— Organic Lewis Acid Catalysis — Vinylogous Mukaiyama Aldol Reactions And New Catalysts

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„Die Menschen sind verschieden, doch die Wahrheit ist Eine, und alle, die sie suchen, auf welchem Gebiet es sei, helfen einander.“

Gottfried Wilhelm Freiherr von Leibniz (1646-1716)

(loose transl.: Humans are different, but the truth is One, and all seeking for it, in whatever field, are helping each other.)

„Viele sind hartnäckig in Bezug auf den einmal eingeschlagenen Weg, wenige in Bezug auf das Ziel.“

Friedrich Nietzsche (1844-1900)

(loose transl.: Many are insistent regarding the way they took, few regarding the goal.)

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Gracias Lolo. Te quiero!

Outline

Abbreviation Index

A – anion or acid
Å – Ångström
Ac – acetyl
ACDC – asymmetric counteranion directed catalysis
Alk – alkyl
Ar – aryl, aromatic
BINAP – (2-2'-Bis(diphenylphosphino)-1,1'-binaphthyl
BINOL – 1,1'-bi-2-naphthol
Bn – benzyl
Boc – *tert*-butyloxycarbonyl
c – concentration
C – cation
calcd. – calculated
cat. – catalyst/catalytic
CFF – condensed fukui function
CI – chemical ionization
Cy – cyclohexyl
d – days
δ – chemical shift (NMR)
Δ – heat
dba – dibenzylideneacetone
DCC – dicyclohexylcarbodiimide
DFT – density functional theory
DMAP – 4-dimethylaminopyridine
DMF – dimethylformamide
DMPU – 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO – dimethylsulfoxide
dr – diastereomeric ratio
DVMAR – double VMAR
E – electrophile
(*E*) – double bond geometry (entgegen)
EDG – electron donating group
EI – electron ionization
eq – equation
equiv – equivalents/equivalent
er – enantiomeric ratio
ESI – electospray ionization
EWG – electron withdrawing group
F^- – source of fluoride
GC – gas chromatography
GSP – general synthetic procedure
h – hours
HMPT – hexamethylphosphoric triamide
HOMO – highest occupied molecular orbital
HPLC – high performance liquid chromatography
HRMS – high resolution mass spectrometry
HSAB – hard/soft, acid/base-theory
∫ – integral (NMR)
IR – infrared spectroscopy
KHMDS – potassium hexamethyldisilazide
L – ligand
LA – Lewis acid
LB – Lewis base
LC – liquid chromatography
LDA – lithium diisopropylamide
lit. – literature
LUMO – lowest unoccupied molecular orbital
m- – *meta*-position
M – mass or metal
M – molarity

MM – molecular mechanics
MS – mass spectrometry
NCS – N-chlorosuccinimide
n.d. – not detected
neg – negative
NMR – nuclear magnetic resonance spectroscopy
NOE – nuclear Overhauser effect
Nu – nucleophile
o- – *ortho*-position
p- – *para*-position
P – product
PCC – pyridiniumchlorochromate
Ph – phenyl
pos – positive
ppm – parts per million
PyBox – 2,6-bis(oxazolin-2-yl)pyridine
quant. – quantitative
R – rest
r.t. – room temperature
SM – starting material
TBS – *tert*-butyl(dimethyl)silyl
Tf – trifluoromethanesulfonyl
THF – tetrahydrofuran
TIPS – triisopropylsilyl
TLC – thin layer chromatography
TMEDA – N,N,N',N'-tetramethylethylenediamine
TMS – trimethylsilyl
TOF – turnover frequency (per hour)
Tol – tolyl
TON – turnover number
Tr – trityl
TRIP – 3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl-2,2'-diylhydrogenphosphate
Ts – tosyl
UV – ultraviolet
VMAR – vinylogous Mukaiyama aldol reaction
X – electronegative group
(*Z*) – double bond geometry (zusammen)

1. Introduction

Chirality is ubiquitous in nature, embodied for example in the interaction of optically pure drugs with its binding sites. This phenomenon is called molecular recognition and its fundamentals were first discussed as "Schlüssel-Schloss-Prinzip – (key-lock-principle)" by Emil Fischer in 1894 (Fig. 1).[1]

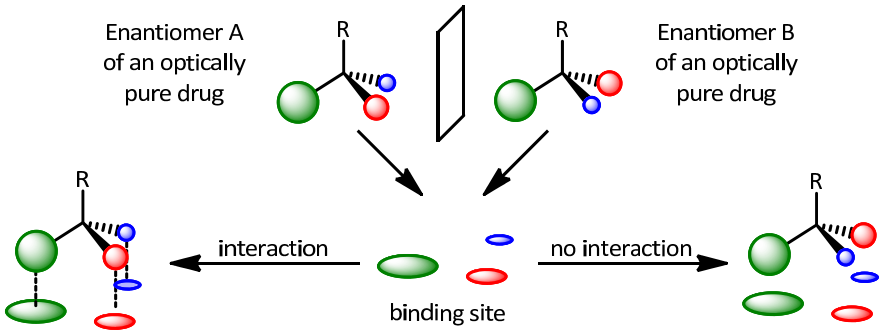


Figure 1. *Illustration of the key lock principle and chirality.*

Thus it was not surprising, that an interest in the production of enantiomerically enriched products developed very early: asymmetric synthesis.[2] Asymmetric synthesis in general, and *asymmetric catalysis* in particular, ranks among the most stimulating and challenging concepts in organic chemistry. Since countless organic transformations can be conducted in an asymmetric way, its possibilities are truly manifold.[3] To develop a successful method, one has to consider various parameters, eventually encountering new reaction mechanisms and opening up unknown pathways. Almost infinite numbers of contributions make it one of the most fruitful areas of scientific research, a steadily growing pool of solutions to almost any problem one might face in synthesis and catalysis.[4]

Summoning early studies by Louis Pasteur[5] and Emil Fischer, Willi Marckwald carved the cornerstone of asymmetric synthesis in 1904.[6] Reacting achiral ethylmethylmalonic acid **1** with enantiomerically pure brucine, he obtained a mixture of salts which were separable by crystallization. Selecting the crystals of one enantiomerically pure salt, decarboxylating the free carboxylic acid function and subsequently hydrolizing, he was able to isolate optically active 2-methyl-butanoic-acid **2**. As such, the transformation achieved enantioenrichment during the reaction pathway, an *asymmetric synthesis* (Fig. 2).

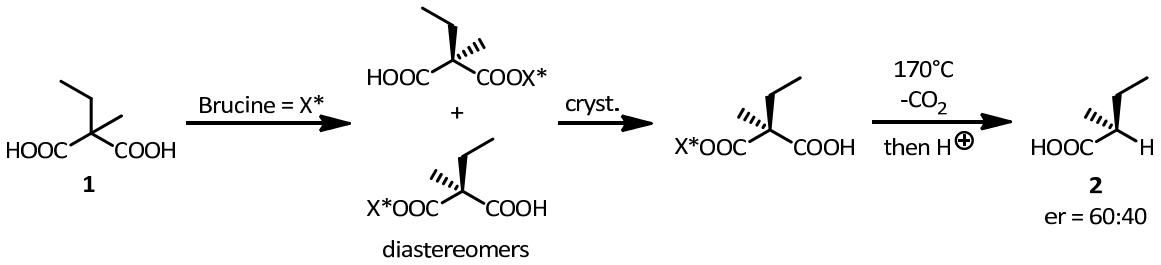


Figure 2. *First asymmetric synthesis by Marckwald.*

Reviewing his achievements, Marckwald described asymmetric syntheses as follows:

"Asymmetrische Synthesen sind solche, welche aus symmetrisch constituirten Verbindungen unter intermediärer Benutzung optisch-activer Stoffe, aber unter Vermeidung jedes analytischen Vorganges, optisch-active Substanzen erzeugen."[7] (loose transl.: Asymmetric syntheses are those which convert symmetrically substituted compounds, under the governance of optically active substances and avoiding any analytic operation, into optically active substances.)

The key attribute of operational simplicity was already present in the very first definition. In this context it seems inconsistent, that many catalytic systems developed for asymmetric organic synthesis, approach the addressed problem on a level which eliminates operational simplicity in the root. Surely numerous contributions to asymmetric catalysis are very appealing and bear a non-dismissible beauty, however their successful synthetic application at low cost, as the ultimate goal in organic synthesis, is unlikely. Quality and financial demands for compounds in pharmaceutical-, crop-protection-, material- or food-industry forbid impurities (both with undesired compounds *and* the wrong enantiomer) and operationally complex methods. With these requirements in mind it becomes clear, that a catalysis approach for the production of enantiomerically enriched substances is superior over an auxiliary- or a resolution-strategy. A good catalytic method avoids the generation of waste in form of undesired compounds *and* the wrong enantiomer. However, cost-factors often obviate the use of catalytic syntheses, since common auxiliaries or separations of racemates are cheap.

The 2001 Nobel-prize winning achievements by Knowles,[8] Noyori[9] and Sharpless[10] impressively illustrate the potential of asymmetric catalysis. These methods, based on Rh-, Ru- and Ti-catalysts, found industrial applications and are widely accepted by industrial chemists. Unfortunately these examples are rare exceptions, and catalytic methods are not

yet common for the production of chemical products. Multi-step syntheses of catalysts, laborious removal of trace metal impurities, excessive additive employment and very low reaction temperatures are characteristics which often deny the entry of asymmetric catalysis into industrial processes.

Thus, due to its outstanding potential, asymmetric catalysis is an area of eager research. For a long time this research was solely based on metals or enzymes. Around the millennium break organocatalysis was pioneered: a complementary and very powerful approach, making use of small organic molecules. In seminal contributions by List and MacMillan, proline and other amino acid derivatives found application in aldol and Diels-Alder reactions.[11]

Starting from these reports, the field of asymmetric organocatalysis underwent a rapid progression.[12] The structures appearing in new organocatalysts are multifaceted, making use of various chiral skeletons. The superior potential of organocatalysis is obvious due to economic and ecologic reasons. Furthermore, it is a general concept which can be adapted in Brønsted acid-, Brønsted base-, Lewis acid- and Lewis base-catalyzed transformations.[13] Thus the development of new, highly reactive, easily accessible and general organocatalysts represents a unique opportunity for the future.

2. Background

2.1 Lewis acid catalysis in organic synthesis

Acids and bases are widely abundant in nature and as a result there has been a need for their exact definition. Based on his PhD-studies, Svante A. Arrhenius defined acids as substances dissociating into protons (H^+) and the corresponding anions (A^-) in an aqueous medium.[14] Correspondingly, bases were characterized as substances dissociating into hydroxy-anions (OH^-) and its respective cations (C^+). Clearly this concept is restricted to acids and bases like HBr or KOH in water. In 1923 Johannes N. Brønsted and Thomas M. Lowry independently elaborated the extension of the acid-base theory by defining acids as proton-(H^+)-donors and bases as proton-acceptors, no longer restricting the concept to specific substance classes or solvents.[15] Following these ideas, a larger number of reactions could be interpreted accordingly (see Fig. 3).

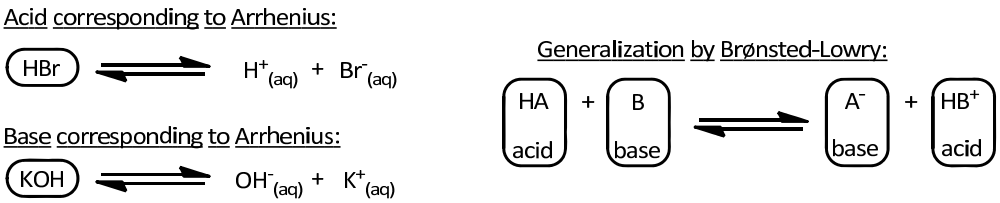


Figure 3. *Acid-Base Concepts by Arrhenius and Brønsted-Lowry.*

Since many reactions do not involve direct proton transfers, the generalization of the acid-base definition by Gilbert N. Lewis in 1938, was an important step for the understanding of chemical compounds and their transformations.[16] A Lewis acid is a compound with an electron demand, an unoccupied orbital which is able to accept an electron pair. On the other hand a Lewis base donates an electron-pair from an occupied orbital. The reaction products of Lewis acids and bases are Lewis adducts, bound through a coordinative (or dative) bond (Fig. 4). By joining the two concepts it becomes clear, that a Brønsted acid is a compound consisting of a Lewis base and a proton. This leaves the proton as the smallest of all Lewis acids, bearing free space in its 1s-orbital.

Further refined by Ralph G. Pearson in 1963, Lewis acids and bases are categorized into hard and soft acids and bases (HSAB-concept).[17] This approach describes the quality of a bond in a Lewis adduct by consideration of atomic or ionic radii, charge distribution and polarizability.

Accordingly, moieties of small size, high charge density and high polarizing potential are considered “hard”, whereas large radii, low charge densities and low polarizing potential characterize “soft” acids or bases (see Fig. 4). The association of hard acids with hard bases, and soft acids with soft bases is preferred. This preference is based on the bond character present in these combinations. A bond between a hard acid and a hard base, as in NaCl, has an ionic character, whereas the bond between a soft acid and a soft base results in a combination exhibiting a covalent bond character. With these concepts a manifold of chemical reactions and compounds can be qualitatively described. Especially for the understanding of structure and reactivity of transition metal complexes, the HSAB-concept is of very high value.

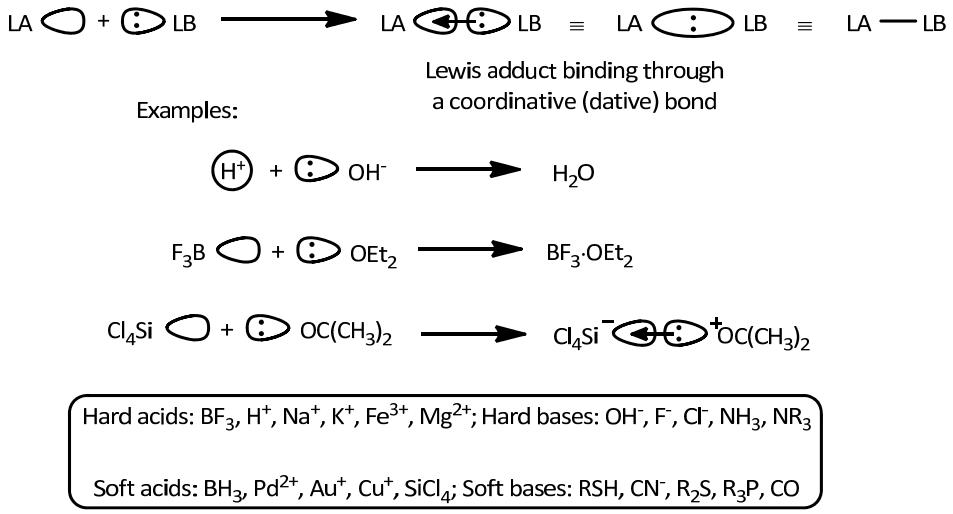


Figure 4. *Interaction of Lewis acids and Lewis bases and the HSAB-categorization.*

A great potential of Lewis acids is their application in the activation of molecules bearing Lewis basic sites.[I] Thus Lewis acids play a key role for the activation of σ- and π-systems. The formation of σ-complexes is present in the activation of substrates such as carbonyl compounds or imines.[18] Due to the interaction of the lowest unoccupied molecular orbital (LUMO) of the Lewis acid with the highest occupied molecular orbital (HOMO) of the Lewis base, adjacent bonds get polarized and a nucleophilic attack from external or internal nucleophiles is facilitated. This mode of action can be summarized in a commonly accepted catalytic cycle which accounts for this activation mode, “Lewis acid catalysis” (Fig. 5).

I Since the proton is a Lewis acid as well, Brønsted acids are powerful activators for Lewis basic sites.

Together with Lewis base activation, Brønsted acid activation and Brønsted base activation it represents the pillars of asymmetric catalysis.[13]

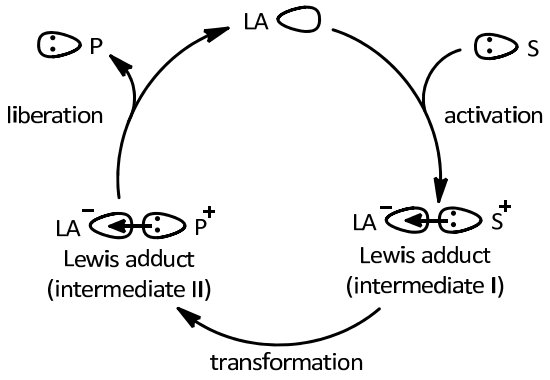


Figure 5. *General reactive principle of Lewis acid catalysis.*

However, Lewis acid activation is not restricted to σ-electron donors. Some Lewis acids are very powerful catalysts for the activation of π-electron-systems as well. By these interactions nucleophilic attacks on allenes, alkenes and alkynes can be efficiently triggered. Usually these catalysts are complexes bearing a "soft" metal center.[19]

2.1.1 σ-Lewis acids

Some archetypical Lewis acids for σ-donor activations are group 3- and 4-element halides, such as BF_3, $AlCl_3$, $SnCl_4$ or $SiCl_4$. Many other σ-Lewis acids are based on transition metals, such as $TiCl_4$ and $FeCl_3$ (see Fig. 4). Based on the periodic table, a vaguely defined borderline between (transition)-metal and (transition)-metal-free Lewis acids can be drawn. As a common example from the main group elements, $AlCl_3$ finds its application for various purposes.[20] One important example is the Friedel-Crafts alkylation (see Fig. 6). This reaction, first reported in 1877 by French chemist Charles Friedel and american chemist James Crafts, is an electrophilic aromatic substitution, occurring through an addition-elimination mechanism.[21] The role of the Lewis acid is the interaction of its empty orbital with a lone pair of electrons on chlorine (Fig. 6, eq 1). This interaction polarizes the halogen-carbon bond in MeCl and results in a higher electrophilicity on carbon. Subsequently a nucleophilic attack by the aromatic ring takes place. Upon rearomatization via elimination of a proton, the product and the catalyst are liberated.

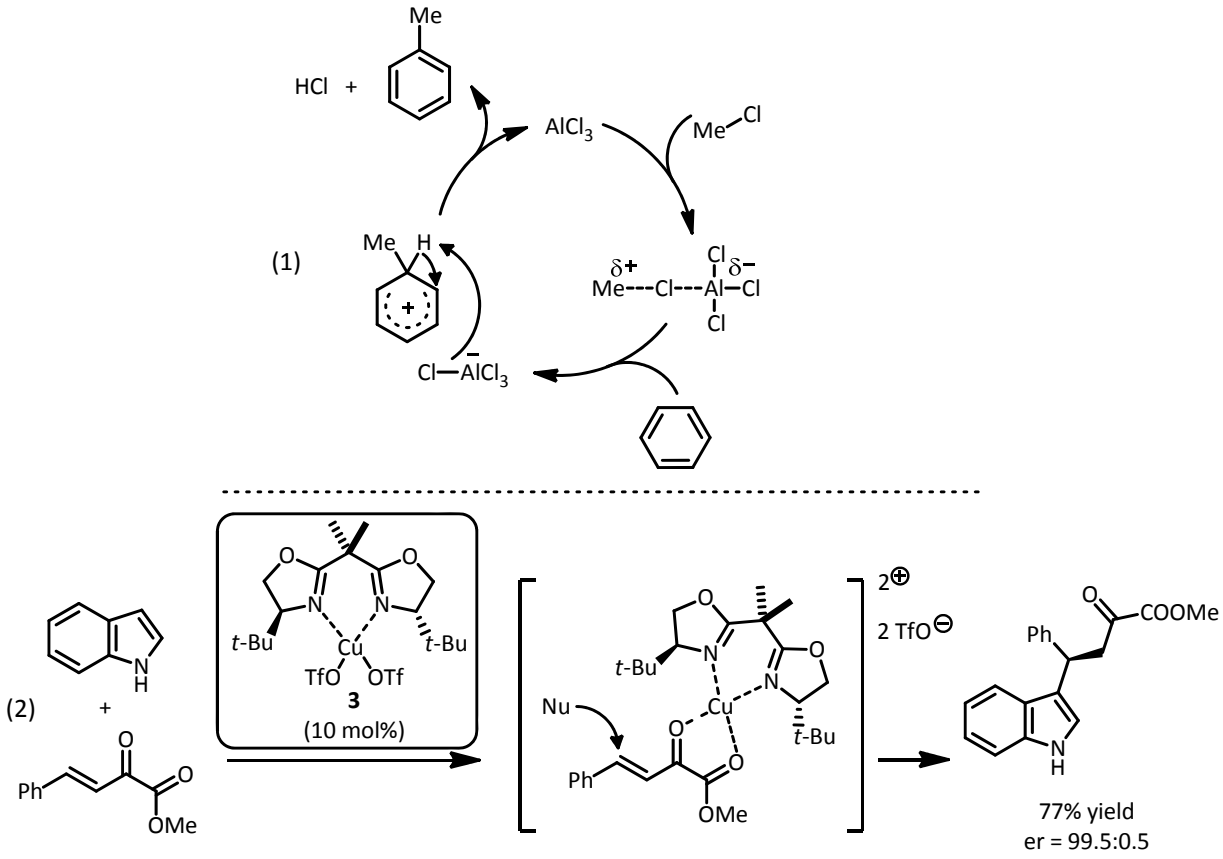


Figure 6. *Mechanism of the Friedel-Crafts alkylation of benzene and a highly asymmetric version.*

In recent years the Friedel-Crafts-reaction, especially utilizing indoles as nucleophiles, experienced a remarkable renaissance.[22] The use of chiral Lewis acids and prochiral electrophiles set the stage for various highly enantioselective versions. A highly enantioselective example for Friedel-Crafts alkylations was presented by the group of Jørgensen in 2001. The reaction between indoles and α,β-unsaturated ketoesters was selectively catalyzed by copper-(II)-bisoxazoline complex **3** (Fig. 6, eq 2).[23] The interaction between copper and the electrophile relies on the activation of the oxygen lone-pairs in the ketoester by the copper-center in **3**, removing electron density from the conjugated system, facilitating nucleophilic attack by the indole. The rigid intermediate is actually cyclic, resulting in an outstanding enantioselectivity of the process.

Another very illustrative reaction based on Lewis acid-/base-interactions is the Corey-Bakshi-Shibata-(CBS) reduction of ketones and aldehydes, reported in 1987.[24] Seminal studies towards the parent catalytic system, a chiral oxazaborolidine **4**, were already reported by

Itsuno and Hirao in 1981,[25] although the real synthetic potential was discovered only later. [II] The mechanism of this transformation nicely demonstrates the subtle interplay of Lewis acidity and Lewis basicity (Fig. 7).

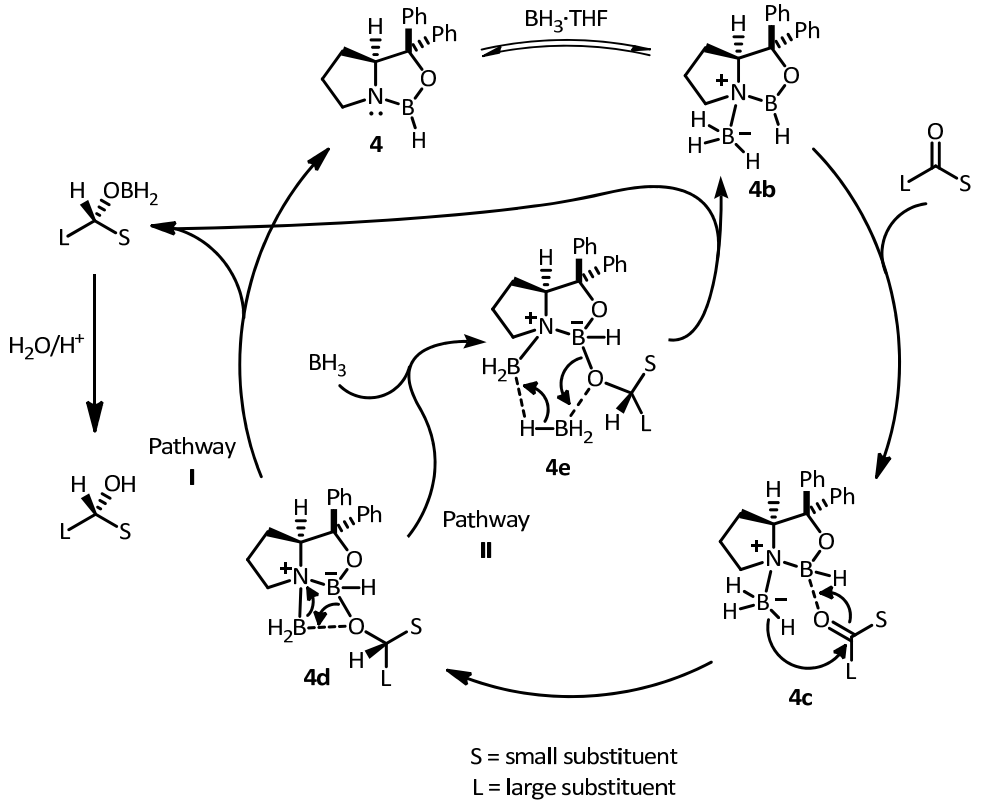


Figure 7. *Mechanism of the Corey-Bakshi-Shibata-reduction.*

The oxazaborolidine **4** is readily available from the inexpensive amino-acid proline in a simple synthetic operation. Under the reaction conditions, the Lewis basic nitrogen interacts with the external Lewis acid BH_3, resulting in adduct **4b**, in which the internal Lewis acidic site gains additional reactivity. The ring boron center uses its empty orbital for the activation of a carbonyl compound. In the resulting intermediate **4c**, the substituents of the carbonyl compound align with least steric repulsion, arranging the substrate for the subsequent hydride transfer from the formerly external BH_3. The resulting intermediate **4d** can break down in two different pathways. In pathway **I** a ligand-exchange on the boron atoms of the four-membered-ring is involved, liberating catalyst **4** and the product. Pathway **II** leads through an insertion of an external borane into the boron-oxygen bond, followed by subsequent ligand-exchange via six-membered ring **4e,** resulting in the liberation of catalyst

[II] Sometimes this reaction is referred to as the Corey-Itsuno reduction accordingly.

4b and the products respectively. The borane-products are hydrolyzed to the corresponding optically active alcohols after work-up.

Another reaction that is archetypical in Lewis acid catalysis is the Diels-Alder reaction of dienes with dienophiles. This reaction was first systematically studied by the German chemists Otto Diels and Kurt Alder from the Universität Kiel in 1928, being awarded with the Nobel Prize in 1950.[26]

Diels-Alder reactions, [4+2]-cycloadditions, occur either as normal- or inverse-electron-demand reactions under thermal conditions. These transformations provide rapid access to complex cyclic structural subunits and are a very powerful tool for the synthesis of natural products.[III] They are driven by an overlap between the HOMO and the LUMO of the two reactants, triggering the subsequent bond formation. The counterintuitive occurence of the sterically less favourable endo-products can possibly be explained by secondary orbital interactions of the substrates.[27]

However as already commented, these transformations are very efficiently catalyzed by Lewis acids, avoiding thermal conditions which can be inconvenient if dealing with complex molecules (see Fig. 8).[28] In the normal electron-demand Diels-Alder reaction, the electron withdrawing group on the dienophile, often a carbonyl-oxygen, can be activated by a Lewis acid which lowers the LUMO-energy towards interaction with the HOMO of the diene. One example for an enantioselective version of this transformation is related to studies towards prostaglandins by the group of E. J. Corey (Fig. 8, eq 1)[29]. In this procedure the chiral Al-complex **5** is used as catalyst, providing the Diels-Alder product of cyclopentadiene and an acrylate with excellent regio- and enantiocontrol.

In an inverse electron demand Diels-Alder reaction a Lewis acid can activate an electron-poor diene towards interaction with an electron-rich dienophile. This principle was used in the activation of tropones towards enolates with chiral Al-based Lewis acid **6** by the group of Yamamoto in 2009 (Fig. 8, eq 2).[30]

[III] Interestingly Diels and Alder anticipated the synthetic potential of the method, stating the following in their original publication: „Wir behalten uns die Anwendung der von uns gefundenen Reaktionen zur Lösung derartiger Probleme ausdrücklich vor. – We explicitly reserve the right for the application of our findings regarding the solution of such problems."

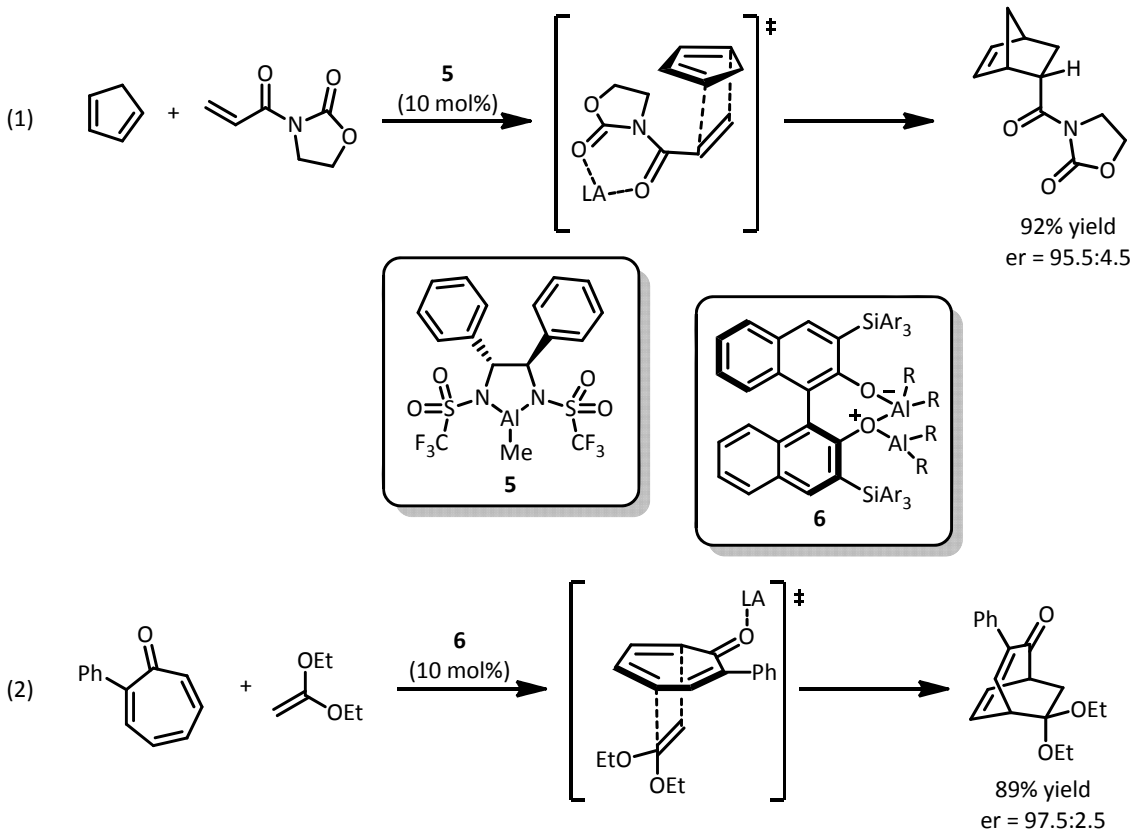


Figure 8. *Chiral Lewis acid-catalyzed Diels-Alder reactions presented by Corey and Yamamoto.*

2.1.2 π-Lewis acids

As already mentioned, the activation of multiple carbon-carbon bonds is another domain of Lewis-acid catalysis. Here the π-systems of, for example, allenes, alkenes and alkynes are activated. An extremely important reaction using this slightly different mode of action is the Ziegler-Natta polymerization of ethylene or propylene. This milestone-contribution[IV] was developed in the laboratories of the Nobel-laureates Karl Ziegler and Giulio Natta in the 1950s.[31]

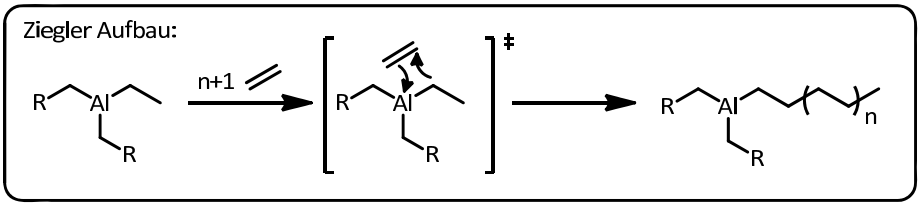


Figure 9. *The Ziegler-Aufbau reaction.*

[IV] Resulting in the Nobel prize of chemistry in the year 1963.

In early studies Ziegler developed the so-called Aufbau-reaction (Aufbau (Ger.) = assembly), the multiple insertion of ethylene into the carbon-aluminium bond of trialkylaluminium compounds (Fig. 9).

In an original contribution from 1955 Karl Ziegler retrospectively[V] describes the development of extremely efficient catalysts for the quantitative dimerization of ethylene and as well its polymerization to polyethylene.[31a] Along these lines Ziegler and his group studied transition metal additives and other aluminium-based Lewis acids to obtain more efficient butane formation. However, they found that the incorporation of Ti, Zr and other metals from the auxiliary groups 4-6 led to quantitative production of a white solid, polyethylene, instead. These transition metal sources formed complexes, now widely referred to as the Ziegler-Natta polymerization catalysts **7** (Fig. 10).

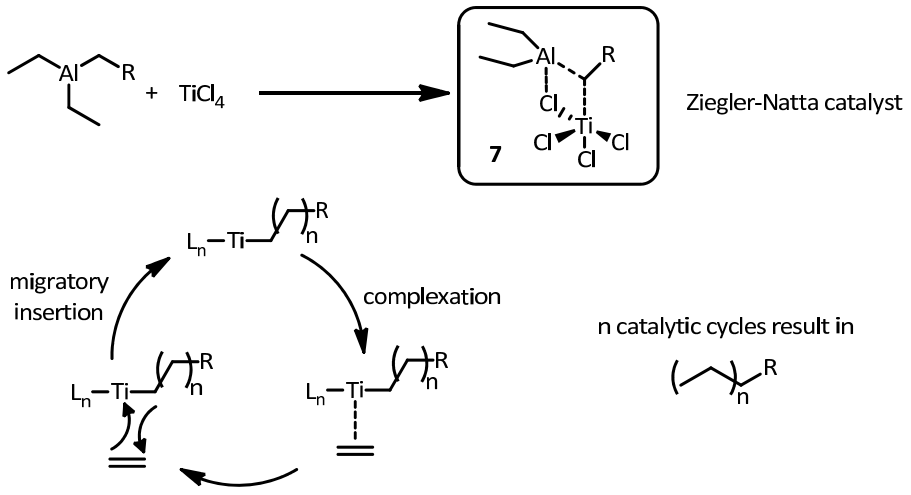


Figure 10. *Proposed mechanism for the Ziegler-Natta polymerization of ethene.*

Over the years several classes of catalysts have been developed. One important class are mixtures of $TiCl_4$ and $Al(Cl)Et_2$ or closely related compounds. The crucial π-Lewis-acid activation is delivered by the free binding site on titanium, triggering a mechanism presumably following complexation and migratory insertion.[32] [VI]

Gold-(I)-species are particularly suited for the activation of π-systems as well, due to their soft, carbophilic character.[33] Au-(III)-species generally act more like oxophilic Lewis acids. Most reserach regarding chiral gold-complexes focused on Au-(I). Here the utilization of

[V] This publication is a synopsis of previous works from the laboratory of Karl Ziegler.

[VI] Although a well-known reaction, the exact mechanism and binding status in the catalyst remains elusive.

phosphine ligands proved particularly useful. Investigations by the group of Hayashi from 1986 on enantioselective aldol reactions provided an early example of chiral gold-(I)-catalysis. However, in this case it was acting like a σ-acid (**8**), long before the field started exploding over the recent years (Fig. 11, eq 1).[34]

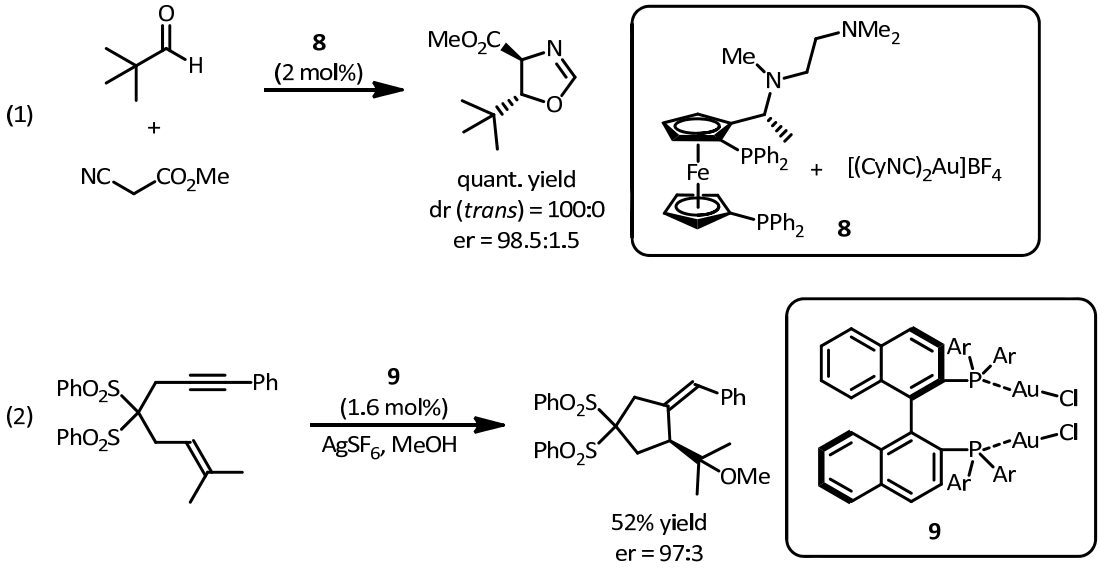


Figure 11. *Au-(I)-catalyzed aldol reaction by Hayashi and alkoxycyclization by Echavarren.*

In 2005 the group of Echavarren reported the alkoxycyclization of enynes, catalyzed by chiral bis-Au-(I)-complexes like **9** (Fig. 11, eq 2).[35] The fact that simple and ubiquitous phosphine ligands could be used, stimulated further research. Following these and other seminal reports, a vast array of gold-(I)-catalyzed reactions was reported. However, not only the strategy of ligand design was followed, stereoinduction by chiral counterions in transformations with cationic Au-(I)-complexes was also disclosed.[36] Although Lewis acid catalysis is clearly versatile and propagates throughout the complete periodic table, the use of transition-metal centers as the electron accepting unit is the most frequent strategy.

2.1.3 Cooperative effects in Lewis-acid catalysis

One fascinating possibility for reactivity enhancement of Lewis acids is the installation of secondary interacting entities, such as Brønsted acids or other Lewis acids. These cooperative effect activations of Lewis acid catalysts can be considered as combined acid approaches, reviewed by the group of Yamamoto recently.[37] With this in mind, one has different possibilities for the enhancement of the catalytic performance of a Lewis acid catalyst. As Yamamoto et al. very well pointed out, two combined acid activations of Lewis

acids are possible: “Lewis acid assisted Lewis acids (LLA)” and “Brønsted acid assisted Lewis acids (BLA)”.

As already shown earlier, the interplay of multiple Lewis acidic sites can increas overall reactivity substantially. In line with the observations on the Al-complex **6** (Fig. 8), Kobayashi and co-workers presented a bis-Zr-BINOL-complex **10** as a very powerful catalyst for the Strecker reaction (Fig. 12, eq 1).[38] In this catalyst system two Lewis acidic sites in one complex influence each other. One Zr-atom delivers an empty orbital towards an interaction with a lone pair of an oxygen-ligand on the other Zr-center, rendering it more electron-withdrawing and increasing the overall Lewis acidity of the catalytically active center.

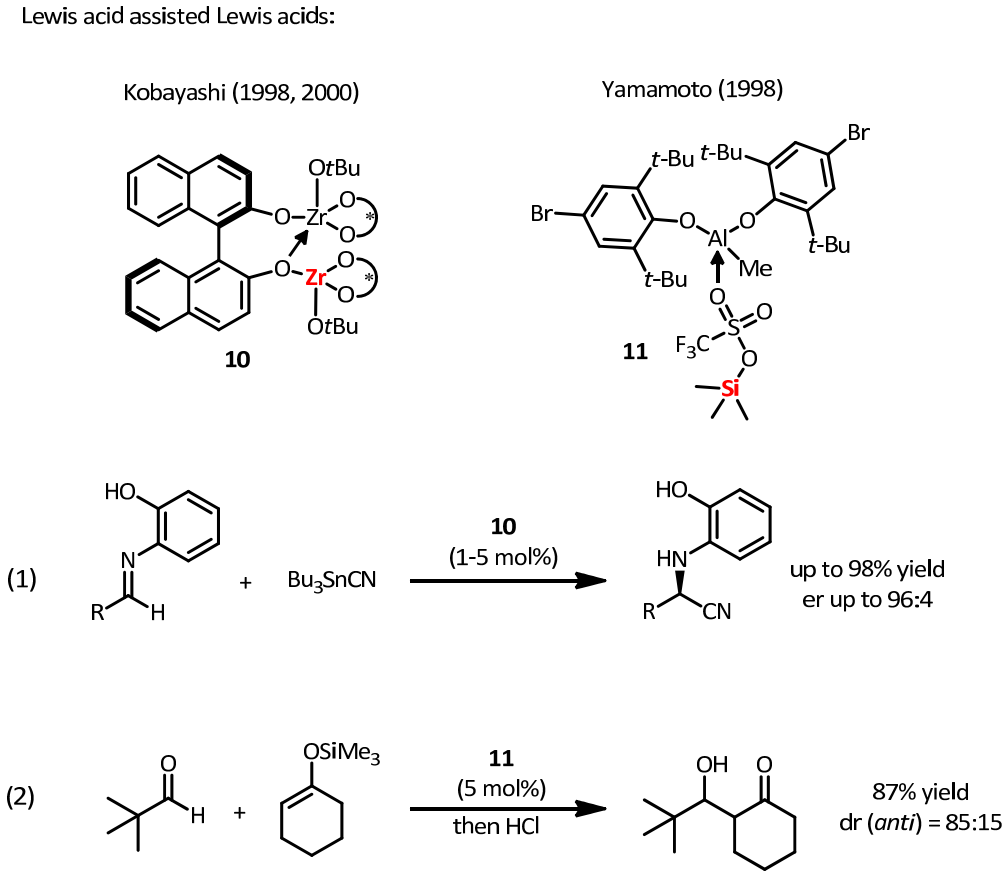


Figure 12. *Lewis acid assisted Lewis acid catalysts reported by Kobayashi and Yamamoto.*

Another application of Lewis acid activation of Lewis acids was reported by the group of Yamamoto in the year 1998.[39] They described the use of Me_3SiOTf in combination with an Al-based Lewis acid **11** for Mukaiyama aldol reactions (Fig. 12, eq 2). The activation mode is discussed as the interaction of the Al-species with the sulfonyl oxygen atoms on the triflate, increasing the overall electron-demand on silicon.

Different from this concept is the activation of Lewis acids by Brønsted acids. The wide abundance of Brønsted acids offers various opportunities regarding this mode of double activation. Here Ishihara and Yamamoto reported a BINOL-derived tetraol-borane **12** as an efficient catalyst for Diels-Alder reactions (Fig. 13, eq 1).[40] In this complex, three alcohol moieties ligate to the catalytically active boron, whereas one oxygen-atom stays protonated and delivers a hydrogen-bond activation of one of the oxygen-ligands. However, the role of this dual activation is considered as twofold, one being the increase in Lewis acidity at boron, the second is the increase in π-stacking ability of the aromatic substituent, rendering the orientation of the substrate more effective.

