl-2-(propionamido)butanoate (13.61 g, 72.8 mmol) and PCl_5 (15.3 g, 70.3 mmol), the crude product is fractionally distilled using Büchi-distillation apparatus (125 °C at about 90 torr using water-vacuum pump) to give the oxazole (7.38 g, 43.7 mmol) as yellow oil.

Yield: 60 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

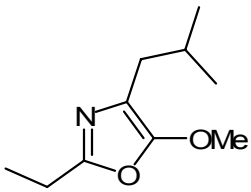
δ (ppm) = 1.07 (d, 6H, *J* = 6.90 Hz, $(C\underline{H}_3)_2CH$), 1.13 (t, 3H, *J* = 7.50 Hz, $C\underline{H}_3CH_2$), 2.50 (q, 2H, *J* = 6.50 Hz, $C\underline{H}_2CH_3$), 2.64 (septet, 1H, *J* = 6.90 Hz, $C\underline{H}(CH_3)_2$), 3.72 (s, 3H, $OC\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 11.0 (q, $\underline{C}H_3CH_2$), 21.4 (2 x q, $(\underline{C}H_3)_2CH$), 21.8 (t, $\underline{C}H_2CH_3$), 24.9 (d, $\underline{C}H(CH_3)_2$), 61.1 (q, $O\underline{C}H_3$), 120.9 (s, C-4), 153.0 (s, C-5), 156.0 (s, C-2).

2-Ethyl-4-isobutyl-5-methoxyoxazole (20f)

(elid 489a)



The preparation and work-up were carried out according to **GP-13** using Methyl 4-methyl-2-(propionamido)pentanoate (16.63 g, 82.7 mmol) and PCl_5 (18.0g, 82.7 mmol), the crude product is fractionally distilled using Büchi-distillation apparatus (237.5 °C at about 90 torr using water-vacuum pump) to give the oxazole (9.85 g, 53.8 mmol) as yellow oil.

Yield: 65 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.74 (d, 6H, *J* = 6.75 Hz, $(C\underline{H}_3)_2CH$), 1.10 (t, 3H, *J* = 7.65 Hz, $C\underline{H}_3CH_2$), 1.75 (septet, 1H, *J* = 6.75 Hz, $C\underline{H}(CH_3)_2$), 2.04 (d, 2H, $C\underline{H}_2CH$), 2.47 (q, 2H, *J* = 7.65 Hz, $C\underline{H}_2CH_3$), 3.69 (s, 3H, $OC\underline{H}_3$).

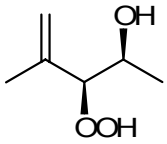
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 10.8 (q, $\underline{C}H_3CH_2$), 21.7 (t, $\underline{C}H_2CH_3$), 22.0 (2 x q, $(\underline{C}H_3)_2CH$), 27.5 (d, $\underline{C}HCH_2$), 33.4 (t, $\underline{C}H_2CH$), 60.7 (q, $O\underline{C}H_3$), 114.5 (s, C-4), 154.7 (s, 5-C), 155.9 (s, C-2).

4.5 Singlet Oxygen Photooxygenation Reactions of Different Substrates

(2RS,3RS)-3-Hydroperoxy-4-methylpent-4-en-2-ol[37a] **(*syn*-7a)**

(elid 278c)



Photooxygenation of 4-methylpent-3-en-2-ol **(6a)** (1.0 g, 10 mmol) for 48 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 75:25) of β-hydroxy allylic hydroperoxides (1.10 g, 8.33 mmol, 83 %) as colorless oil.

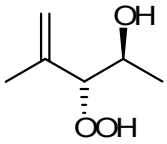
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.07 (d, 3H, *J* = 6.48 Hz, C$\underline{H}_3$CH), 1.67 (s, 3H, C$\underline{H}_3$C=), 3.80 (dq, 1H, *J* = 6.45, 8.52 Hz, C$\underline{H}$-OH), 4.08 (d, 1H, *J* = 8.67 Hz, C$\underline{H}$-OOH), 5.0 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.7 (q, $\underline{C}H_3$CH), 18.7 (q, $\underline{C}H_3$C=), 67.1 (d, $\underline{C}$H-OH), 94.8 (d, $\underline{C}$H-OOH), 116.5 (t, $\underline{C}H_2$=C), 141.4 (s, $\underline{C}$=CH_2).

(2RS,3SR)-3-Hydroperoxy-4-methylpent-4-en-2-ol (*anti*-7a)



^{1}H-NMR: (300 MHz, $CDCl_3$)

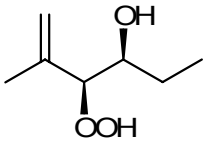
δ (ppm) = 1.14 (d, 3H, *J* = 6.45 Hz, C$\underline{H}_3$CH), 1.74 (s, 3H, C$\underline{H}_3$C=), 3.94 (dq, 1H, *J* = 4.56, 6.48 Hz, C$\underline{H}$-OH), 4.25 (d, 1H, *J* = 4.56 Hz, C$\underline{H}$-OOH), 5.03 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.0 (q, $\underline{C}H_3$CH), 19.2 (q, $\underline{C}H_3$C=), 67.0 (d, $\underline{C}$H-OH), 92.1 (d, $\underline{C}$H-OOH), 115.1 (t, $\underline{C}H_2$=C), 141.1 (s, $\underline{C}$=CH_2).

(3RS,4RS)-4-Hydroperoxy-5-methylhex-5-en-3-ol (*syn*-7b)

(elid 322b)



Photooxygenation of 5-methylhex-4-en-3-ol **(6b)** (1.0 g, 8.77 mmol) for 48 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 77:23) of β-hydroxy allylic hydroperoxides (0.92 g, 6.30 mmol, 72 %) as colorless oil.

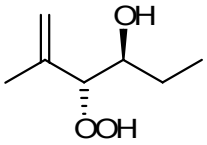
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.92 (t, 3H, *J* = 7.50 Hz, C$\underline{H}_3$CH$_2$), 1.23-1.58 (m, 2H, C$\underline{H}_2$CH$_3$), 1.68 (m, 3H, C$\underline{H}_3$C=), 3.55 (ddd, 1H, *J* = 5.95, 5.95, 8.53 Hz, C$\underline{H}$-OH), 4.15 (d, 1H, *J* = 8.53 Hz, C$\underline{H}$-OOH), 5.01 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.6 (q, $\underline{C}H_3CH_2$), 17.8 (q, $\underline{C}H_3C$=), 25.5 (t, $\underline{C}H_2CH_3$), 71.8 (d, $\underline{C}$H-OH), 93.4 (d, $\underline{C}$H-OOH), 116.5 (t, $\underline{C}H_2$=C), 141.4 (s, $\underline{C}$=CH$_2$).

(3RS,4SR)-4-Hydroperoxy-5-methylhex-5-en-3-ol (*anti*-7b)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

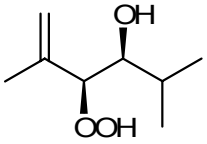
δ (ppm) = 0.93 (t, 3H, *J* = 7.35 Hz, C$\underline{H}_3$CH$_2$), 1.76 (s, 3H, C$\underline{H}_3$C=), 3.69 (m, 1H, C$\underline{H}$-OH), 4.30 (d, 1H, *J* = 4.70 Hz, C$\underline{H}$-OOH), 5.04 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 10.3 (q, $\underline{C}H_3CH_2$), 19.3 (q, $\underline{C}H_3C$=), 25.0 (t, $\underline{C}H_2CH_3$), 72.2 (d, $\underline{C}$H-OH), 91.4 (d, $\underline{C}$H-OOH), 115.3 (t, $\underline{C}H_2$=C), 141.2 (s, $\underline{C}$=CH$_2$).

(3RS,4RS)-4-Hydroperoxy-2,5-dimethylhex-5-en-3-ol (*syn*-7c)

(elid 326b)



Photooxygenation of 2,5-dimethylhex-4-en-3-ol **(6c)** (1.0 g, 7.81 mmol) for 48 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 81:19) of β-hydroxy allylic hydroperoxides (0.90 g, 5.63 mmol, 72 %) as colorless oil.

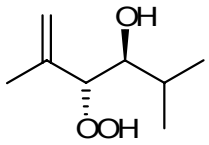
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.85 (d, 3H, *J* = 6.75 Hz, C$\underline{H}_3$CH), 0.95 (d, 3H, *J* = 7.05 Hz, C$\underline{H}_3$CH), 1.65 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 1.70 (m, 3H, C$\underline{H}_3$C=), 3.49 (dd, 1H, *J* = 2.79, 8.67 Hz, C$\underline{H}$-OH), 4.28 (d, 1H, *J* = 8.67 Hz, C$\underline{H}$-OOH), 5.07 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.7 (q, $\underline{C}H_3$CH), 17.7 (q, $\underline{C}H_3$CH), 20.3 (q, $\underline{C}H_3$C=), 29.0 (d, $\underline{C}$H(CH$_3$)$_2$), 74.5 (d, $\underline{C}$H-OH), 92.0 (d, $\underline{C}$H-OOH), 116.5 (t, $\underline{C}H_2$=C), 141.3 (s, $\underline{C}$=CH$_2$).

(3RS,4SR)-4-Hydroperoxy-2,5-dimethylhex-5-en-3-ol (*anti*-7c)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

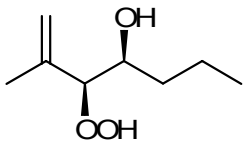
δ (ppm) = 0.85 (d, 3H, C$\underline{H}_3$CH), 0.92 (d, 3H, C$\underline{H}_3$CH), 1.78 (m, 3H, C$\underline{H}_3$C=), 3.51 (dd, 1H, C$\underline{H}$-OH), 4.34 (d, 1H, *J* = 8.67 Hz, C$\underline{H}$-OOH), 5.10 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.7 (q, $\underline{C}H_3$CH), 18.7 (q, $\underline{C}H_3$CH), 19.7 (q, $\underline{C}H_3$C=), 29.5 (d, $\underline{C}$H(CH$_3$)$_2$), 74.2 (d, $\underline{C}$H-OH), 89.9 (d, $\underline{C}$H-OOH), 116.4 (t, $\underline{C}H_2$=C), 141.8 (s, $\underline{C}$=CH$_2$).

(3RS,4RS)-3-Hydroperoxy-2-methylhept-1-en-4-ol (*syn*-7d)

(elid 451q)



Photooxygenation of 2-methylhept-2-en-4-ol **(6d)** (1.0 g, 7.81 mmol) for 48 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 79:21) of β-hydroxy allylic hydroperoxides (0.98 g, 6.13 mmol, 78 %) as colorless oil.

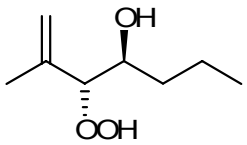
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.87 (t, 3H, *J* = 7.05 Hz, $C\underline{H}_3CH_2$), 1.20-1.58 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 1.68 (m, 3H, $C\underline{H}_3C$=), 3.63 (m, 1H, C<u>H</u>-OH), 4.13 (d, 1H, *J* = 8.52 Hz, C<u>H</u>-OOH), 5.01 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.8 (q, $\underline{C}H_3CH_2$), 17.8 (t, $\underline{C}H_2CH_3$), 18.3 (q, $\underline{C}H_3C$=), 34.6 (t, $\underline{C}H_2CH_2$) 70.3 (d, <u>C</u>H-OH), 93.8 (d, <u>C</u>H-OOH), 116.6 (t, $\underline{C}H_2$=C), 141.4 (s, <u>C</u>=CH_2).

(3RS,4SR)-3-Hydroperoxy-2-methylhept-1-en-4-ol (*anti*-7d)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

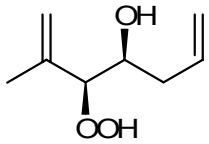
δ (ppm) = 0.87 (t, 3H, *J* = 7.05 Hz, $C\underline{H}_3CH_2$), 1.76 (m, 3H, $C\underline{H}_3C$=), 3.78 (m, 1H, C<u>H</u>-OH), 4.29 (d, 1H, *J* = 4.41 Hz, C<u>H</u>-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 19.0 (t, $\underline{C}H_2CH_3$), 19.4 (q, $\underline{C}H_3C$=), 34.0 (t, $\underline{C}H_2CH_2$) 70.5 (d, <u>C</u>H-OH), 91.6 (d, <u>C</u>H-OOH), 115.2 (t, $\underline{C}H_2$=C), 141.2 (s, <u>C</u>=CH_2).

(3RS,4RS)-3-Hydroperoxy-2-methylhepta-1,6-dien-4-ol (*syn*-7e)

(elid 465n)



Photooxygenation of 6-methylhepta-1,5-dien-4-ol **(6e)** (1.16 g, 9.21 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 75:25) of β-hydroxy allylic hydroperoxides (1.0 g, 6.33 mmol, 69 %) as faint yellow oil.

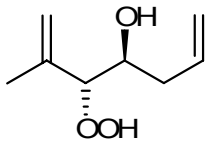
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.70 (m, 3H, $C\underline{H}_3C$=), 2.02-2.37 (m, 2H, $C\underline{H}_2$), 3.71 (ddd, 1H, *J* = 3.66, 8.31, 8.31 Hz, C<u>H</u>-OH), 4.17 (d, 1H, *J* = 8.40 Hz, C<u>H</u>-OOH), 5.05 (m, 4H, $C\underline{H}_2$=C and $C\underline{H}_2$=CH), 5.79 (m, 1H, C<u>H</u>=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, $\underline{C}H_3C$=), 37.1 (t, $\underline{C}H_2$), 70.0 (d, <u>C</u>H-OH), 92.8 (d, <u>C</u>H-OOH), 116.8 (t, $\underline{C}H_2$=CH), 118.1 (t, $\underline{C}H_2$=C), 133.8 (d, <u>C</u>H=CH_2), 141.1 (s, <u>C</u>=CH_2).

(3RS,4SR)-3-Hydroperoxy-2-methylhepta-1,6-dien-4-ol (*anti*-7e)



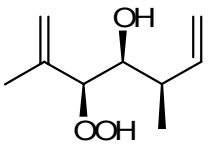
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

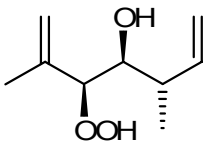
δ (ppm) = 1.76 (m, 3H, $C\underline{H}_3C$=), 3.82 (m, 1H, C<u>H</u>-OH), 4.31 (d, 1H, *J* = 4.86 Hz, C<u>H</u>-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.1 (q, $\underline{C}H_3C$=), 36.6 (t, $\underline{C}H_2$), 69.9 (d, <u>C</u>H-OH), 91.0 (d, <u>C</u>H-OOH), 115.6 (t, $\underline{C}H_2$=CH), 117.9 (t, $\underline{C}H_2$=C), 134.5 (d, <u>C</u>H=CH_2), 141.0 (s, <u>C</u>=CH_2).

(3RS,4RS,5SR)-3-Hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol (*syn,syn*-7f) and (3RS,4RS,5RS)-3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol (*syn,anti*-7f) (elid 498s)





Photooxygenation of 3,6-dimethylhepta-1,5-dien-4-ol **(6f)** (1.20 g, 8.57 mmol) for 60 h according to **GP-9a** afforded an oil composed of the inseparable diastereomeric mixture (0.92 g, 5.35 mmol, 63 %) composed of *syn,syn*-**7f**, *syn,anti*-**7f** (d.r. 1:1) of β-hydroxy allylic hydroperoxides as major product and a diastereomeric mixture of *anti*,*syn*-**7f**, *anti*,*anti*-**7f** (d.r. 1:1) as minor product.

^{1}H-NMR: (300 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 0.90 (d, 3H, *J* = 6.84 Hz, C$\underline{H_3}$CH), 1.63 (s, 3H, C$\underline{H_3}$C=), 2.17 (m, 1H, C$\underline{H}$CH$_3$), 3.50 (m, 1H, C$\underline{H}$-OH), 4.12 (d, 1H, *J* = 8.76 Hz, C$\underline{H}$-OOH), 4.94 (m, 4H, C$\underline{H_2}$=C and C$\underline{H_2}$=CH), 5.74 (m, 1H, C$\underline{H}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 12.1 (q, $\underline{C}H_3CH$), 17.8 (q, $\underline{C}H_3C$=), 38.7 (d, $\underline{C}HCH_3$), 73.1 (d, $\underline{C}$H-OH), 90.8 (d, $\underline{C}$H-OOH), 114.3 (t, $\underline{C}H_2$=CH), 116.2 (t, $\underline{C}H_2$=C), 141.1 (s, $\underline{C}$=CH$_2$), 141.2 (d, $\underline{C}$H=CH$_2$).

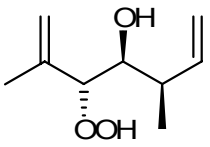
^{1}H-NMR: (300 MHz, $CDCl_3$, 2nd diastereomer, additional significant signals)

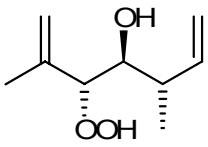
δ (ppm) = 0.99 (d, 3H, *J* = 5.40 Hz, C$\underline{H_3}$CH), 3.52 (m, 1H, C$\underline{H}$-OH), 4.22 (d, 1H, *J* = 8.04 Hz, C$\underline{H}$-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 2nd diastereomer, additional significant signals)

δ (ppm) = 17.6 (q, $\underline{C}H_3C$=), 39.0 (d, $\underline{C}HCH_3$), 73.4 (d, $\underline{C}$H-OH), 91.3 (d, $\underline{C}$H-OOH), 116.2 (t, $\underline{C}H_2$=CH), 116.8 (t, $\underline{C}H_2$=C), 137.8 (d, $\underline{C}$H=CH$_2$), 140.6 (s, $\underline{C}$=CH$_2$).

(3RS,4SR,5RS)-3-Hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol (*anti*,*syn*-7f) and (3RS,4SR,5SR)-3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol (*anti*,*anti*-7f)





Only the signal of CH_3C= in ^{1}H-NMR (δ = 1.69 ppm) can be seen for both minor diastereomers.

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer, additional significant signals)

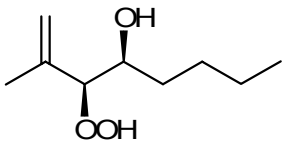
δ (ppm) = 72.5 (d, CH-OH), 89.2 (d, CH-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 2nd diastereomer, additional significant signals)

δ (ppm) = 72.5 (d, CH-OH), 89.5 (d, CH-OOH).

(3RS,4RS)-3-Hydroperoxy-2-methyloct-1-en-4-ol (*syn*-7g)

(elid 451j)



Photooxygenation of 2-methyloct-2-en-4-ol **(6g)** (1.19 g, 8.38 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 79:21) of β-hydroxy allylic hydroperoxides (1.14 g, 6.55 mmol, 78 %) as faint yellow oil.

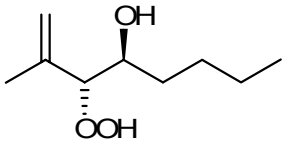
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.85 (t, 3H, *J* = 7.05 Hz, C$\underline{H}_3$CH$_2$), 1.21-1.57 (m, 6H, C$\underline{H}_2$C$\underline{H}_2$C$\underline{H}_2$), 1.70 (s, 3H, C$\underline{H}_3$C=), 3.64 (m, 1H, C$\underline{H}$-OH), 4.15 (d, 1H, *J* = 8.37 Hz, C$\underline{H}$-OOH), 5.03 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 17.9 (q, $\underline{C}H_3C$=), 22.5 (t, $\underline{C}H_2CH_3$), 27.3 (t, $\underline{C}H_2CH_2$), 32.2 (t, $\underline{C}H_2CH_2$) 70.6 (d, $\underline{C}$H-OH), 93.7 (d, $\underline{C}$H-OOH), 116.6 (t, $\underline{C}H_2$=C), 141.3 (s, $\underline{C}$=CH$_2$).

(3RS,4SR)-3-Hydroperoxy-2-methyloct-1-en-4-ol (*anti*-7g)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

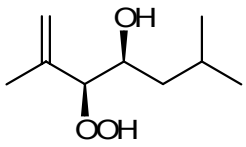
δ (ppm) = 1.77 (s, 3H, C$\underline{H}_3$C=), 3.75 (m, 1H, C$\underline{H}$-OH), 4.30 (d, 1H, *J* = 4.68 Hz, C$\underline{H}$-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 19.3 (q, $\underline{C}H_3C$=), 22.5 (t, $\underline{C}H_2CH_3$), 28.0 (t, $\underline{C}H_2CH_2$), 32.2 (t, $\underline{C}H_2CH_2$) 70.7 (d, $\underline{C}$H-OH), 91.7 (d, $\underline{C}$H-OOH), 116.6 (t, $\underline{C}H_2$=C), 141.2 (s, $\underline{C}$=CH$_2$).

(3RS,4RS)-3-Hydroperoxy-2,6-dimethylhept-1-en-4-ol (*syn*-7h)

(elid 365a)



Photooxygenation of 2,6-dimethylhept-2-en-4-ol **(6h)** (1.25 g, 8.80 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 80:20) of β-hydroxy allylic hydroperoxides (1.18 g, 6.78 mmol, 77 %) as colorless oil.

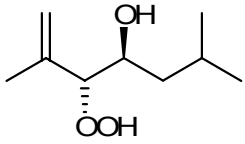
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.83 (d, 3H, *J* = 6.48 Hz, C$\underline{H_3}$CH), 0.87 (d, 3H, *J* = 6.75 Hz, C$\underline{H_3}$CH), 1.03 (m, 1H, C$\underline{H_2}$CH), 1.32 (m, 1H, C$\underline{H_2}$CH), 1.68 (s, 3H, C$\underline{H_3}$C=), 1.81 (m, 1H, C$\underline{H}CH_2$), 3.68 (m, 1H, C$\underline{H}$-OH), 4.09 (d, 1H, *J* = 8.37 Hz, C$\underline{H}$-OOH), 5.0 (m, 2H, C$\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, $\underline{C}H_3CH$), 21.1 (q, $\underline{C}H_3C$=), 23.8 (d, $\underline{C}HCH_2$) 24.0 (q, $\underline{C}H_3CH$), 41.6 (t, $\underline{C}H_2CH$), 68.7 (d, $\underline{C}$H-OH), 94.2 (d, $\underline{C}$H-OOH), 116.6 (t, $\underline{C}H_2$=C), 141.4 (s, $\underline{C}$=CH_2).

(3RS,4SR)-3-Hydroperoxy-2,6-dimethylhept-1-en-4-ol (*anti*-7h)



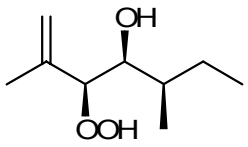
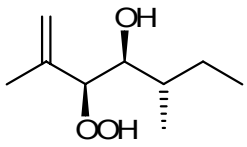
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 0.84 (d, 3H, *J* = 6.72 Hz, C$\underline{H_3}$CH), 1.76 (s, 3H, C$\underline{H_3}$C=), 3.83 (m, 1H, C$\underline{H}$-OH), 4.26 (d, 1H, *J* = 4.53 Hz, C$\underline{H}$-OOH), 5.05 (m, 2H, C$\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.4 (q, $\underline{C}H_3CH$), 21.4 (q, $\underline{C}H_3C$=), 23.6 (d, $\underline{C}HCH_2$) 24.7 (q, $\underline{C}H_3CH$), 41.1 (t, $\underline{C}H_2CH$), 68.9 (d, $\underline{C}$H-OH), 92.0 (d, $\underline{C}$H-OOH), 115.2 (t, $\underline{C}H_2$=C), 141.3 (s, $\underline{C}$=CH_2).

(3RS,4RS,5SR)-3-Hydroperoxy-2,5-dimethylhept-1-en-4-ol (*syn,syn*-7i) and (3RS,4RS,5RS)-3-hydroperoxy-2,5-dimethylhept-1-en-4-ol (*syn,anti*-7i) (elid 473i, 497t)

Photooxygenation of 2,5-dimethylhept-2-en-4-ol **(6i)** (1.10 g, 7.75 mmol) for 60 h according to **GP-9a** afforded an oil composed of the β-hydroxy allylic hydroperoxides (0.98 g, 5.63 mmol, 73 %) in 83:17 diastereomeric mixtures of *syn,syn*-**7i**, *syn,anti*-**7i** as major products and *anti,syn*-**7i** , *anti,anti*-**7i** as minor products.

^{1}H-NMR: (300 MHz, $CDCl_3$, both major diastereomers)

δ (ppm) = 0.80 (m, 6H, $C\underline{H}_3CH$ and $C\underline{H}_3CH_2$), 1.02-1.55 (m, 3H, $C\underline{H}_2C\underline{H}$), 1.70 (s, 3H, CH_3C=), 3.60 (m, 1H, C<u>H</u>-OH), 4.15 (d, 1H, *J* = 8.37 Hz, C<u>H</u>-OOH), 5.05 (m, 2H, $C\underline{H}_2$=C).

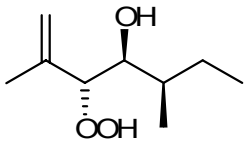
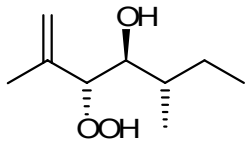
^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 11.1 (q, $\underline{C}H_3CH_2$), 17.7 (q, $\underline{C}H_3CH$), 19.0 (q, $\underline{C}H_3C$=), 29.4 (t, $\underline{C}H_2$), 34.1 (d, $\underline{C}HCH_3$), 70.8 (d, <u>C</u>H-OH), 93.4 (d, <u>C</u>H-OOH), 116.2 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 2nd diastreomer, additional significant signals)

δ (ppm) = 11.0 (q, $\underline{C}H_3CH_2$), 18.7 (q, $\underline{C}H_3CH$), 29.0 (t, $\underline{C}H_2$), 34.0 (d, $\underline{C}HCH_3$), 70.6 (d, <u>C</u>H-OH), 93.5 (d, <u>C</u>H-OOH), 116.2 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

(3RS,4SR,5RS)-3-Hydroperoxy-2,5-dimethylhept-1-en-4-ol (*anti,syn*-7i) and (3RS,4SR,5SR)-3-hydroperoxy-2,5-dimethylhept-1-en-4-ol (*anti,anti*-7i)

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals for both minor diastereomers)

δ (ppm) = 1.77 (s, 3H, CH_3C=), 3.73 (m, 1H, C<u>H</u>-OH), 4.29 (d, 1H, *J* = 4.71 Hz, C<u>H</u>-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer, significant signals)

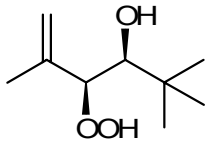
δ (ppm) = 11.1 (q, $\underline{C}H_3CH_2$), 33.9 (d, $\underline{C}HCH_3$), 70.9 (d, <u>C</u>H-OH), 92.3 (d, <u>C</u>H-OOH), 116.0 (t, $\underline{C}H_2$=C), 141.2 (s, $\underline{C}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 2nd diastereomer, significant signals)

δ (ppm) = 34.2 (d, CHCH_3), 71.1 (d, CH-OH), 92.4 (d, CH-OOH), 116.1 (t, CH_2=C), 141.2 (s, C=CH_2).

(3RS,4RS)-4-Hydroperoxy-2,2,5-trimethylhex-5-en-3-ol (*syn*-7j)

(elid 454a)



Photooxygenation of 2,2,5-trimethylhex-4-en-3-ol **(6j)** (1.25 g, 8.80 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 78:22) of β-hydroxy allylic hydroperoxides (0.90 g, 5.17 mmol, 59 %) as faint yellow oil.

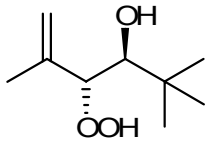
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.92 (s, 9H, (CH_3)$_3$C), 1.75 (m, 3H, CH_3C=), 3.28 (d, 1H, *J* = 4.56 Hz, CH-OH), 4.33 (d, 1H, *J* = 4.41 Hz, CH-OOH), 5.0 (m, 1H, CH_2=C), 5.07 (m, 1H, CH_2=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.8 (q, CH_3C=), 26.2 (q, (CH_3)$_3$C), 34.9 (s, C(CH_3)$_3$), 78.6 (d, CH-OH), 88.0 (d, CH-OOH), 114.7 (t, CH_2=C), 143.2 (s, C=CH_2).

(3RS,4SR)-4-Hydroperoxy-2,2,5-trimethylhex-5-en-3-ol (*anti*-7j)



^{1}H-NMR: (300 MHz, $CDCl_3$)

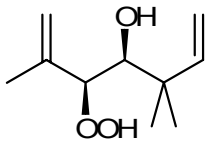
δ (ppm) = 0.92 (s, 9H, (CH_3)$_3$C), 1.75 (m, 3H, CH_3C=), 3.28 (d, 1H, *J* = 4.56 Hz, CH-OH), 4.33 (d, 1H, *J* = 4.41 Hz, CH-OOH), 5.0 (m, 1H, CH_2=C), 5.07 (m, 1H, CH_2=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.2 (q, CH_3C=), 27.0 (q, (CH_3)$_3$C), 34.6 (s, C(CH_3)$_3$), 76.1 (d, CH-OH), 90.1 (d, CH-OOH), 116.4 (t, CH_2=C), 143.8 (s, C=CH_2).

(3RS,4RS)-3-Hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol (*syn*-7k)

(elid 451m)



Photooxygenation of 3,3,6-trimethylhepta-1,5-dien-4-ol (*artemesia alcohol*) **(6k)** (1.04 g, 6.75 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 72:28) of β-hydroxy allylic hydroperoxides (0.92 g, 4.95 mmol, 73 %) as faint yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

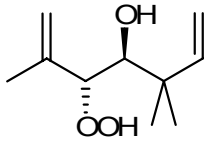
δ (ppm) = 1.01 (d, 6H, $(C\underline{H}_3)_2C$), 1.70 (s, 3H, $C\underline{H}_3C$=), 3.34 (d, 1H, *J* = 4.41 Hz, C<u>H</u>-OH), 4.28 (d, 1H, *J* = 4.14 Hz, C<u>H</u>-OOH), 4.97 (m, 4H, $C\underline{H}_2$=C and $C\underline{H}_2$=CH), 5.84 (dd, 1H, *J* = 10.42 , 17.92 Hz, C<u>H</u>=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.8 (q, $\underline{C}H_3C$=), 22.6 (q, $\underline{C}H_3C$), 23.9 (q, $\underline{C}H_3C$), 41.2 (s, $\underline{C}(CH_3)_2$), 77.8 (d, <u>C</u>H-OH), 87.5 (d, <u>C</u>H-OOH), 112.8 (t, $\underline{C}H_2$=CH), 114.7 (t, $\underline{C}H_2$=C), 142.8 (s, <u>C</u>=CH_2), 144.5 (d, <u>C</u>H=CH_2).

(3RS,4SR)-3-Hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol (*anti*-7k)

(elid 482l)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

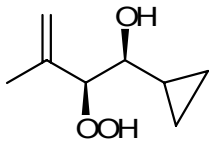
δ (ppm) = 0.95 (d, 6H, $(C\underline{H}_3)_2C$), 1.72 (s, 3H, $C\underline{H}_3C$=), 3.26 (d, 1H, *J* = 6.62 Hz, C<u>H</u>-OH), 4.27 (d, 1H, *J* = 6.76 Hz, C<u>H</u>-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.2 (q, $\underline{C}H_3C$=), 23.0 (q, $\underline{C}H_3C$), 23.3 (q, $\underline{C}H_3C$), 40.9 (s, $\underline{C}(CH_3)_2$), 75.1 (d, <u>C</u>H-OH), 89.8 (d, <u>C</u>H-OOH), 112.8 (t, $\underline{C}H_2$=CH), 116.4 (t, $\underline{C}H_2$=C), 143.2 (s, <u>C</u>=CH_2), 144.3 (d, <u>C</u>H=CH_2).

(1RS,2RS)-1-Cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol (*syn*-7p)

(elid 384a)



Photooxygenation of 1-cyclopropyl-3-methylbut-2-en-1-ol **(6p)** (1.0 g, 7.94 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 62:38) of β-hydroxy allylic hydroperoxides (1.0 g, 6.33 mmol, 80 %) as colorless oil.

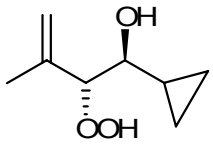
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.20-0.52 (m, 4H, $C\underline{H_2}C\underline{H_2}$), 0.78-0.99 (m, 1H, C<u>H</u>), 1.75 (m, 3H, $C\underline{H_3}C$=), 3.07 (dd, 1H, *J* = 7.95, 7.95 Hz, C<u>H</u>-OH), 4.29 (d, 1H, *J* = 9.30 Hz, C<u>H</u>-OOH), 5.05 (m, 2H, $C\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.8 (t, $\underline{C}H_2CH_2$), 3.2 (t, $\underline{C}H_2CH_2$), 14.0 (d, <u>C</u>H), 18.9 (q, $\underline{C}H_3C$=), 75.0 (d, <u>C</u>H-OH), 93.3 (d, <u>C</u>H-OOH), 115.5 (t, $\underline{C}H_2$=C), 141.6 (s, <u>C</u>=CH_2).

(1RS,2SR)-1-Cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol (*anti*-7p)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

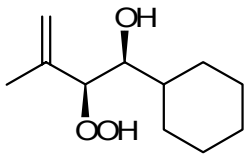
δ (ppm) = 1.82 (m, 3H, $C\underline{H_3}C$=), 3.14 (dd, 1H, *J* = 4.26, 8.82 Hz, C<u>H</u>-OH), 4.41 (d, 1H, *J* = 4.26 Hz, C<u>H</u>-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 2.6 (t, $\underline{C}H_2CH_2$), 2.9 (t, $\underline{C}H_2CH_2$), 13.3 (d, <u>C</u>H), 19.6 (q, $\underline{C}H_3C$=), 75.6 (d, <u>C</u>H-OH), 91.2 (d, <u>C</u>H-OOH), 115.4 (t, $\underline{C}H_2$=C), 141.3 (s, <u>C</u>=CH_2).

(1RS,2RS)-1-Cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol (*syn*-7q)

(elid 500c)



Photooxygenation of 1-cyclohexyl-3-methylbut-2-en-1-ol **(6q)** (1.30 g, 7.74 mmol) for 60 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 88:12) of β-hydroxy allylic hydroperoxides (1.0 g, 5.0 mmol, 65 %) as faint yellow oil.

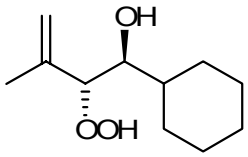
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.83-1.90 (m, 11H, C<u>H</u> and C<u>H$_2$</u>), 1.64 (s, 3H, C<u>H$_3$</u>C=), 3.43 (m, 1H, C<u>H</u>-OH), 4.24 (d, 1H, *J* = 8.49 Hz, C<u>H</u>-OOH), 4.97 (s, 2H, C<u>H$_2$</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.7 (q, <u>C</u>H$_3$C=), 25.3 (t, <u>C</u>H$_2$), 25.9 (t, <u>C</u>H$_2$), 26.1 (t, <u>C</u>H$_2$), 26.4 (t, <u>C</u>H$_2$), 30.3, 30.5 (t, <u>C</u>H$_2$), 39.1 (d, <u>C</u>H), 74.3 (d, <u>C</u>H-OH), 91.0 (d, <u>C</u>H-OOH), 115.9 (t, <u>C</u>H$_2$=C), 141.6 (s, <u>C</u>=CH$_2$).

(1RS,2SR)-1-Cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol (*anti*-7q)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 4.29 (d, 1H, *J* = 5.97 Hz, C<u>H</u>-OOH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 39.3 (d, <u>C</u>H), 89.2 (d, <u>C</u>H-OOH), 112.9 (t, <u>C</u>H$_2$=C).

1-(6-Methyl-3,4-dihydro-[1,2]dioxin-3-yl)ethanol[188] **(*syn*-9 and *anti*-9)**

(elid 477a)

Photooxygenation of (3E,5E)-hepta-3,5-dien-2-ol **(8)** (100 mg, 0.89 mmol) for 5 h according to **GP-9b** using TSP-S-DVB copolymer afforded a diastereomeric mixture (d.r. 59:41) of the endoperoxide (97 mg, 0.67 mmol, 76 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 1.17 (d, 3H, C$\underline{H_3}$CHOO), 1.19 (d, 3H, *J* = 6.78 Hz, C$\underline{H_3}$CHOH), 4.03 (m, 1H, C$\underline{H}$OH), 4.17 (m, 1H, C$\underline{H}$OO), 4.64 (m, 1H, C$\underline{H}$CH$_3$), 5.85 (m, 1H, C$\underline{H}$=CH), 5.95 (m, 1H, C$\underline{H}$=CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 17.7 (q, $\underline{C}H_3$CHOO), 19.0 (q, $\underline{C}H_3$CHOH), 68.1 (d, $\underline{C}$HOH), 74.2 (d, $\underline{C}$HOO(CH$_3$)), 81.6 (s, $\underline{C}$HOO(CH)), 123.1 (d, $\underline{C}$H=CH), 130.7 (d, $\underline{C}$H=CH).

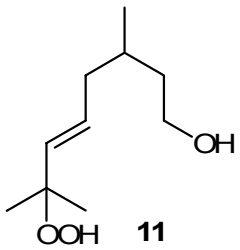
^{1}H-NMR: (300 MHz, $CDCl_3$, minor diastereomer)

δ (ppm) = 1.11 (d, 3H, *J* = 6.75 Hz C$\underline{H_3}$CHOO), 1.16 (d, 3H, C$\underline{H_3}$CHOH), 3.93-4.0 (m, 2H, C$\underline{H}$OO and C$\underline{H}$OH), 4.74 (q, 1H, *J* = 6.78 Hz, C$\underline{H}$CH$_3$), 5.85 (m, 1H, C$\underline{H}$=CH), 5.95 (m, 1H, C$\underline{H}$=CH).

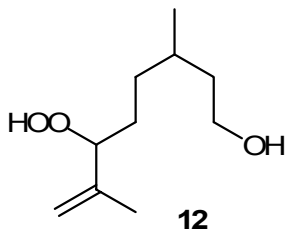
^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer)

δ (ppm) = 17.3 (q, $\underline{C}H_3$CHOO), 17.9 (q, $\underline{C}H_3$CHOH), 69.7 (d, $\underline{C}$HOH), 74.2 (d, $\underline{C}$HOO(CH$_3$)), 83.2 (s, $\underline{C}$HOO(CH)), 122.9 (d, $\underline{C}$H=CH), 130.8 (d, $\underline{C}$H=CH).

(E)-7-Hydroperoxy-3,7-dimethyloct-5-en-1-ol (11) and 6-hydroperoxy-3,7-dimethyloct-7-en-1-ol (12) (elid 371a)



11



12

Photooxygenation of 3,7-Dimethyloct-6-en-1-ol (citronellol, **10**) (350 mg, 2.24 mmol) for 37 h according to **GP-9b** using TSP-S-DVB copolymer afforded 310 mg (1.66 mmol, 74 %) yellow oil composed of a regioisomeric mixture of the hydroperoxides **11** and **12** in ratio 1.3:1, respectively. The regioisomer **12** is obtained as 1:1 diastereomeric mixture.

^{1}H-NMR: (300 MHz, $CDCl_3$, **11** and **12**)

δ (ppm) = 0.79 (d, 3H, *J* = 6.45 Hz, C$\underline{H}_3$CH), 0.80 (d, 3H, J = 6.60 Hz, C$\underline{H}_3$CH), 1.10-1.60 (m, 10H, C$\underline{H}_2$C$\underline{H}$C$\underline{H}_2$ of **11** and **12**), 1.21 (s, 6H, (C$\underline{H}_3$)$_2$C of **11**), 1.62 (s, 3H, C$\underline{H}_3$C= of **12**), 1.90 (m, 2H, C$\underline{H}_2$CHOOH of **12**), 3.55 (m, 2H, C$\underline{H}_2$OH of **11** and **12**), 4.14 (m, 1H, C$\underline{H}$-OOH of **12**), 4.86 (s, 2H, C$\underline{H}_2$=C of **12**), 5.45 (d, 1H, *J* = 15.87 Hz, C$\underline{H}$=CH of **11**), 5.53 (m, 1H, C$\underline{H}$=CH of **11**).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, regioisomer **11**)

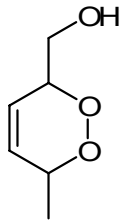
δ (ppm) = 19.5 (q, $\underline{C}H_3CH$), 27.8 (d, $\underline{C}HCH_3$), 29.4 (q, ($\underline{C}H_3$)$_2$C), 38.6 (t, $\underline{C}H_2CH$=CH), 39.6 (t, $\underline{C}H_2CH_2OH$), 60.5 (t, $\underline{C}H_2OH$), 81.6 (s, $\underline{C}$q-OOH), 129.2 (d, $\underline{C}H$=CH-Cq), 135.1 (d, $\underline{C}H$=CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, two diastereomers of regioisomer **12**)

δ (ppm) = 16.7/16.8 (q, $\underline{C}H_3CH$), 19.2/19.3 (q, $\underline{C}H_3C$=), 24.1/24.2 (t, $\underline{C}H_2CH$-OOH), 28.8/29.1 (d, $\underline{C}HCH_3$), 32.4/32.6 (t, $\underline{C}H_2CH_2CH$-OOH), 39.1/39.3 (t, $\underline{C}H_2CH_2OH$), 60.5 (t, $\underline{C}H_2OH$), 89.1/89.5 (d, $\underline{C}H$-OOH), 113.5/113.8 (t, $\underline{C}H_2$=C), 143.8/144.0 (s, $\underline{C}$=CH_2).

(3,6-Dihydro-6-methyl-1,2-dioxin-3-yl)methanol[189] **(14)**

(elid 368a, 477e)



Photooxygenation of (2E,4E)-hexa-2,4-dien-1-ol **(13)** (100 mg, 1.02 mmol) for 6 h according to **GP-9b** using TSP-S-DVB copolymer afforded the endoperoxide (110 mg, 0.85 mmol, 83 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

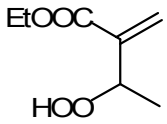
δ (ppm) = 1.16 (d, 3H, *J* = 6.75 Hz, C$\underline{H}_3$CH), 3.65 (dd, 1H, *J* = 3.06, 12.21 Hz, C$\underline{H}_2$OH), 3.82 (dd, 1H, *J* = 7.80, 12.33 Hz, C$\underline{H}_2$OH), 4.39 (m, 1H, C$\underline{H}$CH$_2$), 4.77 (m, 1H, C$\underline{H}$CH$_3$), 5.83 (m, 1H, C$\underline{H}$=CH), 5.93 (m, 1H, C$\underline{H}$=CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.5 (q, $\underline{C}H_3CH$), 63.2 (t, $\underline{C}H_2$), 74.3 (d, $\underline{C}HCH_3$), 79.7 (d, $\underline{C}HCH_2$), 84.3 (d, $\underline{C}H$), 122.9 (d, $\underline{C}H$=CH), 131.3 (d, $\underline{C}H$=CH).

Ethyl 3-hydroperoxy-2-methylenebutanoate (16)

(elid 444a, 451w, 490p)



Photooxygenation of (E)-ethyl 2-methylbut-2-enoate **(15)** (1.0 g, 7.81 mmol) for 48 h according to **GP-9a** afforded the allylic hydroperoxides (1.02 g, 6.38 mmol, 82 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

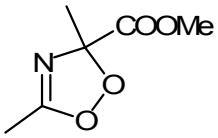
δ (ppm) = 1.23 (m, 6H, $C\underline{H}_3CH$ and $C\underline{H}_3CH_2$), 4.14 (dq, 2H, *J* = 1.17, 7.05 Hz, $C\underline{H}_2CH_3$), 4.90 (dq, 1H, *J* = 1.02, 6.63 Hz, C<u>H</u>-OOH), 5.85 (d, 1H, *J* = 1.02 Hz, $C\underline{H}_2$=C), 6.26 (s, 1H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3$), 18.4 (q, $\underline{C}H_3$), 60.8 (t, $\underline{C}H_2$), 79.0 (d, <u>C</u>H-OOH), 125.4 (t, $\underline{C}H_2$=C), 140.6 (s, <u>C</u>=CH_2), 166.2 (s, <u>C</u>OO).

3,5-Dimethyl-3-methoxycarbonyl-1,2,4-dioxazole (21a)

(elid 497k)



Photooxygenation of **(20a)** 0.20 g (1.6 mmol) according to **GP-14** affords the dioxazole as yellow oil.

Yield: 0.18 g (60 %) using TSP-S-DVB and 0.13 g (44 %) using PP-S-DVB.

^{1}H-NMR: (300 MHz, $CDCl_3$)

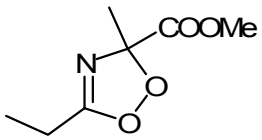
δ (ppm) = 1.63 (s, 3H, $C\underline{H}_3$), 1.98 (s, 3H, $C\underline{H}_3$-C=), 3.71 (s, 3H, $COOC\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.4 (q, $\underline{C}H_3$C=), 22.1 (q, $\underline{C}H_3$), 52.8 (q, $COO\underline{C}H_3$), 106.1 (s, <u>Cq</u>), 160.7 (s, <u>C</u>=N), 168.4 (s, $\underline{C}OOCH_3$).

5-Ethyl-3-methoxycarbonyl-3-methyl-1,2,4-dioxazole (21b)

(elid 498e)



Photooxygenation of **20b** 0.20 g (1.4 mmol) according to **GP-14** affords the dioxazole as yellow oil.

Yield: 0.20 g (86 %) using TSP-S-DVB and 0.21 g (90 %) using PP-S-DVB.

^{1}H-NMR: (300 MHz, $CDCl_3$)

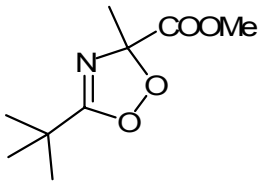
δ (ppm) = 1.18 (t, 3H, *J* = 7.5 Hz, $C\underline{H_3}CH_2$), 1.66 (s, 3H, $C\underline{H_3}$), 2.30 (q, 2H, *J* = 7.5 Hz, $C\underline{H_2}CH_3$), 3.72 (s, 3H, $COOC\underline{H_3}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.9 (q, $\underline{C}H_3CH_2$), 17.4 (t, $\underline{C}H_2CH_3$), 22.2 (q, $\underline{C}H_3$), 52.9 (q, $COO\underline{C}H_3$), 106.0 (s, C_q), 164.9 (s, $\underline{C}$=N), 168.6 (s, $\underline{C}OOCH_3$).

3-Methoxycarbonyl-3-methyl-5-*tert*-butyl-1,2,4-dioxazole (21c)

(elid 498d)



Photooxygenation of **20c** 0.20 g (1.2 mmol) according to **GP-14** affords the dioxazole as yellow oil.

Yield: 0.20 g (84 %) using PP-S-DVB.

^{1}H-NMR: (300 MHz, $CDCl_3$)

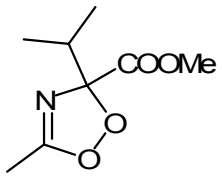
δ (ppm) = 1.18 (s, 9H, $(C\underline{H_3})_3C$), 1.62 (s, 3H, $C\underline{H_3}$), 3.69 (s, 3H, $COOC\underline{H_3}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 22.0 (q, $\underline{C}H_3$), 27.2 (s, $\underline{C}(CH_3)_3$), 27.6 (q, $(\underline{C}H_3)_3C$), 52.7 (q, $COO\underline{C}H_3$), 105.9 (s, C_q), 168.6 (s, $\underline{C}OOCH_3$), 170.0 (s, $\underline{C}$=N).

3-Isopropyl-3-methoxycarbonyl-5-methyl-1,2,4-dioxazole (21d)

(elid 499c)



Photooxygenation of **20d** 0.20 g (1.3 mmol) according to **GP-14** affords the dioxazole as yellow oil.

Yield: 0.19 g (79 %) using PP-S-DVB.

^{1}H-NMR: (300 MHz, $CDCl_3$)

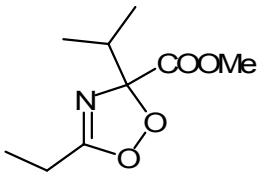
δ (ppm) = 0.87 (d, 3H, *J* = 6.91 Hz, $(C\underline{H}_3)_2CH$), 0.92 (d, 3H, *J* = 6.91 Hz, $(C\underline{H}_3)_2CH$), 2.01 (s, 3H, $C\underline{H}_3C$=), 2.40 (septet, 1H, C<u>H</u>), 3.79 (s, 3H, $COOC\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.4 (q, $\underline{C}H_3C$=), 15.6 (q, $(\underline{C}H_3)_2CH$), 15.7 (q, $(\underline{C}H_3)_2CH$), 33.3 (d, <u>C</u>H), 52.7 (q, $COO\underline{C}H_3$), 111.3 (s, C_q), 160.3 (s, <u>C</u>=N), 168.8 (s, $\underline{C}OOCH_3$).

5-Ethyl-3-isopropyl-3-methoxy-carbonyl-1,2,4-dioxazole (21e)

(elid 490b)



Photooxygenation of **20e** 0.30 g (1.8 mmol) according to **GP-14** affords the dioxazole as yellow oil.

Yield: 0.32 g (90 %) using TSP-S-DVB and 0.31 g (86 %) using PP-S-DVB.

^{1}H-NMR: (300 MHz, $CDCl_3$)

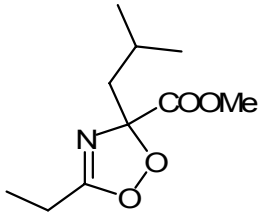
δ (ppm) = 0.80 (d, 3H, *J* = 6.91 Hz, $(C\underline{H}_3)_2CH$), 0.85 (d, 3H, *J* = 6.91 Hz, $(C\underline{H}_3)_2CH$), 1.12 (t, 3H, *J* = 7.64 Hz, $C\underline{H}_3CH_2$), 2.25 (q, 2H, *J* = 7.64 Hz, $C\underline{H}_2CH_3$), 2.34 (septet, C<u>H</u>), 3.68 (s, 3H, $COOC\underline{H}_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 10.0 (q, $\underline{C}H_3CH_2$), 15.4 (q, $(\underline{C}H_3)_2CH$), 15.5 (q, $(\underline{C}H_3)_2CH$), 17.3 (t, $\underline{C}H_2CH_3$), 33.1 (d, $\underline{C}H$), 52.5 (q, $COO\underline{C}H_3$), 111.0 (s, C_q), 164.3 (s, $\underline{C}$=N), 168.6 (s, $\underline{C}OOCH_3$).

5-Ethyl-3-isobutyl-3-methoxy-carbonyl-1,2,4-dioxazole (21f)

(elid 489m)



Photooxygenation of **20f** 0.20 g (1.09 mmol) according to **GP-14** affords the dioxazole as yellow oil.

Yield: 209 mg (89 %) using TSP-S-DVB and 186 mg (79 %) using PP-S-DVB.

^{1}H-NMR: (300 MHz, $CDCl_3$)

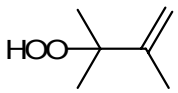
δ (ppm) = 0.81 (d, 6H, *J* = 6.6 Hz, $(C\underline{H_3})_2CH$), 1.11 (t, 3H, *J*= 7.5 Hz $C\underline{H_3}CH_2$), 1.66 (m, 1H, C<u>H</u>), 1.86 (dd, 2H, $C\underline{H_2}CH$), 2.23 (q, 2H, *J* = 7.5 Hz, $C\underline{H_2}CH_3$), 3.66 (s, 3H, $COOC\underline{H_3}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.9 (q, $\underline{C}H_3CH_2$), 17.3 (t, $\underline{C}H_2CH_3$), 23.1 (q, $(\underline{C}H_3)_2CH$), 23.3 (q, $(\underline{C}H_3)_2CH$), 23.5 (t, $\underline{C}H_2CH$), 43.4 (d, $\underline{C}H$), 52.5 (q, $COO\underline{C}H_3$), 108.3 (s, C_q), 164.4 (s, $\underline{C}$=N), 168.7 (s, $\underline{C}OOCH_3$).

3-Hydroperoxy-2,3-dimethylbut-1-ene[190] **(24)**

(elid 473f)



Irradiation of tetramethylethylene (1g, 11.9 mmol) for 24 h according to **GP-7a** followed by usual work-up gives the allylic hydroperoxide (0.87 g, 7.50 mmol, 63 %) as an oil which is used without further purification.

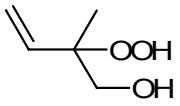
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.31 (s, 6H, 2 x C<u>H</u>$_3$), 1.76 (t, 3H, *J* = 0.75 Hz, CH_3C=), 4.89-4.94 (m, 2H, C<u>H</u>$_2$=C), 7.99 (br s, 1H, OO<u>H</u>).

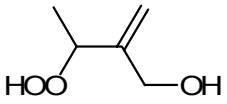
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.6 (q, <u>C</u>H_3C=), 23.8 (q, 2 x <u>C</u>H_3), 84.2 (s, <u>C</u>-OOH), 111.7 (t, <u>C</u>H_2=C), 148.0 (s, <u>C</u>=CH_2).