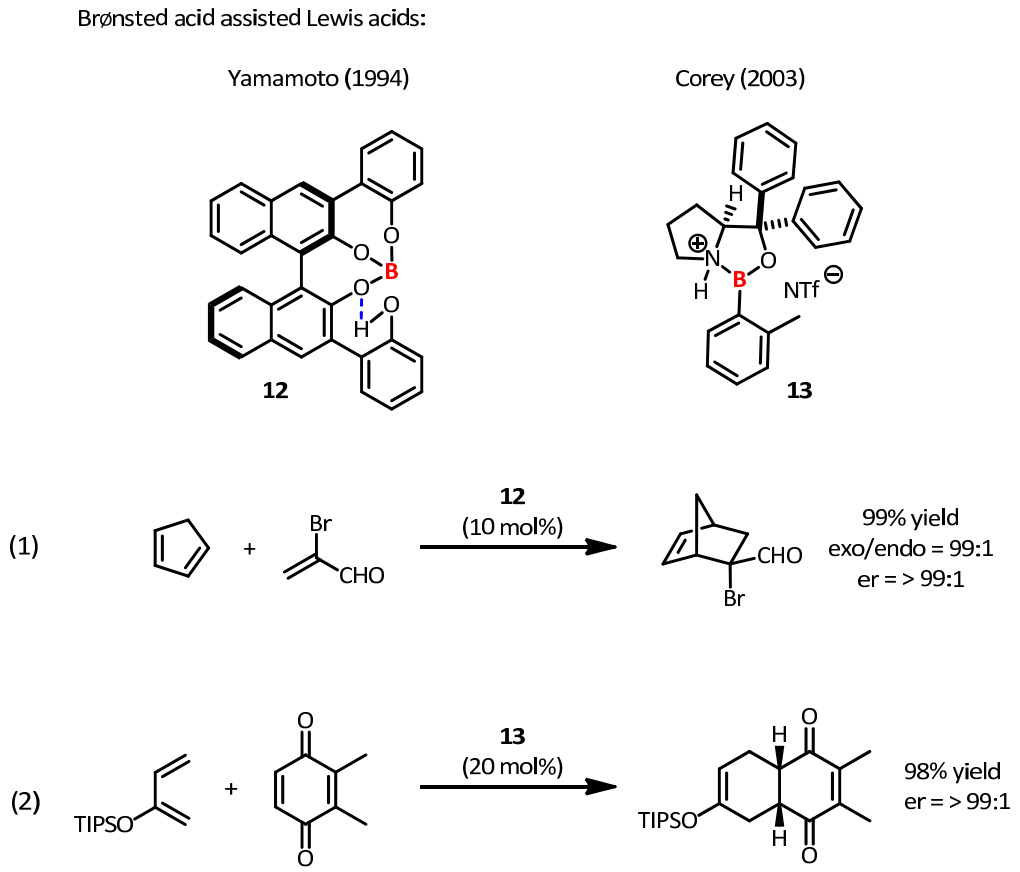


Figure 13. *Brønsted acid assisted Lewis acid catalysts as presented by Yamamoto and Corey.*

Later the laboratory of Corey identified the potential of protonated chiral oxazaborolidines, such as **13**, as highly efficient catalysts for Diels-Alder reactions (Fig. 13, eq 2).[41] For this purpose, oxazaborolidines were treated with very strong Brønsted acids, such as triflic acid or triflimide, resulting in nitrogen protonation and an increase in Lewis acidity on boron. The substrate spectrum with these catalysts was remarkable, involving otherwise unreactive dienophiles and dienes.

2.2 Aldol reactions

One of the most important and well investigated reactions for the generation of carbon-carbon bonds is the aldol reaction. Nature developed some impressively efficient solutions for aldol transformations, *e.g.* embodied in glycolysis or the citric acid cycle. Research on the activity of enzymes[42] or antibodies[42-43] in aldol reactions, further underlines the ease with which natural and bioinspired systems are able to solve this synthetic challenge.

First synthetic reports go back to the 18th century, when Russian chemist Alexander P. Borodin and French chemist Charles A. Wurtz performed experiments combining aldehydes with acids or bases.[44] The corresponding products of these transformations bearing an aldehyde- and an alcohol-function, were named aldols accordingly (Fig. 14).

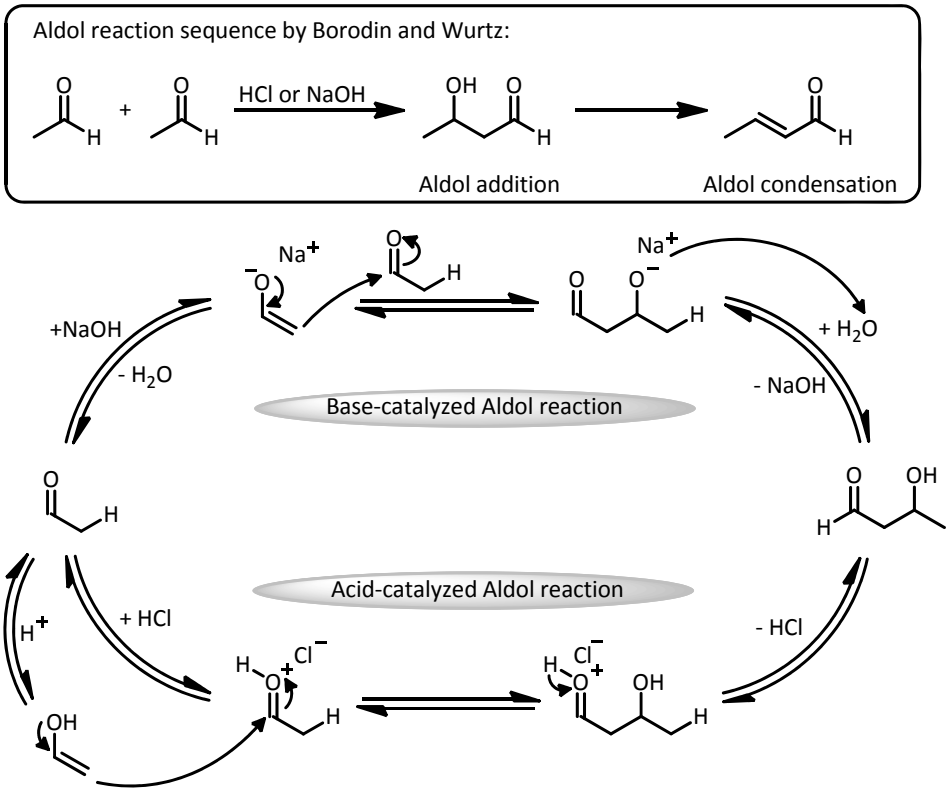


Figure 14. *The aldol reaction catalyzed by acids and bases, originally observed by Borodin and Wurtz.*

However, aldol reactions are not restricted to aldehydes. Ketones can be utilized as electrophiles as well, and the role of the nucleophile can, in theory, be represented by a vast array of enolizable carbonyl compound, such as ketones, esters and others. The enolization of the nucleophilic counterpart can be accomplished using acids or bases as catalyst, already illustrated in the original publications of Borodin and Wurtz.

2.2.1 Stereoselectivity in aldol reactions

Obviously aldol products bear stereocenters, a fact that led to massive research efforts towards stereoselective aldol reaction processes. To get diastereo- and enantioinduction, two major strategies can be followed:

1. the installation of stereocenters in the starting materials (auxiliary- or substrate-controlled aldol reaction),

2. the use of chiral catalysts (catalyst-controlled aldol reaction).

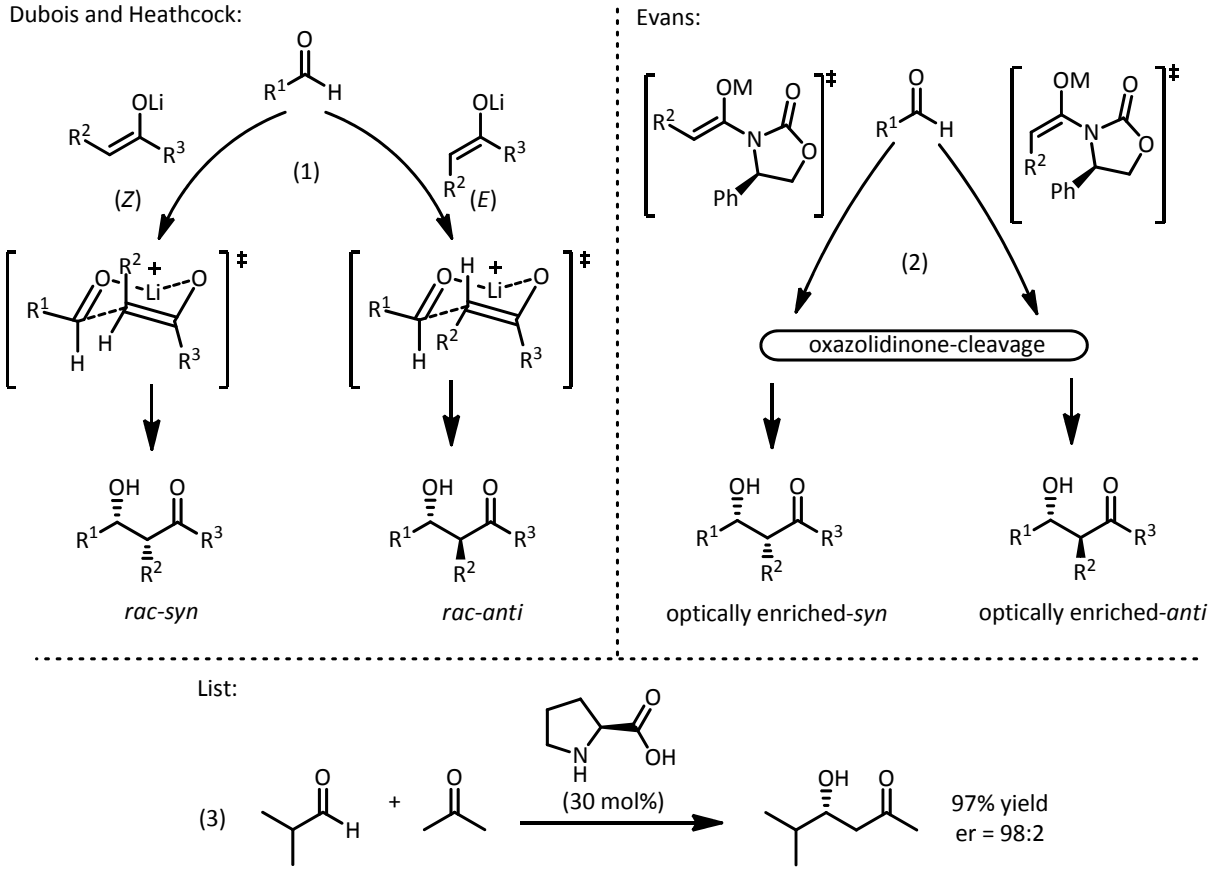


Figure 15. *Different approaches towards selective aldol reactions.*

The diastereoselectivity of aldol reactions can be controlled by the enolate geometry. First studies regarding this behaviour go back to the groups of Dubois and Heathcock in 1967 and 1976 respectively.[45] They described the reaction outcome of lithium enolate additions to aldehydes, resulting in the *syn*-diastereomers for (*Z*)-enolates and *vice versa* (Fig. 15, eq 1). These selectivities can be explained using six-membered Zimmermann-Traxler transition states. Later Evans and many others extensively studied the influence of chiral auxiliaries attached to the enolates.[46] With this strategy various aldol reactions could be realized with

high enantioselectivities as well (Fig. 15, eq 2). The use of stoichiometric chiral promoters on the enolate proved very useful.[47] Although reliable, the aforementioned transformations require stoichiometric amounts of a Lewis acid *and*/*or* a chiral auxiliary, leading to large amounts of waste, encumbering the atom economy.

An ideal solution to this problem is the direct, catalytic asymmetric aldol addition of unmodified starting materials. This idea goes back to the Hajos-Parrish-Eder-Sauer-Wiechert reaction from 1971, an intramolecular aldol-reaction using the amino-acid proline as catalyst.[48] However it was not until the year 2000, that List and co-workers became aware of the true potential of proline **14** for the biologically inspired direct aldol addition of acetone to aldehydes (Fig. 15, eq 3).[11a] The reactive intermediate is an enamine, related to Stork's enamine chemistry,[49] which attacks the electrophile with high enantioinduction. This approach and later examples stimulated eager research in the field of aminocatalysis.[50] However, a major bottleneck of these organocatalytic transformations is the catalyst turnover, often resulting in high catalyst loadings (usually between 10 and 20 mol%). Artificial peptide-catalysts, as presented by Wennemers et al., are a powerful exception, allowing for catalyst loadings of 1 mol% or lower.[51] Other approaches towards the direct aldol reaction of unmodified starting materials are scarce, often based on complicated catalyst systems or especially reactive substrates.

Leading contributions by Trost and Shibasaki make use of bimetallic or heteropolymetallic Zn- or Ln-based systems, offering a double activation of electrophile and nucleophile at the same time (see Fig. 16).[52] Recently, another much simpler activation mode emerged, the Brønsted-acid catalyzed direct aldolization. Stimulated by seminal studies from the Akiyama group,[53] Blanchet and co-workers illustrated, that chiral phosphoric acids mediate the transformation of cyclohexanones and glyoxylates efficiently (Fig. 16)[54]. However this system is not applicable to a broader aldehyde scope yet and glyoxylates are among the most reactive electrophiles for aldol chemistry. A particular difficulty in the field of aldol reactions is the lacking employment of ketones or very simple aldehydes, since these electrophiles are much less reactive. Concerning nucleophiles, it is disadvantageous that esters can not be employed directly, although products arising from such transformations would be highly valuable.

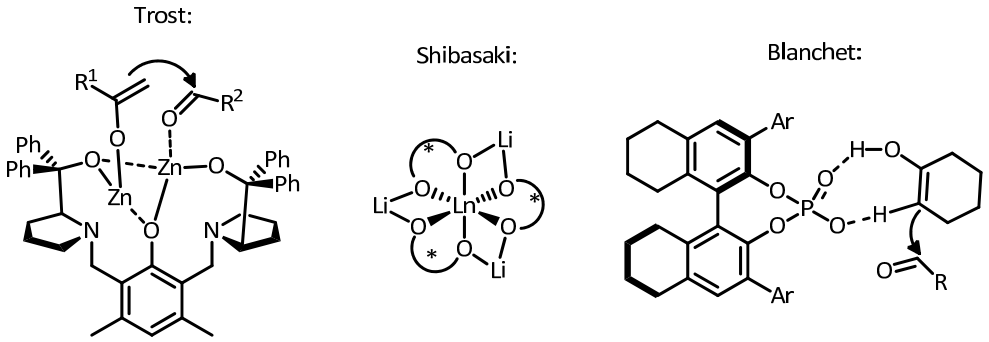


Figure 16. *Direct aldol reaction approaches by Trost, Shibasaki and Blanchet.*

2.2.2 Mukaiyama-type aldol reactions

The most powerful approach for general catalytic asymmetric aldol reactions is based on the preformation of stable, isolable latent enolates, derived from structurally diverse aldehydes, ketones or esters.[55] The cornerstone of this important concept was set by the workgroup of Mukaiyama in the 1970s.[56] In these early studies the use of preformed silyl enolates derived from ketones and esters was described which gave the name to all following reactions using latent silyl enolates: *the Mukaiyama-type reactions*. These preformed enolates reacted smoothly with carbonyl compounds, under stoichiometric Lewis acid activation of the electrophiles (Fig. 17).

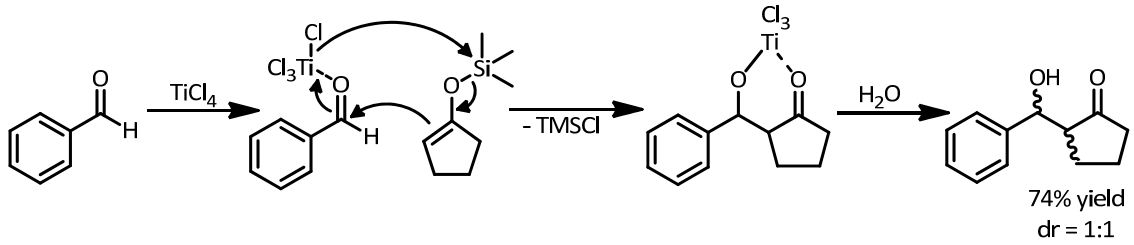


Figure 17. *The first Mukaiyama aldol reaction.*

In the original procedure the titanium-chelate intermediate had to be hydrolyzed for the liberation of the product, obviating a catalytic use of the Lewis acid by strong ligation. However, the potential of this method for truly catalytic versions became clear. The same laboratory reported trityl perchlorate **15** ($TrClO_4$) as an efficient catalyst for these transformations in an early organocatalytic example (Fig. 18).[57] These studies also discuss, that the (*E*)-, (*Z*)-geometry of the silyl enolates does not influence the diastereoselectivity, a trend that was corroborated in other catalytic systems. This led to the proposal, that a lack of chelation can lead through an open transition state rather than a Zimmermann-Traxler situation.[58] The products obtained incorporated the silyl group on the alcohol oxygen,

showing the complete silyl transfer during the mechanism, presumably featuring a terminal formal transsilylation.

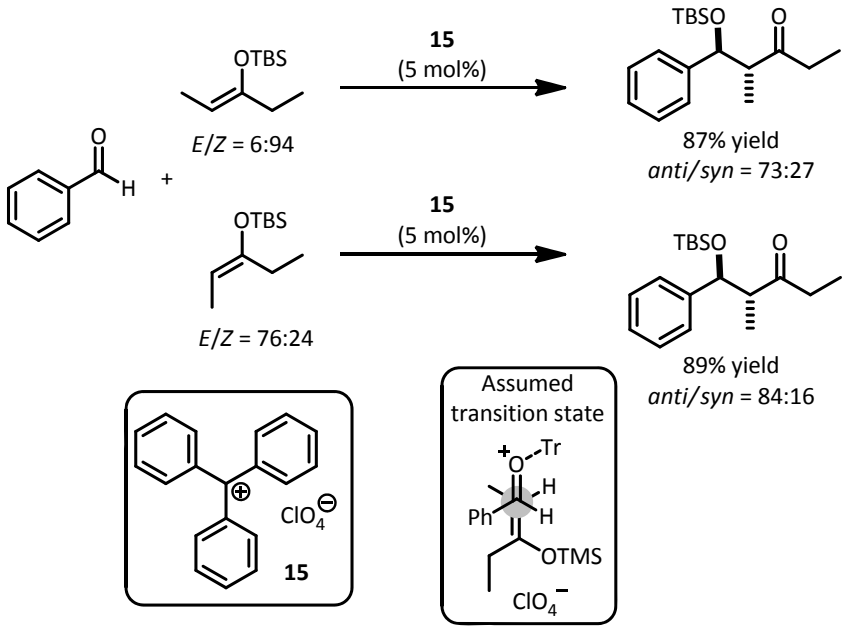


Figure 18. *The first catalytic, diastereoselective Mukaiyama aldol reaction.*

Subsequent studies towards enhanced diastereoselectivity were carried out, showing that by proper choice of the substituents and the Lewis acid activator the diastereoselectivity can be controlled for a wide range of substrates.[59] An approach to obtain high enantioselectivity in Mukaiyama-type aldol additions was the installation of defined stereocenters in the nucleophile. With this strategy, analogously to the Evans auxiliary approach, Gennnari and Helmchen obtained products with remarkably high enantioselectivities.[60]

However, a catalytic enantioselective version of the reaction remained elusive. As a first, and only moderately successful example, Reetz et al. reported the use of Al- and Ti-based Lewis acids **16** and **17** offering promising catalyst turnover (see Fig. 19).[61]

This seminal report stimulated further research, and an impressive number of studies towards catalytic enantioselective reactions followed.

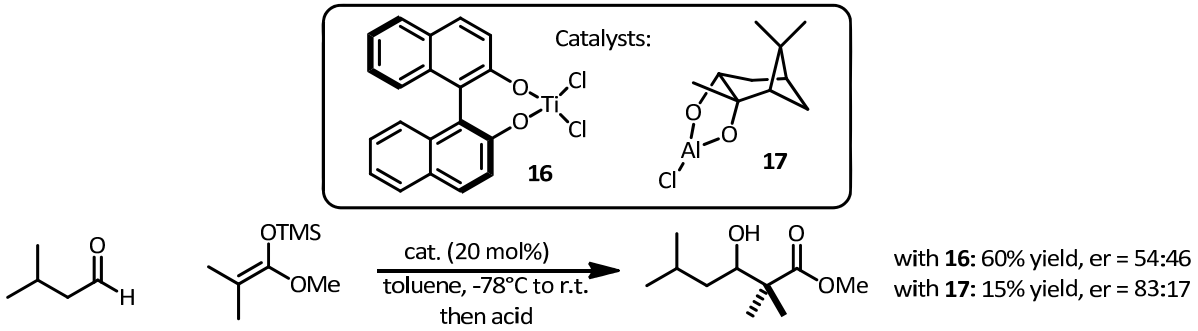
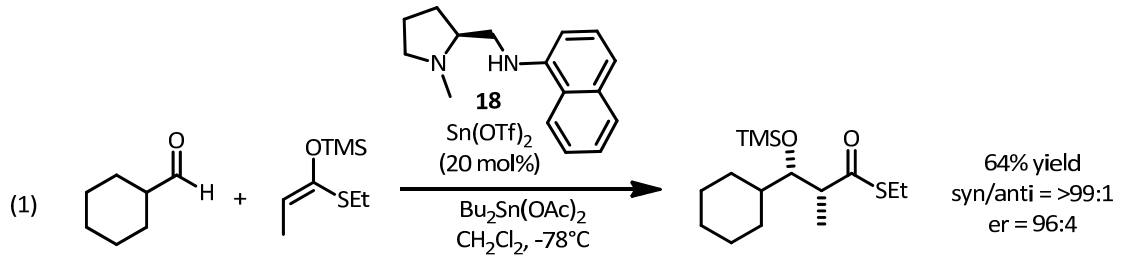


Figure 19. *The first catalytic enantioselective Mukaiyama aldol reaction.*

As one very potent system, the group of Mukaiyama presented Sn-based chiral Lewis acids with ligand **18**. By these catalysts highly enantioenriched products could be observed for the first time (see Fig. 20, eq 1).[62]



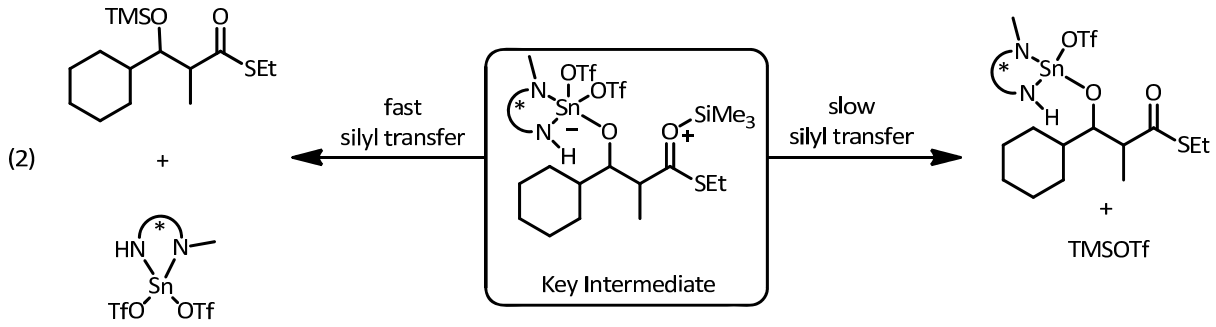


Figure 20. *Sn-(II)-catalyzed Mukaiyama aldol reaction.*

One very important assumption from these seminal contributions was the existence of an achiral reaction pathway compromising the enantioselectivity. The genesis of this pathway was ascribed to TMSOTf, which is a powerful achiral Lewis acid itself, arising from a slow silyl transfer step in the key intermediate (see Fig. 20, eq 2).[63] The Sn-(IV)-additive is thus believed to trap this achiral pathway. Later the same group showed the incorporation of a polar solvent, such as propionitrile, enhancing the rate of silyl transfer and avoiding the use of an additive.[64]

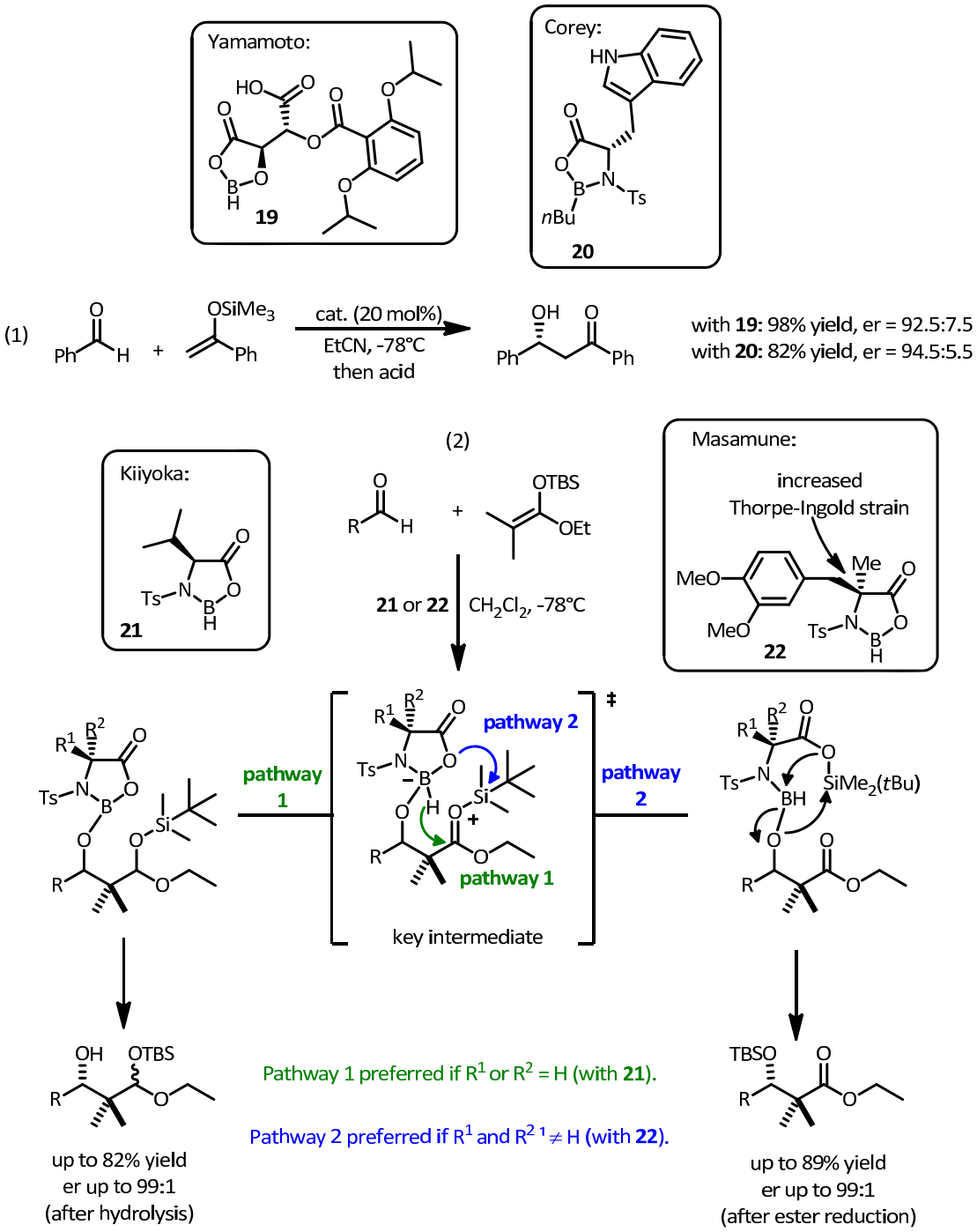


Figure 21. *Boron Lewis-acid catalyzed Mukaiyama aldol reactions.*

Another very abundant catalyst-class is based on boranes which are ligated by carboxylic- or amino-acids. Originally the group of Yamamoto described the tartaric acid derived borane **19** as an efficient catalyst for Diels-Alder reactions.[65] However, these catalysts proved equally efficient for the activation of aldehydes in Mukaiyama-aldol reactions (Fig. 21, eq 1).[66] The boranes **20**, introduced by Corey and co-workers, are based on the natural amino acid tryptophane, offering an indole moiety as a π-stacking entity (Fig. 21, eq 1).[67] With these

catalysts high enantioselectivities were observed aswell, most probably due to very well ordered transition states.

The Kiiyoka group employed amino acid sulfonamide-derived boranes **21** as stoichiometric carbonyl group activators (Fig. 21, eq 2).[68] Interestingly they showed that the incorporation of a TBS- rather than a TMS-group led to the formation of an acetal product. Possibly this behavior can again be explained by a slow silyl transfer on the alcohol oxygen, leading to a competing intramolecular hydride transfer pathway, obviating the efficient catatytic use of **21**.

To circumvent this undesired side reaction, the group of Masamune introduced catalysts like **22** with a geminal substitution in the backbone, increasing the silicon-shuttling rate by a Thorpe-Ingold effect (Fig. 21, eq 2).[69] Kiiyoka and co-workers simply changed the solvent to nitromethane, resulting in a reaction which also circumvented acetal-formation efficiently.[70]

The already mentioned studies by the workgroups of Mukaiyama and Reetz showed the high potential of Ti-(IV)-catalysts for their use in enantioselective aldol chemistry. However, the preparation of the catalyst proved unreliable, diminishing its synthetic use. For this reason much effort was spent to develop other Ti-based complexes for Mukaiyama aldol reactions. The influence of titanium-(IV)-catalysts was extensively studied by the group of Mikami.

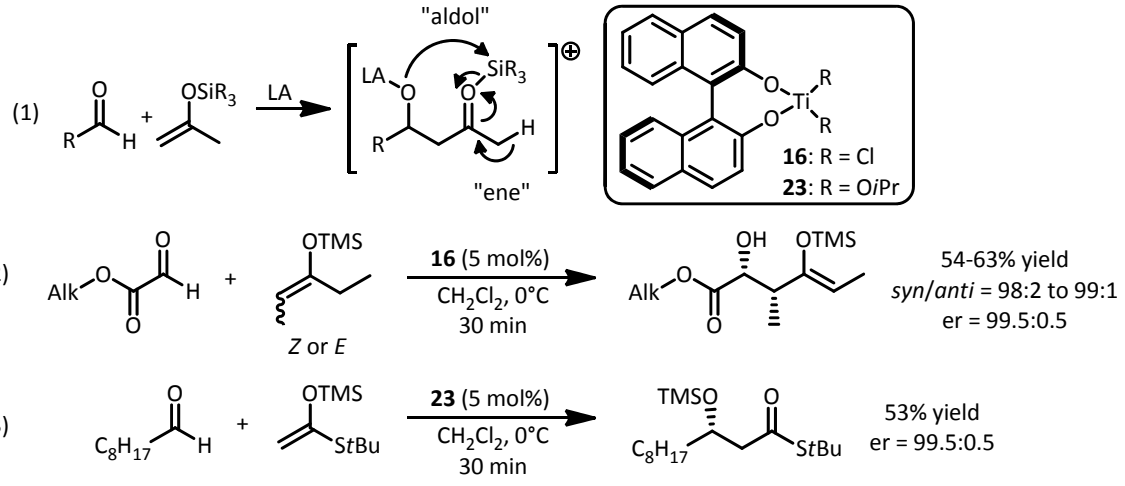


Figure 22. *Ti-(IV)-catalyzed Mukaiyama aldol- and Ene-reactions.*

The problem of an inhibited silyl transfer as a consequence of the concurrence between an aldol- and ene-reaction pathway was identified as an important issue for the development of really efficient catalyst systems (Fig. 22, eq 1).[71]

In the reported reactions the products obtained were accordingly the protected hydroxy-enols (Fig. 22, eq 2). The same observations were made by the group of Kuwajima, however using achiral Al-based catalysts instead.[72] The Mikami group also studied titanium-alkoxide complexes **23** as very efficient and selective catalysts (Fig 22, eq 3).[73]

Later the workgroup of Carreira further addressed the problem of silyl transfer by studying new ligand systems in Ti-(IV)-complexes (Fig. 23, eq 1).

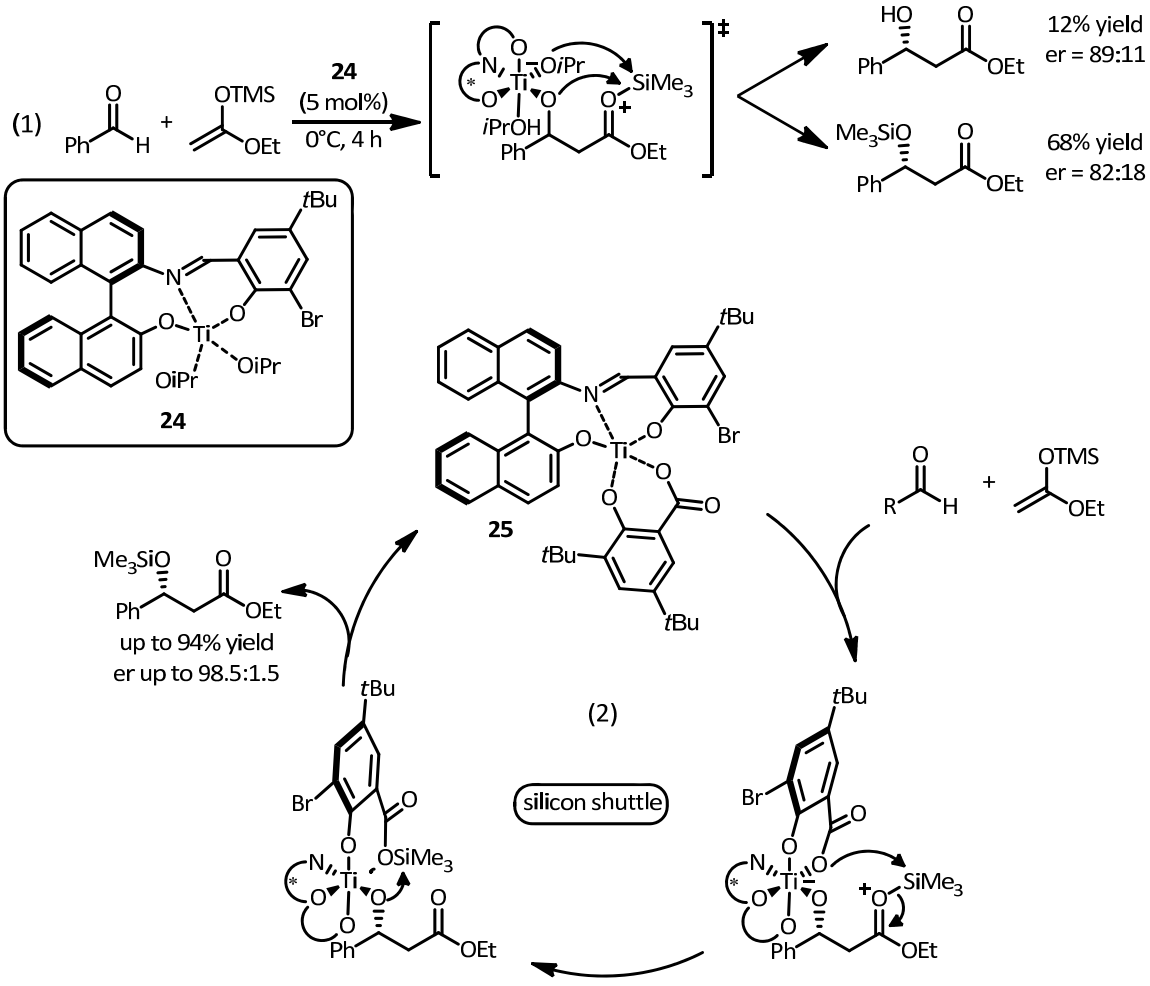


Figure 23. *Ti-(IV)-Schiff base complexes for Mukaiyama aldol reactions.*

The introduction of a chiral BINOL-derived Schiff-base in combination with Ti(O*i*Pr)$_4$ led to a very reactive and efficient catalyst (**24**) for reactions between aldehydes and silyl ketene acetals. Remarkably though, the product distribution was not well defined, consisting of silylated and non-silylated β-hydroxyesters.[74]

By changing the two isopropoxides to a less basic ligand, namely a salicylate (as in structure **25**), the reactions were successfully tuned towards complete silyl transfer with excellent

enantiocontrol and full conversions (Fig. 23, eq 2). This ligand system seems to have the following major advantages:

1. a weakening of the ligand-titanium interaction strengthens the Ti-aldehyde binding, increasing the enantiocontrol by a tighter contact.

2. the labile, but tethered salicylate ligand shuttles the silicon group to the aldolate oxygen, suppressing the achiral silicon-catalyzed pathway which was already discussed.[75]

Until now, although more than 15 years old, this procedure is still a landmark for Mukaiyama aldol reactions regarding aldehyde and nucleophile scope, catalyst loading, enantiocontrol and conversion.[VII] However this method bears some drawbacks, such as the catalysts synthesis and stability and operational simplicity.

Despite the reported catalytic systems focusing on B-, Al- and Ti-species, there are many other developments concerning Lewis acid catalysts for aldol reactions (Mukaiyama-type and others). Among these are various metal systems, *e.g.* based on Rh-,[76] Zn-,[77] Ln-,[78] Cu-,[79] Sn-[80] or Gd.[81] However, although there might be an ideal catalyst for each individual problem in Mukaiyama aldol chemistry, a lack of generality and efficiency, may it be with regard to the electrophile/nucleophile scope or catalyst performance, can still be observed. Remarkably for example, ketones remain a notoriously difficult substrate class, only being solved with extremely activated substrates and high catalyst loadings, as demonstrated by *e.g.* Harada using a very reactive nucleophile.[82]

[VII] The "Lewis base activation of Lewis acids", an activation mode introduced by the group of Denmark is another powerful approach, which will be discussed later.

2.3 Vinylogous Mukaiyama aldol reactions (VMARs)

A far less developed Mukaiyama-type transformation is the vinylogous extension of the aldol reaction: *the vinylogous Mukaiyama aldol reaction (VMAR).* While the normal aldol reaction adds two carbon-atoms to the carbonyl compound (Fig. 24, eq 1), the VMAR adds four carbons in a single operation by means of a formal dienolate addition (Fig. 24, eq 2).

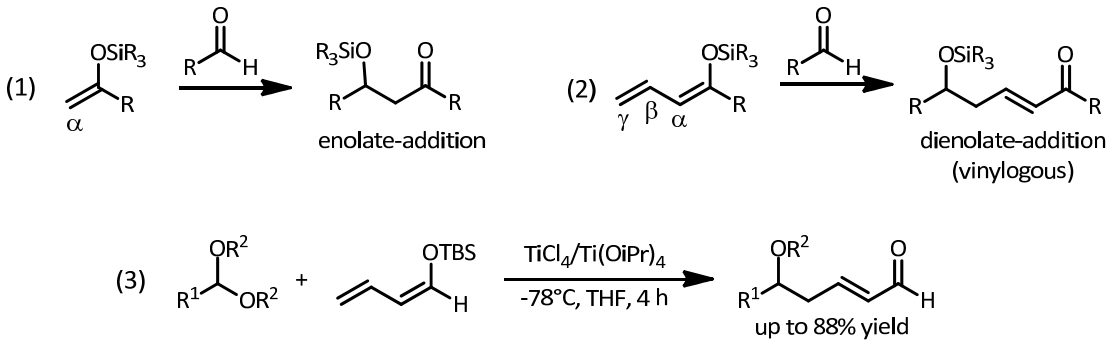


Figure 24. *Vinylogous aldol addition and first examples by Mukaiyama.*

The first studies on these extended aldol reactions were likewise reported by Teruaki Mukaiyama in 1975.[83] Ti-(IV)-catalysts proved to be efficient mediators as well (Fig. 24, eq 3).

2.3.1 The principle of vinylogy

Whereas enolates for aldol reactions are pretty simple nucleophiles, their vinylogous congeners possess significant differences. The fact that they act under the governance of a conjugated π-system over four carbon-atoms, raises a concern about site selectivity, namely α- vs. γ-addition. Fuson already discussed in 1935, that conjugated esters such as crotonates or sorbates react with ethyl oxalate at their peripheric carbon atoms.[84]

Rathke (Fig. 25, eq 1) and Schlessinger (Fig. 25, eq 2) examined the possibility and potential of (metallo)-dienolate formation.[85] However, they showed that for metallodienolates α-reactivity is a common phenomenon, which can be synthetically useful as well. It was until 1975, that Mukaiyama developed the silyl-version of the above mentioned reaction,[83] in which a dienolate reacts preferably in its peripheric position, most probably due to the electronic and steric influence of the silicon.[86]

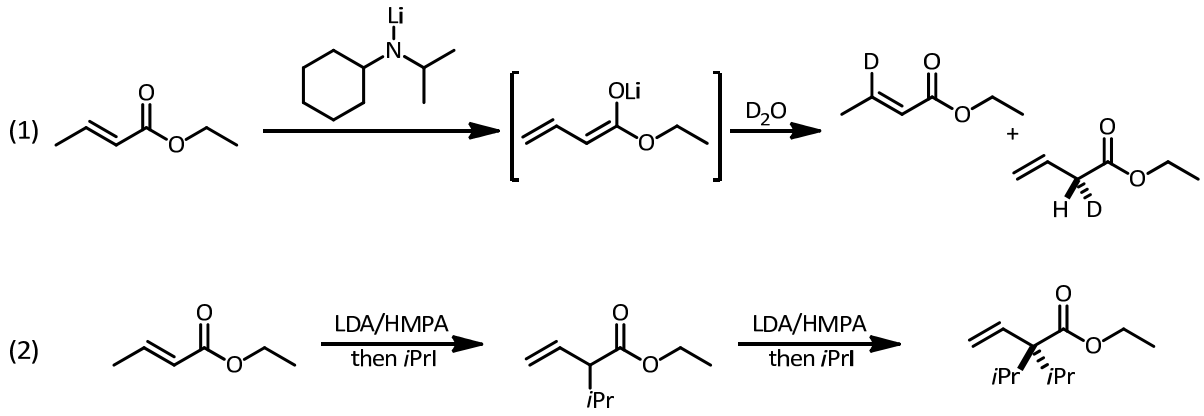


Figure 25. *Dienolate-reactivity experiments described by Rathke and Schlessinger.*

As a consequence, various strategies for the exploitation of vinylogous aldol reactivity followed (Fig. 26) and different research groups utilized *e.g.* acetoacetate equivalents, dioxinone-derivatives, silyloxy-furanes and -pyranes and crotonic ester-derivatives, with the first three substrate classes being most commonly used for various synthetic purposes.[87]

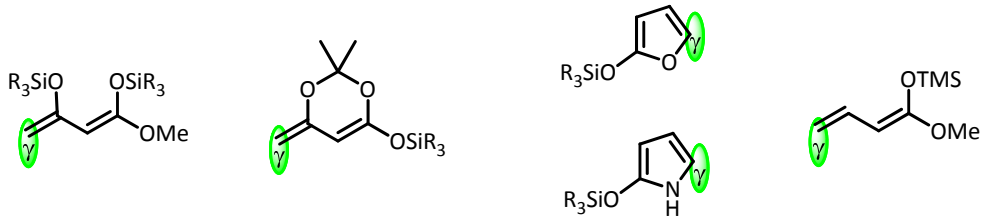


Figure 26. *Different classes of vinylogous nucleophiles.*

This may be due to their inherent reactivity and rather straightforward reaction control, considering the site-selectivity. However, it is clear that open chain dienolates of the latter class are particularly underrepresented in general enantioselective approaches, although offering very valuable synthetic possibilities. This survey therefore concentrates more on acyclic substrates, however not without addressing groundbreaking methods developed for the previously mentioned nucleophile classes.

2.3.2 Vinylogy in stereoselective aldol reactions

Following the seminal work of Mukaiyama, and entering the realm of asymmetric catalysis, the group of Sato and Kaneko was the first to investigate a catalytic enantioselective version of the VMAR in 1994 (Fig. 27),[88] utilizing the tartaric-acid derived acyloxyborane complex **19**, previously described by the Yamamoto group.[66]

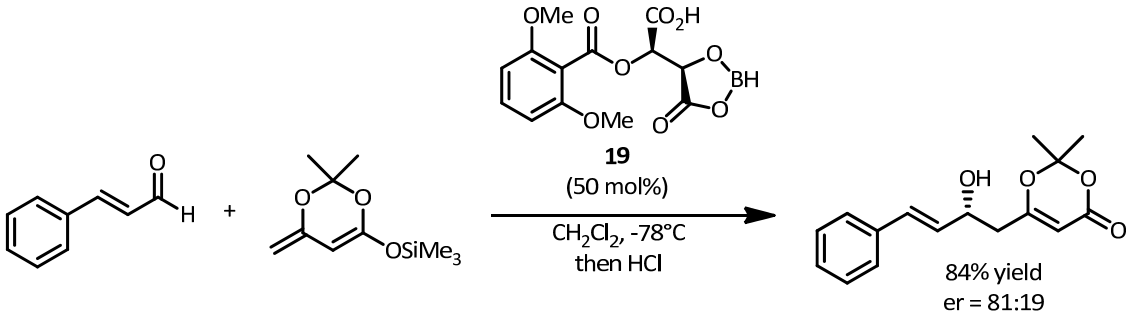


Figure 27. *The first catalytic asymmetric VMAR reported by Sato et al.*

Due to the relatively close similarities in structure and reactivity of the nucleophilic reaction partners, many developments in VMAR were based on systems originally introduced for normal Mukaiyama aldol reactions. Equally, these reactions suffer from the same drawbacks, such as possible achiral silyl-cation catalyzed reactions. Therefore at the outset of these developments, high catalyst loadings and slow additions of reactants were necessary. It is not surprising, that the group of Sato and Kaneko identified the previously introduced Mikami-catalyst **23**[71] as equally powerful for the vinylogous aldol additions of dioxinone-derived nucleophiles to aldehydes (Fig. 28).[89]

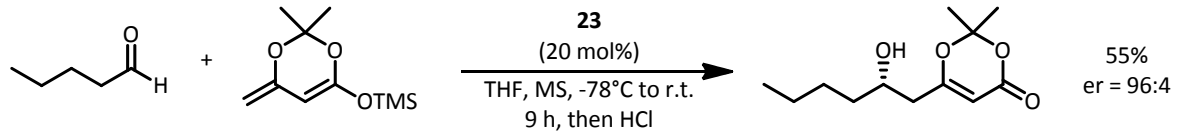


Figure 28. *Improved catalytic asymmetric VMAR by Sato et al. featuring Mikami's catalyst.*

The same catalytic system was further improved and adapted to acetoacetate-derived nucleophiles by the group of Scettri.[90]

Shortly after the achievements of Sato, the group of Carreira reported their previously introduced catalyst **25** as very efficient for dienolate additions to aldehydes. Again the success of this system lies in the labile ligands, giving efficient turnover at low catalyst loadings, resulting in no product inhibition and a tight Ti-substrate binding, which leads to high enantiocontrol (Fig. 29).[91]

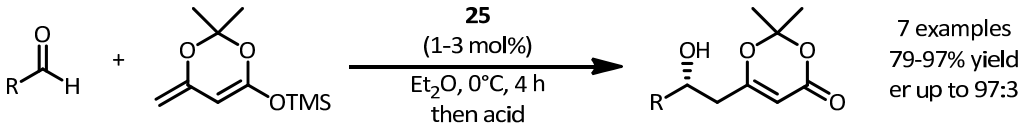


Figure 29. *The first highly enantioselective VMAR reported by Carreira.*

The potential of this method found application in the elegant total synthesis of Macrolactin A.[92]

Due to the rapid assembly of complex molecules offered by VMARs, several research groups focused on the development of more efficient methods. In 1996 the group of Evans reported the Cu-(II)-PyBox-complex **26** as a powerful chiral Lewis acid for the conduction of vinylogous Mukaiyama aldol reactions of dioxinone- and acetoacetate-derived nucleophiles with certain electrophiles (Fig. 30).[79] They implemented this strategy in their synthetic studies towards the complex natural product Phorboxazole B.[93]

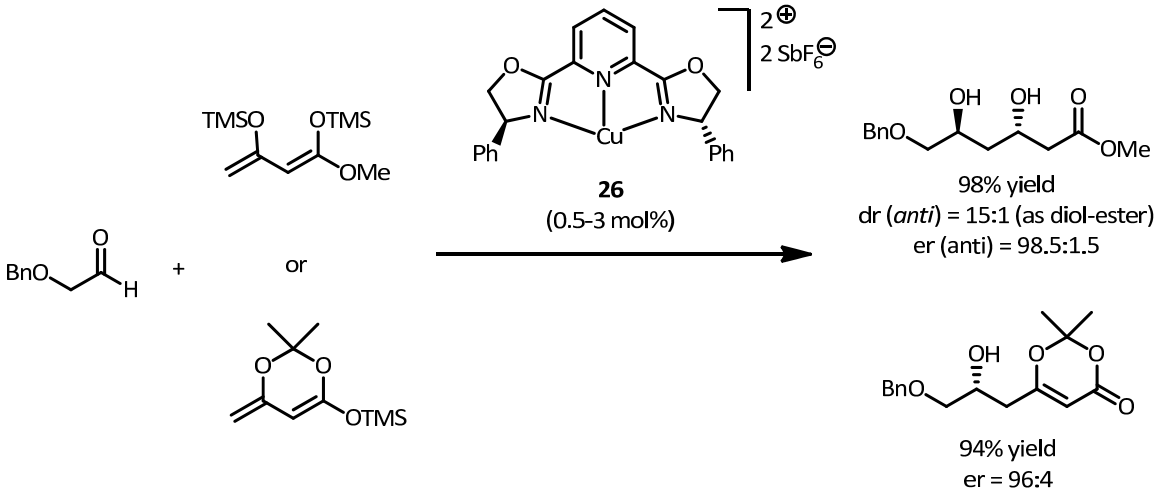


Figure 30. *Cu-Lewis acid catalyzed VMAR by Evans et al.*

As a method which was specifically designed for the aldol addition with dienolate equivalents, Carreira described the use of Cu-(II)-complexes **27** with Tol-BINAP-ligands (Fig. 31, eq 1).[94] A very remarkable feature of this procedure is the mechanistical assumption made by the same group later.[95] They actually identified metalloenolate **I** as the key intermediate. This intermediate is presumably formed by the reaction of a Cu-(I)-species which is generated transiently, and renders the entry into the catalytic cycle possible.

The group of Campagne used the same catalytic method for the conversion of open dienolates (derived from crotonic-acid derivatives) in synthetic procedures towards Macrolactin A (Fig. 31, eq 2) and the Prelog-Djerassi Lactone (Fig. 31, eq 3).[96]

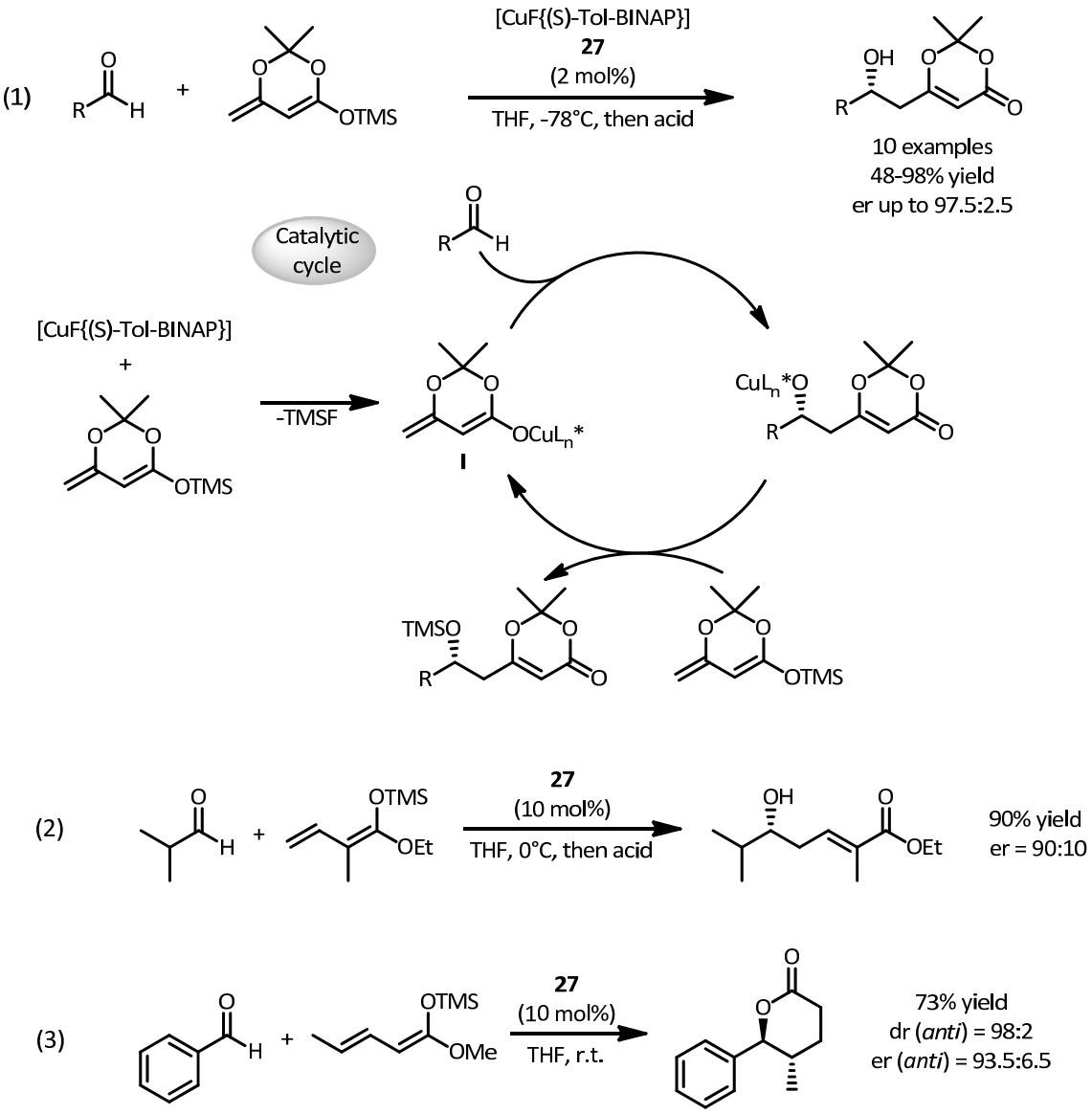


Figure 31. *The CuF{Tol-BINAP}-system* ***27*** *developed by Carreira and further used by Campagne et al.*

Exploiting the same class of open chain substrates in the context of the synthesis of structurally complex polyols and polyketides, the group of Kalesse extensively developed chiral borolidinones **28** as catalysts and mediators for VMARs (Fig. 32).[97]

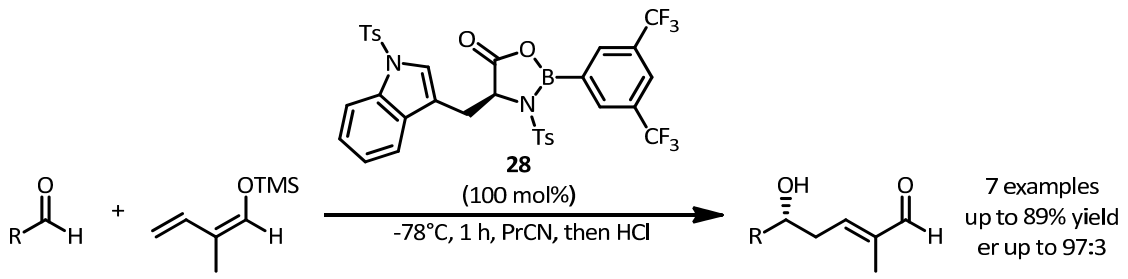


Figure 32. *Oxazaborolidinone-mediated VMAR between aldehydes and aldehyde-derived dienolates.*

Very recently they were able to make use of their systems with aldehyde-derived nucleophiles, transformations which proved very difficult with previous methods.[98] Unfortunately, the binding of the boron species is rather strong, so that a stoichiometric use of the 'catalys' is necessary, and the material has to be treated with HCl to liberate the desired reaction product.

Another example which illustrates the power of metal-based Lewis acids, are Cr-based Salen-complexes **29** which were introduced by the group of Katsuki in the year 2003 (Fig. 33).[99] Although not used for open dienolate-systems, the results considering enantioinduction achieved with the silyloxyfurane- and dioxinone-derived nucleophiles were outstanding.[100]

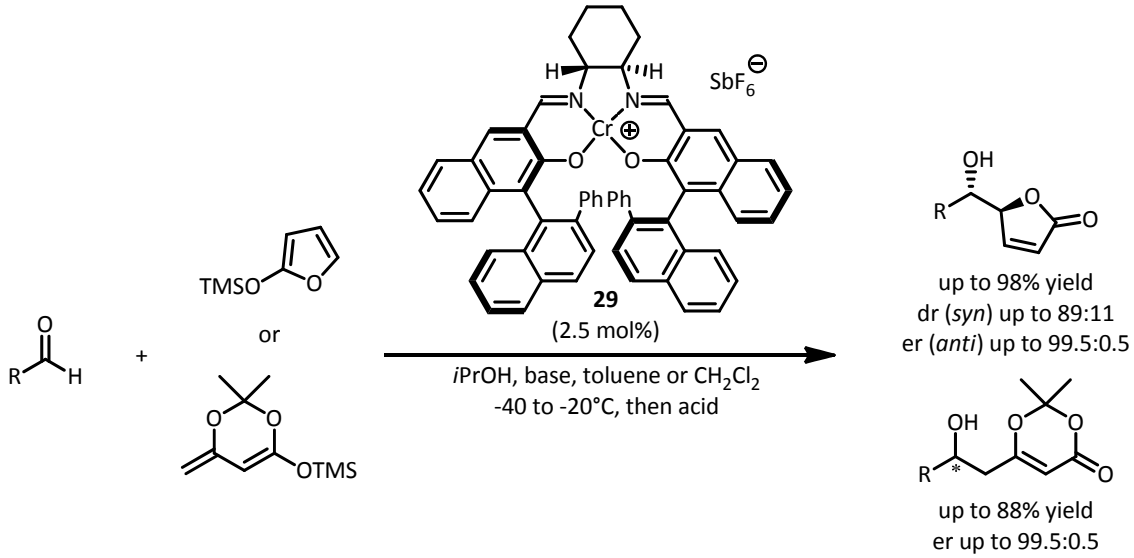


Figure 33. *Cr-salen complexes introduced by the group of Katsuki.*

As an observation from all previous examples, asymmetric Mukaiyama aldol chemistry in general and VMAR in particular is rather difficult to achieve by truly organocatalytic methods. One of the main reasons is that these catalysts can not offer a sufficient activation of the electrophiles towards the attack of these rather weak nucleophiles.[101] Nevertheless, there are some organocatalytic methods in the literature, which are based on either hydrogen bonding catalysis (general Brønsted acid catalysis) or activation by protonation (specific Brønsted acid catalysis).

Probably the first real organocatalytic example was introduced by the group of Rawal in 2005 (Fig. 34, eq 1).[102] In these studies the utility of a double activation is described. Following their mechanistic assumptions, an internally hydrogen-bond activated TADDOL-derivative **30** acts as a Brønsted acid and activates very reactive aldehydes, such as

glyoxylates. The nucleophiles presented in the substrate scope are the previously discussed dioxinone-derivatives. Following this seminal work, the groups of Scettri and Soriente (achiral version, Fig. 34, eq 2) used the strategy of hydrogen bonding catalysis (**31**) in combination with acetoacetate- and silyloxypyran-nucleophiles.[103]

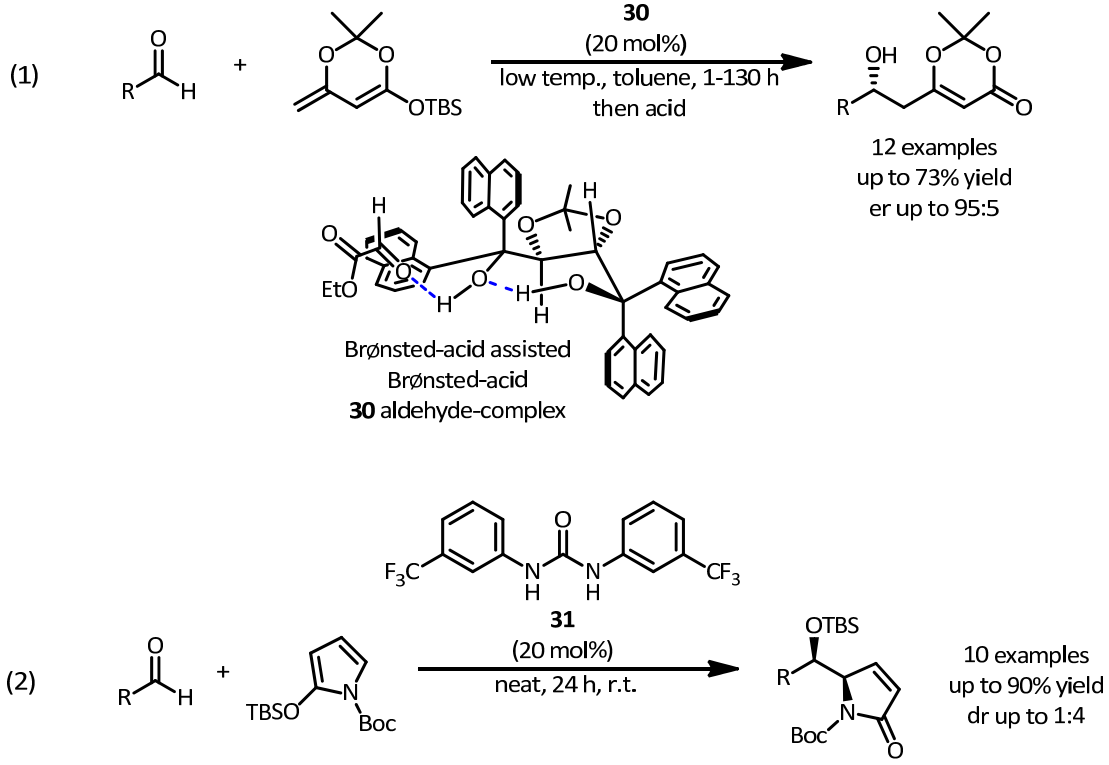


Figure 34. *Hydrogen bonding approaches presented by Rawal and Soriente.*

Following these strategies, other hydrogen bonding catalysts were successfully introduced. These achievements were based on chiral backbones attached to the hydrogen bond donors, thus rendering asymmetric vinylogous aldol reactions possible. Very useful catalysts were cinchona-alkaloid derived thioureas like **32**, as illustrated by Wang (Fig. 35, eq 1).[104]

Later the group of Feng showed that the tertiary amine moiety is basic enough to deprotonate the parent lactone *in situ*, offering the chance of a direct vinylogous aldol reaction (Fig. 35, eq 2).[105] Terada and co-workers introduced chiral guanidine catalyst **33**, activating similar substrates in the same manner (Fig. 35, eq 3).[106]

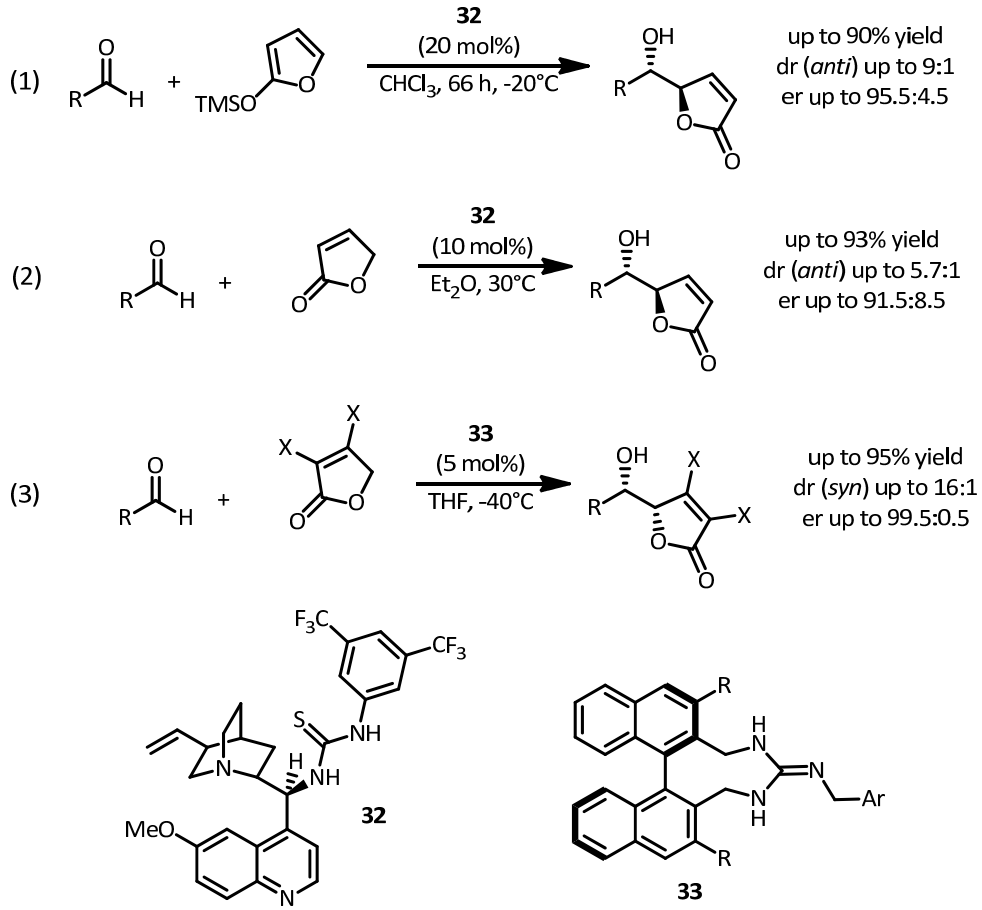


Figure 35. *Hydogen-bonding and dual-mode-catalyzed VMAR and direct vinylogous aldol reactions.*

These last examples illustrate the significance of Mukaiyama aldol reactions in current organic chemistry. Surely, a direct aldol approach is the ideal solution to all the previously described reactions and might well be realized at one point. Nevertheless with current methods one can only rudimentarily face this challenge without the help of preformed enolates. The difficulty of the employment of simple esters in direct aldol reactions further underlines the synthetic importance of the Mukaiyama aldol reaction. Since the use of silicon enolates emerged as the most convenient approach, catalysts which incorporate the inherent silicon in the catalytic cycle offer special opportunities.

2.4 Silicon Lewis-acids for aldol reactions

The incorporation of silicon into otherwise metal free catalyst systems enters the realm of Lewis acid catalysis.[107] However it is very difficult to explicitly distinguish between a Lewis acid activation or specific Brønsted acid catalysis. With this in mind it is obvious, that the Mukaiyama aldol reaction is ideally suited for catalysis which incorporates silicon in the active center. As already shown previously, silicon based Lewis acids are very powerful.

However, the complexity of silicon catalysis is unambiguous. The bond-formation between the silicon and the catalyst moiety, thus the formation of the active catalyst, occurs *in situ*. This interrelationship between the pre-catalyst and the active catalyst always opens up the possibility of a pathway without the incorporation of the (possibly chiral) catalyst moiety. This delicate behavior of Mukaiyama aldol reactions in general, and silicon-based-Lewis acids incorporating triflates in particular, was described by the group of Bosnich earlier.[108]

2.4.1 Silylated Brønsted acids as powerful Lewis acids

The Brønsted-acidity of triflic acid (TfOH) in aqueous media was shown to be in the range of very strong acids (pK_a = -5.9).[109] Furthermore it can form silylated species, which represent strong Lewis acids.[110] The parent nitrogen-based triflic-Brønsted acid, triflimide (Tf_2NH), shows a higher pK_a-value in water (pK_a = 1.7).[111] Contrarily, in gas-phase calculations Tf_2NH was shown to be more acidic than TfOH.[112] In any case, both acids can be counted to the strong acids (superacids, which are defined stronger than H_2SO_4) and a similar silylation and Lewis acid generation behavior for triflimide could also be expected.

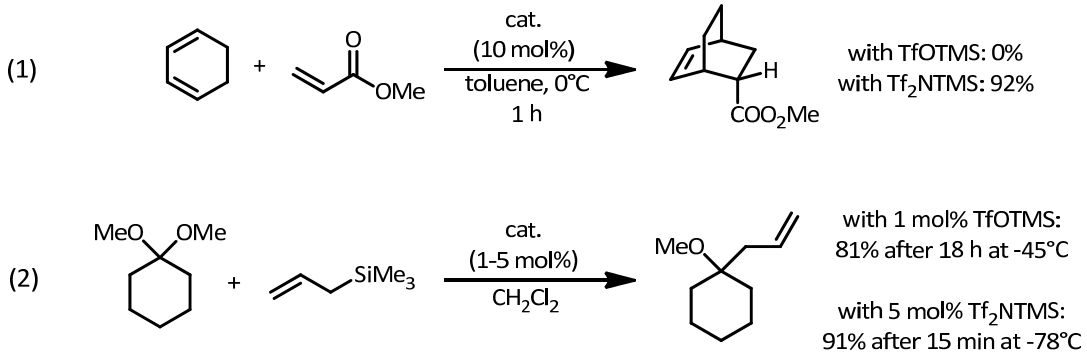


Figure 36. *First silyl-triflimide catalyzed Diels-Alder reaction and allylations by Ghosez and Mikami.*

In 1997 the groups of Ghosez (Fig. 36, eq 1) and Mikami (Fig. 36, eq 2) reported the first use of $TMSNTf_2$ as a very effective Lewis acid with a significantly better performance than the parent silyl triflate.[113] Following these reports, several groups elaborated other silyltriflimide-catalyzed non-asymmetric transformations, such as conjugate allylations of α,β-unsaturated carbonyl compounds [114] or glycosidations.[115]

After the efficiency of the catalytic system incorporating silylated triflimide had been established, it was obvious to use it for other classical reactions incorporating silicon in the reaction partners, such as the Mukaiyama aldol reactions.[116] During these studies, the mechanistical complexity became more and more apparent, thus obviating a facile

development of chiral catalyst motifs using this activation mode. Nevertheless the different possibilities of silicon-transfer reactions during the reaction mechanism led to eager studies on the real reaction intermediates. Here the group of Yamamoto intensively studied the mechanism, making use of crossover experiments, showing that the silylated triflimide most probably acts as a real Lewis acid towards the activation of aldehydes in Mukaiyama aldol transformations. However, double cross-over experiments showed the possibility of second stage intermediates as catalysts, generated from catalyst-substrate complexes *in situ* (Fig. 37).[117]

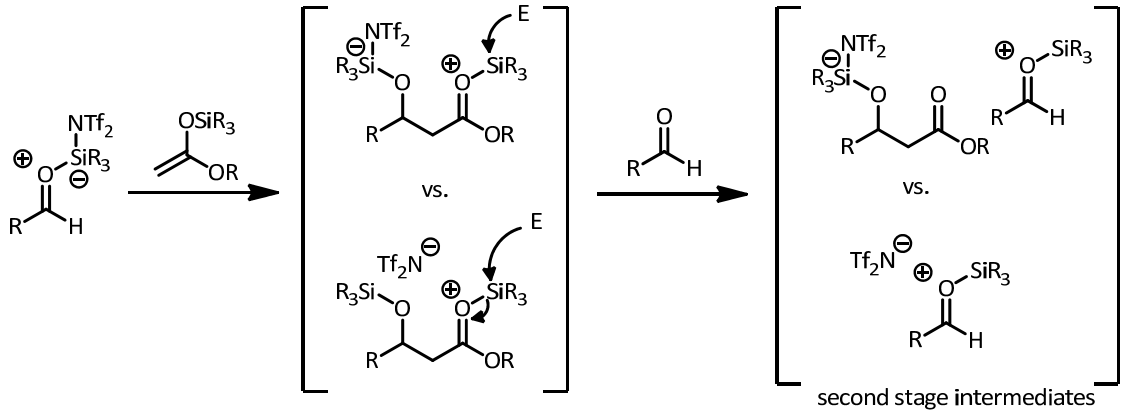


Figure 37. *Possible reaction intermediates discussed by the group of Yamamoto.*

Another cornerstone underlining the superiority of silylated strong Brønsted acids are studies from the groups of Yamamoto and later Taguchi, making use of carbon based triflated acids. Although the group of Yamamoto introduced their tetrafluorophenylbis(triflyl)methane **34** as a truly Brønsted acidic catalyst for esterifications, Friedel-Crafts acylations, acetalizations, Mukaiyama aldol reactions and Hosomi-Sakurai allylations,[118] they (Fig. 38, eq 1) and the group of Taguchi (Fig. 38, eq 2) later impressively demonstrated the potential of C-silylation of carbon-based Brønsted acids (like in **35** and **35a**).[117, 119]

In comparison studies it was shown, that the Lewis acidity of carbon-based silylated Lewis acids can be ranked even higher than that of triflate or triflimide-derived catalysts. One common feature of all silylated Brønsted acid-based Lewis acid catalysts is the self repairing mechanism, which occurs in the presence of silylated nucleophiles, such as silyl enolates (Fig. 38, eq 3).

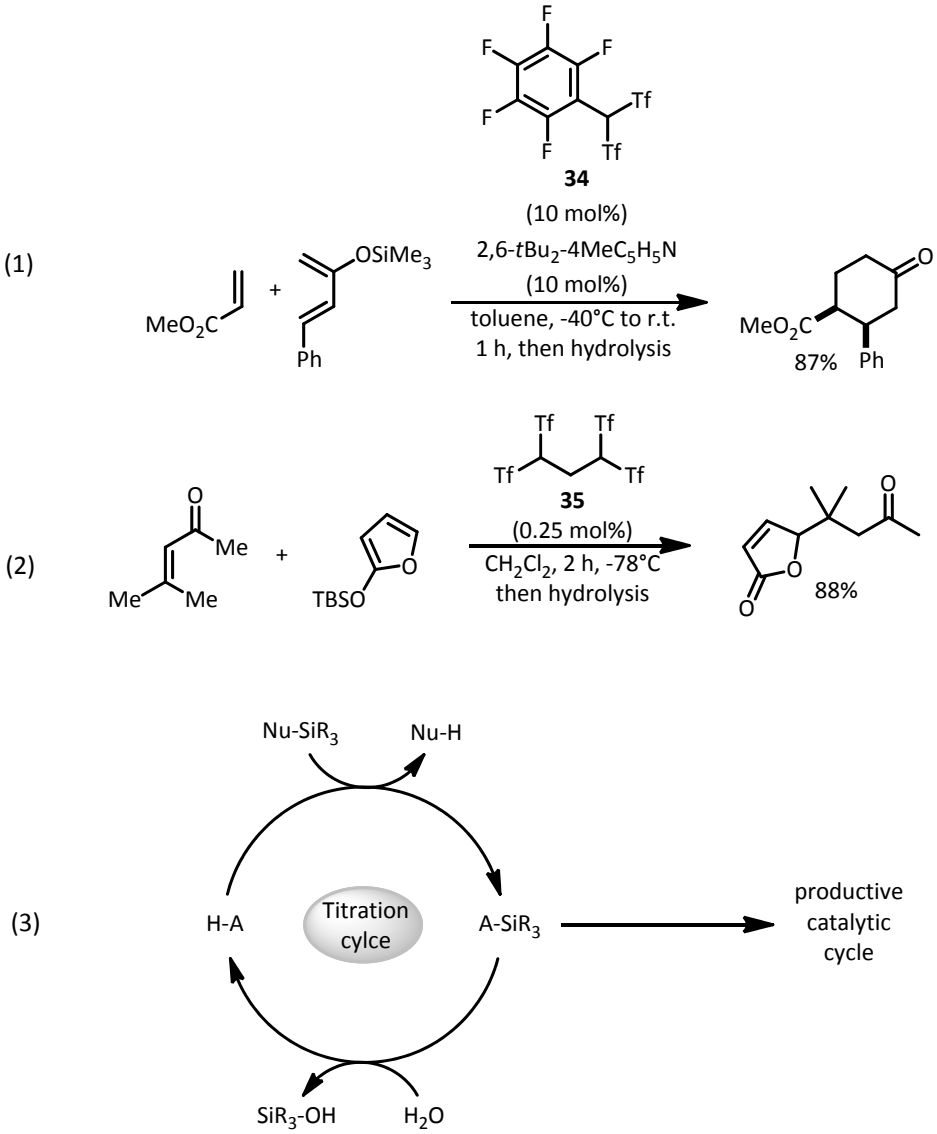


Figure 38. *Very strong carbon based Lewis acids and hydrolysis cycle for silylated Brønsted acids.*

Water traces, which may be present in the reaction mixture, are removed by a protodesilylation event which consumes nucleophile under formation of silanol and the corresponding desilylated ester, until the water is completely removed. Thus, this event can be considered as a preceeding water exclusion cycle, which occurs before the silylated Brønsted acid can enter into the "productive" catalytic cycle.

2.4.2 Lewis base activation of Lewis acids

Another very powerful strategy for the asymmetric catalysis of Mukaiyama aldol reactions is based on the principle of "Lewis-base activation of Lewis-acids", introduced by the group of Denmark.[120] Since this concept is based on very reactive hexacoordinate silicon-intermediates, it can be traced back to the previously developed Lewis-base catalyzed aldol reactions with trichlorosilyl enolates.[121] In these early studies of the Denmark group, the combination of trichlorosilyl enolates and Lewis base catalyst **36** presumably leads the reaction through a closed transition-state (Fig. 39), resulting in *anti*-diastereoselectivity which is normally not observed in Mukaiyama type aldol reactions. In a sense, the inherent reactivity of trichlorosilyl enolates can be considered as the attached Lewis acid, which is only further activated through Lewis-base coordination.

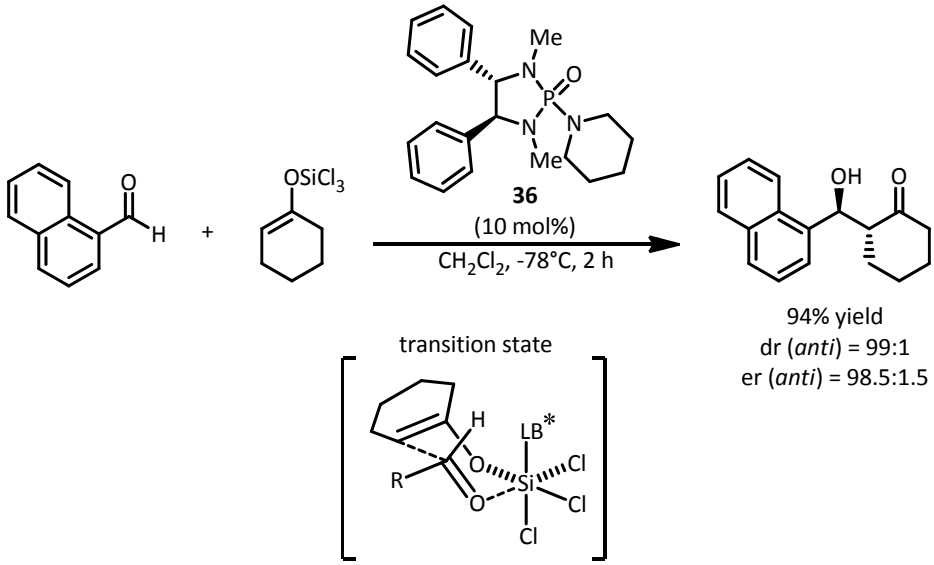


Figure 39. *Lewis base catalyzed Mukaiyama aldol reactions of trichlorosilyl enolates.*

In the concept of Lewis-base activation of Lewis acids, the rather weak Lewis acid $SiCl_4$ (**37**) coordinated by a chiral bidentate Lewis base **38**, is converted into a much stronger hexavalent Lewis acid **39** (Fig. 40, eq 1). With this concept for aldol chemistry, Denmark and co-workers did not only realize a very powerful method for 1,2-selective Mukaiyama aldol reactions (Fig. 40, eq 2),[122] but also the most versatile solution for vinylogous Mukaiyama aldol reactions known to date (Fig. 40, eq 3).[123]

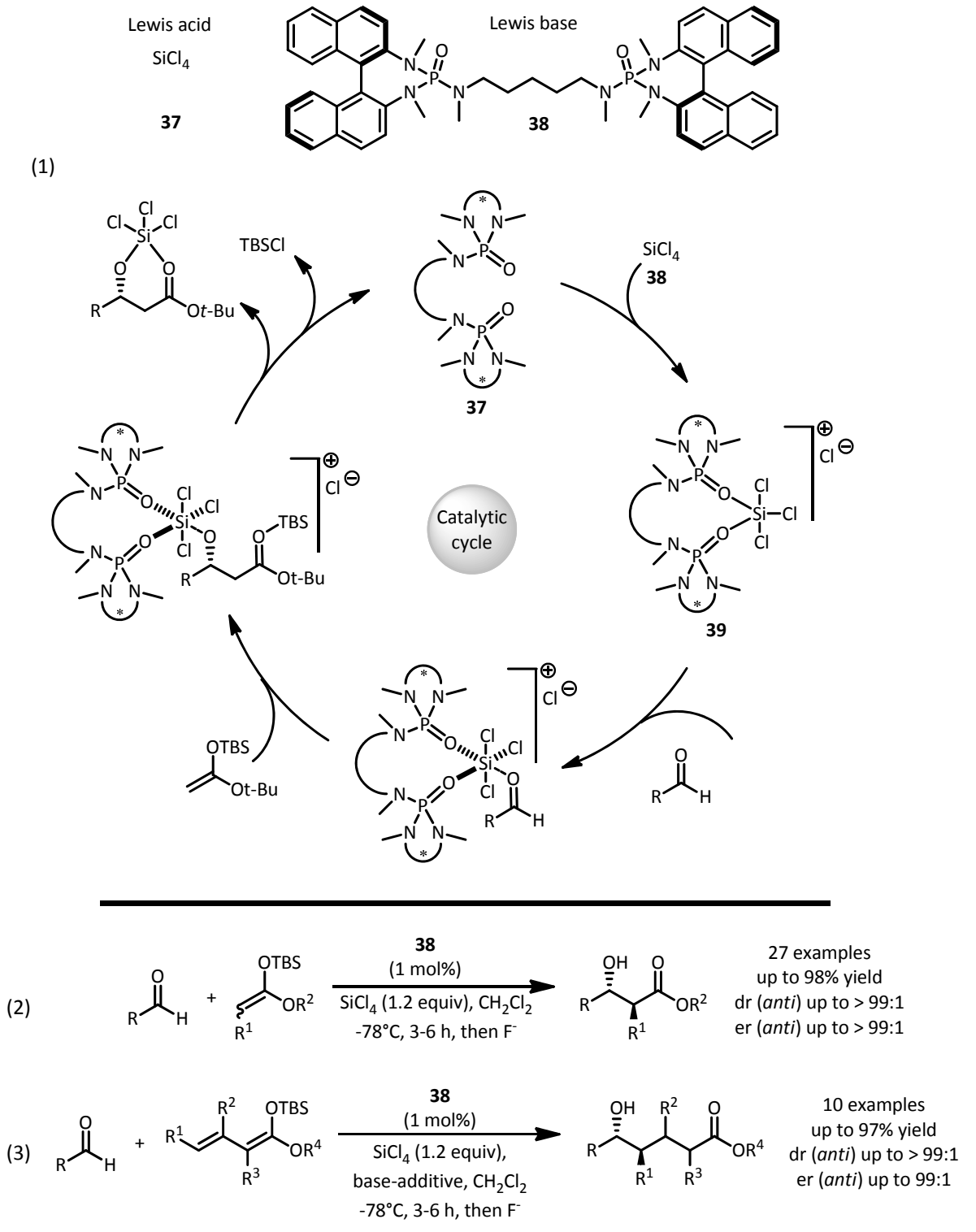


Figure 40. *Lewis base activation of Lewis acids.*

Nevertheless the reaction has one major drawback which is implemented in the mechanism. Since both silyl groups, the one from the former nucleophile *and* the one incorporated in the LA-LB-complex leave the catalytic cycle after the transformation, the reaction is not catalytic in silicon and requires one full equivalent of $SiCl_4$. Nevertheless, the reaction is still catalytic

in Lewis base at a very low loadings (1 mol%). Furthermore the very ordered and complex transition state provides excellent levels of diastereo- and enantiocontrol.

2.4.3 Disulfonimides as powerful Lewis acid pre-catalysts

When considering operational simplicity, the silylated Brønsted acids described in chapter 2.4.1 show the higher potential for a simple and general solution to Mukaiyama aldol reactions. One main point that did not find consideration previously, is that in principle the catalyst does not have to be preformed in a prior operation, as illustrated before in the series of TMSOTf, $TMSNTf_2$ and $TMSCTf_3$. Furthermore the self-repairing mechanism discussed earlier can provide high operational simplicity as well.

For this purpose we sought a platform which allows for the implementation of this activation mode into a more complex backbone, to render asymmetric transformations possible. Already in 1926, the group of Smiles showed a synthesis of *o*-benzenedisulfonimide **40** (Fig. 41).[124] Later the group of Blaschette reconsidered this Brønsted acid and intensively studied the silylation-behavior of the nitrogen and oxygen-atom (silatropy) in disulfonimide entities (Fig. 41, eq 1).[125] Simchen et al. later described the differences between silyl groups with different steric demands incorporated in the triflimide substructure.[126] They assumed that bulkier silyl groups did not only lead to a higher degree of silatropy favouring oxygen-silylation, but also rendered the catalyst more reactive for different silyl transfer reactions.

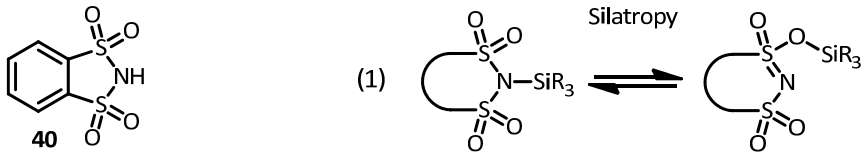


Figure 41. *Early developments on disulfonimides.*

For the first catalytic application of disulfonimide catalyst **40** one had to wait another 10 years, until the group of Barbero introduced **40** as a powerful Brønsted acid for etherifications, esterifications and acetalizations (Fig. 42).[127] Although not yet identified as a pre-Lewis acid catalyst, **40** was applied in the Hosomi-Sakurai- and the Mukaiyama aldol-reaction shortly after.[128] However, the authors discuss the mechanism of these transformations as Brønsted acid activation rather than Lewis acid catalysis.

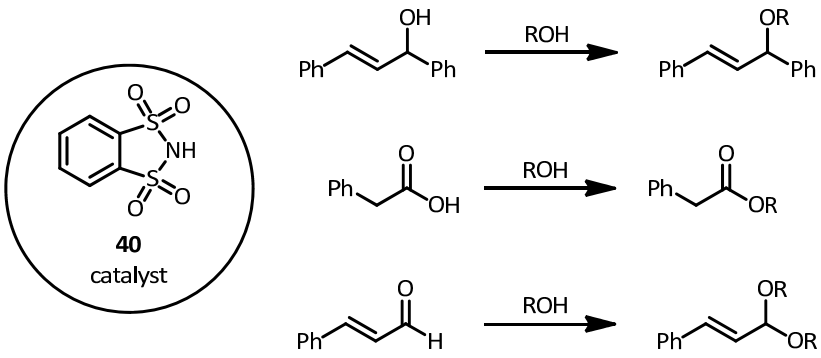


Figure 42. 40 *as a Brønsted acid catalyst as presented by Barbero et al.*

Inspired by these studies, and in continuation of our studies on asymmetric counteranion directed catalysis,[36b] we reported the implementation of the disulfonimide moiety in a 3,3'-3,5-$(CF_3)_2$-C_6H_3-substituted BINOL-backbone (**41**) and the successful use of these catalysts in the Mukaiyama aldol reaction of unactivated aldehydes with silyl ketene acetals (see Fig. 43).[129] The first generation catalyst synthesis (Fig. 43, scheme 1) was based on a substituted BINOL-**42**[130]-carbamoylation with the subsequent Newman-Kwart rearrangement, furnishing the S,O-rearranged key intermediate **43**. This step was followed by an NCS/HCl-induced oxychlorination to obtain the sulfonyl chloride, which could then be smoothly converted into the enantioenriched disulfonimide **41** by treatment with ammonia.[VIII] The catalytic performance of this catalyst in Mukaiyama aldol reactions appeared to be privileged, since neither chiral phosphoric acids[131] nor strongly Brønsted acidic phosphoric acid triflimides[132] or chiral sulfonic acids[133] could catalyze the reaction in a similar efficiency (Fig. 43, eq 2). NMR-studies showed the presence of a silylated catalyst intermediate, most probably pointing towards a mechanism including the previously discussed silatropically siliylated imide structure. Another remarkable fact was the low catalyst loading, which could be reached (0.01 mol%) without interfering with the catalytic performance. Only shortly after these accomplishments, the group of Giernoth independently reported a synthesis of the unsubstituted disulfonimide **44** following an identical strategy (Fig. 44), however lacking any catalytic application.[134]

[VIII] Since enantiopure BINOL was used, a racemate separation was not needed and racemization was not observed throughout the synthetic procedure developed by FRANK LAY / PhD thesis University of Cologne presumably 2012.

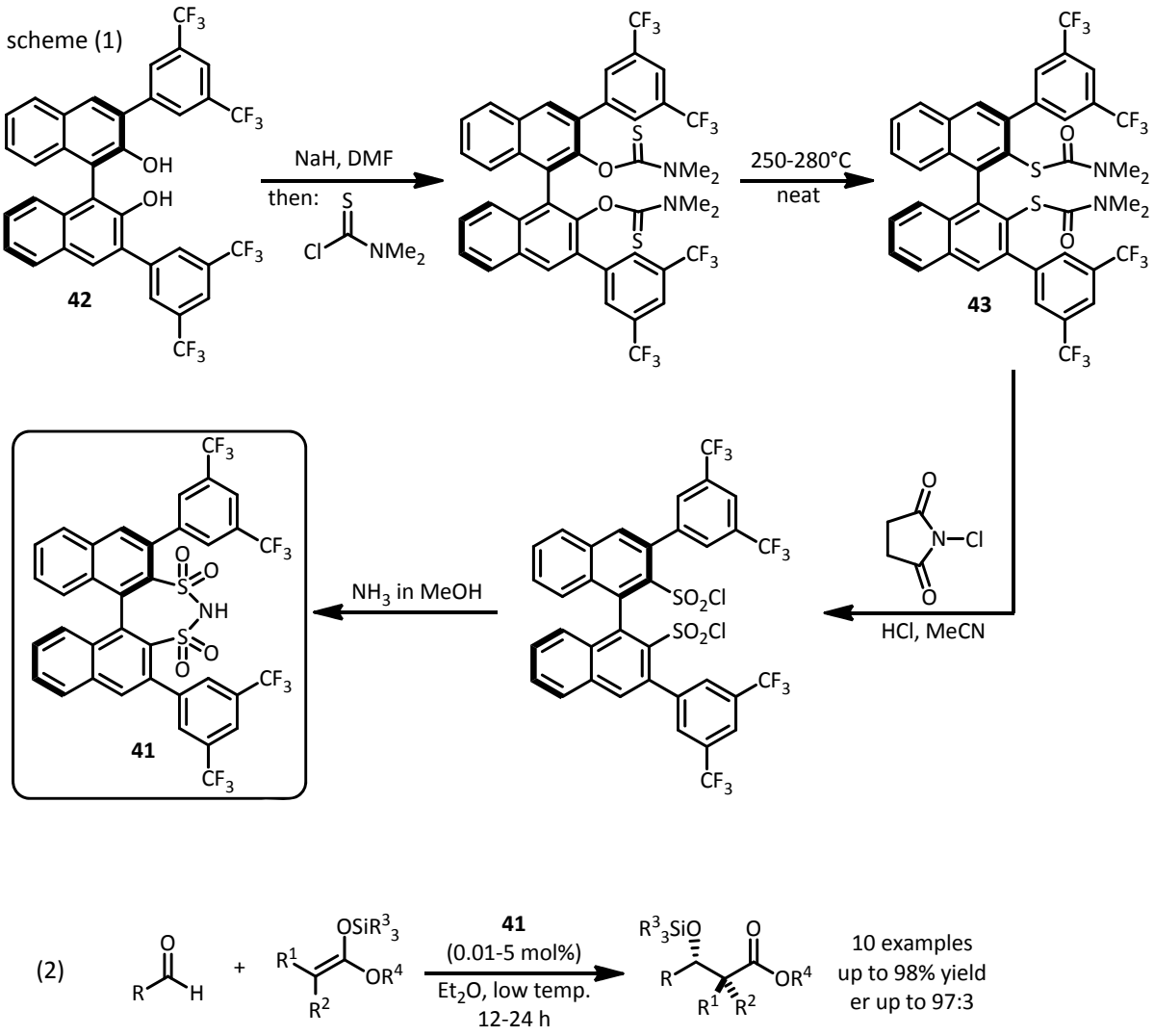


Figure 43. *Development of a chiral disulfonimide-synthesis and catalytic performance in asymmetric Mukaiyama aldol reactions.*

With these key contributions, a new class of organocatalysts entered the community, and approaches towards these and similar motifs were subsequently reported by the groups of Lee (Fig. 44, scheme 1) and [135] Berkessel (JINGLEs **45**) (Fig. 44).[136] Remarkably, the group of Lee investigated a modular approach for the installation of substituents in the 3,3'-positions of the BINOL-backbone, in line with studies conducted in our laboratories at the same time.[IX] Apart from reactions which open up a Lewis-acid reaction pathway, chiral disulfonimides very recently found an entry as powerful Brønsted acid catalysts for the Friedel-Crafts alkylation of indoles.[137]

[IX] These strategic improvements of the disulfonimide-synthesis will be presented in the PhD-thesis of FRANK LAY / University of Cologne 2012.