2-Hydroperoxy-2-methylbut-3-en-1-ol (36a) and 3-hydroperoxy-2-methylenebutan-1-ol[191] **(36b)** (elid 433b)



36a



36b

Photooxygenation of (E)-2-methylbut-2-en-1-ol **(6o)** (1.2 g, 14.0 mmol) for 60 h according to **GP-9a** afforded 0.88 g (7.5 mmol, 54 %) of a faint yellow oil composed of a regioisomeric mixture of the allylic hydroperoxides **36a** and **36b** in ratio 53:47, respectively.

^{1}H-NMR: (300 MHz, $CDCl_3$, regioisomer **36a**)

δ (ppm) = 1.24 (m, 3H, C<u>H</u>$_3$), 3.57 (dd, 1H, *J* = 1.62, 12.03 Hz, C<u>H</u>$_2$-OH), 3.70 (d, 1H, *J* = 12.06 Hz, C<u>H</u>$_2$-OH), 5.20 (m, 2H, C<u>H</u>$_2$=CH), 5.90 (ddd, 1H, *J* = 0.87, 11.01, 17.76 Hz, C<u>H</u>=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, regioisomer **36a**)

δ (ppm) = 19.1 (q, <u>C</u>H_3), 65.3 (t, <u>C</u>H_2-OH), 84.6 (s, <u>C</u>q-OOH), 116.5 (t, <u>C</u>H_2=CH), 137.9 (d, <u>C</u>H=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, regioisomer **36b**)

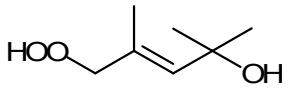
δ (ppm) = 1.25 (d, 3H, *J* = 6.78 Hz, C<u>H</u>$_3$CH), 4.08 (d, 1H, *J* = 12.93 Hz, C<u>H</u>$_2$-OH), 4.22 (m, 1H, C<u>H</u>$_2$-OH), 4.59 (q, 1H, *J* = 6.60 Hz, C<u>H</u>-OOH), 5.20 (m, 2H, C<u>H</u>$_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, regioisomer **36b**)

δ (ppm) = 17.5 (q, <u>C</u>H_3), 62.4 (t, <u>C</u>H_2-OH), 82.9 (d, <u>C</u>H-OOH), 115.6 (t, <u>C</u>H_2=C), 147.5 (s, <u>C</u>=CH_2).

(E)-4-(hydroperoxymethyl)-2-methylpent-3-en-2-ol (37b)

(elid 139)



Photooxygenation of 2,4-dimethylpent-3-en-2-ol **(6n)** (1.0 g, 8.77 mmol) for 48 h according to **GP-7b** afforded the rearranged allylic hydroperoxides (1.03 g, 7.05 mmol, 80 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.22 (s, 6H, 2 x C<u>H</u>$_3$), 1.63 (s, 3H, C<u>H</u>$_3$C=), 4.26 (s, 2H, C<u>H</u>$_2$-OOH), 5.46 (s, 1H, C<u>H</u>=C).

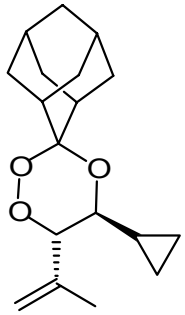
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, <u>C</u>H$_3$C=), 25.2 (q, 2 x <u>C</u>H$_3$), 72.3 (t, <u>C</u>H$_2$-OOH), 77.7 (s, <u>C</u>-OH), 126.9 (d, <u>C</u>H=C), 129.6 (s, <u>C</u>=CH$_2$).

4.6 Synthesis of 1,2,4-Trioxanes

4.6.1 Derived from 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol (7p)

(5RS,6RS)-5-Cyclopropyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (38) (elid 409c)



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (1.88 g, 11.9 mmol) and adamantanone (1.78 g, 11.9 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.81) affords the pure 1,2,4-trioxane as faint yellow oil which crystallizes upon standing (0.25 g, 0.86 mmol, 7 %).

M.p. 79-81 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.31-0.49 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.78 (m, 1H, C$\underline{H}$(CH$_2$)$_2$), 1.50-2.19 (m, 13H, C$\underline{H}$ and C$\underline{H_2}$), 1.79 (m, 3H, C$\underline{H_3}$C=), 2.82 (m, 1H, C$\underline{H}$), 3.33 (dd, 1H, *J* = 7.35, 9.41 Hz, OC$\underline{H}$), 4.38 (d, 1H, *J* = 9. 40 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.9 (t, $\underline{C}H_2$), 3.1 (t, $\underline{C}H_2$), 12.2 (d, $\underline{C}H(CH_2)_2$), 21.0 (q, $\underline{C}H_3C$=), 27.5 (d, $\underline{C}$H), 27.6 (d, $\underline{C}$H), 30.2 (d, $\underline{C}$H), 36.9 (d, $\underline{C}$H), 33.4 (t, $\underline{C}H_2$), 33.7 (t, $\underline{C}H_2$), 33.8 (t, $\underline{C}H_2$), 34.0 (t, $\underline{C}H_2$), 37.6 (t, $\underline{C}H_2$), 73.0 (d, O$\underline{C}$H), 87.9 (d, OO$\underline{C}$H), 105.0 (s, O$\underline{C}$OO), 117.2 (t, $\underline{C}H_2$=), 140.4 (s, $\underline{C}$=CH$_2$).

IR: (Film)

ν (cm^{-1}) = 3079, 2931, 2917, 1653, 1112, 1079, 1025, 926, 910, 891.

MS: (EI, 70 eV)

m/z (%) = 290 (M^+, less than 1), 220 (M^+-C_4H_6O, 1), 150 ($C_{10}H_{14}O^+$, 57), 108 ($C_8H_{12}^+$, 47), 93 ($C_7H_9^+$, 57), 81 ($C_6H_9^+$, 37), 80 ($C_6H_8^+$, 97), 79 ($C_6H_7^+$, 100), 67 ($C_5H_7^+$, 32), 55 ($C_3H_3O^+$, 27).

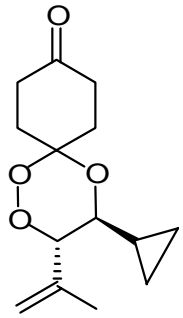
Elemental Analysis: ($C_{18}H_{26}O_3$, M = 290.40)

Calcd: C 74.45 H 9.02

Found: C 73.61 H 8.94

(3RS,4RS)-4-Cyclopropyl-3-isopropenyl-1,2,5-trioxa-spiro[5.5]undecan-9-one (39)

(elid 495p)



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (1.10 g, 6.96 mmol) and cyclohex-1,4-dione (0.40 g, 3.57 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of excess ketone followed by purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.30) affords the pure 1,2,4-trioxane as yellow oil (0.15 g, 0.60 mmol, 17 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

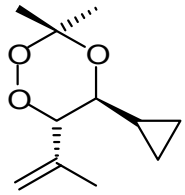
δ (ppm) = 0.09-0.62 (m, 4H, ($C\underline{H}_2)_2$CH), 0.66-0.97 (m, 1H, C$\underline{H}$($CH_2)_2$), 1.03-1.23 (m, 2H, $C\underline{H}_2CH_2$), 1.78 (s, 3H, $C\underline{H}_3$C=), 1.95 (m, 2H, $C\underline{H}_2CH_2$), 2.20-2.52 (m, 4H, 2 x $C\underline{H}_2$CO), 3.30 (dd, 1H, *J* = 7.50, 9.54 Hz, OC$\underline{H}$), 4.43 (d, 1H, *J* = 9. 54 Hz, OOC$\underline{H}$), 5.04 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.7 (t, $\underline{C}H_2$CH), 2.7 (t, $\underline{C}H_2$CH), 11.7 (d, $\underline{C}$H($CH_2)_2$), 20.5 (q, $\underline{C}H_3$C=), 27.6 (t, $\underline{C}H_2$), 33.5 (t, $\underline{C}H_2$), 36.4 (t, $\underline{C}H_2$), 36.6 (t, $\underline{C}H_2$), 74.6 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 101.1 (s, O$\underline{C}$OO), 117.2 (t, $\underline{C}H_2$=C), 139.4 (s, $\underline{C}$=CH_2), 209.8 (s, $\underline{C}$=O).

(5RS,6RS)-5-Cyclopropyl-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (40)

(elid 391a)



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (1.0 g, 6.33 mmol) and excess acetone (2.0 g, 34.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of excess ketone affords the pure 1,2,4-trioxane as yellow oil (0.51 g, 2.58 mmol, 41 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

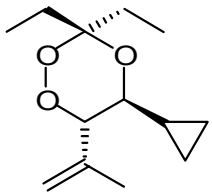
δ (ppm) = 0.20-0.60 (m, 4H, $C\underline{H_2}C\underline{H_2}$), 0.70-0.81 (m, 1H, $C\underline{H}(CH_2)_2$), 1.33 (s, 3H, $C\underline{H_3}$), 1.57 (s, 3H, $C\underline{H_3}$), 1.79 (s, 3H, $C\underline{H_3}C=$), 3.24 (dd, 1H, *J* = 7.95, 9.42 Hz, O$C\underline{H}$), 4.35 (d, 1H, *J* = 9.54 Hz, OO$C\underline{H}$), 5.07 (m, 2H, $C\underline{H_2}=$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.9 (t, $\underline{C}H_2$), 2.8 (t, $\underline{C}H_2$), 11.9 (d, $\underline{C}H(CH_2)_2$), 20.4 (q, $\underline{C}H_3C=$), 20.5 (q, $\underline{C}H_3$), 25.9 (q, $\underline{C}H_3$), 74.8 (d, O$\underline{C}$H), 87.4 (d, OO$\underline{C}$H), 102.6 (s, O$\underline{C}$OO), 116.7 (t, $\underline{C}H_2=$), 139.9 (s, $\underline{C}=CH_2$).

(5RS,6RS)-5-Cyclopropyl-3,3-diethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (41)

(elid 496m)



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (0.69 g, 4.37 mmol) and excess 3-pentanone (2.0 g, 23.3 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of excess ketone followed by purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.81) affords the pure 1,2,4-trioxane as yellow oil (0.10 g, 0.44 mmol, 10 %).

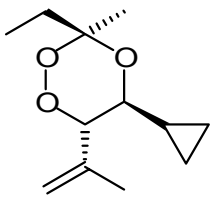
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.25-0.53 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.76 (m, 1H, C$\underline{H}$(CH_2)$_2$), 0.84 (t, 3H, *J* = 7.44 Hz, C$\underline{H_3}$$CH_2$), 0.88 (t, 3H, *J* = 7.44 Hz, C$\underline{H_3}$$CH_2$), 1.60 (m, 2H, C$\underline{H_2}$$CH_3$), 1.79 (s, 3H, C$\underline{H_3}$C=), 1.80-2.16 (m, 2H, C$\underline{H_2}$$CH_3$), 3.28 (dd, 1H, *J* = 7.41, 9.24 Hz, OC$\underline{H}$), 4.33 (d, 1H, *J* = 9. 48 Hz, OOC$\underline{H}$), 5.05 (s, 2H, C$\underline{H_2}$=C).

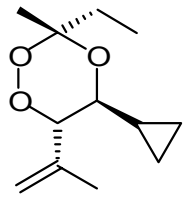
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.7 (t, $\underline{C}H_2CH$), 2.4 (t, $\underline{C}H_2CH$), 6.8 (q, $\underline{C}H_3CH_2$), 8.0 (q, $\underline{C}H_3CH_2$), 11.8 (d, $\underline{C}H(CH_2)_2$), 20.6 (q, $\underline{C}H_3C$=), 22.9 (t, $\underline{C}H_2CH_3$), 28.3 (t, $\underline{C}H_2CH_3$), 73.4 (d, O$\underline{C}$H), 87.2 (d, OO$\underline{C}$H), 105.8 (s, O$\underline{C}$OO), 116.7 (t, $\underline{C}H_2$=C), 140.0 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Cyclopropyl-3-ethyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (42a) and (3RS,5SR,6SR)-5-cyclopropyl-3-ethyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (42b) (elid 391b) major



42a



42b

Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (0.6 g, 3.80 mmol) and excess 2-butanone (2.0 g, 27.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of excess ketone affords a yellow oil of 1,2,4-trioxanes diastereomeric mixture **42a,b** in 72:28 ratio (0.50 g, 2.36 mmol, 62 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **42a**)

δ (ppm) = 0.18-0.56 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.75 (m, 1H, C$\underline{H}$(CH_2)$_2$), 0.91 (t, 3H, *J* = 7.47 Hz, C$\underline{H_3}$$CH_2$), 1.51 (s, 3H, C$\underline{H_3}$), 1.60 (q, 2H, *J* = 7.65 Hz, C$\underline{H_2}$$CH_3$), 1.79 (m, 3H, C$\underline{H_3}$C=), 3.34 (dd, 1H, *J* = 7.35, 9.41 Hz, OC$\underline{H}$), 4.31 (d, 1H, *J* = 9. 41 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **42a**)

δ (ppm) = 1.5 (t, $\underline{C}H_2$), 2.3 (t, $\underline{C}H_2$), 7.1 (q, $\underline{C}H_3CH_2$), 11.8 (d, $\underline{C}H(CH_2)_2$), 18.5 (q, $\underline{C}H_3$), 20.4 (q, $\underline{C}H_3C$=), 32.1 (t, $\underline{C}H_2CH_3$), 73.6 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 103.9 (s, O$\underline{C}$OO), 116.7 (t, $\underline{C}H_2$=), 139.9 (s, $\underline{C}$=CH_2).

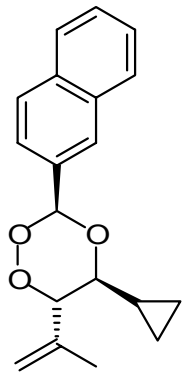
^{1}H-NMR: (300 MHz, $CDCl_3$, minor diastereomer **42b**)

δ (ppm) = 0.18-0.56 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.75 (m, 1H, C$\underline{H}$(CH_2)$_2$), 0.84 (t, 3H, *J* = 7.65 Hz, C$\underline{H_3}$$CH_2$), 1.24 (s, 3H, C$\underline{H_3}$), 1.87-2.13 (m, 2H, C$\underline{H_2}$$CH_3$), 1.78 (m, 3H, C$\underline{H_3}$C=), 3.16 (dd, 1H, *J* = 7.86, 9.41 Hz, OC$\underline{H}$), 4.34 (d, 1H, *J* = 9. 41 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **42b**)

δ (ppm) = 1.9 (t, $\underline{C}H_2$), 2.8 (t, $\underline{C}H_2$), 8.2 (q, $\underline{C}H_3CH_2$), 11.9 (d, $\underline{C}H(CH_2)_2$), 20.5 (q, $\underline{C}H_3C$=), 22.6 (q, $\underline{C}H_3$), 25.1 (t, $\underline{C}H_2CH_3$), 74.5 (d, O$\underline{C}$H), 87.1 (d, OO$\underline{C}$H), 104.9 (s, O$\underline{C}$OO), 116.7 (t, $\underline{C}H_2$=), 139.9 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Cyclopropyl-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (43)
(elid 440c)



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (1.25 g, 7.91 mmol) and β-naphthaldehyde (1.23 g, 7.88 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.67) affords the pure 1,2,4-trioxane as yellow oil which crystallizes upon standing (0.72 g, 2.43 mmol, 31 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.39-0.64 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.98 (m, 1H, C$\underline{H}$(CH_2)$_2$), 1.87 (m, 3H, C$\underline{H_3}$C=), 3.44 (dd, 1H, *J* = 7.43, 9.12 Hz, OC$\underline{H}$), 4.68 (d, 1H, *J* = 9.12 Hz, OOC$\underline{H}$), 5.14 (m, 2H, C$\underline{H_2}$=), 6.31 (s, 1H, OC$\underline{H}$OO), 7.46-7.98 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 2.0 (t, $\underline{C}H_2$), 2.8 (t, $\underline{C}H_2$), 11.6 (d, $\underline{C}H(CH_2)_2$), 20.7 (q, $\underline{C}H_3C$=), 81.0 (d, O$\underline{C}$H), 87.8 (d, OO$\underline{C}$H), 104.0 (d, O$\underline{C}$HOO), 117.5 (t, $\underline{C}H_2$=), 124.2 (d, $\underline{C}H_{arom}$), 126.2

(d, $\underline{C}H_{arom}$), 126.7 (d, $\underline{C}H_{arom}$), 127.0 (d, $\underline{C}H_{arom}$), 127.7 (d, $\underline{C}H_{arom}$), 128.2 (d, $\underline{C}H_{arom}$), 128.5 (d, $\underline{C}H_{arom}$), 131.8 (s, $\underline{C}q_{arom}$), 132.9 (s, $\underline{C}q_{arom}$), 134.1 (s, $\underline{C}q_{arom}$), 139.9 (s, $\underline{C}=CH_2$).

IR: (Film)

ν (cm^{-1}) = 3088, 3011, 2968, 2934, 1647, 1603, 1126, 1071, 904, 859, 814.

HRMS: (EI, 70 eV, $C_{19}H_{20}O_3$)

Calcd: M = 296.141 g/mol

Found: M = 296.141 ±0.005 g/mol

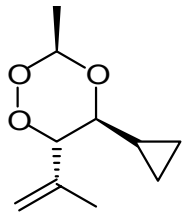
Elemental Analysis: ($C_{19}H_{20}O_3$, M = 296.36)

Calcd: C 77.00 H 6.80

Found: C 76.47 H 6.83

(3RS,5RS,6RS)-5-Cyclopropyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (44a)

(elid 493w)



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol (**7p**) (1.20 g, 7.59 mmol) and acetaldehyde diethylacetal (0.93 g, 7.88 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.70) afforded colorless oil composed of a diastereomeric mixture of the pure 1,2,4-trioxanes **44a** as major product and **44b**,**c** as minor products (363 mg, 1.97 mmol, 26 %).

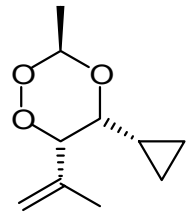
^{1}H-NMR: (300 MHz, $CDCl_3$, **44a**)

δ (ppm) = 0.20-0.60 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 0.78 (m, 1H, $C\underline{H}(CH_2)_2$), 1.21 (d, 3H, *J* = 5.46 Hz, $C\underline{H}_3$), 1.73 (m, 3H, $C\underline{H}_3C=$), 3.03 (dd, 1H, *J* = 8.07, 8.79 Hz, $OC\underline{H}$), 4.39 (d, 1H, *J* = 8.97 Hz, $OOC\underline{H}$), 5.0 (m, 2H, $C\underline{H}_2=$), 5.26 (q, 1H, J = 5.46 Hz, $OC\underline{H}OO$).

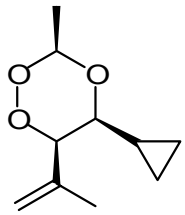
^{13}C-NMR: (75.5 MHz, $CDCl_3$, **44a**)

δ (ppm) = 1.7 (t, $\underline{C}H_2$), 2.8 (t, $\underline{C}H_2$), 11.4 (d, $\underline{C}H(CH_2)_2$), 17.7 (q, $\underline{C}H_3$), 20.4 (q, $\underline{C}H_3C=$), 80.6 (d, $O\underline{C}H$), 87.3 (d, $OO\underline{C}H$), 101.1 (d, $O\underline{C}HOO$), 117.0 (t, $\underline{C}H_2=C$), 139.2 (s, $\underline{C}=CH_2$).

(3RS,5RS,6RS)-5-Cyclopropyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (44b) and (3RS,5RS,6SR)-5-cyclopropyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (44c)



44b



44c

^{1}H-NMR: (300 MHz, $CDCl_3$, additional signals of both minor diastreomers **44b**,**c**)

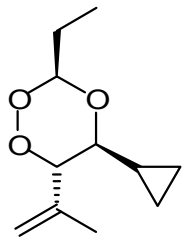
δ (ppm) = 0.20-0.60 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 0.78 (m, 1H, C$\underline{H}$(CH_2)$_2$), 1.19 (d, 3H, *J* = 5.31 Hz, C$\underline{H}_3$), 1.66 (s, 3H, C$\underline{H}_3$C=), 3.10 (m, 1H, OC$\underline{H}$), 4.05 (d, 1H, *J* = 3.81 Hz, OOC$\underline{H}$), 5.06 (m, 2H, C$\underline{H}_2$=), 5.67 (q, 1H, J = 5.31 Hz, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional signals of both minor diastreomers **44b**,**c**)

δ (ppm) = 3.6/6.5 (t, $\underline{C}H_2$), 8.0/11.6 (d, $\underline{C}H(CH_2)_2$), 18.0 (q, $\underline{C}H_3$) 19.8/22.9 (q, $\underline{C}H_3C$=), 78.7/81.4 (d, O$\underline{C}$H), 83.5/84.0 (d, OO$\underline{C}$H), 95.9/101.4 (d, O$\underline{C}$HOO), 111.9/118.1 (t, $\underline{C}H_2$=C), 138.9/141.8 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Cyclopropyl-3-ethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (45a)

(elid 493u) major



Following **GP-15**, a solution of 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (1.20 g, 7.59 mmol) and propionaldehyde diethylacetal (1.0 g, 7.58 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (0.67 g, 3.38 mmol, 45 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.76) afforded colorless oil composed of a diastereomeric mixture of the pure 1,2,4-trioxanes **45a** as major product and **45b**,**c** as minor products (315 mg, 1.59 mmol, 21 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, **45a**)

δ (ppm) = 0.31-0.62 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.79 (m, 1H, C$\underline{H}$(CH_2)$_2$), 0.90 (t, 3H, *J* = 7.50 Hz, C$\underline{H_3}$$CH_2$), 1.56 (dq, 2H, *J* = 5.31, 7.50 Hz, C$\underline{H_2}$$CH_3$), 1.75 (m, 3H, C$\underline{H_3}$C=), 3.08 (dd, 1H, *J* = 7.65, 9.09 Hz, OC$\underline{H}$), 4.41 (d, 1H, *J* = 9.09 Hz, OOC$\underline{H}$), 5.01 (m, 2H, C$\underline{H_2}$=), 5.08 (t, 1H, *J* = 5.37 Hz, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, **45a**)

δ (ppm) = 1.6 (t, $\underline{C}H_2$), 2.6 (t, $\underline{C}H_2$), 8.1 (q, $\underline{C}H_3CH_2$), 11.4 (d, $\underline{C}H(CH_2)_2$), 20.4 (q, $\underline{C}H_3C$=), 25.3 (t, $\underline{C}H_2CH_3$), 80.3 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 105.1 (d, O$\underline{C}$HOO), 117.0 (t, $\underline{C}H_2$=C), 139.3 (s, $\underline{C}$=CH_2).

IR: (Film)

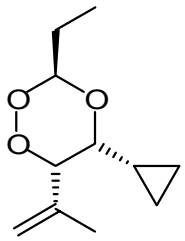
ν (cm^{-1}) = 3085, 3009, 2973, 2927, 2881, 1653, 1648, 1116, 1088, 1047, 943, 904.

Elemental Analysis: ($C_{11}H_{18}O_3$, M = 198.26)

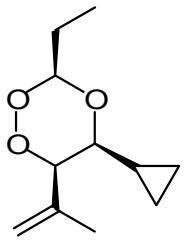
Calcd: C 66.64 H 9.15

Found: C 66.55 H 9.15

(3RS,5RS,6RS)-5-Cyclopropyl-3-ethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (45b)
and (3RS,5RS,6SR)-5-cyclopropyl-3-ethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (45c)



45b



45c

^{1}H-NMR: (300 MHz, $CDCl_3$, additional signals of both minor diastreomers **45b**,**c**)

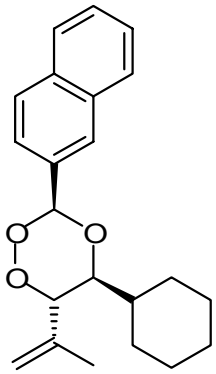
δ (ppm) = 0.91 (t, 3H, *J* = 7.62 Hz, C$\underline{H_3}$$CH_2$), 1.57 (m, 2H, C$\underline{H_2}$$CH_3$), 1.68 (m, 3H, C$\underline{H_3}$C=), 3.10 (m, 1H, OC$\underline{H}$), 4.07 (d, 1H, *J* = 3.84 Hz, OOC$\underline{H}$), 4.87 (m, 2H, C$\underline{H_2}$=), 5.48 (t, 1H, J = 5.37 Hz, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, signals of both minor diastreomers **45b**,**c**)

δ (ppm) = 1.4/1.7 (t, $\underline{C}H_2$), 3.6/6.7 (t, $\underline{C}H_2$), 7.9/8.0 (q, $\underline{C}H_3CH_2$), 8.1/11.6 (d, $\underline{C}H(CH_2)_2$), 19.8/22.0 (q, $\underline{C}H_3C$=), 25.3/25.7 (t, $\underline{C}H_2CH_3$), 78.6/81.4 (d, O$\underline{C}$H), 83.8/84.3 (d, OO$\underline{C}$H), 99.9/105.4 (d, O$\underline{C}$HOO), 111.9/118.1 (t, $\underline{C}H_2$=C), 139.0/141.9 (s, $\underline{C}$=CH_2).

4.6.2 Derived from 1-cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol (7q)

(3RS,5RS,6RS)-5-Cyclohexyl-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (46)
(elid 493t)



Following **GP-15**, a solution of 1-cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7q)** (1.20 g, 6.0 mmol) and β-naphthaldehyde (0.94 g, 6.03 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, $R_f = 0.65$) afforded the pure 1,2,4-trioxanes (0.83 mg, 2.46 mmol, 41 %) as white solid.

M.p. 88-90 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.06-1.94 (m, 11H, C<u>H</u> and C<u>H</u>$_2$), 1.85 (s, 3H, C<u>H</u>$_3$C=), 3.87 (d, 1H, *J* = 9.54 Hz, OC<u>H</u>), 4.87 (d, 1H, *J* = 9.54 Hz, OOC<u>H</u>), 5.18 (m, 2H, C<u>H</u>$_2$=), 6.38 (s, 1H, OC<u>H</u>OO), 7.47-8.02 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (q, <u>C</u>H$_3$C=), 26.2 (t, <u>C</u>H$_2$), 26.2 (t, <u>C</u>H$_2$), 26.3 (t, <u>C</u>H$_2$), 26.5 (t, <u>C</u>H$_2$), 30.1 (t, <u>C</u>H$_2$), 38.4 (d, <u>C</u>H), 81.4 (d, O<u>C</u>H), 85.2 (d, OO<u>C</u>H), 104.1 (d, O<u>C</u>HOO), 118.5 (t, <u>C</u>H$_2$=C), 124.1 (d, <u>C</u>H$_{arom}$), 126.1 (d, <u>C</u>H$_{arom}$), 126.6 (d, <u>C</u>H$_{arom}$), 126.9 (d, <u>C</u>H$_{arom}$), 127.6 (d, <u>C</u>H$_{arom}$), 128.0 (d, <u>C</u>H$_{arom}$), 128.4 (d, <u>C</u>H$_{arom}$), 132.1 (s, <u>C</u>q$_{arom}$), 132.8 (s, <u>C</u>q$_{arom}$), 133.9 (s, <u>C</u>q$_{arom}$), 138.9 (s, <u>C</u>=CH$_2$).

IR: (CsI)

ν (cm^{-1}) = 2933, 2856, 1653, 1647, 1605, 1560, 1112, 1074, 1004, 906, 822.

MS: (EI, 70 eV)

m/z (%) = 338 (M^+, 1), 226 (M^+-$C_5H_{10}O$, 2), 156 ($C_{11}H_8O^+$, 95), 155 ($C_{11}H_7O^+$, 96), 128 ($C_{10}H_8^+$, 27), 127 ($C_{10}H_7^+$, 100), 83 ($C_6H_{11}^+$, 17).

HRMS: (EI, 70 eV, $C_{22}H_{26}O_3$)

Calcd: M = 338.188 g/mol

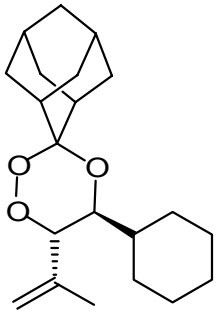
Found: M = 338.188 ±0.005 g/mol

Elemental Analysis: ($C_{22}H_{26}O_3$, M = 338.44)

Calcd: C 78.07 H 7.74

Found: C 77.49 H 7.90

(5RS,6RS)-5-Cyclohexyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (47) (elid 496i, 500h)



Following **GP-15**, a solution of 1-cyclohexyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7q)** (1.20 g, 6.0 mmol) and adamantanone (0.91 g, 6.07 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.69) afforded the 1,2,4-trioxanes **47** and **48** in a ratio 3:1, respectively, as colorless oil (0.20 g, 10 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.92-2.12 (m, 24H, C<u>H</u> and C<u>H$_2$</u>), 1.73 (s, 3H, C<u>H$_3$</u>C=), 2.88 (br. s, 1H, C<u>H</u>), 3.77 (d, 1H, *J* = 9.93 Hz, OC<u>H</u>), 4.49 (d, 1H, *J* = 9.93 Hz, OOC<u>H</u>), 5.05 (m, 2H, C<u>H$_2$</u>=).

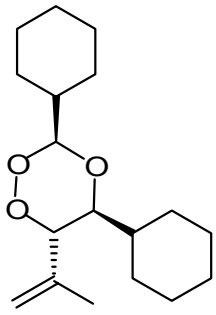
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.9 (q, <u>C</u>H$_3$C=), 25.6 (t, cyclohexane <u>C</u>H$_2$), 26.2 (t, cyclohexane <u>C</u>H$_2$), 26.4 (t, cyclohexane <u>C</u>H$_2$), 26.6 (t, cyclohexane <u>C</u>H$_2$), 27.2 (d, <u>C</u>H), 27.3 (d, <u>C</u>H), 29.6 (d, <u>C</u>H), 30.4 (t, cyclohexane <u>C</u>H$_2$), 32.9 (t, adamantane <u>C</u>H$_2$), 33.3 (t, adamantane <u>C</u>H$_2$), 33.3 (t, adamantane <u>C</u>H$_2$), 33.6 (t, adamantane <u>C</u>H$_2$), 36.6 (d, <u>C</u>H), 37.2 (t, adamantane <u>C</u>H$_2$), 38.2 (d, cyclohexane <u>C</u>H), 72.3 (d, O<u>C</u>H), 84.9 (d, OO<u>C</u>H), 104.5 (s, O<u>C</u>OO), 117.7 (t, <u>C</u>H$_2$=C), 139.6 (s, <u>C</u>=CH$_2$).

IR: (Film)

ν (cm^{-1}) = 3080, 2922, 2851, 1648, 1450, 1111, 1097, 1071, 1026, 1005, 926, 908.

(3RS,5RS,6RS)-3,5-Dicyclohexyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (48)



^{1}H-NMR: (300 MHz, $CDCl_3$)

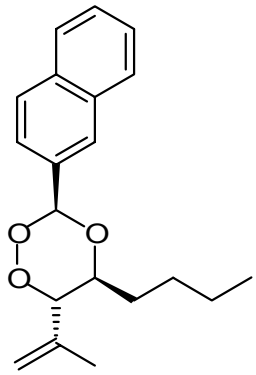
δ (ppm) = 0.92-2.12 (m, 22H, C<u>H</u> and C<u>H$_2$</u>), 1.71 (s, 3H, C<u>H$_3$</u>C=), 3.48 (d, 1H, *J* = 9.63 Hz, OC<u>H</u>), 4.54 (d, 1H, *J* = 9.51 Hz, OOC<u>H</u>), 4.95 (d, 1H, *J* = 5.55 Hz, OC<u>H</u>OO), 5.05 (m, 2H, C<u>H$_2$</u>=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (q, <u>C</u>H$_3$C=), 25.7 (t, <u>C</u>H$_2$), 25.7 (t, <u>C</u>H$_2$), 25.8 (t, <u>C</u>H$_2$), 26.0 (t, <u>C</u>H$_2$), 26.2 (t, <u>C</u>H$_2$), 26.3 (t, <u>C</u>H$_2$), 26.5 (t, <u>C</u>H$_2$), 27.1 (t, <u>C</u>H$_2$), 27.3 (t, <u>C</u>H$_2$), 30.1 (t, <u>C</u>H$_2$), 38.3 (d, <u>C</u>H), 40.6 (d, <u>C</u>H), 80.6 (d, O<u>C</u>H), 85.2 (d, OO<u>C</u>H), 107.1 (d, O<u>C</u>HOO), 118.1 (t, <u>C</u>H$_2$=C), 139.1 (s, <u>C</u>=CH$_2$).

4.6.3 Derived from 3-hydroperoxy-2-methyloct-1-en-4-ol (7g)

(3RS,5RS,6RS)-5-Butyl-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (49)
(elid 464k)



Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.24 g, 7.13 mmol) and β-naphthaldehyde (1.11 g, 7.12 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.85) afforded the pure 1,2,4-trioxane (0.96 g, 3.08 mmol, 43 %) as viscous oil which crystallizes on standing.

M.p. 51-53 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.96 (t, 3H, *J* = 7.20 Hz, $C\underline{H_3}CH_2$), 1.25-1.70 (m, 6H, $C\underline{H_2}$), 1.85 (s, 3H, $C\underline{H_3}C$=), 4.01 (m, 1H, OC<u>H</u>), 4.64 (d, 1H, *J* = 9.26 Hz, OOC<u>H</u>), 5.18 (m, 1H, $C\underline{H_2}$=), 5.22 (s, 1H, $C\underline{H_2}$=), 6.41 (s, 1H, OC<u>H</u>OO), 7.49-8.05 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 19.7 (q, $\underline{C}H_3C$=), 22.6 (t, $\underline{C}H_2CH_3$), 27.0 (t, $\underline{C}H_2CH_2$), 30.1 (t, $\underline{C}H_2CH_2$), 77.4 (d, O<u>C</u>H), 87.7 (d, OO<u>C</u>H), 104.1 (d, O<u>C</u>HOO), 118.5 (t, $\underline{C}H_2$=C), 124.1 (d, CH_{arom}), 126.1 (d, CH_{arom}), 126.6 (d, CH_{arom}), 126.8 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.1 (d, CH_{arom}), 128.4 (d, CH_{arom}), 132.0 (s, Cq_{arom}), 132.8 (s, Cq_{arom}), 133.9 (s, Cq_{arom}), 138.8 (s, $\underline{C}$=CH_2).

MS: (EI, 70 eV)

m/z (%) = 312 (M^+, 1), 226 (M^+-$C_5H_{10}O$, less than 1), 156 ($C_{11}H_8O^+$, 100), 155 ($C_{11}H_7O^+$, 93), 127 ($C_{10}H_7^+$, 72), 124 ($C_9H_{16}^+$, 38).

HRMS: (EI, 70 eV, $C_{20}H_{24}O_3$)

Calcd: M = 312.173 g/mol

Found: M = 312.173 ±0.005 g/mol

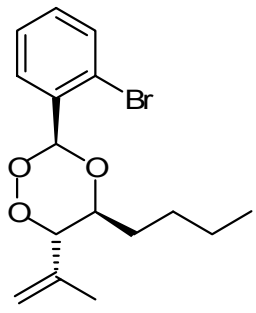
Elemental Analysis: ($C_{20}H_{24}O_3$, M = 312.40)

Calcd: C 76.89 H 7.74

Found: C 76.61 H 7.78

(3RS,5RS,6RS)-3-(2-Bromophenyl)-5-butyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (50)

(elid 464m, 492l)



Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.24 g, 7.13 mmol) and 2-bromobenzaldehyde (1.30 g, 7.03 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.83) afforded the pure 1,2,4-trioxane (0.69 g, 2.02 mmol, 29 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.82 (t, 3H, *J* = 7.20 Hz, C$\underline{H_3}$CH$_2$), 1.17-1.55 (m, 6H, C$\underline{H_2}$), 1.72 (m, 3H, C$\underline{H_3}$C=), 3.88 (m, 1H, OC$\underline{H}$), 4.48 (d, 1H, *J* = 9.24 Hz, OOC$\underline{H}$), 5.06 (m, 1H, C$\underline{H_2}$=), 5.09 (s, 1H, C$\underline{H_2}$=), 6.42 (s, 1H, OC$\underline{H}$OO), 7.12-7.60 (m, 4H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 19.8 (q, $\underline{C}H_3C$=), 22.5 (t, $\underline{C}H_2CH_3$), 26.9 (t, $\underline{C}H_2CH_2$), 30.1 (t, $\underline{C}H_2CH_2$), 77.5 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 103.1 (d, O$\underline{C}$HOO), 118.6 (t, $\underline{C}H_2$=C), 123.2 (s, Cq_{arom}), 127.4 (d, CH_{arom}), 128.9 (d, CH_{arom}), 131.1 (d, CH_{arom}), 132.7 (d, CH_{arom}), 133.8 (s, Cq_{arom}), 138.6 (s, $\underline{C}$=CH_2).

IR: (Film)

ν (cm^{-1}) = 3078, 2955, 2930, 2871, 1651, 1647, 1570, 1125, 1081, 1025, 1000, 948, 911.

MS: (EI, 70 eV)

m/z (%) = 342/340 (M^+, not observed), 256/254 (M^+-$C_5H_{10}O$, 2), 186 ($C_7H_5{}^{81}Br^+$, 73), 185 ($C_7H_4{}^{81}Br^+$, 100), 184 ($C_7H_5{}^{79}Br^+$, 80), 183 ($C_7H_4{}^{79}Br^+$, 50), 157 ($C_6H_4{}^{81}Br^+$, 28), 155 ($C_6H_4{}^{79}Br^+$, 25), 124 ($C_9H_{16}{}^+$, 57), 95 ($C_7H_{11}{}^+$, 30), 76 ($C_6H_4{}^+$, 55), 69 ($C_4H_5O^+$, 51), 51 ($C_4H_3{}^+$, 32), 50 ($C_4H_2{}^+$, 31).

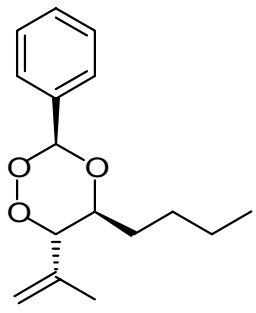
Elemental Analysis: ($C_{16}H_{21}BrO_3$, M = 341.24)

Calcd: C 56.32 H 6.20

Found: C 56.33 H 6.33

(3RS,5RS,6RS)-5-Butyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (51)

(elid 464v, 491r,v)



Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.32 g, 7.59 mmol) and benzaldehyde dimethylacetal (1.15 g, 7.57 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, $R_f = 0.76$) afforded the pure 1,2,4-trioxane (0.96 g, 3.66 mmol, 48 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.91 (t, 3H, *J* = 7.21 Hz, C<u>H</u>$_3$CH$_2$), 1.23-1.61 (m, 6H, C<u>H</u>$_2$), 1.80 (m, 3H, C<u>H</u>$_3$C=), 3.92 (m, 1H, OC<u>H</u>), 4.54 (d, 1H, *J* = 9.27 Hz, OOC<u>H</u>), 5.13 (m, 1H, C<u>H</u>$_2$=), 5.16 (s, 1H, C<u>H</u>$_2$=), 6.22 (s, 1H, OC<u>H</u>OO), 7.37-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, <u>C</u>H$_3$CH$_2$), 19.7 (q, <u>C</u>H$_3$C=), 22.6 (t, <u>C</u>H$_2$CH$_3$), 27.0 (t, <u>C</u>H$_2$CH$_2$), 30.1 (t, <u>C</u>H$_2$CH$_2$), 77.3 (d, O<u>C</u>H), 87.6 (d, OO<u>C</u>H), 104.0 (d, O<u>C</u>HOO), 118.5 (t, <u>C</u>H$_2$=C), 126.9 (d, CH_{arom}), 128.3 (d, CH_{arom}), 129.7 (d, CH_{arom}), 134.6 (s, Cq_{arom}), 138.8 (s, <u>C</u>=CH$_2$).

MS: (EI, 70 eV)

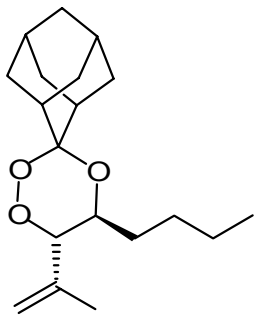
m/z (%) = 262 (M^+, not observed), 124 ($C_9H_{16}^+$, 13), 106 ($C_7H_6O^+$, 32), 105 ($C_7H_5O^+$, 100), 77 ($C_6H_5^+$, 33), 51 ($C_4H_3^+$, 13).

Elemental Analysis: ($C_{16}H_{22}O_3$, M = 262.34)

Calcd: C 73.25 H 8.45

Found: C 73.11 H 8.46

(5RS,6RS)-5-*n*-Butyl-6-(prop-1-en-2yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (52) (elid 437a)



Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (0.49 g, 2.82 mmol) and adamantanone (0.52 g, 3.47 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by

preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.88) afforded the pure 1,2,4-trioxane (0.10 g, 0.33 mmol, 12 %) as viscous colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

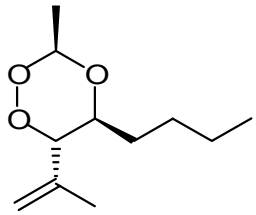
δ (ppm) = 0.88 (t, 3H, *J* = 7.35 Hz, C<u>H</u>$_3$CH$_2$), 1.15-2.10 (m, 17H, C<u>H</u> and CH$_2$), 1.73 (m, 3H, C<u>H</u>$_3$C=), 2.90 (m, 1H, C<u>H</u>), 3.86 (m, 1H, OC<u>H</u>), 4.24 (d, 1H, *J* = 9.55 Hz, OOC<u>H</u>), 5.05 (m, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.0 (q, <u>C</u>H$_3$CH$_2$), 19.8 (q, <u>C</u>H$_3$C=), 22.6 (t, <u>C</u>H$_2$CH$_3$), 27.1 (t, <u>C</u>H$_2$CH$_2$), 27.2 (d, <u>C</u>H), 27.3 (d, <u>C</u>H), 29.8 (d, <u>C</u>H), 30.6 (t, <u>C</u>H$_2$CH$_2$), 36.7 (d, <u>C</u>H), 33.0 (t, <u>C</u>H$_2$), 33.3 (t, <u>C</u>H$_2$), 33.4 (t, <u>C</u>H$_2$), 33.6 (t, <u>C</u>H$_2$), 37.2 (t, <u>C</u>H$_2$), 68.6 (d, O<u>C</u>H), 87.7 (d, OO<u>C</u>H), 104.8 (s, O<u>C</u>OO), 117.9 (t, <u>C</u>H$_2$=C), 139.4 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-5-Butyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (53)

(elid 464s)



Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.22 g, 7.01 mmol) and acetaldehyde diethylacetal (0.83 g, 7.03 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.84) afforded the pure 1,2,4-trioxane (0.37 g, 1.85 mmol, 26 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

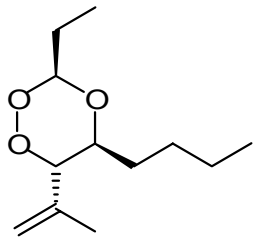
δ (ppm) = 0.87 (t, 3H, *J* = 7.05 Hz, C<u>H</u>$_3$CH$_2$), 1.19-1.57 (m, 6H, C<u>H</u>$_2$), 1.26 (d, 3H, *J* = 5.44 Hz, C<u>H</u>$_3$CH), 1.70 (m, 3H, C<u>H</u>$_3$C=), 3.65 (m, 1H, OC<u>H</u>), 4.33 (d, 1H, *J* = 9.26 Hz, OOC<u>H</u>), 5.05 (m, 2H, C<u>H</u>$_2$=), 5.36 (q, 1H, *J* = 5.44 Hz, O<u>C</u>HOO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, <u>C</u>H$_3$CH$_2$), 17.9 (<u>C</u>H$_3$CH), 19.7 (q, <u>C</u>H$_3$C=), 22.6 (t, <u>C</u>H$_2$CH$_3$), 27.0 (t, <u>C</u>H$_2$CH$_2$), 30.1 (t, <u>C</u>H$_2$CH$_2$), 76.8 (d, O<u>C</u>H), 87.4 (d, OO<u>C</u>H), 101.5(d, O<u>C</u>HOO), 118.3 (t, <u>C</u>H$_2$=C), 138.8 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-5-Butyl-3-ethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (54)

(elid 464t, 491y)



Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.27 g, 7.30 mmol) and propionaldehyde diethylacetal (0.96 g, 7.27 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, $R_f = 0.79$) afforded the pure 1,2,4-trioxane (0.41 g, 1.92 mmol, 26 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.87 (t, 3H, *J* = 7.35 Hz, C<u>H</u>$_3$(CH$_2$)$_3$), 0.94 (t, 3H, *J* = 7.65 Hz, C<u>H</u>$_3$CH$_2$), 1.15-1.64 (m, 8H, C<u>H</u>$_2$), 1.71 (m, 3H, C<u>H</u>$_3$C=), 3.65 (m, 1H, OC<u>H</u>), 4.32 (d, 1H, *J* = 9.12 Hz, OOC<u>H</u>), 5.05 (m, 2H, C<u>H</u>$_2$=), 5.16 (t, 1H, *J* = 5.43 Hz, O<u>C</u>HOO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 8.2 (q, <u>C</u>H$_3$CH$_2$), 13.9 (q, <u>C</u>H$_3$(CH$_2$)$_3$), 19.7 (q, <u>C</u>H$_3$C=), 22.6 (t, CH$_3$<u>C</u>H$_2$(CH$_2$)$_2$), 25.4 (t, <u>C</u>H$_2$CH$_3$), 27.1 (t, <u>C</u>H$_2$CH$_2$), 30.1 (t, <u>C</u>H$_2$CH$_2$), 76.7 (d, O<u>C</u>H), 87.7 (d, OO<u>C</u>H), 105.5 (d, O<u>C</u>HOO), 118.2 (t, <u>C</u>H$_2$=C), 138.9 (s, <u>C</u>=CH$_2$).

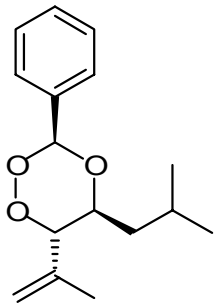
IR: (Film)

ν (cm^{-1}) = 2962, 2875, 1653, 1260, 1096, 1020, 865, 800.

4.6.4 Derived from 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol (7h)

(3RS,5RS,6RS)-5-Isobutyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (55)

(elid 408c, 467c, 492q)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (0.87 g, 5.0 mmol) and benzaldehyde (0.53 g, 5.0 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (0.74 g, 2.82 mmol, 56.5 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) affords the 1,2,4-trioxane (0.26 g, 1.0 mmol, 20 %) as an oil

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.93 (d, 3H, *J* = 6.63 Hz, C$\underline{H_3}$CH), 0.96 (d, 3H, *J* = 6.78 Hz, C$\underline{H_3}$CH), 1.25 (m, 1H, C$\underline{H_2}$CH), 1.57 (m, 1H, C$\underline{H_2}$CH), 1.79 (m, 3H, C$\underline{H_3}$C=), 1.97 (m, 1H, C$\underline{H}$CH$_2$), 4.0 (ddd, 1H, *J* = 2.34, 9.24, 12.04 Hz, OC$\underline{H}$), 4.51 (d, 1H, *J* = 9.24 Hz, OOC$\underline{H}$), 5.13 (m, 2H, C$\underline{H_2}$=), 6.22 (s, 1H, OC$\underline{H}$OO), 7.36-7.52 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (q, $\underline{C}H_3C$=), 21.5 (q, $\underline{C}H_3CH$), 23.6 (d, $\underline{C}HCH_2$), 23.7 (q, $\underline{C}H_3CH$), 39.2 (t, $\underline{C}H_2CH$), 75.6 (d, O$\underline{C}$H), 88.1 (d, OO$\underline{C}$H), 103.9 (d, O$\underline{C}$HOO), 118.7 (t, $\underline{C}H_2$=C), 126.9 (d, $\underline{C}H_{arom}$), 128.3 (d, $\underline{C}H_{arom}$), 129.7 (d, $\underline{C}H_{arom}$), 134.6 (s, Cq_{arom}), 138.7 (s, $\underline{C}$=CH$_2$).

MS: (EI, 70 eV)

m/z (%) = 262 (M^+, not observed), 106 ($C_7H_6O^+$, 30), 105 ($C_7H_5O^+$, 100), 77 ($C_6H_5^+$, 35), 51 ($C_4H_3^+$, 13).

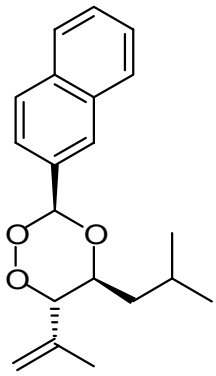
Elemental Analysis: ($C_{16}H_{22}O_3$, M = 262.34)

Calcd: C 73.25 H 8.45

Found: C 73.02 H 8.43

(3RS,5RS,6RS)-5-Isobutyl-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (56)

(elid 493n)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.21 g, 6.95 mmol) and β-naphthaldehyde (1.09 g, 6.99 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.71) affords the 1,2,4-trioxane (0.46 g, 1.47 mmol, 21 %) as an oil which crystallizes on standing to white solid.

M.p. 60-62 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.01 (d, 3H, *J* = 6.60 Hz, C$\underline{H_3}$CH), 1.04 (d, 3H, *J* = 6.75 Hz, C$\underline{H_3}$CH), 1.33 (m, 1H, C$\underline{H_2}$CH), 1.70 (m, 1H, C$\underline{H_2}$CH), 1.87 (s, 3H, C$\underline{H_3}$C=), 2.08 (m, 1H, C$\underline{H}$CH$_2$), 4.12 (ddd, 1H, *J* = 2.34, 9.09, 10.32 Hz, OC$\underline{H}$), 4.65 (d, 1H, *J* = 9.09 Hz, OOC$\underline{H}$), 5.19 (m, 1H, C$\underline{H_2}$=), 5.24 (m, 1H, C$\underline{H_2}$=), 6.45 (s, 1H, OC$\underline{H}$OO), 7.49-8.07 (m, 5H, H_{arom}) .

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.6 (q, $\underline{C}H_3C$=), 21.5 (q, $\underline{C}H_3CH$), 23.6 (d, $\underline{C}HCH_2$), 23.7 (q, $\underline{C}H_3CH$), 39.2 (t, $\underline{C}H_2CH$), 75.6 (d, O$\underline{C}$H), 88.0 (d, OO$\underline{C}$H), 104.0 (d, O$\underline{C}$HOO), 118.7 (t, $\underline{C}H_2$=), 124.0 (d, $\underline{C}H_{arom}$), 126.1 (d, $\underline{C}H_{arom}$), 126.6 (d, $\underline{C}H_{arom}$), 126.7 (d, $\underline{C}H_{arom}$), 127.6 (d, $\underline{C}H_{arom}$), 128.0 (d, $\underline{C}H_{arom}$), 128.3 (d, $\underline{C}H_{arom}$), 131.9 (s, Cq_{arom}), 132.8 (s, Cq_{arom}), 133.9 (s, Cq_{arom}), 138.6 (s, $\underline{C}$=CH$_2$).

IR: (CsI)

ν (cm^{-1}) = 3095, 2956, 2934, 1605, 1347, 1098, 1080, 997, 863, 817.

MS: (EI, 70 eV)

m/z (%) = 312 (M^+, 3), 226 (M^+-$C_5H_{10}O$, 2), 156 ($C_{11}H_8O^+$, 100), 155 ($C_{11}H_7O^+$, 97), 128 ($C_{10}H_8^+$, 30), 127 ($C_{10}H_7^+$, 70), 124 ($C_9H_{16}^+$, 27), 109 ($C_8H_{13}^+$, 17).

HRMS: (EI, 70 eV, $C_{20}H_{24}O_3$)

Calcd: M = 312.173 g/mol

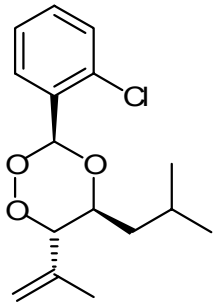
Found: M = 312.173 ±0.005 g/mol

Elemental Analysis: ($C_{20}H_{24}O_3$, M = 312.40 g/mol)

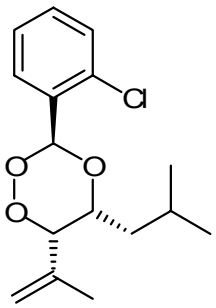
Calcd: C 76.89 H 7.74

Found: C 76.61 H 7.63

(3RS,5RS,6RS)-3-(2-Chlorophenyl)-5-isobutyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (57a) and (3RS,5SR,6RS)-3-(2-chlorophenyl)-5-isobutyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (57b) (elid 450k)



57a



57b

Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.42 g, 8.16 mmol) and 2-chlorobenzaldehyde (1.40 g, 9.69 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) afforded a diastereomeric mixture of the 1,2,4-trioxanes **57a**,**b** in a ratio 88:12 (0.46 g, 1.55 mmol, 19 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **57a**)

δ (ppm) = 0.85 (d, 3H, *J* = 6.32 Hz, C$\underline{H_3}$CH), 0.87 (d, 3H, *J* = 6.47 Hz, C$\underline{H_3}$CH), 1.16 (m, 1H, C$\underline{H_2}$CH), 1.49 (m, 1H, C$\underline{H_2}$CH), 1.73 (m, 3H, C$\underline{H_3}$C=), 1.85 (m, 1H, C$\underline{H}$CH$_2$), 3.96 (ddd, 1H, *J* = 2.35, 9.26, 10.14 Hz, OC$\underline{H}$), 4.44 (d, 1H, *J* = 9.26 Hz, OOC$\underline{H}$), 5.06 (m, 2H, C$\underline{H_2}$=), 6.46 (s, 1H, OC$\underline{H}$OO), 7.17-7.60 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **57a**)

δ (ppm) = 19.7 (q, $\underline{C}H_3C$=), 21.4 (q, $\underline{C}H_3CH$), 23.6 (d, $\underline{C}HCH_2$), 23.7 (q, $\underline{C}H_3CH$), 39.2 (t, $\underline{C}H_2CH$), 75.9 (d, O$\underline{C}$H), 88.2 (d, OO$\underline{C}$H), 101.0 (d, O$\underline{C}$HOO), 118.9 (t, $\underline{C}H_2$=C), 126.8 (d, $\underline{C}H_{arom}$), 128.6 (d, $\underline{C}H_{arom}$), 129.5 (d, $\underline{C}H_{arom}$), 130.9 (d, $\underline{C}H_{arom}$), 132.2 (s, Cq_{arom}), 133.5 (s, Cq_{arom}), 138.6 (s, $\underline{C}$=CH_2).

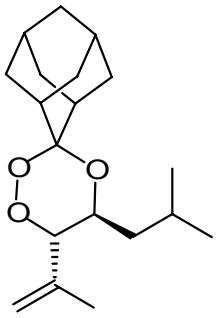
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of **57b**)

δ (ppm) = 1.38 (m, 1H, C$\underline{H_2}$CH), 2.02 (s, 3H, C$\underline{H_3}$C=), 4.06 (d, 1H, *J* = 3.82 Hz, OOC$\underline{H}$), 4.30 (m, 1H, OC$\underline{H}$), 6.50 (s, 1H, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of **57b**)

δ (ppm) = 75.6 (d, O$\underline{C}$H), 85.1 (d, OO$\underline{C}$H), 101.4 (d, O$\underline{C}$HOO), 118.7 (t, $\underline{C}H_2$=C), 126.9 (d, $\underline{C}H_{arom}$), 128.6 (d, $\underline{C}H_{arom}$), 129.5 (d, $\underline{C}H_{arom}$), 130.9 (d, $\underline{C}H_{arom}$), 132.4 (s, Cq_{arom}), 133.5 (s, Cq_{arom}), 141.6 (s, $\underline{C}$=CH_2).

(5RS,6RS)-5-Isobutyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (58) (elid 375f)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.70 g, 9.77 mmol) and adamantanone (2.10 g, 13.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.80) affords the 1,2,4-trioxane (0.28 g, 0.92 mmol, 10 %) as an oil which crystallizes on standing to white solid.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.87 (d, 3H, *J* = 6.63 Hz, C$\underline{H}_3$CH), 0.90 (d, 3H, *J* = 6.78Hz, C$\underline{H}_3$CH), 1.01-1.10 (m, 1H, C$\underline{H}_2$CH), 1.34 (m, 1H, C$\underline{H}_2$CH), 1.50-2.09 (m, 14H, C$\underline{H}$, C$\underline{H}_2$ and C$\underline{H}$(CH$_3$)$_2$), 1.72 (t, 3H, *J* = 1.17 Hz, C$\underline{H}_3$C=), 2.91 (br. d, 1H, C$\underline{H}$), 3.99 (ddd, 1H, *J* = 2.97, 9.54, 9.54 Hz, OC$\underline{H}$), 4.20 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (q, $\underline{C}H_3$C=), 21.4 (q, $\underline{C}H_3$CH), 23.5 (d, $\underline{C}$HCH$_2$), 23.8 (q, $\underline{C}H_3$CH), 27.2 (2 x d, CH), 29.9 (d, CH), 33.1 (t, CH$_2$), 33.3 (2 x t, CH$_2$), 33.5 (t, CH$_2$), 36.6 (d, CH), 37.2 (t, CH$_2$), 39.9 (t, $\underline{C}$H$_2$CH), 66.6 (d, O$\underline{C}$H), 87.8 (d, OO$\underline{C}$H), 104.7 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}$H$_2$=C), 139.3 (s, $\underline{C}$=CH$_2$).

MS: (EI, 20 eV)

m/z (%) = 150 ($C_{10}H_{14}O^+$, 100), 124 ($C_9H_{16}^+$, 27).

HRMS: (EI, 70 eV, $C_{19}H_{30}O_3$)

Calcd: M = 306.2195 g/mol

Found: M = 306.219 ± 0.005 g/mol

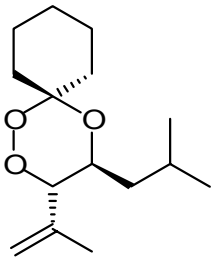
Elemental Analysis: ($C_{19}H_{30}O_3$, M = 306.44 g/mol)

Calcd: C 74.47 H 9.87

Found: C 74.06 H 9.78

(3RS,4RS)-4-Isobutyl-3-isopropenyl-1,2,5-trioxa-spiro[5.5]undecane (59)

(elid 368i)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (0.75 g, 4.31 mmol) and cyclohexanone (0.41 g, 4.18 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of excess ketone affords the 1,2,4-trioxane **No** (0.52 g, 2.05 mmol, 48 %) as an oil

^{1}H-NMR: (300 MHz, $CDCl_3$)

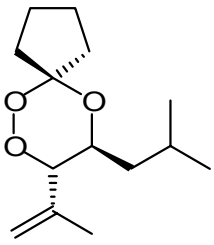
δ (ppm) = 0.87 (d, 3H, *J* = 6.60 Hz, C$\underline{H_3}$CH), 0.90 (d, 3H, *J* = 6.60 Hz, C$\underline{H_3}$CH), 1.05 (m, 1H, C$\underline{H_2}$CH), 1.34 (m, 1H, C$\underline{H_2}$CH), 1.30-1.65 (m, 8H, C$\underline{H_2}$), 1.73 (m, 3H, C$\underline{H_3}$C=), 1.85 (m, 1H, C$\underline{H}$CH$_2$), 2.0 (m, 1H, C$\underline{H_2}$), 2.18 (m, 1H, C$\underline{H_2}$), 3.98 (ddd, 1H, *J* = 2.37, 9.54, 10.14 Hz, OC$\underline{H}$), 4.22 (d, 1H, *J* = 9.56 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (q, $\underline{C}H_3C$=), 21.3 (q, $\underline{C}H_3CH$), 22.3 (t, $\underline{C}H_2$), 22.5 (t, $\underline{C}H_2$), 23.6 (d, $\underline{C}HCH_2$), 23.7 (q, $\underline{C}H_3CH$), 25.7 (t, $\underline{C}H_2$), 29.4 (t, $\underline{C}H_2$), 35.1 (t, $\underline{C}H_2$), 39.7 (t, $\underline{C}H_2CH$), 67.2 (d, O$\underline{C}$H), 88.0 (d, OO$\underline{C}$H), 102.8 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}H_2$=C), 139.3 (s, $\underline{C}$=CH_2).

(8RS,9RS)-9-Isobutyl-8-isopropenyl-6,7,10-trioxa-spiro[4.5]decane (60)

(elid 368j, 389a)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.04 g, 5.98 mmol) and cyclopentanone (0.50 g, 5.95 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of excess ketone affords the crude

product (0.50 g, 2.08 mmol, 35 %) as yellow oil which is further purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) to afford the pure 1,2,4-trioxane (0.16 g, 0.67 mmol, 11 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

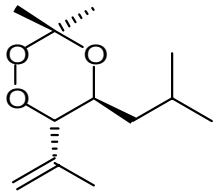
δ (ppm) = 0.84 (d, 3H, *J* = 6.45 Hz, $C\underline{H_3}CH$), 0.88 (d, 3H, *J* = 6.75 Hz, $C\underline{H_3}CH$), 1.05 (m, 1H, $C\underline{H_2}CH$), 1.34 (m, 1H, $C\underline{H_2}CH$), 1.48-1.90 (m, 8H, $C\underline{H}CH_2$ and $C\underline{H_2}$), 1.71 (t, 3H, *J* = 1.17 Hz, $C\underline{H_3}C$=), 2.51 (m, 1H, $C\underline{H_2}$), 3.85 (ddd, 1H, *J* = 2.52, 9.39, 10.14 Hz, $OC\underline{H}$), 4.29 (d, 1H, *J* = 9.39 Hz, $OOC\underline{H}$), 5.03 (m, 2H, $C\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.5 (q, $\underline{C}H_3C$=), 21.2 (q, $\underline{C}H_3CH$), 23.1 (d, $\underline{C}HCH_2$), 23.5 (q, $\underline{C}H_3CH$), 23.6 (t, $\underline{C}H_2$), 24.7 (t, $\underline{C}H_2$), 32.9 (t, $\underline{C}H_2$), 37.3 (t, $\underline{C}H_2$), 39.3 (t, $\underline{C}H_2CH$), 70.1 (d, $O\underline{C}H$), 87.9 (d, $OO\underline{C}H$), 114.7 (s, $O\underline{C}OO$), 118.1 (t, $\underline{C}H_2$=C), 138.7 (s, $\underline{C}$=CH_2).

(5RS,6RS)-5-Isobutyl-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (61)

(elid 368a, 476y)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.50 g, 8.62 mmol) and excess acetone (2.0 g, 34.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.88) affords the 1,2,4-trioxane (0.60 g, 2.80 mmol, 33 %) as colorless oil

^{1}H-NMR: (300 MHz, $CDCl_3$)

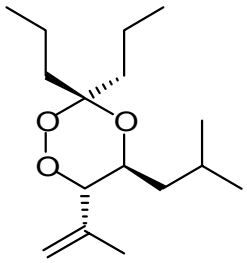
δ (ppm) = 0.81 (d, 3H, *J* = 6.61 Hz, $C\underline{H_3}CH$), 0.84 (d, 3H, *J* = 6.77 Hz, $C\underline{H_3}CH$), 1.01 (m, 1H, $C\underline{H_2}CH$), 1.28 (s, 3H, $C\underline{H_3}$), 1.33 (m, 1H, $C\underline{H_2}CH$), 1.59 (s, 3H, $C\underline{H_3}$), 1.70 (m, 3H, $C\underline{H_3}C$=), 1.80 (m, 1H, $C\underline{H}CH_2$), 3.93 (ddd, 1H, *J* = 2.50, 8.0, 9.55 Hz, $OC\underline{H}$), 4.17 (d, 1H, *J* = 9.55 Hz, $OOC\underline{H}$), 5.0 (m, 2H, $C\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.4 (q, $\underline{C}H_3C$=), 20.3 (q, $\underline{C}H_3$), 21.1 (q, $\underline{C}H_3CH$), 23.4 (d, $\underline{C}HCH_2$), 23.6 (q, $\underline{C}H_3CH$), 25.8 (q, $\underline{C}H_3$), 39.5 (t, $\underline{C}H_2CH$), 68.0 (d, O$\underline{C}$H), 87.8 (d, OO$\underline{C}$H), 102.6 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}H_2$=C), 139.1 (s, $\underline{C}$=CH_2).

(5RS,6RS)-5-Isobutyl-6-(prop-1-en-2-yl)-3,3-dipropyl-1,2,4-trioxane (62)

(elid 402b)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.0 g, 5.75 mmol) and 4-heptanone (0.66 g, 5.79 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) affords the 1,2,4-trioxane (0.28 g, 1.0 mmol, 18 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

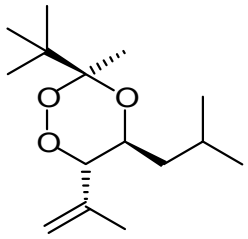
δ (ppm) = 0.84-0.97 (m, 12 H, 2 x $C\underline{H}_3CH$ and 2 x $C\underline{H}_3CH_2$), 1.06 (m, 1H, $C\underline{H}_2CH$), 1.22-1.57 (m, 8H, $C\underline{H}_2CH$ and $C\underline{H}_2C\underline{H}_2$), 1.73 (s, 3H, $C\underline{H}_3C$=), 1.83 (m, 1H, $C\underline{H}CH_2$), 1.99 (m, 1H, $C\underline{H}_2CH_2$), 3.95 (ddd, 1H, *J* = 2.22, 9.54, 9.99 Hz, OC$\underline{H}$), 4.17 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.04 (m, 2H, $C\underline{H}_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.4 (q, $\underline{C}H_3CH_2$), 14.5 (q, $\underline{C}H_3CH_2$), 15.9 (t, $\underline{C}H_2CH_3$), 17.1 (t, $\underline{C}H_2CH_3$), 19.7 (q, $\underline{C}H_3C$=), 21.4 (q, $\underline{C}H_3CH$), 23.6 (d, $\underline{C}HCH_2$), 23.7 (q, $\underline{C}H_3CH$), 32.8 (t, $\underline{C}H_2CH_2$), 38.2 (t, $\underline{C}H_2CH_2$), 39.8 (t, $\underline{C}H_2CH$), 67.4 (d, O$\underline{C}$H), 87.8 (d, OO$\underline{C}$H), 105.6 (s, O$\underline{C}$OO), 117.9 (t, $\underline{C}H_2$=C), 139.4 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3-*tert*-Butyl-5-isobutyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (63)

(elid 368g)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (0.75 g, 4.31 mmol) and excess 3,3-dimethyl2-butanone (2.0 g, 20.0 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of excess ketone affords the 1,2,4-trioxane (0.24 g, 0.94 mmol, 22 %) as yellow oil

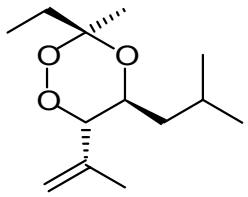
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.84 (d, 3H, *J* = 6.61 Hz, C$\underline{H_3}$CH), 0.88 (d, 3H, *J* = 6.76 Hz, C$\underline{H_3}$CH), 0.94 (s, 9H, (C$\underline{H_3}$)$_3$)C), 1.03 (m, 1H, C$\underline{H_2}$CH), 1.32 (m, 1H, C$\underline{H_2}$CH), 1.55 (s, 3H, C$\underline{H_3}$), 1.72 (m, 3H, C$\underline{H_3}$C=), 1.81 (m, 1H, C$\underline{H}$CH$_2$), 3.97 (ddd, 1H, *J* = 2.35, 9.56, 10.14 Hz, OC$\underline{H}$), 4.13 (d, 1H, *J* = 9.56 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.3 (q, $\underline{C}H_3$), 19.6 (q, $\underline{C}H_3$C=), 21.4 (q, $\underline{C}H_3$CH), 23.7 (d, $\underline{C}$HCH$_2$), 23.8 (q, $\underline{C}H_3$CH), 24.7 (q, ($\underline{C}H_3$)$_3$C), 38.6 (s, $\underline{C}$(CH$_3$)$_3$), 39.5 (t, $\underline{C}H_2$CH), 67.7 (d, O$\underline{C}$H), 87.8 (d, OO$\underline{C}$H), 106.4 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}H_2$=C), 139.2 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3-Ethyl-5-isobutyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (64a)
(elid 368e)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.0 g, 5.75 mmol) and excess 2-butanone (2.0 g, 27.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of excess ketone afforded yellow oil of the 1,2,4-trioxanes diastereomeric mixture **64a** as major product (85 %), **64b-d** as minor products (0.68 g, 2.98 mmol, 52 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

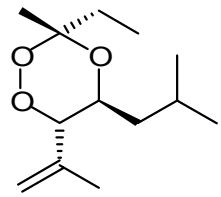
δ (ppm) = 0.82 (d, 3H, *J* = 6.45 Hz, C$\underline{H_3}$CH), 0.88 (d, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH), 0.89 (t, 3H, *J* = 7.65 Hz, C$\underline{H_3}$CH$_2$), 1.04 (m, 1H, C$\underline{H_2}$CH), 1.31 (m, 1H, C$\underline{H_2}$CH), 1.55 (s, 3H, C$\underline{H_3}$), 1.56 (q, 2H, *J* = 7.65 Hz, C$\underline{H_2}$CH$_3$), 1.71 (m, 3H, C$\underline{H_3}$C=), 1.82 (m, 1H, C$\underline{H}$CH$_2$), 3.96 (ddd, 1H, *J* = 2.50, 7.64, 9.41 Hz, OC$\underline{H}$), 4.17 (d, 1H, *J* = 9.41 Hz, OOC$\underline{H}$), 5.02 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.1 (q, $\underline{C}$H$_3$CH$_2$), 18.2 (q, $\underline{C}$H$_3$), 19.5 (q, $\underline{C}$H$_3$C=), 21.3 (q, $\underline{C}$H$_3$CH), 23.6 (d, $\underline{C}$HCH$_2$), 23.6 (q, $\underline{C}$H$_3$CH), 32.0 (t, $\underline{C}$H$_2$CH$_3$), 39.4 (t, $\underline{C}$H$_2$CH), 67.9 (d, O$\underline{C}$H), 88.0 (d, OO$\underline{C}$H), 104.0 (s, O$\underline{C}$OO), 117.9 (t, $\underline{C}$H$_2$=C), 139.2 (s, $\underline{C}$=CH$_2$).

(3RS,5SR,6SR)-3-Ethyl-5-isobutyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (64b)

Minor (9%)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

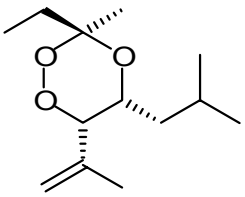
δ (ppm) = 0.83 (d, 3H, *J* = 6.46 Hz, C$\underline{H_3}$CH), 1.21 (s, 3H, C$\underline{H_3}$), 1.69 (m, 3H, C$\underline{H_3}$C=), 3.89 (ddd, 1H, *J* = 2.36, 8.23, 11.3 Hz, OC$\underline{H}$), 4.10 (d, 1H, *J* = 8.23 Hz, OOC$\underline{H}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 8.3 (q, $\underline{C}$H$_3$CH$_2$), 39.8 (t, $\underline{C}$H$_2$CH), 67.6 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 105.0 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}$H$_2$=C), 141.3 (s, $\underline{C}$=CH$_2$).

(3RS,5SR,6RS)-3-Ethyl-5-isobutyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (64c)

Minor (6%)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

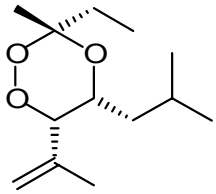
δ (ppm) = 3.83 (m, 1H, OC$\underline{H}$), 4.24 (d, 1H, *J* = 4.70 Hz, OOC$\underline{H}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 41.6 (t, $\underline{C}H_2CH$), 68.8 (d, O$\underline{C}$H), 94.1 (d, OO$\underline{C}$H), 116.6 (t, $\underline{C}H_2$=C), 141.3 (s, $\underline{C}$=CH_2).

(3RS,5RS,6SR)-3-Ethyl-5-isobutyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (64d)

(less than 6%)



^{1}H-NMR: (300 MHz, $CDCl_3$)

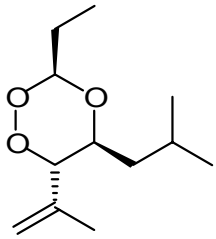
All signals are overlapped.

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 41.2 (t, $\underline{C}H_2CH$), 68.6 (d, O$\underline{C}$H), 92.1 (d, OO$\underline{C}$H), 115.3 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3-Ethyl-5-isobutyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (65)

(elid 387)



Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.14 g, 6.55 mmol) and propionaldehyde diethylacetal (0.87 g, 6.59 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of excess orthoester affords the 1,2,4-trioxane (0.70 g, 3.27 mmol, 50 %) as yellow oil

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.85 (d, 3H, *J* = 6.48 Hz, C$\underline{H}_3$CH), 0.89 (d, 3H, *J* = 6.75 Hz, C$\underline{H}_3$CH), 0.92 (t, 3H, *J* = 7.50 Hz, C$\underline{H}_3CH_2$), 1.10 (m, 1H, C$\underline{H}_2$CH), 1.38 (m, 1H, C$\underline{H}_2$CH), 1.55 (m, 2H, C$\underline{H}_2CH_3$), 1.68 (m, 3H, C$\underline{H}_3$C=), 1.85 (m, 1H, C$\underline{H}CH_2$), 3.71 (ddd, 1H, *J* = 2.34,

9.09, 10.44 Hz, OC<u>H</u>), 4.28 (d, 1H, *J* = 9.09 Hz, OOC<u>H</u>), 5.03 (m, 2H, C<u>H</u>$_2$=), 5.14 (t, 1H, *J* = 5.58 Hz, OC<u>H</u>OO).

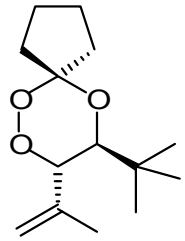
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 8.2 (q, <u>C</u>H$_3$CH$_2$), 19.6 (q, <u>C</u>H$_3$C=), 21.4 (q, <u>C</u>H$_3$CH), 23.6 (d, <u>C</u>HCH$_2$), 23.6 (q, <u>C</u>H$_3$CH), 25.3 (t, <u>C</u>H$_2$CH$_3$), 39.1 (t, <u>C</u>H$_2$CH), 75.0 (d, O<u>C</u>H), 88.0 (d, OO<u>C</u>H), 105.5 (d, O<u>C</u>HOO), 118.4 (t, <u>C</u>H$_2$=C), 138.7 (s, <u>C</u>=CH$_2$).

4.6.5 Derived from 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol

(8RS,9RS)-9-*tert*-Butyl-8-isopropenyl-6,7,10-trioxa-spiro[4.5]decane (66)

(elid 415c)



Following **GP-15**, a solution of 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol **(7j)** (0.75 g, 4.31 mmol) and excess cyclopentanone (2.0 g, 23.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum afforded the crude product (206.9 mg, 0.86 mmol, 20 %) which was further purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) afforded the pure 1,2,4-trioxanes (82.8 mg, 0.34 mmol, 8 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.91 (s, 9H, (C<u>H</u>$_3$)$_3$C), 1.55-1.90 (m, 7H, C<u>H</u>$_2$), 1.75 (m, 3H, C<u>H</u>$_3$C=), 2.37 (m, 1H, C<u>H</u>$_2$), 3.57 (d, 1H, *J* = 9.70 Hz, OC<u>H</u>), 4.90 (d, 1H, *J* = 9.70 Hz, OOC<u>H</u>), 5.04 (m, 1H, C<u>H</u>$_2$=), 5.13 (s, 1H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

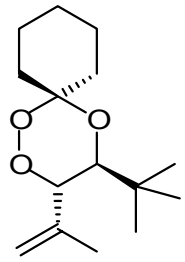
δ (ppm) = 19.3 (q, <u>C</u>H$_3$C=), 23.1 (t, <u>C</u>H$_2$), 24.6 (t, <u>C</u>H$_2$), 26.3 (q, (<u>C</u>H$_3$)$_3$C), 32.8 (t, <u>C</u>H$_2$), 33.8 (s, <u>C</u>(CH$_3$)$_3$), 37.1 (t, <u>C</u>H$_2$), 77.7 (d, O<u>C</u>H), 85.8 (d, OO<u>C</u>H), 114.3 (s, O<u>C</u>OO), 118.9 (t, <u>C</u>H$_2$=), 141.0 (s, <u>C</u>=CH$_2$).

MS: (EI, 70 eV)

m/z (%) = 240 (M^+, not observed), 109 ($C_8H_{13}^+$, 27), 85 ($C_5H_9O^+$, 57), 84 ($C_5H_8O^+$, 33), 57 ($C_4H_9^+$, 100), 55 ($C_4H_7^+$, 71).

(3RS,4RS)-4-*tert*-Butyl-3-isopropenyl-1,2,5-trioxa-spiro[5.5]undecane (67)

(elid 450w)



Following **GP-15**, a solution of 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol **(7j)** (0.75 g, 4.31 mmol) and cyclohexanone (0.48 g, 4.90 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum and further purification by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.79) afforded the pure 1,2,4-trioxanes (0.12 g, 0.47 mmol, 11 %) as colorless oil.

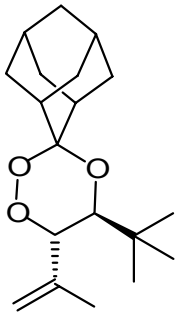
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.92 (s, 9H, $(C\underline{H}_3)_3C$), 1.27-1.60 (m, 9H, $C\underline{H}_2$), 1.78 (m, 3H, $C\underline{H}_3C$=), 2.26 (m, 1H, $C\underline{H}_2$), 3.67 (d, 1H, *J* = 9.71 Hz, OC<u>H</u>), 4.43 (d, 1H, *J* = 9.70 Hz, OOC<u>H</u>), 5.04 (m, 1H, $C\underline{H}_2$=), 5.13 (s, 1H, $C\underline{H}_2$=).

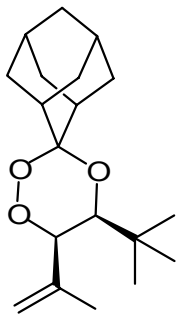
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.5 (q, $\underline{C}H_3C$=), 22.2 (t, $\underline{C}H_2$), 22.4 (t, $\underline{C}H_2$), 25.7 (t, $\underline{C}H_2$), 26.3 (q, $(\underline{C}H_3)_3C$), 29.3 (t, $\underline{C}H_2$), 33.9 (s, $\underline{C}(CH_3)_3$), 34.9 (t, $\underline{C}H_2$), 74.9 (d, O<u>C</u>H), 85.8 (d, OO<u>C</u>H), 102.4 (s, O<u>C</u>OO), 118.8 (t, $\underline{C}H_2$=), 141.2 (s, $\underline{C}$=CH_2).

(5RS,6RS)-5-*tert*-Butyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (68a) and (5RS,6SR)-5-*tert*-butyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (68b) (elid 491s or elid 450j)



68a



68b

Following **GP-15**, a solution of 4-hydroperoxy-2,2,5-trimethylhex-5-en-3-ol **(7j)** (0.76 g, 4.37 mmol) and adamantanone (1.30 g, 8.67 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by further purification by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) afforded a colorless oil of the pure 1,2,4-trioxanes diastereomeric mixture **68a,b** in ratio 84:16, respectively, (0.16 g, 0.52 mmol, 12 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **68a**)

δ (ppm) = 0.93 (s, 9H, $(C\underline{H}_3)_3C$), 1.50-2.19 (m, 13H, CH and $C\underline{H}_2$), 1.77 (m, 3H, $C\underline{H}_3C$=), 2.85 (br. s, 1H, C<u>H</u>), 3.70 (d, 1H, *J* = 9.69 Hz, OC<u>H</u>), 4.43 (d, 1H, *J* = 9.69 Hz, OOC<u>H</u>), 5.05 (m, 1H, $C\underline{H}_2$=), 5.13 (s, 1H, $C\underline{H}_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **68a**)

δ (ppm) = 19.6 (q, $\underline{C}H_3C$=), 26.4 (q, $(\underline{C}H_3)_3C$), 27.2 (d, <u>C</u>H), 27.3 (d, <u>C</u>H), 29.8 (d, <u>C</u>H), 33.0 (t, $\underline{C}H_2$), 33.3 (2 x t, 2 x $\underline{C}H_2$), 33.6 (t, $\underline{C}H_2$), 34.1 (s, $\underline{C}(CH_3)_3$), 36.6 (d, <u>C</u>H), 37.2 (t, $\underline{C}H_2$), 74.4 (d, O<u>C</u>H), 85.5 (d, OO<u>C</u>H), 104.3 (s, O<u>C</u>OO), 118.9 (t, $\underline{C}H_2$=C), 141.2 (s, <u>C</u>=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **68b**)

δ (ppm) = 0.88 (s, 9H, $(C\underline{H}_3)_3C$), 1.77 (m, 3H, $C\underline{H}_3C$=), 3.63 (d, 1H, *J* = 3.39 Hz, OC<u>H</u>), 4.83 (d, 1H, *J* = 3.36 Hz, OOC<u>H</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **68b**)

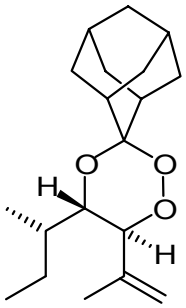
δ (ppm) = 15.3 (q, $\underline{C}H_3C$=), 25.5 (q, $(\underline{C}H_3)_3C$), 26.8 (d, <u>C</u>H), 27.1 (d, <u>C</u>H), 29.8 (d, <u>C</u>H), 32.3 (t, $\underline{C}H_2$), 34.5 (2 x t, 2 x $\underline{C}H_2$), 34.8 (t, $\underline{C}H_2$), 35.0 (s, $\underline{C}(CH_3)_3$), 36.8 (d, <u>C</u>H), 38.1 (t, $\underline{C}H_2$), 63.4 (d, O<u>C</u>H), 89.0 (d, OO<u>C</u>H), 102.4 (s, O<u>C</u>OO), 113.0 (t, $\underline{C}H_2$=C), 141.2 (s, <u>C</u>=CH_2).

MS: (EI, 70 eV)

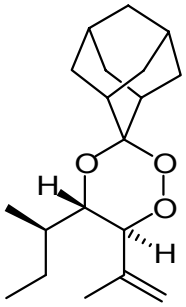
m/z (%) = 306 (M^+, less than 1), 150 ($C_{10}H_{14}O^+$, 100), 124 ($C_9H_{16}^+$, 31), 109 ($C_8H_{13}^+$, 32), 81 ($C_6H_9^+$, 19), 80 ($C_6H_8^+$, 38), 79 ($C_6H_7^+$, 47), 67 ($C_5H_7^+$, 17), 55 ($C_3H_3O^+$, 16).

4.6.6 Derived from 3-hydroperoxy-2,5-dimethylhept-1-en-4-ol (7i)

(5RS,6RS)-5-((RS)-But-2-yl)-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (69a) (5RS,6RS)-5-((SR)-but-2-yl)-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (69b) (elid 474a, 491x)



69a



69b

Following **GP-15**, a solution of 3-hydroperoxy-2,5-dimethylhept-1-en-4-ol **(7i)** (1.50 g, 8.62 mmol) and adamantanone (1.58 g, 10.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (2.07 g, 6.76 mmol, 78.5 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.83) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **69a,b** in a 1:1 ratio (0.52 g, 1.70 mmol, 20 %) as viscous colorless liquid.

^{1}H-NMR: (300 MHz, $CDCl_3$, both diastereomers)

δ (ppm) = 0.81 (m, 6H, C$\underline{H}_3$CH$_2$ and C$\underline{H}_3$CH), 1.01-1.45 (m, 3H, C$\underline{H}$C$\underline{H}_2$), 1.49-2.10 (m, 13H, C$\underline{H}$ and C$\underline{H}_2$), 1.72 (s, 3H, C$\underline{H}_3$C=), 2.88 (br. d, 1H, C$\underline{H}$), 3.83 (m, 1H, OC$\underline{H}$), 4.22 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H}_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 11.2 (q, $\underline{C}$H$_3$CH$_2$), 19.0 (q, $\underline{C}$H$_3$CH), 19.8 (q, $\underline{C}$H$_3$C=), 27.1 (d, $\underline{C}$H), 27.2 (d, $\underline{C}$H), 28.2 (t, $\underline{C}$H$_2$), 29.6 (t, $\underline{C}$H$_2$), 29.8 (d, $\underline{C}$H), 32.0 (t, $\underline{C}$H$_2$), 33.0 (t, $\underline{C}$H$_2$), 33.2 (t, $\underline{C}$H$_2$), 33.3 (t, $\underline{C}$H$_2$), 33.5 (t, $\underline{C}$H$_2$), 34.3 (d, $\underline{C}$HCH$_3$), 36.6 (d, $\underline{C}$H), 37.2 (t, $\underline{C}$H$_2$), 68.6 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 104.7 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}$H$_2$=C), 139.4 (s, $\underline{C}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of 2nd diastereomer)

δ (ppm) = 11.4 (q, $\underline{C}$H$_3$CH$_2$), 19.2 (q, $\underline{C}$H$_3$CH), 19.8 (q, $\underline{C}$H$_3$C=), 28.3 (t, $\underline{C}$H$_2$), 29.1 (t, $\underline{C}$H$_2$), 29.8 (d, $\underline{C}$H), 31.6 (t, $\underline{C}$H$_2$), 33.0 (t, $\underline{C}$H$_2$), 33.2 (t, $\underline{C}$H$_2$), 33.3 (t, $\underline{C}$H$_2$), 33.5 (t, $\underline{C}$H$_2$), 34.1 (d, $\underline{C}$HCH$_3$), 37.2 (t, $\underline{C}$H$_2$), 69.1 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 104.7 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}$H$_2$=C), 139.4 (s, $\underline{C}$=CH$_2$).

IR: (Film)

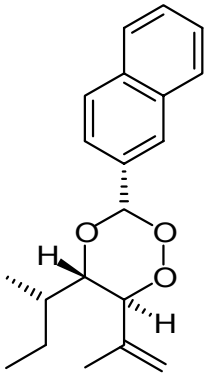
ν (cm^{-1}) = 3081, 2914, 2857, 1648, 1450, 1379, 1109, 1096, 1024, 925, 908.

Elemental Analysis: ($C_{19}H_{30}O_3$, M = 306.44)

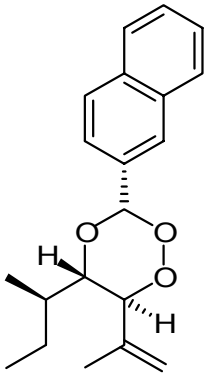
Calcd: C 74.47 H 9.87

Found: C 74.58 H 10.05

(3RS,5RS,6RS)-5-((RS)-But-2-yl)-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (70a) and (3RS,5RS,6RS)-5-((SR)-but-2-yl)-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (70b) (elid 499f)



70a



70b

Following **GP-15**, a solution of 3-hydroperoxy-2,5-dimethylhept-1-en-4-ol **(7i)** (1.0 g, 5.75 mmol) and β-naphthaldehyde (0.90 g, 5.77 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **70a,b** in a 1:1 ratio (0.31 g, 0.99 mmol, 17 %) as viscous colorless liquid.

^{1}H-NMR: (300 MHz, $CDCl_3$, both diastereomers)

δ (ppm) = 0.90 (m, 12H, $C\underline{H_3}CH_2$ and $C\underline{H_3}CH$), 1.08-1.71 (m, 12H, $C\underline{H}C\underline{H_2}$), 1.84 (s, 3H, $C\underline{H_3}C$=) 3.98 (m, 1H, OC$\underline{H}$), 4.62 (d, 1H, *J* = 9.21 Hz, OOC$\underline{H}$), 5.17 (m, 1H, $C\underline{H_2}$=), 5.21 (s, 1H, $C\underline{H_2}$=), 6.39 (s, 1H, OOC$\underline{H}$O), 7.46-8.02 (m, 1H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 11.2 (q, $\underline{C}H_3CH_2$), 18.9 (q, $\underline{C}H_3CH$), 19.8 (q, $\underline{C}H_3C$=), 28.0 (t, $\underline{C}H_2$), 29.5 (t, $\underline{C}H_2$), 31.5 (t, $\underline{C}H_2$), 34.3 (d, $\underline{C}HCH_3$), 77.6 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 104.1 (s, O$\underline{C}$HOO), 118.5 (t, $\underline{C}H_2$=C), 124.1 (d, $\underline{C}$H), 126.2 (d, $\underline{C}$H), 126.7 (d, $\underline{C}$H), 126.8 (d,

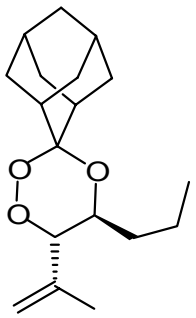
CH), 127.7 (d, CH), 128.1 (d, CH), 128.4 (d, CH), 132.0 (Cq_{arom}), 132.8 (Cq_{arom}), 134.0 (Cq_{arom}), 138.8 (s, C=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of 2nd diastereomer)

δ (ppm) = 11.4 (q, CH_3CH_2), 19.2 (q, CH_3CH), 28.1 (t, CH_2), 29.0 (t, CH_2), 31.7 (t, CH_2), 34.3 (d, $CHCH_3$).

4.6.7 Derived from 3-hydroperoxy-2-methylhept-1-en-4-ol (7d)

(5RS,6RS)-6-(Prop-1-en-2-yl)-5-*n*-propyl-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (71) (elid 437b)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.34 g, 8.38 mmol) and adamantanone (1.57 g, 10.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.88) afforded the pure 1,2,4-trioxane (0.73 g, 2.50 mmol, 30 %) as viscous colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.89 (t, 3H, *J* = 7.05 Hz, CH_3CH_2), 1.28-1.40 (m, 4H, CH_2CH_2), 1.50-2.10 (m, 13H, CH and CH_2), 1.72 (m, 3H, CH_3C=), 2.90 (br. s, 1H, CH), 3.88 (m, 1H, OCH), 4.22 (d, 1H, *J* = 9.54 Hz, OOCH), 5.03 (s, 2H, CH_2=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, CH_3CH_2), 18.3 (t, CH_2CH_3), 19.8 (q, CH_3C=), 27.1 (d, CH), 27.2 (d, CH), 29.8 (d, CH), 32.9 (t, CH_2CH_2), 33.0 (t, CH_2), 33.3 (t, CH_2), 33.3 (t, CH_2), 33.5 (t, CH_2), 37.1 (t, CH_2), 68.3 (d, OCH), 87.6 (d, OOCH), 104.7 (s, OCOO), 117.8 (t, CH_2=C), 139.4 (s, C=CH_2).

IR: (Film)

ν (cm^{-1}) = 2913, 2858, 1648, 1135, 1109, 1095, 1002, 926, 908.

MS: (EI, 70 eV)

m/z (%) = 292 (M^+, not observed), 150 ($C_{10}H_{14}O^+$, 100), 110 ($C_8H_{14}^+$, 37), 81 ($C_6H_9^+$, 21), 80 ($C_6H_8^+$, 32), 79 ($C_6H_7^+$, 47).

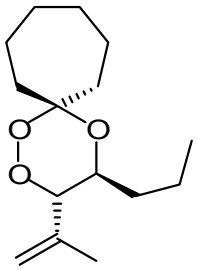
Elemental Analysis: ($C_{18}H_{28}O_3$, M = 292.41)

Calcd: C 73.93 H 9.65

Found: C 73.93 H 9.65

(3RS,4RS)-3-Isopropenyl-4-propyl-1,2,5-trioxa-spiro[5.6]dodecane (72)

(elid 425a)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.56 g, 9.75 mmol) and cycloheptanone (1.10 g, 9.82 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.83) afforded the pure 1,2,4-trioxane (0.45 g, 1.77 mmol, 18 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

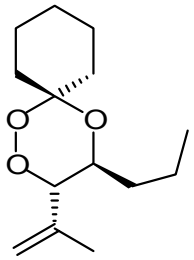
δ (ppm) = 0.88 (t, 3H, *J* = 7.05 Hz, C$\underline{H}_3$CH$_2$), 1.30-1.65 (m, 14H, C$\underline{H}_2$ and C$\underline{H}_2$C$\underline{H}_2$), 1.73 (s, 3H, C$\underline{H}_3$C=), 2.21 (m, 2H, C$\underline{H}_2$), 3.85 (m, 1H, OC$\underline{H}$), 4.22 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.03 (s, 2H, C$\underline{H}_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}$H$_3$CH$_2$), 18.1 (t, $\underline{C}$H$_2$CH$_3$), 19.6 (q, $\underline{C}$H$_3$C=), 22.0 (t, $\underline{C}$H$_2$), 22.2 (t, $\underline{C}$H$_2$), 29.0 (t, $\underline{C}$H$_2$), 29.5 (t, $\underline{C}$H$_2$), 31.2 (t, $\underline{C}$H$_2$), 33.0 (t, $\underline{C}$H$_2$CH$_2$) 38.6 (t, $\underline{C}$H$_2$), 69.1 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 107.2 (s, O$\underline{C}$OO), 117.7 (t, $\underline{C}$H$_2$=C), 139.5 (s, $\underline{C}$=CH$_2$).

(3RS,4RS)-3-Isopropenyl-4-propyl-1,2,5-trioxa-spiro[5.5]undecane (73)

(elid 467j)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.20 g, 7.50 mmol) and propionaldehyde diethylacetal (0.73 g, 7.45 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, $R_f = 0.80$) afforded the pure 1,2,4-trioxane (0.88 g, 3.67 mmol, 49 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

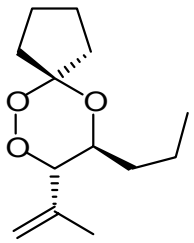
δ (ppm) = 0.87 (t, 3H, *J* = 6.90 Hz, C<u>H</u>$_3$CH$_2$), 1.20-1.65 (m, 12H, C<u>H</u>$_2$ and CH$_2$C<u>H</u>$_2$), 1.71 (m, 3H, C<u>H</u>$_3$C=), 2.0 (m, 1H, C<u>H</u>$_2$), 2.14 (m, 1H, C<u>H</u>$_2$), 3.87 (m, 1H, OC<u>H</u>), 4.21 (d, 1H, *J* = 9.54 Hz, OOC<u>H</u>), 5.02 (s, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.8 (q, <u>C</u>H$_3$CH$_2$), 18.1 (t, <u>C</u>H$_2$CH$_3$), 19.6 (q, <u>C</u>H$_3$C=), 22.2 (t, <u>C</u>H$_2$), 22.4 (t, <u>C</u>H$_2$), 25.6 (t, <u>C</u>H$_2$), 29.4 (t, <u>C</u>H$_2$), 35.0 (t, <u>C</u>H$_2$), 32.9 (t, <u>C</u>H$_2$CH$_2$), 68.8 (d, O<u>C</u>H), 87.7 (d, OO<u>C</u>H), 102.7 (s, O<u>C</u>OO), 117.7 (t, <u>C</u>H$_2$=), 139.3 (s, <u>C</u>=CH$_2$).

(8RS,9RS)-8-Isopropenyl-9-propyl-6,7,10-trioxa-spiro[4.5]decane (74)

(elid 425c)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.55 g, 9.69 mmol) and cyclopentanone (0.81 g, 9.64 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) afforded the pure 1,2,4-trioxane (0.42 g, 1.86 mmol, 19 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

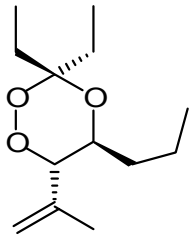
δ (ppm) = 0.86 (t, 3H, *J* = 6.90 Hz, C<u>H</u>$_3$CH$_2$), 1.29-1.55 (m, 4H, C<u>H</u>$_2$C<u>H</u>$_2$), 1.59-1.85 (m, 7H, CH_2), 1.71 (s, 3H, C<u>H</u>$_3$C=), 2.48 (m, 1H, C<u>H</u>$_2$), 3.77 (m, 1H, OC<u>H</u>), 4.30 (d, 1H, *J* = 9.54 Hz, OOC<u>H</u>), 5.03 (s, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.8 (q, <u>C</u>H$_3$CH$_2$), 18.0 (t, <u>C</u>H$_2$CH$_3$), 19.5 (q, <u>C</u>H$_3$C=), 23.1 (t, <u>C</u>H$_2$), 24.7 (t, <u>C</u>H$_2$), 32.6 (t, <u>C</u>H$_2$), 32.9 (t, <u>C</u>H$_2$CH$_2$), 37.2 (t, <u>C</u>H$_2$), 71.6 (d, O<u>C</u>H), 87.5 (d, OO<u>C</u>H), 114.7 (s, O<u>C</u>OO), 117.9 (t, <u>C</u>H$_2$=C), 139.1 (s, <u>C</u>=CH$_2$).

(5RS,6RS)-3,3-Diethyl-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (75)

(elid 496n)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.10 g, 6.88 mmol) and 3-pentanone (2.0 g, 23.3 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.79) afforded the pure 1,2,4-trioxane (0.22 g, 0.96 mmol, 14 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.84-0.91 (m, 9H, 2 x C<u>H</u>$_3$CH$_2$ and C<u>H</u>$_3$(CH$_2$)$_2$), 1.21-1.65 (m, 6H, C<u>H</u>$_2$CH$_3$ and C<u>H</u>$_2$C<u>H</u>$_2$), 1.88-2.19 (m, 2H, C<u>H</u>$_2$CH$_3$), 1.73 (m, 3H, C<u>H</u>$_3$C=), 3.86 (m, 1H, OC<u>H</u>), 4.21 (d, 1H, *J* = 9.48 Hz, OOC<u>H</u>), 5.04 (s, 2H, C<u>H</u>$_2$=).

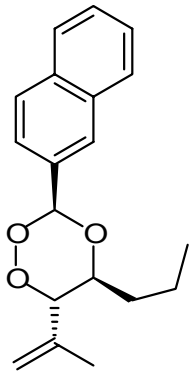
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 6.8 (q, <u>C</u>H$_3$CH$_2$), 8.0 (q, <u>C</u>H$_3$CH$_2$), 14.0 (q, <u>C</u>H$_3$CH$_2$CH$_2$), 18.1 (t, <u>C</u>H$_2$CH$_2$), 19.7 (q, <u>C</u>H$_3$C=), 22.8 (t, <u>C</u>H$_2$CH$_3$), 28.3 (t, <u>C</u>H$_2$CH$_3$), 33.0 (t, <u>C</u>H$_2$CH$_2$), 69.1 (d, O<u>C</u>H), 87.3 (d, OO<u>C</u>H), 106.0 (d, O<u>C</u>OO), 117.8 (t, <u>C</u>H$_2$=), 139.4 (s, <u>C</u>=CH$_2$).

IR: (Film)

ν (cm^{-1}) = 3082, 2971, 2940, 2880, 1648, 1460, 1162, 1146, 1091, 1004, 924.

(3RS,5RS,6RS)-3-(Naphthalen-2-yl)-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (76)
(elid 493m)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.20 g, 7.50 mmol) and β-naphthaldehyde (1.18 g, 7.56 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.66) afforded the pure 1,2,4-trioxane (0.89 g, 2.99 mmol, 40 %) as colorless oil which crystallizes on standing.

M.p. 78-80 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.02 (t, 3H, *J* = 7.06 Hz, $C\underline{H_3}CH_2$), 1.47-1.79 (m, 4H, $C\underline{H_2}C\underline{H_2}$), 1.86 (m, 3H, $C\underline{H_3}C$=), 4.04 (ddd, 1H, *J* = 3.09, 8.09, 9.26 Hz, OC<u>H</u>), 4.67 (d, 1H, *J* = 9.26 Hz, OOC<u>H</u>), 5.19 (m, 1H, $C\underline{H_2}$=), 5.24 (s, 1H, $C\underline{H_2}$=), 6.43 (s, 1H, OC<u>H</u>OO), 7.47-8.07 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 18.1 (t, $\underline{C}H_2CH_3$), 19.7 (q, $\underline{C}H_3C$=), 32.5 (t, $\underline{C}H_2CH_2$), 77.1 (d, O<u>C</u>H), 87.7 (d, OO<u>C</u>H), 104.0 (d, O<u>C</u>HOO), 118.5 (t, $\underline{C}H_2$=), 124.0 (d, $\underline{C}H_{arom}$), 126.1 (d, $\underline{C}H_{arom}$), 126.6 (d, $\underline{C}H_{arom}$), 126.7 (d, $\underline{C}H_{arom}$), 127.6 (d, $\underline{C}H_{arom}$), 128.0 (d, $\underline{C}H_{arom}$), 128.3 (d, $\underline{C}H_{arom}$), 131.9 (s, Cq_{arom}) , 132.8 (s, Cq_{arom}), 133.9 (s, Cq_{arom}), 138.7 (s, $\underline{C}$=CH_2).

IR: (CsI)

ν (cm^{-1}) = 2957, 2934, 1664, 1605, 1576, 1362, 1340, 1092, 1075, 907.

MS: (EI, 70 eV)

m/z (%) = 298 (M^+, 3), 226 (M^+-C_4H_8O, 2), 156 ($C_{11}H_8O^+$, 92), 155 ($C_{11}H_7O^+$, 100), 128 ($C_{10}H_8^+$, 22), 127 ($C_{10}H_7^+$, 77), 110 ($C_8H_{14}^+$, 27), 95 ($C_7H_{11}^+$, 8).

HRMS: (EI, 70 eV, $C_{19}H_{22}O_3$)

Calcd: M = 298.157 g/mol

Found: M = 298.157 ±0.005 g/mol

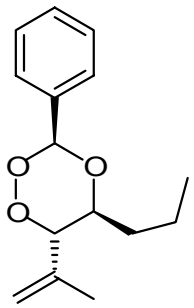
Elemental Analysis: ($C_{19}H_{22}O_3$, M = 298.39)

Calcd: C 76.48 H 7.43

Found: C 76.25 H 7.27

(3RS,5RS,6RS)-3-Phenyl-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (77)

(elid 467e)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.20 g, 7.50 mmol) and benzaldehyde dimethylacetal (1.13 g, 7.43 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.80) afforded the pure 1,2,4-trioxane (0.67 g, 2.70 mmol, 36 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

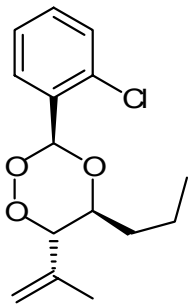
δ (ppm) = 0.96 (t, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH$_2$), 1.40-1.74 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 1.81 (m, 3H, C$\underline{H_3}$C=), 3.95 (m, 1H, OC$\underline{H}$), 4.56 (d, 1H, *J* = 9.26 Hz, OOC$\underline{H}$), 5.14 (m, 2H, C$\underline{H_2}$=), 6.24 (s, 1H, OC$\underline{H}$OO), 7.36-7.60 (m, 4H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

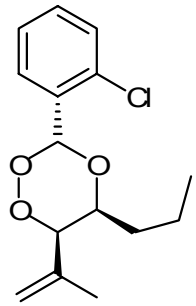
δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 18.0 (t, $\underline{C}H_2CH_3$), 19.7 (q, $\underline{C}H_3C$=), 32.5 (t, $\underline{C}H_2CH_2$), 77.0 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 103.9 (d, O$\underline{C}$HOO), 118.5 (t, $\underline{C}H_2$=C), 126.9 (d, $\underline{C}H_{arom}$), 128.2 (d, $\underline{C}H_{arom}$), 129.6 (d, $\underline{C}H_{arom}$), 134.6(s, Cq_{arom}), 138.7 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3-(2-Chlorophenyl)-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (78a) and (3RS,5SR,6RS)-3-(2-chlorophenyl)-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (78b)

(elid 450e)



78a



78b

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7d)** (0.85 g, 5.31 mmol) and 2-chlorobenzaldehyde (0.93 g, 6.62 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.67) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **78a**,**b** in a ratio 88:12 (0.60 g, 2.13 mmol, 40 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **78a**)

δ (ppm) = 0.86 (t, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH$_2$), 1.32-1.58 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 1.73 (m, 3H, C$\underline{H_3}$C=), 3.90 (m, 1H, OC$\underline{H}$), 4.48 (d, 1H, *J* = 9.26 Hz, OOC$\underline{H}$), 5.07 (m, 2H, C$\underline{H_2}$=), 6.47 (s, 1H, OC$\underline{H}$OO), 7.18-7.61 (m, 4H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **78a**)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 18.0 (t, $\underline{C}H_2CH_3$), 19.7 (q, $\underline{C}H_3C$=), 32.5 (t, $\underline{C}H_2CH_2$), 77.3 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 101.0 (d, O$\underline{C}$HOO), 118.7 (t, $\underline{C}H_2$=C), 126.8 (d, $\underline{C}H_{arom}$), 128.7 (d, $\underline{C}H_{arom}$), 129.5 (d, $\underline{C}H_{arom}$), 130.9 (d, $\underline{C}H_{arom}$), 132.1 (s, Cq_{arom}), 133.5 (s, Cq_{arom}), 138.7 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **78b**)

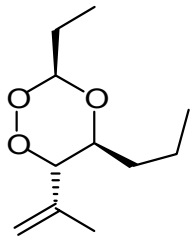
δ (ppm) = 0.88 (t, 3H, *J* = 7.08 Hz, C$\underline{H_3}$CH$_2$), 2.03 (m, 3H, C$\underline{H_3}$C=), 3.62 (m, 1H, OC$\underline{H}$), 4.09 (d, 1H, *J* = 3.82 Hz, OOC$\underline{H}$), 6.49 (s, 1H, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of minor diastereomer **78b**)

δ (ppm) = 77.1 (d, O$\underline{C}$H), 85.0 (d, OO$\underline{C}$H), 101.4 (d, O$\underline{C}$HOO), 118.2 (t, $\underline{C}H_2$=C), 126.9 (d, $\underline{C}H_{arom}$), 128.6 (d, $\underline{C}H_{arom}$), 129.5 (d, $\underline{C}H_{arom}$), 130.9 (d, $\underline{C}H_{arom}$), 132.1 (s, Cq_{arom}), 133.5 (s, Cq_{arom}), 141.6 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3-Ethyl-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (79)

(elid 467i)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (1.43 g, 8.94 mmol) and propionaldehyde diethylacetal (1.17 g, 8.86 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, $R_f = 0.80$) afforded the pure 1,2,4-trioxane (0.73 g, 3.65 mmol, 41 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

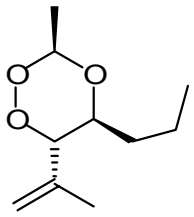
δ (ppm) = 0.89 (t, 3H, *J* = 6.90 Hz, $C\underline{H_3}(CH_2)_2$), 0.93 (t, 3H, *J* = 7.65 Hz, $C\underline{H_3}CH_2$), 1.30-1.63 (m, 6H, $C\underline{H_2}CH_3$ and $C\underline{H_2}C\underline{H_2}$), 1.70 (m, 3H, $C\underline{H_3}C$=), 3.66 (m, 1H, OC<u>H</u>), 4.33 (d, 1H, *J* = 9.12 Hz, OOC<u>H</u>), 5.05 (m, 2H, $C\underline{H_2}$=), 5.15 (t, 1H, J = 5.43 Hz, $C\underline{H}CH_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

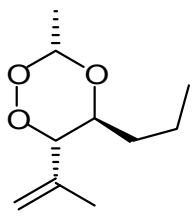
δ (ppm) = 8.2 (q, $\underline{C}H_3CH_2$), 13.9 (q, $\underline{C}H_3(CH_2)_2$), 18.1 (t, $\underline{C}H_2CH_2$), 19.7 (q, $\underline{C}H_3C$=), 25.4 (t, $\underline{C}H_2CH_3$), 32.5 (t, $\underline{C}H_2CH_2$), 76.5 (d, O<u>C</u>H), 87.7 (d, OO<u>C</u>H), 105.5 (d, O<u>C</u>HOO), 118.2 (t, $\underline{C}H_2$=C), 138.8 (s, <u>C</u>=CH_2).