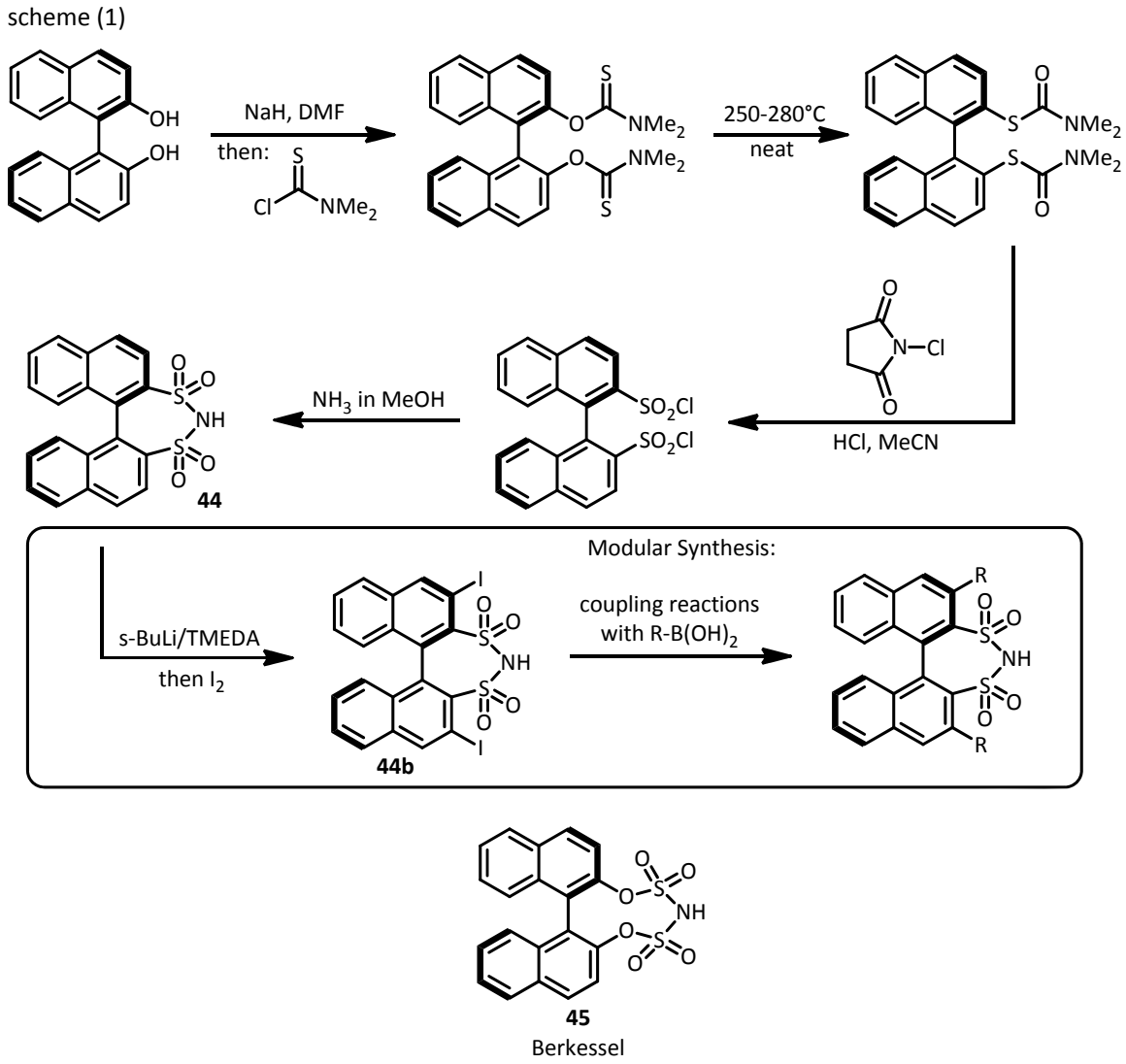


Figure 44. *Simplified, modular disulfonimide-synthesis and a disulfonimide-related catalyst motif by Berkessel.*

Without a doubt, this catalyst-development was one of the major improvements in recent asymmetric "organic catalysis",[138] rendering possible the use of the inherent reactivity of very strong Brønsted acids such as triflimide, however implemented in a chiral backbone. Furthermore, the Lewis acid reactivity apparent in disulfonimides opens up an entire group of reactions feasible for asymmetric organic metal free catalysis.

3. Research Goals

The research fields covered by this thesis are divided in three parts:

• the development of vinylogous and double vinylogous disulfonimide-catalyzed Mukaiyama aldol reactions;

• the investigation of the reaction mechanism which is operative in disulfonimide-catalysis;

• the development of improved disulfonimide-catalysts.

3.1 Towards an efficient protocol of metal-free catalyzed vinylogous and double vinylogous Mukaiyama aldol reactions

A large number of compounds present in nature bear subunits accessible via aldol reactions, such as the group of polyketides.[139] The importance of these transformations becomes even more blatant if one considers the manifold of synthetic molecules from pharmaceutical-, crop- or material-science. Thus there is a high demand for catalytic, stereoselective versions of these C-C bond forming reactions. Reviewing existing research shows quite plainly, that the Mukaiyama-type reaction is the most versatile present method for aldol processes (see chapter 2). However there is a lack of procedures which are generally applicable with regard to electrophile and nucleophile scope. From this point of view, it would be more than eligible to have a method available, which does not only allow access to normal aldol addition products, but also to the more challenging vinylogous aldol transformations. Since the seminal reports by Mukaiyama, until the most recent improvements by Denmark, Kalesse and others, these extended aldol reactions proved notoriously difficult to solve.[140] However, their synthetic potential for the production of natural products and pharmaceutics is obvious and a longstanding challenge in organic synthesis.[86, 141] Regarding vinylogous reactions it becomes clear that the principle of this reactive behavior can, in theory, be further extended. These double vinylogous aldol reactions are however only rudimentarily known at present, although representing a very precious synthetic tool.[142]

Previous work in our group has shown that disulfonimides are efficient catalysts for the reaction of aldehydes with silyl enolates.[129a] The aim of this research project was to further extend the scope of these reactions and provide efficient access to vinylogous Mukaiyama

aldol products. Following successful completion of this goal, we envisaged the extension of the method towards unprecedented ε-selective double vinylogous Mukaiyama aldol reactions. This would represent the first general procedure for the canonical Mukaiyama aldol reactions, from the normal transformation to multiple vinylogous versions. With these aims in mind, we were especially interested in the use of extended enolates derived from crotonic and sorbic acid esters (Fig. 45).

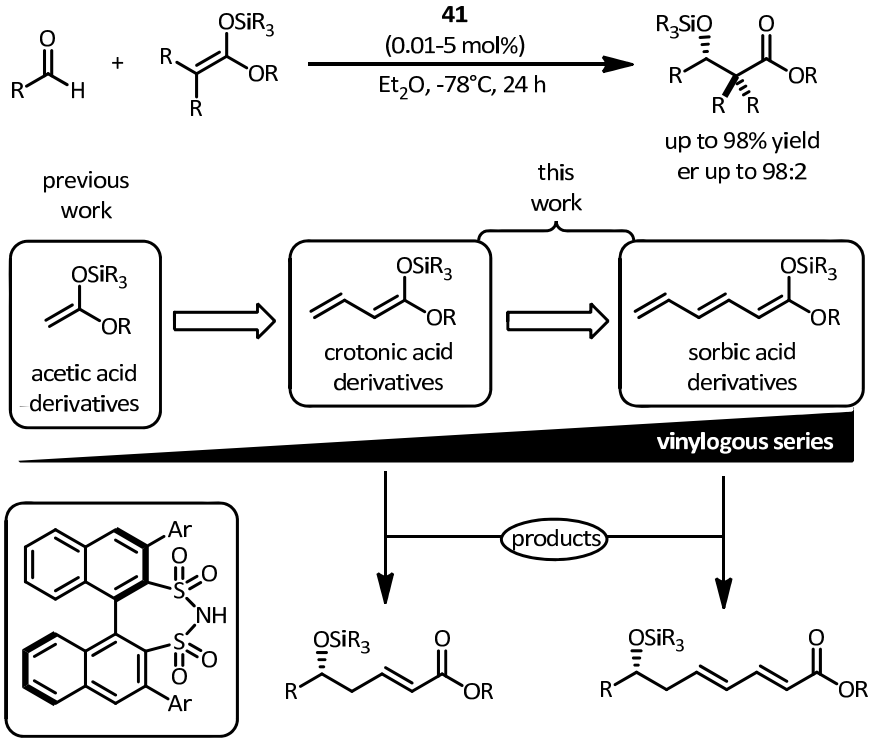


Figure 45. *Development of vinylogous Mukaiyama aldol reactions employing disulfonimide-catalysis.*

These entities are on one hand strikingly simple, on the other hand they offer the possibility to introduce a complex structural motif with an interesting and useful δ- and ζ-hydroxyester relationship. Many reported VMAR-protocols use especially reactive acetoacetate- and oxyfuranoyl-derived nucleophiles, leaving simpler nucleophile-classes as a widely unsolved synthetic problem.[87]

3.2 Mechanism elucidation of disulfonimide-catalysts

The ideal catalyst for asymmetric reactions should meet the following criteria:

• highly stereoselective,

• very efficient,

• applicable for a wide variety of substrates,

• applicable at ambient temperatures,

• tolerant to moisture and air,

• useful in low catalyst loadings / easy to recover.

At present, high enantioselectivities *and* yields can only be achieved using extended reaction times (up to 112 h) *and* low temperatures (-78°C).[129a] Additionally, aliphatic aldehydes and ketones remain challenging substrate classes. This is a general trend in Mukaiyama aldol chemistry and shows the demands which have to be addressed in the future.[143] However, since further improvement of a catalyst structure is challenging without shining light on the reaction mechanism, the elucidation of the latter was one important content of these studies. Especially the differentiation between a rather complex Lewis acid mechanism, in line with the studies provided by Yamamoto et al,[116-117] and an alternative Lewis acid initiated mechanism with subsequent cission of the N-Si-bond,[X] was of fundamental interest (see Fig. 46).[36, 144]

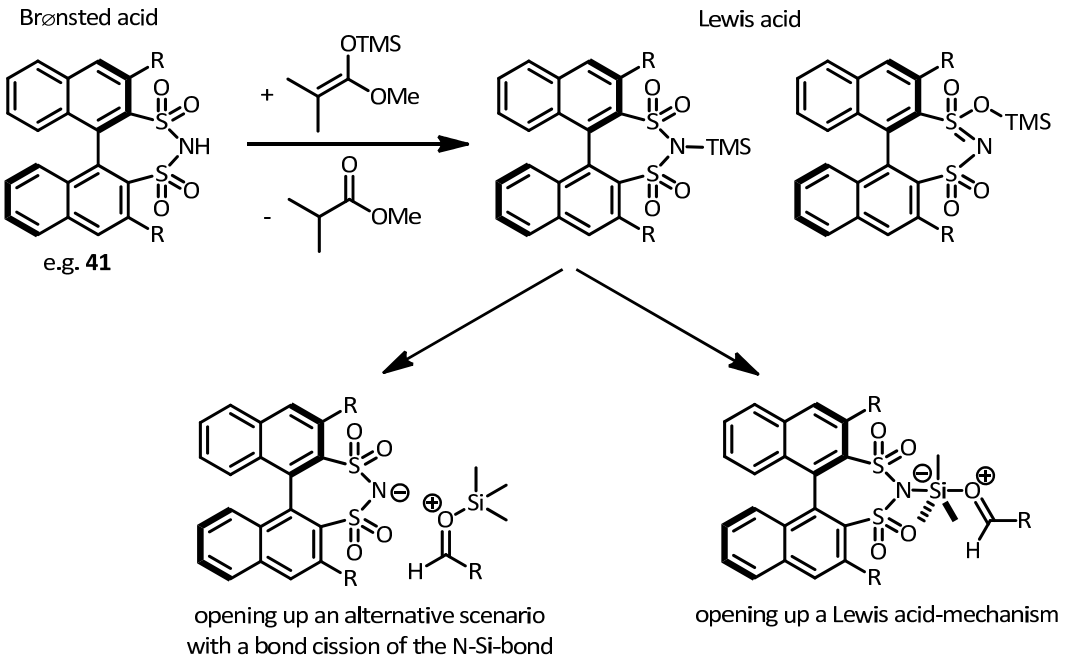


Figure 46. *Possible mechanisms offered by disulfonimide-catalysis.*

[X] Both mechanism fall into the category of ACDC, asymmetric-counteranion-directed-catalysis, as previously defined by our labs, since in both cases a disulfonimide is the anion for a Lewis acidic species.

3.3 Development of improved disulfonimide-catalysts

Based on the mechanistic studies, it was contemplated to further improve disulfonimide-catalysis by not only changing the substitution patterns, but improving the catalyst structure and its intrinsic reactivity. Already quoting the possibility of cooperative effects, we identified this approach for the tuning of our catalysts. Analyzing the catalyst structure regarding the substitution in 3,3'-position on the BINOL-backbone shows the potential for the installation of additional hydrogen bonding entities, thus Brønsted-acidic side chains. By following a suitable synthetic pathway, a modular construction from a common intermediate, in line with exisiting disulfonimide-syntheses, seems very appealing (Fig. 47).[135]

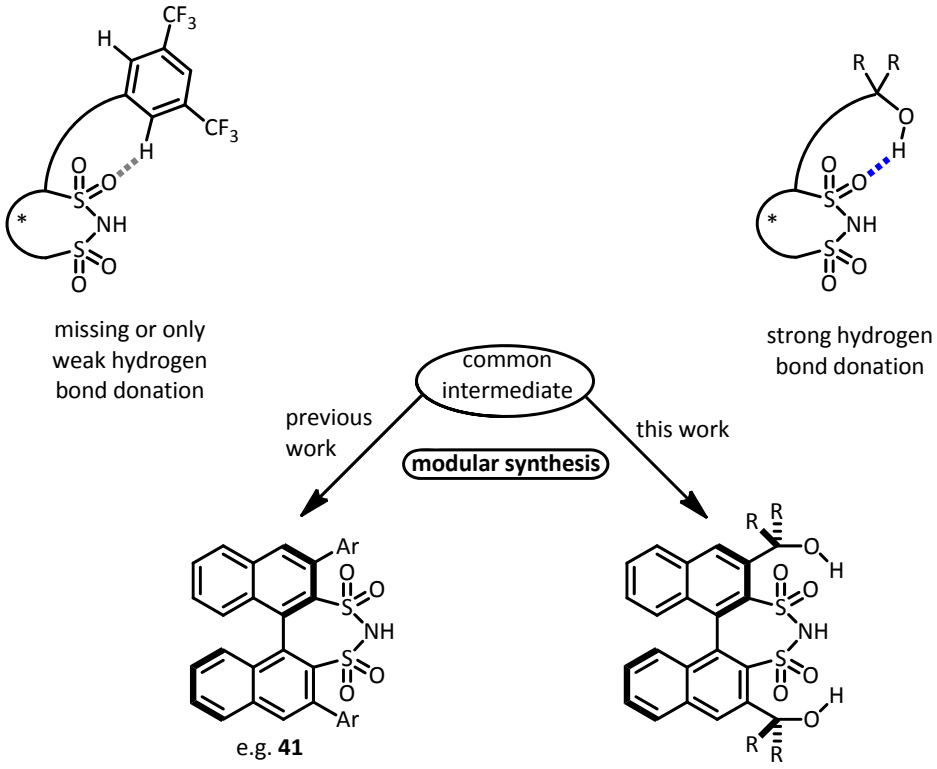


Figure 47. *Modular synthesis of improved disulfonimides.*

Since most BINOL-derived metal-free catalysts, or ligands for metal catalytic systems, are only available through long synthetic routes, this modular approach can be deemed very powerful for the preparation of new catalyst motifs. Previous studies by *e.g.* Yamamoto[37] or Mattson[145] showed that cooperative internal activation modes, either through Brønsted- or Lewis-acids, can raise reaction rates and catalyst activities by several orders of magnitude.

4. Results and Discussion

4.1 Disulfonimide-catalyzed vinylogous Mukaiyama aldol reactions

4.1.1 Synthesis of crotonic-acid derived nucleophiles

At the outset of our studies we were interested in the identification and synthesis of nucleophiles which are less established in VMARs. Accordingly, acetoacetate- and oxyfurane-derivatives, which have been extensively investigated in seminal reports, were of little interest.[87] This led us to consider crotonic acid esters and its derivatives. Considering the studies by Denmark, Kalesse, Campagne and others, the preparation of these substrates was already sufficiently described in the literature.[123a] The synthesis can be easily varied regarding the silyl group, the ester substituent, and the substitution in the vinylogous portion. Since crotonic acid is commonly used as a copolymerization agent and starting material for the synthesis of threonine, most of the corresponding educts are commercially available at low cost. Following the principle of vinylogy, these α,β-unsaturated esters can be easily deprotonated with LDA as a strong non-nucleophilic base (**GSP 1**). In all the reactions DMPU was added as a co-solvent to avoid lithium cluster formation. This molecule, developed by Seebach and co-workers, has now widely superseded HMPT, historically used for the same purpose.[146] Eventually possible side products from deconjugation reactions were not observed, and distillation afforded the products **47**-**56** cleanly (Fig. 48). Under these conditions many differently substituted nucleophiles arising from crotonic acid esters (**47**-**54**), ethyl 3,3-dimethylacrylate (**55**) and ethyl tiglate (**56**) were synthesized as mixtures of *E*/*Z*-isomers (Fig 48). The *E*/*Z*-ratio proved particularly dependent on the size of the protecting group, the ester portion and the substitution pattern introduced. The same behaviour was already shown and studied by the group of Denmark. They also assigned the geometry of the corresponding dienolates by studying the nuclear Overhauser effect (NOE),[123a, 147] coming to the conclusion, that the main isomer bears (*Z*)-configuration in all cases.

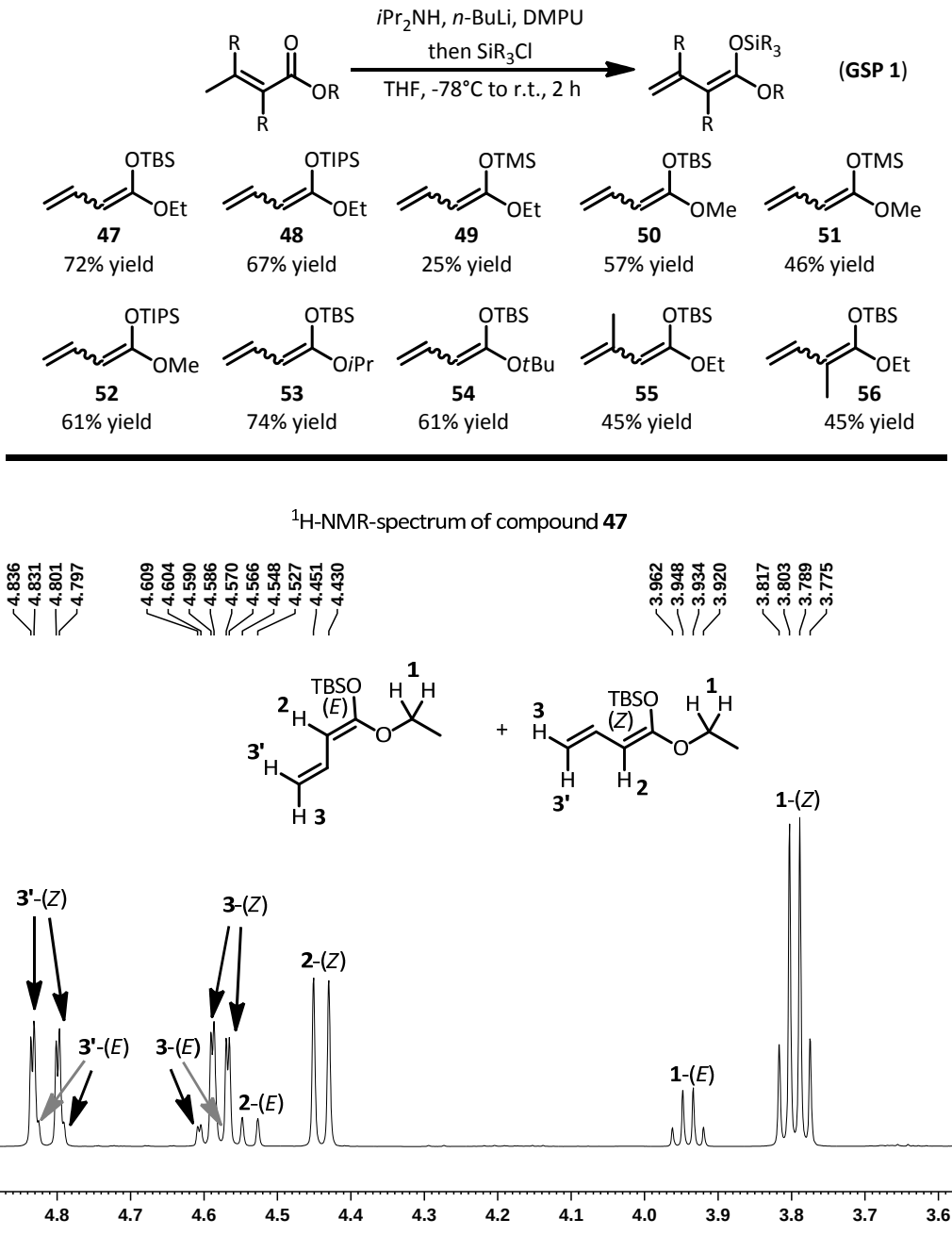


Figure 48. *Synthesis of simple crotonic acid nucleophiles* ***47*****-*****56*** *and NMR-spectrum of the region between 3.5 and 5.0 ppm for compound* ***47****.*

The synthesized silyl crotonates proved storable for long time under Argon at 4°C. A general trend could be observed, in which nucleophiles with sterically more demanding silicon groups and ester-substitutions showed higher stability.

4.1.2 Synthesis of alternative nucleophiles

For a better comparison of a catalytic method with other existing protocols, common substrates should be chosen as well. For this reason we synthesized the well studied silylated nucleophile arising from the cheap diketene acetone adduct. This compound (**57**) could be readily prepared following the general synthetic procedure (**GSP 1**) (Fig. 49).

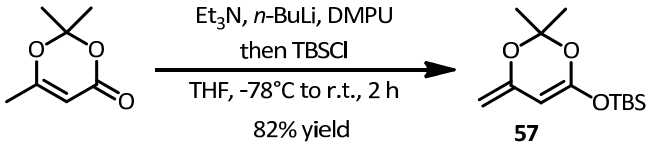


Figure 49. *Diketene acetone adduct derived nucleophile* ***57****.*

Another substrate class, recently introduced by the workgroup of Scott Denmark in the context of Lewis base activation of Lewis acids, are crotonic acid amides.[147] In collaboration with the workgroup of NUNO MAULIDE we became interested in the corresponding crotonic acid amide silyl dienolate of pyrollidine **58**. This substrate was studied in the context of an ongoing research towards a macrolactonization protocol. For this purpose we synthesized the compound according to the literature procedure. The applied base was KHMDS, affording the corresponding unstable product after high-vacuum distillation (Fig. 50).

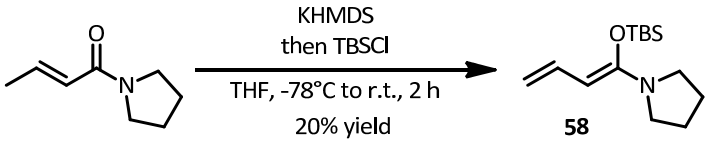


Figure 50. *Crotonic acid amide-derived nucleophile* ***58****.*

For the synthetic application of VMARs, we envisaged the late stage manipulation of hormone structures. In this context, testosterone with its α,β-unsaturated subunit was particularly interesting. Substitution of hormone moieties is an interesting approach to tune their biologic properties.[148] After optimization, we found, that testosterone could be smoothly deprotonated and silylated with TMEDA as a mild base and TBSOTf to give the corresponding silylated nucleophile **59**. X-Ray analysis of this material gave unambiguous proof of the corresponding double bond constitution, showing typical C=C bond lengths between 1.329 Å and 1.332 Å in the respective dienolate portion (Fig. 51).

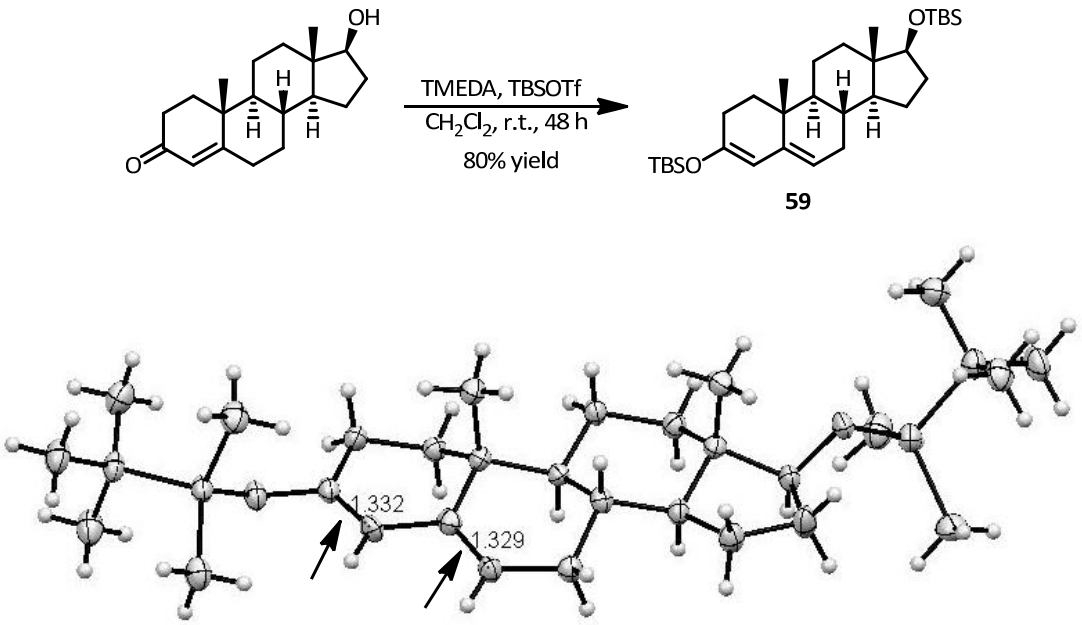


Figure 51. *Preparation of a testosterone-derived vinylogous nucleophile* ***59*** *and ORTEP-presentation of its crystal structure.*

4.1.3 Optimization of the disulfonimide-catalyzed VMAR

At the outset of our studies we required a catalyst for the preparation of racemic products of the VMARs. As described earlier in this work, Ghosez, and later Yamamoto, investigated the Brønsted and Lewis acidic properties of simple trimethylsilyl-derivatives of triflic acid and triflimide (Fig. 52). The conclusion of these studies was, that triflic acid is a stronger Brønsted acid than triflimide. In contrast, the silylated triflimide Lewis acid was found to be stronger than the corresponding Lewis acid derived from triflic acid. Considering this and the fact that triflimide is difficult to handle, we sought a simple, easily handled alternative to triflimide.

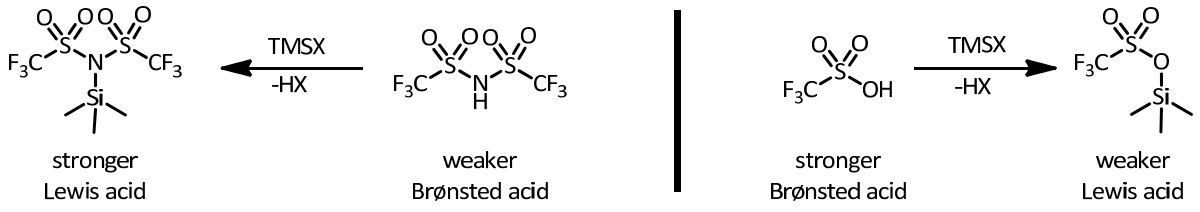


Figure 52. *Triflimide- vs. triflate-reactivity.*

We reasoned, that benzenedisulfonimide **40**, prepared from the corresponding sulfonyldichloride, could act as an effective catalyst (Fig. 53, eq 1). It was reported as an efficient Brønsted acid catalyst for various reactions by Barbero,[127-128] although not for

reactions involving Lewis acid catalysis. Satisfyingly, **40** catalyzed the reaction between nucleophile **47** and benzaldehyde to give product **60** in full conversion at r.t. in CH_2Cl_2 (Fig. 53, eq 2). Remarkably the corresponding products were obtained in completely silylated form, suggesting a full transfer of the silyl-group during the mechanism.

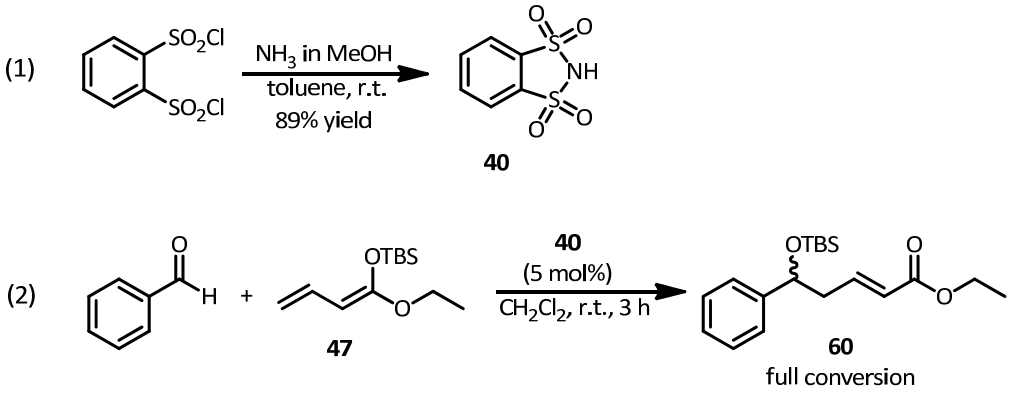


Figure 53. *A first vinylogous Mukaiyama aldol reaction catalyzed by catalyst* ***40****.*

With these results in hand we turned our attention to the use of the chiral catalysts **44**, **61** and **41** (Fig. 54). We decided to adapt 2 mol% catalyst loading and Et_2O as the standard reaction conditions.[129a]

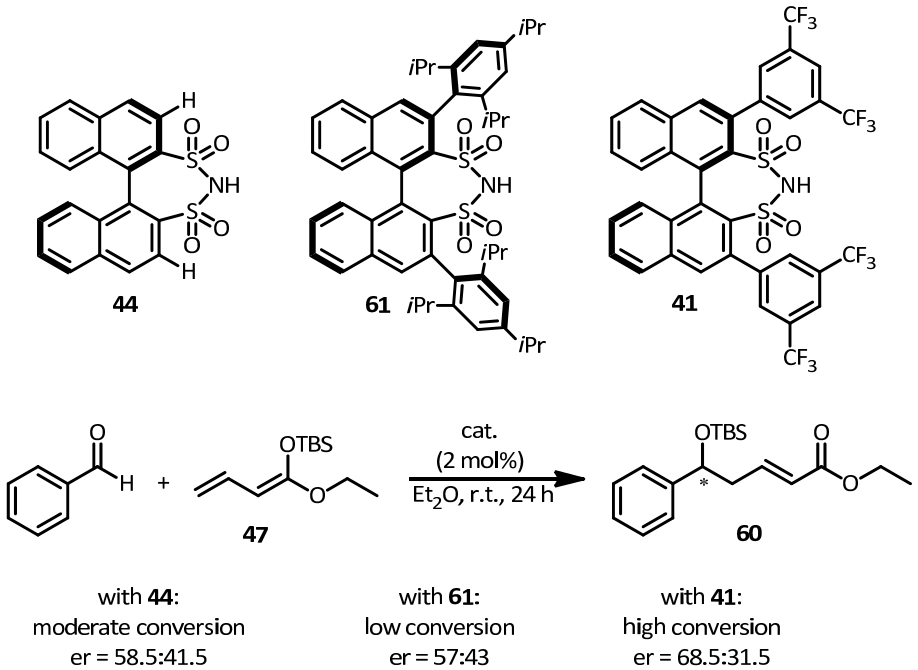
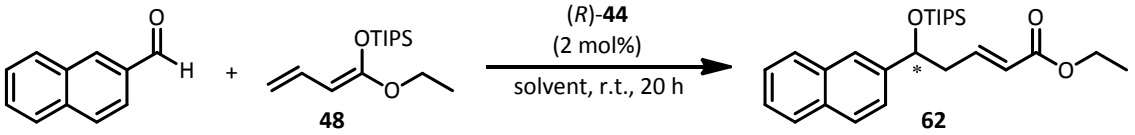


Figure 54. *Asymmetric VMARs for the preparation of* ***60****.*

Quite remarkably, although giving generally low enantioinduction, the 3,3'-unsubstituted disulfonimide **44** provided superior results compared to the TRIP-analogue **61** regarding enantioselectivity and conversion. However it was shown, that the 3,3'-(3,5-CF_3-phenyl)-

substituted disulfonimide **41** was privileged. Based on these results, we decided to screen a series of common reaction solvents for the reaction between 2-napthaldehyde and TIPS-protected nucleophile **48**, in the presence of unsubstituted disulfonimide **44**. The choice of 2-naphtaldehyde was taken, because it proved to be especially reactive in disulfonimide-catalyzed 1,2-selective Mukaiyama aldol reactions.[129a]

Table 1. *Solvent-Screening for the disulfonimide-catalyzed vinylogous Mukaiyama aldol reaction.*



solvent	NMR-yield	e.r.
DMSO	n.d.	n.d.
acetone	n.d.	n.d.
CH_2Cl_2	88%	52.5:47.5
$CHCl_3$	76%	54:46
THF	n.d.	n.d.
1,4-dioxane	n.d.	n.d.
Et_2O	61%	56.5:43.5
toluene	46%	58.5:41.5
pentane	n.d.	n.d.
methanol	n.d.	n.d.

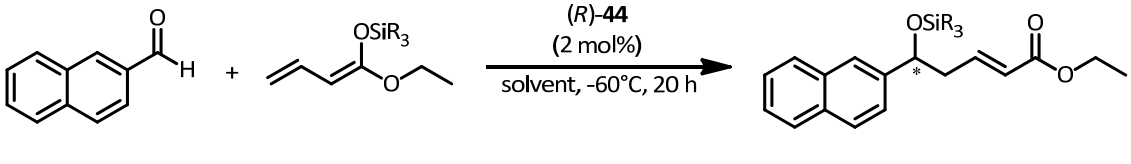
triphenylmethane was used as an internal NMR-standard

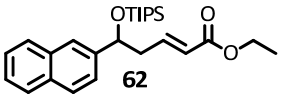
Chlorinated solvents, such as $CHCl_3$ and CH_2Cl_2, as well as Et_2O and toluene were found to be effective solvents. In contrast, polar or protic solvents such as DMSO, acetone or methanol did not lead to any reactivity, probably due to degradation of the reactive intermediate. Surprisingly, pentane and etheric solvents other than Et_2O led to no reactivity at all.

In order to study the influence of the protecting group we conducted a screening of ethyl crotonate derived nucleophiles **47**-**49** in the reaction with 2-naphtaldehyde. Unsubstituted catalyst **44** and reduced reaction temperature (-60°C) was used throughout this study (Table 2). The results illustrated, that the size of the protecting group had a pronounced effect on both, the enantioselectivity and the yield. Whereas smaller protecting groups (TBS and TMS) delivered the products in high yields and promising optical purity, the more demanding TIPS-group had a contrary effect, decreasing the yield and giving the corresponding product **62** in virtually racemic form. Between the TMS- and the TBS-protected hydroxyesters the

difference was much less distinct. However, although delivering products in high yields and enantioselectivities, the TMS-group proved problematic. On one hand, product **63** was partially deprotected after workup, requiring an additional deprotection to further analyze the material, on the other hand the starting dienolate **49** proved to be substantially less stable than its TBS-congener **47**. As a result, the yields obtained were often irreproducible. Due to its enhanced stability and superior reaction behavior, we decided to use the nucleophile **47** for further screenings.

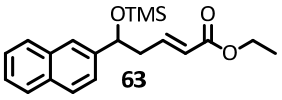
Table 2. *Investigation of the influence of the protecting group using catalyst* ***44****.*





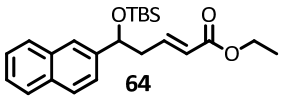
62

solvent	NMR-yield	e.r.
CH_2Cl_2	74%	53:47
Et_2O	54%	55.5:44.5
toluene	68%	57.5:42.5



63

solvent	NMR-yield	e.r.
CH_2Cl_2	86%	61:39
Et_2O	86%	79:21
toluene	83%	83.5:16.5



64

solvent	NMR-yield	e.r.
CH_2Cl_2	84%	60:40
Et_2O	87%	76.5:23.5
toluene	88%	79.5:20.5

triphenylmethane was used as an internal NMR-standard

To further increase the reactivity and enantioselectivity, we focused on substituted disulfonimides, such as the reported and very reactive **41**, which was available in our laboratories. With this catalyst, under the initially optimized conditions at -78°C, we obtained the product **64** in an e.r. of 92:8 at quantitative conversion after 3 days reaction time (not shown in the table). We decided to increase the reaction time, because in some cases the reactions were not complete after 20 h.

Furthermore, we were interested in the influence of the double bond geometry in the nucleophile. With the help of preparative gas chromatography, we were able to enrich the (*E*)- and (*Z*)-isomers and investigate the particular reactivities (Fig. 55, eq 1).

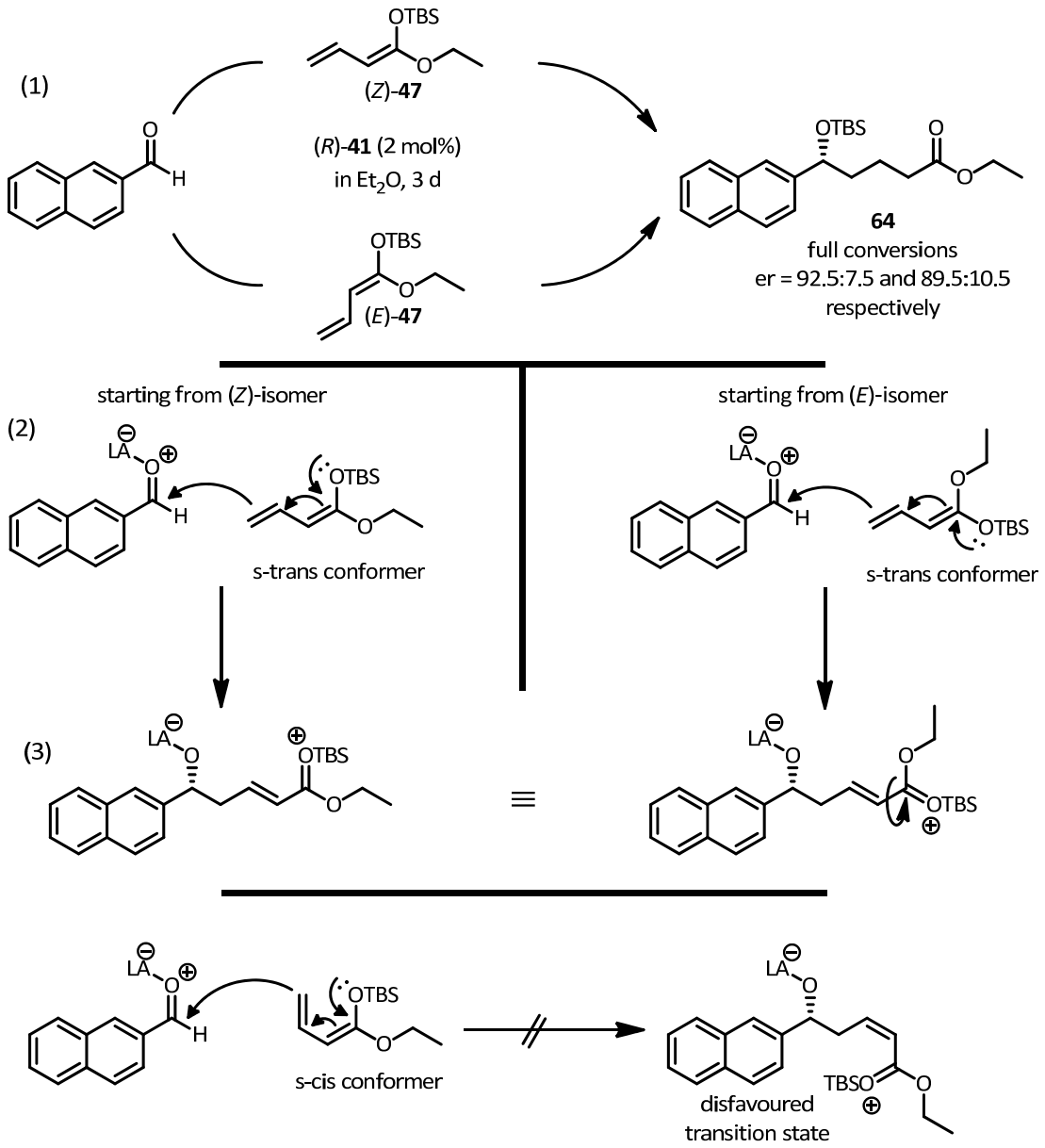


Figure 55. *Investigation and rationalization of the influence of the (E,Z)-geometry on the reaction outcome.*

In accordance with previous VMAR-studies, the desired product **64** was obtained with the same (*E*)-double bond geometry and virtually identical enantioselectivites and yields for the (*E*)- *and* the (*Z*)-configured nucleophile respectively. A simple explanation for this behaviour can be found if one considers the possible reaction pathways (Fig. 55, eq 2). Since the most favourable s-trans conformers of the (*E*)- and (*Z*)-isomer lead to a common transient intermediate, the same product forms in both cases. In order to provide the (*Z*)-configured product the nucleophile would have to attack as its disfavored s-cis conformer, leading to a transition state which seems unfavourable as well (Fig. 55, eq 3).

We next examined the effect of the catalyst structure in an effort to further improve the enantioselectivities and yields. The syntheses of these BINOL-derived catalyst candidates were approached in a modular way from previously described common intermediates, such as **44** or **44b**, which allowed for various coupling reactions or trapping of ortho-lithiated disulfonimides with ketones.[XI]

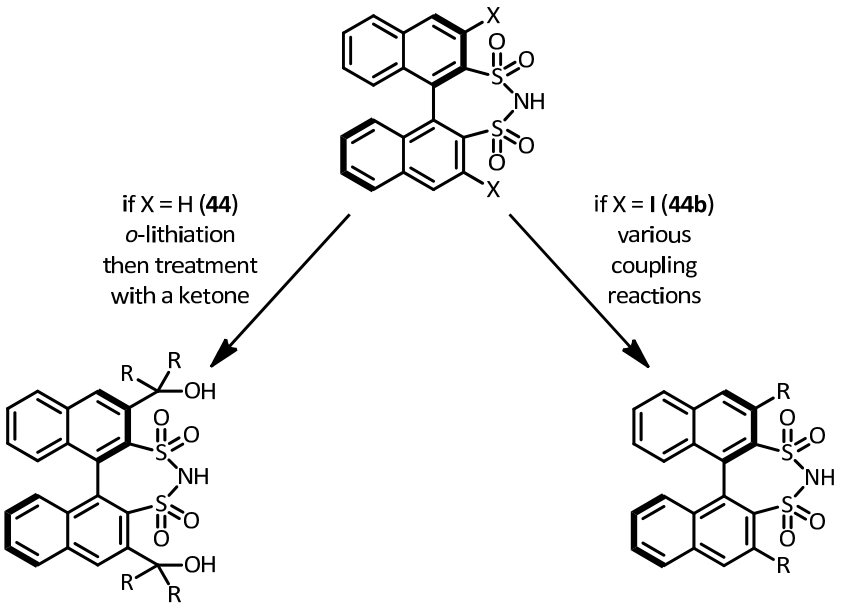


Figure 56. *Strategies towards the modular syntheses of differently substituted disulfonimides.*

With these catalysts we were able to investigate the catalytic activity and especially the enantioinduction provided. We utilized 2-naphtaldehyde as an electrophile and the nucleophile **47** under our standard conditions with several 3,3'-aryl substituted disulfonimides.

Electron-poor aromatic substitution patterns gave significantly better results in terms of activity and stereoselectivity (Fig. 57). The catalyst **41**, already tested in the beginning of our studies, proved to be superior throughout all our reaction attempts. Other electron-poor substituents provided efficient catalysts as well, however giving inferior results than **41**, especially concerning the enantioselectivity. Interestingly, electron-rich, electron-neutral or polyaromatically substituted disulfonimides were not efficient at all. These catalysts neither gave any synthetically useful conversion, nor did they provide the product in promising

[XI] The coupling procedures and and the catalysts produced by couplings were elaborated and described by FRANK LAY and will be presented in his doctoral thesis/University of Cologne 2012. The treatment of *o*-lithiated disulfonimides with electrophiles such as ketones will find further reference in the second part of this work.

optical purity. Additionally, raising the catalyst loading to 5 mol% gave better results for catalyst **41**, significantly advancing the enantioselectivity.

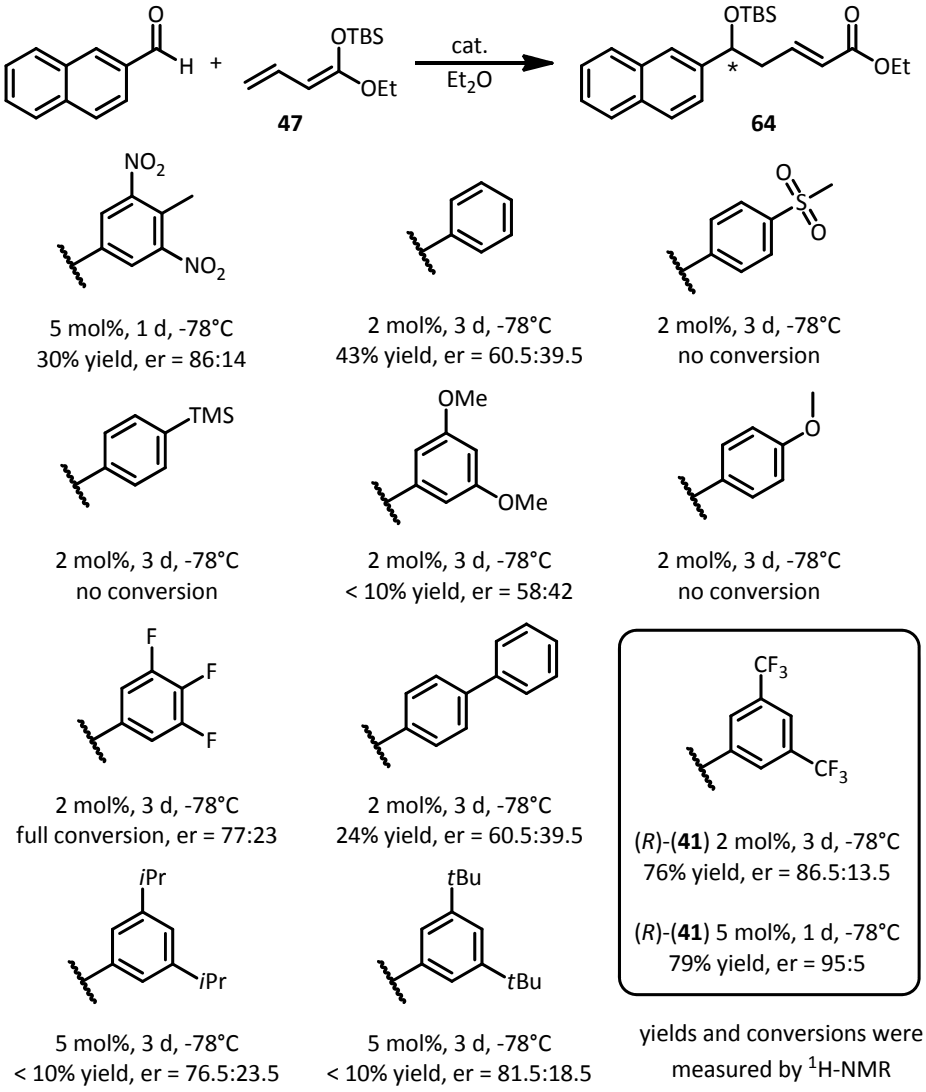


Figure 57. *Investigation of various substitution patterns on the disulfonimide-catalyzed VMAR.*

However the performance provided by catalyst **41** illustrates the requirement for the electron poor 3,5-CF_3-substituents. It was assumed that the silylated catalyst represents the Lewis acid which mediates the reaction. Hence the substituents on silicon will have a strong influence. One could argue that the electron-withdrawing effect results in a catalyst with higher activity on silicon.[XII] Considering that tetra-alkysilanes are not very strong Lewis acids themselves, an electron-withdrawing ligand should increase the Lewis-acidic properties substantially, removing electron-density from the silicon center (Fig. 58).[149] Thus the LUMO

[XII] In both possible scenarios, the Lewis acid and the alternative mechanism stated in chapter 3.

on silicon will be lowered and provide a better overlap with the lone pair on the aldehyde-oxygen.

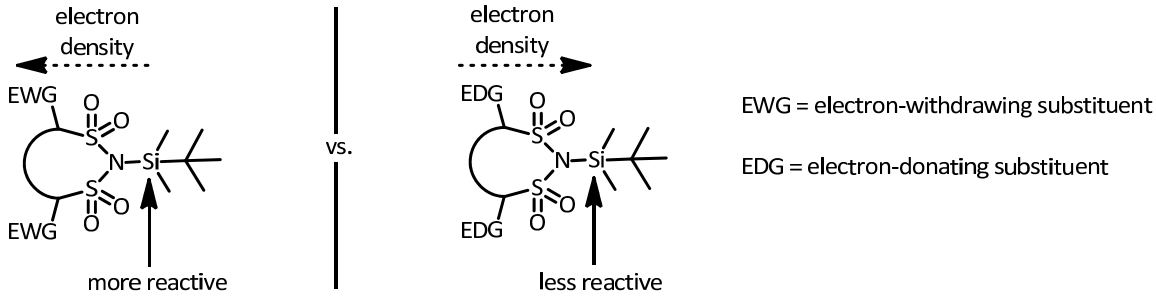


Figure 58. *Rationalization for the intrinsic difference in silicon Lewis acidity of electron-poor and electron-rich silylated disulfonimides.*

For the stereoselectivity provided, an explanation has to be found regarding sterics and electronics. Only by consideration of sterics the difference in optical purity of the product resulting from the reaction catalyzed by **41** versus its 3,5-MeO-substituted congener cannot be explained, because these two groups bear similar steric demand.

Obviously the combination of electron-poor aromatic substituents with the chiral information from the backbone allows for a specific alignment of the substrate, which is not possible with other catalysts. Here one might have to consider the specific π-interaction properties provided by the substituents, since this will also influence the π-system of the BINOL-backbone. This situation could lead to a complex coherence of these factors, allowing for an optimal combination of backbone *and* substituent which has to be found for the observation of the best results.

These studies led us to consider other catalysts bearing CF_3-substituents and/or electron-withdrawing groups offering secondary interactions. In these studies (Fig. 57 and 59) the CF_3-group showed superior reactivity profiles, however, yields and enantioselectivities were always lower than those obtained with catalyst **41**.

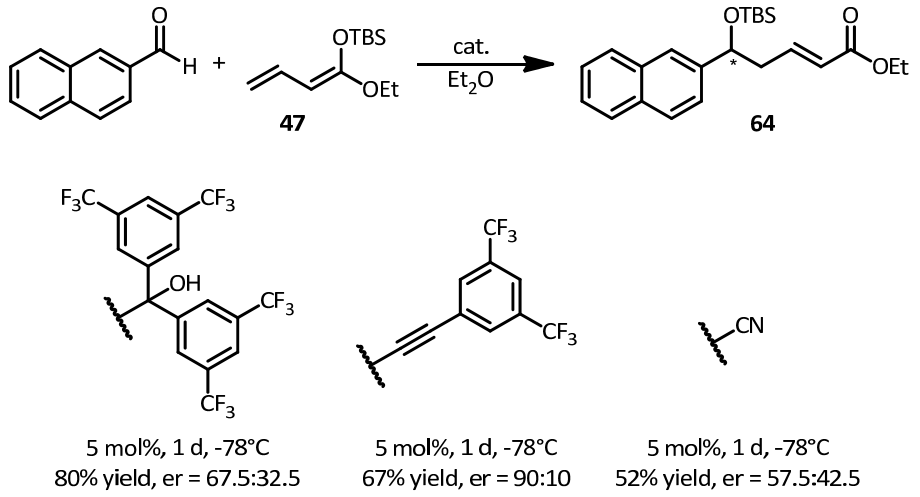


Figure 59. *Investigation of various substitution patterns on the disulfonimide-catalyzed VMAR (continued I).*

Later in our studies we focused on nucleophile **50**, since we discovered that yield and enantioselectivity improved with this reactant. These reactions were conducted with other catalysts bearing polyfluorinated substituents in 3,5-position of the aromatic ring or a new catalyst class with 3,3-carboxylic acid amide subunits (Fig. 60).[XIII]

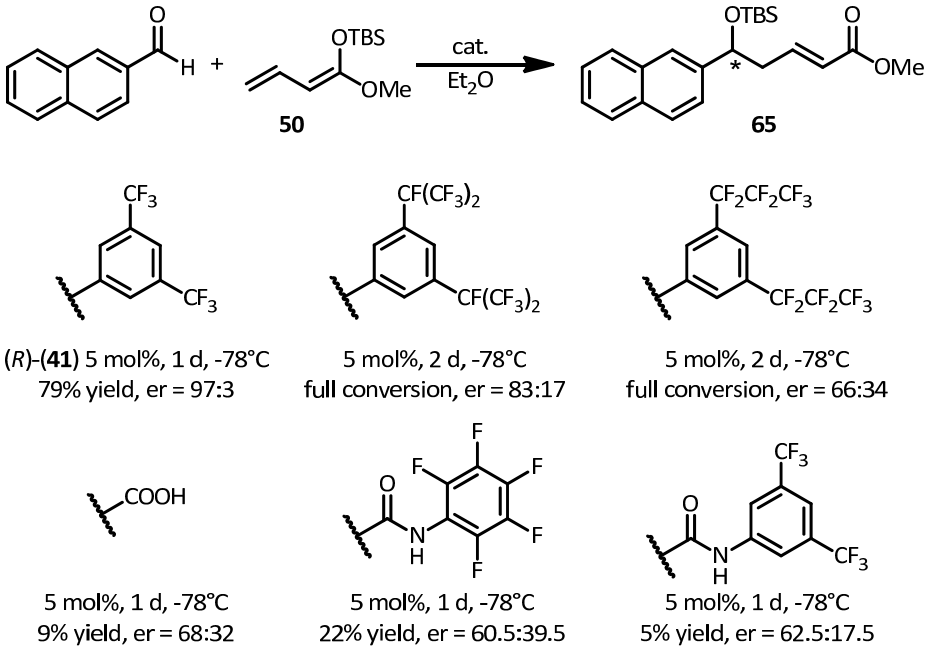


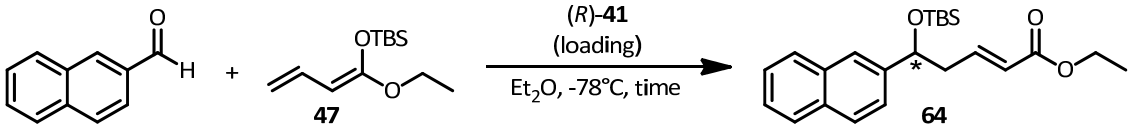
Figure 60. *Investigation of various substitution patterns on the disulfonimide-catalyzed VMAR (continued II).*

However, among the catalyst examined, **41** remained the most effective. For this reason it was used throughout our further studies.

[XIII] These catalysts were generously provided by Dr. ARTUR PINTO and Dr. CONSTANTINOS RABALAKOS.

We were occasionally faced with poor reproducibility and wished to develop more robust reaction conditions. In some cases we realized, that conversions were not full and we started studying the catalyst loading and the behaviour of the enantioselectivity over time. For these reactions we chose nucleophile **47**. Hence we looked at the behaviour of the reaction with 10, 5 and 2 mol% catalyst loading. Additionally, we took samples from the reactions with 10 mol% and 5 mol% after 1, 2 and 3 days in order to test for possible enantioselectivity deterioration (Table 3). In this study we had problems to reproduce previous results, namely to reach full conversion and high enantioselectivity with the catalyst loading of 2 mol%. Probably this behaviour could be explained with variabilities in the catalyst and nucleophile quality, which we sometimes observed at the outset of our studies. The different catalytic behaviour of chiral phosphoric acids in its protonated and its salt form was studied by us as well, and that could be equally true for disulfonimides.[150] Furthermore, the nucleophiles might bear acid impurities from slow decomposition processes or their preparation. This could account for the appearance of achiral reaction pathways. Through these studies it was shown that, although the yields varied in a certain range, the enantioenrichment of the products did not degrade over time. The use of 5 and 10 mol% catalyst-loading gave similar results, so that we decided to further work with 5 mol% catalyst loadings for 3 days to reach complete conversion and high enantioselectivity, even for less reactive nucleophiles and electrophiles.

Table 3. *Investigation of the catalyst loading on the disulfonimide-catalyzed VMAR.*

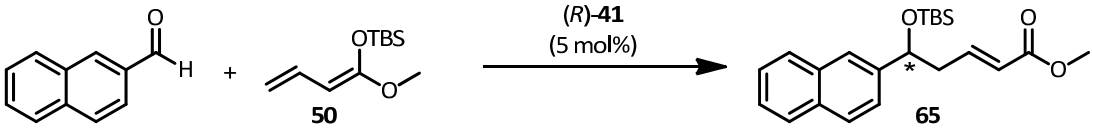


loading	time	NMR-yield	e.r.
10 mol%	1 d	88%	95:5
10 mol%	2 d	69%	95.5:4.5
10 mol%	3 d	73%	95:5
5 mol%	1 d	81%	95:5
5 mol%	2 d	75%	95.5:4.5
5 mol%	3 d	73%	95.5:4.5
2 mol%	2 d	20%	67:33
2 mol%	2 d	76%	86.5:13.5:33

triphenylmethane was used as an internal NMR-standard

With these optimized conditions in hand, we turned our attention to examine the effect of temperature and solvent on the reaction of 2-naphtaldehyde and nucleophile **50** in the presence of catalyst **41** (Table 4). With the data obtained from these reactions, we could identify Et_2O as the best solvent. Interestingly, solvents like dichloromethane or acetonitrile allowed for an efficient reaction, but provided the product in only poor enantioenrichment. This behaviour cannot be explained easily, and an incorporation of solvent in the mechanism, as discussed by Yamamoto, cannot be ruled out at present.[117]

Table 4. *Reinvestigation of solvents in combination with the temperature dependence of disulfonimide-catalyzed VMAR.*



solvent	temperature	time	isolated yield	e.r.
MeCN	0°C	1 d	74%	52:48
pentane	0°C	1 d	66%	80:20
toluene	0°C	1 d	85%	74:26
CH_2Cl_2	0°C	1 d	88%	68:32
Et_2O	0°C	1 d	62%	83:17
pentane	-20°C	1 d	85%	85:15
toluene	-20°C	1 d	99%	77:23
Et_2O	-20°C	1 d	99%	87:13
Et_2O	-78°C	3 d	96%	97:3

yields correspond to isolated material after column chromatography

The temperature effect could be shown quite plainly, revealing results from other methods, describing that Mukaiyama aldol reactions work most selectively at low temperatures (-78°C). At this point we switched from analytical scale to a synthetically useful and reliable 0.2 mmol scale for the conduction of our further experiments and determined isolated yields. Increasing the reaction scale had no adverse effect on the reaction outcome, and we could finally achieve almost quantitative yields and enantioselectivities of 97:3 for our optimized conditions.

4.1.4 Disulfonimide-catalyzed VMAR – Nucleophile scope

After identifying the optimum reaction conditions for our catalyst system, we turned our attention towards the nucleophile scope. For this purpose we subjected silyl enol ethers **47**-**57** (see Fig. 48) to the optimized reaction conditions (Fig. 61).

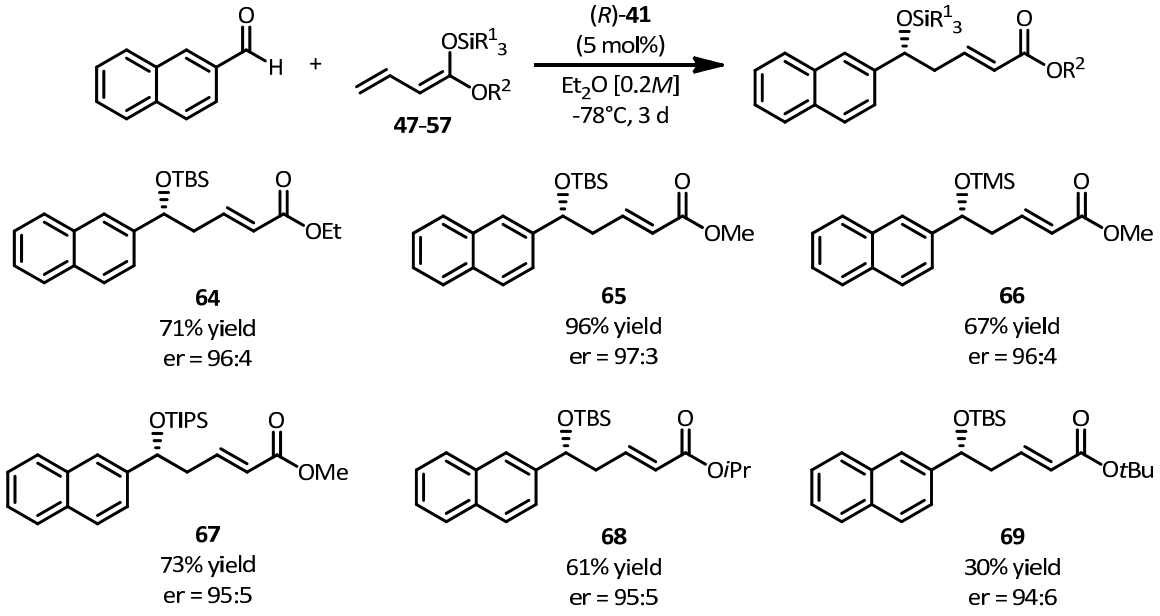


Figure 61. *Influence of the silyl protecting group and the ester portion of the nucleophile on the disulfonimide-catalyzed VMAR.*

Pleasingly, the reaction conditions proved to be robust and all nucleophiles, besides the ones already tested in the optimization studies, converted smoothly to the corresponding products. Interestingly the silyl-group had little influence on the observed enantioselectivity. However, subtle differences in reactivity could be noted. The TMS-group gave full conversion, however the isolated yield of the desired product **66** decreased because of the appearance of the α-product. The much bulkier TIPS-group provided the reaction product **67** in slightly decreased yield, most probably due to its lower reactivity. Thus the reactivities of the nucleophile can be correlated to the size of the protecting group. Actually this behaviour is coherent with the stability of the nucleophiles. Whereas **51** (TMS-group and Me-ester) had to be resynthesized after some weeks, nucleophile **52** (TIPS-group and Me-ester) was almost indefinetly stable. In our optimization studies with unsubstituted catalyst **44**, the nucleophile bearing the TIPS-protecting group gave almost racemic products, whereas with the correspondingly substituted catalyst **41** good enantioselectivities were observed. For smaller protecting groups both catalysts **41** and **44** provided products with good enantioenrichment. It is presumed, that the very bulky TIPS-group in the unsubstituted catalyst prevents the

aldehyde from a favourable alignment with the BINOL-backbone, whereas a shielding by 3,3'-substituents allows for this orientation, enabling a highly face-selective nucleophilic attack.

The substituent in the ester portion also had an influence on the reactivity (in accordance with Mayr's nucleophilicity scale).[101] As already shown by the reactions involving nucleophile **47** and **50**, the difference between the ethyl and the methyl group was notable. This effect was more drastic when we changed the substitution to secondary or tertiary alkyl groups on the ester. Whereas the installation of an *i*Pr-group to the nucleophilic portion resulted in the product **68** with acceptable 61% yield, the product **69** bearing a *t*Bu-group on the ester was only obtained in 30% isolated yield, as a mixture of rotamers. Thus this behavior might correlate with the steric influence of the alkyl groups:

$$-CH_3 < -CH_2\text{-}CH_3 < -CH(CH_3)_2 < -C(CH_3)_3$$

decreasing the observed nucleophilicity accordingly.

Installation of methyl groups in the nucleophilic portion, as present in products **70** and **71** showed interesting effects on the reaction outcome (Fig. 62).

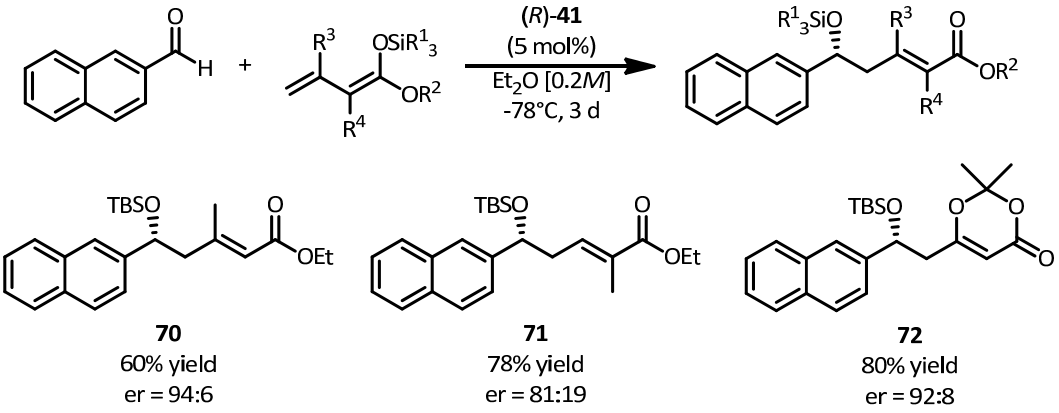


Figure 62. *Influence of substituents in the nucleophile in the disulfonimide-catalyzed VMAR.*

Whilst product **70** was obtained in only 60% yield, the optical purity remained high. Product **71** on the other hand showed a noteable decrease in optical purity in comparison to all the other examples, however high reactivity was retained. Interestingly this behaviour contrasts results from the Denmark group, where nucleophiles with the methyl group in α-position, such as **56**, provided higher enantioselectivities.[123a]

Also quite remarkable is the fact, that nucleophile **57** provided the corresponding product **72** in good yield, however decreased optical purity (Fig. 62). This nucleophile proved remarkably

general and highly selective in many seminal reports. These observations illustrate the complementary character to existing methods which can be possibly offered by disulfonimide-catalysis.

Although being of high interest from a synthetic viewpoint, the testosterone-derived nucleophile **59** could not be successfully used in our VMAR-protocol.

4.1.5 Disulfonimide-catalyzed VMAR – Electrophile scope

Existing catalytic methods for the synthesis of δ-hydroxy esters often lack generality in electrophile scope (see chapter 2). Several methods have been reported which only allow the conversion of aliphatic *or* aromatic aldehydes. Techniques converting both classes of substrates are much less established. With our catalyst system involving **41** at low temperatures we were able to use a wide range of aromatic, as well as aliphatic aldehydes. However, we could demonstrate a remarkable preference towards naphtaldehyde- and cinnamaldehyde-derivatives (Fig. 63).

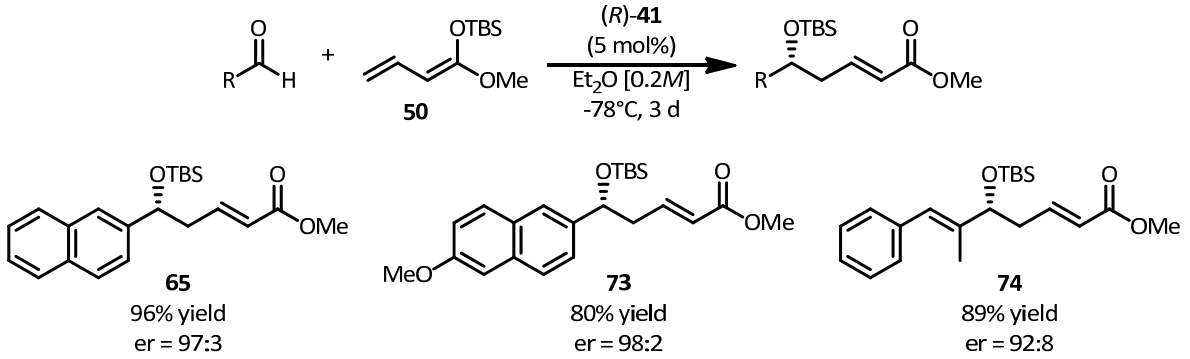


Figure 63. *Electrophile scope of the disulfonimide-catalyzed VMAR.*

This behaviour could probably be explained by a privileged interaction of the extended π-system of the electrophile with the π-system of catalyst **41**. Regarding the scope towards other aromatic aldehydes we observed a high generality in reactivity towards various structures. However the enantioselectivities achieved with naphtaldehydes and cinnamaldehydes could only be approximately corroborated with rather electron-rich entities with defined substitution, for example resulting in products **75**, **76**, **77** and **80** (Fig. 64). As can be seen in the series **80**-**82**, *m*-substitution plays a special role, providing the products in notably higher enantioselectivities.

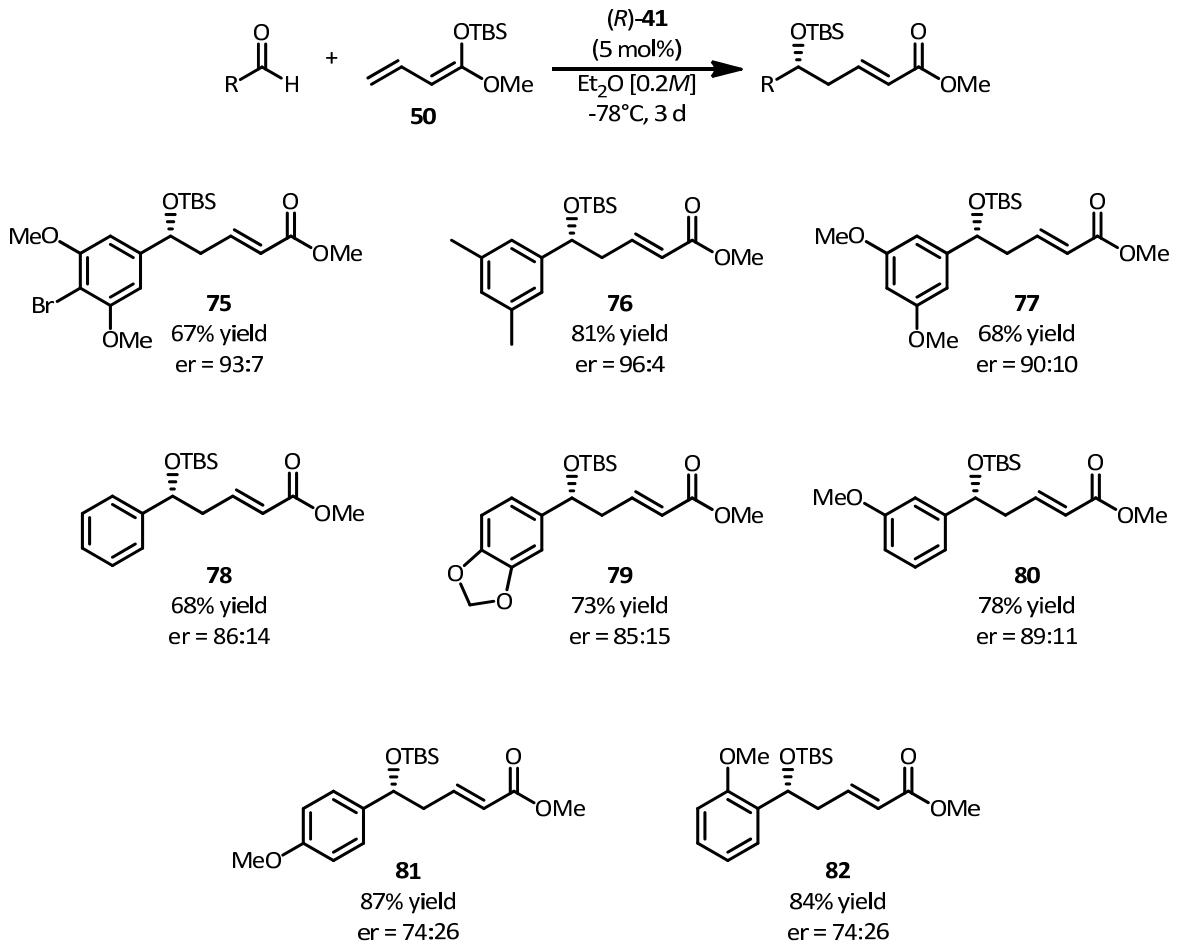


Figure 64. *Electrophile scope of the disulfonimide-catalyzed VMAR (continued I).*

The VMARs of other aromatic aldehydes, such as heteroaromatic or electron-poor ones occurred smoothly too, however the levels of enantioinduction proved inferior compared to naphtaldehyde-, and cinnamaldehyde-derivatives (Fig. 65). The difference between **76** and its congeners **83** and **84** was remarkable, approving *m*-substituents as particularly well suited for our catalyst system. One could be tempted to predict, that for high enantioselectivities the substrate should bear some unique structural features, namely α,β-unsaturation and substituents in α- and in γ-position.

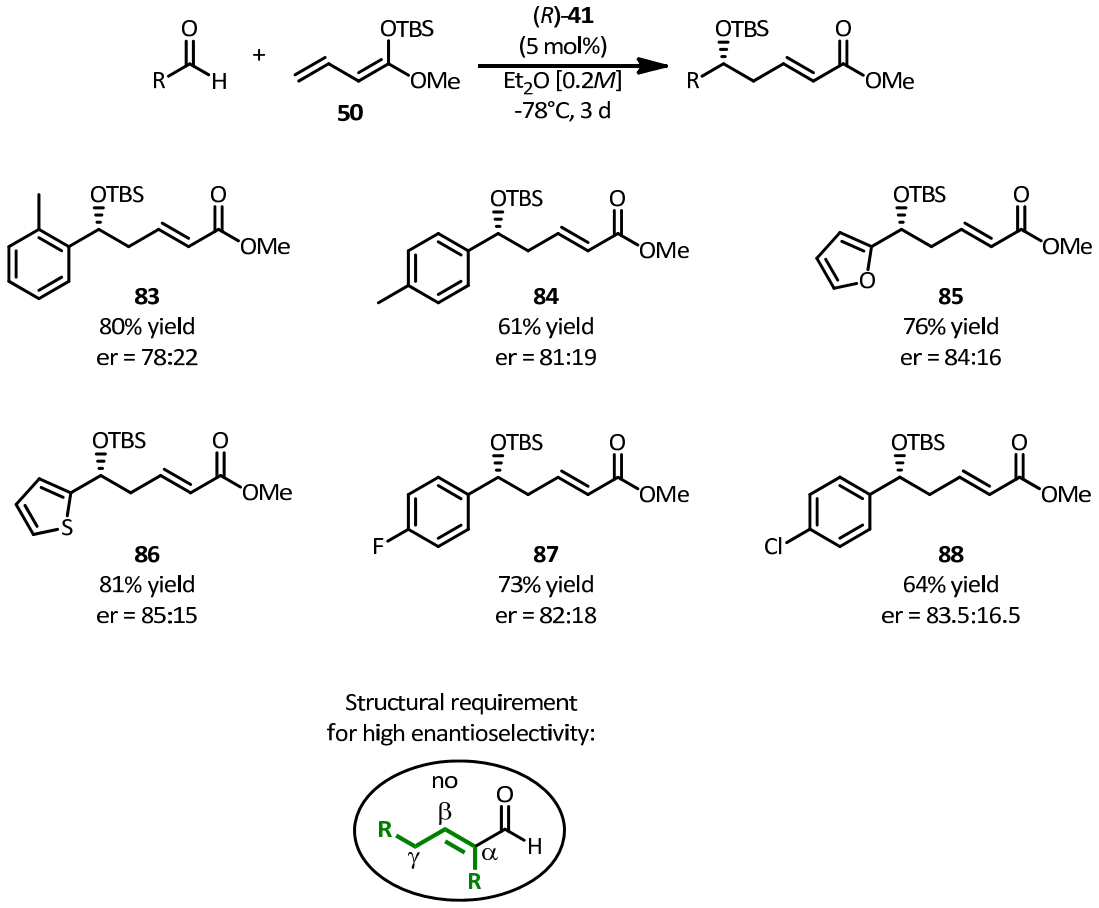


Figure 65. *Electrophile scope of the disulfonimide-catalyzed VMAR (continued II) and analysis of the quintessential structural requirement.*

Simple aliphatic aldehydes proved to be difficult substrates for several previous catalytic VMAR methods frequently resulting in extremely low conversions. Remarkably, our disulfonimide-system converted selected aliphatic aldehydes as well, however resulting in low yields and very poor enantioenrichment (Fig. 66, eq 1). This fact could point towards a crucial π-π-interaction for efficient orientation of the substrate, in order to induce high enantioinductions. Remarkably, we could even access the products **92**-**94** from aliphatic aldehydes and nucleophile **55**. This nucleophile gave a notably higher enantioselectivity than for example the nucleophile **50**. Although speculative, one might imagine that for aliphatic aldehydes, in lieu of π-interactions, the enantioselectivity can be controlled by other effects which are not yet clear.

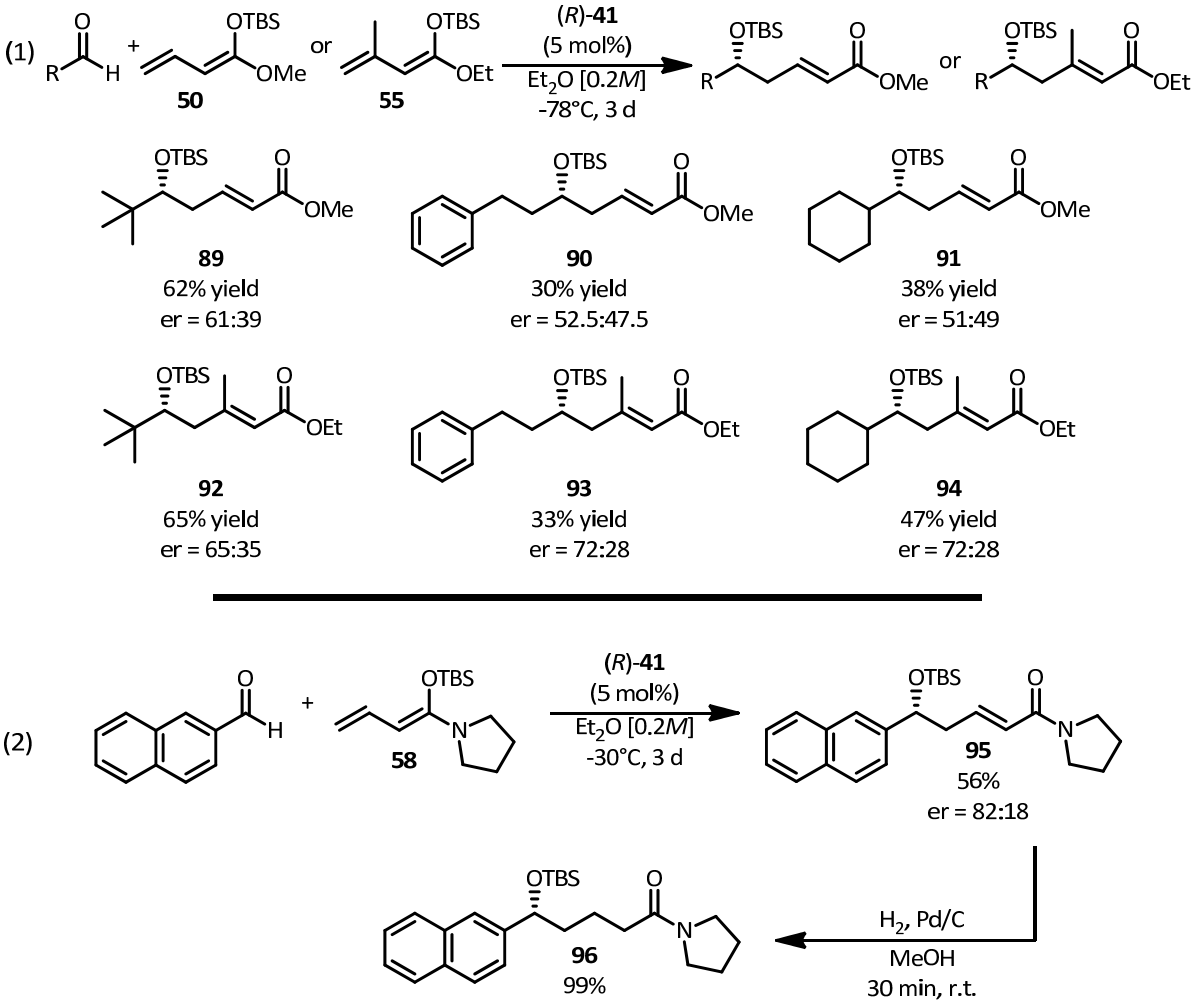


Figure 66. *Electrophile scope of the disulfonimide-catalyzed VMAR (continued III) and an example with amide derived nucleophile* ***58****.*

Nevertheless, the reported substrate scope concerning nucleophiles and electrophiles is remarkably broad compared to existing methods. Although the enantioselectivities are not yet generally high, the synthetic potential of disulfonimide-catalysis is clear.

Besides crotonic acid ester derived nucleophiles, crotonic acid amide **58** was also synthesized, which was subjected to the previously optimized reaction conditions (Fig. 66, eq 2). Under these conditions, we could obtain the α,β-unsaturated enamide **95** in 56% yield with an optical purity of 82:18 er. Furthermore the material could be quantitatively hydrogenated to the corresponding fully saturated amide **96**, which is used in an ongoing cooperation with the group of NUNO MAULIDE.

4.2 Disulfonimide-catalyzed double vinylogous Mukaiyama aldol reactions (DVMAR)

4.2.1 Synthesis of sorbic acid-derived nucleophiles

In contrast to normal and vinylogous Mukaiyama aldol reactions, the double vinylogous version is not well studied to date.[151] The C_2-homologue of crotonic acid is sorbic acid, and its potassium salt is widely used in food industry, *e.g.* as an antidegradant.[152] Thus it is not surprising, that sorbic acid derivatives are cheap and commercially available. To begin our studies in this area, we synthesized the corresponding esters (Fig. 67).

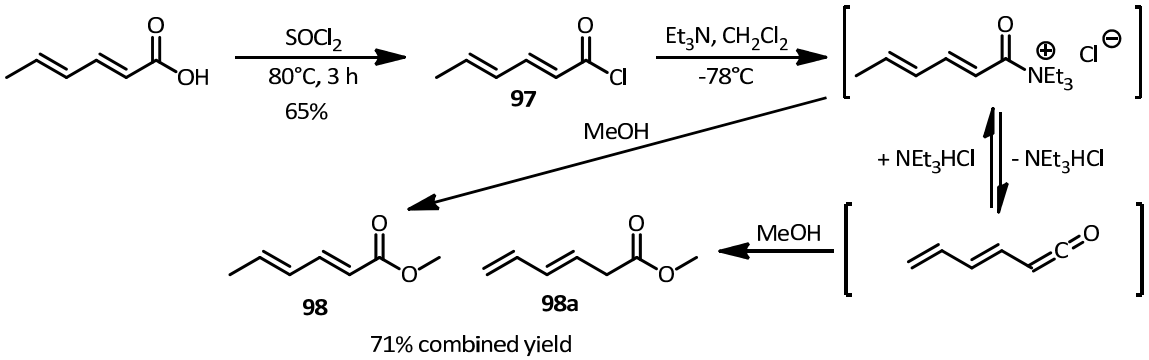


Figure 67. *Synthesis of the trienolate-precursor **98** / **98a** for the double vinylogous Mukaiyama aldol reaction (DVMAR).*

Starting from sorbic acid, we first synthesized sorbic chloride **97** by treatment with of $SOCl_2$. Subsequent distillation afforded the desired product in 65% yield. For the generation of the corresponding methyl ester we became aware of a report from the workgroup of Hoye.[153] In this report, **97** was treated with triethylamine and MeOH in CH_2Cl_2 to afford mixtures of the corresponding sorbic acid methyl ester **98** and its deconjugated derivative **98a**. This reaction is believed to proceed via initial acetyltriethylammonium ion generation, which can either undergo direct nucleophilic attack by the alcohol (**98**), or lead to ketene formation by elimination of NEt_3HCl and subsequent trapping with the alcohol, furnishing **98a**. In the course of the reaction, we were only able to synthesize mixtures of the two compounds, each as an *E*/*Z*-mixture in a combined yield of 71%. Nevertheless with compounds **98** and **98a** in hand, we envisioned that treatment with LDA and TBSCl in the presence of DMPU might lead to one single product, regardless of the double bond distribution in the parent ester. With this in mind we followed the general procedure **GSP 1** and were pleased that the desired reaction to compound **99** occurred smoothly, giving an *E*/*Z*-ratio of > 50:1 (Fig. 68).

Following this method we synthesized the TIPS-protected trienolate **100** and the TIPS-protected ethyl sorbate-derived trienolate **101**. Unfortunately we were not able to obtain any TMS-protected trienolates, due to the instability of these compounds.

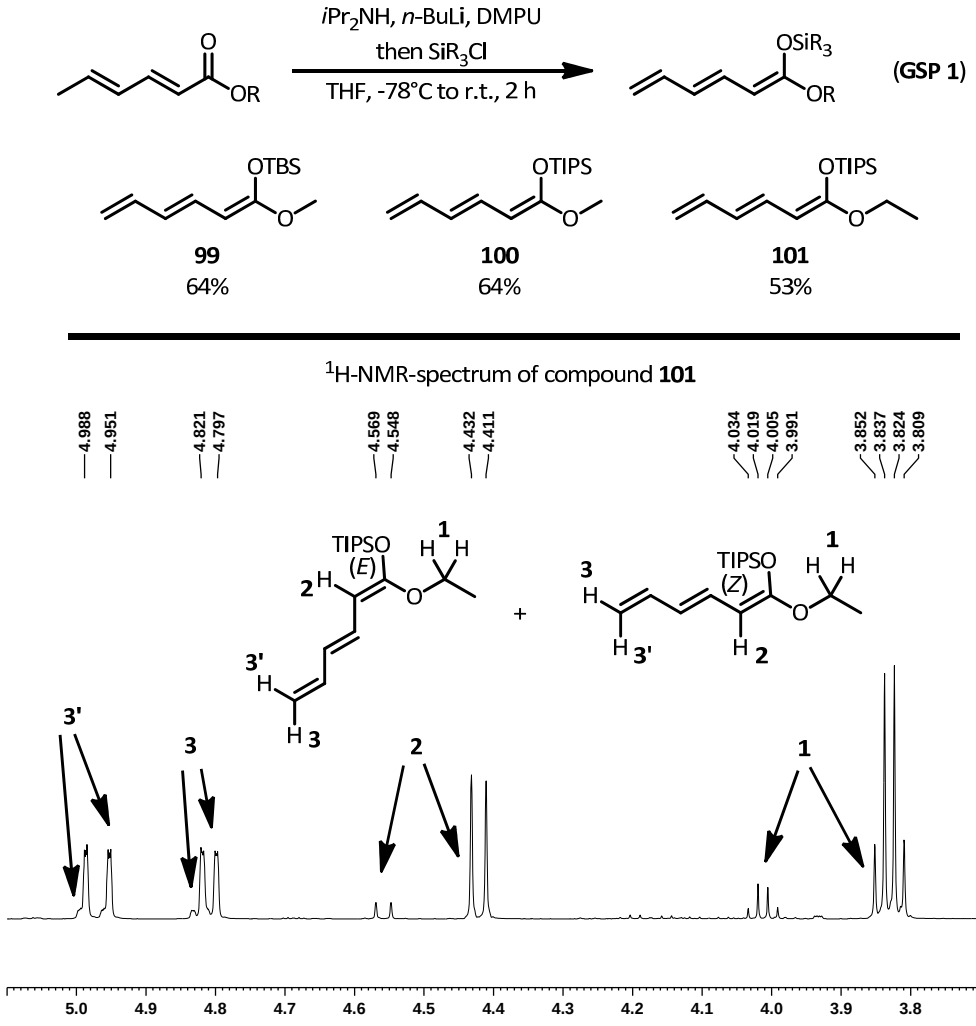


Figure 68. *Trienolate-synthesis and illustration of the (E,Z)-mixtures obtained.*

For substituted trienolates a more elaborate synthesis was required, since sorbates bearing substituents are not commercially available. We were interested in the synthesis of compounds with methyl-substituents in γ-, or δ-position. For this purpose we synthesized both esters analogously to literature procedures, via Horner-Wadsworth-Emmons reaction or Heck coupling respectively (Fig. 69). The Horner-Wadsworth-Emmons reaction between α-methyl-crotonaldehyde and triethyl phosphonoacetate, with sodium hydride as a base, was reported by the group of Serebryakov and delivered compound **102** in 42% yield.[154] Subsequent reaction of **102** following **GSP 1** gave the desired trienolate **103** (Fig. 69, eq 1).