(3RS,5RS,6RS)-3-Methyl-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (80a) and (3RS,5SR,6SR)-3-methyl-6-(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (80b)

(elid 467l)



80a



80b

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7d)** (1.0 g, 6.25 mmol) and acetaldehyde diethylacetal (0.73 g, 6.19 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer

chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.77) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **80a**,**b** in a ratio 90:10 (0.55 g, 2.96 mmol, 48 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **80a**)

δ (ppm) = 0.88 (t, 3H, *J* = 6.91 Hz, $C\underline{H_3}CH_2$), 1.25 (d, 3H, *J* = 5.44 Hz, $C\underline{H_3}CH$), 1.27-1.60 (m, 4H, $C\underline{H_2}C\underline{H_2}$), 1.72 (m, 3H, $C\underline{H_3}C$=), 3.66 (m, 1H, OC<u>H</u>), 4.32 (d, 1H, *J* = 9.12 Hz, OOC<u>H</u>), 5.05 (m, 2H, $C\underline{H_2}$=C), 5.35 (q, 1H, J = 5.44 Hz, $C\underline{H}CH_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **80a**)

δ (ppm) = 13.8 (q, $\underline{C}H_3CH_2$), 17.8 (q, $\underline{C}H_3CH$), 18.0 (t, $\underline{C}H_2CH_3$), 19.5 ($\underline{C}H_3C$=), 32.4 (t, $\underline{C}H_2CH$), 76.4 (d, O<u>C</u>H), 87.4 (d, OO<u>C</u>H), 101.4 (d, OO<u>C</u>HO), 118.2 (t, $\underline{C}H_2$=C), 138.7 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **80b**)

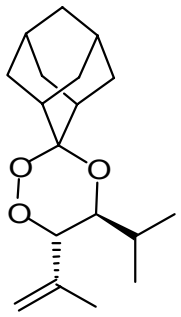
δ (ppm) = 1.75 (m, 3H, $C\underline{H_3}C$=), 3.75 (m, 1H, OC<u>H</u>), 4.38 (d, 1H, *J* = 9.27 Hz, OOC<u>H</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **80b**)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 17.6 (q, $\underline{C}H_3CH$), 17.9 (t, $\underline{C}H_2CH_3$), 19.5 ($\underline{C}H_3C$=), 33.4 (t, $\underline{C}H_2CH$), 75.9 (d, O<u>C</u>H), 84.5 (d, OO<u>C</u>H), 101.6 (d, OO<u>C</u>HO), 118.3 (t, $\underline{C}H_2$=C), 138.8 (s, $\underline{C}$=CH_2).

4.6.8 Derived from 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol (7c)

(5RS,6RS)-6-(Prop-1-en-2-yl)-5-isopropyl-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (81) (elid 475z)



Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (1.35 g, 8.44 mmol) and adamantanone (1.27 g, 8.47 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer chromatography

(SiO_2, EA/*n*-hex, 1:10, R_f = 0.76) afforded the pure 1,2,4-trioxane (0.69 g, 2.36 mmol, 28 %) as viscous colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.89 (d, 3H, *J* = 6.77 Hz, C<u>H</u>$_3$CH), 0.97 (d, 3H, *J* = 7.06 Hz, C<u>H</u>$_3$CH), 1.48-2.10 (m, 14H, C<u>H</u>(CH$_3$)$_2$, C<u>H</u> and C<u>H</u>$_2$), 1.72 (m, 3H, C<u>H</u>$_3$C=), 2.87 (br. s, 1H, CH), 3.78 (dd, 1H, *J* = 2.65, 9.85 Hz, OC<u>H</u>), 4.41 (d, 1H, *J* = 9.85 Hz, OOC<u>H</u>), 5.02 (m, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.9 (q, <u>C</u>H$_3$CH), 19.6 (q, <u>C</u>H$_3$C=), 20.2 (q, <u>C</u>H$_3$CH), 27.17 (d, CH), 27.22 (d, CH), 29.7 (d, CH), 36.5 (d, CH), 28.1 (d, <u>C</u>H(CH$_3$)$_2$), 32.9 (t, CH$_2$), 33.2 (2 x t, CH$_2$), 33.5 (t, CH$_2$), 37.2 (t, CH$_2$), 72.1 (d, O<u>C</u>H), 85.4 (d, OO<u>C</u>H), 104.4 (s, O<u>C</u>OO), 117.6 (t, <u>C</u>H$_2$=C), 139.5 (s, <u>C</u>=CH$_2$).

IR: (Film)

ν (cm^{-1}) = 3081, 2913, 2857, 1649, 1450, 1380, 1110, 1097, 1077, 1025, 925, 908

MS: (EI, 70 eV)

m/z (%) = 292 (M^+, less than 1), 220 (M^+-C_4H_8O, 1), 150 ($C_{10}H_{14}O^+$, 58), 110 ($C_8H_{14}^+$, 78), 95 ($C_7H_{11}^+$, 50), 81 ($C_6H_9^+$, 36), 80 ($C_6H_8^+$, 88), 79 ($C_6H_7^+$, 100), 67 ($C_5H_7^+$, 31), 55 ($C_3H_3O^+$, 27).

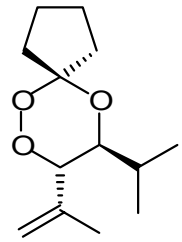
Elemental Analysis: ($C_{18}H_{28}O_3$, M = 292.41)

Calcd: C 73.93 H 9.65

Found: C 73.64 H 9.33

(8RS,9RS)-8-Isopropenyl-9-isopropyl-6,7,10-trioxa-spiro[4.5]decane (82)

(elid 348f)



Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.90 g, 5.63 mmol) and excess cyclopentanone (2.0 g, 23.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum

followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) afforded the pure 1,2,4-trioxane (0.19 g, 0.84 mmol, 15 %) as colorless liquid.

^{1}H-NMR: (300 MHz, $CDCl_3$)

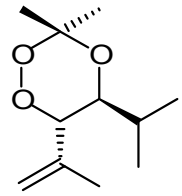
δ (ppm) = 0.89 (d, 3H, *J* = 6.91 Hz, C$\underline{H_3}$CH), 0.94 (d, 3H, *J* = 6.90 Hz, C$\underline{H_3}$CH),1.58-1.85 (m, 7H, C$\underline{H_2}$ (cyclopentane)), 1.70 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 1.72 (m, 3H, C$\underline{H_3}$C=), 2.45 (m, 1H, C$\underline{H_2}$ (cyclopentane)), 3.67 (dd, 1H, *J* = 2.35, 9.70 Hz, OC$\underline{H}$), 4.49 (d, 1H, *J* = 9.70 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 15.2 (q, $\underline{C}H_3CH$), 19.4 (q, $\underline{C}H_3C$=), 19.9 (q, $\underline{C}H_3CH$), 23.1 (t, $\underline{C}H_2$), 24.7 (t, $\underline{C}H_2$), 33.0 (t, $\underline{C}H_2$), 37.2 (t, $\underline{C}H_2$), 28.0 (d, $\underline{C}H(CH_3)_2$), 75.6 (d, O$\underline{C}$H), 85.6 (d, OO$\underline{C}$H), 114.7 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}H_2$=C), 139.4 (s, $\underline{C}$=CH_2).

(5RS,6RS)-5-Isopropyl-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (83)

(elid 330e)



Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.86 g, 5.38 mmol) and excess acetone (2.0 g, 34.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum affords the 1,2,4-trioxane (0.46 g, 2.30 mmol, 43 %) as yellow oil.

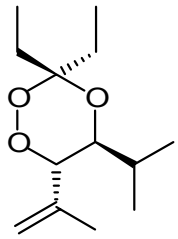
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.88 (d, 3H, *J* = 6.91 Hz, C$\underline{H_3}$CH), 0.94 (d, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH), 1.31 (s, 3H, CH3), 1.60 (s, 3H, CH3), 1.68 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 1.74 (m, 3H, C$\underline{H_3}$C=), 3.79 (dd, 1H, *J* = 2.35, 9.84 Hz, OC$\underline{H}$), 4.41 (d, 1H, *J* = 10.0 Hz, OOC$\underline{H}$), 5.05 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 15.0 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 19.8 (q, $\underline{C}H_3CH$), 20.5 (q, $\underline{C}H_3$), 25.8 (q, CH3), 28.0 (d, $\underline{C}H(CH_3)_2$), 73.6 (d, O$\underline{C}$H), 85.5 (d, OO$\underline{C}$H), 102.6 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}H_2$=C), 139.5 (s, $\underline{C}$=CH_2).

(5RS,6RS)-3,3-Diethyl-5-isopropyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (84)
(elid 330a)



Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.17 g, 1.06 mmol) and excess 3-pentanone (2.0 g, 23.3 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum affords the 1,2,4-trioxane (0.12 g, 0.53 mmol, 50 %) as yellow oil.

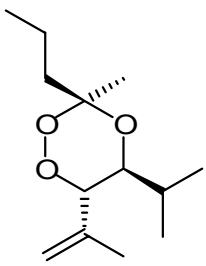
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.83 (t, 3H, *J* = 7.62 Hz, C<u>H</u>$_3$CH$_2$), 0.86 (t, 3H, *J* = 7.50 Hz, C<u>H</u>$_3$CH$_2$), 0.93 (d, 3H, *J* = 6.90 Hz, C<u>H</u>$_3$CH), 1.43-1.65 (m, 2H, C<u>H</u>$_2$CH$_3$), 1.69 (m, 1H, C<u>H</u>(CH$_3$)$_2$), 1.71 (m, 3H, C<u>H</u>$_3$C=), 1.80-2.20 (m, 2H, C<u>H</u>$_2$CH$_3$), 3.72 (dd, 1H, *J* = 2.34, 9.84 Hz, OC<u>H</u>), 4.37 (d, 1H, *J* = 9.99 Hz, OOC<u>H</u>), 5.0 (m, 2H, C<u>H</u>$_2$=).

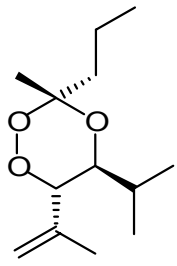
^{13}C-NMR: ($CDCl_3$)

δ (ppm) = 6.6 (q, <u>C</u>H$_3$CH$_2$), 7.9 (q, <u>C</u>H$_3$CH$_2$), 14.9 (q, <u>C</u>H$_3$CH), 19.5 (q, <u>C</u>H$_3$C=), 19.9 (q, <u>C</u>H$_3$CH), 23.2 (t, <u>C</u>H$_2$CH$_3$), 28.2 (d, <u>C</u>H(CH$_3$)$_2$), 28.4 (t, <u>C</u>H$_2$CH$_3$), 72.8 (d, O<u>C</u>H), 85.2 (d, OO<u>C</u>H), 105.6 (s, O<u>C</u>OO), 117.6 (t, <u>C</u>H$_2$=C), 139.5 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-5-Isopropyl-3-methyl-6-(prop-1-en-2-yl)-3-propyl-1,2,4-trioxane (85a) and (3RS,5SR,6SR)-5-isopropyl-3-methyl-6-(prop-1-en-2-yl)-3-propyl-1,2,4-trioxane (85b) (elid 400b)



85a



85b

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.85 g, 5.31 mmol) and excess 2-pentanone (2.0 g, 23.3 mmol) in CH_2Cl_2 was treated with a catalytic

amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **85a**,**b** in a ratio 87:13 (0.21 g, 0.92 mmol, 17 %) as colorless liquid.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **85a**)

δ (ppm) = 0.89 (t, 3H, *J* = 7.20 Hz, C$\underline{H_3}$CH$_2$), 0.89 (d, 3H, *J* = 6.90 Hz, C$\underline{H_3}$CH), 0.94 (d, 3H, *J* = 6.90 Hz, C$\underline{H_3}$CH), 0.91-0.98 (m, 2H, C$\underline{H_2}$CH$_3$), 1.38-1.62 (m, 2H, C$\underline{H_2}$CH$_2$), 1.56 (s, 3H, C$\underline{H_3}$), 1.69 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 1.75 (m, 3H, C$\underline{H_3}$C=), 3.80 (dd, 1H, *J* = 2.35, 9.85 Hz, OC$\underline{H}$), 4.41 (d, 1H, *J* = 9.99 Hz, OOC$\underline{H}$), 5.05 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **85a**)

δ (ppm) = 14.4 (q, $\underline{C}$H$_3$CH$_2$), 15.1 (q, $\underline{C}$H$_3$CH), 16.1 (t, $\underline{C}$H$_2$CH$_3$), 19.2 (q, $\underline{C}$H$_3$C=), 19.6 (q, $\underline{C}$H$_3$CH), 19.9 (q, $\underline{C}$H$_3$), 28.2 (d, $\underline{C}$H(CH$_3$)$_2$), 41.4 (t, $\underline{C}$H$_2$CH$_2$), 73.4 (d, O$\underline{C}$H), 85.6 (d, OO$\underline{C}$H), 103.8 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}$H$_2$=C), 139.6 (s, $\underline{C}$=CH$_2$).

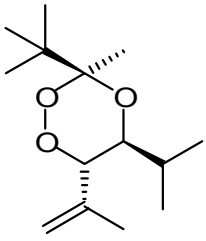
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signal of minor diastereomer **85b**)

δ (ppm) = 3.74 (dd, 1H, *J* = 2.27, 9.84 Hz, OC$\underline{H}$).

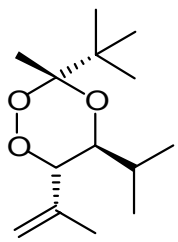
^{13}C-NMR: (75.5 MHz, $CDCl_3$, of minor diastereomer **85b**)

δ (ppm) = 14.4 (q, $\underline{C}$H$_3$CH$_2$), 14.7 (q, $\underline{C}$H$_3$CH), 17.1 (t, $\underline{C}$H$_2$CH$_3$), 19.1 (q, $\underline{C}$H$_3$C=), 19.6 (q, $\underline{C}$H$_3$CH), 23.1 (q, $\underline{C}$H$_3$), 27.8 (d, $\underline{C}$H(CH$_3$)$_2$), 34.4 (t, $\underline{C}$H$_2$CH$_2$), 73.0 (d, O$\underline{C}$H), 85.1 (d, OO$\underline{C}$H), 104.3 (s, O$\underline{C}$OO), 117.9 (t, $\underline{C}$H$_2$=C), 139.2 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3-*tert*-Butyl-5-isopropyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (86a) and (3RS,5SR,6SR)-3-*tert*-butyl-5-isopropyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (86b) (elid 330d)



86a



86b

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.58 g, 3.63 mmol) and excess 3,3-dimethyl-2-butanone (2.0 g, 20 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under

vacuum afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **86a**,**b** in a ratio 83:17 (0.32 g, 1.32 mmol, 36 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **86a**)

δ (ppm) = 0.88 (d, 3H, *J* = 6.76 Hz, C$\underline{H_3}$CH), 0.93 (d, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH), 0.95 (s, 9H, (C$\underline{H_3}$)$_3$C), 1.51 (s, 3H, C$\underline{H_3}$), 1.68 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 1.72 (m, 3H, C$\underline{H_3}$C=), 3.78 (dd, 1H, *J* = 2.35, 9.85 Hz, OC$\underline{H}$), 4.37 (d, 1H, *J* = 9.85 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **86a**)

δ (ppm) = 14.3 (q, $\underline{C}H_3$), 15.1 (q, $\underline{C}H_3$CH), 19.5 (q, $\underline{C}H_3$C=), 20.0 (q, $\underline{C}H_3$CH), 24.7 (q, ($\underline{C}H_3$)$_3$C), 28.3 (d, $\underline{C}$H(CH$_3$)$_2$), 39.0 (s, $\underline{C}$(CH$_3$)$_3$), 73.1 (d, O$\underline{C}$H), 85.3 (d, OO$\underline{C}$H), 106.3 (s, O$\underline{C}$OO), 117.6 (t, $\underline{C}H_2$=C), 139.4 (s, $\underline{C}$=CH$_2$).

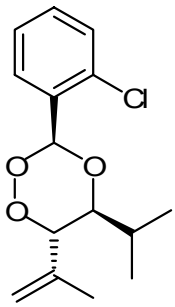
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **86b**)

δ (ppm) = 1.10 (s, 9H, (C$\underline{H_3}$)$_3$C), 3.50 (m, 1H, OC$\underline{H}$), 4.29 (d, 1H, *J* = 8.22 Hz, OOC$\underline{H}$).

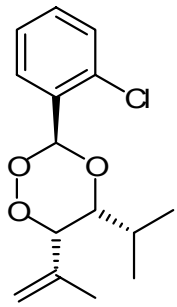
^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of minor diastereomer **86b**)

δ (ppm) = 74.7 (d, O$\underline{C}$H), 91.7 (d, OO$\underline{C}$H), 104.8 (s, O$\underline{C}$OO), 141.2 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3-(2-Chlorophenyl)-5-isopropyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (87a) and (3RS,5SR,6RS)-3-(2-chlorophenyl)-5-isopropyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (87b) (elid 450g)



87a



87b

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.90 g, 5.63 mmol) and 2-chlorobenzaldehyde (0.98 g, 6.98 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.80) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **87a**,**b** in a ratio 91:9 (0.52 g, 1.84 mmol, 33 %) as oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **87a**)

δ (ppm) = 0.97 (d, 3H, *J* = 6.75 Hz, C$\underline{H_3}$CH), 0.98 (d, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH), 1.71 (m, 3H, C$\underline{H_3}$C=), 1.81 (m, 1H, C$\underline{H}(CH_3)_2$), 3.78 (dd, 1H, *J* = 2.20, 9.41 Hz, OC$\underline{H}$), 4.64 (d, 1H, *J* = 9.57 Hz, OOC$\underline{H}$), 5.04-5.10 (m, 2H, C$\underline{H_2}$=), 6.46 (s, 1H, OC$\underline{H}$OO), 7.15-7.61 (m, 4H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **87a**)

δ (ppm) = 15.5 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 20.0 (q, $\underline{C}H_3CH$), 28.2 (d, $\underline{C}H(CH_3)_2$), 81.2 (d, O$\underline{C}$H), 85.8 (d, OO$\underline{C}$H), 101.0 (d, O$\underline{C}$HOO), 118.6 (t, $\underline{C}H_2$=C), 126.8 (d, CH_{arom}), 128.7 (d, CH_{arom}), 129.4 (d, CH_{arom}), 130.9 (d, CH_{arom}), 132.2 (s, Cq_{arom}), 133.5 (s, Cq_{arom}), 138.7 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **87b**)

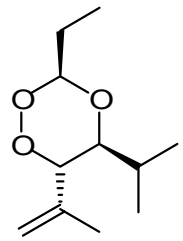
δ (ppm) = 0. 79 (br. s, 3H, C$\underline{H_3}$CH), 0.81 (br. s, 3H, C$\underline{H_3}$CH), 2.0 (m, 3H, C$\underline{H_3}$C=), 3.74 (dd, 1H, *J* = 3.54, 10.29 Hz, OC$\underline{H}$), 4.15 (d, 1H, *J* = 3.54 Hz, OOC$\underline{H}$), 6.44 (s, 1H, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **87b**)

δ (ppm) = 17.9 (q, $\underline{C}H_3CH$), 19.2 (q, $\underline{C}H_3C$=), 23.2 (q, $\underline{C}H_3CH$), 29.4 (d, $\underline{C}H(CH_3)_2$), 83.1 (d, O$\underline{C}$H), 83.7 (d, OO$\underline{C}$H), 101.5 (d, O$\underline{C}$HOO), 119.1 (t, $\underline{C}H_2$=C), 127.0 (d, CH_{arom}), 128.3 (d, CH_{arom}), 128.5 (d, CH_{arom}), 129.3 (d, CH_{arom}), 130.5 (s, Cq_{arom}), 135.0 (s, Cq_{arom}), 141.0 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3-Ethyl-5-isopropyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (88)

(elid 387b)



Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.92 g, 5.75 mmol) and propionaldehyde diethyl acetal (0.76 g, 5.76 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum afforded the pure 1,2,4-trioxane (0.51 g, 2.55 mmol, 44 %) as faint yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

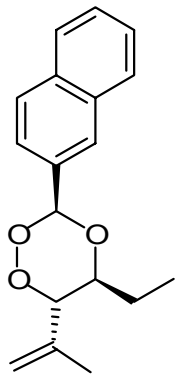
δ (ppm) = 0.90 (d, 3H, *J* = 6.76 Hz, C$\underline{H_3}$CH), 0.92 (t, 3H, *J* = 7.64 Hz, C$\underline{H_3}$CH$_2$), 0.97 (d, 3H, *J* = 6.91 Hz, C$\underline{H_3}$CH), 1.52-1.62 (dq, 2H, *J* = 5.29, 7.64 Hz, C$\underline{H_2}$CH$_3$), 1.70 (m, 3H, C$\underline{H_3}$C=), 1.72 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 3.54 (dd, 1H, *J* = 2.34, 9.42 Hz, OC$\underline{H}$), 4.49 (d, 1H, *J* = 9.42 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H_2}$=), 5.13 (t, 1H, *J* = 5.29 Hz, C$\underline{H}$CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 8.0 (q, $\underline{C}$H$_3$CH$_2$), 15.3 (q, $\underline{C}$H$_3$CH), 19.5 (q, $\underline{C}$H$_3$C=), 19.9 (q, $\underline{C}$H$_3$CH), 25.3 (t, $\underline{C}$H$_2$CH$_3$), 28.1 (d, $\underline{C}$H(CH$_3$)$_2$), 80.4 (d, O$\underline{C}$H), 85.7 (d, OO$\underline{C}$H), 105.3 (d, $\underline{C}$HCH$_2$), 118.1 (t, $\underline{C}$H$_2$=), 138.9 (s, $\underline{C}$=CH$_2$).

4.6.9 Derived from 4-hydroperoxy-5-methylhex-5-en-3-ol (7b)

(3RS,5RS,6RS)-5-Ethyl-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (89)
(elid 493l)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (1.22 g, 8.36 mmol) and β-naphthaldehyde (1.30 g, 8.33 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.71) affords the 1,2,4-trioxane (0.57 g, 2.0 mmol, 24 %) as viscous oil which crystallizes into white solid on standing.

M.p. 73-75 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.14 (dd, 3H, *J* = 7.35, 7.35 Hz, C$\underline{H_3}$CH$_2$), 1.70 (m, 2H, C$\underline{H_2}$CH$_3$), 1.86 (m, 3H, C$\underline{H_3}$C=), 3.96 (ddd, 1H, *J* = 3.75, 7.86, 9.26 Hz, OC$\underline{H}$), 4.67 (d, 1H, *J* = 9.26 Hz,

OOC<u>H</u>), 5.18 (m, 1H, C<u>H$_2$</u>=), 5.23 (s, 1H, C<u>H$_2$</u>=), 6.43 (s, 1H, OC<u>H</u>OO), 7.48- 8.07 (m, 7H, <u>H$_{arom}$</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.4 (q, <u>C</u>H$_3$CH$_2$), 19.9 (q, CH$_3$<u>C</u>=), 23.6 (t, <u>C</u>H$_2$CH$_3$), 78.5 (d, O<u>C</u>H), 87.4 (d, OO<u>C</u>H), 104.0 (d, O<u>C</u>HOO), 118.4 (t, <u>C</u>H$_2$=C), 124.0 (d, <u>C</u>H$_{arom}$), 126.1 (d, <u>C</u>H$_{arom}$), 126.6 (d, <u>C</u>H$_{arom}$), 126.8 (d, <u>C</u>H$_{arom}$), 127.6 (d, <u>C</u>H$_{arom}$), 128.0 (d, <u>C</u>H$_{arom}$), 128.3 (d, <u>C</u>H$_{arom}$), 131.9 (s, <u>C</u>q$_{arom}$), 132.8 (s, <u>C</u>q$_{arom}$), 133.9 (s, <u>C</u>q$_{arom}$), 138.7 (s, <u>C</u>=CH$_2$).

IR: (CsI)

ν (cm^{-1}) = 3064, 2980, 2925, 2898, 1664, 1605, 1071, 908, 824.

MS: (EI, 70 eV)

m/z (%) = 284 (M^+, 4), 156 ($C_{11}H_8O^+$, 100), 155 ($C_{11}H_7O^+$, 95), 128 ($C_{10}H_8^+$, 22), 127 ($C_{10}H_7^+$, 73), 96 ($C_7H_{12}^+$, 47), 81 ($C_6H_9^+$, 17).

HRMS: (EI, 70 eV, $C_{18}H_{20}O_3$)

Calcd: M = 284.141 g/mol

Found: M = 284.141 ±0.005 g/mol

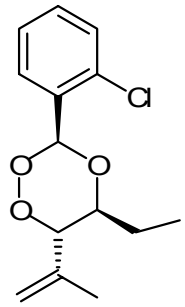
Elemental Analysis: ($C_{18}H_{20}O_3$, M = 284.35 g/mol)

Calcd: C 76.03 H 7.09

Found: C 75.53 H 7.11

(3RS,5RS,6RS)-3-(2-Chlorophenyl)-5-ethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (90)

(elid 446b, 492n)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (1.50 g, 10.3 mmol) and 2-chlorobenzaldehyde (1.44 g, 10.2 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10) affords the 1,2,4-trioxane (0.60 g, 2.23 mmol, 22 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.97 (dd, 3H, *J* = 7.41, 7.41 Hz, $C\underline{H_3}CH_2$), 1.43-1.62 (m, 2H, $C\underline{H_2}CH_3$), 1.73 (m, 3H, $C\underline{H_3}C$=), 3.82 (ddd, 1H, *J* = 3.54, 8.10, 9.24 Hz, OC<u>H</u>), 4.48 (d, 1H, *J* = 9.24 Hz, OOC<u>H</u>), 5.05 (m, 2H, $C\underline{H_2}$=), 5.48 (s, 1H, OC<u>H</u>OO), 7.21- 7.65 (m, 4H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.3 (q, $\underline{C}H_3CH_2$), 19.7 (q, $\underline{C}H_3C$=), 23.6 (t, $\underline{C}H_2CH_3$), 78.7 (d, O<u>C</u>H), 87.4 (d, OO<u>C</u>H), 101.0 (d, O<u>C</u>HOO), 118.5 (t, $\underline{C}H_2$=C), 126.8 (d, $\underline{C}H_{arom}$), 128.7 (d, $\underline{C}H_{arom}$), 129.5 (d, $\underline{C}H_{arom}$), 130.9 (d, $\underline{C}H_{arom}$), 132.1 (s, $\underline{C}q_{arom}$), 133.5 (s, $\underline{C}q_{arom}$), 138.7 (s, $\underline{C}$=CH_2).

IR: (Film)

ν (cm^{-1}) = 3079, 2971, 2925, 2879, 1647, 1597, 1576, 1445, 1086, 1053, 1003, 960, 916.

MS: (EI, 70 eV)

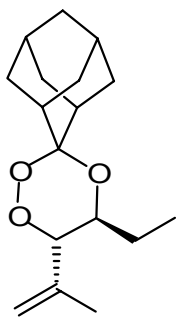
m/z (%) = 268 (M^+, not observed), 142 ($C_7H_5{}^{37}Cl^+$, 13), 141 ($C_7H_4{}^{37}Cl^+$, 42), 140 ($C_7H_5{}^{35}Cl^+$, 39), 139 ($C_7H_4{}^{35}Cl^+$, 100), 113 ($C_6H_5{}^{37}Cl^+$, 7), 111 ($C_6H_5{}^{35}Cl^+$, 21), 96 ($C_7H_{12}{}^+$, 30), 81 ($C_6H_9{}^+$, 20).

Elemental Analysis: ($C_{14}H_{17}ClO_3$, M = 268.74 g/mol)

Calcd: C 62.57 H 6.38

Found: C 62.55 H 6.36

(5RS,6RS)-5-Ethyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (91) (elid 489r, 489z)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (1.56 g, 10.7 mmol) and adamantanone (1.62 g, 10.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by

preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.83) affords the 1,2,4-trioxane (0.15 g, 0.54 mmol, 5 %) as viscous colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.97 (dd, 3H, *J* = 7.35, 7.35 Hz, C<u>H</u>$_3$CH$_2$), 1.16-2.10 (m, 15H, C<u>H</u>$_2$CH$_3$, C<u>H</u> and C<u>H</u>$_2$), 1.73 (m, 3H, C<u>H</u>$_3$C=), 2.90 (br. s, 1H, C<u>H</u>), 3.80 (ddd, 1H, *J* = 2.79, 9.42, 9.54 Hz, OC<u>H</u>), 4.24 (d, 1H, *J* = 9.54 Hz, OOC<u>H</u>), 5.04 (m, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.7 (q, <u>C</u>H$_3$CH$_2$), 19.9 (q, <u>C</u>H$_3$C=), 24.0 (t, <u>C</u>H$_2$CH$_3$), 27.2 (d, CH), 27.3 (d, CH), 29.8 (d, CH), 36.7 (d, CH), 33.0 (t, CH_2), 33.3 (t, CH_2), 33.4 (t, CH_2), 33.6 (t, CH_2), 37.2 (t, CH_2), 70.0 (d, O<u>C</u>H), 87.5 (d, OO<u>C</u>H), 104.8 (s, O<u>C</u>OO), 117.7 (t, <u>C</u>H$_2$=C), 139.5 (s, <u>C</u>=CH$_2$).

IR: (Film)

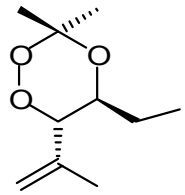
ν (cm^{-1}) = 3082, 2937, 2914, 2857, 1648, 1450, 1379, 1109, 1093, 1072, 1024, 925, 910.

MS: (EI, 70 eV)

m/z (%) = 278 (M^+, less than 1), 220 (M^+-C_3H_6O, 1), 150 ($C_{10}H_{14}O^+$, 65), 96 ($C_7H_{12}^+$, 100), 81 ($C_6H_9^+$, 25), 80 ($C_6H_8^+$, 36), 79 ($C_6H_7^+$, 43).

(5RS,6RS)-5-Ethyl-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (92)

(elid 329e)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (0.64 g, 4.38 mmol) and excess 2,2-dimethoxy propane (2.0 g, 19.2 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum affords the 1,2,4-trioxane (0.26 g, 1.40 mmol, 32 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

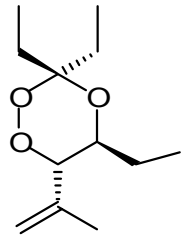
δ (ppm) = 0.91 (dd, 3H, *J* = 7.42, 7.42 Hz, C$\underline{H_3}$CH$_2$), 1.25-1.54 (m, 2H, C$\underline{H_2}$CH$_3$), 1.32 (s, 3H, C$\underline{H_3}$), 1.61 (s, 3H, C$\underline{H_3}$), 1.73 (m, 3H, C$\underline{H_3}$C=), 3.81 (ddd, 1H, *J* = 3.24, 8.25, 9.69 Hz, OC$\underline{H}$), 4.24 (d, 1H, *J* = 9.69 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.3 (q, $\underline{C}$H$_3$CH$_2$), 19.6 (q, $\underline{C}$H$_3$C=), 20.6 (q, $\underline{C}$H$_3$), 23.9 (t, $\underline{C}$H$_2$CH$_3$), 25.9 (q, $\underline{C}$H$_3$), 71.2 (d, O$\underline{C}$H), 87.2 (d, OO$\underline{C}$H), 102.7 (s, O$\underline{C}$OO), 117.8 (t, $\underline{C}$H$_2$=C), 139.3 (s, $\underline{C}$=CH$_2$).

(5RS,6RS)-3,3,5-Triethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (93)

(elid 399b, 413c, 491t)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (1.14 g, 7.80 mmol) and 3-pentanone (0.67 g, 7.79 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up affords the 1,2,4-trioxane (0.37 g, 1.73 mmol, 22 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

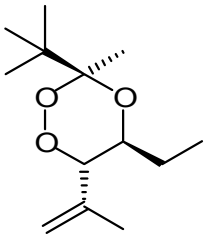
δ (ppm) = 0.87 (t, 3H, *J* = 7.65 Hz, C$\underline{H_3}$CH$_2$), 0.88 (t, 3H, *J* = 7.50 Hz, C$\underline{H_3}$CH$_2$), 0.91 (dd, 3H, *J* = 7.35, 7.35 Hz, C$\underline{H_3}$CH$_2$CH), 1.30-1.74 (m, 4H, C$\underline{H_2}$CH and C$\underline{H_2}$CH$_3$), 1.74 (m, 3H, C$\underline{H_3}$C=), 1.88-2.20 (m, 2H, C$\underline{H_2}$CH$_3$), 3.78 (ddd, 1H, *J* = 3.06, 8.25, 9.69 Hz, OC$\underline{H}$), 4.21 (d, 1H, *J* = 9.69 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 6.8 (q, $\underline{C}$H$_3$), 8.0 (q, $\underline{C}$H$_3$), 9.3 (q, $\underline{C}$H$_3$CH$_2$CH), 19.7 (q, $\underline{C}$H$_3$C=), 23.0 (t, $\underline{C}$H$_2$CH), 24.0 (t, $\underline{C}$H$_2$CH$_3$), 28.4 (t, $\underline{C}$H$_2$CH$_3$), 70.5 (d, O$\underline{C}$H), 87.0 (d, OO$\underline{C}$H), 106.0 (s, O$\underline{C}$OO), 117.7 (t, $\underline{C}$H$_2$=C), 139.5 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3-*tert*-Butyl-5-ethyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (94)

(elid 329b, 413b)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (0.50 g, 3.42 mmol) and excess 3,3-dimethyl-2-butanone (2.0 g, 20.0 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum affords the 1,2,4-trioxane (0.30 g, 1.32 mmol, 39 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

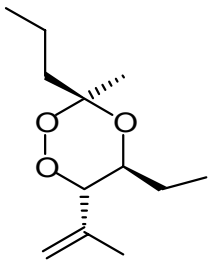
δ (ppm) = 0.92 (dd, 3H, *J* = 7.42, 7.42 Hz, $C\underline{H_3}CH_2$), 0.96 (s, 9H, $(C\underline{H_3})_3C$), 1.22-1.51 (m, 2H, $C\underline{H_2}CH_3$), 1.55 (s, 3H, $C\underline{H_3}$), 1.74 (m, 3H, $C\underline{H_3}C$=), 3.82 (ddd, 1H, *J* = 3.17, 8.18, 9.69 Hz, OC<u>H</u>), 4.20 (d, 1H, *J* = 9.69 Hz, OOC<u>H</u>), 5.03 (m, 2H, $C\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

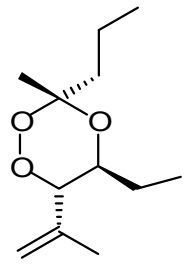
δ (ppm) = 9.2 (q, $\underline{C}H_3CH_2$), 14.4 (q, $\underline{C}H_3$), 19.7 (q, $\underline{C}H_3C$=), 24.0 (t, $\underline{C}H_2CH_3$), 24.7 (q, $(\underline{C}H_3)_3C$), 38.7 (s, $\underline{C}(CH_3)_3$), 70.6 (d, O<u>C</u>H), 87.1 (d, OO<u>C</u>H), 106.4 (s, O<u>C</u>OO), 117.6 (t, $\underline{C}H_2$=C), 139.4 (s, <u>C</u>=CH_2).

(3RS,5RS,6RS)-5-Ethyl-3-methyl-6-(prop-1-en-2-yl)-3-propyl-1,2,4-trioxane (95a) and (3RS,5SR,6SR)-5-ethyl-3-methyl-6-(prop-1-en-2-yl)-3-propyl-1,2,4-trioxane (95b)

(elid 329c)



95a



95b

Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (0.50 g, 3.42 mmol) and excess 2-pentanone (2.0 g, 23.2 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up, evaporation of the excess ketone under vacuum affords a yellow oil of the 1,2,4-trioxanes diastereomeric mixture **95a,b** in 83:17 ratio (0.28 g, 1.31 mmol, 38 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **95a**)

δ (ppm) = 0.88 (t, 3H, *J* = 7.20 Hz, C<u>H</u>$_3$(CH$_2$)$_2$), 0.91 (dd, 3H, *J* = 7.40, 7.40 Hz, C<u>H</u>$_3$CH$_2$), 1.25-1.55 (m, 6H, C<u>H</u>$_2$CH$_3$ and C<u>H</u>$_2$C<u>H</u>$_2$), 1.57 (s, 3H, C<u>H</u>$_3$), 1.73 (s, 3H, C<u>H</u>$_3$C=), 3.82 (ddd, 1H, *J* = 3.24, 8.22, 9.54 Hz, OC<u>H</u>), 4.23 (d, 1H, *J* = 9.54 Hz, OOC<u>H</u>), 5.03 (m, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **95a**)

δ (ppm) = 9.2 (q, <u>C</u>H$_3$CH$_2$), 14.3 (q, CH$_3$), 16.1 (q, CH$_3$), 19.0 (t, CH$_2$), 19.7 (q, <u>C</u>H$_3$C=), 23.9 (t, <u>C</u>H$_2$CH$_3$), 41.4 (t, <u>C</u>H$_2$), 70.9 (d, O<u>C</u>H), 87.3 (d, OO<u>C</u>H), 104.0 (s, O<u>C</u>OO), 117.7 (t, <u>C</u>H$_2$=C), 139.4 (s, <u>C</u>=CH$_2$).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **95b**)

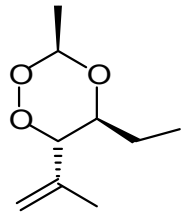
δ (ppm) = 0.89 (t, 3H, C<u>H</u>$_3$(CH$_2$)$_2$), 0.94 (dd, 3H, *J* = 7.20, 7.20 Hz, C<u>H</u>$_3$CH$_2$), 3.76 (ddd, 1H, *J* = 3.09, 8.22, 9.57 Hz, OC<u>H</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **95b**)

δ (ppm) = 9.3 (q, <u>C</u>H$_3$CH$_2$), 14.3 (q, CH$_3$), 17.3 (q, CH$_3$), 19.0 (t, CH$_2$), 19.6 (t, <u>C</u>H$_3$C=), 23.3 (t, <u>C</u>H$_2$CH$_3$), 34.7 (t, CH$_2$), 70.1 (d, O<u>C</u>H), 87.0 (d, OO<u>C</u>H), 104.6 (s, O<u>C</u>OO), 117.7 (t, <u>C</u>H$_2$=C), 139.4 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-5-Ethyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (96)

(elid 413a)



Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (1.0 g, 6.85 mmol) and acetaldehyde diethylacetal (0.81 g, 6.86 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up affords the 1,2,4-trioxane (0.44 g, 2.56 mmol, 37 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.93 (dd, 3H, *J* = 7.50, 7.50 Hz, C<u>H</u>$_3$CH$_2$), 1.23 (d, 3H, *J* = 5.43 Hz, C<u>H</u>$_3$CH), 1.10-1.54 (m, 2H, C<u>H</u>$_2$CH$_3$), 1.68 (m, 3H, C<u>H</u>$_3$C=), 3.57 (ddd, 1H, *J* = 3.21,

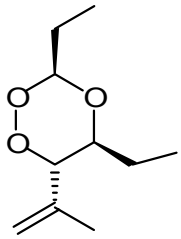
8.55, 9.24 Hz, OC<u>H</u>), 4.30 (d, 1H, J = 9.24 Hz, OOC<u>H</u>), 5.0 (m, 2H, C<u>H</u>$_2$=), 5.33 (q, 1H, *J* = 5.43 Hz, C<u>H</u>CH$_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

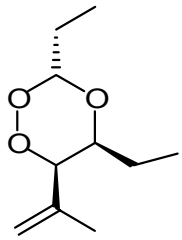
δ (ppm) = 9.3 (q, <u>C</u>H$_3$CH$_2$), 17.8 (q, <u>C</u>H$_3$CH), 19.6 (q, <u>C</u>H$_3$C=), 23.5 (t, <u>C</u>H$_2$CH$_3$), 77.9 (d, O<u>C</u>H), 87.2 (d, OO<u>C</u>H), 101.5 (d, <u>C</u>HCH$_3$), 118.1 (t, <u>C</u>H$_2$=C), 138.7 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-3,5-Diethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129b) and (3RS,5SR,6RS)-3,5-diethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (97)

(elid 387a)



129b



97

Following **GP-15**, a solution of 4-hydroperoxy-5-methylhex-5-en-3-ol (**7b**) (0.67 g, 4.59 mmol) and propionaldehyde diethyl acetal (0.61 g, 4.62 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up afforded the 1,2,4-trioxanes diastereomeric mixture **129b** and **97** in 89:11 ratio (0.42 g, 2.26 mmol, 49 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **129b**)

δ (ppm) = 0.93 (dd, 3H, *J* = 7.65, 7.65 Hz, C<u>H</u>$_3$CH$_2$), 0.96 (dd, 3H, *J* = 7.35, 7.35 Hz, C<u>H</u>$_3$CH$_2$), 1.34-1.63 (m, 4H, 2 x C<u>H</u>$_2$CH$_3$), 1.70 (m, 3H, C<u>H</u>$_3$C=), 3.57 (ddd, 1H, *J* = 3.24, 8.70, 9.24 Hz, OC<u>H</u>), 4.32 (d, 1H, *J* = 9.24 Hz, OOC<u>H</u>), 5.04 (m, 2H, C<u>H</u>$_2$=), 5.16 (t, 1H, *J* = 5.45 Hz, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **129b**)

δ (ppm) = 8.1 (q, <u>C</u>H$_3$), 9.4 (q, <u>C</u>H$_3$), 19.7 (q, <u>C</u>H$_3$C=), 23.6 (t, CH$_2$), 25.4 (t, CH$_2$), 77.9 (d, O<u>C</u>H), 87.5 (d, OO<u>C</u>H), 105.5 (d, O<u>C</u>HOO), 118.1 (t, <u>C</u>H$_2$=C), 138.9 (s, <u>C</u>=CH$_2$).

^{1}H-NMR: (300 MHz, $CDCl_3$, minor diastereomer **97**)

δ (ppm) = 0.93 (dd, 3H, *J* = 7.65, 7.65 Hz, C<u>H</u>$_3$CH$_2$), 0.96 (dd, 3H, *J* = 7.35, 7.35 Hz, C<u>H</u>$_3$CH$_2$), 1.34-1.63 (m, 4H, 2 x C<u>H</u>$_2$CH$_3$), 1.98 (m, 3H, C<u>H</u>$_3$C=), 3.88 (m, 1H, OC<u>H</u>),

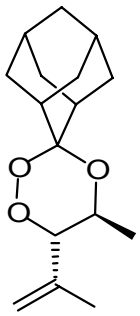
4.02 (d, 1H, *J* = 3.84 Hz, OOC<u>H</u>), 5.04 (m, 2H, C<u>H</u>$_2$=), 5.16 (t, 1H, *J* = 5.45 Hz, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of minor diastereomer **97**)

δ (ppm) = 18.5 (q, <u>C</u>H$_3$C=), 77.7 (d, O<u>C</u>H), 84.6 (d, OO<u>C</u>H), 105.6 (d, O<u>C</u>HOO), 118.3 (t, <u>C</u>H$_2$=), 141.8 (s, <u>C</u>=CH$_2$).

4.6.10 Derived from 3-hydroperoxy-4-methylpent-4-en-2-ol (7a)

(5RS,6RS)-5-Methyl-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (98) (elid 487j)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (2.0 g, 15.2 mmol) and adamantanone (2.28 g, 15.2 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.89) afforded the pure 1,2,4-trioxane as colorless oil which crystallizes on standing (0.47 g, 1.78 mmol, 12 %).

M.p. 48-49 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.07 (d, 3H, *J* = 6.18 Hz, C<u>H</u>$_3$CH), 1.52-2.11 (m, 13H, C<u>H</u> and C<u>H</u>$_2$), 1.73 (m, 3H, C<u>H</u>$_3$C=), 2.90 (br. d, 1H, C<u>H</u>), 4.04 (dq, 1H, *J* = 6.18, 9.56 Hz, OC<u>H</u>), 4.17 (d, 1H, *J*= 9.56 Hz, OOC<u>H</u>), 5.04 (m, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.0 (q, <u>C</u>H$_3$CH), 19.8 (q, <u>C</u>H$_3$C=), 27.1 (d, <u>C</u>H), 27.2 (d, <u>C</u>H), 29.8 (d, <u>C</u>H) , 36.5 (d, <u>C</u>H), 33.1 (t, <u>C</u>H$_2$), 33.3 (t, <u>C</u>H$_2$), 33.4 (t, <u>C</u>H$_2$), 33.5 (t, <u>C</u>H$_2$), 37.2 (t, <u>C</u>H$_2$), 65.0 (d, O<u>C</u>H), 88.7 (d, OO<u>C</u>H), 104.8 (s, O<u>C</u>OO), 117.6 (t, <u>C</u>H$_2$=), 139.3 (s, <u>C</u>=CH$_2$).

IR: (Film)

ν (cm^{-1}) = 2912, 1648, 1222, 1109, 1090, 1023, 999, 926.

MS: (EI, 70 eV)

m/z (%) = 264 (M^+, 4), 220 (M^+-C_2H_4O, 55), 150 ($C_{10}H_{14}O^+$, 34), 82 ($C_6H_{10}^+$, 100), 81 ($C_6H_9^+$, 53), 80 ($C_6H_8^+$, 82), 79 ($C_6H_7^+$, 97), 67 ($C_5H_7^+$, 67), 55 ($C_3H_3O^+$, 42).

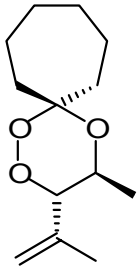
Elemental Analysis: ($C_{16}H_{24}O_3$, M = 264.36)

Calcd: C 72.69 H 9.15

Found: C 72.69 H 9.05

(3RS,4RS)-3-Isopropenyl-4-methyl-1,2,5-trioxa-spiro[5.6]dodecane (99)

(elid 382f)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.73 g, 5.53 mmol) and cycloheptanone (0.61 g, 5.45 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (0.52 g, 2.30 mmol, 42 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) afforded the pure 1,2,4-trioxane as colorless oil (0.20 g, 0.88 mmol, 16 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

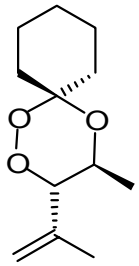
δ (ppm) = 1.07 (d, 3H, *J* = 6.18 Hz, C$\underline{H}_3$CH), 1.50-1.70 (m, 10H, C$\underline{H}_2$), 1.73 (m, 3H, C$\underline{H}_3$C=), 2.15 (m, 1H, C$\underline{H}_2$), 2.33 (m, 1H, C$\underline{H}_2$), 4.01 (dq, 1H, *J* = 6.18, 9.57 Hz, OC$\underline{H}$), 4.17 (d, 1H, *J* = 9.57 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H}_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.0 (q, $\underline{C}H_3$CH), 19.7 (q, $\underline{C}H_3$C=), 22.2 (t, $\underline{C}H_2$), 22.3 (t, $\underline{C}H_2$), 29.4 (t, $\underline{C}H_2$), 29.9 (t, $\underline{C}H_2$), 31.4 (t, $\underline{C}H_2$), 38.9 (t, $\underline{C}H_2$), 65.9 (d, O$\underline{C}$H), 88.7 (d, OO$\underline{C}$H), 107.5 (s, O$\underline{C}$OO), 117.5 (t, $\underline{C}H_2$=), 139.4 (s, $\underline{C}$=CH_2).

(3RS,4RS)-3-Isopropenyl-4-methyl-1,2,5-trioxa-spiro[5.5]undecane (100)

(elid 474z)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.26 g, 9.55 mmol) and cyclohexanone (0.94 g, 9.59 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). After usual work-up the crude product (1.40 g, 6.59 mmol, 69 %) was purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) to afford the pure 1,2,4-trioxane (0.53 g, 2.50 mmol, 26 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.06 (d, 3H, *J* = 6.0 Hz, C$\underline{H_3}$CH), 1.30-1.60 (m, 8H, 4 x C$\underline{H_2}$), 1.73 (m, 3H, CH_3C=), 1.94 (m, 1H, C$\underline{H_2}$), 2.24 (m, 1H, C$\underline{H_2}$), 4.07 (dq, 1H, *J* = 9.50, 6.0 Hz, OC$\underline{H}$), 4.18 (d, 1H, *J* = 9.50 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.0 (q, $\underline{C}H_3$CH), 19.7 (q, $\underline{C}H_3$C=), 22.3 (t, $\underline{C}H_2$), 22.4 (t, $\underline{C}H_2$), 25.6 (t, $\underline{C}H_2$), 29.5 (t, $\underline{C}H_2$), 35.1 (t, $\underline{C}H_2$), 65.6 (d, O$\underline{C}$H), 88.8 (d, OO$\underline{C}$H), 102.8 (s, O$\underline{C}$OO), 117.6 (t, $\underline{C}H_2$=C), 139.3 (s, $\underline{C}$=CH_2).

IR: (Film)

ν (cm^{-1}) = 2937, 1684, 1669, 1653, 1646, 1362, 1163, 1095, 1008, 919.

MS: (EI, 70 eV)

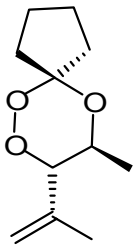
m/z (%) = 98 ($C_6H_{10}O^+$, 80), 82 ($C_6H_{10}^+$, 94), 70 ($C_4H_6O^+$, 52), 69 ($C_4H_5O^+$, 62), 67 ($C_5H_7^+$, 33), 55 ($C_3H_3O^+$, 100).

Elemental Analysis: ($C_{12}H_{20}O_3$, M = 212.29)

Calcd: C 67.89 H 9.50

Found: C 67.45 H 9.45

(8RS,9RS)-8-Isopropenyl-9-methyl-6,7,10-trioxa-spiro[4.5]decane (101)
(elid 121)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.0 g, 7.58 mmol, prepared according to **GP-7b**) and excess cyclopentanone (6.37 g, 75.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of the excess ketone under vacuum afforded the product (1.10 g, 5.53 mmol, 73 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.07 (d, 3H, *J* = 6.3 Hz, C$\underline{H_3}$CH), 1.60-1.87 (m, 7H, C$\underline{H_2}$), 1.71 (m, 3H, CH_3C=), 2.50 (m, 1H, C$\underline{H_2}$), 3.29 (dq, 1H, *J* = 9.40, 6.30 Hz, OC$\underline{H}$), 4.24 (d, 1H, *J* = 9.40 Hz, OOC$\underline{H}$), 5.03 (m, 2H, C$\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

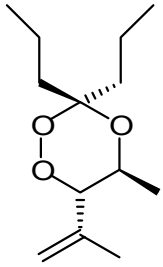
δ (ppm) = 16.7 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 23.1 (t, $\underline{C}H_2$), 24.7 (t, $\underline{C}H_2$), 32.9 (t, $\underline{C}H_2$), 37.3 (t, $\underline{C}H_2$), 68.4 (d, O$\underline{C}$H), 88.6 (d, OO$\underline{C}$H), 114.7 (s, O$\underline{C}$OO), 117.7 (t, $\underline{C}H_2$=C), 139.1 (s, $\underline{C}$=CH_2).