The Heck reaction of isocrotyl bromide and methyl acrylate reported by Gilbertson et al.,[155] furnished the desired substituted ester **104** in 50% yield. Treatment of **104** under the conditions developed for **GSP 1**, resulted in the desired trienolate **105** as a mixture of isomers (Fig. 69, eq 2).

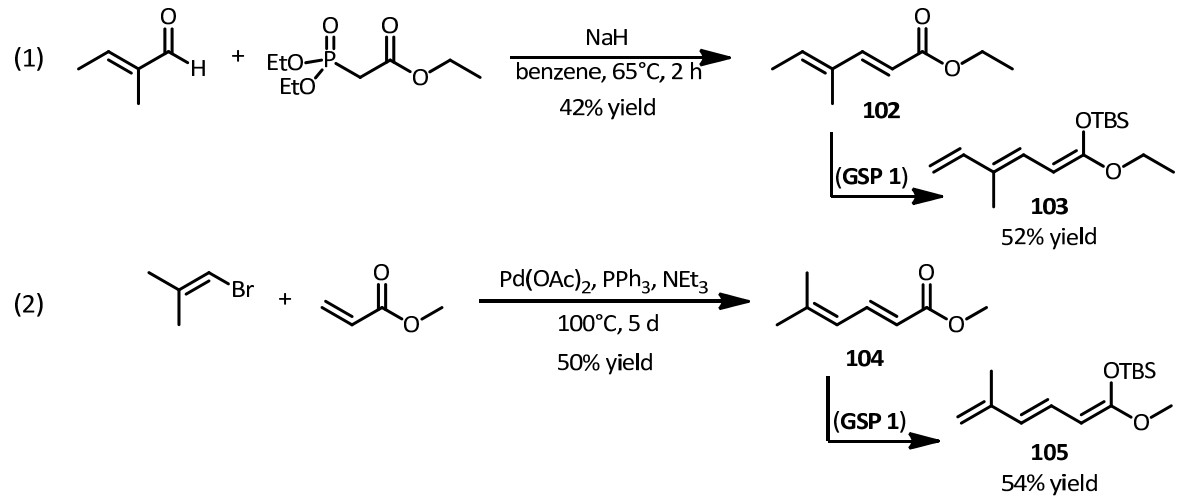


Figure 69. *Synthesis of branched trienolates **103** and **105**.*

The stability of the resulting products **99**, **100**, **101**, **103** and **105** was comparable to the corresponding crotonate-derived enolates and in Schlenck- or Young-tubes the material could be stored for weeks under Argon at 4°C.

4.2.2 Theoretical studies towards the nucleophilic behaviour of silyl trienolates

As already mentioned previously, the reactivity of trienolates has not been extensively investigated to date. Theoretical studies offer a good tool for the evaluation of the regioselectivity issues one might possibly face when conducting vinylogous Mukaiyama aldol reactions. Previously the group of Denmark discussed this possibility regarding calculations for electrophilic susceptibilities and orbital coefficients of dienolates such as **51**.[86] Following this stimulus, we sought a measure of expectable regioselectivities for double vinylogous Mukaiyama aldol reactions of trienolate-nucleophiles. A cooperation with the theoretical chemistry department of the Bayer CropScience AG, resulted in DFT-calculations of the corresponding theoretical nucleophilic behaviour of nucleophiles like **99**. We calculated the

Fukui functions ($f^-(\boldsymbol{r})$),[XIV] which provide an estimate for the probability of reaction with an electrophile at any given atom of the unsaturated carbon-chain (Fig. 70).

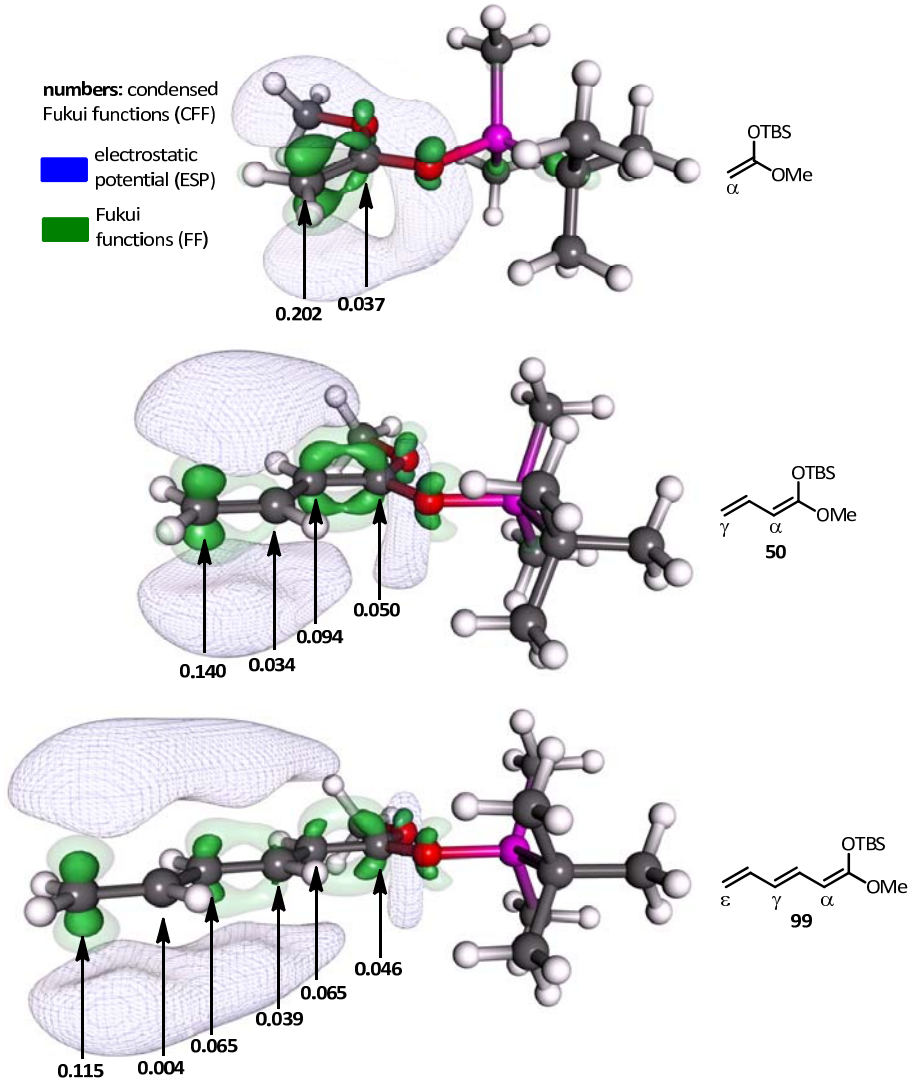


Figure 70. *DFT-calculations on the nucleophilicity and predicted reactive behavior of a silyl enolate, a dienolate and a trienolate.*

From the same calculations, we obtained the electrostatic potential and the condensed Fukui functions (CFF) of the molecule. These CFFs offer values which can be roughly compared with the data obtained by the group of Denmark. Furthermore the potential reactivities and regioselectivities can be predicted to some extent.

To set the data in a more global context, identical calculations were made for the *mono*-enolate *tert*-butyl((1-methoxyvinyl)oxy)dimethylsilane, the corresponding *di*-enolate **50** and the *tri*-enolate **99**.

[XIV] Named after the 1981-nobel prize winning theoretical chemist Kenichi Fukui (* 1918; †1998).

From these calculations it became obvious that the terminal positions are favoured, bearing highest nucleophilicities. Naturally, *mono*enolates do not offer any regioselectivity-issues, but the CFF of 0.202 can possibly be used to estimate its absolute reactivity in comparison to **50** and **99**. Accordingly, the *di*enolate **50** showed similar tendencies, with a clear preference for nucleophilic attack from the terminal γ-position (with a CFF of 0.14), however possessing significant electron density at the internal α-position.[XV] For the homologous *tri*enolate **99** similar tendencies were predicted with the highest estimate of nucleophilicity at the ε-position, however bearing considerable concurrence by the two internal positions at the γ- and α-carbons (CFF of 0.115 at ε- over 0.065 and 0.065 at γ- and α-position, respectively). With this in mind it becomes clear that for vinylogous aldol reactions one has to consider regioselectivity-challenges as already shown in previous reports. Interestingly our calculations and geometry optimizations resulted in geometries of the dienolate **50** different to the ones from the Denmark-group (Fig. 71). Whereas in our studies the silyl group *and* the methyl ester orientated *in-plane*, as defined by the double bonds of the crotonate, the calculations reported by Denmark offered an *out-of-plane* alignment of these two groups.

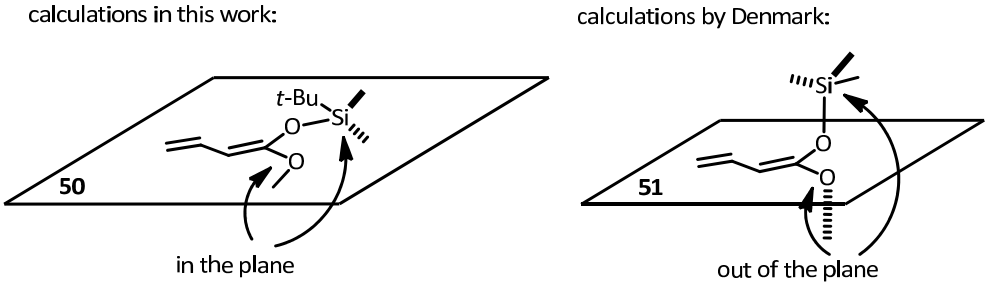


Figure 71. *In plane vs. out-of-plane orientation of the dienolates **50** and **51** as a result from geometrical optimization.*

Whether this issue can be traced back to the differences in basis sets (for details see experimental part and the respective literature), or to any other effect occurring in the calculation process, remains speculative. Another chemical reason might be the different steric demand delivered by a TBS- over a TMS-group, although intuitively the effect should have been opposite following this consideration. However, the principle reactivity of the vinylogous aldol reactions could be rationalized and the expected reactivity for double

[XV] The calculations provided in the literature[86] are conducted for compound **51** and specify the values for the orbital coefficient O.C. (0.302 at the γ- and 0.230 at the α-position) and the electrophilic susceptibility E. S. (0.592 at the γ- and 0.451 at the α-position), for further details see experimental part.

VMARs predicted, strengthening the feasibility of double vinylogous Mukaiyama aldol transformations. The absolute numbers obtained can be roughly correlated with those obtained in previous reports.[XVI]

4.2.3 The disulfonimide-catalyzed DVMAR

Having successfully synthesized trienolates **99**, **100**, **101**, **103** and **105**, we turned our attention to their application in double vinylogous Mukaiyama aldol reactions. Since the reaction conditions were already established for the vinylogous aldol version (see previous chapters), we decided to keep the procedure and the catalysts identical. Indeed we were very satisfied to see, that first trials using achiral benzene-disulfonimide **40** in combination with 2-naphtaldehyde and nucleophile **99** resulted in the corresponding reaction delivering the product in good conversion. The reaction mixtures were more complex, accounting for undesired side product. A decrease of the reaction temperature and the utilization of the chiral disulfonimide **41**, led to a significantly cleaner conversion. The expected ε-product **106** was formed in major amounts, along with an undesired product arising from reaction at an internal position of the nucleophile. Quite strikingly, the optical purity of the desired product was high (Fig. 72, er of 89:11).

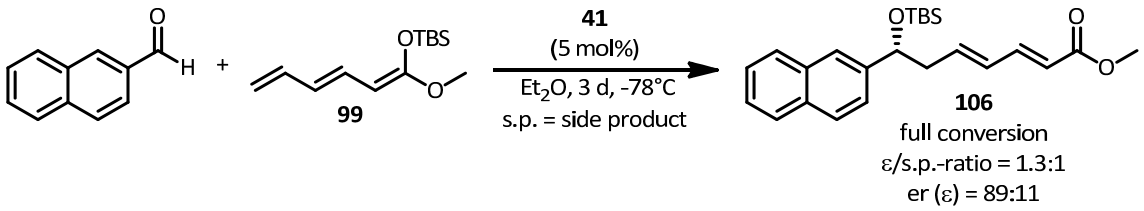


Figure 72. *The first disulfonimide-catalyzed double vinylogous Mukaiyama aldol reaction (DVMAR).*

In order to see whether we could extend this reactivity to other aldehydes, we screened a series of substrates under identical conditions. From these experiments it became clear, that the catalytic system showed the same substrate preference than the corresponding vinylogous aldol reaction (Fig. 73). It was observed, that cinnamaldehyde-derivatives, exemplarily present in **107**, were very well suited for a highly regioselective nucleophilic attack. Interestingly, electron-rich aldeyhdes, such as anisaldehyde, delivered no desired product **111**, but exclusively a side product. To allow further speculation about the exact role

[XVI] For further CFF-values of compounds not directly related to this work, such as ketone-derived silyl enolates or lithium enolates, see tables in the supplementary information.

of the aldehyde, we had to unambiguously identify the exact structure of the reaction products first. For this purpose we carefully interpreted the 1D-, and 2D-^{1}H-NMR-spectra of respective candidates.

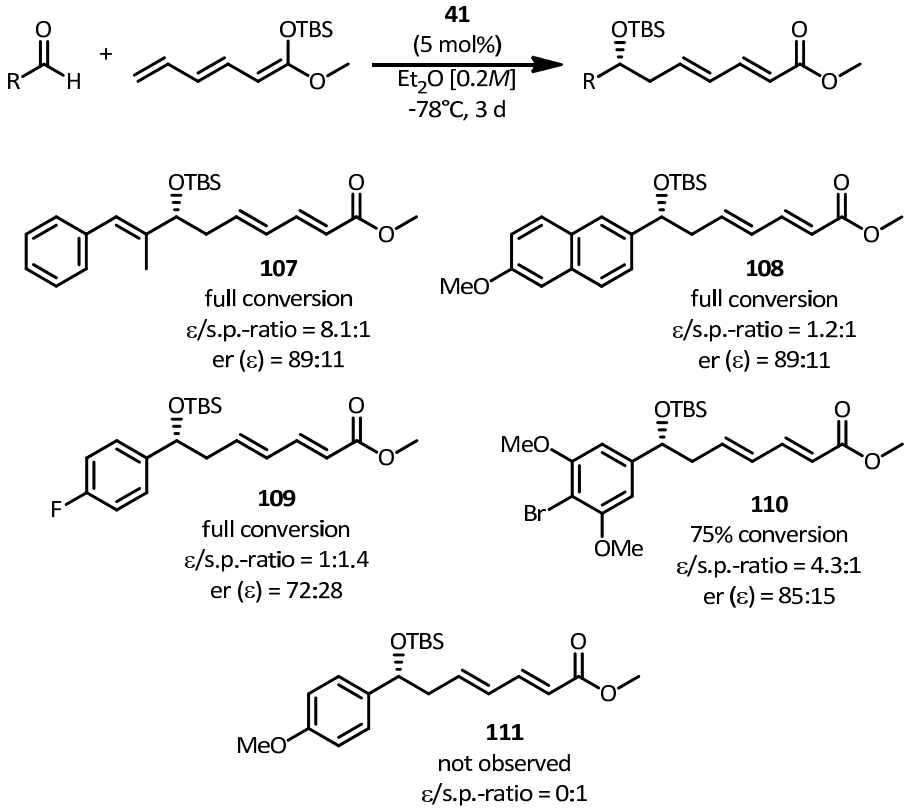


Figure 73. *First trial experiments towards the electrophile scope of the disulfonimide* ***41****-catalyzed DVMAR.*

To establish the double bond geometry as the depicted all-*E*-pattern, we looked at the coupling constants of the corresponding proton-signals in product **106** (Fig. 74). A similar coupling pattern and signal appearance could be observed for all double vinylogous Mukaiyama aldol products. The most characteristic peak for these compounds is the multiplet-signal at 2.5 ppm integrating to 2 protons, which corresponds to the crucial CH_2-signals. With this in mind, the crosspeak-distribution can be analyzed accordingly, leading to the clear determination of the structure. The *E*-geometry of the two newly formed double-bonds was analyzed by the values of coupling constants, being in the range of 15.0 and 16.0 Hz, the archetypical area for *trans*-aligned olefinic protons.

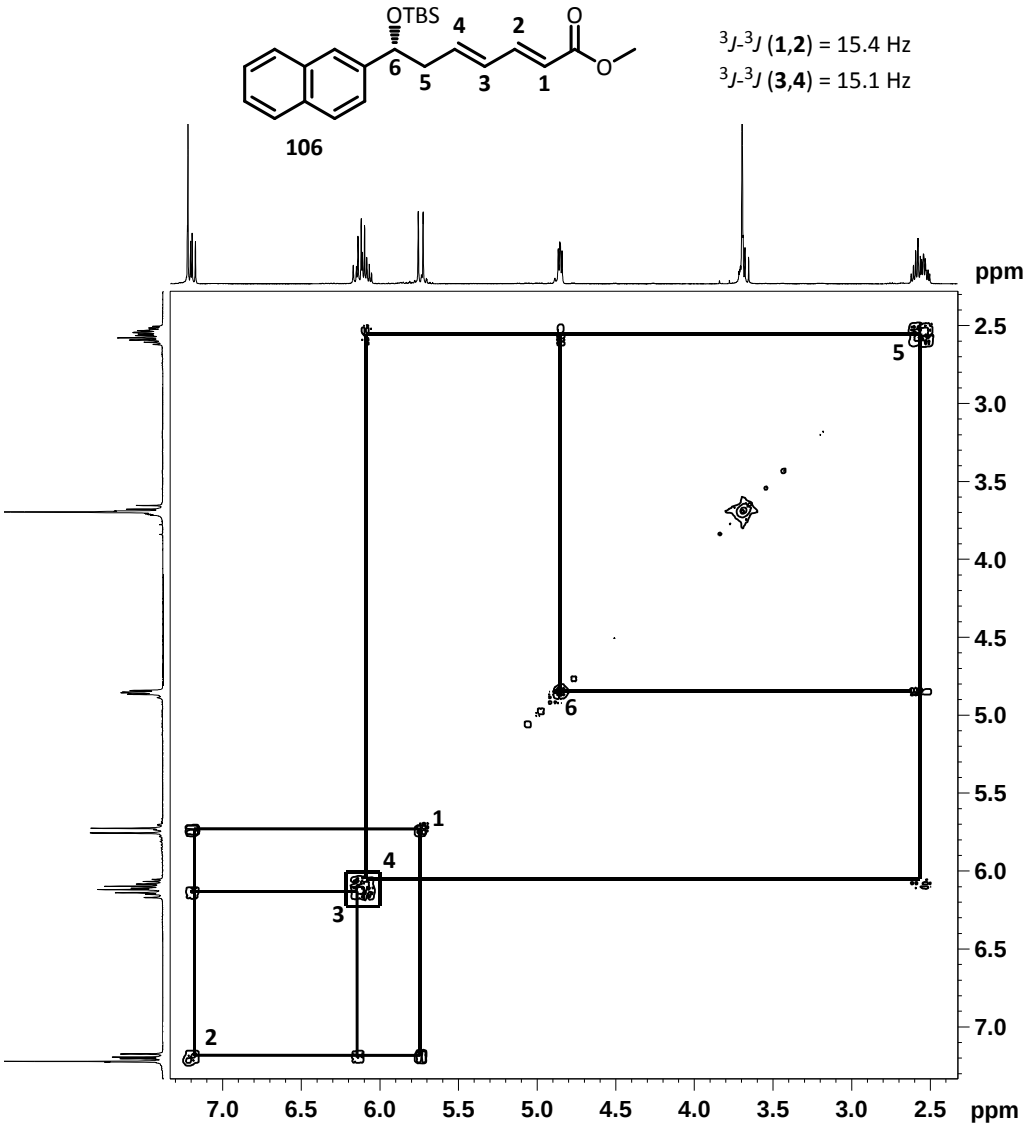


Figure 74. *^{1}H-^{1}H-COSY-analysis of the desired ε-DVMAR-product **106**.*

After the unambiguous assignment of the NMR-signals of the expected double vinylogous Mukaiyama aldol products, we turned our attention to the structure determination of the side product. Our theoretical studies showed that the Fukui functions were equal in α- and in γ-position, suggesting an according product distribution. However, it is noteworthy that we were only able to isolate one side product in clean form. The second side product is only produced in very minor quantities, if at all. Nevertheless our endeavour was to identify the exact structure of the isolable side product (exemplarily on compound **111a**, Fig. 75).

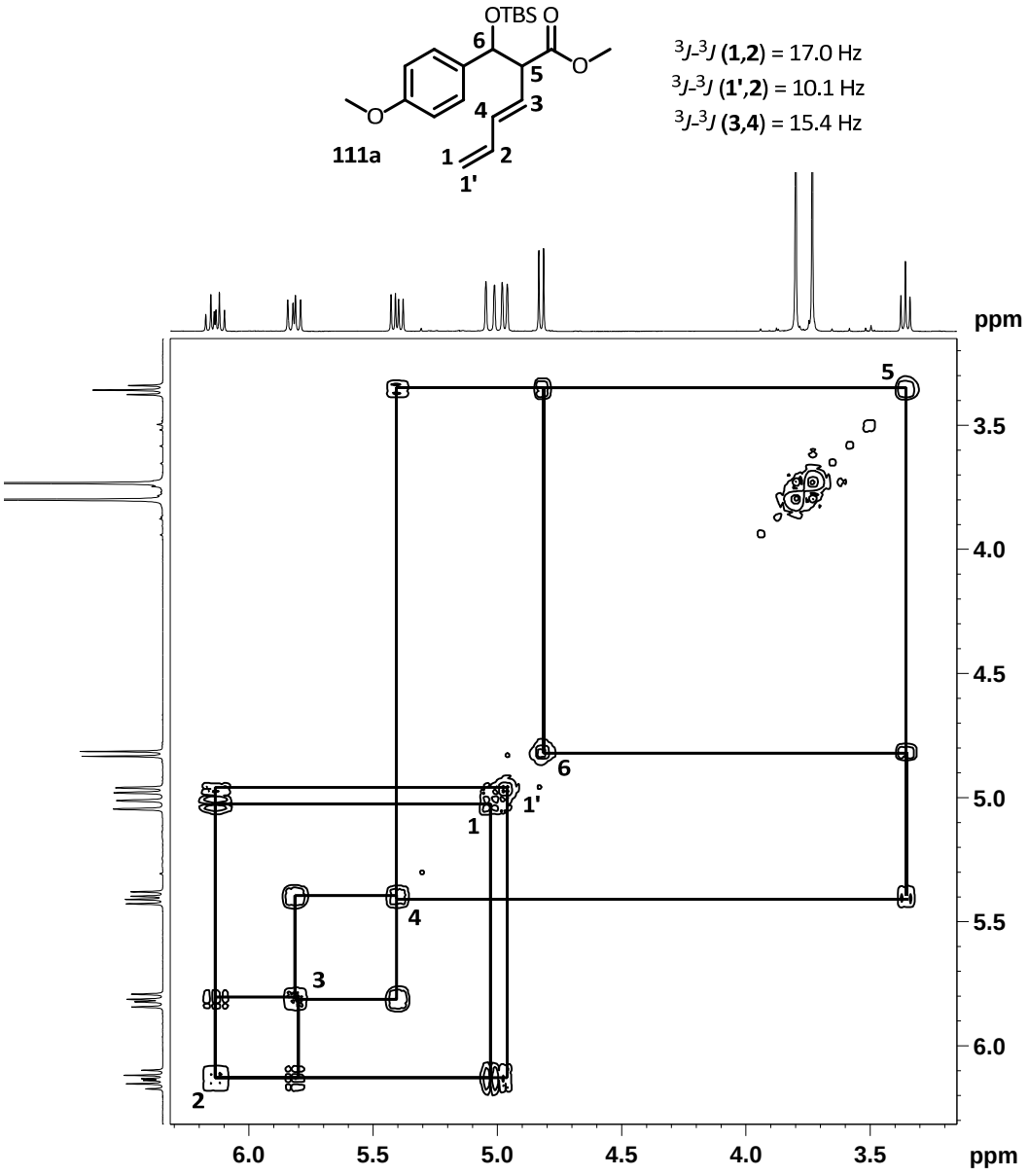


Figure 75. *^{1}H-^{1}H-COSY-analysis of the undesired α-DVMAR-product **111a**.*

Careful investigations of coupling constants and 2D-^{1}H-NMR experiments were very helpful. Quite clearly, the coupling of the two terminal protons in the double bond system (10.1 Hz and 17.0 Hz), the alignment of the alkyl chain as a conjugated diene, as well as the crosspeaks between the two sp^3-CH-protons, showed the constitution of the side product. Its appearance however raised the question of the destiny of a possible γ-product. When considering the size of a TBS-protecting group, one might argue to expect remote reactivity preferably due to steric reasons, thus the γ-product should be obtained. However, an argument towards the production of the α-product might be the fact that in this case a conjugated diene system is produced. Consideration of the geometrical arrangement of a TBS-group shows that its steric bulk is not very different from a TMS-group: two thirds of the

total steric demand are occupied by methyl-groups. The combination of these two factors gives a good explanation towards the outcome of this aldol reaction.

To provide further support of these assumptions, we investigated the substrate scope and were able to optimize yields and enantioselectivities substantially (Fig. 76). This reaction proved to have the same scope and limitations than the earlier discussed vinylogous version. Although we were not able to isolate the side products in all cases, we determined the regioselectivity by NMR-analysis of the crude reaction mixtures. With this in mind, we synthesized the corresponding α,β,γ,δ-unsaturated silyloxy esters in synthetically useful yields and high enantiopurities. The reaction conditions chosen were identical to those presented in Fig. 73.

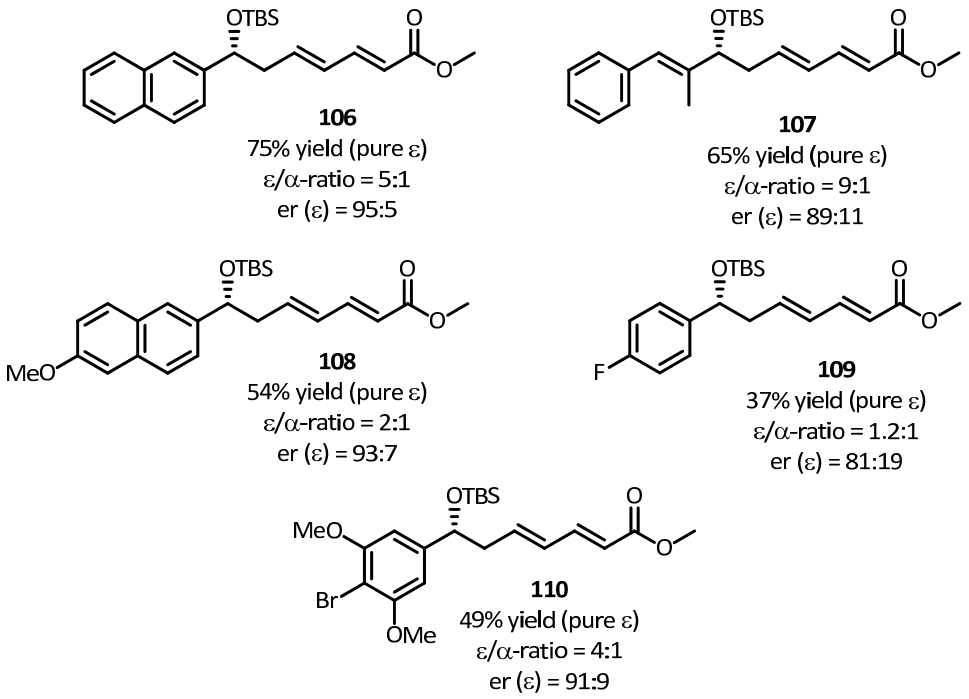


Figure 76. *Electrophile scope of the DVMAR under optimized conditions and on preparative scale (for conditions see Fig. 73).*

Following these optimized results we quickly found that the method is equally well applicable to a larger variety of aldehydes, however, the regioselectivities proved to be very variable. The use of low reaction temperatures, which is crucial to obtain a maximum enantioselectivity, suppressed the conversions in some cases, resulting in low isolated yields (Fig. 77).

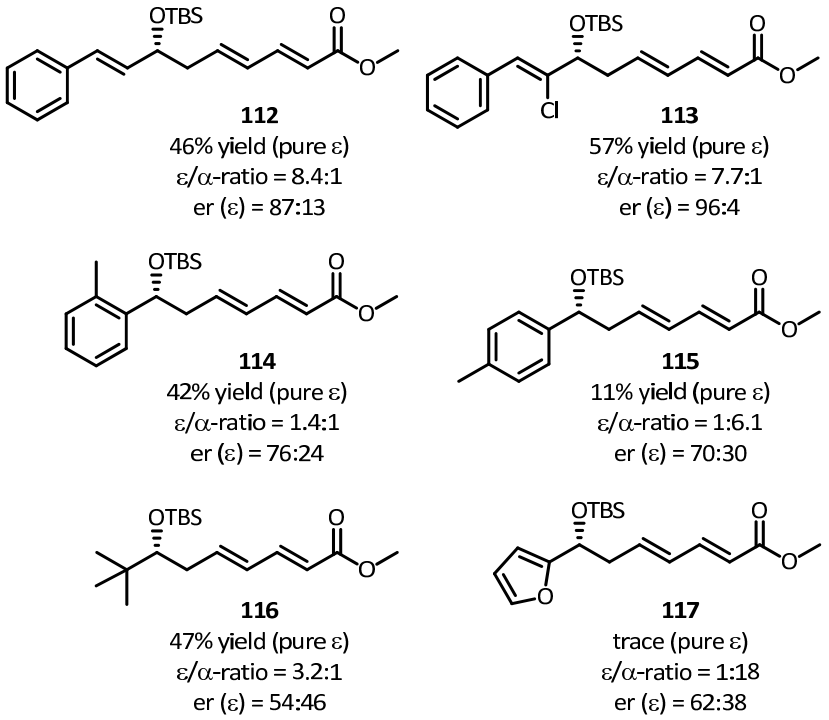


Figure 77. *Electrophile scope of the DVMAR (continued I, for conditions see Fig. 73).*

Interestingly pivalic aldehyde gave product **116** in 47% yield, although the product was virtually racemic. Reactions with other aliphatic aldehydes, such as hydrocinnamaldehyde or cyclohexane-carboxaldehyde, were unsuccessful. For these substrates the products could only be isolated in the racemic reaction using catalysts **40** at room temperature. To further show the applicability of the new ε-selective aldol method, we investigated the branched nucleophiles **103** and **105** (Fig. 78).

The γ-branched trienolate **103** delivered the desired product in good enantioselectivities, but only in moderate yields and regioselectivities. Unfortunately, the nucleophile **105** with its methyl substituent at the δ-position did not give any desired product. Thus, although our developed Mukaiyama aldol reactions work well with unbranched sorbic acid-derived trienolates, the applicability towards branched reaction partners is limited so far. This behavior might be due to the instability of the nucleophiles as well, since the corresponding trienolates **103** and **105** showed a stronger tendency to decompose.

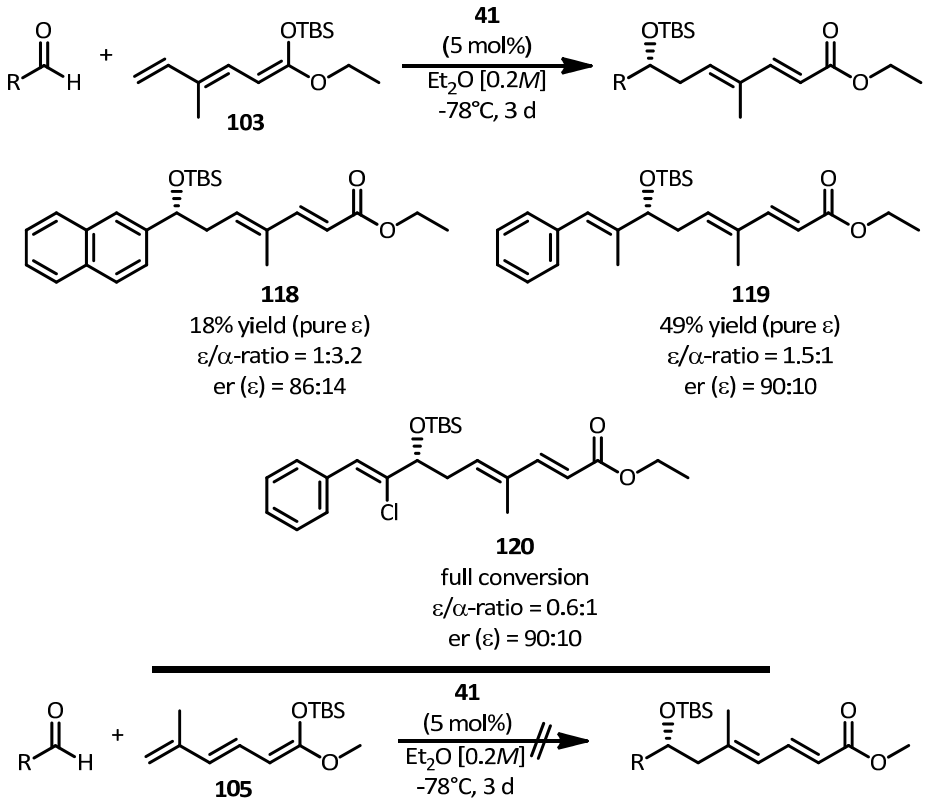


Figure 78. *Towards the introduction of complexity in the DVMAR.*

Being especially intrigued by the synthetic potential of the ε-products arising from nucleophiles like **99**, we endeavoured towards increasing the regioselectivity. We envisaged that for the double vinylogous Mukaiyama aldol reaction the influence of the silyl protection group should be higher than for the vinylogous version. Indeed the installation of a TIPS-protecting-group, as present in nucleophile **100**, significantly increased the ε-selectivity (Fig. 79).

Probing the reactivity for six different electrophiles, we showed a drastic improvement of the synthetic utility of the procedure. One drawback of the reactions featuring nucleophile **100**, were the extended reaction times. These reaction mixtures had to be stirred for 5 days to reach full conversions. When we tried to utilize nucleophile **101**, we did not observe any product formation (Fig. 79, eq 2).

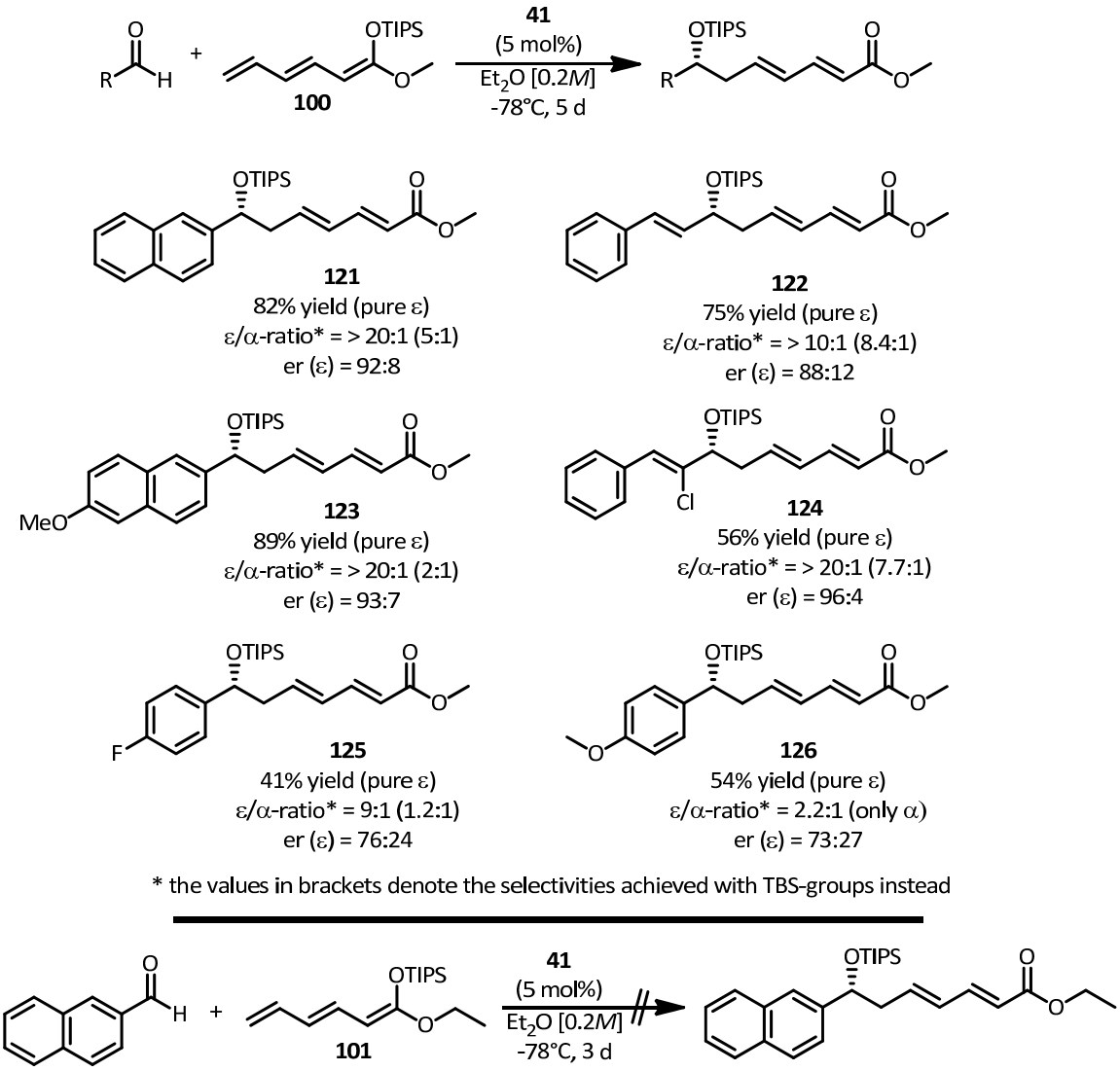


Figure 79. *Considerable regioselectivity-improvement by means of a different protecting group in disulfonimide catalyzed DVMARs.*

Hence, overall we developed a very efficient and mild protocol for the preparation of not only α,β-unsaturated, but also α,β,γ,δ-unsaturated esters. Although showing some limitations in electrophile scope, the nucleophile-applicability proved to be quite general for both, substituted and unsubstituted *di*- and *tri*-enolates.

4.2.4 Determination of the absolute configuration

To corroborate the stereochemical outcome of our catalytic system we investigated the absolute configuration of the reaction products. For this purpose we chose compound **72**, since it has been thoroughly explored before (Fig. 80). Satisfyingly we could deprotect this reaction product by simple treatment with 10% HCl in THF. The optical rotation $[\alpha]^D$ of alcohol **72a** after deprotection gave data correlating to the (*R*)-configuration.[91]

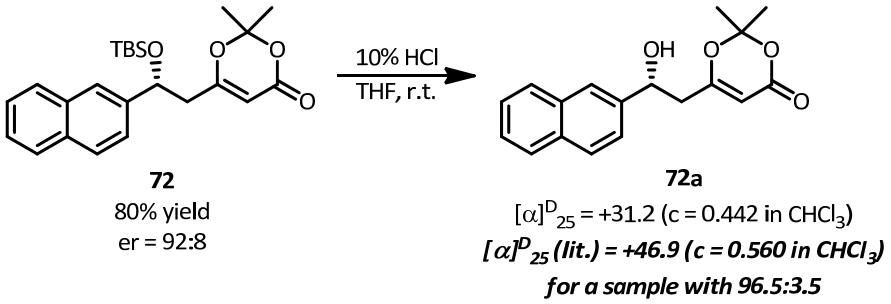
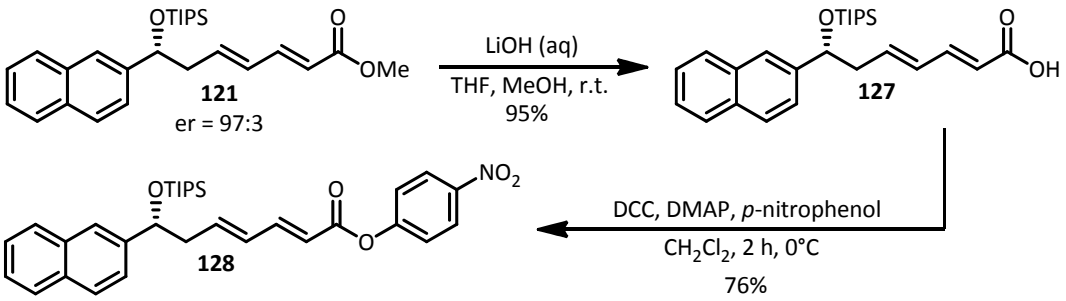


Figure 80. *Evaluation of the absolute configuration of product* ***72*** *by means of its free alcohol* ***72a****.*

However, we were even more interested in establishing the absolute configuration of our double vinylogous Mukaiyama aldol products (Fig. 81). An X-Ray-structure would not only show the configuration of the stereocenter, but could also confirm the all-*E*-double bond geometry. To realize this, a highly enantioenriched sample of product **121** was converted into the corresponding nitrophenolate **128**.



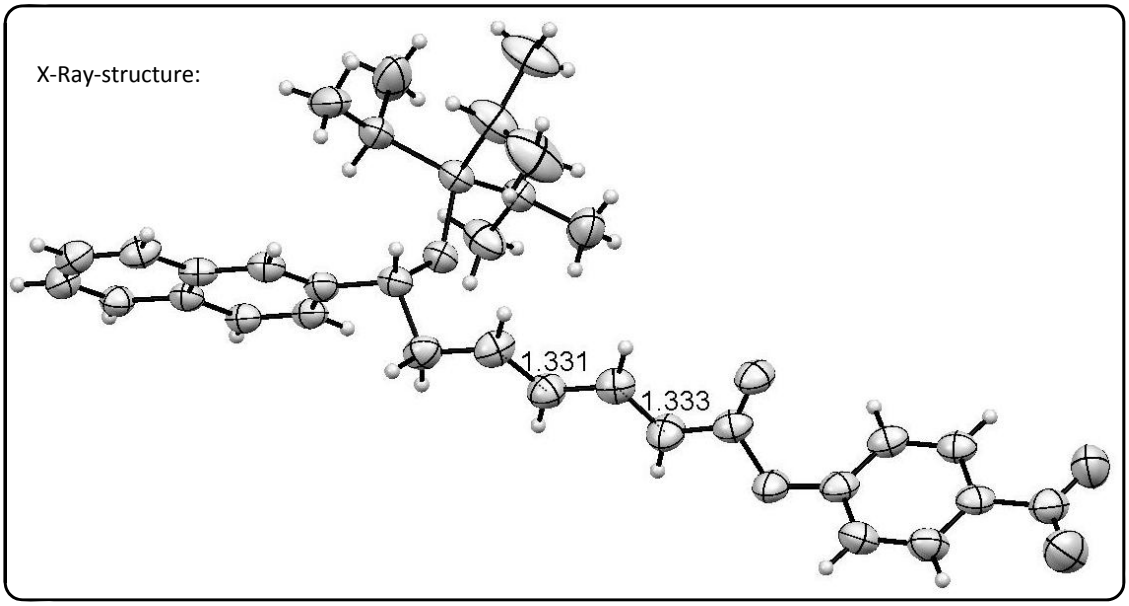


Figure 81. *Determination of the absolute configuration of the disulfonimide-catalyzed DVMAR product* ***121*** *by means of its p-nitrobenzoate* ***128*** *and crystal structure, double bond lengths (in Å) are highlighted.*

Satisfyingly, this material crystallized in form of white needles, which could be examined by X-ray single crystal analysis. The stereocenter exhibited (*R*)-configuration and the double bond geometry was shown as all-*E*, distributing typical double bond lengths of 1.33 Å.

4.2.5 Synthetic application of the double vinylogous Mukaiyama aldol reaction

The synthetic utility of vinylogous Mukaiyama aldol products was already illustrated in the syntheses of several natural products.[87] The groups of Carreira, Evans, Kalesse and Denmark successfully showed the comprehension of either enantio- or diastereoselective vinylogous Mukaiyama aldol reactions for syntheses of Macrolactin A,[92] Phorboxazole B,[93] Ratjadone[156] and Macrolide RK-397.[157] From these approaches one can realize that the available products are versatile and can set the stage for subsequent transformations.

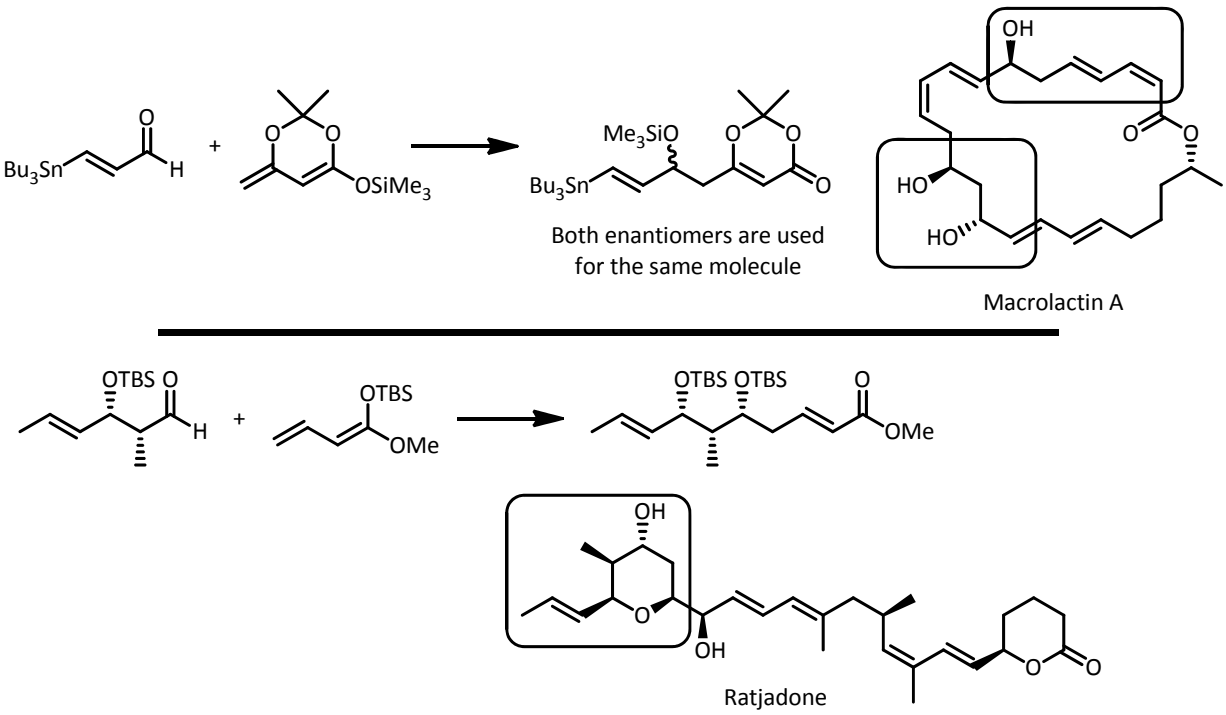


Figure 82. *Natural products potentially accessible by VMAR-methods.*

By considering the structure of Macrolactin A (Fig. 82) it is obvious, that a double vinylogous Mukaiyama aldol procedure could be valuable. The appearance of α,β,γ,δ-unsaturated hydroxycarbonyls can be illustrated by other natural products, with Lasonolide as one of their most complex examples.[158] Nevertheless, we were interested in another potential

arising from this transformation: the construction of eight-membered ring lactones (ζ-lactones).

4.2.5.1 Synthesis of eigth-membered ring lactones (ζ-lactones)

Since sorbic-acid derived nucleophiles readily install six carbon atoms onto an aldehyde moiety, the products can possibly be used for the construction of eight-membered ring lactone structures. If one considers the possibilities of variation in the nucleophilic *and* electrophilic portion, the true potential of the method becomes clear. A variety of natural products bear fully saturated ζ-lactones, such as the marine oxylipins Solandelactone A-D,[159] Cephalosporolide D[160] and Octalactins[161] as prominent examples (Fig. 83). Previous syntheses of such structures, as shown by the groups of Pietruszka and White,[162] illustrated the difficulty of the construction of the eight membered ring.

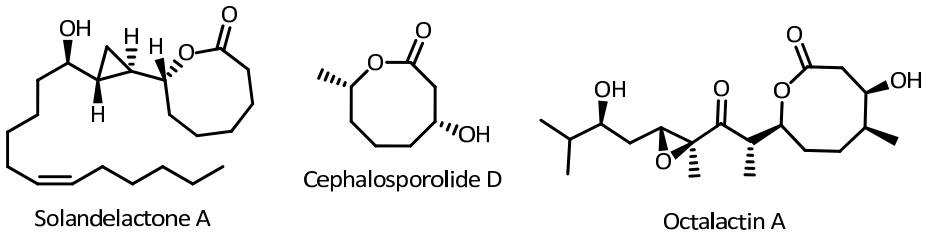


Figure 83. *Selected natural products bearing a ζ-lactone subunit.*

Thus we envisioned a direct route to ζ-lactones, utilizing our highly enantiopure α,β,γ,δ-unsaturated esters. Pleasingly with a sequence of deprotection, hydrogenation, ester-hydrolysis and Yamaguchi-macrolactonization, we were able to synthesize different eight-membered macrolactones **132**, **137** and **141** in up to 64% overall yield without the loss of enantiopurity (Fig. 84). After optimization of the reaction conditions, we were able to carry out the sequence without any intermediate column chromatography, which underlines its operational simplicity. Nevertheless it should be noted, that the reaction intermediates can be sensitive towards the elimination of the alcohol. We observed this behaviour during the hydrogenation, aswell as the hydrolysis of the ester portion, leading to elimination products. After the hydrogenation of **129**, which should be accurately controlled by TLC, one can observe the completely conjugated α,β,γ,δ,ε,ζ-unsaturated ester **133**, the acid-sensitivity of similar compounds was reported earlier.[163] However, also the ester hydrolysis with the concomitant acidification can lead to the elimination of the alcohol function, resulting in ε,ζ-unsaturated acids, as observed in the synthesis of compound **137**.

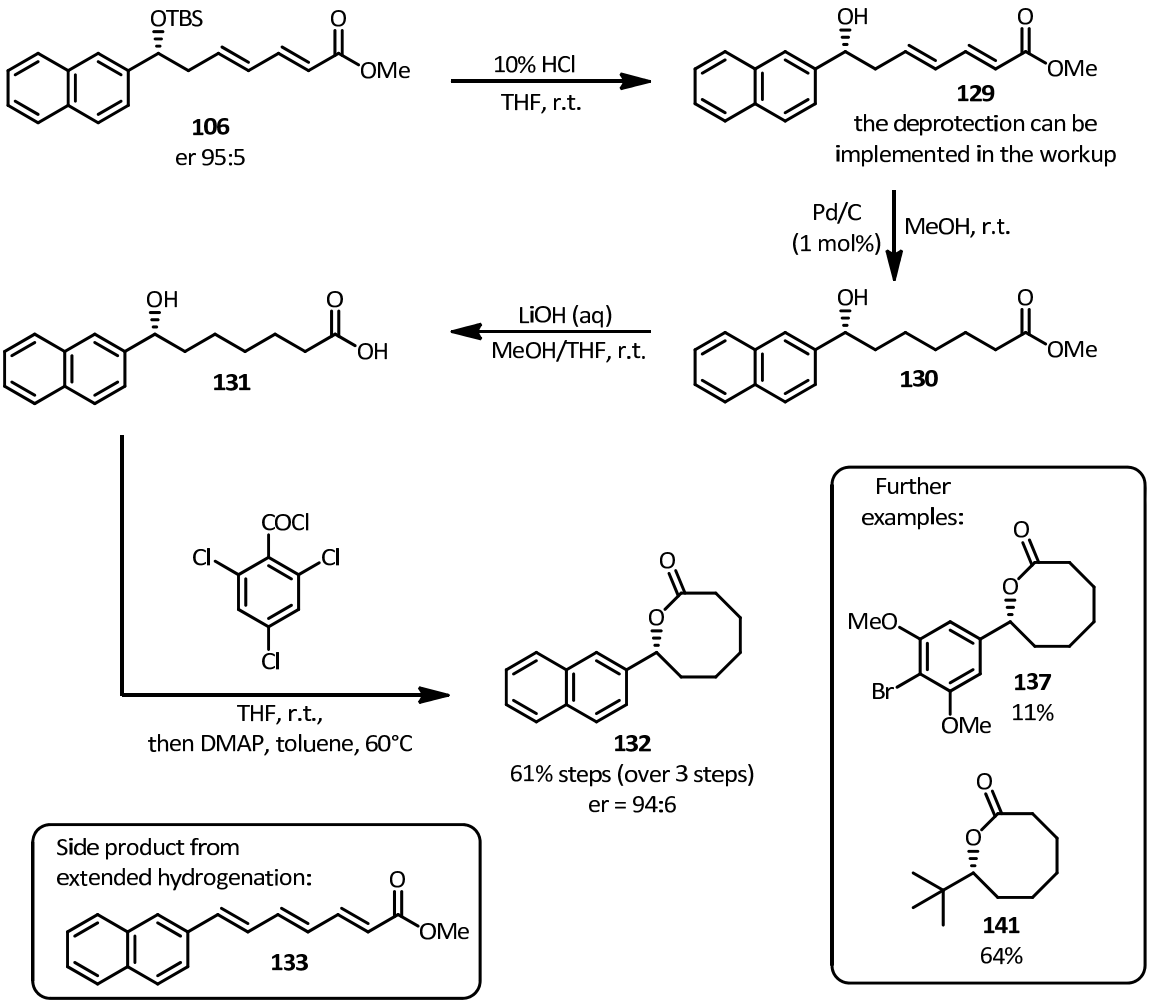


Figure 84. *Four-step approach towards highly enantioenriched eight-membered lactones (ζ-lactones).*

Although bearing some sensitive reaction steps, this approach probably represents the most direct entry to eight-membered ring lactones known to date.

4.3. Mechanism Elucidation

4.3.1 Preliminary studies towards establishing the reaction mechanism

The general performance offered through disulfonimide-catalysis is very intriguing. However, although disulfonimides possessed excellent activity towards various electrophiles and nucleophiles, the substrate scope and enantioinductions still left room for improvement.[XVII] In order to tune the catalyst in a more efficient manner, we were interested in the mechanism of disulfonimide-catalyzed reactions. In the very beginning of the research project, the working hypothesis was based on ACDC, asymmetric-counteranion-directed catalysis.[36, 144a-d] This hypothesis implied the initial silylation of the disulfonimide-structure. This catalyst activation, occuring off cycle, should give rise to an N- and / or O-silylated disulfonimide. These species have been previously discussed by Blaschette and others,[125] possibly being in a silatropic equilibrium in solution. The conversion of the catalyst can be observed by on-line ^{1}H-NMR-spectroscopy.[129a] In any case, this type of catalysis falls into the operating area of Lewis acid catalysis, since a Brønsted acidic precursor converts into a Lewis acid, initiating the catalytic cycle. To rule out the appearance of Brønsted acid-catalysis in these processes, the reaction was shown successfully in the presence of 2,6-di-*tert*butyl-4-methyl pyridine in the original paper.[129a] This base is frequently used to differentiate between activation modes, scavenging protons from the reaction mixture, though not silyl groups.

In a first possible **mechanism 1** (Fig. 85), the silyl group is transmitted from the catalyst molecule to the oxygen-atom of the carbonyl compound, resulting in a reactive oxocarbenium ***chiral ion pair I*** or an equivalent. Obviously the counterion is the chiral disulfonimide, potentially governing the observed enantioselective nucleophilic attack of a silyl enolate. The arising second intermediate would be a disilylated silyloxycarbenium ***chiral ion pair II*** (Fig. 85), in which the labile silyl group on the former enolate-oxygen could be possibly transferred to the disulfonimide-anion. The catalyst would be liberated, and the reaction product would bear the silicon from the enolate initially activating the catalyst.

[XVII] In this research program a large variety of different reactions, namely Mannich and Michael reactions, allylations and methallylations, cyanations, formal cycloadditions and other transformations were attempted by colleagues, possessing similar reactivity profiles with respect to the aldehyde scope.

Trace amounts of other Lewis acids could possibly lead to the liberation of a "R_3Si^+"-species, which can open up an achiral pathway of the reaction, as discussed by Bosnich.[108]

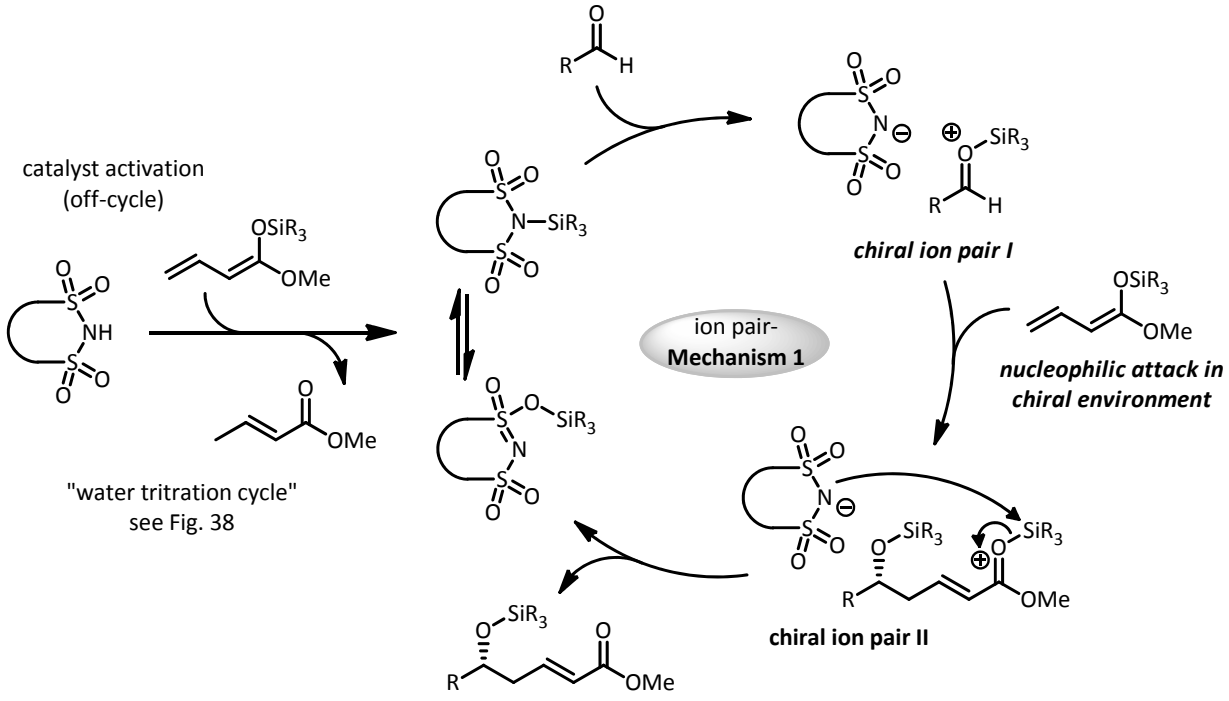


Figure 85. *Hypothetical ion pair* ***mechanism 1*** *of disulfonimide-catalyzed Mukaiyama aldol reactions.*

Another scenario in accordance with initial catalyst silylation is a Lewis acid **mechanism 2** as proposed *e.g.* by Yamamoto (Fig. 86).[116] Here, the N- or O-silylated disulfonimide-species would form a ***pentavalent silicon-species*** with the aldehyde, lowering the LUMO of the carbonyl-carbon towards nucleophilic attack. An additional hypothesis could be a further activation of the silicon center by an interaction of a Lewis basic oxygen (or nitrogen, if the O-silylated catalyst species is operative). This would further increase the reactivity at silicon, in line with research by the group of Denmark.[122a, 122b, 123] The catalyst regeneration in this scenario would occur through a ***transsilylation*** (Fig. 86) from the second intermediate. The silyl-group initially present in the disulfonimide-catalyst would presumably stay unchanged, representing a 'true' Lewis acid catalyst where the silyl group is not exchanged during an N-Si-bond cission.

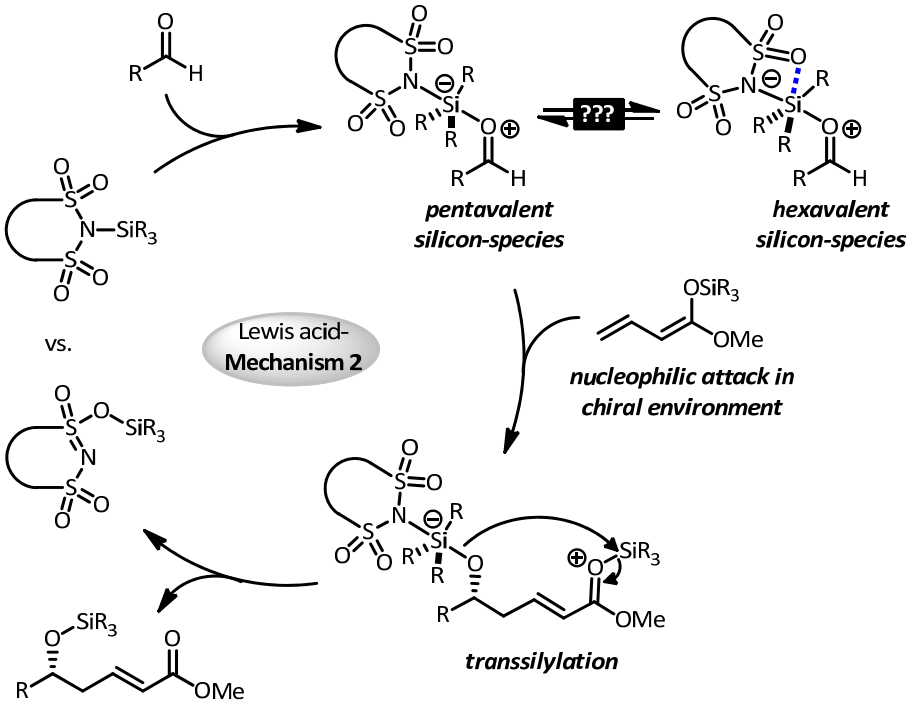


Figure 86. *Hypothetical* ***mechanism 2*** *of disulfonimide-catalyzed Mukaiyama aldol reactions.*

The discussion about these two 'extreme' scenarios is not new and goes back to seminal studies discussed before.[117] In these studies, the involvement of an achiral Me_3SiOTf-catalyzed reaction pathway in asymmetric Ti-catalyzed Mukaiyama aldolizations prevented appreciable enantioinduction.[108] This illustrates the possibility of achiral reaction pathways involving strongly Lewis acidic R_3Si^+-species. Of course these thoughts have to be considered regarding the present method as well, although our actual catalyst system is not based on a triflate species but on a presumably more nucleophilic triflimide.

Based on research by Ghosez et al.[113a] regarding the high activity of triflimide-derived silyl Lewis-acids in Diels-Alder reactions, the group of Yamamoto undertook careful investigation of the mechanism and ligand influence in silyl Lewis acid-catalyzed Mukaiyama aldol reactions.[117] Remarkably both studies revealed that triflimide-derived silyl Lewis acids are much more active than the corresponding triflates.

To evaluate whether the first mechanism (Fig. 85) or the second mechanism (Fig. 86) was operative in our case, cross-over experiments were conducted. These experiments were in line with the ones previously reported by Yamamoto,[116] Denmark[164] and Carreira[75] (for a schematical sketch Fig. 87, eq 1). Therefore we presynthesized silylated disulfonimide-catalysts from stoichiometric amounts of disulfonimide **40** with a nucleophile bearing a particular silyl protecting group in CD_2Cl_2 as a solvent at r.t. The consumption of the

nucleophile was followed by ^{1}H-NMR-spectroscopy of the mixture. The solution with the active catalyst was then injected to a mixture of 3,5-dimethylbenzaldehyde, followed by addition of a nucleophile bearing a different protecting group. The reaction was conducted at r.t., because the tendency for a scrambling should be highest at elevated temperature.

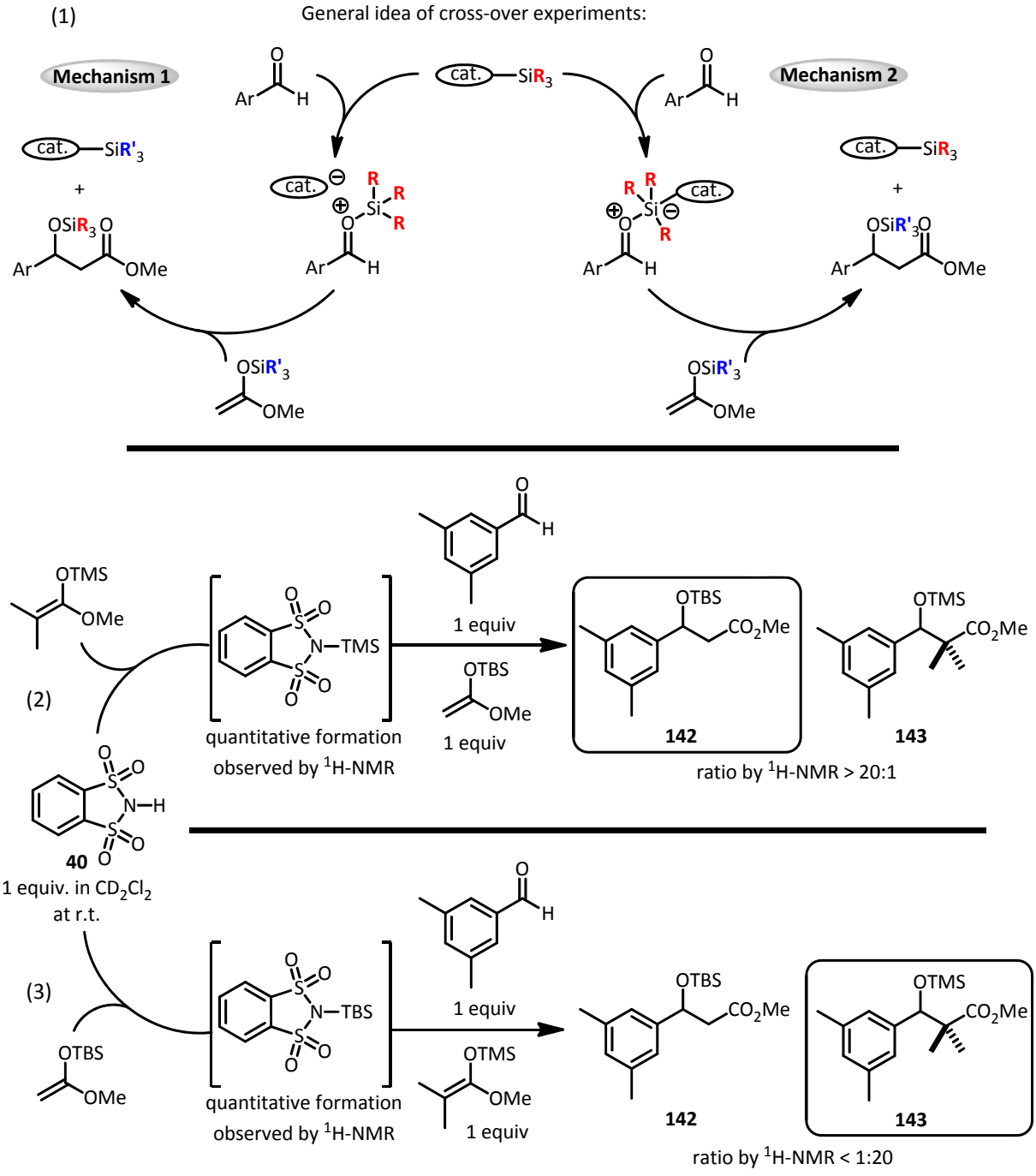


Figure 87. *Simple cross-over experiments with benzenedisulfonimide* ***40*** *and non-vinylogous enolates.*

The product was found to bear the silyl group from the actual nucleophile, which points towards a scenario like **mechanism 2**. The **mechanism 1** should involve the cission of the

disulfonimide-silicon bond and most probably result in a considerable scrambling. The steric effects of the different silyl groups on the catalyst had no influence on the reaction outcome. The TMS-incorporating catalyst provided the product with the TBS-group exclusively when the TBS-containing nucleophile was used (Fig. 87, eq 2). Analogously, the TBS-catalyst gave the TMS-group on the product when utilizing the TMS-protected nucleophile (Fig. 87, eq 3).

However, switching to the presumably less nucleophilic *vinylogous* nucleophiles **50** and **51**, changed the scrambling behavior considerably (Fig. 88, eq 1 and 2).

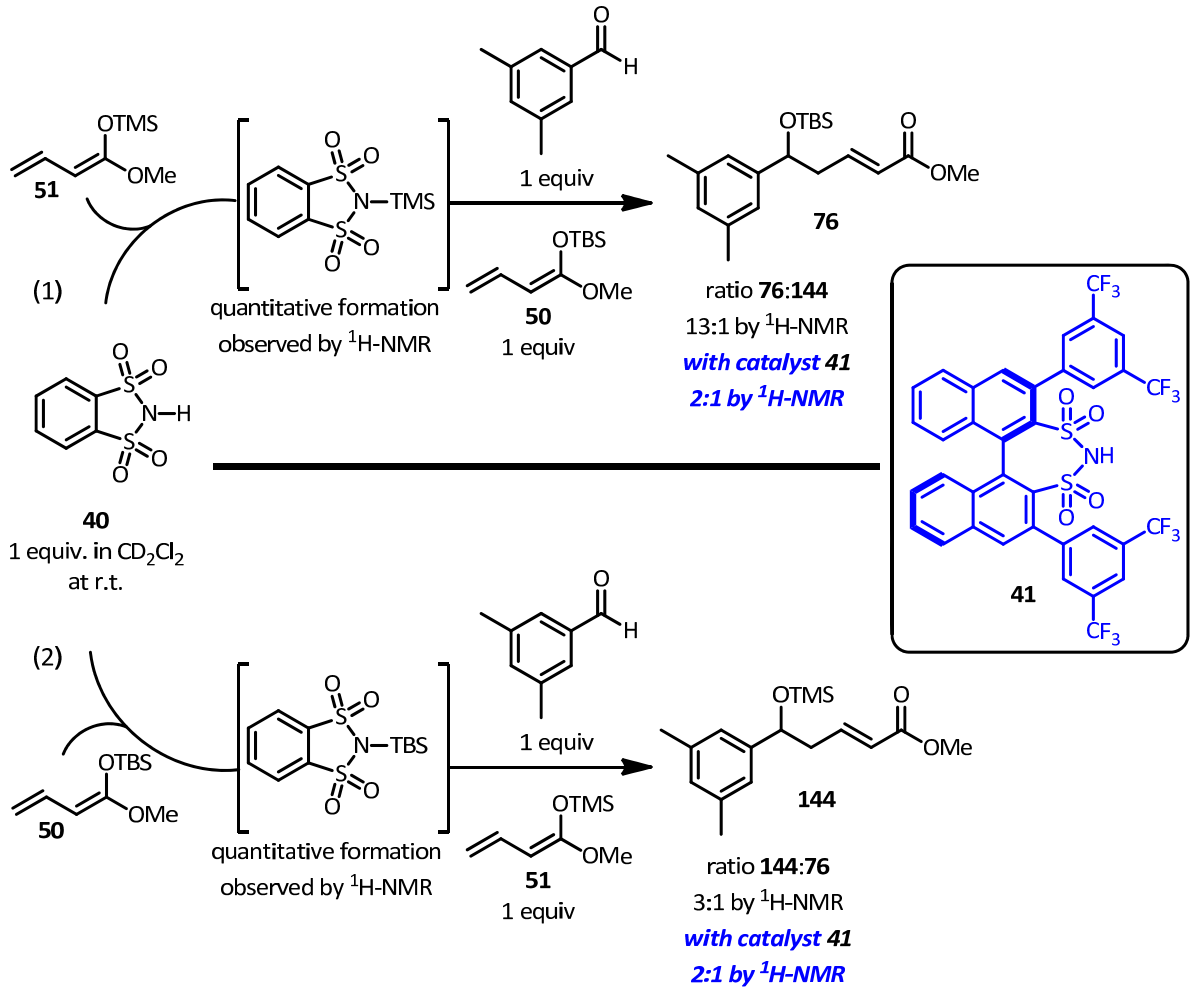


Figure 88. *Simple cross-over experiments with disulfonimide **40** and **41** and vinylogous enolates **50** and **51**.*

Significant amounts of the scrambled reaction products could be observed by ^{1}H-NMR-analysis. This behaviour was even more pronounced when we used the less reactive chiral catalyst **41**. To rationalize this behavior, one has to consider the reactivity of the nucleophile and the activity of the catalyst. Generally, the more nucleophilic non-vinylogous nucleophiles did not result in considerable scrambling.

Another observation from these studies is that the TMS-preformed catalyst led to lower scrambling than its TBS-derived congener when using pre-catalyst **40** (Fig. 88, eq 1). This could be possibly explained by a difference in reactivity of the differently bulky silicon Lewis acids, or different kinetics of a possible silyl transfer. If this comes to play, the interchange of silyl groups from the former catalyst could possibly become favourable (a scenario more in line with **mechanism 1**). One fact that should not be neglected is the consideration of sterics. The 1,4-selective vinylogous aldol system offers simply a larger distance between the newly formed center and the oxocarbenium-ion. This could possibly lead to preference for a scrambling event (**mechanism 1**) rather than a transsilylation (**mechanism 2**). Nevertheless exact conclusions can not be drawn and neither can one mechanism be excluded, nor is the interplay of both impossible.

To further investigate the fashion of silicon-transfer, we used a double cross-over experiment. Here a non-preformed catalyst was reacted with the different nucleophiles **47** and **52**, with regard to the ester portion *and* the silyl group. The product distribution was then analyzed by GC-MS (Fig. 89).

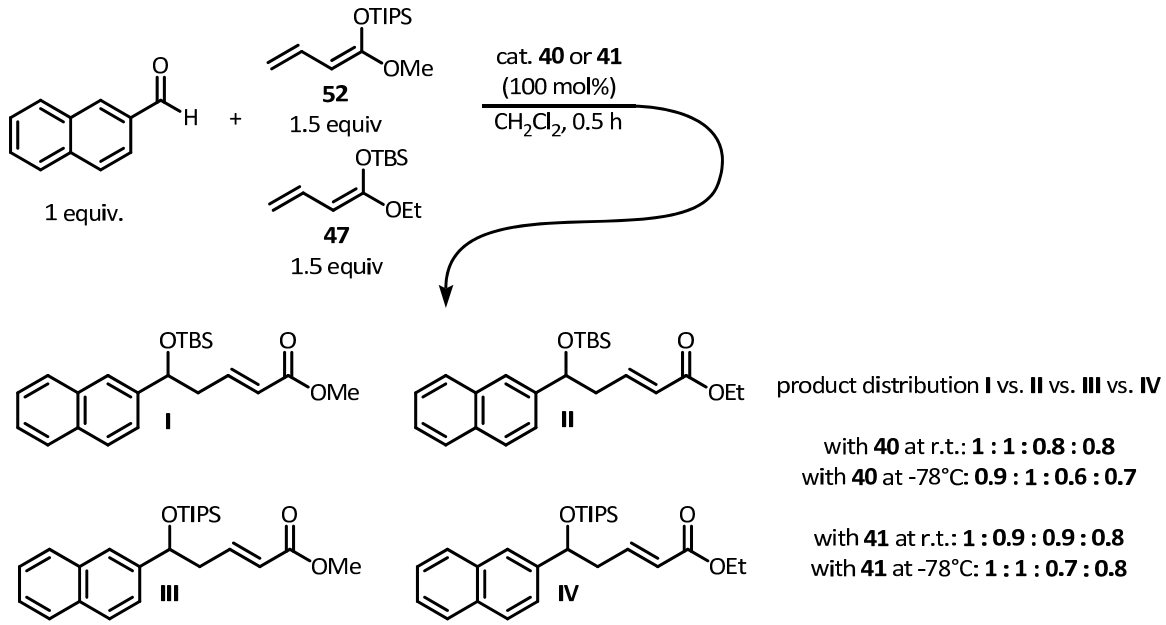


Figure 89. *Double cross-over experiment with disulfonimides **40** and **41** and vinylogous enolates **47** and **52**.*

Interestingly the product distribution proved to be complex, accounting for a very distinct silicon transfer. Trying both, achiral and chiral catalyst **40** and **41** at r.t and -78°C resulted in a complete double cross-over of the reaction products. It became obvious that the TBS-products were more favoured than the TIPS-products. Another interesting observation is

that the concentration of products bearing the TBS-group becomes even higher at decreased temperatures. A clear tendency of preference of the corresponding ester-substitution was not drawn, presumably leaving it as a rather unimportant factor. Yamamoto and co-workers already illustrated, that silyl enolates and silylated aldol products are stable towards silyl group exchange under similar reaction conditions, so that an explanation with more complex reaction intermediates might become feasible.

To see whether we were facing more complex reaction intermediates as catalytically active species, we designed an experiment with a catalyst presilylated by a TMS-protected nucleophile (Fig. 90). This active species was then subjected to a reaction mixture containing an electrophile and two vinylogous nucleophiles varying in silyl-protection (TIPS and TBS) and ester portion (Et and Me), such as for the reaction reported in Fig. 89.

Interestingly there was almost no incorporation of TMS-silylation in the products, further underlining the appearance of a Lewis acid rather than an alternative mechanism. This behavior was the same, even when a completely different TMS-source was used (compare Fig. 90, left and right side). Again we found, that TBS-incorporation in the products was preferred, which could be possibly explained by a faster transsilylation occurring with smaller protecting groups. Remarkably the silyl group scrambling was found to be lower at decreased temperature, where significantly lower amounts of TIPS-products were found. Nevertheless, even at lower temperatures the TMS-group from the former catalyst could not be found in the products in any appreciable amount (the same reaction outcome could be observed, when catalytic amounts of the disulfonimide were used).[XVIII]

These experimental findings actually underlined some of the previous observations:

1. the catalytically active species (if bearing the apparently more reactive TMS-group) does not transfer its inherent silyl-group to the product in an appreciable manner,

2. although the TIPS-protected products are less populated at lower temperature, their distribution regarding the ester is still completely scrambeled, accounting for a pronounced silyl exchange during the reaction course (either inter- or inramolecular),

[XVIII] The experiment with catalytic amounts of disulfonimide was conducted by MANUEL MAHLAU.

3. a solvent dependency of the product distribution can be observed, possibly suggesting, that Lewis acid-base interactions with solvent molecules can further influence the outcome of the transformation.

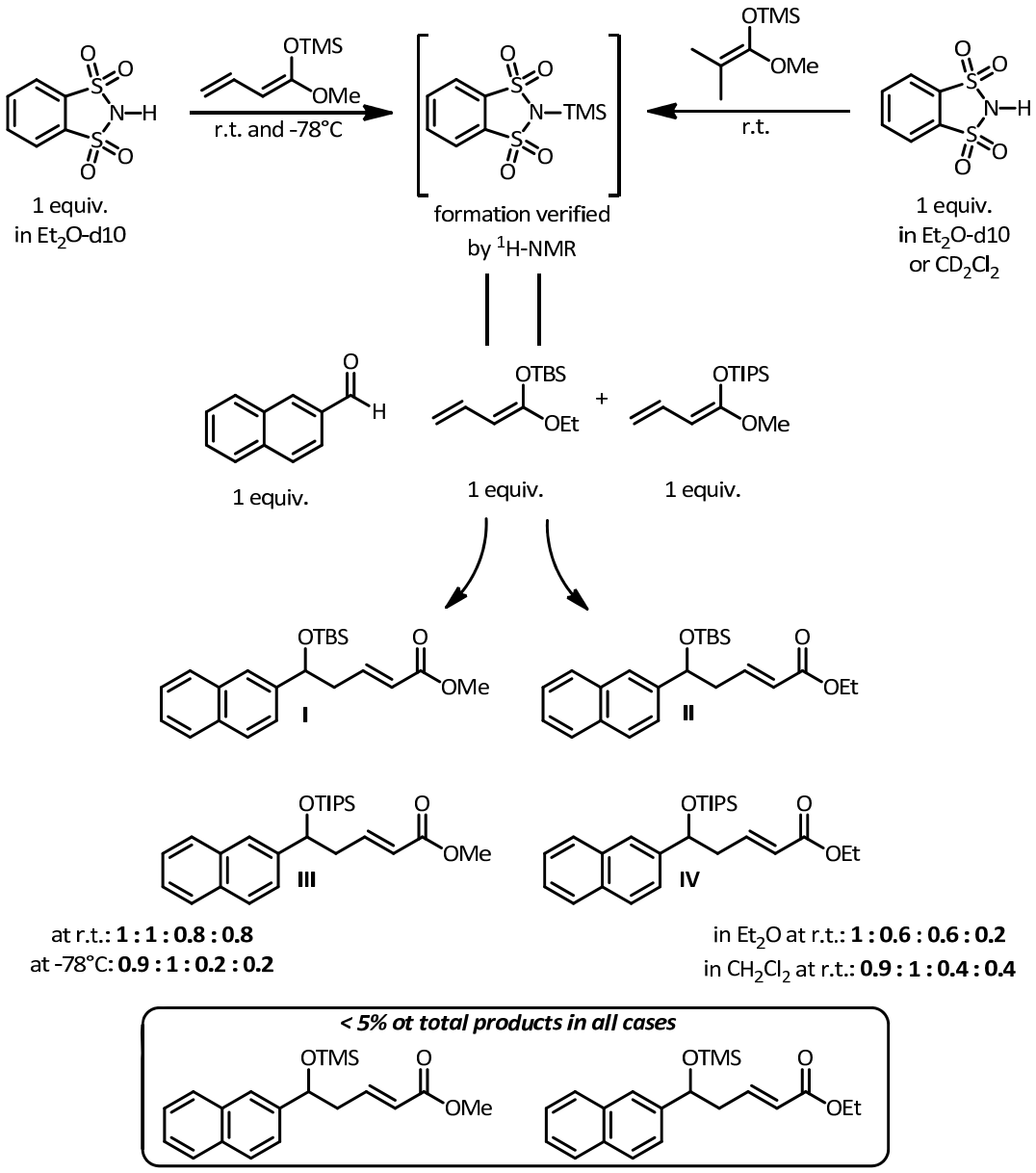


Figure 90. *Double cross-over experiment with benzenedisulfonimide* ***40****, non-vinylogous enolate and vinylogous enolates.*

From all previous studies one can only predict a more complex mechanism for disulfonimide-catalyzed vinylogous Mukaiyama aldol reactions at the moment. The high diversity of products observed in the double cross-over experiment is most probably provided during the critical silyl-transfer step, which also represents the crucial step for the catalyst regeneration. The possibility of N- vs. O-silylation opens up various directions for different silyl transfer events as well.

One very interesting argumentation about the actual catalysts, which is based on studies by Yamamoto et al., deals with second stage intermediates, *i.e.* aldol addition products (Fig. 91). In this sense, the active catalyst provided, could arise from second intermediates of the Lewis-acid mechanism, where a peripheric silyl group acts as the actual catalyst. This scenario can be imagined in an *open* (Fig. 91, eq 1) or *closed* (Fig. 91, eq 2) transition state form. Upon formulating these transition states it becomes apparent, that the closed transition state offers parallels to the Lewis-base activation of Lewis acids discussed earlier. Whereas the open species would activate the aldehyde via a penta-coordinated silicon (Fig. 91, eq. 1), the closed activation could occur through a presumably more reactive hexavalent silicon (Fig. 91, eq. 2). Furthermore, these two scenarios possess very different transmissions of chiral information.

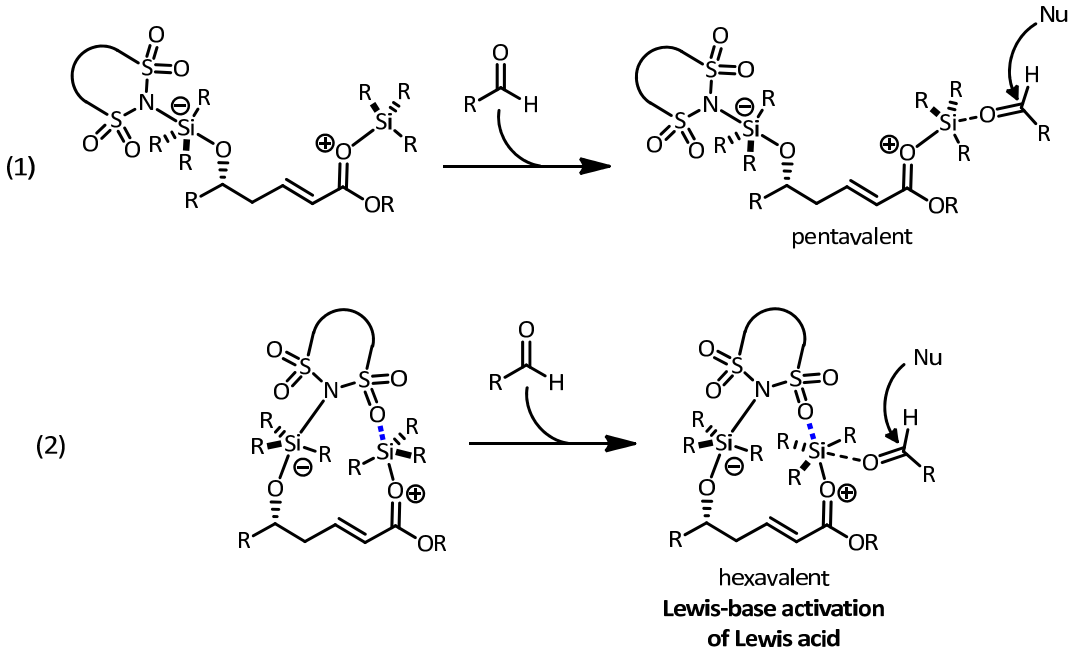


Figure 91. *Possible alternative scenarios involving second stage intermediates.*

The open chain intermediate would bear the chiral BINOL-backbone in a remote position and chiral induction could be transmitted from the stereocenter which is already formed during the reaction. A closed mechanism however, offers a more rigid structure and possibly a tighter control. The exact nature of silyl transfer reactions however remains unclear to date.

Although it is not possible to preclude any mechanism at the moment, the previous mechanistic experiments show quite plainly that the two simplistic mechanisms described initially are improbable. To fully account for the outcome of the scrambling experiments

conducted at present, one has to consider mechanisms with second stage intermediates, such as described above (Fig. 91). Another facette of the discussion can be the distinct reactivity provided by differently silylated disulfonimides. To further elaborate the reaction mechanism, experiments along these lines are needed and subject of ongoing research in our laboratories.

4.4 Catalyst improvement by means of cooperative effects

4.4.1 Synthesis and theroretical investigations of hydroxy-disulfonimides

Even though the actual mode of action in disulfonimide-catalysis is still blurry, the need for improved catalysts regarding reactivity and selectivity is clear. As already pointed out, the influence of cooperative effects can dramatically improve the performance, especially the reactivity, of catalytic systems.[37] For this purpose we turned our attention to a structure offering this possibility, already synthesized earlier during our catalyst screening of VMARs, but not further studied (see Fig. 59, example 1). The synthesis of this type of catalysts was accomplished in a modular way, using a single step operation starting from disulfonimide **44**. This strategy was deemed to be advantageous, as already pointed out in the previous chapters.

Having identified the need of electron-withdrawing substituents in 3,3'-position for disulfonimides, we concentrated on the installation of electron-poor tertiary alcohol moieties first. Treatment of **44** with *sec*-butyllithium in the presence of TMEDA in THF at -78°C delivered the trilithiated disulfonimide **44a** smoothly, which could be reacted with bis(3,5-bis(trifluoromethyl)phenyl)methanone, resulting in catalyst **145** (Fig. 92).