MS: (EI, 70 eV)

m/z (%) = 84 ($C_5H_8O^+$, 81), 82 ($C_6H_{10}^+$, 69), 67 ($C_5H_7^+$, 30), 56 ($C_3H_4O^+$, 52), 55 ($C_3H_3O^+$, 100).

(5RS,6RS)-5-Methyl-6-(prop-1-en-2-yl)-3,3-dipropyl-1,2,4-trioxane (102)

(elid 383b, 476z)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.40 g, 10.6 mmol) and 4-heptanone (1.30 g, 11.4 mmol) in CH_2Cl_2 was treated with a catalytic amount of

$BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (0.60 g, 2.63 mmol, 24.8 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.79) afforded the pure 1,2,4-trioxane as colorless oil (0.33 g, 1.45 mmol, 14 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

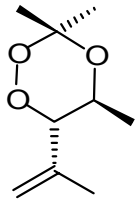
δ (ppm) =0.86 (t, 3H, *J* = 7.35 Hz, C<u>H</u>$_3$CH$_2$), 0.94 (t, 3H, *J* = 7.35 Hz, C<u>H</u>$_3$CH2), 1.06 (d, 3H, *J* = 6.03 Hz, C<u>H</u>$_3$CH), 1.23-1.57 (m, 6H, 3 x C<u>H</u>$_2$), 1.75 (m, 3H, C<u>H</u>$_3$C=), 1.88-2.11 (m, 2H, C<u>H</u>$_2$CH$_2$), 4.01 (dq, 1H, *J* = 6.03, 9.57 Hz, OC<u>H</u>), 4.14 (d, 1H, *J* = 9.57 Hz, OOC<u>H</u>), 5.04 (m, 2H, C<u>H</u>$_2$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 14.3 (q, <u>C</u>H$_3$CH$_2$), 14.4 (q, <u>C</u>H$_3$CH$_2$), 15.8 (t, <u>C</u>H$_2$CH$_3$), 16.9 (q, <u>C</u>H$_3$CH), 17.1 (t, <u>C</u>H$_2$CH$_3$), 19.7 (q, <u>C</u>H$_3$C=), 33.1 (t, <u>C</u>H$_2$CH$_2$), 38.3 (t, <u>C</u>H$_2$CH$_2$), 65.9 (d, O<u>C</u>H), 88.5 (d, OO<u>C</u>H), 105.6 (s, O<u>C</u>OO), 117.5 (t, <u>C</u>H$_2$=), 139.4 (s, <u>C</u>=CH$_2$).

(5RS,6RS)-3,3,5-Trimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (103)

(elid 151)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.0 g, 7.58 mmol, prepared according to **GP-7b**) and excess acetone (5.0 g, 86.2 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of the excess ketone under vacuum afforded the product (0.85 g, 4.93 mmol, 65 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.93 (d, 3H, *J* = 6.20 Hz, C<u>H</u>$_3$CH), 1.19 (s, 3H, C<u>H</u>$_3$), 1.50 (s, 3H, C<u>H</u>$_3$), 1.61 (t, 3H, *J* = 1.32 Hz, CH$_3$C=), 3.91 (dq, 1H, *J* = 9.57, 6.20 Hz, OC<u>H</u>), 4.03 (d, 1H, *J* = 9.57 Hz, OOC<u>H</u>), 4.92 (m, 2H, C<u>H</u>$_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

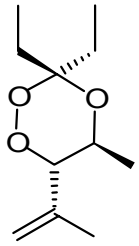
δ (ppm) = 16.6 (q, <u>C</u>H$_3$CH), 19.2 (q, <u>C</u>H$_3$C=), 20.2 (q, <u>C</u>H$_3$), 25.6 (q, <u>C</u>H$_3$), 66.2 (d, O<u>C</u>H), 88.4 (d, OO<u>C</u>H), 102.3 (s, O<u>C</u>OO), 117.3 (t, <u>C</u>H$_2$=C), 139.0 (s, <u>C</u>=CH$_2$).

MS: (EI, 70 eV)

m/z (%) = 115 (M^+-C_3H_7O, 35), 97 ($C_6H_9O^+$, 41), 85 ($C_5H_9O^+$, 38), 83 ($C_5H_7O^+$, 34), 69 ($C_4H_5O^+$, 54), 59 ($C_3H_7O^+$, 100).

(5RS,6RS)-3,3-Diethyl-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (104a)

(elid 109)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.0 g, 7.58 mmol, prepared according to **GP-7b**) and excess 3-pentanone (6.52 g, 75.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of the excess ketone under vacuum afforded the product (1.06 g, 5.31 mmol, 70 %) as an oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.87 (t, 6H, *J* = 7.30 Hz, 2 x $C\underline{H}_3CH_2$), 1.06 (d, 3H, *J* = 6.20 Hz, $C\underline{H}_3CH$), 1.52-1.61 (m, 2H, $C\underline{H}_2CH_3$), 1.72 (t, 3H, *J* = 1.25 Hz, CH_3C=), 1.91-2.16 (m, 2H, $C\underline{H}_2CH_3$), 3.99 (dq, 1H, *J* = 9.55, 6.20 Hz, OC<u>H</u>), 4.13 (d, 1H, *J* = 9.55 Hz, OOC<u>H</u>), 5.03 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

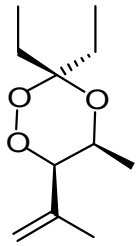
δ (ppm) = 6.7 (q, $\underline{C}H_3CH_2$), 8.1 (q, $\underline{C}H_3CH_2$), 16.9 (q, $\underline{C}H_3CH$), 19.7 (q, $\underline{C}H_3C$=), 23.0 (t, $\underline{C}H_2CH_3$), 28.3 (t, $\underline{C}H_2CH_3$), 65.8 (d, O<u>C</u>H), 88.4 (d, OO<u>C</u>H), 106.0 (s, O<u>C</u>OO), 117.5 (t, $\underline{C}H_2$=C), 139.3 (s, <u>C</u>=CH_2).

MS: (EI, 70 eV)

m/z (%) = 82 ($C_6H_{10}^+$, 87), 70 ($C_4H_6O^+$, 74), 69 ($C_4H_5O^+$, 100), 67 ($C_5H_7^+$, 57).

(5RS,6SR)-3,3-Diethyl-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (104b)

(elid 163)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.0 g, 7.58 mmol, prepared according to **GP-7a**) and excess 3-pentanone (6.52 g, 75.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). After usual work-up and evaporation of the excess ketone under vacuum, a diastereomeric mixture of the 1,2,4-trioxanes **104a**,**b** were obtained as an oil in the ratio 78:22, respectively.

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

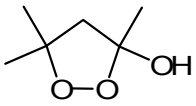
δ (ppm) = 1.06 (d, 3H, *J* = 6.40 Hz, C<u>H</u>$_3$CH), 1.69 (m, 3H, CH_3C=), 3.80 (m, 1H, OC<u>H</u>), 4.19 (d, 1H, *J* = 5.40 Hz, OOC<u>H</u>), 4.95 (m, 2H, C<u>H</u>$_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 7.8 (q, <u>C</u>H$_3$CH$_2$), 8.2 (q, <u>C</u>H$_3$CH$_2$), 30.4 (t, <u>C</u>H$_2$CH$_3$), 30.7 (t, <u>C</u>H$_2$CH$_3$), 75.1 (d, O<u>C</u>H), 87.0 (d, OO<u>C</u>H), 114.0 (t, <u>C</u>H$_2$=C), 141.6 (s, <u>C</u>=CH$_2$).

3,5,5-Trimethyl-1,2-dioxolan-3-ol (104c)

(elid 163)



This compound is obtained in traces amount as byproduct in the photooxygention of 4-methylpent-3-en-2-ol **(6a)** using **GP-7** by cyclization of the minor regioisomer.

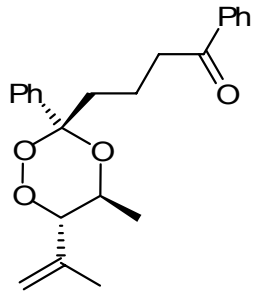
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.16 (d, 1H, *J* = 6.0 Hz, C<u>H</u>$_2$), 1.22 (d, 1H, *J* = 6.0 Hz, C<u>H</u>$_2$), 1.26 (s, 3H, C<u>H</u>$_3$), 1.30 (s, 3H, C<u>H</u>$_3$), 1.67 (s, 3H, C<u>H</u>$_3$C-OH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.2 (t, <u>C</u>H$_2$), 24.9 (q, <u>C</u>H$_3$), 25.0 (q, <u>C</u>H$_3$), 30.1 (q, <u>C</u>H$_3$), 93.3 (s, OO<u>C</u>), 114.9 (s, OO<u>C</u>OH).

4-((3RS,5SR,6SR)-5-Methyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxan-3-yl)-1-phenyl-butan-1-one (105) (elid 482o or elid 488a)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (2.0 g, 15.2 mmol) and 1,5-diphenyl-1,5-pentandione (1.90 g, 7.54 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.49) afforded the pure 1,2,4-trioxane as viscous colorless oil (0.10 g, 0.27 mmol, 4 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.03 (d, 3H, *J* = 6.33 Hz, $C\underline{H}_3CH$), 1.06-1.30 (m, 2H, $CH_2C\underline{H}_2CH_2$), 1.40 (s, 3H, $C\underline{H}_3C$=), 1.62-1.83 (m, 2H, $C\underline{H}_2$), 2.82 (t, 2H, *J* = 7.20 Hz, $C\underline{H}_2CO$), 3.74 (dq, 1H, *J* = 6.33, 9.39 Hz, OC<u>H</u>), 4.27 (d, 1H, J = 9.39 Hz, OOC<u>H</u>), 4.78 (s, 1H, $C\underline{H}_2$=), 4.86 (m, 1H, $C\underline{H}_2$=), 7.18-7.82 (m, 10H, H_{arom}).

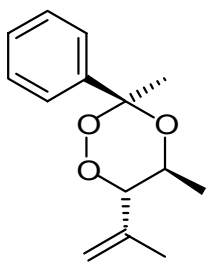
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.4 (q, $\underline{C}H_3CH$), 17.5 (t, $\underline{C}H_2$), 19.4 (q, $\underline{C}H_3C$=), 38.3 (t, $\underline{C}H_2$), 40.9 (t, $\underline{C}H_2$), 67.2 (d, O<u>C</u>H), 88.6 (d, OO<u>C</u>H), 106.4 (s, O<u>C</u>OO), 117.7 (t, $\underline{C}H_2$=), 127.1 (d, $\underline{C}H_{arom}$), 127.7 (d, $\underline{C}H_{arom}$), 127.9 (d, $\underline{C}H_{arom}$), 128.1 (d, $\underline{C}H_{arom}$), 128.4 (d, $\underline{C}H_{arom}$), 132.8 (d, $\underline{C}H_{arom}$), 136.9 (s, $\underline{C}q_{arom}$), 138.9 (s, $\underline{C}q_{arom}$), 139.7 (s, $\underline{C}$=CH_2), 199.7 (s, C=O).

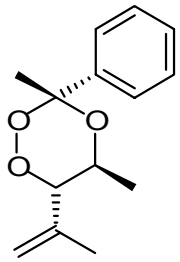
IR: (Film)

ν (cm^{-1}) = 2975, 1726, 1687, 1642, 1598, 1378, 1176, 1003, 917.

(3RS,5RS,6RS)-3,5-Dimethyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (106a) and (3RS,5SR,6SR)-3,5-dimethyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (106b)
(elid 255h)



106a



106b

Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.24 g, 1.82 mmol, prepared according to **GP-7b**) and acetophenone (0.22 g, 1.83 mmol) in Et_2O was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up afforded an oil composed of a diastereomerc mixture of the 1,2,4-trioxanes **106a**, **b** in the ratio 1:1 (128 mg, 0.55 mmol, 30 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, first diastereomer **106a**)

δ (ppm) = 1.16 (d, 3H, *J* = 6.03 Hz, $C\underline{H_3}CH$), 1.54 (m, 3H, $C\underline{H_3}$), 1.81 (m, 3H, $C\underline{H_3}C$=), 3.99 (dq, 1H, *J* = 6.03, 8.4 Hz, OC<u>H</u>), 3.84 (d, 1H, *J* = 8.4 Hz, OOC<u>H</u>), 4.89-4.99 (m, 2H, $C\underline{H_2}$=), 7.25-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, first diastereomer **106a**)

δ (ppm) = 17.7 (q, $\underline{C}H_3CH$), 17.3 (q, $\underline{C}H_3C$=), 29.4 (q, $\underline{C}H_3$), 76.0 (d, O<u>C</u>H), 86.3 (d, OO<u>C</u>H), 108.4 (s, O<u>C</u>OO), 114.1 (t, $\underline{C}H_2$=), 125.1 (d, $\underline{C}H_{arom}$), 127.5 (d, $\underline{C}H_{arom}$), 127.9 (d, $\underline{C}H_{arom}$), 141.1 (s, $\underline{C}$=CH_2), 144.9 (s, Cq_{arom}).

^{1}H-NMR: (300 MHz, $CDCl_3$, other diastereomer **106b**)

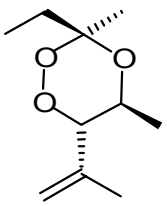
δ (ppm) = 1.29 (d, 3H, *J* = 6.03 Hz, $C\underline{H_3}CH$), 1.64 (m, 3H, $C\underline{H_3}C$=), 1.80 (m, 3H, $C\underline{H_3}$), 3.71 (dq, 1H, *J* = 6.03, 8.82 Hz, OC<u>H</u>), 4.05 (d, 1H, *J* = 8.82 Hz, OOC<u>H</u>), 4.89-4.99 (m, 2H, $C\underline{H_2}$=), 7.25-7.55 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, other diastereomer **106b**)

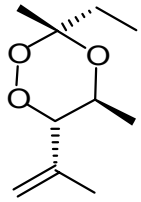
δ (ppm) = 16.4 (q, $\underline{C}H_3CH$), 17.7 (q, $\underline{C}H_3C$=), 28.6 (q, $\underline{C}H_3$), 75.0 (d, O<u>C</u>H), 87.4 (d, OO<u>C</u>H), 108.3 (s, O<u>C</u>OO), 114.5 (t, $\underline{C}H_2$=), 124.9 (d, $\underline{C}H_{arom}$), 127.4 (d, $\underline{C}H_{arom}$), 127.9 (d, $\underline{C}H_{arom}$), 141.3 (s, $\underline{C}$=CH_2), 144.8 (s, Cq_{arom}).

(3RS,5RS,6RS)-3-Ethyl-3,5-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (107a) and (3RS,5SR,6SR)-3-ethyl-3,5-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (107b)

(elid 141b)



107a



107b

Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.60 g, 4.55 mmol, prepared according to **GP-7b**) and excess 2-butanone (5.0 g, 69.4 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of the excess ketone under vacuum afforded a diastereomerc mixture of the 1,2,4-trioxanes **a**, **b** as an oil in the ratio 80:20, respectively, (0.65 g, 3.49 mmol, 77 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **107a**)

δ (ppm) = 0.92 (t, 3H, *J* = 7.60 Hz, C$\underline{H_3}$CH$_2$), 1.06 (d, 3H, *J* = 6.0 Hz, C$\underline{H_3}$CH), 1.59 (s, 3H, C$\underline{H_3}$), 1.62 (q, 2H, *J* = 7.60 Hz, C$\underline{H_2}$CH$_3$), 1.75 (m, 3H, CH$_3$C=), 4.06 (dq, 1H, *J* = 9.50, 6.0 Hz, OC$\underline{H}$), 4.16 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.05 (m, 2H, C$\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **107a**)

δ (ppm) = 7.1 (q, $\underline{C}$H$_3$CH$_2$), 16.9 (q, $\underline{C}$H$_3$CH), 18.6 (q, $\underline{C}$H$_3$), 19.7 (q, $\underline{C}$H$_3$C=), 32.2 (t, $\underline{C}$H$_2$CH$_3$), 66.3 (d, O$\underline{C}$H), 88.8 (d, OO$\underline{C}$H), 104.1 (s, O$\underline{C}$OO), 117.6 (t, $\underline{C}$H$_2$=C), 139.3 (s, $\underline{C}$=CH$_2$).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of the minor diastereomer **107b**)

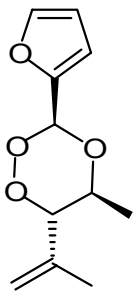
δ (ppm) = 1.26 (s, 3H, C$\underline{H_3}$), 4.0 (m, 1H, OC$\underline{H}$), 4.18 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$),

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **107b**)

δ (ppm) = 8.4 (q, $\underline{C}$H$_3$CH$_2$), 16.9 (q, $\underline{C}$H$_3$CH), 19.7 (q, $\underline{C}$H$_3$C=), 22.7 (q, $\underline{C}$H$_3$), 25.2 (t, $\underline{C}$H$_2$CH$_3$), 66.1 (d, O$\underline{C}$H), 88.4 (d, OO$\underline{C}$H), 105.0 (s, O$\underline{C}$OO), 117.7 (t, $\underline{C}$H$_2$=C), 139.2 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3-(Furan-2-yl)-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (108)

(elid 493e)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.71 g, 5.38 mmol) and furan-2-carboxaldehyde (0.65 g, 6.77 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, $R_f = 0.57$) afforded the pure 1,2,4-trioxane as viscous colorless oil (0.38 g, 1.81 mmol, 34 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.22 (d, 3H, *J* = 6.33 Hz, C$\underline{H_3}$CH), 1.74 (m, 3H, C$\underline{H_3}$C=), 4.0 (dq, 1H, *J* = 6.33, 9.12 Hz, OC$\underline{H}$), 4.45 (d, 1H, *J* = 9.12 Hz, OOC$\underline{H}$), 5.09 (m, 2H, C$\underline{H_2}$=), 6.25 (s, 1H, OC$\underline{H}$OO), 6.34 (m, 1H, CH), 6.53 (m, 1H, CH), 7.39 (m, 1H, CH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.2 (q, $\underline{C}H_3$CH), 19.5 (q, $\underline{C}H_3$C=), 74.1 (d, O$\underline{C}$H), 88.7 (d, OO$\underline{C}$H), 98.4 (d, O$\underline{C}$HOO), 110.0 (d, $\underline{C}$H=), 110.3 (d, $\underline{C}$H=), 118.4 (t, $\underline{C}H_2$=C), 138.4 (s, $\underline{C}$=CH_2), 143.3 (d, O$\underline{C}$H=), 147.3 (s, O$\underline{C}$q=).

IR: (Film)

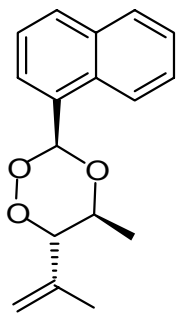
ν (cm^{-1}) = 3126, 3085, 2979, 2901, 1647, 1636, 1601, 1149, 1087, 1065, 1000, 984, 915.

Elemental Analysis: ($C_{11}H_{14}O_4$, M = 210.23)

Calcd: C 62.85 H 6.71

Found: C 62.80 H 6.70

(3RS,5RS,6RS)-5-Methyl-3-(naphthalen-1-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (109)
(elid 450b)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.77 g, 5.83 mmol) and 1-naphthaldehyde (0.91 g, 5.83 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by

preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.56) afforded the pure 1,2,4-trioxane as yellow solid (0.72 g, 2.67 mmol, 46 %).

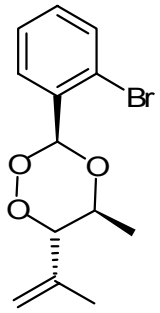
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.33 (d, 3H, *J* = 6.76 Hz, C<u>H</u>$_3$CH), 1.85 (m, 3H, C<u>H</u>$_3$C=), 4.20 (dq, 1H, *J* = 6.76, 9.12 Hz, OC<u>H</u>), 4.61 (d, 1H, *J* = 9.12 Hz, OOC<u>H</u>), 5.16-5.21 (m, 2H, C<u>H</u>$_2$=), 6.84 (s, 1H, OC<u>H</u>OO), 7.45-7.61 (m, 3H, H_{arom}), 7.81-7.89 (m, 3H, H_{arom}), 8.30 (d, 1H, *J* = 8.52 Hz, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.5 (q, <u>C</u>H$_3$CH), 19.8 (q, <u>C</u>H$_3$C=), 74.2 (d, O<u>C</u>H), 88.9 (d, OO<u>C</u>H), 102.6 (d, O<u>C</u>HOO), 118.4 (t, <u>C</u>H$_2$=), 123.9 (d, <u>C</u>H$_{arom}$), 125.0 (d, <u>C</u>H$_{arom}$), 125.6 (d, <u>C</u>H$_{arom}$), 125.8 (d, <u>C</u>H$_{arom}$), 126.5 (d, <u>C</u>H$_{arom}$), 128.5 (d, <u>C</u>H$_{arom}$), 130.4 (d, <u>C</u>H$_{arom}$), 129.8 (s, <u>C</u>q$_{arom}$), 130.7 (s, <u>C</u>q$_{arom}$), 133.6 (s, <u>C</u>q$_{arom}$), 138.7 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-3-(2-Bromophenyl)-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (110)
(elid 501c)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.77 g, 5.83 mmol) and 2-bromobenzaldehyde (1.10 g, 5.95 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.57) afforded the pure 1,2,4-trioxane as viscous colorless oil (0.92 g, 3.08 mmol, 53 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

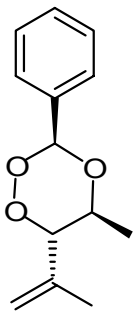
δ (ppm) = 1.24 (d, 3H, *J* = 6.27 Hz, C<u>H</u>$_3$CH), 1.77 (t, 3H, *J* = 1.17Hz, C<u>H</u>$_3$C=), 4.08 (dq, 1H, *J* = 6.42, 9.21 Hz, OC<u>H</u>), 4.47 (d, 1H, *J* = 9.21 Hz, OOC<u>H</u>), 5.09 (m, 1H, C<u>H</u>$_2$=C), 5.14 (s, 1H, C<u>H</u>$_2$=C), 6.52 (s, 1H, OC<u>H</u>OO), 7.16-7.67 (m, 4H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.3 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 73.8 (d, O$\underline{C}$H), 88.7 (d, OO$\underline{C}$H), 102.9 (d, O$\underline{C}$HOO), 118.4 (t, $\underline{C}H_2$=), 122.9 (s, $\underline{C}q_{arom}$), 127.3 (d, $\underline{C}H_{arom}$), 128.9 (d, $\underline{C}H_{arom}$), 131.1 (d, $\underline{C}H_{arom}$), 132.6 (d, $\underline{C}H_{arom}$), 133.4 (s, $\underline{C}q_{arom}$), 138.5 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Methyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (111a)

(elid 491u, 128)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol (**7a**) (0.88 g, 6.67 mmol) and benzaldehyde dimethyl acetal (1.0 g, 6.58 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and purification by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.88) afforded the pure diastereomerc mixture **111a**,**b** in the ratio 97:3, respectively, (0.47 g, 2.14 mmol, 33 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.26 (d, 3H, *J* = 6.30 Hz, $C\underline{H}_3CH$), 1.79 (t, 3H, *J* = 1.20 Hz, CH_3C=), 4.05 (dq, 1H, *J* = 9.10, 6.30 Hz, OC$\underline{H}$), 4.46 (d, 1H, *J* = 9.10 Hz, OOC$\underline{H}$), 5.13 (m, 2H, $C\underline{H}_2$=C), 6.21 (s, 1H, OC$\underline{H}$OO), 7.34-7.51 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.5 (q, $\underline{C}H_3CH$), 19.7 (q, $\underline{C}H_3C$=), 73.8 (d, O$\underline{C}$H), 88.8 (d, OO$\underline{C}$H), 104.1 (d, O$\underline{C}$HOO), 118.3 (t, $\underline{C}H_2$=C), 127.0 (d, $\underline{C}H_{arom}$), 128.5 (d, $\underline{C}H_{arom}$), 129.9 (d, $\underline{C}H_{arom}$), 134.4 (s, Cq_{arom}), 138.7 (s, $\underline{C}$=CH_2).

IR: (Film)

ν (cm^{-1}) = 2978, 1635, 1617, 1374, 1134, 1089, 1061, 1000, 914.

MS: (EI, 70 eV)

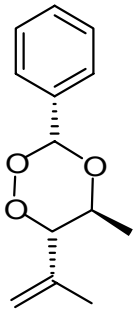
m/z (%) = 106 ($C_7H_6O^+$, 59), 105 ($C_7H_5O^+$, 100), 82 ($C_6H_{10}^+$, 63), 77 ($C_6H_5^+$, 65), 67 ($C_5H_7^+$, 24), 51 ($C_4H_3^+$, 23).

Elemental Analysis: ($C_{13}H_{16}O_3$, M = 220.26)

Calcd: C 70.89 H 7.32

Found: C 70.81 H 7.29

(3RS,5SR,6SR)-5-Methyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (111b)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

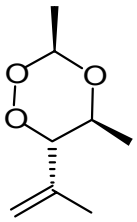
δ (ppm) = 1.33 (d, 3H, *J* = 6.75 Hz, C<u>H$_3$</u>CH), 1.72 (s, 3H, CH_3C=), 3.90 (m, 1H, OC<u>H</u>), 6.40 (s, 1H, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 15.3 (q, <u>C</u>H$_3$CH), 18.3 (q, <u>C</u>H$_3$C=), 79.7 (d, O<u>C</u>H), 84.2 (d, OO<u>C</u>H), 126.0 (d, <u>C</u>H$_{arom}$), 128.4 (d, <u>C</u>H$_{arom}$).

(3RS,5RS,6RS)-3,5-Dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129e)

(elid 162)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol (**7a**) (0.60 g, 4.55 mmol, prepared according to **GP-7b**) and excess acetaldehyde (2.0 g, 45.5 mmol) in Et_2O was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of the excess ketone under vacuum afforded an oil composed of a mixture (0.49 g, 78 %).of the 1,2,4-trioxane **129e** and 1,3,5-trioxane **112** in a ratio 23:77 respectively.

^{1}H-NMR: (300 MHz, $CDCl_3$)

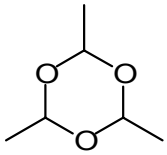
δ (ppm) = 1.12 (d, 3H, *J* = 6.33 Hz, C$\underline{H_3}$CH), 1.25 (d, 3H, *J* = 5.43 Hz, C$\underline{H_3}$CH), 1.70 (t, 3H, *J* = 1.32 Hz, CH_3C=), 3.79 (dq, 1H, *J* = 9.10, 6.30 Hz, OC$\underline{H}$), 4.25 (d, 1H, *J* = 9.10 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=C), 5.36 (q, 1H, *J* = 5.40 Hz, C$\underline{H}$$CH_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.3 (q, $\underline{C}H_3$CH), 17.9 (q, $\underline{C}H_3$CH), 19.6 (q, $\underline{C}H_3$C=), 73.2 (d, O$\underline{C}$H), 88.5 (d, OO$\underline{C}$H), 101.4 (d, O$\underline{C}$HOO), 118.1 (t, $\underline{C}H_2$=C), 138.7 (s, $\underline{C}$=CH_2).

2,4,6-Trimethyl-1,3,5-trioxane (112)

(elid 162)



^{1}H-NMR: (300 MHz, $CDCl_3$)

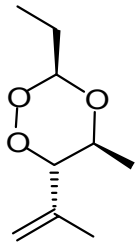
δ (ppm) = 1.34 (d, 3H, *J* = 5.10 Hz, C$\underline{H_3}$), 5.0 (q, 1H, *J* = 5.10 Hz, C$\underline{H}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.5 (q, $\underline{C}H_3$), 98.4 (d, $\underline{C}$H).

(3RS,5RS,6RS)-3-Ethyl-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (113)

(elid 158)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol (**7a**) (0.60 g, 4.55 mmol, prepared according to **GP-7b**) and excess propionaldehyde (2.0 g, 34.5 mmol) in Et_2O was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of the excess ketone under vacuum afforded an oil composed of a mixture of the 1,2,4-trioxane **113** and 1,3,5-trioxane **114** in a ratio 16:84, respectively.

^{1}H-NMR: (300 MHz, $CDCl_3$)

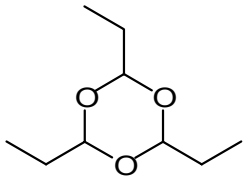
δ (ppm) = 0.90 (t, 3H, *J* = 7.70 Hz, C<u>H</u>$_3$CH$_2$), 1.10 (d, 3H, *J* = 6.30 Hz, C<u>H</u>$_3$CH), 1.56 (m, 2H, C<u>H</u>$_2$CH$_3$), 1.68 (m, 3H, CH$_3$C=), 3.78 (dq, 1H, *J* = 9.10, 6.30 Hz, OC<u>H</u>), 4.24 (d, 1H, *J* = 9.10 Hz, OOC<u>H</u>), 5.02 (m, 2H, C<u>H</u>$_2$=C), 5.15 (t, 1H, *J* = 5.50 Hz, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.9 (q, <u>C</u>H$_3$CH$_2$), 16.3 (q, <u>C</u>H$_3$CH), 19.6 (q, <u>C</u>H$_3$C=), 25.4 (t, <u>C</u>H$_2$CH$_3$), 73.0 (d, O<u>C</u>H), 88.7 (d, OO<u>C</u>H), 105.4 (d, O<u>C</u>HOO), 118.0 (t, <u>C</u>H$_2$=C), 138.7 (s, <u>C</u>=CH$_2$).

2,4,6-Triethyl-1,3,5-trioxane (114)

(elid 158)



^{1}H-NMR: (300 MHz, $CDCl_3$)

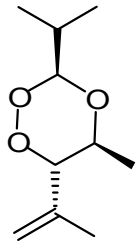
δ (ppm) = 0.89 (t, 3H, *J* = 7.50 Hz, C<u>H</u>$_3$), 1.63 (m, 2H, C<u>H</u>$_2$), 4.73 (t, 1H, *J* = 5.30 Hz, C<u>H</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.8 (q, <u>C</u>H$_3$), 27.5 (t, <u>C</u>H$_2$), 102.4 (d, <u>C</u>H).

(3RS,5RS,6RS)-3-Isopropyl-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (115)

(elid 159)



Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol (**7a**) (0.60 g, 4.55 mmol, prepared according to **GP-7b**) and excess propionaldehyde (2.0 g, 34.5 mmol) in Et_2O was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and evaporation of

the excess ketone under vacuum afforded an oil composed of a mixture of the 1,2,4-trioxane **115** and 1,3,5-trioxane **116** in a ratio 27:73, respectively.

^{1}H-NMR: (300 MHz, $CDCl_3$)

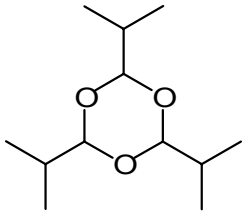
δ (ppm) = 0.92 (d, 3H, *J* = 6.90 Hz, $(C\underline{H}_3)_2CH$), 1.08 (d, 3H, *J* = 7.05 Hz, $C\underline{H}_3CH$), 1.12 (d, 3H, *J* = 6.45 Hz, $(C\underline{H}_3)_2CH$), 1.69 (m, 3H, CH_3C=), 2.38 (m, 1H, $C\underline{H}(CH_3)_2$), 3.76 (dq, 1H, *J* = 9.09, 6.30 Hz, OC<u>H</u>), 4.24 (d, 1H, *J* = 9.09 Hz, OOC<u>H</u>), 4.96 (d, 1H, *J* = 5.43 Hz, OC<u>H</u>OO), 5.02 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 15.4 (q, $\underline{C}H_3CH$), 16.3 (q, $\underline{C}H_3CH$), 16.9 (q, $\underline{C}H_3CH$), 19.6 (q, CH_3C=), 31.1 (d, <u>C</u>H), 73.1 (d, O<u>C</u>H), 88.8 (d, OO<u>C</u>H), 107.8 (d, O<u>C</u>HOO), 117.9 (t, $\underline{C}H_2$=C), 138.8 (s, <u>C</u>=CH_2).

2,4,6-Triisopropyl-1,3,5-trioxane (116)

(elid 159)



^{1}H-NMR: (300 MHz, $CDCl_3$)

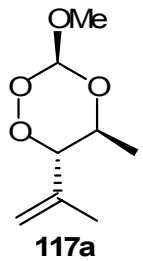
δ (ppm) = 0.89 (d, 6H, *J* = 6.70 Hz, $C\underline{H}_3$), 1.81 (m, 1H, $CH(CH_3)_2$), 4.45 (d, 1H, *J* = 5.40 Hz, OC<u>H</u>O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

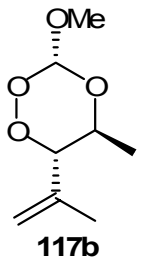
δ (ppm) = 16.6 (q, 2 x $\underline{C}H_3$), 32.4 (d, <u>C</u>H), 104.7 (d, <u>C</u>H).

(3RS,5RS,6RS)-3-Methoxy-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (117a) and (3RS,5SR,6SR)-3-methoxy-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (117b)

(elid 332a)



117a



117b

Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.50 g, 3.79 mmol, prepared according to **GP-7b**) and excess trimethyl orthoformate (0.50 g, 4.72 mmol) in Et_2O was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up afforded an oil composed of a diastereomerc mixture of the 1,2,4-trioxanes in the ratio 57:43 (0.21 g, 1.21 mmol, 32 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 1.18 (d, 3H, *J* = 6.33 Hz, C$\underline{H_3}$CH), 1.72 (t, 3H, *J* = 1.32 Hz, C$\underline{H_3}$C=), 3. 54 (s, 3H, OC$\underline{H_3}$), 4.02 (dq, 1H, *J* = 6.33, 9.27 Hz, OC$\underline{H}$), 4.20 (d, 1H, *J* = 9.27 Hz, OOC$\underline{H}$), 5.07 (m, 2H, C$\underline{H_2}$=), 5.72 (s, 1H, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 16.2 (q, $\underline{C}H_3$CH), 19.6 (q, $\underline{C}H_3$C=), 54.5 (q, O$\underline{C}H_3$), 74.2 (d, O$\underline{C}$H), 87.5 (d, OO$\underline{C}$H), 113.6 (d, O$\underline{C}$HOO), 118.6 (t, $\underline{C}H_2$=), 137.7 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, minor diastereomer)

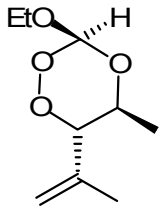
δ (ppm) = 1.08 (d, 3H, *J* = 5.88 Hz, C$\underline{H_3}$CH), 1.74 (m, 3H, C$\underline{H_3}$C=), 3.41 (s, 3H, OC$\underline{H_3}$), 4.30 (dq, 1H, *J* = 5.88, 9.27 Hz, OC$\underline{H}$), 4.36 (d, 1H, *J* = 9.27 Hz, OOC$\underline{H}$), 5.07 (m, 2H, CH_2=), 5.48 (s, 1H, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer)

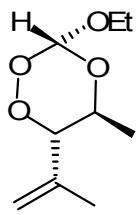
δ (ppm) = 16.1 (q, $\underline{C}H_3$CH), 19.6 (q, $\underline{C}H_3$C=), 53.4 (q, O$\underline{C}H_3$), 65.9 (d, O$\underline{C}$H), 88.9 (d, OO$\underline{C}$H), 111.0 (d, O$\underline{C}$HOO), 118.3 (t, $\underline{C}H_2$=), 138.9 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3-Ethoxy-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (118a) and (3RS,5SR,6SR)-3-ethoxy-5-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (118b)

(elid 115)



118a



118b

Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.75 g, 5.68 mmol, prepared according to **GP-7b**) and triethylorthoformate (5.0 g, 33.8 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by

evaporation of excess orthoester afforded an oil composed of a diastereomerc mixture of the 1,2,4-trioxanes **118a**,**b** in the ratio 72:28, respectively, (0.75 g, 3.99 mmol, 70 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **118a**)

δ (ppm) = 1.19 (d, 3H, *J* = 6.33 Hz, $C\underline{H}_3CH$), 1.24 (t, 3H, *J* = 7.20 Hz, $C\underline{H}_3CH_2$), 1.72 (t, 3H, *J* = 1.32 Hz, CH_3C=), 3.83 (m, 2H, $C\underline{H}_2CH_3$), 4.02 (dq, 1H, *J* = 9.20, 6.30 Hz, OC<u>H</u>), 4.20 (d, 1H, *J* = 9.20 Hz, OOC<u>H</u>), 5.07 (m, 2H, $C\underline{H}_2$=C), 5.77 (s, 1H, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **118a**)

δ (ppm) = 15.2 (q, $\underline{C}H_3CH_2$), 16.2 (q, $\underline{C}H_3CH$), 19.6 (q, $\underline{C}H_3C$=), 63.8 (d, O<u>C</u>H), 74.3 (t, $\underline{C}H_2CH_3$), 87.5 (d, OO<u>C</u>H), 113.3 (d, O<u>C</u>HOO), 118.5 (t, $\underline{C}H_2$=C), 137.8 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of the minor diastereomer **118b**)

δ (ppm) = 1.74 (t, 3H, *J* = 1.05 Hz, CH_3C=), 3.60 (dq, 1H, *J* = 9.70, 7.06 Hz, OC<u>H</u>), 3.71 (m, 2H, $C\underline{H}_2CH_3$), 5.58 (s, 1H, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **118b**)

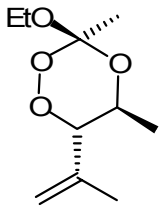
δ (ppm) = 14.7 (q, $\underline{C}H_3CH_2$), 16.1 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 61.6 (t, $\underline{C}H_2CH_3$), 65.8 (d, O<u>C</u>H), 88.9 (d, OO<u>C</u>H), 110.0 (d, O<u>C</u>HOO), 118.2 (t, $\underline{C}H_2$=C), 139.0 (s, $\underline{C}$=CH_2).

MS: (EI, 70 eV)

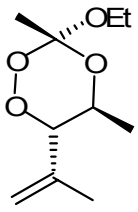
m/z (%) = 82 ($C_6H_{10}^+$, 100), 70 ($C_4H_6O^+$, 28), 69 ($C_4H_5O^+$, 27), 67 ($C_5H_7^+$, 68).

(3RS,5RS,6RS)-3-Ethoxy-3,5-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (119a) and (3RS,5SR,6SR)-3-ethoxy-3,5-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (119b)

(elid 126)



119a



119b

Following **GP-15**, a solution of 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (0.75 g, 5.68 mmol, prepared according to **GP-7b**) and triethylorthoacetate (4.0 g, 24.7 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by

evaporation of excess orthoester afforded an oil composed of a diastereomerc mixture of the 1,2,4-trioxanes **119a,b** in the ratio 1:1 (0.86 g, 4.26 mmol, 75 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, both diastereomers)

δ (ppm) = 1.06 (d, 3H, *J* = 6.20 Hz, $C\underline{H_3}CH$), 1.21 (t, 3H, *J* = 7.05 Hz, $C\underline{H_3}CH_2$), 1.42 (s, 3H, $C\underline{H_3}$), 1.72 (m, 3H, CH_3C=), 3.68 (q, 2H, *J* = 7.05 Hz, $C\underline{H_2}CH_3$), 4.14 (dq, 1H, *J* = 9.40, 6.20 Hz, OC<u>H</u>), 4.24 (d, 1H, *J* = 9.42 Hz, OOC<u>H</u>), 5.06 (m, 2H, $C\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 15.1 (q, $\underline{C}H_3CH_2$), 16.1 (q, $\underline{C}H_3CH$), 19.4 (q, $\underline{C}H_3C$=), 20.5 (q, $\underline{C}H_3$), 58.4 (t, $\underline{C}H_2CH_3$), 66.1 (d, O<u>C</u>H), 87.8 (d, OO<u>C</u>H), 113.8 (s, O<u>C</u>OO), 118.1 (t, $\underline{C}H_2$=C), 138.9 (s, $\underline{C}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

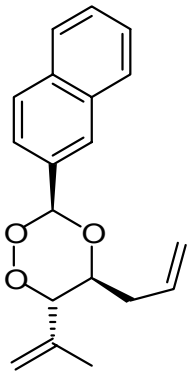
δ (ppm) = 18.3 (q, $\underline{C}H_3CH_2$), 18.6 (q, $\underline{C}H_3$), 59.3 (t, $\underline{C}H_2CH_3$), 114.3 (s, O<u>C</u>OO).

MS: (EI, 70 eV)

m/z (%) = 82 ($C_6H_{10}^+$, 100), 70 ($C_4H_6O^+$, 58), 67 ($C_5H_7^+$, 56).

4.6.11 Derived from 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol (7e)

(3RS,5RS,6RS)-5-Allyl-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (120)
(elid 474q, 475e, 497p)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (0.39 g, 2.47 mmol) and β-naphthaldehyde (388 mg, 2.49 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.69) afforded the pure 1,2,4-trioxanes (30 mg, 0.10 mmol, 4 %) as viscous colorless oil which crystallizes on standing.

M.p. 55-57 °C

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.82 (m, 3H, $C\underline{H}_3C$=), 2.47 (m, 2H, $C\underline{H}_2$), 4.06 (ddd, 1H, *J* = 3.96, 7.23, 9.24 Hz, OC<u>H</u>), 4.64 (d, 1H, *J* = 9.24 Hz, OOC<u>H</u>), 5.15 (m, 4H, $C\underline{H}_2$=CH and $C\underline{H}_2$=C), 6.0 (m, 1H, C<u>H</u>=CH_2), 6.37 (s, 1H, OC<u>H</u>OO), 7.45-8.0 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (q, $\underline{C}H_3C$=), 35.1 (t, $C\underline{H}_2$), 76.8 (d, O<u>C</u>H), 87.1 (d, OO<u>C</u>H), 104.1 (d, O<u>C</u>HOO), 117.7 (t, $\underline{C}H_2$=CH), 119.0 (t, $\underline{C}H_2$=C), 124.1 (d, $\underline{C}H_{arom}$), 126.2 (d, $\underline{C}H_{arom}$), 126.7 (d, $\underline{C}H_{arom}$), 126.9 (d, $\underline{C}H_{arom}$), 127.7 (d, $\underline{C}H_{arom}$), 128.2 (d, $\underline{C}H_{arom}$), 128.5 (d, $\underline{C}H_{arom}$), 131.8 (s, Cq_{arom}), 132.9 (s, Cq_{arom}), 134.0 (s, Cq_{arom}), 133.4 (d, <u>C</u>H=CH_2), 138.5 (s, <u>C</u>=CH_2).

MS: (EI, 70 eV)

m/z (%) = 296 (M^+, 7), 156 ($C_{11}H_8O^+$, 100). 155 ($C_{11}H_7O^+$, 86), 127 ($C_{10}H_7^+$, 62).

HRMS: (EI, 70 eV, $C_{19}H_{20}O_3$)

Calcd: M = 296.141 g/mol

Found: M = 296.141 ±0.005 g/mol

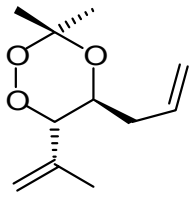
Elemental Analysis: ($C_{19}H_{20}O_3$, M = 296.36)

Calcd: C 77.00 H 6.80

Found: C 76.85 H 6.71

(5RS,6RS)-5-Allyl-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (121)

(elid 475y, 480f, 480z, 480n, 496p)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (1.20 g, 7.59 mmol) and excess acetone (2.0 g, 34.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (1.11 g, 5.61 mmol, 73.9 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.80) the pure 1,2,4-trioxane as colorless oil (0.25 g, 1.26 mmol, 17 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

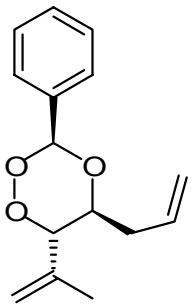
δ (ppm) = 1.32 (s, 3H, C$\underline{H}_3$), 1.62 (s, 3H, C$\underline{H}_3$), 1.74 (s, 3H, C$\underline{H}_3$C=), 2.23 (m, 2H, C$\underline{H}_2$), 3.98 (ddd, 1H, *J* = 3.83, 7.20, 9.70 Hz, OC$\underline{H}$), 4.28 (d, 1H, *J* = 9.70 Hz, OOC$\underline{H}$), 5.04 (m, 4H, C$\underline{H}_2$=CH and C$\underline{H}_2$=C), 5.80 (m, 1H, C$\underline{H}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

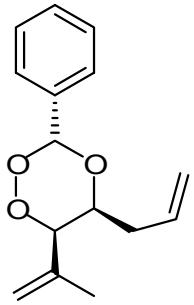
δ (ppm) = 19.5 (q, $\underline{C}H_3$C=), 20.5 (q, $\underline{C}H_3$), 25.8 (q, $\underline{C}H_3$), 35.3 (t, $\underline{C}H_2$), 69.6 (d, O$\underline{C}$H), 86.7 (d, OO$\underline{C}$H), 102.7 (s, O$\underline{C}$OO), 117.0 (t, $\underline{C}H_2$=CH), 118.2 (t, $\underline{C}H_2$=C), 133.7 (d, $\underline{C}$H=CH_2), 138.9 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Allyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (122a) and (3RS,5SR,6RS)-5-allyl-3-phenyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (122b)

(elid 473z, 501t)



122a



122b

Following **GP-15**, a solution of 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (1.0 g, 6.33 mmol) and benzaldehyde dimethyl acetal (0.96 g, 6.32 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.74) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **122a**,**b** in a ratio 93:7 respectively (0.41 g, 1.66 mmol, 26 %) as colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer **122a**)

δ (ppm) = 1.81 (t, 3H, *J* = 1.02 Hz, C$\underline{H}_3$C=), 2.41 (m, 2H, C$\underline{H}_2$), 4.03 (ddd, 1H, *J* = 3.96, 7.05, 9.27 Hz, OC$\underline{H}$), 4.61 (d, 1H, *J* = 9.27 Hz, OOC$\underline{H}$), 5.15 (m, 4H, C$\underline{H}_2$=CH and C$\underline{H}_2$=C), 5.97 (m, 1H, C$\underline{H}$=CH_2), 6.23 (s, 1H, OC$\underline{H}$OO), 7.37-7.54 (m, 5H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer **122a**)

δ (ppm) = 19.6 (q, $\underline{C}H_3$C=), 35.0 (t, $\underline{C}H_2$), 76.6 (d, O$\underline{C}$H), 86.9 (d, OO$\underline{C}$H), 103.9 (d, O$\underline{C}$HOO), 117.6 (t, $\underline{C}H_2$=CH), 118.8 (t, $\underline{C}H_2$=C), 126.9 (d, $\underline{C}H_{arom}$), 128.3 (d, $\underline{C}H_{arom}$), 129.8 (d, $\underline{C}H_{arom}$), 133.3 (d, $\underline{C}$H=CH_2), 134.4 (s, Cq_{arom}), 138.4 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer **122b**)

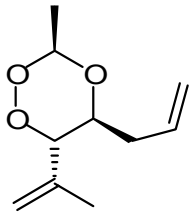
δ (ppm) = 2.12 (m, 3H, C<u>H</u>$_3$C=), 4.22 (d, 1H, *J* = 3.66 Hz, OOC<u>H</u>), 4.31 (m, 1H, OC<u>H</u>), 5.85 (m, 1H, C<u>H</u>=CH$_2$), 6.38 (s, 1H, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer **122b**)

δ (ppm) = 19.7 (q, <u>C</u>H$_3$C=), 35.8 (t, C<u>H</u>$_2$), 76.4 (d, O<u>C</u>H), 84.1 (d, OO<u>C</u>H), 104.4 (d, O<u>C</u>HOO), 117.2 (t, <u>C</u>H$_2$=CH), 118.8 (t, <u>C</u>H$_2$=C), 127.0 (d, <u>C</u>H$_{arom}$), 128.2 (d, <u>C</u>H$_{arom}$), 129.7 (d, <u>C</u>H$_{arom}$), 133.0 (d, <u>C</u>H=CH$_2$), 134.5 (s, Cq$_{arom}$), 138.4 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-5-Allyl-3-methyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (123)

(elid 467k)



Following **GP-15**, a solution of 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (1.0 g, 6.33 mmol) and acetaldehyde diethyl acetal (0.74 g, 6.27 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (1.13 g, 6.14 mmol, 98 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.77) the pure 1,2,4-trioxane as colorless oil (0.47 g, 2.55 mmol, 41 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

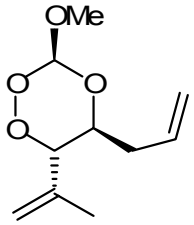
δ (ppm) = 1.27 (d, 3H, *J* = 5.43 Hz, C<u>H</u>$_3$), 1.71 (s, 3H, C<u>H</u>$_3$C=), 2.36 (m, 2H, C<u>H</u>$_2$), 3.76 (ddd, 1H, *J* = 3.70, 7.64, 9.24 Hz, OC<u>H</u>), 4.38 (d, 1H, *J* = 9.24 Hz, OOC<u>H</u>), 5.04 (m, 4H, C<u>H</u>$_2$=CH and C<u>H</u>$_2$=C), 5.37 (q, 1H, *J* = 5.43 Hz, C<u>H</u>), 5.86 (m, 1H, C<u>H</u>=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

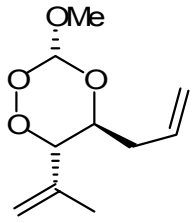
δ (ppm) = 17.8 (q, <u>C</u>H3), 19.6 (q, <u>C</u>H$_3$C=), 34.9 (t, C<u>H</u>$_2$), 76.2 (d, O<u>C</u>H), 86.8 (d, OO<u>C</u>H), 101.5 (d, O<u>C</u>HOO), 117.3 (t, <u>C</u>H$_2$=CH), 118.7 (t, <u>C</u>H$_2$=C), 133.5 (d, <u>C</u>H=CH$_2$), 138.5 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-5-Allyl-3-methoxy-6-(prop-1-en-2-yl)-1,2,4-trioxane (124a) and (3RS,5SR,6SR)-5-allyl-3-methoxy-6-(prop-1-en-2-yl)-1,2,4-trioxane (124b)

(elid 475v,u)



124a



124b

Following **GP-15**, a solution of 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (1.20 g, 7.59 mmol) and excess trimethyl orthoformate (2.0 g, 18.9 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography allowed the separation of one of the 1,2,4-trioxane diastereoisomers (SiO_2, EA/*n*-hex, 1:10, R_f = 0.58). Besides, a diastereomeric mixture of the pure 1,2,4-trioxanes (SiO_2, EA/*n*-hex, 1:10, R_f = 0.78) in a ratio 45:55 were obtained as colorless oil (0.32 g, 1.6 mmol, 21 %).

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 1.70 (m, 3H, C$\underline{H_3}$C=), 2.0-2.40 (m, 2H, C$\underline{H_2}$), 3.50 (s, 3H, OC$\underline{H_3}$), 3.94 (m, 1H, OC$\underline{H}$), 4.28 (d, 1H, *J* = 9.39 Hz, OOC$\underline{H}$), 5.02 (m, 4H, C$\underline{H_2}$=CH and C$\underline{H_2}$=C), 5.69 (s, 1H, OC$\underline{H}$OO), 5.81 (m, 1H, C$\underline{H}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 19.4 (q, $\underline{C}H_3$C=), 34.7 (t, C$\underline{H_2}$), 54.2 (q, O$\underline{C}H_3$), 76.9 (d, O$\underline{C}$H), 85.5 (d, OO$\underline{C}$H), 113.5 (d, O$\underline{C}$HOO), 117.8 (t, $\underline{C}H_2$=CH), 119.0 (t, $\underline{C}H_2$=C), 132.7 (d, $\underline{C}$H=CH_2), 137.5 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, minor diastereomer)

δ (ppm) = 1.72 (m, 3H, C$\underline{H_3}$C=), 2.0-2.40 (m, 2H, C$\underline{H_2}$), 3.38 (s, 3H, OC$\underline{H_3}$), 4.25 (m, 1H, OC$\underline{H}$), 4.45 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.02 (m, 4H, C$\underline{H_2}$=CH and C$\underline{H_2}$=C), 5.48 (s, 1H, OC$\underline{H}$OO), 5.81 (m, 1H, C$\underline{H}$=CH_2).

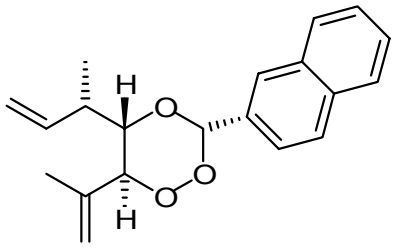
^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer)

δ (ppm) = 19.4 (q, $\underline{C}H_3$C=), 34.6 (t, C$\underline{H_2}$), 53.2 (q, O$\underline{C}H_3$), 68.8 (d, O$\underline{C}$H), 87.0 (d, OO$\underline{C}$H), 111.0 (d, O$\underline{C}$HOO), 117.6 (t, $\underline{C}H_2$=CH), 118.7 (t, $\underline{C}H_2$=C), 133.0 (d, $\underline{C}$H=CH_2), 138.6 (s, $\underline{C}$=CH_2).

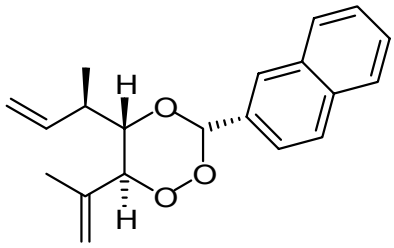
4.6.12 Derived from 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol (7f)

(3RS,5RS,6RS)-5-((RS)-But-3-en-2-yl)-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxa-ne (125a) and (3RS,5RS,6RS)-5-((SR)-but-3-en-2-yl)-3-(naphthalen-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (125b)

(elid 493r)



125a



125b

Following **GP-15**, a solution of 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol **(7f)** (1.16 g, 6.74 mmol) and 2-naphthaldehyde (1.07 g, 6.86 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (1.62 g, 5.23 mmol, 77.5 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.69) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **125a**,**b** in a ratio 1:1 (0.31 g, 1.0 mmol, 15 %) as white solid.

^{1}H-NMR: (300 MHz, $CDCl_3$, one diastereomer)

δ (ppm) = 1.30 (d, 3H, *J* = 7.05 Hz, C$\underline{H}_3$CH), 1.88 (t, 3H, *J* = 1.47 Hz, C$\underline{H}_3$C=), 2.55 (m, 1H, C$\underline{H}$CH$_3$), 4.02 (dd, 1H, *J* = 1.90, 9.54 Hz, OC$\underline{H}$), 4.83 (d, 1H, *J* = 9.54 Hz, OOC$\underline{H}$), 5.20 (m, 4H, C$\underline{H}_2$=CH and C$\underline{H}_2$=), 6.15 (m, 1H, C$\underline{H}$=CH$_2$), 6.40 (s, 1H, OC$\underline{H}$OO), 7.50-8.10 (m, 7H, H_{arom}).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, one diastereomer)

δ (ppm) = 13.5 (q, $\underline{C}H_3$CH), 19.5 (q, $\underline{C}H_3$C=), 38.1 (d, $\underline{C}$HCH$_3$), 79.9 (d, O$\underline{C}$H), 85.4 (d, OO$\underline{C}$H), 103.9 (d, O$\underline{C}$HOO), 114.3 (t, $\underline{C}H_2$=CH), 118.9 (t, $\underline{C}H_2$=C), 124.0 (d, CH_{arom}), 126.1 (d, CH_{arom}), 126.6 (d, CH_{arom}), 126.8 (d, CH_{arom}), 126.9 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.0 (d, CH_{arom}), 131.9 (s, Cq_{arom}), 132.7 (s, Cq_{arom}), 133.9 (s, Cq_{arom}), 138.5 (d, $\underline{C}$H=CH$_2$), 138.6 (s, $\underline{C}$=CH$_2$).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional signals of the other diastereomer)

δ (ppm) = 4.12 (dd, 1H, *J* = 2.51, 9.57 Hz, OC$\underline{H}$), 4.89 (d, 1H, *J* = 9.57 Hz, OOC$\underline{H}$), 6.41 (s, 1H, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, other diastereomer)

δ (ppm) = 18.2 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 38.8 (d, $\underline{C}HCH_3$), 80.0 (d, O$\underline{C}$H), 85.6 (d, OO$\underline{C}$H), 104.0 (d, O$\underline{C}$HOO), 116.1 (t, $\underline{C}H_2$=CH), 118.9 (t, $\underline{C}H_2$=C), 124.0 (d, CH_{arom}), 126.1 (d, CH_{arom}), 126.6 (d, CH_{arom}), 126.8 (d, CH_{arom}), 126.9 (d, CH_{arom}), 127.6 (d, CH_{arom}), 128.3 (d, CH_{arom}), 131.9 (s, Cq_{arom}), 132.7 (s, Cq_{arom}), 133.9 (s, Cq_{arom}), 138.4 (s, $\underline{C}$=CH_2), 140.8 (d, $\underline{C}$H=CH_2).

IR: (CsI)

ν (cm^{-1}) = 3078, 2978, 2923, 1653, 1647, 1605, 1127, 1076, 999, 987, 904, 866, 818.

MS: (EI, 70 eV)

m/z (%) = 310 (M^+, 2), 226 (M^+-C_5H_8O, 1), 156 ($C_{11}H_8O^+$, 100), 155 ($C_{11}H_7O^+$, 89), 128 ($C_{10}H_8^+$, 20), 127 ($C_{10}H_7^+$, 68), 107 ($C_8H_{11}^+$, 20).

HRMS: (EI, 70 eV, $C_{20}H_{22}O_3$)

Calcd: M = 310.157 g/mol

Found: M = 310.157 ±0.005 g/mol

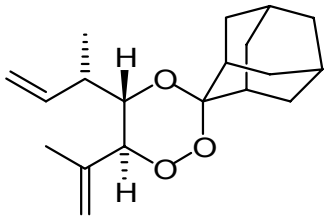
Elemental Analysis: ($C_{20}H_{22}O_3$, M = 310.39)

Calcd: C 77.39 H 7.14

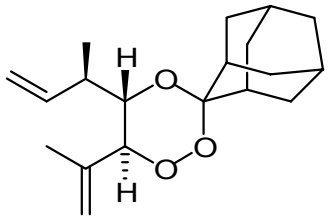
Found: C 77.28 H 7.02

(5RS,6RS)-5-((RS)-But-3-en-2-yl)-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (126a) (5RS,6RS)-5-((SR)-but-3-en-2-yl)-6-(prop-1-en-2-yl)-spiro[1,2,4-trioxacyclohexane-3,2´-adamantane] (126b)

(elid 487w)



126a



126b

Following **GP-15**, a solution of 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol **(7f)** (1.40 g, 8.14 mmol) and adamantanone (1.22 g, 8.13 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (1.57 g, 5.16 mmol, 63.5 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.81) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **126a**,**b** in a ratio 31:69 (0.10 g, 3.29 mmol, 4 %) as viscous colorless liquid.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 1.10 (d, 3H, *J* = 7.05 Hz, $C\underline{H}_3CH$), 1.50-2.30 (m, 14H, $C\underline{H}CH_3$, CH and $C\underline{H}_2$), 1.74 (s, 3H, $C\underline{H}_3C$=), 2.88 (br. s, 1H, CH), 3.86 (dd, 1H, *J* = 2.13, 9.99 Hz, OC<u>H</u>), 4.39 (d, 1H, *J* = 9.99 Hz, OOC<u>H</u>), 4.92 (m, 4H, $C\underline{H}_2$=CH and $C\underline{H}_2$=), 5.88 (m, 1H, $C\underline{H}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 18.5 (q, $\underline{C}H_3CH$), 19.7 (q, $\underline{C}H_3C$=), 27.2 (d, CH), 27.3 (d, CH), 29.6 (d, CH), 33.0 (t, CH_2), 33.3 (t, CH_2), 33.6 (t, CH_2), 34.5 (t, CH_2), 36.5 (d, CH), 37.2 (t, CH_2), 38.8 (d, $\underline{C}HCH_3$), 71.5 (d, O<u>C</u>H), 85.3 (d, OO<u>C</u>H), 104.6 (s, O<u>C</u>OO), 115.6 (t, $\underline{C}H_2$=CH), 118.1 (t, $\underline{C}H_2$=C), 138.9 (d, $\underline{C}H$=CH_2), 139.4 (s, $\underline{C}$=CH_2).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional signals of the minor diastereomer)

δ (ppm) = 1.04 (d, 3H, *J* = 6.75 Hz, $C\underline{H}_3CH$), 3.93 (dd, 1H, *J* = 3.09, 9.84 Hz, OC<u>H</u>), 4.44 (d, 1H, *J* = 9.84 Hz, OOC<u>H</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer)

δ (ppm) = 13.3 (q, $\underline{C}H_3CH$), 19.9 (q, $\underline{C}H_3C$=), 26.8 (d, CH), 27.0 (d, CH), 29.8 (d, CH), 32.9 (t, CH_2), 33.3 (t, CH_2), 33.6 (t, CH_2), 34.9 (t, CH_2), 36.5 (d, CH), 37.2 (t, CH_2), 38.4 (d, $\underline{C}HCH_3$), 71.5 (d, O<u>C</u>H), 85.2 (d, OO<u>C</u>H), 103.5 (s, O<u>C</u>OO), 113.8 (t, $\underline{C}H_2$=CH), 118.2 (t, $\underline{C}H_2$=C), 139.1 (s, $\underline{C}$=CH_2), 141.5 (d, $\underline{C}H$=CH_2).

IR: (Film)

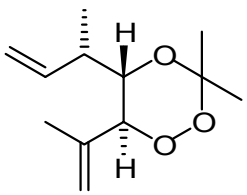
ν (cm^{-1}) = 3078, 2913, 1647, 1315, 1222, 1110, 1031, 912.

Elemental Analysis: ($C_{19}H_{28}O_3$, M = 304.42)

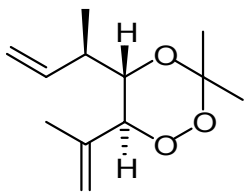
Calcd: C 74.96 H 9.27

Found: C 74.11 H 9.36

(5RS,6RS)-5-((RS)-But-3-en-2-yl)-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (127a) and (5RS,6RS)-5-((SR)-but-3-en-2-yl)-3,3-dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (127b) (elid 487x)



127a



127b

Following **GP-15**, a solution of 3-hydroperoxy-2,5-dimethylhepta-1,6-dien-4-ol **(7f)** (0.99 g, 5.76 mmol) and excess acetone (3.3 g, 56.9 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (0.65 g, 3.07 mmol, 53.2 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.80) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes **127a**,**b** in a ratio 48:52 (0.17 g, 0.8 mmol, 14 %) as colorless liquid.

^{1}H-NMR: (300 MHz, $CDCl_3$, one diastereomer)

δ (ppm) = 1.0 (d, 3H, *J* = 6.90 Hz, C$\underline{H_3}$CH), 1.31 (s, 3H, C$\underline{H_3}$), 1.59 (s, 3H, C$\underline{H_3}$), 1.73 (m, 3H, C$\underline{H_3}$C=), 2.24 (m, 1H, C$\underline{H}$CH$_3$), 3.84 (dd, 1H, *J* = 2.07, 9.99 Hz, OC$\underline{H}$), 4.36 (d, 1H, *J* = 9.99 Hz, OOC$\underline{H}$), 5.0 (m, 4H, C$\underline{H_2}$=CH and C$\underline{H_2}$=), 5.85 (m, 1H, C$\underline{H}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, one diastereomer)

δ (ppm) = 18.1 (q, $\underline{C}H_3$CH), 19.4 (q, $\underline{C}H_3$C=), 20.4 (q, $\underline{C}H_3$), 25.7 (q, $\underline{C}H_3$), 38.7 (d, $\underline{C}$HCH$_3$), 72.8 (d, O$\underline{C}$H), 85.3 (d, OO$\underline{C}$H), 102.6 (s, O$\underline{C}$OO), 115.6 (t, $\underline{C}H_2$=CH), 118.2 (t, $\underline{C}H_2$=C), 139.0 (d, $\underline{C}$H=CH$_2$), 139.2 (s, $\underline{C}$=CH$_2$).

^{1}H-NMR: (300 MHz, $CDCl_3$, additional signals of the other diastereomer)

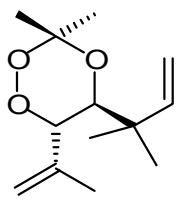
δ (ppm) = 1.04 (d, 3H, J = 7.08 Hz, C$\underline{H_3}$CH), 1.74 (m, 3H, C$\underline{H_3}$C=), 3.94 (dd, 1H, *J* = 2.79, 9.84 Hz, OC$\underline{H}$), 4.43 (d, 1H, *J* = 9.84 Hz, OOC$\underline{H}$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional signals of the other diastereomer)

δ (ppm) = 13.0 (q, $\underline{C}H_3$CH), 19.5 (q, $\underline{C}H_3$C=), 20.3 (q, $\underline{C}H_3$), 37.9 (d, $\underline{C}$HCH$_3$), 72.7 (d, O$\underline{C}$H), 85.1 (d, OO$\underline{C}$H), 113.8 (t, $\underline{C}H_2$=CH), 118.2 (t, $\underline{C}H_2$=), 138.8 (s, $\underline{C}$=CH$_2$), 141.2 (d, $\underline{C}$H=CH$_2$).

4.6.13 Derived from 3-hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol (7k)

(5RS,6RS)-3,3-Dimethyl-5-(2-methylbut-3-en-2-yl)-6-(prop-1-en-2-yl)-1,2,4-trioxane (128) (elid 482k)



Following **GP-15**, a solution of 3-hydroperoxy-2,5,5-trimethylhepta-1,6-dien-4-ol **(7k)** (0.90 g, 4.84 mmol) and excess acetone (2.0 g, 34.5 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.87) afforded the pure 1,2,4-trioxane as colorless oil (0.06 g, 0.27 mmol, 6 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.01 (s, 3H, C<u>H$_3$</u>C(vinyl)CH$_3$), 1.03 (s, 3H, C<u>H$_3$</u>C(vinyl)CH$_3$), 1.32 (s, 3H, C<u>H$_3$</u>), 1.58 (s, 3H, C<u>H$_3$</u>), 1.75 (m, 3H, C<u>H$_3$</u>C=), 3.74 (d, 1H, *J* = 9.70 Hz, OC<u>H</u>), 4.34 (d, 1H, *J* = 9.70 Hz, OOC<u>H</u>), 4.90-5.10 (m, 4H, 2 x C<u>H$_2$</u>=), 5.92 (dd, 1H, *J* = 17.49, 10.88 Hz, C<u>H</u>=CH$_2$).

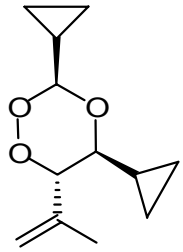
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.9 (q, <u>C</u>H$_3$C=), 20.4 (q, <u>C</u>H$_3$), 23.5 (q, <u>C</u>H$_3$C(vinyl)CH$_3$), 24.0 (q, <u>C</u>H$_3$C(vinyl)CH$_3$), 25.7 (q, <u>C</u>H$_3$), 39.6 (s, <u>C</u>(vinyl)(CH$_3$)$_2$), 75.5 (d, O<u>C</u>H), 85.3 (d, OO<u>C</u>H), 102.4 (s, O<u>C</u>OO), 111.8 (t, <u>C</u>H$_2$=CH), 119.0 (t, <u>C</u>H$_2$=C), 142.8 (s, <u>C</u>=CH$_2$), 144.3 (d, <u>C</u>H=CH$_2$).

4.7 Lewis-Acid Catalyzed Cleavage of β-Hydroperoxy Alcohols and Subsequent Cross-Peroxyacetalization Reaction

(3RS,5RS,6RS)-3,5-Dicyclopropyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129a)

(elid 495s, 488u, 477l)



Following **GP-16** using 1-cyclopropyl-2-hydroperoxy-3-methylbut-3-en-1-ol **(7p)** (1.50 g, 9.5 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129a**, **130a** in a 61:39 ratio (0.66 g, 33 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.81) to separate the 1,2,4-trioxane **129a** as pure product (0.23 g, 1.1 mmol, 12 %).

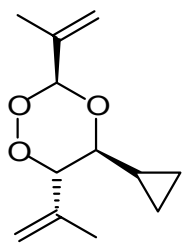
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.24-0.59 (m, 8H, 4 x C$\underline{H}_2$), 0.74-0.95 (m, 2H, 2 x C$\underline{H}$), 1.77 (s, 3H, C$\underline{H}_3$C=), 3.06 (dd, 1H, *J* = 7.92, 8.73 Hz, OC$\underline{H}$), 4.45 (d, 1H, *J* = 9. 21 Hz, OOC$\underline{H}$), 4.73 (d, 1H, *J* = 6.15 Hz, OC$\underline{H}$OO), 5.04 (br. s, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.4 (t, $\underline{C}H_2$CH), 1.7 (t, $\underline{C}H_2$CH), 1.9 (t, $\underline{C}H_2$CH), 2.8 (t, $\underline{C}H_2$CH), 11.5 (d, $\underline{C}$H(CH_2)$_2$), 12.0 (d, $\underline{C}$H(CH_2)$_2$), 20.6 (q, $\underline{C}H_3$C=), 80.8 (d, O$\underline{C}$H), 87.4 (d, OO$\underline{C}$H), 106.4 (d, O$\underline{C}$HOO), 117.1 (t, $\underline{C}H_2$=C), 139.4 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Cyclopropyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130a)



^{1}H-NMR: (300 MHz, $CDCl_3$)

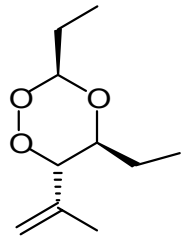
δ (ppm) = 0.17-0.52 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 0.67-1.24 (m, 1H, C$\underline{H}$(CH_2)$_2$), 1.69 (m, 3H, C$\underline{H_3}$C=), 1.74 (t, 3H, *J* = 1.17 Hz, C$\underline{H_3}$C=), 3.21 (dd, 1H, *J* = 7.08, 8.97 Hz, OC$\underline{H}$), 4.43 (d, 1H, *J* = 9.09 Hz, OOC$\underline{H}$), 4.98-5.04 (m, 3H, C$\underline{H_2}$=C), 5.18 (br. s, 1H, C$\underline{H_2}$=C), 5.45 (s, 1H, OOC$\underline{H}$O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 1.5 (t, $\underline{C}H_2$), 2.3 (t, $\underline{C}H_2$), 11.3 (d, $\underline{C}$H(CH_2)$_2$), 17.5 (q, $\underline{C}H_3$C=), 20.4 (q, $\underline{C}H_3$C=), 79.8 (d, O$\underline{C}$H), 87.5 (d, OO$\underline{C}$H), 104.5 (d, OO$\underline{C}$HO), 116.5 (t, $\underline{C}H_2$=C), 117.2 (t, $\underline{C}H_2$=C), 138.7 (s, $\underline{C}$=CH_2), 139.2 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3,5-Diethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129b)

(elid 387a, 475m)

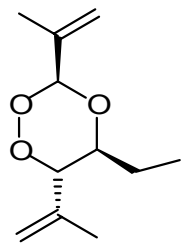


Following **GP-16** using 4-hydroperoxy-5-methylhex-5-en-3-ol **(7b)** (1.1 g, 7.53 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129b**, **130b** in a 63:37 ratio (0.58 g, 41 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0. 84) to obtain the 1,2,4-trioxane **129b** as pure product (0. 09 g, 0.47 mmol, 6 %).

NMR data see previously.

(3RS,5RS,6RS)-5-Ethyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130b)

(elid 407d)



^{1}H-NMR: (300 MHz, DMSO-d_6)

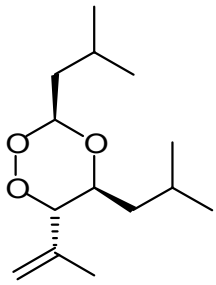
δ (ppm) = 0.93 (t, 3H, *J* = 7.35 Hz, C$\underline{H}_3$CH$_2$), 1.44 (m, 2H, C$\underline{H}_2$CH$_3$), 1.69 (2 x s, 6H, 2 x C$\underline{H}_3$C=), 3.77 (ddd, 1H, *J* = 3.50, 8.07, 9.27 Hz, OC$\underline{H}$), 4.38 (d, 1H, *J* = 9.27 Hz, OOC$\underline{H}$), 5.10 (m, 3H, 2 x C$\underline{H}_2$=C), 5.24 (br. s, 1H, C$\underline{H}_2$=C), 5.60 (s, 1H, OOC$\underline{H}$O).

^{13}C-NMR: (75.5 MHz, DMSO-d_6)

δ (ppm) = 9.0 (q, $\underline{C}$H$_3$), 17.3 (q, $\underline{C}$H$_3$C=), 19.1 (q, $\underline{C}$H$_3$C=), 23.0 (t, CH$_2$), 76.8 (d, O$\underline{C}$H), 86.8 (d, OO$\underline{C}$H), 104.1 (d, O$\underline{C}$HOO), 116.6 (t, $\underline{C}$H$_2$=C), 118.7 (t, $\underline{C}$H$_2$=C), 138.6 (2 x s, 2 x $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3,5-Diisobutyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129c)

(elid 495k, 486u, 501f)



Following **GP-16** using 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (0.80 g, 4.6 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129c**, **130c** in a 83:17 ratio (0.65 g, 59 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.84) to separate the 1,2,4-trioxane **129c** as pure product (184 mg, 0.76 mmol, 17 %).

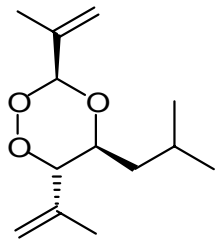
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.87 (d, 3H, *J* = 6.45 Hz, C$\underline{H}_3$CH), 0.88 (d, 3H, C$\underline{H}_3$CH), 0.90 (d, 3H, *J* = 6.75 Hz, C$\underline{H}_3$CH), 0.92 (d, 3H, *J* = 6.63 Hz, C$\underline{H}_3$CH), 1.09 (m, 1H, C$\underline{H}_2$CH), 1.35-1.45 (m, 3H, C$\underline{H}_2$CH and C$\underline{H}_2$CH), 1.69 (m, 3H, C$\underline{H}_3$C=), 1.82 (m, 2H, 2 x C$\underline{H}$CH$_2$), 3.72 (ddd, 1H, *J* = 3.68, 9.11, 9.11 Hz, OC$\underline{H}$), 4.30 (d, 1H, *J* = 9.11 Hz, OOC$\underline{H}$), 5.05 (m, 2H, C$\underline{H}_2$=C), 5.26 (dd, 1H, *J* = 5.57, 5.73 Hz, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.6 (q, $\underline{C}$H$_3$C=), 21.3 (q, $\underline{C}$H$_3$CH), 22.5 (q, $\underline{C}$H$_3$CH), 22.9 (q, $\underline{C}$H$_3$CH), 23.6 (q, $\underline{C}$H$_3$CH), 23.7 (d, $\underline{C}$HCH$_2$), 24.0 (d, $\underline{C}$HCH$_2$), 39.1 (t, $\underline{C}$H$_2$CH), 40.6 (t, $\underline{C}$H$_2$CH), 75.0 (d, O$\underline{C}$H), 88.1 (d, OO$\underline{C}$H), 103.8 (d, O$\underline{C}$HOO), 118.4 (t, $\underline{C}$H$_2$=C), 138.7 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-5-Isobutyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130c)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

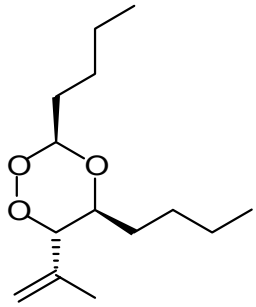
δ (ppm) = 1.70 (m, 3H, C<u>H</u>$_3$C=), 1.74 (m, 3H, C<u>H</u>$_3$C=), 3.80 (m, 1H, OC<u>H</u>), 4.34 (d, 1H, *J* = 9.12 Hz, OOC<u>H</u>), 5.54 (s, 1H, OC<u>H</u>OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 39.1 (t, <u>C</u>H$_2$CH), 75.2 (d, O<u>C</u>H), 88.0 (d, OO<u>C</u>H), 104.6 (d, O<u>C</u>HOO), 116.1 (t, <u>C</u>H$_2$=C), 118.5 (t, <u>C</u>H$_2$=C), 138.7 (s, <u>C</u>=CH$_2$), 138.9 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-3,5-Dibutyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129d)

(elid 472c, 492p)



Following **GP-16** using 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.60 g, 9.2 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129d**, **130d** in a 68:32 ratio (1.30 g, 59.7 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.82) to obtain the 1,2,4-trioxane **129d** as pure product (0.32 g, 1.32 mmol, 14 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

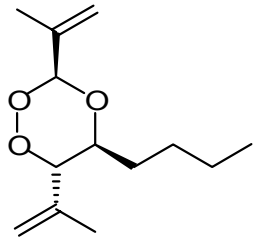
δ (ppm) = 0.88 (t, 6H, *J* = 6.99 Hz, C<u>H</u>$_3$CH$_2$), 1.18-1.65 (m, 12H, C<u>H</u>$_2$), 1.71 (m, 3H, C<u>H</u>$_3$C=), 3.65 (m, 1H, OC<u>H</u>), 4.33 (d, 1H, *J* = 9.09 Hz, OOC<u>H</u>), 5.06 (s, 2H, C<u>H</u>$_2$=), 5.21 (t, 1H, *J* = 5.36 Hz, O<u>C</u>HOO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.8 (q, $\underline{C}H_3CH_2$), 14.0 (q, $\underline{C}H_3CH_2$), 19.7 (q, $\underline{C}H_3C$=), 22.4 (t, $\underline{C}H_2CH_3$), 22.6 (t, $\underline{C}H_2CH_3$), 26.0 (t, $\underline{C}H_2CH_2$), 27.1 (t, $\underline{C}H_2CH_2$), 30.1 (t, $\underline{C}H_2CH_2$), 31.8 (t, $\underline{C}H_2CH_2$), 76.8 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 104.8 (d, O$\underline{C}$HOO), 118.3 (t, $\underline{C}H_2$=C), 138.9 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Butyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130d)

(elid 464p)



^{1}H-NMR: (300 MHz, $CDCl_3$)

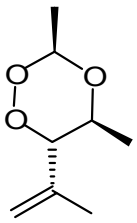
δ (ppm) = 0.87 (t, 3H, *J* = 7.05 Hz, $C\underline{H}_3CH_2$), 1.24-1.65 (m, 6H, 3 x $C\underline{H}_2$), 1.72 (s, 3H, $C\underline{H}_3C$=), 1.75 (s, 3H, $C\underline{H}_3C$=), 3.74 (m, 1H, OC$\underline{H}$), 4.38 (d, 1H, *J* = 9.24 Hz, OOC$\underline{H}$), 5.05 (m, 3H, 2 x $C\underline{H}_2$=C), 5.24 (br. s, 1H, $C\underline{H}_2$=C), 5.55 (s, 1H, OO$\underline{C}$HO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.8 (q, $\underline{C}H_3CH_2$), 17.7 (q, $\underline{C}H_3C$=), 19.7 (q, $\underline{C}H_3C$=), 22.6 (t, $\underline{C}H_2CH_3$), 26.9 (t, $\underline{C}H_2CH_2$), 30.1 (t, $\underline{C}H_2CH_2$), 76.8 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 104.7 (d, OO$\underline{C}$HO), 116.3 (t, $\underline{C}H_2$=C), 118.3 (t, $\underline{C}H_2$=C), 138.8 (s, $\underline{C}$=CH_2) 138.9 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3,5-Dimethyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129e)

(elid 486i)



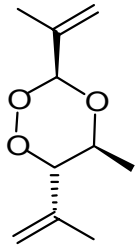
Following **GP-16** using 3-hydroperoxy-4-methylpent-4-en-2-ol **(7a)** (1.40 g, 10.6 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129e**, **130e** in a 79:21 ratio (1.1 g, 62 %). The yellow oil was then purified by preparative thick-layer

chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.74) to separate the 1,2,4-trioxane **130e** as pure product (0.13 g, 0.71 mmol, 7 %).

For the NMR data of **129e** see before.

(3RS,5RS,6RS)-5-Methyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130e)

(elid 477f)



^{1}H-NMR: (300 MHz, $CDCl_3$)

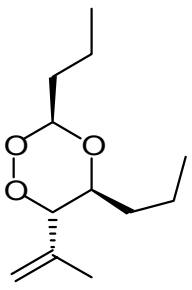
δ (ppm) = 1.16 (d, 3H, C<u>H</u>$_3$CH), 1.72 (s, 3H, C<u>H</u>$_3$C=), 1.75 (s, 3H, C<u>H</u>$_3$C=), 3.88 (dq, 1H, *J* = 6.33, 9.12 Hz, OC<u>H</u>), 4.32 (d, 1H, *J* = 9.12 Hz, OOC<u>H</u>), 5.05 (m, 3H, C<u>H</u>$_2$=C), 5.24 (s, 1H, C<u>H</u>$_2$=C), 5.56 (s, 1H, OOC<u>H</u>O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 16.3 (q, <u>C</u>H$_3$CH), 17.6 (q, <u>C</u>H$_3$C=), 19.6 (q, <u>C</u>H$_3$C=), 73.2 (d, O<u>C</u>H), 88.7 (d, OO<u>C</u>H), 104.8 (d, O<u>C</u>HOO), 116.6 (t, <u>C</u>H$_2$=C), 118.1 (t, <u>C</u>H$_2$=C), 138.7 (s, <u>C</u>=CH$_2$), 138.8 (s, <u>C</u>=CH$_2$).

(3RS,5RS,6RS)-6-(Prop-1-en-2-yl)-3,5-dipropyl-1,2,4-trioxane (129f)

(elid 473q)



Following **GP-16** using 3-hydroperoxy-2-methylhept-1-en-4-ol **(7d)** (0.78 g, 4.88 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129f**, **130f** (0.25 g, 24 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.83) to obtain the pure 1,2,4-trioxanes mixture **129f**, **130f** in a 95:5 ratio (0.08 g, 8 %).

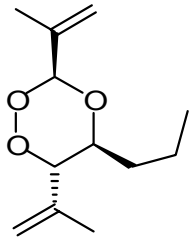
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.88 (t, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH$_2$), 0.89 (t, 3H, *J* = 7.35 Hz, C$\underline{H_3}$CH$_2$), 1.28-1.57 (m, 8H, 2 x C$\underline{H_2}$C$\underline{H_2}$), 1.70 (m, 3H, C$\underline{H_3}$C=), 3.65 (m, 1H, OC$\underline{H}$), 4.32 (d, 1H, *J* = 9.12 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H_2}$=C), 5.21 (t, 1H, *J* = 5.28 Hz, OC$\underline{H}$OO).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, 2 x $\underline{C}$H$_3$CH$_2$), 17.2 (t, $\underline{C}$H$_2$CH$_3$), 18.1 (t, $\underline{C}$H$_2$CH$_3$), 19.6 (q, $\underline{C}$H$_3$C=), 32.4 (t, $\underline{C}$H$_2$CH$_2$), 34.0 (t, $\underline{C}$H$_2$CH$_2$), 76.5 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 104.5 (d, O$\underline{C}$HOO), 118.3 (t, $\underline{C}$H$_2$=C), 138.8 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3,6-Di(prop-1-en-2-yl)-5-propyl-1,2,4-trioxane (130f)



^{1}H-NMR: (300 MHz, $CDCl_3$)

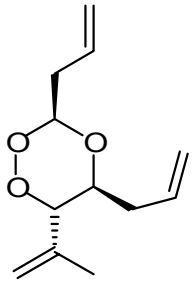
δ (ppm) = 0.90 (t, 3H, *J* = 7.20 Hz, C$\underline{H_3}$CH$_2$), 1.33-1.58 (m, 4H, C$\underline{H_2}$C$\underline{H_2}$), 1.73 (t, 3H, *J* = 1.47 Hz, C$\underline{H_3}$C=), 1.76 (t, 3H, *J* = 1.05 Hz, C$\underline{H_3}$C=), 3.76 (m, 1H, OC$\underline{H}$), 4.39 (d, 1H, *J* = 9.24 Hz, OOC$\underline{H}$), 5.07 (m, 3H, C$\underline{H_2}$=C), 5.25 (br. s, 1H, C$\underline{H_2}$=C), 5.56 (s, 1H, OOC$\underline{H}$O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.9 (q, $\underline{C}$H$_3$CH$_2$), 17.8 (q, $\underline{C}$H$_3$C=), 18.1 (t, $\underline{C}$H$_2$CH$_3$), 19.7 (q, $\underline{C}$H$_3$C=), 32.5 (t, $\underline{C}$H$_2$CH$_2$), 76.6 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 104.7 (d, OO$\underline{C}$HO), 116.3 (t, $\underline{C}$H$_2$=C), 118.3 (t, $\underline{C}$H$_2$=C), 138.8 (s, $\underline{C}$=CH$_2$), 138.9 (s, $\underline{C}$=CH$_2$).

(3RS,5RS,6RS)-3,5-Diallyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129g)

(elid 474x, 486t)



Following **GP-16** using 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (0.74 g, 4.68 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129g**, **130g** in a 80:20 ratio (0.51 g, 2.43 mmol, 52 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.85) to give the pure 1,2,4-trioxanes mixture **129g**, **130g** in a 90:10 ratio (0.05 g, 5 %).

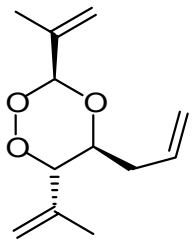
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.72 (t, 3H, *J* = 1.32 Hz, C$\underline{H_3}$C=), 2.35 (m, 4H, 2 x C$\underline{H_2}$), 3.77 (ddd, 1H, *J* = 3.81, 7.50, 9.42 Hz, OC$\underline{H}$), 4.40 (d, 1H, *J* = 9.42 Hz, OOC$\underline{H}$), 5.04-5.15 (m, 6H, 2 x C$\underline{H_2}$=CH and C$\underline{H_2}$=C), 5.27 (t, 1H, *J* = 5.46 Hz, OOC$\underline{H}$O), 5.70-5.97 (m, 2H, 2 x C$\underline{H}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.6 (q, $\underline{C}H_3$C=), 34.9 (t, $\underline{C}H_2$), 36.7 (t, $\underline{C}H_2$), 76.3 (d, O$\underline{C}$H), 87.0 (d, OO$\underline{C}$H), 103.7 (d, OO$\underline{C}$HO), 117.4 (t, $\underline{C}H_2$=CH), 118.3 (t, $\underline{C}H_2$=), 118.7 (t, $\underline{C}H_2$=), 131.2 (d, $\underline{C}$H=CH_2), 133.5 (d, $\underline{C}$H=CH_2), 138.4 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-5-Allyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130g)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

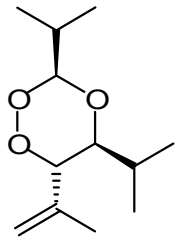
δ (ppm) = 1.74 (t, 3H, *J* = 1.17 Hz, C$\underline{H_3}$C=), 1.76 (m, 3H, C$\underline{H_3}$C=), 2.26 (m, 2H, C$\underline{H_2}$), 3.85 (m, 1H, OC$\underline{H}$), 4.45 (d, 1H, *J* = 9.42 Hz, OOC$\underline{H}$), 5.26 (br. s, 1H, C$\underline{H_2}$=C), 5.57 (s, 1H, OOC$\underline{H}$O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.7 (q, $\underline{C}H_3$C=), 19.6 (q, $\underline{C}H_3$C=), 35.0 (t, $\underline{C}H_2$), 76.2 (d, O$\underline{C}$H), 86.9 (d, OO$\underline{C}$H), 104.7 (d, OO$\underline{C}$HO), 116.6 (t, $\underline{C}H_2$=C), 117.5 (t, $\underline{C}H_2$=CH), 118.7 (t, $\underline{C}H_2$=C), 133.4 (d, $\underline{C}$H=CH_2), 138.5 (s, $\underline{C}$=CH_2), 138.8 (s, $\underline{C}$=CH_2).

(3RS,5RS,6RS)-3,5-Diisopropyl-6-(prop-1-en-2-yl)-1,2,4-trioxane (129h)

(elid 486s, 473p)



Following **GP-16** using 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (0.90 g, 5.6 mmol), followed by usual work-up afforded the crude 1,2,4-trioxanes mixture **129h**, **130h** in a 91:9 ratio (0.60 g, 50 %). The yellow oil was then purified by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.80) to obtain the pure 1,2,4-trioxanes mixture **129h**, **130h** in ratio 94:6 (0.14 g, 12 %).

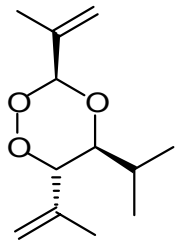
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.90-1.0 (m, 12H, 2 x ($C\underline{H}_3)_2CH$), 1.70 (m, 3H, $C\underline{H}_3C$=), 1.79 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 3.54 (dd, 1H, *J* = 2.34, 9.42 Hz, OC<u>H</u>), 4.49 (d, 1H, *J* = 9.54 Hz, OOC<u>H</u>), 4.95 (d, 1H, *J* = 5.28 Hz, OOC<u>H</u>O), 5.02-5.12 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 15.3 (q, $\underline{C}H_3CH$), 16.7 (q, $\underline{C}H_3CH$), 17.3 (q, $\underline{C}H_3CH$), 19.5 (q, $\underline{C}H_3C$=), 19.9 (q, $\underline{C}H_3CH$), 28.2 (d, $\underline{C}H(CH_3)_2$), 31.1 (d, $\underline{C}H(CH_3)_2$), 80.3 (d, O<u>C</u>H), 85.7 (d, OO<u>C</u>H), 107.6 (s, O<u>C</u>HOO), 118.1 (t, $\underline{C}H_2$=C), 139.0 (s, <u>C</u>=CH_2).

(3RS,5RS,6RS)-5-Isopropyl-3,6-di(prop-1-en-2-yl)-1,2,4-trioxane (130h)



^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

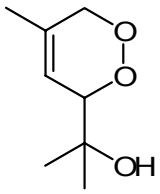
δ (ppm) = 0.98 (m, 6H, ($C\underline{H}_3)_2CH$), 1.72 (m, 3H, $C\underline{H}_3C$=), 1.75 (m, 3H, $C\underline{H}_3C$=), 1.79 (m, 1H, $C\underline{H}(CH_3)_2$), 3.65 (dd, 1H, *J* = 2.37, 9.42 Hz, OC<u>H</u>), 4.56 (d, 1H, *J* = 9.57 Hz, OOC<u>H</u>), 5.24 (br. s, 1H, $C\underline{H}_2$=C), 5.55 (s, 1H, *J* = 5.28 Hz, OOC<u>H</u>O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 15.4 (q, $\underline{C}H_3CH$), 17.6 (q, $\underline{C}H_3C$=), 19.5 (q, $\underline{C}H_3C$=), 20.0 (q, $\underline{C}H_3CH$), 80.5 (d, O$\underline{C}$H), 85.7 (d, OO$\underline{C}$H), 104.8 (s, O$\underline{C}$HOO), 116.3 (t, $\underline{C}H_2$=C), 118.3 (t, $\underline{C}H_2$=C), 138.9 (s, $\underline{C}$=CH_2), 139.1 (s, $\underline{C}$=CH_2).

2-(3,6-Dihydro-5-methyl-1,2-dioxin-3-yl)propan-2-ol (131)

(elid 475l)



Photooxygenation of (E)-2,5-Dimethylhexa-3,5-dien-2-ol **(6u)** (1.10 g, 8.73 mmol) for 65 h according to **GP-9a** afforded the endoperoxide (0.92 g, 5.82 mmol, 67 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.15 (d, 6H, $(C\underline{H}_3)_{\underline{2}}C$), 1.68 (s, 3H, $C\underline{H}_3C$=), 4.20 (m, 1H, C$\underline{H}$), 4.28 (s, 2H, $C\underline{H}_2$), 5.65 (m, 1H, C$\underline{H}$=C).

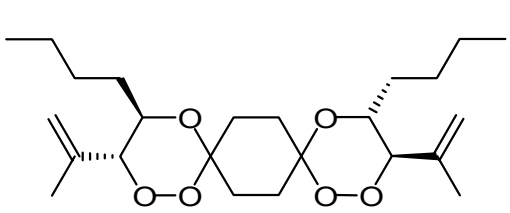
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.2 (q, $\underline{C}H_3C$=), 25.7 (q, $(\underline{C}H_3)_2C$), 72.6 (t, $\underline{C}H_2$), 72.8 (s, $\underline{C}(CH_3)_2$), 84.3 (d, $\underline{C}$H), 117.1 (d, $\underline{C}$H=C), 133.5 (s, $\underline{C}$=CH).

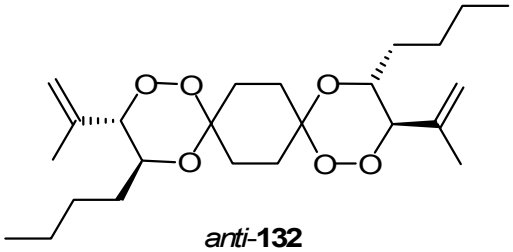
4.8 Bis Spiro-1,2,4-Trioxanes Synthesis

(3RS,4RS,12RS,13RS)-4,13-Dibutyl-3,12-diisopropenyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*syn*-132) and (3RS,4RS,12SR,13SR)-4,13-dibutyl-3,12-diisopropenyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*anti*-132)

(elid 492j)



syn-**132**



anti-**132**

Following **GP-15**, a solution of 3-hydroperoxy-2-methyloct-1-en-4-ol **(7g)** (1.45 g, 8.33 mmol) and cyclohexane-1,4-dione (0.46 g, 4.11 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.53) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes *syn*-**132** and *anti*-**132** in a ratio 1:1 (0.07 g, 0.17 mmol, 4 %) as oil which crystallizes on standing.

^{1}H-NMR: (300 MHz, $CDCl_3$, both diastereomers)

δ (ppm) = 0.86 (t, 3H, *J* = 7.05 Hz, C$\underline{H_3}$CH$_2$), 1.05-1.72 (m, 8H, C$\underline{H_2}$), 1.60 (m, 3H, C$\underline{H_3}$C=), 2.20 (m, 2H, CH$_2$), 3.86 (m, 1H, OC$\underline{H}$), 4.25 (d, 1H, *J* = 9.55 Hz, OOC$\underline{H}$), 5.04 (s, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 13.9 (q, $\underline{C}$H$_3$CH$_2$), 19.7 (q, $\underline{C}$H$_3$C=), 22.5 (t, $\underline{C}$H$_2$CH$_3$), 25.2 (t, $\underline{C}$H$_2$), 27.0 (t, $\underline{C}$H$_2$CH$_2$), 30.4 (t, $\underline{C}$H$_2$CH$_2$), 30.8 (t, $\underline{C}$H$_2$), 69.8 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 102.4 (s, O$\underline{C}$OO), 118.1 (t, $\underline{C}$H$_2$=C), 139.2 (s, $\underline{C}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of the 2nd diastereomer)

δ (ppm) = 19.8 (q, $\underline{C}$H$_3$C=), 22.5 (t, $\underline{C}$H$_2$CH$_3$), 24.9 (t, $\underline{C}$H$_2$), 27.1 (t, $\underline{C}$H$_2$CH$_2$), 30.5 (t, $\underline{C}$H$_2$CH$_2$), 31.2 (t, $\underline{C}$H$_2$), 69.8 (d, O$\underline{C}$H), 87.7 (d, OO$\underline{C}$H), 102.3 (s, O$\underline{C}$OO), 118.1 (t, $\underline{C}$H$_2$=C), 139.1 (s, $\underline{C}$=CH$_2$).

IR: (Film)

ν (cm^{-1}) = 3083, 2957, 2873, 1648, 1455, 1373, 1258, 1105, 1007, 928, 911.

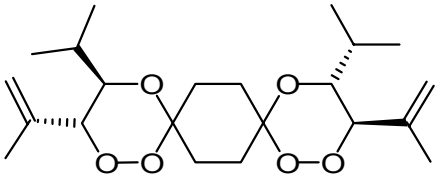
Elemental Analysis: ($C_{24}H_{40}O_6$, M = 424.57)

Calcd: C 67.89 H 9.50

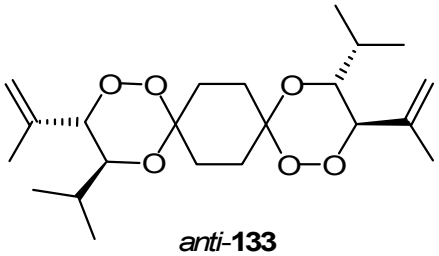
Found: C 67.43 H 9.37

(3RS,4RS,12RS,13RS)-3,12-Diisopropenyl-4,13-diisopropyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*syn*-133) and (3RS,4RS,12SR,13SR)-3,12-diisopropenyl-4,13-diisopropyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*anti*-133)

(elid 476g)



syn-**133**



anti-**133**

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7c)** (1.60 g, 10.0 mmol) and cyclohexane-1,4-dione (0.56 g, 5.0 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.70) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes *syn*-**133** and *anti*-**133** in a ratio 1:1 (0.36 g, 0.91 mmol, 18 %) as oil which crystallizes on standing into yellow crystals.

^{1}H-NMR: (300 MHz, $CDCl_3$, both diastereomers)

δ (ppm) = 0.90 (d, 3H, *J* = 6.93 Hz, C$\underline{H_3}$CH), 0.97 (d, 3H, *J* = 6.75 Hz, C$\underline{H_3}$CH), 0.79-1.10 (m, CH_2), 1.60-1.80 (m, 1H, C$\underline{H}(CH_3)_2$, 1.74 (m, 3H, C$\underline{H_3}$C=), 3.76 (m, 1H, OC$\underline{H}$), 4.45 (d, 1H, *J* = 9.84 Hz, OOC$\underline{H}$), 5.07 (m, 2H, C$\underline{H_2}$=).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 15.0 (q, $\underline{C}H_3CH$), 19.6 (q, $\underline{C}H_3C$=), 19.9 (q, $\underline{C}H_3CH$), 24.8 (t, $\underline{C}H_2$), 28.1 (d, $\underline{C}H(CH_3)_2$), 31.1 (t, $\underline{C}H_2$), 73.4 (d, O$\underline{C}$H), 85.7 (d, OO$\underline{C}$H), 102.2 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}H_2$=C), 139.3 (s, $\underline{C}$=CH_2).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals of 2nd diastereomer)

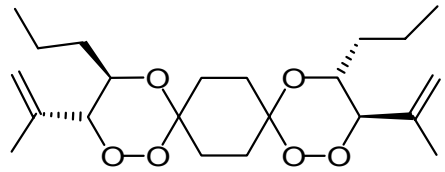
δ (ppm) = 20.0 (q, $\underline{C}H_3CH$), 25.0 (t, $\underline{C}H_2$) 30.7 (t, $\underline{C}H_2$).

IR: (Film)

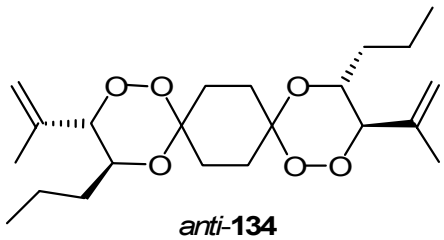
ν (cm^{-1}) = 3083, 2965, 1731, 1649, 1469, 1373, 1258, 1118, 919, 825.

(3RS,4RS,12RS,13RS)-3,12-Diisopropenyl-4,13-dipropyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*syn*-134) and (3RS,4RS,12SR,13SR)-3,12-diisopropenyl-4,13-dipropyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*anti*-134)

(elid 495m)



syn-**134**



anti-**134**

Following **GP-15**, a solution of 4-hydroperoxy-2,5-dimethylhex-5-en-3-ol **(7d)** (1.32 g, 8.25 mmol) and cyclohexane-1,4-dione (0.46 g, 4.11 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up followed by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.64) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes *syn*-**134** and *anti*-**134** in a ratio 1:1 (0.31 g, 0.78 mmol, 19 %) as oil which crystallizes on standing into yellow crystals.

^{1}H-NMR: (300 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 0.88 (t, 3H, *J* = 6.90 Hz, C$\underline{H}_3$CH$_2$), 1.26-1.58 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 1.67 (m, 2H, C$\underline{H}_2$), 1.72 (m, 3H, C$\underline{H}_3$C=), 2.04-2.32 (m, 2H, C$\underline{H}_2$), 3.89 (m, 1H, OC$\underline{H}$), 4.25 (d, 1H, *J* = 9.72 Hz, OOC$\underline{H}$), 5.04 (m, 2H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 13.8 (q, $\underline{C}$H$_3$CH$_2$), 18.1 (t, $\underline{C}$H$_2$CH$_3$), 19.7 (q, $\underline{C}$H$_3$C=), 25.1 (t, $\underline{C}$H$_2$), 30.8 (t, $\underline{C}$H$_2$), 32.9 (t, $\underline{C}$H$_2$CH$_2$), 69.5 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 102.3 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}$H$_2$=C), 139.1 (s, $\underline{C}$=CH$_2$).

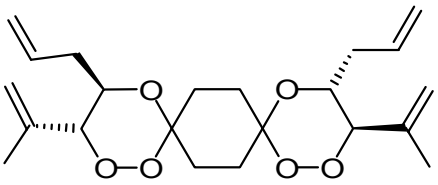
^{13}C-NMR: (75.5 MHz, $CDCl_3$, 2nd diastereomer)

δ (ppm) = 13.9 (q, $\underline{C}$H$_3$CH$_2$), 18.1 (t, $\underline{C}$H$_2$CH$_3$), 19.7 (q, $\underline{C}$H$_3$C=), 24.8 (t, $\underline{C}$H$_2$), 31.2 (t, $\underline{C}$H$_2$), 32.9 (t, $\underline{C}$H$_2$CH$_2$), 69.5 (d, O$\underline{C}$H), 87.6 (d, OO$\underline{C}$H), 102.3 (s, O$\underline{C}$OO), 118.0 (t, $\underline{C}$H$_2$=C), 139.1 (s, $\underline{C}$=CH$_2$).

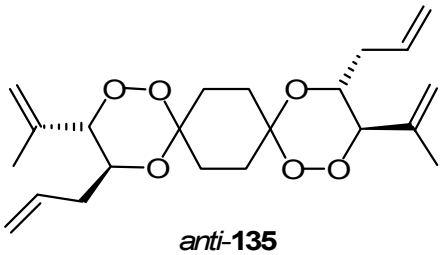
IR: (Film)

ν (cm^{-1}) = 3083, 2956, 2873, 1680, 1649, 1454, 1374, 1258, 1105, 1006, 918.

(3RS,4RS,12RS,13RS)-4,13-Diallyl-3,12-diisopropenyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*syn*-135) and (3RS,4RS,12SR,13SR)-4,13-diallyl-3,12-diisopropenyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*anti*-135) (elid 495t)



syn-**135**



anti-**135**

Following **GP-15**, a solution of 3-hydroperoxy-2-methylhepta-1,6-dien-4-ol **(7e)** (1.30 g, 8.23 mmol) and cyclohexane-1,4-dione (0.46 g, 4.11 mmol, 0.5 equiv.) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product (0.87 g, 2.22 mmol, 54 %) by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.55) afforded a diastereomeric mixture of the pure 1,2,4-trioxanes *syn*-**135** and *anti*-**135** (0.13 g, 0.33 mmol, 8 %) as viscous colorless oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 1.60-2.39 (m, 6H, 3 x C$\underline{H}_2$), 1.74 (s, 3H, C$\underline{H}_3$C=), 3.97 (m, 1H, OC$\underline{H}$), 4.31 (d, 1H, *J* = 9.69 Hz, OOC$\underline{H}$), 5.07 (m, 4H, C$\underline{H}_2$=CH and C$\underline{H}_2$=C), 5.82 (m, 1H, C$\underline{H}$=CH$_2$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 19.7 (q, $\underline{C}$H$_3$C=), 24.8 (t, $\underline{C}$H$_2$), 31.1 (t, $\underline{C}$H$_2$), 35.3 (t, $\underline{C}$H$_2$CH=), 69.5 (d, O$\underline{C}$H), 86.9 (d, OO$\underline{C}$H), 102.4 (s, O$\underline{C}$OO), 117.2 (t, $\underline{C}$H$_2$=CH), 118.4 (t, $\underline{C}$H$_2$=C), 133.6 (d, $\underline{C}$H=CH$_2$), 138.8 (s, $\underline{C}$=CH$_2$).

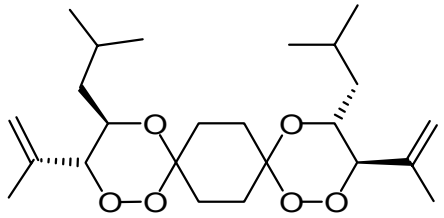
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of 2nd diastereomer)

δ (ppm) = 3.35 (m, 1H, OC$\underline{H}$), 4.30 (d, 1H, *J* = 9.69 Hz, OOC$\underline{H}$).

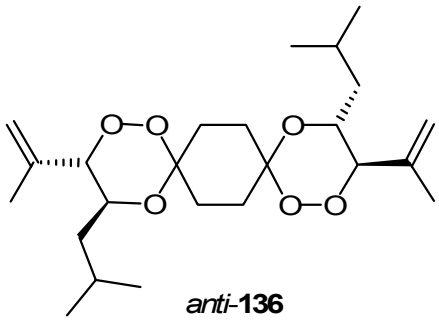
^{13}C-NMR: (75.5 MHz, $CDCl_3$, 2nd diastereomer)

δ (ppm) = 19.7 (q, $\underline{C}$H$_3$C=), 24.8 (t, $\underline{C}$H$_2$), 31.1 (t, $\underline{C}$H$_2$), 35.3 (t, $\underline{C}$H$_2$CH=), 69.5 (d, O$\underline{C}$H), 87.1 (d, OO$\underline{C}$H), 102.4 (s, O$\underline{C}$OO), 117.1 (t, $\underline{C}$H$_2$=CH), 118.4 (t, $\underline{C}$H$_2$=C), 133.7 (d, $\underline{C}$H=CH$_2$), 138.9 (s, $\underline{C}$=CH$_2$).

(3RS,4RS,12RS,13RS)-4,13-Diisobutyl-3,12-diisopropenyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*syn*-136) and (3RS,4RS,12SR,13SR)-4,13-diisobutyl-3,12-diisopropenyl-1,2,5,10,11,14-hexaoxadispiro[5.2.5.2]hexadecane (*anti*-136) (elid 496d)



syn-**136**



anti-**136**

Following **GP-15**, a solution of 3-hydroperoxy-2,6-dimethylhept-1-en-4-ol **(7h)** (1.32 g, 7.59 mmol) and cyclohexane-1,4-dione (0.42 g, 3.75 mmol) in CH_2Cl_2 was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml). Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.71) afforded a diastereomeric mixture of the 1,2,4-trioxanes *syn*-**136** and *anti*-**136** (0.23 g, 0.54 mmol, 15 %) as oil which crystallizes on standing.

^{1}H-NMR: (300 MHz, $CDCl_3$, both diastereomers)

δ (ppm) = 0.81-0.94 (m, 6H, $(C\underline{H}_3)_2CH$), 1.06 (m, 1H, $C\underline{H}_2CH$), 1.33 (m, 1H, $C\underline{H}_2CH$), 1.59-1.89 (m, 3H, $C\underline{H}_2$ and $C\underline{H}CH_2$), 1.72 (m, 3H, $C\underline{H}_3C$=), 2.10-2.35 (m, 2H, $C\underline{H}_2$), 3.97 (m, 1H, O$C\underline{H}$), 4.24 (d, 1H, *J* = 9.54 Hz, OO$C\underline{H}$), 5.05 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, 1st diastereomer)

δ (ppm) = 19.7 (q, $\underline{C}H_3C$=), 21.3 (q, $\underline{C}H_3CH$), 23.5 (d, $\underline{C}HCH_2$), 23.7 (q, $\underline{C}H_3CH$), 25.2 (t, $\underline{C}H_2$), 31.2 (t, $\underline{C}H_2$), 39.6 (t, $\underline{C}H_2CH$), 67.8 (d, O$\underline{C}$H), 88.1 (d, OO$\underline{C}$H), 102.3 (s, O$\underline{C}$OO), 118.2 (t, $\underline{C}H_2$=C), 139.0 (s, $\underline{C}$=CH_2).

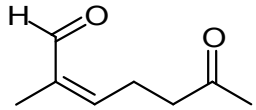
^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional signals of 2nd diastereomer)

δ (ppm) = 19.6 (q, $\underline{C}H_3C$=), 23.5 (d, $\underline{C}HCH_2$), 24.7 (t, $\underline{C}H_2$), 30.7 (t, $\underline{C}H_2$), 39.6 (t, $\underline{C}H_2CH$), 88.1 (d, OO$\underline{C}$H), 102.3 (s, O$\underline{C}$OO), 139.0 (s, $\underline{C}$=CH_2).

4.9 Intramolecular 1,2,4-Trioxanes Synthesis

2-Methyl-6-oxohept-2-enal (139)

(elid 360a)



A solution of SeO_2 (11 g, 100 mmol; caution, selenium compounds are highly toxic and should be handeled carefully !) was stirred at r.t. in CH_2Cl_2 (150 mL) for 30 min, then 6-methylhept-5-en-2-one **(138)** (6.31 g, 50 mmol) was added portionwise over several minutes. The mixture is stirred at r.t. for 48 h and then washed by 10 % aqueous KOH, then with $AcOH/Me_2S$ (4:5, v/v) (45 mL) then with 20 % aqueous K_2CO_3. The aqueous phase is extracted with ether (3 x 50 mL), and the combined organic phase is washed with water, brine and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure affords the dicarbonyl compound (2.88 g, 20.6 mmol) in good purity.

Yield: 41 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

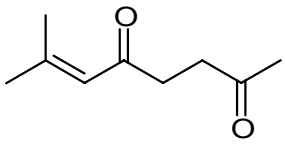
δ (ppm) = 1.71 (s, 3H, C<u>H</u>$_3$CH), 2.13 (s, 3H, C<u>H</u>$_3$CO), 2.56 (m, 4H, C<u>H</u>$_2$C<u>H</u>$_2$), 6.38 (m, 1H, C<u>H</u>=C), 9.32 (s, 1H, C<u>H</u>O).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 9.1 (q, <u>C</u>H$_3$CH), 22.9 (t, <u>C</u>H$_2$CH), 29.8 (q, <u>C</u>H$_3$CO), 41.6 (t, <u>C</u>H$_2$CO), 139.9 (s, <u>C</u>=CH), 152.4 (d, <u>C</u>H=C), 195.0 (d, CHO), 206.8 (s, CO).

7-Methyloct-6-ene-2,5-dione[192] (140)

(elid 496a)



A solution of 3,3-dimethylacrolein (10.0 g, 119 mmol), methylvinylketone (8.33 g, 119 mmol), 3-benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride[193] (3.20 g, 11.9 mmol) and sodium acetate (3.90 g, 47.6 mmol) in ethanol (100 mL) was stirred under nitrogen at 80 °C for 15 h, then the reaction mixture is cooled to r.t. and the solvent was removed under

reduced pressure followed by fractional distillation (b.p. 84 °C, 1.39 torr, Lit. 87-89 °C, 2.5 torr[194]) of the residue to afford the pure 1,4-dione **140** (9.1 g, 59.1 mmol) as yellow oil.

Yield: 50 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

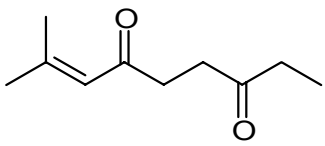
δ (ppm) = 1.81 (s, 3H, $C\underline{H}_3C$=), 2.04 (s, 3H, $C\underline{H}_3C$=), 2.12 (t, 3H, *J* = 2.80 Hz, $C\underline{H}_3CO$), 2.63 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 6.02 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.6 (q, $\underline{C}H_3C$=), 27.5 (q, $\underline{C}H_3C$=), 29.9 (q, $\underline{C}H_3CO$), 36.9 (t, $\underline{C}H_2$), 37.4 (t, $\underline{C}H_2$) 123.3 (d, <u>C</u>H=C), 155.3 (s, <u>C</u>=CH), 198.6 (s, <u>C</u>OCH=), 207.4 (s, $\underline{C}OCH_3$).

8-Methylnon-7-ene-3,6-dione[192] (141)

(elid 483s)



A solution of 3,3-dimethyl acrolein (18.75 g, 223.2 mmol), ethyl vinyl ketone (25 g, 297.6 mmol), 3-benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride (6.0 g, 22.3 mmol) and sodium acetate (7.32 g, 89.3 mmol) in ethanol (250 mL) was stirred under nitrogen at 80 °C for 15 h, then the reaction mixture is cooled to r.t. and the solvent was removed under reduced pressure followed by fractional distillation (b.p. 119 °C, 0.33 torr) of the residue gives the pure 1,4-dione **141** (33.4 g, 198.8 mmol) as yellow oil.

Yield: 89 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

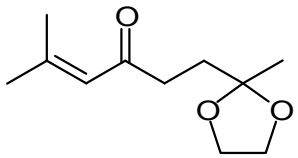
δ (ppm) = 0.95 (dt, 3H, *J* = 1.32, 7.35 Hz, $C\underline{H}_3CH_2$), 1.78 (s, 3H, $C\underline{H}_3C$=), 2.01 (s, 3H, $C\underline{H}_3C$=), 2.39 (q, 2H, *J* = 7.35 Hz, $C\underline{H}_2CH_3$), 2.60 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 6.0 (m, 1H, C<u>H</u>=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.6 (q, $\underline{C}H_3CH_2$), 20.5 (q, $\underline{C}H_3C$=), 27.4 (q, $\underline{C}H_3C$=), 35.6 (t, $\underline{C}H_2$), 35.7 (t, $\underline{C}H_2$), 37.4 (t, $\underline{C}H_2$), 123.3 (d, <u>C</u>H=C), 155.0 (s, <u>C</u>=CH), 198.7 (s, <u>C</u>OCH=), 209.9 (s, $\underline{C}OCH_2$).

5-Methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-3-one[195] (142)

(elid 496q)



A solution of 7-methyloct-6-ene-2,5-dione **(140)** (14.5 g, 94.2 mmol) and ethylene glycol (10.0 g, 161.3 mmol) and pyridinium tosylate (3.58 g, 14.3 mmol) in benzene (100 mL) was refluxed using Dean-Stark apparatus with continuous removal of the separated water. The solvent is removed under reduced pressure and the residue is mixed with ether, washed with saturated $NaHCO_3$ solution (2 x 30 mL), dried over Na_2SO_4 and the ether is evaporated. Fractional distillation (b.p. 100 °C, 0.90 torr, Lit. 48 °C, 0.02 torr[195]) of the residue gives the pure enone acetal **142** (7.46 g, 37.7 mmol) as yellow oil.

Yield: 40 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

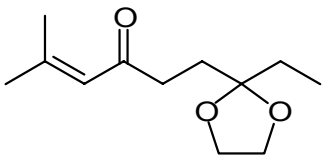
δ (ppm) = 1.19 (s, 3H, C$\underline{H}_3$), 1.76 (d, 3H, *J* = 1.29 Hz, C$\underline{H}_3$C=), 1.85 (t, 2H, *J* = 7.70 Hz C$\underline{H}_2$), 2.01 (d, 3H, *J* = 1.02 Hz, C$\underline{H}_3$C=), 2.39 (t, 2H, *J* = 7.70 Hz C$\underline{H}_2$), 3.81 (m, 4H, 2 x C$\underline{H}_2$O), 5.97 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.4 (q, $\underline{C}H_3$C=), 23.7 (q, $\underline{C}H_3$), 27.4 (q, $\underline{C}H_3$C=), 32.8 (t, $\underline{C}H_2$), 38.5 (t, $\underline{C}H_2$CO), 64.4 (t, 2 x O$\underline{C}H_2$), 109.2 (s, O$\underline{C}$O), 123.6 (d, $\underline{C}$H=C), 154.4 (s, $\underline{C}$=CH), 199.9 (s, $\underline{C}$O).

1-(2-Ethyl-1,3-dioxolan-2-yl)-5-methylhex-4-en-3-one (143)

(elid 494f)



A solution of 8-methylnon-7-ene-3,6-dion **(141)** (30.0 g, 178.6 mmol) and ethylene glycol (12.5 g, 201.6 mmol) and pyridinium tosylate (4.46 g, 17.8 mmol) in benzene (100 mL) was refluxed using Dean-Stark apparatus with continuous removal of the separated water. The solvent is removed under reduced pressure and the residue is mixed with ether, washed with

saturated $NaHCO_3$ solution (2 x 30 mL), dried over Na_2SO_4 and the ether is distilled to afford the enone acetal **143** (30.2 g, 142.3 mmol) as yellow oil.

Yield: 80 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

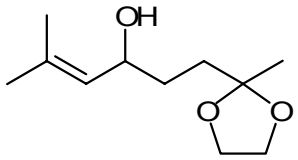
δ (ppm) = 0.80 (t, 3H, *J* = 7.35 Hz, C$\underline{H}_3$CH$_2$), 1.51 (q, 2H, *J* = 7.50 Hz, CH$_2$CH$_3$), 1.76 (s, 3H, C$\underline{H}_3$C=), 1.83 (m, 2H, C$\underline{H}_2$), 2.02 (s, 3H, C$\underline{H}_3$C=), 2.39 (m, 2H, C$\underline{H}_2$), 3.81 (m, 4H, 2 x C$\underline{H}_2$O), 5.96 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.9 (q, $\underline{C}$H$_3$CH$_2$), 20.5 (q, $\underline{C}$H$_3$C=), 27.5 (q, $\underline{C}$H$_3$C=), 30.0 (t, $\underline{C}$H$_2$), 30.5 (t, $\underline{C}$H$_2$), 38.5 (t, $\underline{C}$H$_2$CO), 64.9 (t, 2 x O$\underline{C}$H$_2$), 111.3 (s, O$\underline{C}$O), 123.7 (d, $\underline{C}$H=C), 154.5 (s, $\underline{C}$=CH), 200.2 (s, $\underline{C}$O).

5-Methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-3-ol (144)

(elid 480o)



Under an inert atmosphere, an ether solution of 5-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-3-one **(142)** (8.6 g, 43.4 mmol) was added dropwise at r.t. to a suspension of $LiAlH_4$ (0.64 g, 16.8 mmol) in dry ether at such a rate as to maintain gentle reflux. After complete addition the reaction mixture was treated slowly (caution, vigorous evolution of hydrogen gas !) with 2N aqueous NaOH solution. The precipitate was removed by filteration, digested with ether and the combined ether extracts were washed with brine and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure gives the pure allylic alcohol (5.40 g, 0.027 mmol) as faint yellow oil.

Yield: 62 %

^{1}H-NMR: (300 MHz, $CDCl_3$)

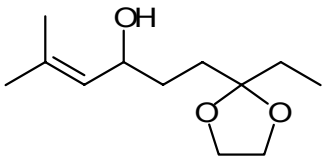
δ (ppm) = 1.25 (s, 3H, C$\underline{H}_3$), 1.44-1.78 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$), 1.61 (d, 2H, *J* = 1.17 Hz, C$\underline{H}_3$C=), 1.65 (d, 3H, *J* = 1.02 Hz, C$\underline{H}_3$C=), 3.87 (m, 4H, 2 x OC$\underline{H}_2$), 4.26 (m, 1H, OC$\underline{H}$), 5.10 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.1 (q, $\underline{C}H_3C$=), 23.7 (q, $\underline{C}H_3$), 25.6 (q, $\underline{C}H_3C$=), 31.9 (t, $\underline{C}H_2$), 34.9 (t, $\underline{C}H_2$), 64.5 (t, 2 x O$\underline{C}H_2$), 109.9 (s, O$\underline{C}$O), 128.0 (d, $\underline{C}$H=C), 134.6 (s, $\underline{C}$=CH).

1-(2-Ethyl-1,3-dioxolan-2-yl)-5-methylhex-4-en-3-ol (145)

(elid 484v)



Under an inert atmosphere, an ether solution of 1-(2-ethyl-1,3-dioxolan-2-yl)-5-methylhex-4-en-3-one **(143)** (28.87 g, 136.2 mmol) was added dropwise at r.t. to a suspension of $LiAlH_4$ (2.0 g, 52.6 mmol) in dry ether at such a rate as to maintain gentle reflux. After complete addition the reaction mixture was treated slowly (caution, vigorous evolution of hydrogen gas !) with 2N aqueous NaOH solution. The precipitate was removed by filteration, digested with ether and the combined ether extracts were washed with brine and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure followed by fractional distillation (b.p. 110 °C, 0.22 torr) gives the pure allylic alcohol (18.0 g, 84.1 mmol) as faint yellow oil.

Yield: 62 %

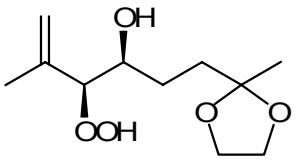
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.71 (t, 3H, *J* = 7.65 Hz, $C\underline{H}_3CH_2$), 1.25-1.59 (m, 6H, 3 x $C\underline{H}_2$), 1.48 (d, 3H, *J* = 1.02 Hz, $C\underline{H}_3C$=), 1.53 (s, 3H, $C\underline{H}_3C$=), 2.65 (br. s, 1H, OH), 3.73 (m, 4H, 2 x O$C\underline{H}_2$), 4.11 (m, 1H, O$C\underline{H}$), 4.96 (m, 1H, $C\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.7 (q, $\underline{C}H_3CH_2$), 17.8 (q, $\underline{C}H_3C$=), 25.3 (q, $\underline{C}H_3C$=), 29.5 (t, $\underline{C}H_2$), 31.5 (t, $\underline{C}H_2$), 32.0 (t, $\underline{C}H_2$), 64.5 (t, 2 x O$\underline{C}H_2$), 68.0 (d, O$\underline{C}$H), 111.6 (s, O$\underline{C}$O), 128.1 (d, $\underline{C}$H=C), 133.6 (s, $\underline{C}$=CH).

(3RS,4RS)-4-Hydroperoxy-5-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-5-en-3-ol (*syn*-146) (elid 497e)



Photooxygenation of 5-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-3-ol **(144)** (1.13 g, 5.65 mmol) for 108 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 77:23) of β-hydroxy allylic hydroperoxides (1.10 g, 4.74 mmol, 84%) as yellow oil.

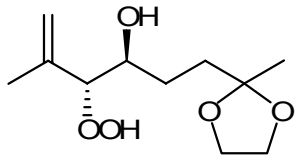
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.21 (s, 3H, $C\underline{H}_3$), 1.64 (s, 3H, $C\underline{H}_3C$=), 1.30-1.90 (m, 4H, $C\underline{H}_2C\underline{H}_2$), 3.84 (br, 4H, 2 x $OC\underline{H}_2$), 4.07 (d, 1H, *J* = 8.07 Hz, OOC<u>H</u>), 4.08 (m, 1H, O<u>CH</u>), 4.95 (br. s, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 17.9 (q, $\underline{C}H_3$), 23.5 (q, $\underline{C}H_3$), 27.0 (t, $\underline{C}H_2$), 34.3 (t, $\underline{C}H_2$), 64.3 (t, 2 x $O\underline{C}H_2$), 70.4 (d, O<u>C</u>H), 93.2 (d, OO<u>C</u>H), 109.8 (s, O<u>C</u>O), 116.1 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

(3RS,4SR)-4-Hydroperoxy-5-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-5-en-3-ol (*anti*-146)



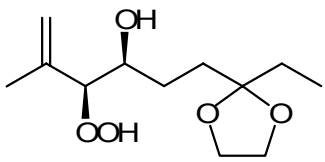
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 1.23 (s, 3H, $C\underline{H}_3$), 1.71 (s, 3H, $C\underline{H}_3C$=), 3.60 (s, 4H, 2 x $OC\underline{H}_2$), 3.70 (m, 1H, O<u>CH</u>).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 64.6 (t, 2 x $O\underline{C}H_2$), 70.3 (d, O<u>C</u>H), 91.5 (d, OO<u>C</u>H), 110.0 (s, O<u>C</u>O), 115.1 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

(3RS,4RS)-1-(2-Ethyl-1,3-dioxolan-2-yl)-4-hydroperoxy-5-methylhex-5-en-3-ol (*syn*-147) (elid 485h)



Photooxygenation of 1-(2-ethyl-1,3-dioxolan-2-yl)-5-methylhex-4-en-3-ol **(145)** (1.12 g, 5.23 mmol) for 120 h according to **GP-9a** afforded a diastereomeric mixture (d.r. *syn*:*anti*, 74:26) of β-hydroxy allylic hydroperoxides (1.17 g, 4.76 mmol, 91 %) as yellow oil.

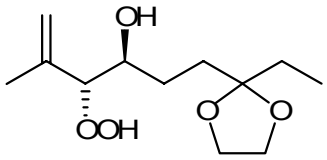
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.78 (m, 3H, $C\underline{H}_3CH_2$), 1.14-1.91 (m, 6H, overlapped signals $C\underline{H}_2CH_3$ and $CH_2C\underline{H}_2$), 1.62 (s, 3H, $C\underline{H}_3C$=), 3.82 (s, 4H, 2 x $OC\underline{H}_2$), 4.05 (d, 1H, *J* = 8.25 Hz, OOC<u>H</u>), 4.09 (m, 1H, O<u>CH</u>), 4.93 (br. s, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.8 (q, $\underline{C}H_3CH_2$), 17.8 (q, $\underline{C}H_3C$=), 26.3 (t, $\underline{C}H_2$), 29.5 (t, $\underline{C}H_2$), 31.8 (t, $\underline{C}H_2$), 64.7 (t, 2 x O$\underline{C}H_2$), 70.5 (d, O<u>C</u>H), 93.1 (d, OO<u>C</u>H), 111.8 (s, O<u>C</u>O), 116.0 (t, $\underline{C}H_2$=C), 141.4 (s, $\underline{C}$=CH_2).

(3RS,4SR)-1-(2-Ethyl-1,3-dioxolan-2-yl)-4-hydroperoxy-5-methylhex-5-en-3-ol (*anti*-147)



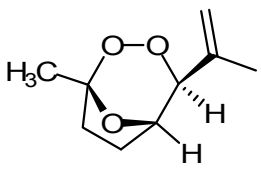
^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 1.69 (s, 3H, $C\underline{H}_3C$=), 3.68 (m, 1H, O<u>CH</u>), 3.83 (s, 4H, 2 x $OC\underline{H}_2$), 4.17 (d, 1H, *J* = 5.16 Hz, OOC<u>H</u>), 4.96 (m, 2H, $C\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, additional significant signals)

δ (ppm) = 64.6 (t, 2 x O$\underline{C}H_2$), 70.5 (d, O<u>C</u>H), 91.4 (d, OO<u>C</u>H), 111.9 (s, O<u>C</u>O), 115.0 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

(1RS,4RS,5RS)-1-Methyl-4-(prop-1-en-2-yl)-2,3,8-trioxa-bicyclo[3.2.1]octane (*exo*-148)
(elid 481h)



Following **GP-15**, a solution of 4-hydroperoxy-5-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-5-en-3-ol **(146)** (2.20 g, 9.48 mmol) in dichloromethane (100 ml) was treated with a catalytic

amount of $BF_3.Et_2O$ (0.2 ml) and then stirred at r.t. for 24 h. Usual work-up and further purification of the crude product by preparative thick-layer chromatography allowed the separation of the pure major 1,2,4-trioxane as yellow oil (SiO_2, EA/*n*-hex, 1:10, R_f = 0.39) beside a diastereomeric mixture of the pure *exo*- and *endo*-1,2,4-trioxanes in a ratio 77:23 (0.30 g, 1.76 mmol, 19 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.41 (s, 3H, C$\underline{H}_3$), 1.88 (t, 3H, *J* = 0.75 Hz, C$\underline{H}_3$C=), 1.81-1.90 (m, 1H, C$\underline{H}_2$), 2.02-2.23 (m, 2H, C$\underline{H}_2$), 2.45-2.55 (m, 1H, C$\underline{H}_2$), 3.94 (d, 1H, *J* = 0.57 Hz, OOC$\underline{H}$), 4.60 (d, 1H, *J* = 6.45 Hz, OC$\underline{H}$), 5.13 (q, 1H, *J* = 1.62 Hz, C$\underline{H}_2$=C), 5.26 (d, 1H, *J* = 0.75 Hz, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.4 (q, $\underline{C}H_3$), 20.9 (q, $\underline{C}H_3$), 28.9 (t, $\underline{C}H_2$), 33.7 (t, $\underline{C}H_2$), 75.0 (d, O$\underline{C}$H), 85.8 (d, OO$\underline{C}$H), 111.0 (s, OO$\underline{C}$O), 113.9 (t, $\underline{C}H_2$=C), 141.5 (s, $\underline{C}$=CH_2).

IR: (Film)

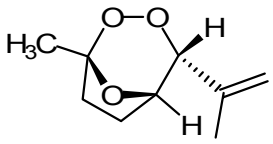
ν (cm^{-1}) = 3092, 2993, 2954, 1650, 1452, 1381, 1189, 1147, 1055, 900, 865.

Elemental Analysis: ($C_9H_{14}O_3$, M = 170.21)

Calcd: C 63.51 H 8.29

Found: C 63.17 H 8.29

(1RS,4SR,5RS)-1-Methyl-4-(prop-1-en-2-yl)-2,3,8-trioxa-bicyclo[3.2.1]octane (*endo*-148) elid (497o)



^{1}H-NMR: (300 MHz, $CDCl_3$)

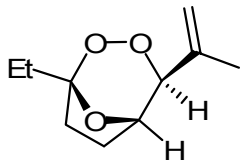
δ (ppm) = 1.34 (s, 3H, C$\underline{H}_3$), 1.61 (d, 3H, *J* = 0.57 Hz, C$\underline{H}_3$C=), 1.71-1.81 (m, 1H, C$\underline{H}_2$), 1.92-2.13 (m, 2H, C$\underline{H}_2$), 2.21-2.27 (m, 1H, C$\underline{H}_2$), 4.30 (d, 1H, *J* = 5.43 Hz, OC$\underline{H}$), 4.65 (br. s, 1H, OOC$\underline{H}$), 4.67 (d, 1H, *J* = 0.90 Hz, C$\underline{H}_2$=C), 4.84 (q, 1H, *J* = 1.47 Hz, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 19.7 (2 x q, 2 x $\underline{C}H_3$), 23.9 (t, $\underline{C}H_2$), 34.1 (t, $\underline{C}H_2$), 76.3 (d, O$\underline{C}$H), 84.4 (d, OO$\underline{C}$H), 110.0 (s, OO$\underline{C}$O), 112.4 (t, $\underline{C}H_2$=C), 138.8 (s, $\underline{C}$=CH_2).

(1RS,4RS,5RS)-1-Ethyl-4-(prop-1-en-2-yl)-2,3,8-trioxa-bicyclo[3.2.1]octane (*exo*-149)

(elid 487k)



Following **GP-15**, a solution of 1-(2-ethyl-1,3-dioxolan-2-yl)-4-hydroperoxy-5-methylhex-5-en-3-ol **(147)** (2.20 g, 8.94 mmol) in dichloromethane (100 ml) was treated with a catalytic amount of $BF_3.Et_2O$ (0.2 ml) and then stirred at r.t. for 24 h. Usual work-up and further purification of the crude product by preparative thick-layer chromatography (SiO_2, EA/*n*-hex, 1:10, R_f = 0.68) afforded a diastereomeric mixture of the pure *exo*- and *endo*-1,2,4-trioxanes in a ratio 77:23 (0.19 g, 1.03 mmol, 12 %).

^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 0.88 (t, 3H, *J* = 7.65, C<u>H</u>$_3$CH$_2$), 1.82 (d, 3H, *J* = 0.75 Hz, C<u>H</u>$_3$C=), 1.53-1.85 (m, 3H, C<u>H</u>$_2$CH$_3$ and CH$_2$), 1.99-2.08 (m, 2H, C<u>H</u>$_2$), 2.30-2.40 (m, 1H, C<u>H</u>$_2$), 3.89 (s, 1H, OOC<u>H</u>), 4.54 (m, 1H, OC<u>H</u>), 5.05 (q, 1H, *J* = 1.47 Hz, C<u>H</u>$_2$=C), 5.19 (d, 1H, *J* = 0.72 Hz, C<u>H</u>$_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.5 (q, <u>C</u>H$_3$CH$_2$), 20.3 (q, <u>C</u>H$_3$C=), 27.6 (t, <u>C</u>H$_2$), 28.3 (t, <u>C</u>H$_2$), 31.2 (t, <u>C</u>H$_2$), 74.8 (d, O<u>C</u>H), 85.8 (d, OO<u>C</u>H), 113.1 (s, OO<u>C</u>O), 113.6 (t, <u>C</u>H$_2$=C), 141.5 (s, <u>C</u>=CH$_2$).

IR: (Film)

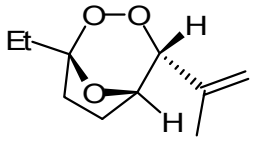
ν (cm^{-1}) = 3094, 2975, 2946, 2883, 1651, 1456, 1178, 1097, 1061, 961, 904.

Elemental Analysis: ($C_{10}H_{16}O_3$, M = 184.23)

Calcd: C 65.19 H 8.75

Found: C 65.13 H 8.58

(1RS,4SR,5RS)-1-Ethyl-4-(prop-1-en-2-yl)-2,3,8-trioxa-bicyclo[3.2.1]octane (*endo*-149)



^{1}H-NMR: (300 MHz, $CDCl_3$)

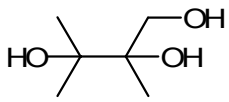
δ (ppm) = 0.91 (t, 3H, *J* = 7.50, $C\underline{H_3}CH_2$), 1.64 (s, 3H, $C\underline{H_3}C$=), 1.53-1.85 (m, 3H, $C\underline{H_2}CH_3$ and CH_2), 1.99-2.08 (m, 2H, $C\underline{H_2}$), 2.18-2.28 (m, 1H, CH_2), 4.35 (d, 1H, *J* = 6.03 Hz, OC<u>H</u>), 4.70 (br. s, 2H, OOC<u>H</u> and $C\underline{H_2}$=C), 4.87 (d, 1H, *J* = 1.32 Hz, $C\underline{H_2}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 7.7 (q, $\underline{C}H_3CH_2$), 19.9 (q, $\underline{C}H_3C$=), 23.6 (t, $\underline{C}H_2$), 27.0 (t, $\underline{C}H_2$), 32.1 (t, $\underline{C}H_2$), 76.3 (d, O<u>C</u>H), 84.8 (d, OO<u>C</u>H), 112.4 (s, OO<u>C</u>O), 112.5 (t, $\underline{C}H_2$=C), 139.0 (s, $\underline{C}$=CH_2).

4.10 Hydroperoxides as Oxygen Donor in Dihydroxylation Reaction

2,3-Dimethylbutane-1,2,3-triol[196] (150)



(a) According to **(GP-18):** (elid 475g)

Using 3-hydroperoxy-2,3-dimethylbut-1-ene **24** (140 mg, 1.2 mmol), water (1 mL), methanol (1 mL) and OsO_4 solution (1 mol %), affords the triol (60 mg, 0.45 mmol, 37%) as yellow oil.

(b) According to **(GP-19):** (elid 500f)

Using 3-hydroperoxy-2,3-dimethylbut-1-ene **24** (140 mg, 1.2 mmol), water (1 mL), methanol (1 mL) and WO_3 (10 mol %), affords the triol (50 mg, 0.37 mmol, 31%) as yellow oil.

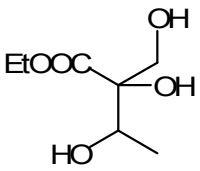
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.04 (s, 3H, C$\underline{H}_3$), 1.20 (s, 3H, C$\underline{H}_3$), 1.23 (s, 3H, C$\underline{H}_3$), 3.45 (d, 1H, *J* = 11.30 Hz, C$\underline{H}_2$OH), 3.86 (d, 1H, *J* = 11.61 Hz, C$\underline{H}_2$OH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 20.1 (q, $\underline{C}H_3$), 24.6 (q, $\underline{C}H_3$), 25.2 (q, $\underline{C}H_3$), 68.3 (t, $\underline{C}H_2$OH), 75.3 (s, Cq-OH), 76.1 (s, Cq-OH).

Ethyl-2,3-dihydroxy-2-(hydroxymethyl)butanoate (151)



(a) According to **(GP-17):** (elid 502d)

Using ethyl 3-hydroperoxy-2-methylenebutanoate **16** (0.10 g, 0.62 mmol), N-methyl-morpholine-N oxide (0.145 g, 1.24 mmol), water (1 mL), *tert*-butanol (1 mL) and OsO_4 solution (0.03 mmol, 4.8 mol %), affords a diastereomeric mixture (d.r. 85:15) of the triol (77 mg, 0.43 mmol, 70 %) as yellow oil.

(b) According to **(GP-18):** (elid 475o)

Using ethyl 3-hydroperoxy-2-methylenebutanoate **16** (0.19 g, 1.2 mmol), water (1 mL), methanol (1 mL) and OsO_4 solution (0.06 mmol, 5 mol %), affords a diastereomeric mixture (d.r. 79:21 as calculated from ^{13}C-NMR) of the triol (40 mg, 0.22 mmol, 19 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 1.17 (d, 3H, *J* = 6.57 Hz, C$\underline{H_3}$CH), 1.29 (t, 3H, *J* = 7.14 Hz, C$\underline{H_3}$CH$_2$), 3.65 (d, 1H, *J* = 11.55 Hz, C$\underline{H_2}$OH), 3.78 (d, 1H, *J* = 11.4 Hz, C$\underline{H_2}$OH), 3.95 (q, 1H, *J* = 6.42 Hz, C$\underline{H}$CH$_3$), 4.28 (q, 2H, *J* = 7.17 Hz, C$\underline{H_2}$CH$_3$).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, major diastereomer)

δ (ppm) = 14.1 (q, $\underline{C}H_3CH_2$), 17.5 (q, $\underline{C}H_3CH$), 62.6 (t, $\underline{C}H_2CH_3$), 64.8 (t, $\underline{C}H_2OH$), 69.4 (d, $\underline{C}HOH$), 81.5 (s, Cq-OH), 174.0 (s, $\underline{C}OO$)

^{1}H-NMR: (300 MHz, $CDCl_3$, additional significant signals of minor diastereomer)

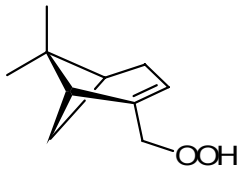
δ (ppm) = 1.11 (d, 3H, *J* = 6.42 Hz, C$\underline{H_3}$CH), 1.28 (t, 3H, *J* = 7.14 Hz, C$\underline{H_3}$CH$_2$), 3.86 (d, 1H, *J* = 5.25 Hz, C$\underline{H_2}$OH).

^{13}C-NMR: (75.5 MHz, $CDCl_3$, minor diastereomer)

δ (ppm) = 13.9 (q, $\underline{C}H_3CH_2$), 17.4 (q, $\underline{C}H_3CH$), 62.5 (t, $\underline{C}H_2CH_3$), 65.8 (t, $\underline{C}H_2OH$), 69.4 (d, $\underline{C}HOH$), 81.0 (s, $\underline{Cq}$-OH), 173.3 (s, $\underline{C}OO$).

(1R)-2-(hydroperoxymethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ene (152)

(elid 462b)



Photooxygenation of β-pinene (1.0 g, 7.35 mmol) for 38 h according to **GP-9a** afforded the allylic hydroperoxides (0.73 g, 4.35 mmol, 59 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

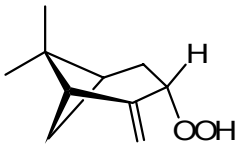
δ (ppm) = 0.79 (s, 3H, C$\underline{H_3}$), 1.24 (s, 3H, C$\underline{H_3}$), 1.95-2.50 (m, 6H, 2 x C$\underline{H_2}$ and 2 x C$\underline{H}$), 3.41 (d, 2H, *J* = 1.02 HZ, C$\underline{H_2}$-OOH), 4.30 (m, 1H, C$\underline{H}$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 21.0 (q, $\underline{C}H_3$), 26.0 (q, $\underline{C}H_3$), 31.3 (t, $\underline{C}H_2$), 31.5 (t, $\underline{C}H_2$), 37.9 (s, $\underline{C}q$), 40.6 (d, $\underline{C}H$), 43.6 (d, $\underline{C}H$), 80.1 (t, $\underline{C}H_2$-OOH), 123.6 (d, $\underline{C}H$=C), 143.3 (s, $\underline{C}$=CH).

(1R)-3-hydroperoxy-6,6-dimethyl-2-methylenebicyclo[3.1.1]heptane[197] **(153)**

(elid 451n, 462a)



Photooxygenation of α-pinene (1.0 g, 7.35 mmol) for 38 h according to **GP-9a** afforded the allylic hydroperoxides (0.62 g, 3.69 mmol, 50 %) as yellow oil.

^{1}H-NMR: (300 MHz, $CDCl_3$)

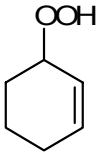
δ (ppm) = 0.65 (s, 3H, C$\underline{H}_3$), 1.24 (s, 3H, C$\underline{H}_3$), 1.48 (d, 1H, *J* = 9.99 Hz, C$\underline{H}$), 1.87-1.95 (m, 2H, C$\underline{H}_2$), 2.14-2.35 (m, 2H, C$\underline{H}_2$), 2.46 (t, 1H, *J* = 5.37 Hz, C$\underline{H}$), 4.59 (d, 1H, *J* = 7.92 HZ, C$\underline{H}$-OOH), 4.96 (m, 1H, C$\underline{H}_2$=C), 5.10 (m, 1H, C$\underline{H}_2$=C).

^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 21.9 (q, $\underline{C}H_3$), 25.9 (q, $\underline{C}H_3$), 27.5 (t, $\underline{C}H_2$), 30.6 (t, $\underline{C}H_2$), 39.3 (s, $\underline{C}$q), 41.1 (d, $\underline{C}$H), 50.4 (d, $\underline{C}$H), 80.6 (d, $\underline{C}$H-OOH), 115.1 (t, $\underline{C}H_2$=C), 148.4 (s, $\underline{C}$=CH_2).

3-Hydroperoxycyclohex-1-ene[198] **(154)**

(elid 476e)



Irradiation of cyclohexene (2.0 g, 24.4 mmol) according to the **GP-7b** for 48 h affords the crude product as an oil (2.61 g, 22.9 mmol, 94 %) which was used without further purification.

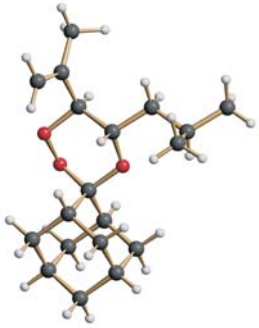
^{1}H-NMR: (300 MHz, $CDCl_3$)

δ (ppm) = 1.47-2.06 (m, 6H, 3 x C$\underline{H}_2$), 4.43 (m, 1H, C$\underline{H}$-OOH), 5.68-5.72 (m, 1H, C$\underline{H}$=CH), 5.92-5.98 (m, 1H, C$\underline{H}$=CH).

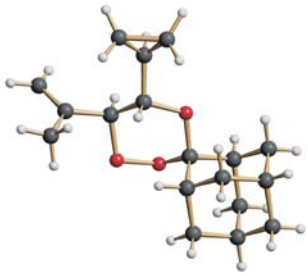
^{13}C-NMR: (75.5 MHz, $CDCl_3$)

δ (ppm) = 18.2 (t, $\underline{C}H_2$), 25.2 (t, $\underline{C}H_2$), 26.2 (t, $\underline{C}H_2$), 78.3 (d, $\underline{C}$H-OOH), 124.0 (d, $\underline{C}$H=CH), 134.2 (d, $\underline{C}$H=CH).

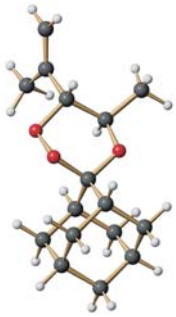
5. Appendix



58



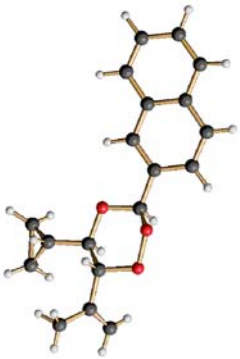
38



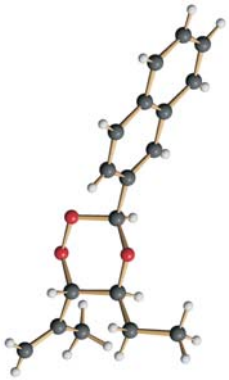
98

Crystal data	**58**	**38**	**98**
Empirical formula	$C_{19}H_{30}O_3$	$C_{18}H_{26}O_3$	$C_{16}H_{24}O_3$
Formula weight	306.43	290.39	264.35
Temperature [°K]	293(2)	100(2)	100(2)
Crystal system	monoclinic	monoclinic	monoclinic
Space group	Pc	P21/n	P21/cx
a [Å]	10.682(1)	7.403(1)	10.776(1)
b [Å]	8.716(1)	10.416(1)	10.691(1)
c [Å]	10.611(1)	20.310(1)	12.315(1)
α [°]	90	90	90
β [°]	117.34(1)	94.18	93.42(1)
γ [°]	90	90	90
Volume [$Å^3$]	877.57(15)	1561.9(3)	1416.2(2)
Z	2	4	4
d_{calcd} [g cm^{-3}]	1.160	1.235	1.240
Crystal size [mm]	0.30 x 0.15 x 0.15	0.30 x 0.30 x 0.08	0.25 x 0.20 x 0.20
No. Refl. collected	7019	9191	6037
No. unique Refl.	3717	3393	3083
No. obs. Refl.[a]	3318	1676	1610
R1[a]	0.0312	0.1796	0.0554
wR2[a]	0.0751	0.4146	0.0999
Largest diff. peak / hole[e/$Å^{-3}$]	0.150 / -0.115	0.732 / -0.472	0.239 / -0.222

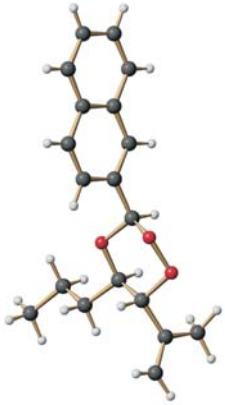
[a] For [I>2sigma(I)]



43



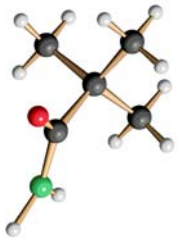
89



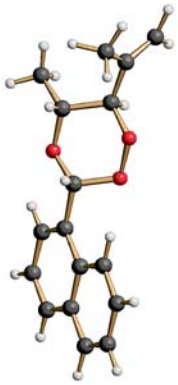
76

Crystal data	**43**	**89**	**76**
Empirical formula	$C_{19}H_{20}O_3$	$C_{18}H_{20}O_3$	$C_{19}H_{22}O_3$
Formula weight	296.35	284.34	298.37
Temperature [°K]	293(2)	100(2)	100(2)
Crystal system	monoclinic	monoclinic	monoclinic
Space group	P21/c	P21/c	C2/c
a [Å]	12.8550(6)	13.614(2)	34.338(1)
b [Å]	14.8204(5)	5.6245(5)	5.362(1)
c [Å]	8.3185(3)	19.903(3)	20.740(1)
α [°]	90	90	90
β [°]	94.9510(10)	97.456(4)	121.32(1)
γ [°]	90	90	90
Volume [$Å^3$]	1578.90(11)	1511.1(4)	3262.2(6)
Z	4	4	8
d_{calcd} [g cm^{-3}]	1.247	1.250	1.215
Crystal size [mm]	0.1 x 0.1 x 0.3	0.1 x 0.1 x 0.3	0.35 x 0.25 x 0.25
No. Refl. collected	9705	6492	10220
No. unique Refl.	3443	3146	3554
No. obs. Refl.[a]	1851	1251	2305
R1[a]	0.0507	0.0663	0.0427
wR2[a]	0.1112	0.1452	0.0900
Largest diff. peak / hole[e/$Å^{-3}$]	0.174 / -0.170	0.428 / -0.215	0.232 / -0.166

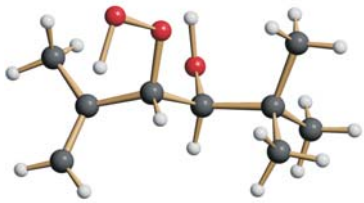
[a] For [I>2sigma(I)]



Pivaloyl amide



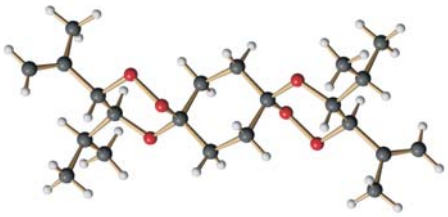
109



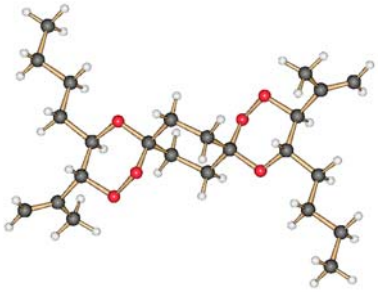
syn-**7j**

Crystal data	**Pivaloyl amide**	**109**	*syn*-**7j**
Empirical formula	$C_{20}H_{44}N_4O_4$	$C_{17}H_{18}O_3$	$C_9H_{18}O_3$
Formula weight	404.59	270.31	174.23
Temperature [°K]	293(2)	100(2)	293(2)
Crystal system	monoclinic	monoclinic	monoclinic
Space group	P21/c	P21/a	P21
a [Å]	10.37(3)	7.1270(5)	9.794(1)
b [Å]	5.861(2)	16.2208(8)	5.958(1)
c [Å]	10.300(9)	12.5650(8)	17.649(3)
α [°]	90	90	90
β [°]	102.393(10)	95.490(3)	94.05(1)
γ [°]	90	90	90
Volume [$Å^3$]	611.4(19)	1445.92(15)	1027.3(3)
Z	1	4	4
d_{calcd} [g cm^{-3}]	1.099	1.242	1.127
Crystal size [mm]	0.2 x 0.6 x 0.03	0.3 x 0.3 x 0.5	0.25 x 0.15 x 0.10
No. Refl. collected	1185	5394	1984
No. unique Refl.	588	3060	1984
No. obs. Refl.[a]	300	1682	1172
R1[a]	0.0554	0.0595	0.2529[b]
wR2[a]	0.1176	0.1261	0.5467[b]
Largest diff. peak / hole[e/$Å^{-3}$]	0.134 / -0.142	0.199 / -0.289	1.094 / -0.936[b]

[a] For [I>2sigma(I)]. [b] Mixture of overlapping enantiomers.



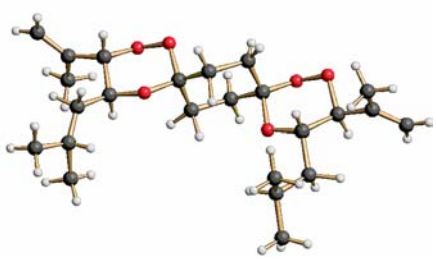
anti-**133**



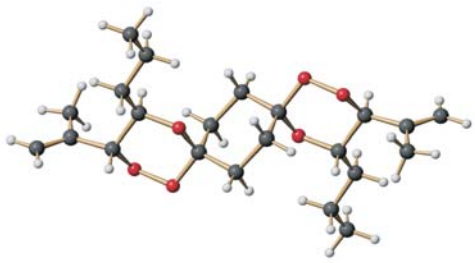
anti-**132**

Crystal data	*anti*-**133**	*anti*-**132**
Empirical formula	$C_{22}H_{36}O_6$	$C_{24}H_{40}O_6$
Formula weight	396.51	424.56
Temperature [°K]	293(2)	100(2)
Crystal system	monoclinic	monoclinic
Space group	P21/c	P21/c
a [Å]	6.467(1)	8.199(2)
b [Å]	12.813(1)	5.3910(10)
c [Å]	13.255(1)	27.400(8)
α [°]	90	90
β [°]	93.38(1)	92.860(10)
γ [°]	90	90
Volume [$Å^3$]	1096.4(2)	1209.6(5)
Z	2	2
d_{calcd} [g cm^{-3}]	1.201	1.166
Crystal size [mm]	0.25 x 0.15 x 0.15	0.06 x 0.2 x 0.2
No. Refl. collected	6664	3553
No. unique Refl.	2398	1986
No. obs. Refl.[a]	1181	1136
R1[a]	0.1635	0.0495
wR2[a]	0.4692	0.0826
Largest diff. peak / hole[e/$Å^{-3}$]	1.073 / -0.404	0.146 / -0.208

[a] For [I>2sigma(I)]



syn-**136**



anti-**134**

Crystal data	*syn*-**136**	*anti*-**134**
Empirical formula	$C_{24}H_{40}O_6$	$C_{22}H_{36}O_6$
Formula weight	424.56	396.51
Temperature [°K]	100(2)	100(2)
Crystal system	monoclinic	orthorhombic
Space group	P21/c	Pbcn
a [Å]	12.200(3)	23.634(1)
b [Å]	14.896(6)	8.201(1)
c [Å]	14.866(5)	11.220(1)
α [°]	90	90
β [°]	116.92(2)	90
γ [°]	90	90
Volume [$Å^3$]	2408.9(14)	2174.7(3)
Z	4	4
d_{calcd} [g cm^{-3}]	1.171	1.211
Crystal size [mm]	0.1 x 0.1 x 0.5	0.20 x 0.08 x 0.08
No. Refl. collected	9309	3951
No. unique Refl.	4095	1441
No. obs. Refl.[a]	1340	321
R1[a]	0.1433	0.0773
wR2[a]	0.3536	0.0682
Largest diff. peak / hole[e/$Å^{-3}$]	0.471 / -0.388	0.208 / -0.214

[a] For [I>2sigma(I)]

6. Summary

In this thesis, a new solvent-free protocol for type-II photooxygenation reactions was developed. I aimed in this protocol to combine the use of a microreactor as reaction medium, visible light and air as reagents. This offers a new and convenient approach towards "green" photooxygenation conditions. Two microreactor systems were used: (1) The commercially available polystyrene beads (PS) crosslinked with divinyl benzene (DVB) and loaded with adsorbed tetraarylporphyrine dye sensitizers; (2) Synthesized polymers covalently bound to porphyrin sensitizers. In the latter approach two singlet oxygen sensitizers with crosslinking properties were used. tetrakis(4-ethenylphenyl)porphyrin (or tetrastyrylporphyrin, TSP) and the natural protoporphyrin-IX (PP). Emulsifier-free emulsion polymerization was applied for copolymerization reaction of both TSP and PP with styrene (S) and DVB resulting in polymer particles that are translucent in color, polyhedral in shape having size range from 200 to 500 nm for TSP-S-DVB and faint rose in color, spherical in shape having size range from 200 to 400 nm for PP-S-DVB (***Figure* 6.1**). The synthesized nanoparticles are characterized by high surface area accounting for their high substrate loading capacity (up to 100 % by wt for both catalysts).

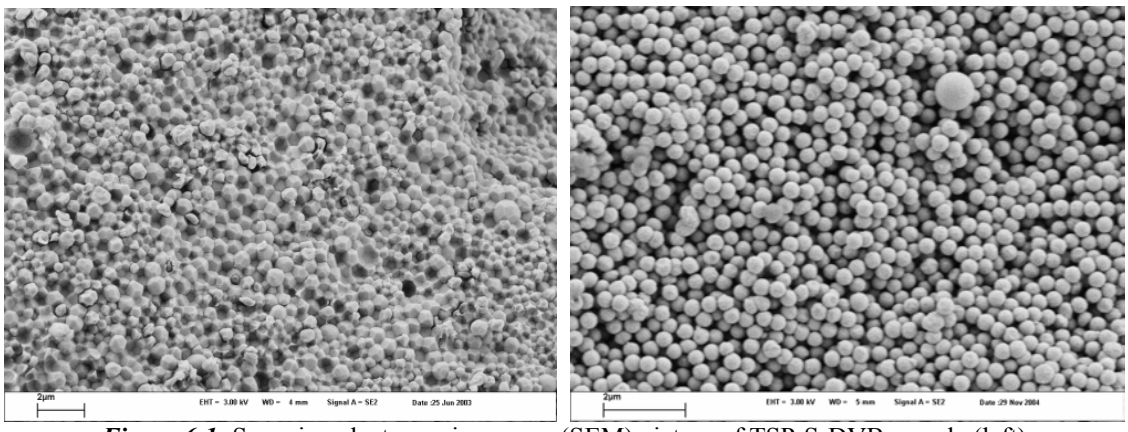
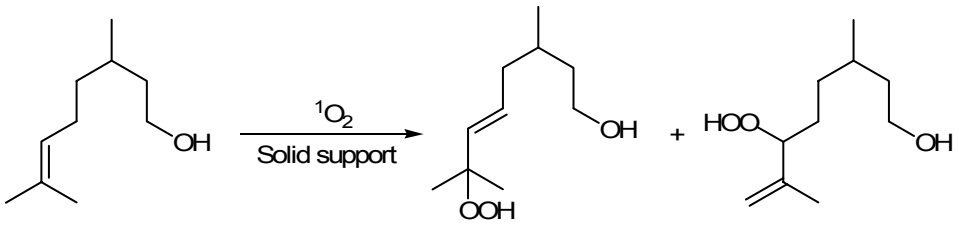


Figure 6.1*:* Scanning electron microscope (SEM) picture of TSP-S-DVB sample (left) and PP-S-DVB sample (right).

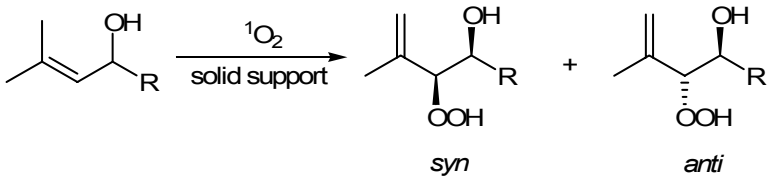
In the developed approach, the photooxygenation reactions are carried out under atmospheric air and the polymeric systems can be recycled and reused several times with negligible decrease in efficiency or dye bleeding yielding sensitizer-free products. Evaluation of the efficiency of the solvent-free approach and identification of its influence on the chemo-, regio- and stereoselectivity pattern in type-II photooxygenation reaction was also investigated by means of oxidation of different substrates that react by different reaction modes. The

photooxygenation of citronellol (the industrial precursor of the fragrant chemical speciality *rose oxide*) was used to study the regioselectivity of the ene reaction of $^1O_2$ (***Scheme 6.1***).

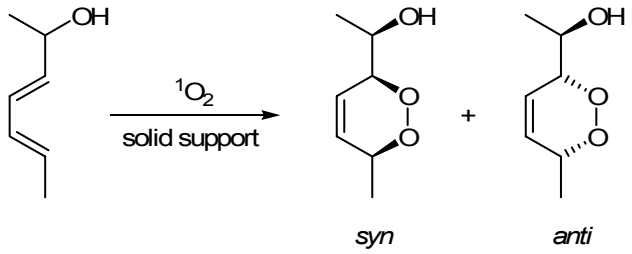


Scheme 6.1

The photooxygenation of different chiral allylic alcohols and the chiral dienol, respectively, where used to investigate the diastereoselectivity of the ene and [4+2]-cycloaddition reactions of $^1O_2$ in the new environments (***Scheme 6.2*** and ***6.3***). The products were obtained in good yields and sensitizer-free (without dye-bleeding).



Scheme 6.2



Scheme 6.3

The solvent-free photooxygenation reaction of a large variety of allylic alcohols resulted in the corresponding 1,2-hydroperoxy alcohols. A literature-novel X-ray structure was obtained as an unambiguous proof of the diastereoselectivity of the ene reaction with allylic alcohols (***Figure 6.2***).

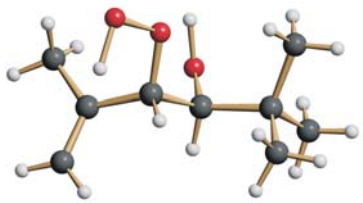
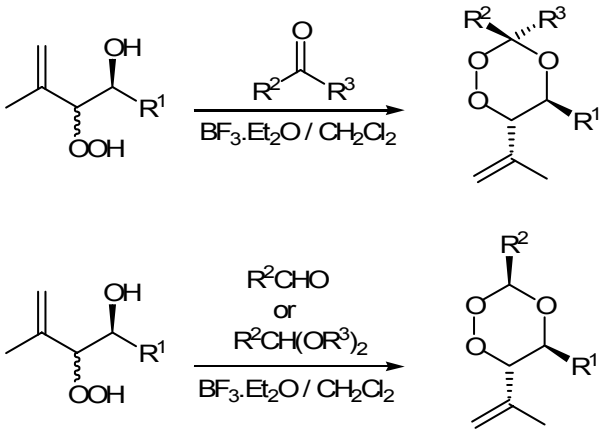


Figure 6.2

The new sensitizer/polymer systems were also used in heterogeneous photooxygenation reactions and compared to the homogeneous conditions. 2,3-Dimethyl-2-butene was applied as model substrate and the kinetics of the oxygen uptake were measured under pseudo-first order reaction conditions in CCl_4 using TPP for the homogeneous reaction and a suspension of TSP-S-DVB or PP-S-DVB in the same solvent for the heterogeneous conditions. From the linear oxygen uptake it was concluded that pseudo-first order conditions exist for longer time without bleaching of the polymer-bound dyestuff. It was also found that the efficiency of TSP-S-DVB is nearly identical and for PP-S-DVB only slightly lower compared to the homogeneous conditions.

I also developed a two-step synthetic route to the 1,2,4-trioxane subunit, the pharmacophore of the naturally occurring antimalarial drug artemisinin. The methodology is based firstly on the conversion of different allylic alcohols to sensitizer-free *vic*-hydroxy allylic hydroperoxides by the reaction of singlet oxygen with allylic alcohols followed by BF_3-catalyzed peroxyacetalization reaction with different carbonyl compounds. (***Scheme 6.4***). Variation of substituents at C-3 and C-5 of the trioxane pharmacophore could be efficiently performed with the formation of wide variety of mono-, polycyclic- and spiro-1,2,4-trioxanes.



Scheme 6.4

The antimalarial activity of a series of the new compounds was also tested *in vitro*. The spiroadamantane-1,2,4-trioxanes with the highest lipophilic properties are the most promising candidates having the best antimalarial activities against the *Plasmodium falciparum* strain. Some of these compounds could be obtained in crystalline form (***Figure 6.3***).

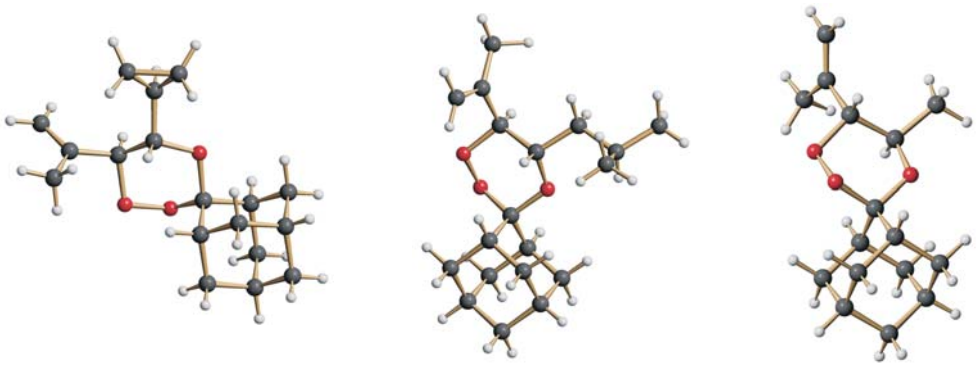


Figure 6.3

In order to insert a naphthyl group into the 1,2,4-trioxane system, several 3-napthyl substituted compounds were synthesized, some of which were also characterized by X-ray analysis (***Figure 6.4***).

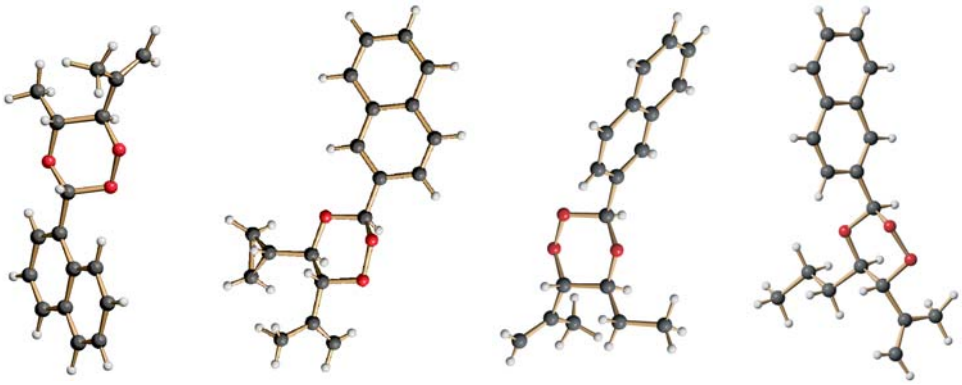
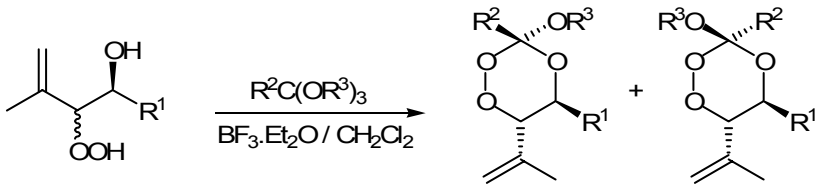


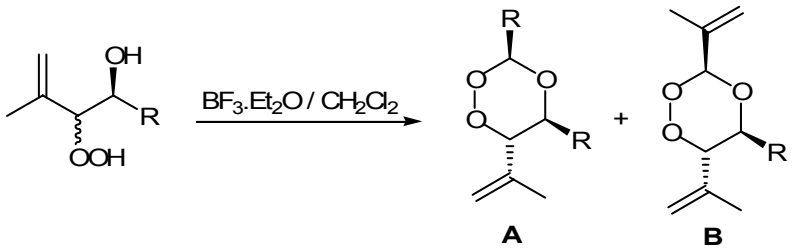
Figure 6.4

The use of orthoesters in the peroxyacetalization reaction enabled a direct route to the synthesis of the first perortho esters with 1,2,4-trioxane substructure described in literature (***Scheme 6.5***).



Scheme 6.5

In absence of external carbonyl compounds, another direct conversion of 1,2-hydroperoxy alcohols to the trioxanes **A** and **B** was also achieved. The reaction proceeds through slow BF_3 catalyzed cleavage of the β-hydroperoxy alcohols to carbonyl fragments that subsequently undergo peroxyacetalization reaction with the excess hydroxy hydroperoxide to furnish the trioxanes (***Scheme 6.6***).



Scheme 6.6

I developed also another concept for integration of two trioxane subunits in the same molecule. Bis spiro-1,2,4-trioxanes are a literature-unknown class of compounds that were synthesized and characterized (***Figure 6.5***). The idea is based on coupling of two 1,2-hydroperoxy alcohols with a central dicarbonyl component (such as cyclohexan-1,4-dione).

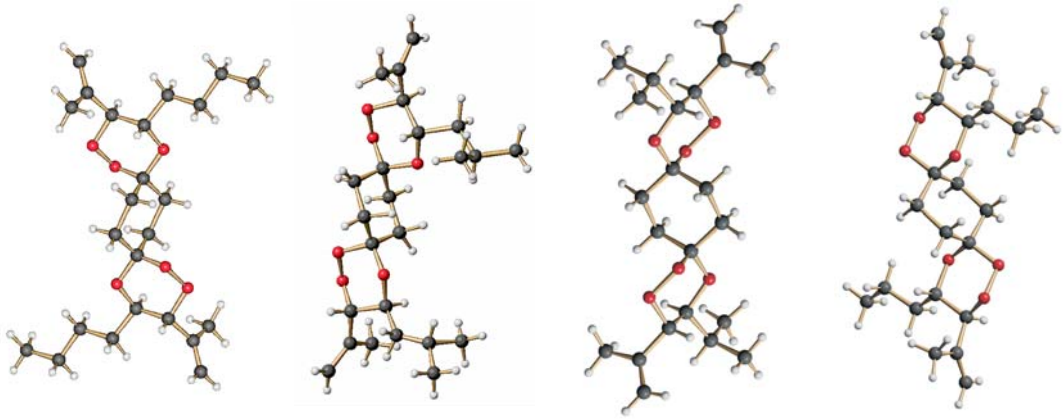
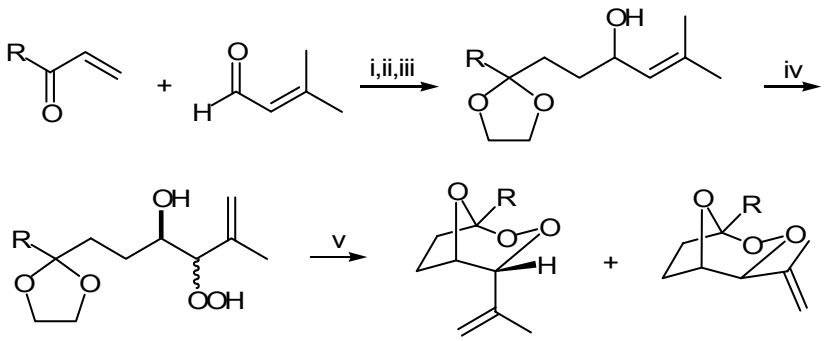


Figure 6.5

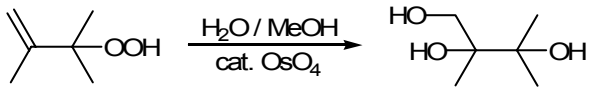
A concise synthetic route to 2,3,8-trioxabicyclo[3.2.1]octanes as ring-contracted analogues to the natural antimalarial artemisinine-pharmacophore was also developed. The synthesized bicyclic 1,2,4-trioxane systems were synthesized by a literature-unknown intramolecular peroxyacetalization reaction (***Scheme 6.7***).



i: thiazolium salt, AcONa, EtOH, 80 °C; ii: ethylene glycol, PPTS; iii: LAH, Et_2O;
iv: $^1O_2$, polymer support; v: BF_3xEt_2O, CH_2Cl_2

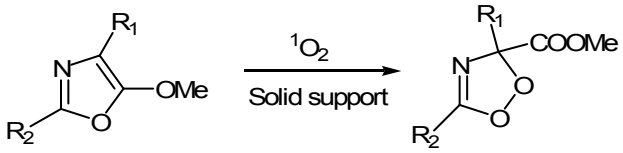
Scheme 6.7

Another synthetic application of allylic hydroperoxides was investigated: their conversion to the corresponding triols in a dihydroxylation reaction using catalytic amounts of OsO_4 or WO_3. Unlike the usual catalyzed bishydroxylation reactions, in our case **no cooxidant was used** and the substrate itself plays role as oxygen donor that reoxidizes the reduced oxidant and simultaneously as oxygen acceptor in a reaction cycle leading to conversion of the allylic hydroperoxide to the corresponding triol product. The effect of the oxidant concentration was also studied showing that an OsO_4 concentration up to 0.001 equivalent is still effective in catalyzing the reaction (***Scheme 6.8***).



Scheme 6.8

The [4+2]-cycloaddition reactions of $^1O_2$ to a series of 5-methoxyoxazoles as substrates under the solvent-free conditions was also studied. 1,2,4-Dioxazoles were found as the reaction products which decompose slowly to give the corresponding amide and dicarbonyl fragments (***Scheme 6.9***).



Scheme 6.9

7. Zusammenfassung

Im Rahmen dieser Arbeit wurde eine neue lösungsmittelfreie Methode für Typ-II Photooxygenierungsreaktionen entwickelt. Mit dieser Methode habe ich das Ziel verfolgt, die Vorteile der Verwendung von Mikroreaktoren als Reaktionsmedium, sichtbares Licht und Luft als Reagenzien zu kombinieren. Diese Methode stellt eine brauchbare Annäherung an „green chemistry“ Photooxygenierungs-Bedingungen dar. Es wurden zwei verschiedene Mikroreaktor-Systeme verwendet: (1) kommerziell erhältliche, mit Divinylbenzol (DVB) quervernetzte Polystyrolkügelchen (PS), die mit Tetraarylporphyrin als Sensibilisator-Farbstoffe beladen wurden, (2) synthetisierte Polymere mit kovalent gebundenen Porphyrin-Sensibilisatoren. Im letztgenannten Fall wurden zwei verschiedene quervernetzbare Sensibilisatoren verwendet: Tetrakis(4-ethenylphenyl)porphyrin (oder Tetrastyrylporphyrin, TSP) und Protoporphyrin-IX (PP). Für beide Sensibilisatoren TSP und PP wurde eine Emulgator-freie Emulsions-Polymerisation zur Copolymerisierung der genannten Farbstoffe mit Styrol (S) und Divinylbenzol verwendet. Daraus resultieren Polymerteilchen mit licht-durchlässigen Eigenschaften und polygonaler Gestalt, deren Grösse im Bereich von 200-500 nm für TSP-S-DVB lag. Im Falle von PP-S-DVB wurden schwach rosa gefärbte Polymerkügelchen mit einer Grösse von 200-400 nm erhalten (***Abb. 7.1***). Die synthetisierten Nanopartikel zeichnen sich durch eine große Oberfläche und eine entsprechende Kapazität hinsichtlich der Beladung mit Substraten aus (bis 100 % der Polymerträger-Einwaage).

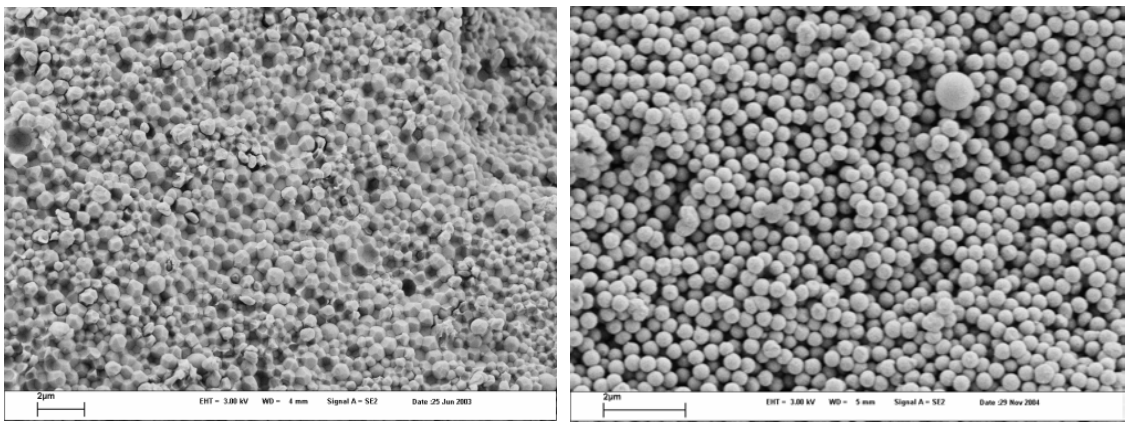
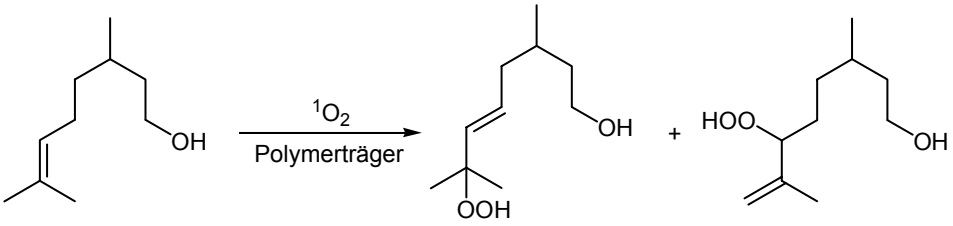


***Abb. 7.1*:** Scanning electron microscope (SEM)-Bild einer TSP-S-DVB Probe (links) und einer PP-S-DVB Probe (rechts).

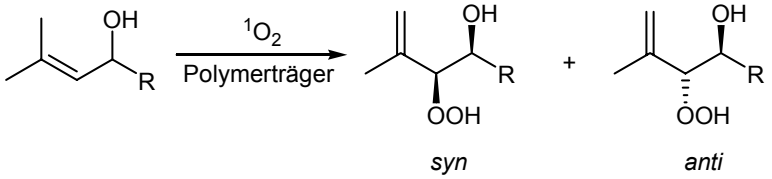
Bei dem entwickelten Verfahren wurden die Photooxygenierungen mit Hilfe von Luft-Sauerstoff in den polymeren Trägersystemen durchgeführt. Die Polymer-Träger mit kovalent

gebundenem Sensibilisator können ohne nennenswerte Abnahme ihrer Effizienz oder Ausblutung des Farbstoffes mehrmals wiederverwendet werden. Zur Bewertung der Effizienz der lösungsmittelfreien Methode und zur Untersuchung des Einflusses auf die Chemo-, Regio- und Stereoselektivität der Typ-II-Reaktion wurde die Oxidation einer Reihe von Substraten unter verschiedenen Bedingungen untersucht. Die Photooxygenierung von Citronellol (industrielle Vorstufe bei der Synthese des Duftstoffes Rosenoxid) diente als Modell, um die Regioselektivität der En- Reaktion von $^1O_2$ zu untersuchen (***Schema 7.1***).

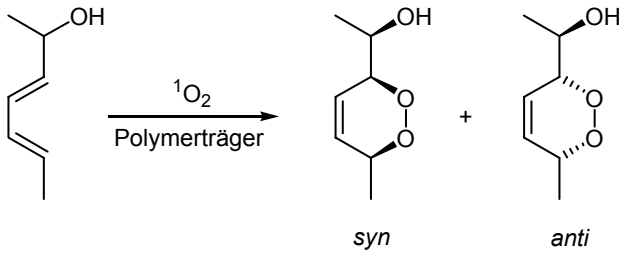


Schema 7.1

Die Photooxygenierungs-Reaktionen von verschiedenen chiralen Allylalkoholen und dem chiralen Dienol wurden jeweils als Modell verwendet, um die Diastereoselektivität der En- und [4+2]-Cycloaddition unter verschiedenen Bedingungen zu untersuchen (***Schema 7.2*** und ***7.3***). Die Produkte wurden in guten Ausbeuten und ohne Farbstoffrückstände erhalten.



Schema 7.2



Schema 7.3

Die lösungsmittelfreie Photooxygenierung einer großen Anzahl von allylischen Alkoholen führte zu den entprechenden 1,2-Hydroperoxy-Alkoholen. Die erhaltene Röntgenstruktur einer noch Literatur-unbekannten Verbindung kann als ein zweifelsfreier Beweis für die

Diastereoselektivität der En-Reaktion von allylischen Alkoholen aufgefasst werden (***Abb. 7.2***).

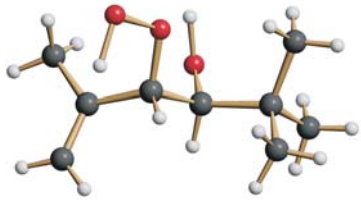
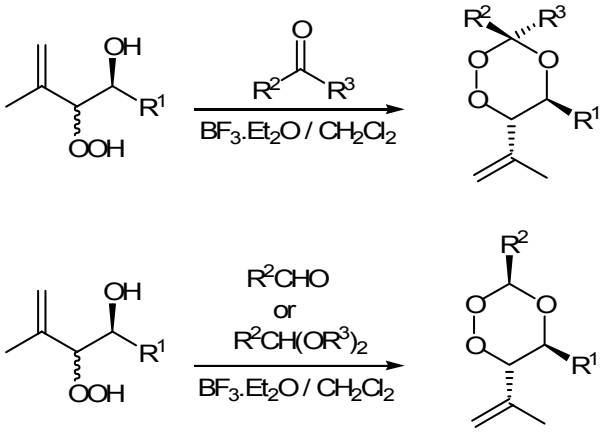


Abb. 7.2

Die neuen polymeren Sensibilisator-Systeme wurden auch auf heterogene Photooxygenierungsreaktionen angewendet und die Ergebnisse mit denen der homogenen Reaktion verglichen. Hierbei diente 2,3-Dimethyl-2-buten als Modelsubstrat. Die Kinetik der Sauerstoff-Aufnahme wurde unter Reaktionsbedingungen pseudo-erster Ordnung in CCl_4 und unter Verwendung von TPP für die homogene Reaktion bzw. einer Suspension von TSP-S-DVB oder PP-S-DVB im gleichen Lösungsmittel gemessen. Aus der linearen Sauerstoffaufnahme konnte geschlossen werden, dass die Bedingungen pseudo-erster Ordnung über einen längeren Zeitraum gelten, ohne dass der Farbstoff ausbleicht. Für TSP-S-DVB wurde eine nahezu gleiche Effizienz und für PP-S-DVB eine geringfügig kleinere Effizienz verglichen mit den homogenen Reaktionsbedingungen gefunden.

Des weiteren habe ich eine zweistufige Syntheseroute zur Darstellung des 1,2,4-Trioxan-Grundgerüstes entwickelt, welches als pharmakophore Grundstruktur im natürlich vorkommenden Antimalaria Mittel Artemisinin enthalten ist. Die Methode gründet sich auf die Umwandlung von verschiedenen Allylalkoholen zu (farbstofffreien) *vic*-Hydroperoxyallylhydroperoxiden durch die Reaktion von Singulettsauerstoff mit Allylalkoholen und anschließender BF_3-katalysierter Peroxoacetalysierung mit verschiedenen Carbonyl-Verbindungen (***Schema 7.4***). Durch die Variation der Substituenten an C-3 und C-5 des Trioxan-Grundgerüstes ist ein weites Spektrum von mono-, polycyclischen- und spiro-1,2,4-Trioxanen zugänglich.



Schema 7.4

Die Antimalariaaktivität einer Reihe von neuen Verbindungen wurde *in-vitro* getestet. Die Spiroadamantan-1,2,4-trioxane mit den am stärksten ausgeprägten lipophilen Eigenschaften sind vielversprechende Kandidaten bezüglich der Antimalariaaktivität gegenüber dem *Plasmodium falciparum*-Parasiten. Einige dieser Verbindungen konnten in kristalliner Form erhalten werden (***Abb. 7.3***).

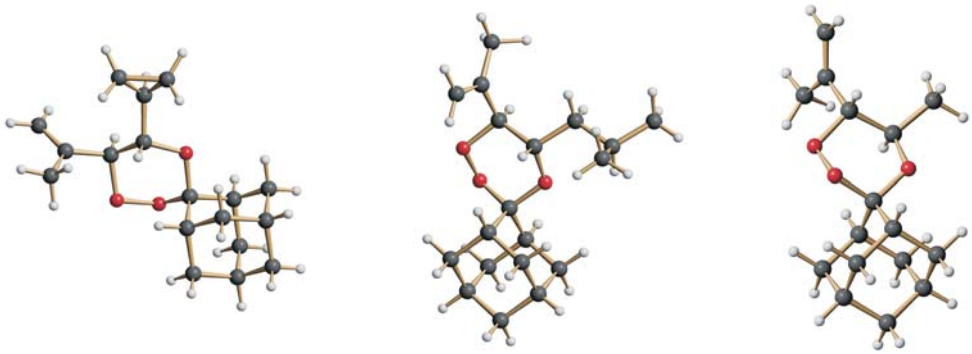
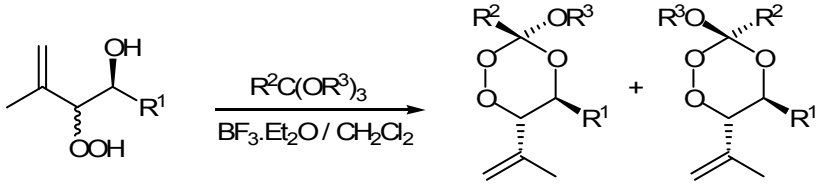


Abb. 7.3

Um eine Naphthyl-Gruppe in die 1,2,4-Trioxane einzuführen, wurden eine Reihe von 3-naphthylsubstituierten Verbindungen dargestellt. Einige hiervon konnten röntgenographisch charakterisiert werden (***Abb. 7.4***).

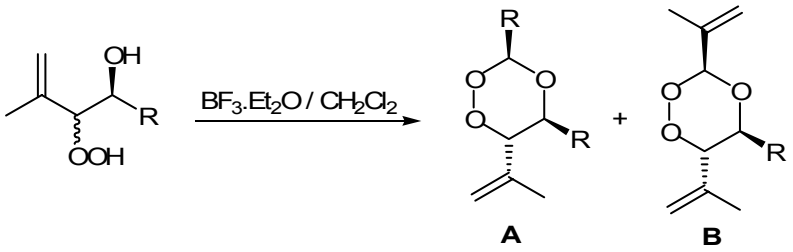
Abb. 7.4

Die Verwendung von Orthoestern bei der Peroxoacetalisierung eröffnete einen direkten Weg zur Synthese der ersten in der Literatur beschriebenen Perorthoester mit einer 1,2,4-Trioxansubstruktur (***Schema 7.5***).



Schema 7.5

In Abwesenheit von Carbonyl-Verbindungen als Reaktionspartner wurde eine direkte Umwandlung vom 1,2-Hydroperoxyalkohol zu den Trioxanen **A** und **B** beobachtet. Die Reaktion läuft über eine langsame, BF_3-katalysierte Spaltung des β-Hydroperoxyalkohols zu Carbonyl- Fragmenten ab, die in einer nachfolgenden Peroxyacetalisierung mit dem noch verbliebenen Hydroxyhydroperoxid zum Trioxan reagieren (***Schema 7.6***).



Schema 7.6

Darüberhinaus habe ich ein Konzept für den Einbau von zwei Trioxan-Untereinheiten in einem Molekül entwickelt. Bis-Spiro-1,2,4-Trioxane sind eine in der Literatur noch nicht bekannte Verbindungskasse. Im Rahmen der vorliegenden Arbeit konnten erstmals Beispiele für Verbindungen dieser Art synthetisiert und charakterisiert werden (***Abb. 7.5***). Die Idee basiert auf der Verknüpfung von zwei 1,2-Hydroperoxyalkoholen mit einer zentralen Dicarbonyl-Komponente (wie z.B. Cyclohexan-1,4-dion).

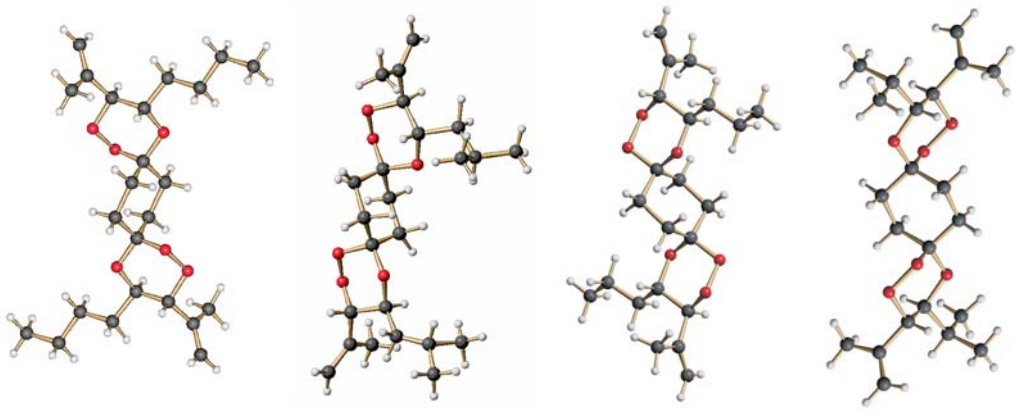
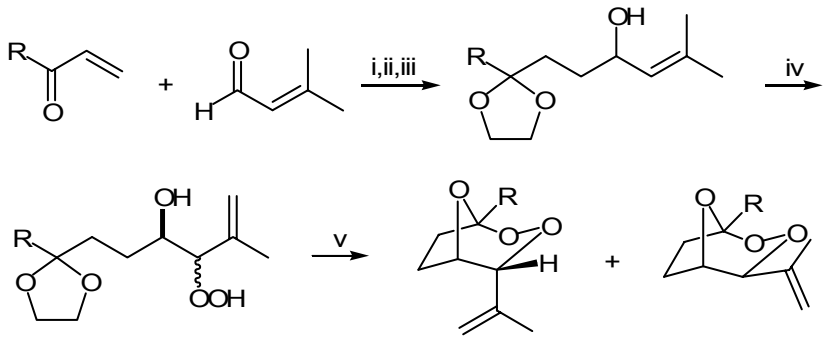


Abb. 7.5

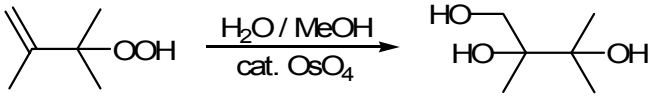
Desweiteren wurde eine effektive Synthesroute zu 2,3,8-Trioxabicyclo[3.2.1]octanen, als ringverkleinerten analogen Verbindungen zum natürlchen Artemisinin-Pharmakophor entwickelt. Die synthetisierten bicyclischen-1,2,4-Trioxansysteme wurden über eine noch literaturunbekannte intramolekulare Peroxoacetalisierungsreaktion erhalten (***Schema 7.7***).



i: Thiazolium Salz, AcONa, EtOH, 80 °C; ii: Ethylenglykol, PPTS; iii: LAH, Et_2O;
iv: $^1O_2$, Polymerträger; v: BF_3xEt_2O, CH_2Cl_2

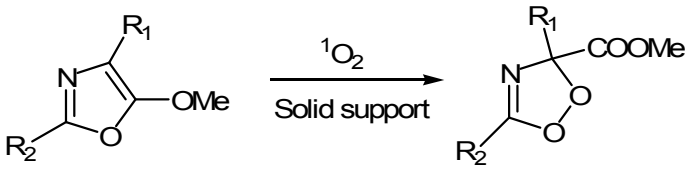
Schema 7.7

Eine weitere synthetische Anwendung der allylischen Hydroperoxide besteht in ihrer Umwandlung zu den entsprechenden Triolen durch Hydroxylierung unter Verwendung von katalytischen Mengen OsO_4 oder WO_3. Im Gegensatz zu den üblichen Hydroxylierungs-reaktionen wurde in unserem Fall kein Cooxidationsmitel verwendet. Stattdessen übernimmt das Substrat selbst die Rolle des Sauerstoffdonors, welcher das reduzierte Oxidationsmittel wieder oxidiert und in einem Reaktionkreislauf die Umwandlung des allylischen Hydroperoxids in das entsprechende Triol-Produkt bewirkt. Bei der Betrachtung des Einflusses der Konzentration des Oxidationsmittels hat sich gezeigt, dass eine Konzentration von 0.001 äquiv OsO_4 die Reaktion noch effektiv katalysiert (***Schema 7.8***).



Schema 7.8

Die [4+2]-Cycloadditions-Reaktionen von $^1O_2$ mit einer Reihe von 5-Methoxyoxazolen als Substrate wurden unter lösungsmittelfreie Bedingungen untersucht. Als Reaktionsprodukte wurden 1,2,5-Dioxazole gefunden, welche sich langsam zu den entsprechenden Amiden und Dicarbonylverbindungen zersetzten (***Schema 7.9***).



Schema 7.9

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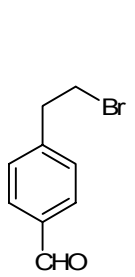
List of compounds



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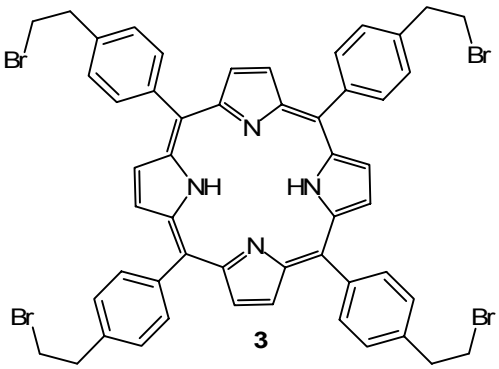

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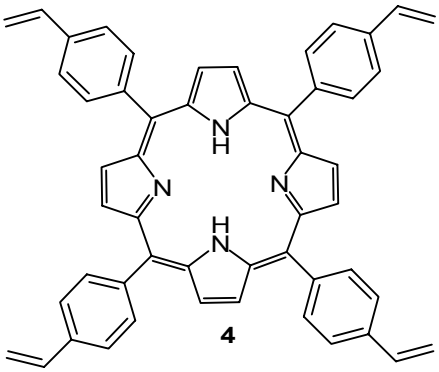

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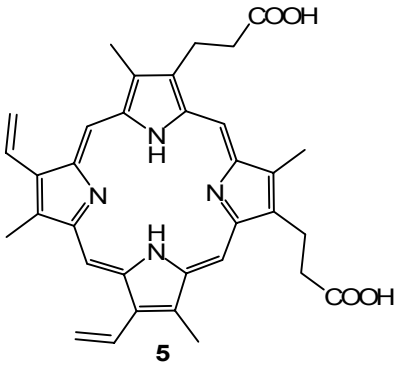

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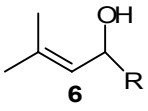
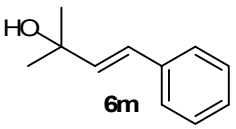


6

R =
a Me
b Et
c *i*-Pr
d *n*-Pr
e $CH_2CH=CH_2$
f $CH(Me)CH=CH_2$
g *n*-Bu

R =
h *i*-Bu
i *sec*-Bu
j *t*-Bu
k $C(Me)_2CH=CH_2$
p *c*-Pr
q *c*-Hex



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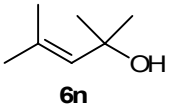

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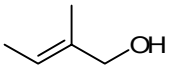

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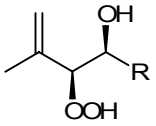
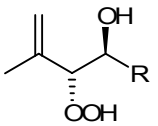


syn-**7**

R =
a Me
b Et
c *i*-Pr
d *n*-Pr
e $CH_2CH=CH_2$
g *n*-Bu

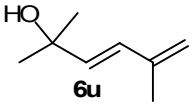
R =
h *i*-Bu
j *t*-Bu
k $C(Me)_2CH=CH_2$
p *c*-Pr
q *c*-Hex



anti-**7**

R =
a Me
b Et
c *i*-Pr
d *n*-Pr
e $CH_2CH=CH_2$
g *n*-Bu

R =
h *i*-Bu
j *t*-Bu
k $C(Me)_2CH=CH_2$
p *c*-Pr
q *c*-Hex



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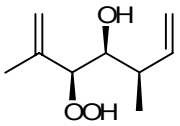

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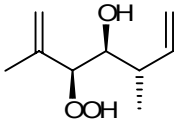

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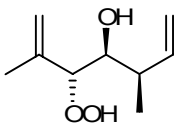

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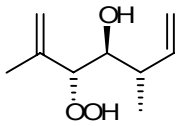

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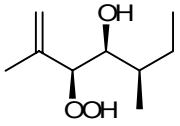

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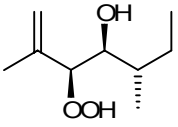

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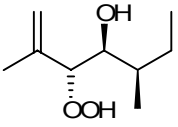

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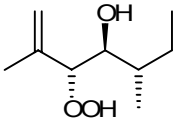

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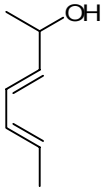

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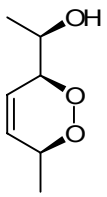
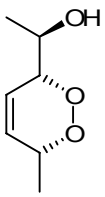
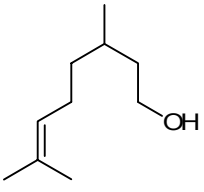


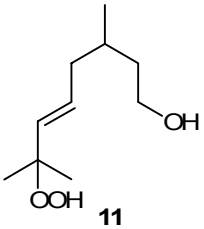
syn-**9**



anti-**9**



10



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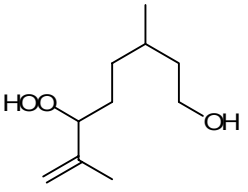
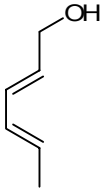
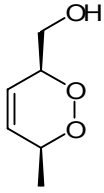


12



13



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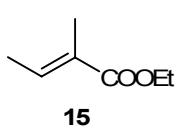

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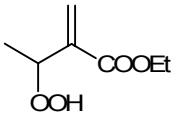
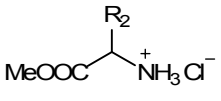
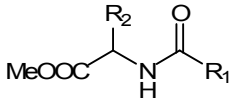


16



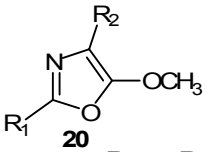
18

R_2 =
a Me
b *i*-Pr
c *i*-Bu



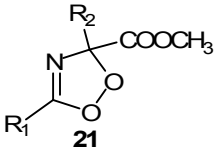
19

	R_1 =	R_2 =
a	Me	Me
b	Me	*i*-Pr
c	Et	Me
d	*t*-Bu	Me



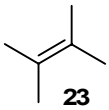
20

	R_1 =	R_2 =
a	Me	Me
b	Et	Me
c	*t*-Bu	Me
d	Me	*i*-Pr
e	Et	*i*-Pr
f	Et	*i*-Bu

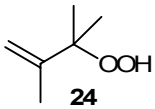


21

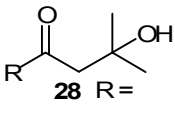
	R_1 =	R_2 =
a	Me	Me
b	Et	Me
c	*t*-Bu	Me
d	Me	*i*-Pr
e	Et	*i*-Pr
f	Et	*i*-Bu



23

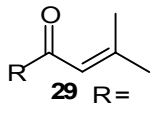


24



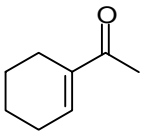
28 R =

a *c*-Pr
b *c*-Hex

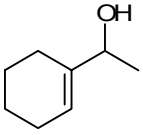


29 R =

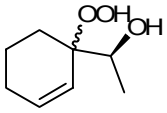
a *c*-Pr
b *c*-Hex



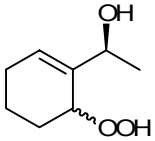
31



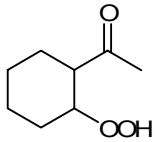
32



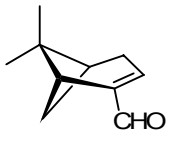
32a



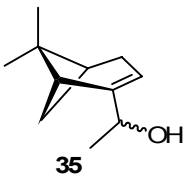
32b



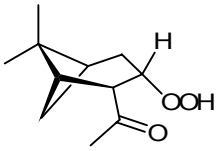
32c



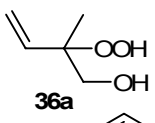
34



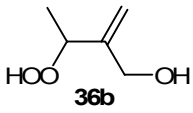
35



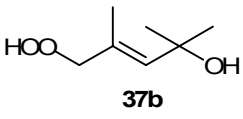
35a



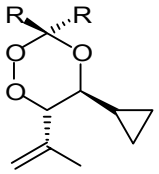
36a



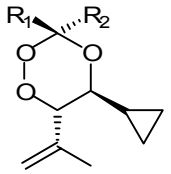
36b



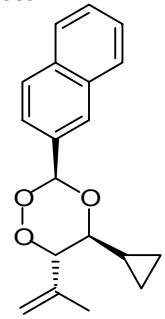
37b



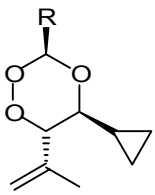
R =
38 adamantane
39 $(CH_2)_2CO(CH_2)_2$
40 Me
41 Et



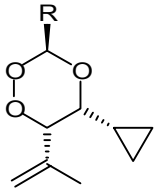
	R_1 =	R_2 =
42a	Et	Me
42b	Me	Et



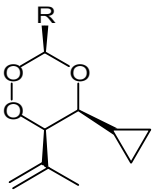
43



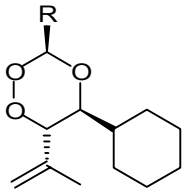
R =
44a Me
45a Et



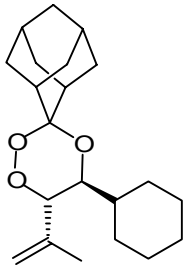
R =
44b Me
45b Et



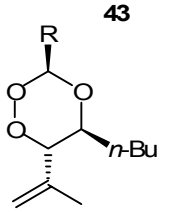
R =
44c Me
45c Et



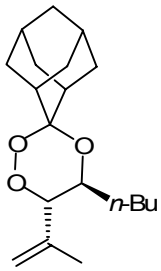
R =
46 2-naphthyl
48 *c*-Hex



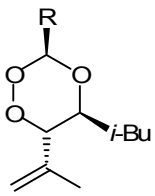
47



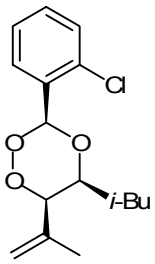
R =
49 2-naphthyl
50 2-Br-C_6H_4
51 Ph
53 Me
54 Et



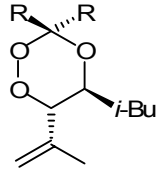
52



R =
55 Ph
56 2-naphthyl
57a 2-Cl-C_6H_4

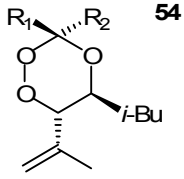


57b

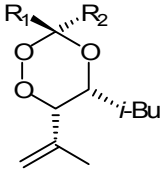


R =
58 adamantane
59 $(CH_2)_5$
60 $(CH_2)_4$

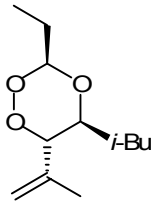
R =
61 Me
62 *n*-Pr



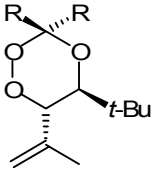
	R_1 =	R_2 =
63	*t*-Bu	Me
64a	Et	Me
64b	Me	Et



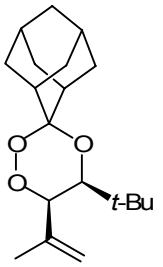
	R_1 =	R_2 =
64c	Et	Me
64d	Me	Et



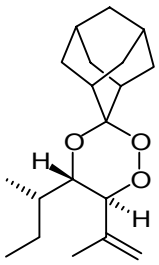
65



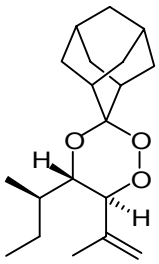
R =
66 $(CH_2)_4$
67 $(CH_2)_5$
68a adamantane



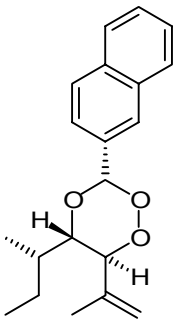
68b



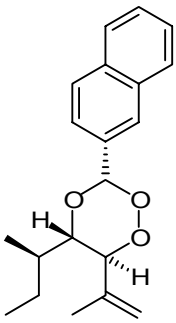
69a



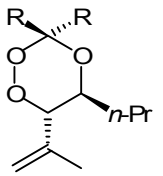
69b



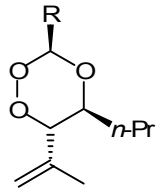
70a



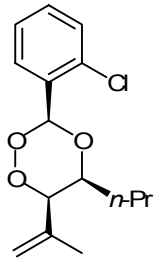
70b



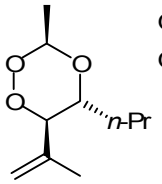
R =
71 adamantane
72 $(CH_2)_6$
73 $(CH_2)_5$
74 $(CH_2)_4$
75 Et



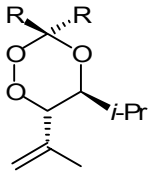
R =
76 2-naphthyl
77 Ph
78a 2-Cl-C_6H_4
79 Et
80a Me



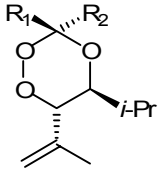
78b



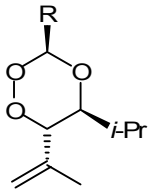
80b



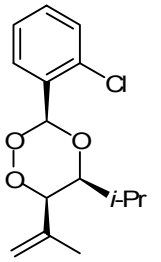
R =
81 adamantane
82 $(CH_2)_4$
83 Me
84 Et



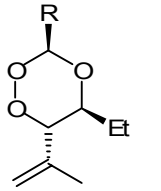
R_1 = R_2 =
85a *n*-Pr Me
85b Me *n*-Pr
86a *t*-Bu Me
86b Me *t*-Bu



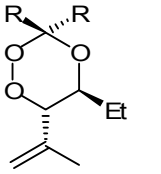
R =
87a 2-Cl-C_6H_4
88 Et



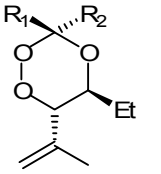
87b



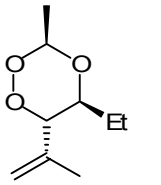
R =
89 2-naphthyl
90 2-Cl-C_6H_4



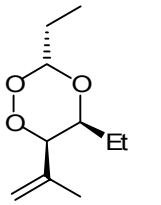
R =
91 adamantane
92 Me
93 Et



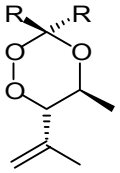
R_1 = R_2 =
94 *t*-Bu Me
95a *n*-Pr Me
95b Me *n*-Pr



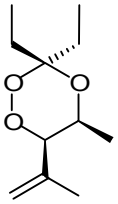
96



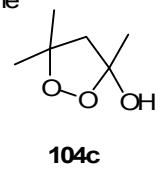
97



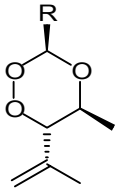
R =
98 adamantane
99 $(CH_2)_6$
100 $(CH_2)_5$
101 $(CH_2)_4$
102 *n*-Pr
103 Me
104a Et



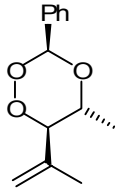
104b



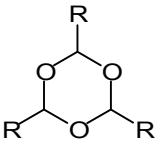
104c



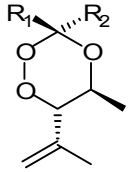
R =
108 2-furyl
109 1-naphthyl
110 2-Br-C_6H_4
111a Ph
113 Et
115 *i*-Pr



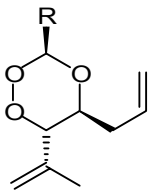
111b



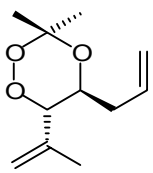
R =
112 Me
114 Et
116 *i*-Pr



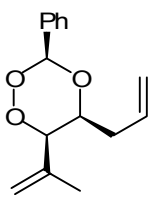
R_1 = R_2 =
105 $(CH_2)_3COPh$ Ph
106a Ph Me
106b Me Ph
107a Et Me
107b Me Et
117a OMe H
117b H OMe
118a OEt H
118b H OEt
119a OEt Me
119b Me OEt



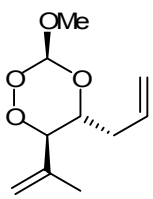
R =
120 2-naphthyl
122a Ph
123 Me
124a OMe



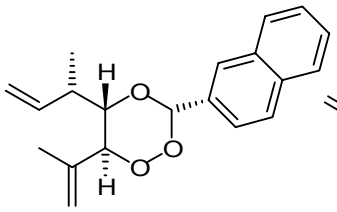
121



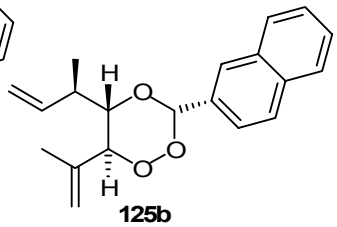
122b



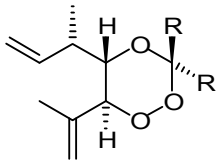
124b



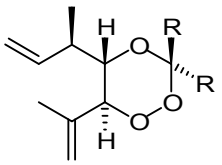
125a



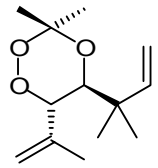
125b



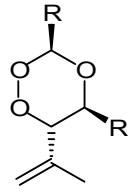
R =
126a adamantane
127a Me



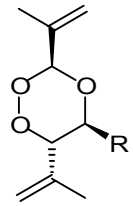
R =
126b adamantane
127b Me



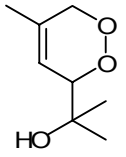
128



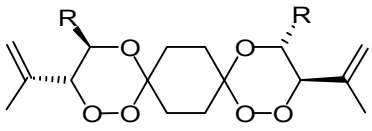
129
R =
a *c*-Pr
b Et
c *i*-Bu
d *n*-Bu
e Me
f *n*-Pr
g $CH_2CH{=}CH_2$
h *i*-Pr



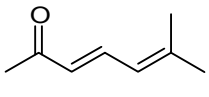
130
R =
a *c*-Pr
b Et
c *i*-Bu
d *n*-Bu
e Me
f *n*-Pr
g $CH_2CH{=}CH_2$
h *i*-Pr



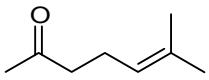
131



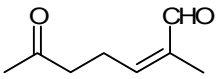
R =
syn-**132** *n*-Bu
syn-**133** *i*-Pr
syn-**134** *n*-Pr
syn-**135** $CH_2CH{=}CH_2$
syn-**136** *i*-Bu



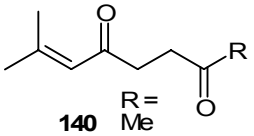
137



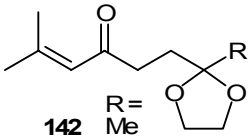
138



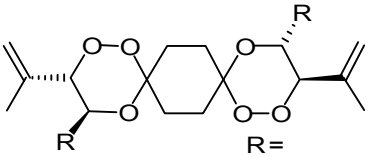
139



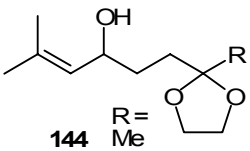
R =
140 Me
141 Et



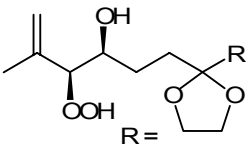
R =
142 Me
143 Et



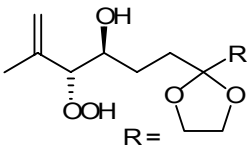
R =
anti-**132** *n*-Bu
anti-**133** *i*-Pr
anti-**134** *n*-Pr
anti-**135** $CH_2CH{=}CH_2$
anti-**136** *i*-Bu



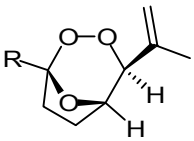
R =
144 Me
145 Et



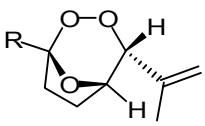
R =
syn-**146** Me
syn-**147** Et



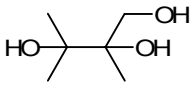
R =
anti-**146** Me
anti-**147** Et



R =
exo-**148** Me
exo-**149** Et



R =
endo-**148** Me
endo-**149** Et



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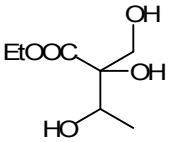

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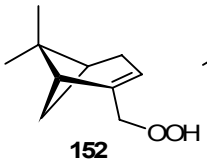

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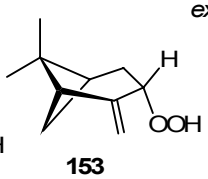

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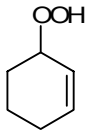

154

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Die von mir vorgelegte Dissertation ist von Herrn Prof. Dr. Axel G. Griesbeck betreut worden.

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Tamer El-Idreesy

Lebenslauf

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