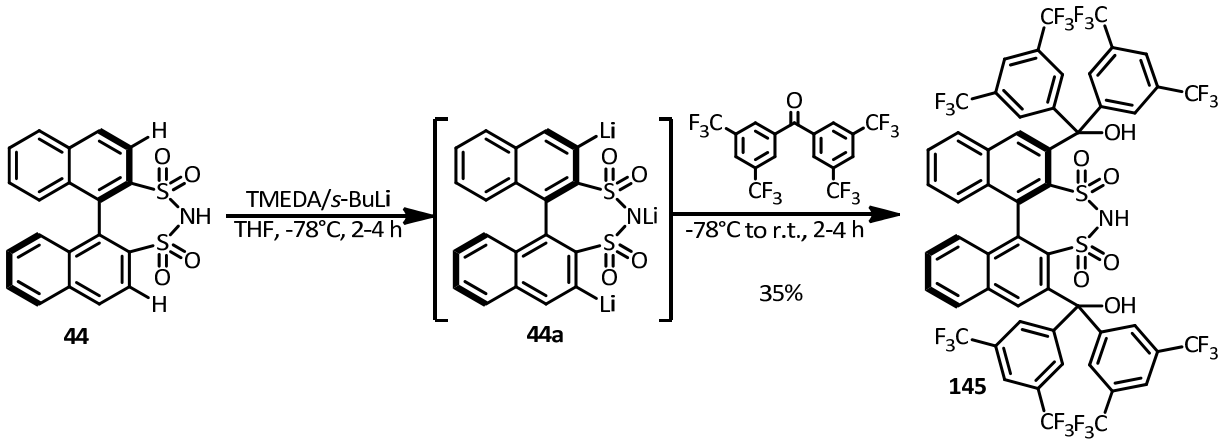


Figure 92. *Synthesis of benzophenone tertiary alcohol substituted disulfonimide* ***145****.*

The substituent present in **145** was previously reported by the group of Maruoka for an efficient phase transfer catalyst which found successful application in the conjugate additions of oxindoles to nitroolefins (see Fig. 93).[165]

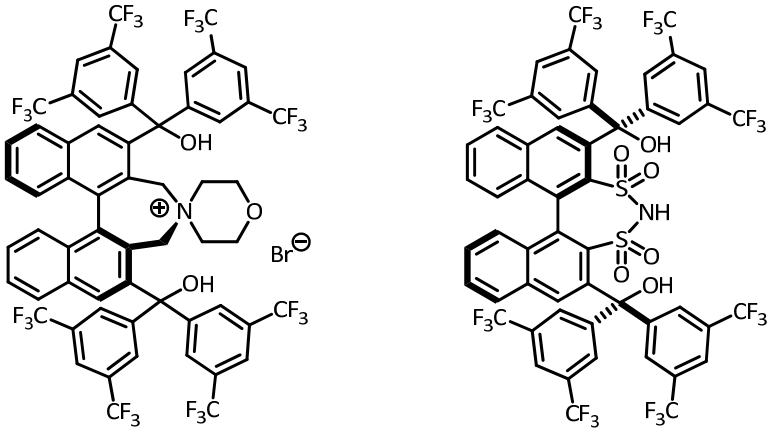


Figure 93. *Structural comparison of Maruoka's phase-transfer catalyst and its related disulfonimide* ***145****.*

We expected the hydrogen bond donation of the hydroxy-group to have an effect on the structure of the disulfonimide-skeleton. Interestingly, we found some remarkable structural features by ^{1}H-NMR-spectroscopy. As indicated by the NMR-signals, the aryl-moieties of the diarylmethanol-substituent orientate themselves. This behavior could be in line with a "locking"-effect between the OH-groups and the Lewis basic oxygens on the disulfonimide-moiety (see Fig. 94, eq 1). Due to the C_2-symmetry of the complete molecule, it would leave the aryl-groups on the substituent as diastereotopic, resulting in two pairs of equivalent diastereotopic aryl-groups. This inequivalence results in two peaks with ∫ = 2 protons for the respective pairs of *p*-protons on the aryl-groups. The corresponding pairs of *m*-protons can also be found, however result in one very broad peak at 40°C with ∫ = 8 protons (Fig. 94, eq 2). Upon heating to 60°C this peak resolves into two multiplets of ∫ = 4 protons, probably accounting for a faster rotation of the diarylmethanol phenyl-rings. This phenomenon can also be observed regarding the NH- and the OH-protons, which resolve from a broad multiplet with ∫ = 3 protons, into two peaks with ∫ = 2 protons and ∫ = 1 proton respectively (Fig. 94, eq 3). Remarkably, the NOE-correlation underlines these assumptions. The ^{19}F-NMR shows two peaks, which further points towards an inequivalence of the two aryl-rings in the diarylmethanol.

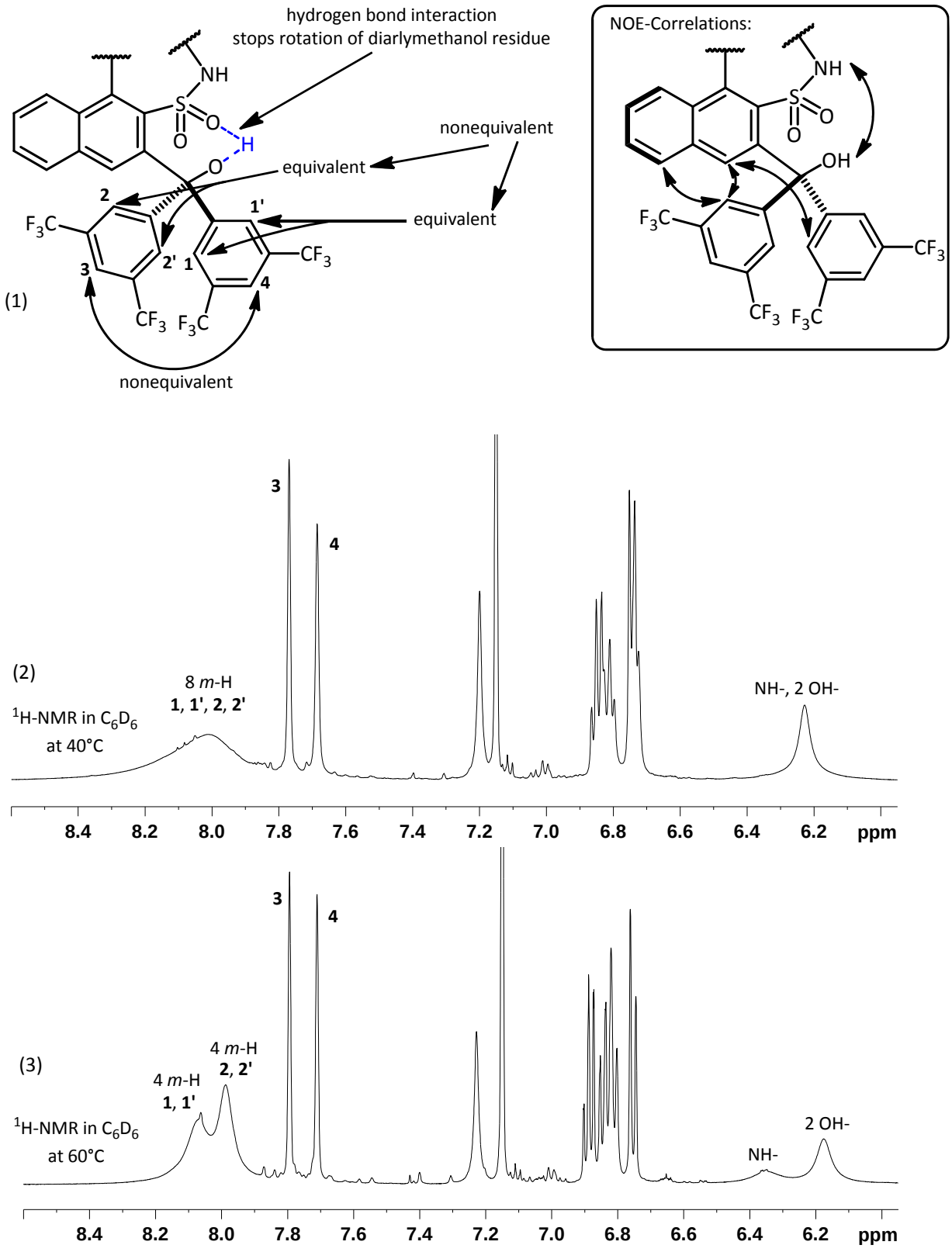
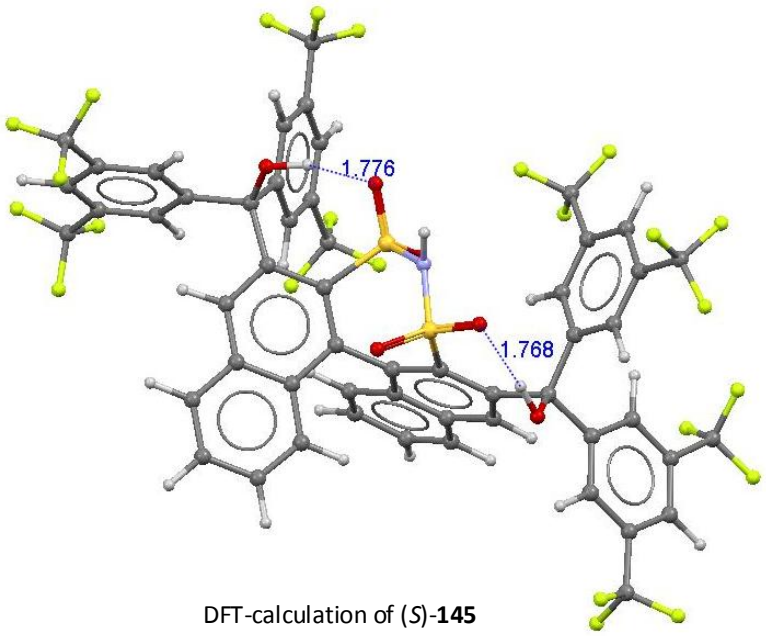


Figure 94. *^{1}H-NMR-analysis of catalyst **145** and a reasoning of its unique structural characteristics.*

Unfortunately, catalyst **145** was not crystalline, so that the corresponding structure could not be unambiguously proved by X-ray-measurements. However, DFT-calculations were

made, resulting in energy-minimized equilibrium geometries which gave a hint towards the actual alignment of the substituents.[XIX] These models confirmed our theory of a significant hydrogen-bonding interaction. This could also lead to an increase of the parent acidity of the imide-proton, thus rendering it more 'naked' and more reactive in the catalyst application. The distance between the Lewis basic sulfon-oxygen and the hydrogens on the hydroxy groups was calculated in a range of 1.76-1.78 Å, which is characteristic for strong hydrogen bonding interactions.



DFT-calculation of (*S*)-**145**
using B3LYP with a 6-31G*-base set

Figure 95. *DFT-geometry optimization of catalyst* ***145*** *and intrinsic hydrogen bond activation, in blue the calculated distance between the alcohol proton and the Lewis-basic oxygen on the imide substructure in Å.*

This increased acidity should presumably lead to a faster initial silylation, and to a stronger Lewis acidic silicon species, since the resulting disulfonimide is less coordinating. Installation of electron-withdrawing groups on silyl Lewis acids to render them more active was earlier reported by Leighton, for example.[149] The increase of Brønsted acidity through an intramolecular hydrogen-bonding was *i.e.* shown by Rawal for the powerful TADDOL-catalysts (Fig. 34).[102]

[XIX] The model calculations depicted in Figs. 95; 100; 101; 103 and 108 were conducted on a WindowsPC with the corresponding DFT-, or MM-Plug-Ins as implemented in Spartan '08 v. 1.2.0 by Wavefunction Inc., Irvine (California), USA.

To prove the catalytic performance of our disulfonimide **145**, we tested it in the Mukaiyama-aldol reaction between 3,5-dimethylbenzaldehyde and tert-butyl((1-methoxyvinyl)oxy)-dimethylsilane for the generation of product **142** (Fig. 96). To set the results into a general context, we investigated the elapsed time to maximum product concentration with catalyst **41** and **145** in a ReactIR apparatus. Catalyst **41** finished the reaction after 6.5 h (validated as 92% NMR-yield) at a loading of 5 mol%, the hydroxy-disulfonimide **145** furnished the product in less than 1 min at 5 mol% and 1 mol% catalyst loading, respectively (corroborated as an NMR-yield of 96%). These striking results support the theory of acidity enhancement by intramolecular hydrogen-bonds.

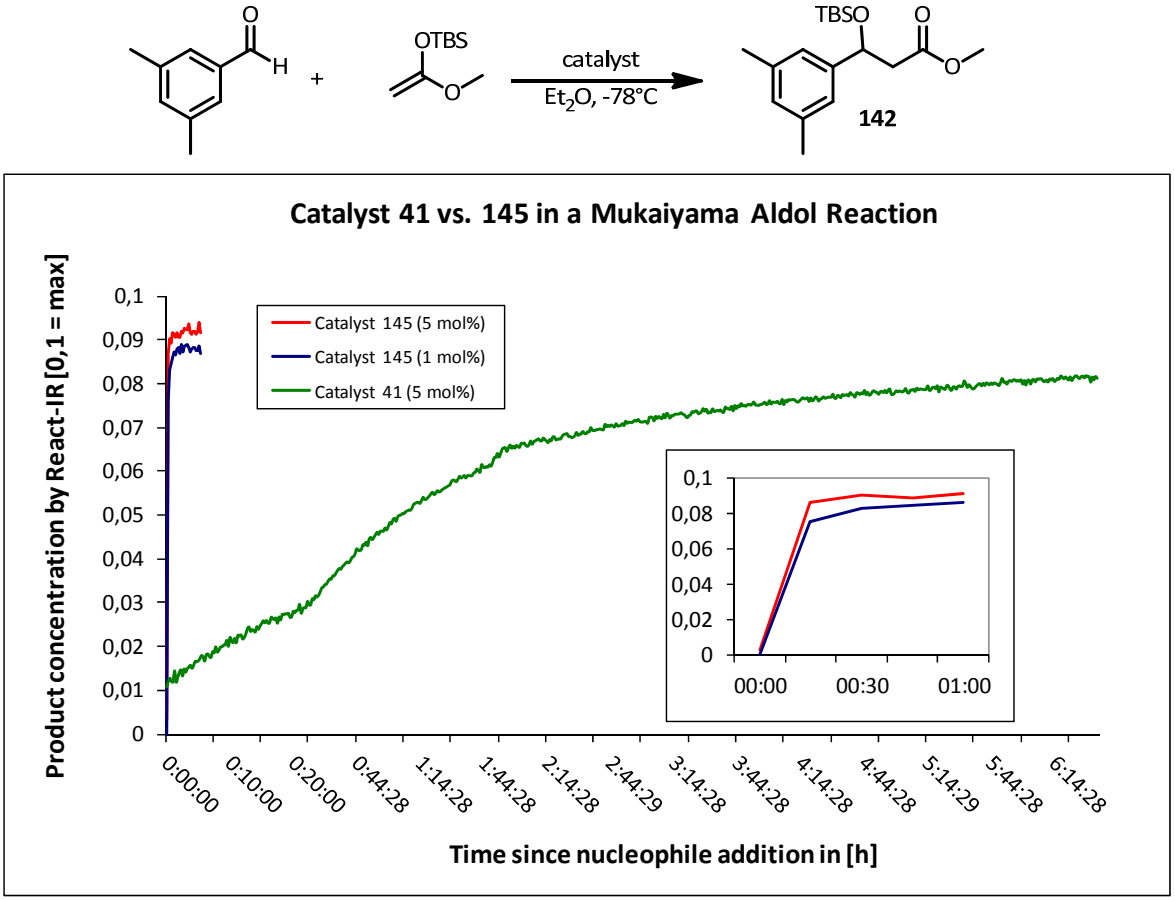


Figure 96. *Catalytic performance of catalyst **41** and catalyst **145**.*

We next turned our attention to some of the asymmetric reactions already studied in the VMARs and DVMARs (Fig 97). Although catalyst **145** was very efficient concerning the conversions, products **64** and **106** could only be synthesized in moderate enantiomeric purity. Interestingly, the double vinylogous aldol product was formed in the oppositie enantiomeric form than the one generated with **41**, although in both cases the (*R*)-form of the BINOL-backbone was used.

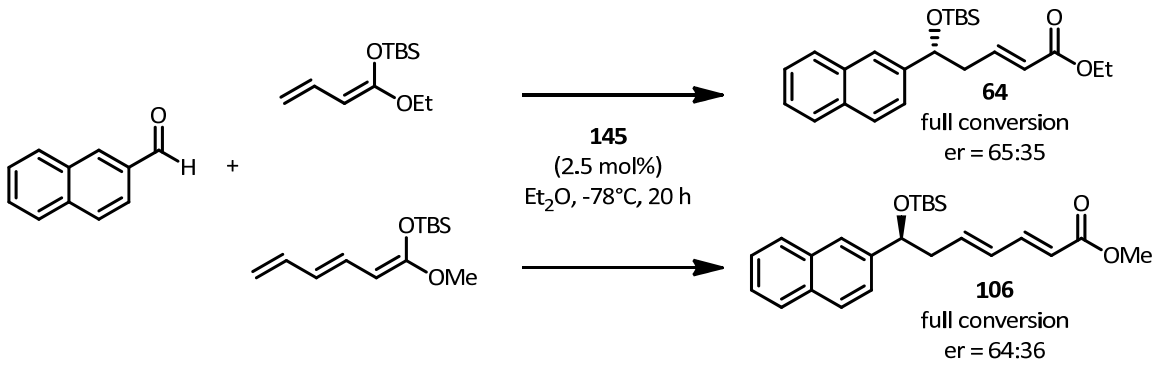


Figure 97. *Asymmetric transformations under the governance of catalyst* ***145****.*

Intrigued by our findings, we attempted to synthesize other hydroxy-disulfonimide catalysts. To exploit the complete range of electronic properties, electron-rich, neutral and electron-poor aromatic groups were installed due to the easy accessibility of the corresponding benzophenones (see Fig. 98).

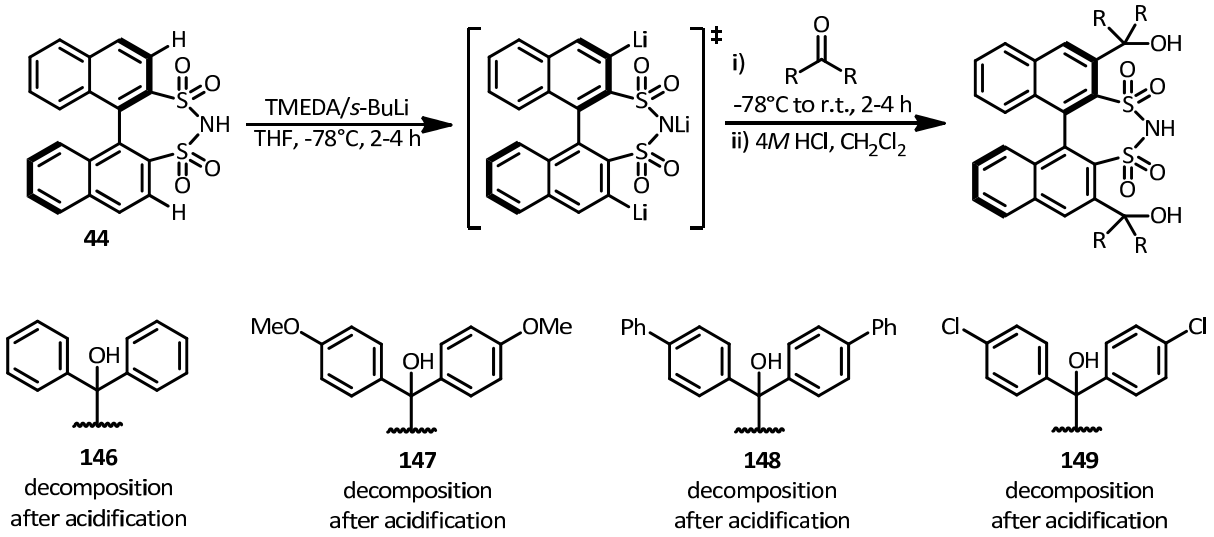


Figure 98. *Syntheses of other diarylmethanol-substituted disulfonimides (hydroxydisulfonimides).*

Although these hydroxy-disulfonimides **146**-**149** were readily synthesized following the above mentioned route,[XX] all candidates except the already mentioned **145** decomposed during the terminal acidification step.

To further explore the reactivity of disulfonimide **145**, we used it in Mukaiyama aldol reactions which are problematic with other catalytic systems (Fig. 99).

[XX] The desired structures could be isolated after column chromatography and analyzed in its salt form only.

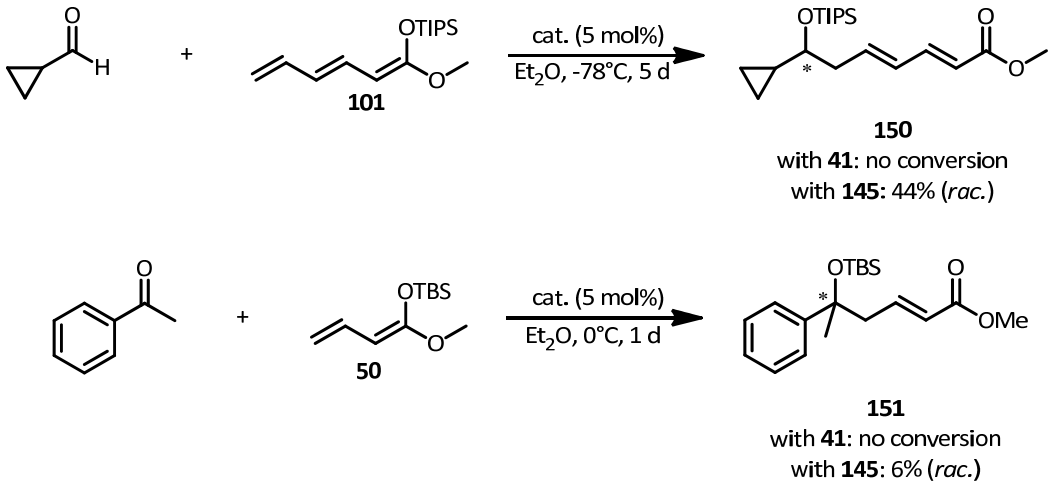


Figure 99. *Challenging Mukaiyama aldol reactions catalyzed by* ***41*** *vs.* ***145****.*

Satisfyingly, cyclopropanecarboxaldehyde and acetophenone could be converted in vinylogous Mukaiyama aldol reactions. Remarkably the catalyst **41** gave no conversions whatsoever. Unfortunately, and in line with the previous results, the enantioinductions delivered by **145** were only poor and delivered the products **150** and **151** in racemic form.

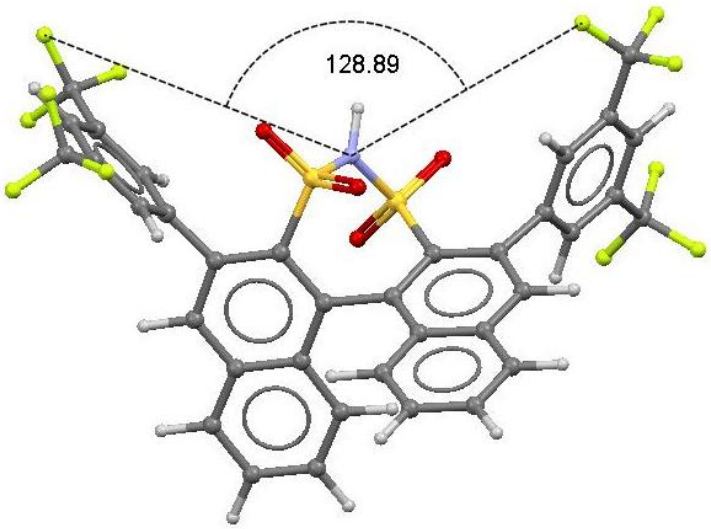


Figure 100. *Molecular mechanics geometry optimization and active angle determination of disulfonimide* ***41****.*

To provide an explanation for this behavior we studied the opening angles, defined by the N-atom and the peripheric atoms on the 3-3'-substituents. To calculate these angles we undertook molecular mechanics (MM)-geometry optimizations of the respective disulfonimide catalysts.[XXI]

[XXI] A crystal structure which goes in line with the reported angles will be presented in the PhD-thesis of FRANK LAY / University of Cologne 2012.

The angle provided by catalyst **41** was calculated with 128.89° (Fig. 100). However, when we undertook the same calculation with the disulfonimide **145**, the angle proved to be much wider, measuring 146.68° (Fig. 101).

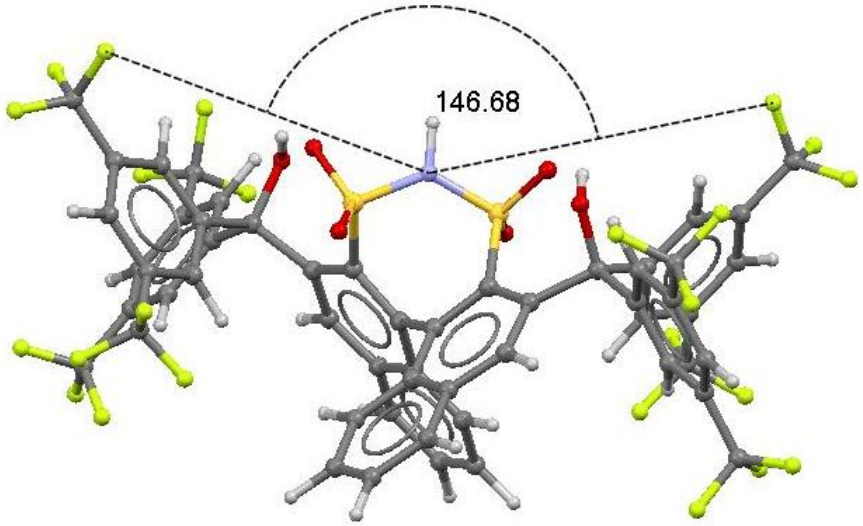
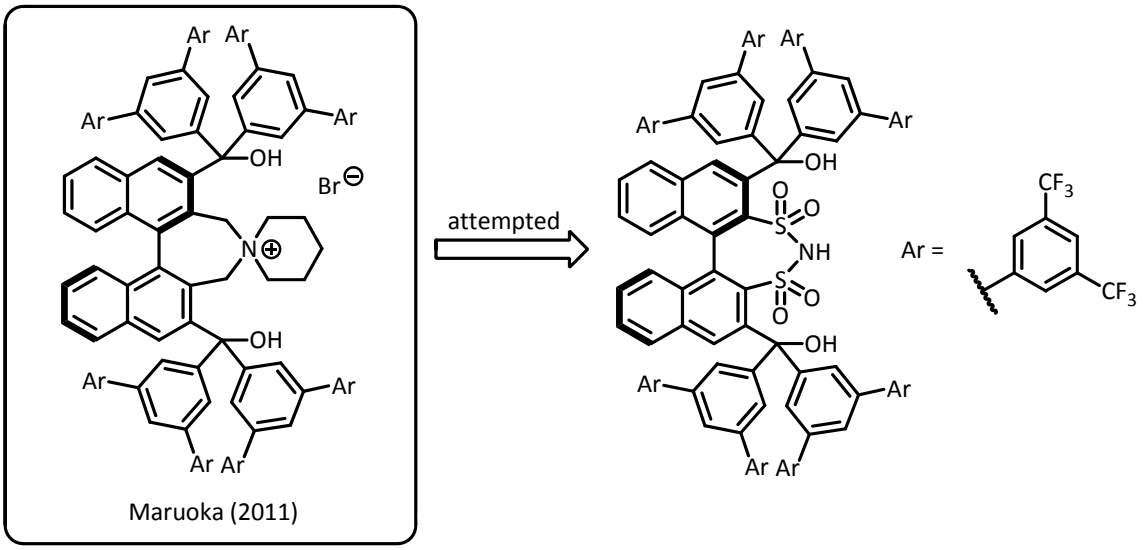


Figure 101. *Molecular mechanics geometry optimization and opening angle determination of diarylmethanol-substituted disulfonimide* ***145****.*

Because of the strong hydrogen bonding interaction, the bulky aromatic substituents undergo an orientation towards the back side of the aromatic system, opening the active angle and diminishing the steric bulk in the actual chiral pocket. This leads to a dramatically reduced flanking in the transition state, resulting in low optical purities of the reaction products when using **145**.

With this in mind, we tried to take advantage of the intrinsic reactivity of the electron poor substituted hydroxy- disulfonimides in combination with a substituent which allows for a more efficient shielding of the active center. In 2011 the group of Maruoka reported a substituent like the one present in Fig. 102, eq 1,[166] bearing a 'second layer' of electron-poor aromatics in the position of the CF_3-groups of **145**. Modeling of the resulting disulfonimide showed the interesting potential of that catalyst (Fig. 102, eq 2). The active center would be strongly flanked by aryl rings (active angle of 125.01°), possibly retaining the reactivity of the parent hydroxy-disulfonimide **145**.

(1)



(2)

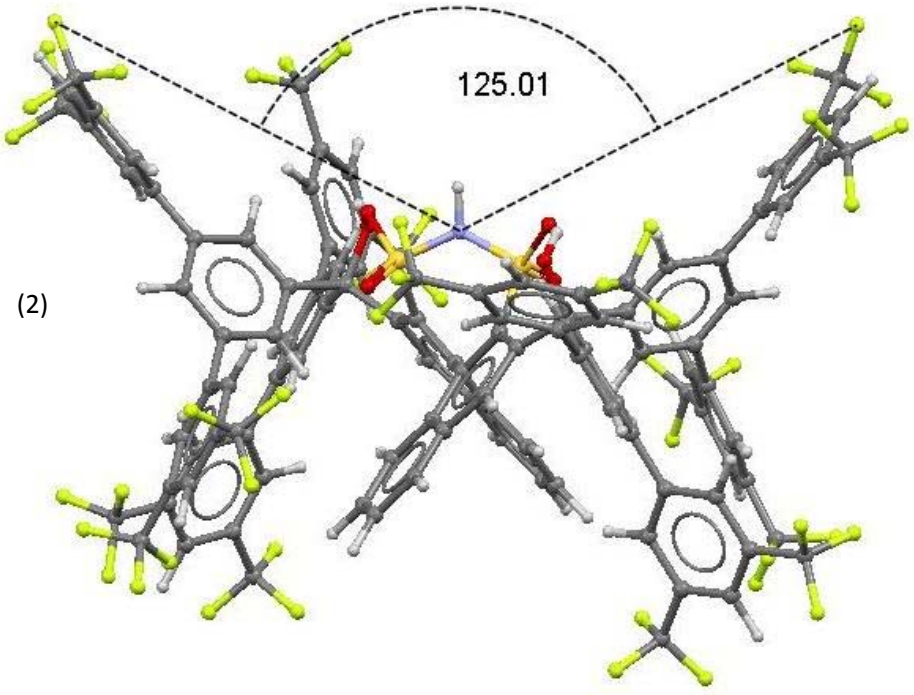


Figure 102. *Structural properties of Maruoka's catalyst and molecular mechanics geometry optimization and active angle determination of an according disulfonimide.*

To install this rest, we decided to synthesize the corresponding ketone (Fig. 103, eq 1). We treated 1,3,5-tribromobenzene with *n*-butyllithium and quenched the monolithiated species with 3,5-dibromobenzaldehyde to obtain the corresponding secondary alcohol **152** in 62% yield. The oxidation to the corresponding ketone **153** could be achieved in a clean way using Dess-Martin-periodinane in 71% yield. Oxidation with pyridiniumchlorochromate (PCC) proved to be less effective and only resulted in a sluggish conversion, diminishing the isolated yields. To install the corresponding 3,5-CF_3-substituted phenyl groups, we

envisioned a coupling protocol with the boronic acid. However, this coupling proved to be difficult, since $Pd(PPh_3)_4$ and Na_2CO_3 as base did not lead to any conversion, starting from the alcohol **152** or the ketone **153** respectively. The combination of Pd_2dba_3, S-Phos as ligand and Cs_2CO_3 as the base in a mixture of toluene and EtOH at 100°C however resulted in 94% isolated yield of the corresponding ketone **154**.

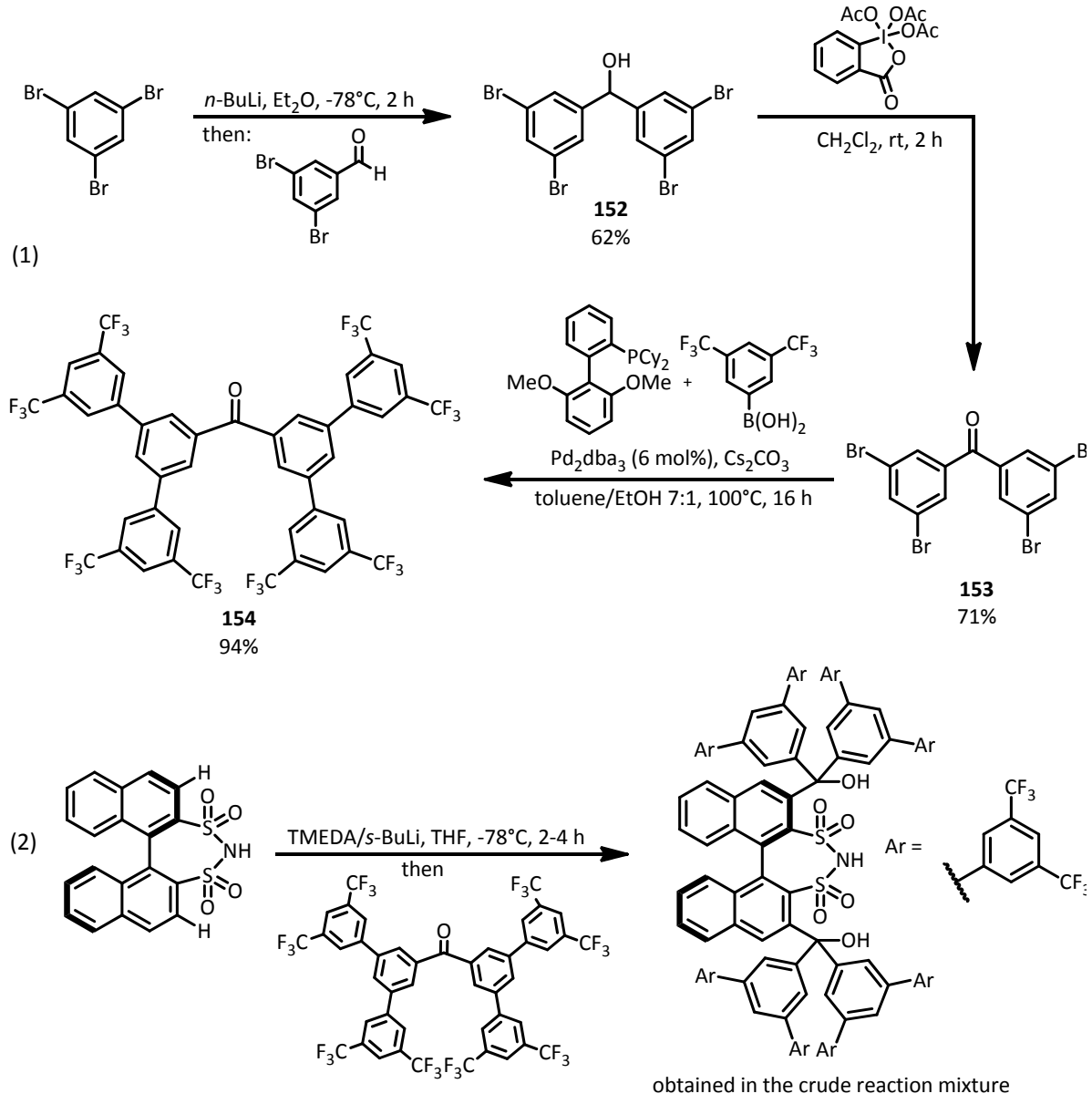


Figure 103. *Synthesis of the ketone precursor **154** and attempted catalyst synthesis.*

However, when we attempted to couple the corresponding ketone to disulfonimide **44**, the resulting material could not be sufficiently purified. For this purpose we subjected the crude mixture to preparative HPLC-conditions, in order to provide sufficiently pure material. Although a separation of the mono-and di-coupled material was accomplished on analytical

scale using LC/MS-techniques, the desired catalyst proved to be acid sensitive, resulting in rapid decomposition with any common workup procedure (Fig. 103, eq 2).

Unfortunately the HPLC-workup could not be improved, resulting in a dead-end for the synthesis of the desired catalyst. The structural similarity of substituted hydroxy-disulfonimides to trityl groups opens up a variety of pathways for decompositions and undesired side reactions. The fact that catalyst **145** did not substantially decompose upon acidic workup, can be explained by its extremely electron-poor substituents, rendering the tertiary alcohol moiety more stable through an intramolecular hydrogen bonding.

Nevertheless we were very intrigued by the catalysts activity and simple accessibility, leading us to adapt the same double activation to the achiral benzenedisulfonimide **40**. To achieve this synthesis, we started with the literature procedure of **40**,[127] followed by double *o*-lithiation with subsequent capture by bis(3,5-bis(trifluoromethyl)phenyl)-methanone resulting in catalyst **155** (Fig. 104).

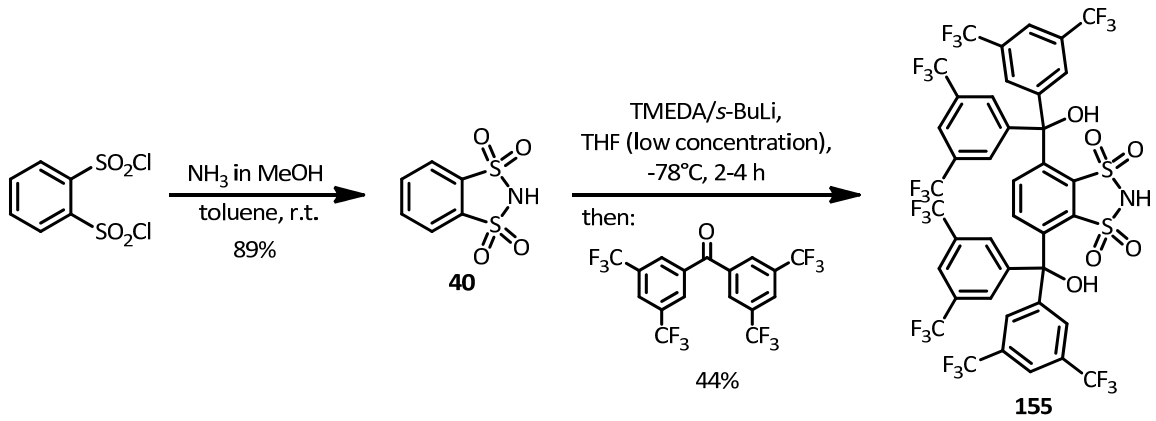


Figure 104. *Preparation of the hydroxybenzene-disulfonimide **155**.*

A very important point is to run the reaction at low concentration [0.01*M*], since at higher concentration the reaction tends to be unstirrable. Remarkably, during acidification of the material obtained after column chromatography, we observed side product, which we identified as a ring opening product of the imide. Most probably this material forms in contact with acids and/or water, requiring storage of **155** under dry and acid-free conditions. The structure of this material was unambiguously shown by X-ray single crystal analysis (Fig. 105).

Since the crystallographic structure did not show whether the open sulfonamide **155a** or the sulfonic acid **155b** was present, we examined the IR-sprectra of the material (see

experimental part for details). From these data we became convinced in having the sulfonamide, which was further underlined by the neutral reaction of the material with pH-paper in aqueous solution. From a mechanistical point of view, it also seems to be more likely to obtain the five-membered sulfonic acid ester as well. The generation of a corresponding imide would have to involve an S_N1-pathway with a formal trityl-cation generation.

With this observation in mind, one might possibly explain the behavior of the other hydroxy-disulfonimides which we attempted to synthesize (see Fig. 98). An analogous side reaction might be feasible for other moieties as well, leaving the catalyst **145** as a special case, due to its very strong intramolecular stabilization against ring opening.

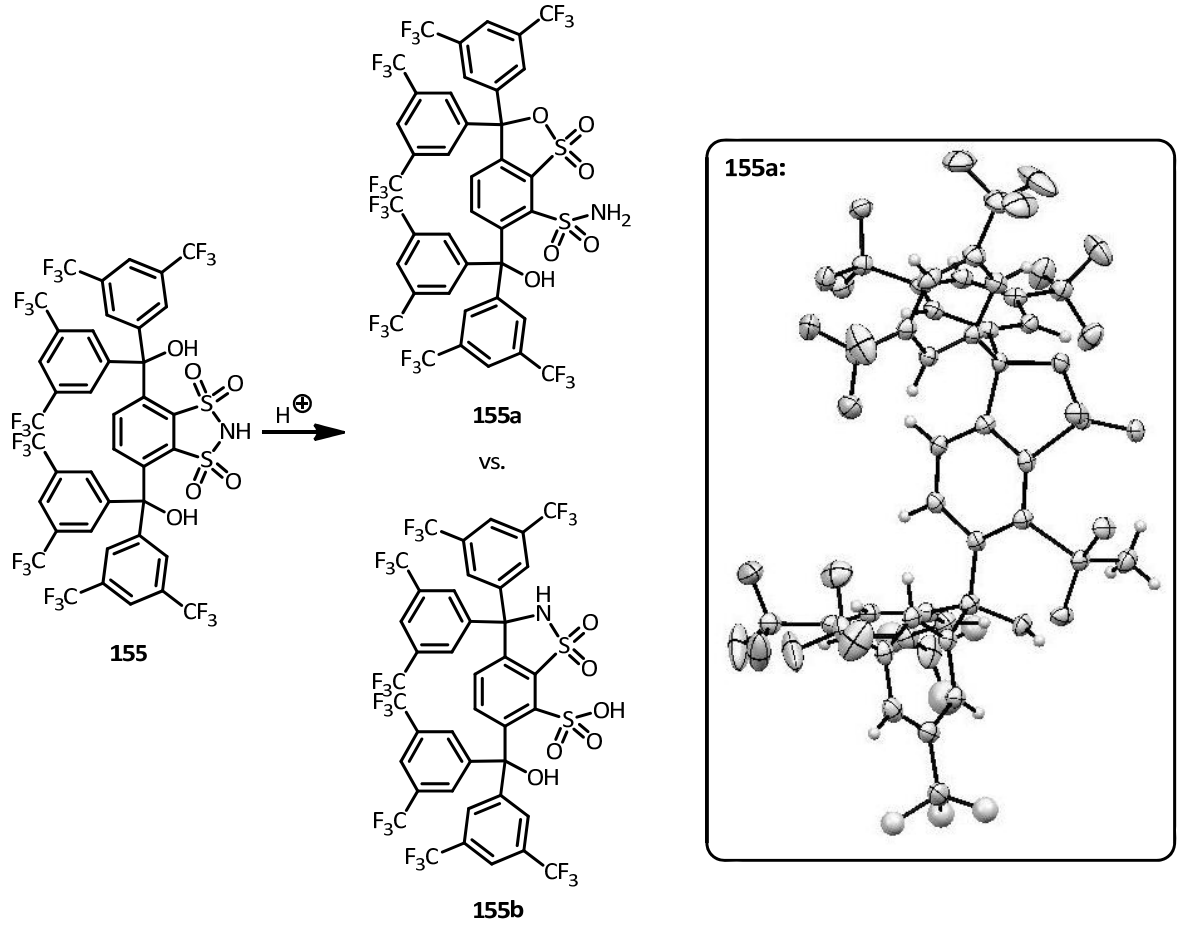


Figure 105. *Side product **155a** from the preparation and acidification of **155** (for IR-Data see experimental part).*

Although giving only little enantioinduction, we were interested in the comparison of the catalytic performance of the hydroxy-disulfonimides **145** and **155** with their parent disulfonimides **40** and **41**. Realizing the high reactivity concerning virtually any kind of carbonyl compound, we became aware of the synthesis of Methallenestril, an estrogen

which was used in a drug against menopausal symptoms, the active compound in Vallestril® (Fig. 106).[167]

The established synthesis requires stoichiometric amounts of CuCN, a Reformatzky-, and a Grignard addition.[168] This would make our hydroxy-disulfonimides privileged for the generation of **156**, since we already showed that **145** can be successfully used for the activation of unactivated ketones in Mukaiyama aldol chemistry.

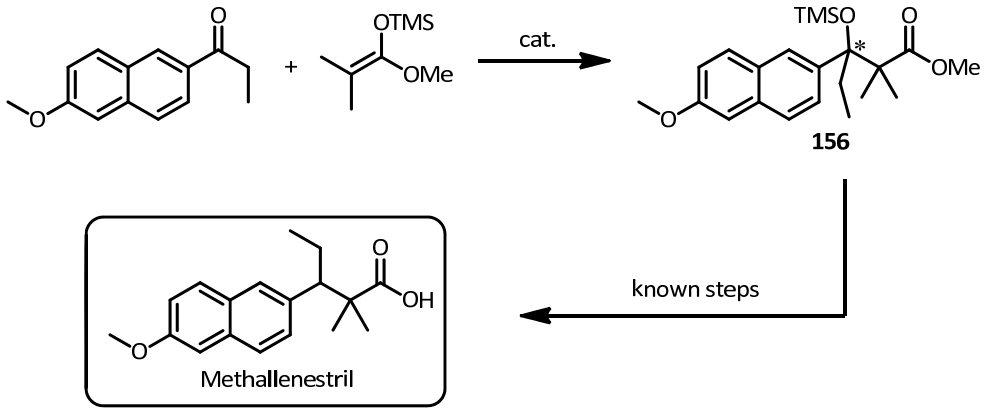


Figure 106. *Partial synthesis of Methallenestril with key intermediate* ***156****.*

Upon conducting this reaction at 1 mol% catalyst loading, we could clearly identify the hydroxydisulfonimide **145** as superior to all other catalyst-candidates tested (Fig. 107). Non-activated disulfonimides **40** and **41** gave no conversion at all, approving previous trends concerning the activation of ketones. However, a quite surprising finding was that catalyst **155** showed significantly inferior activity for this transformation. Analogous to the superior activity of **40** over **41**, our assumption was that **156** should have been more active than **145**.

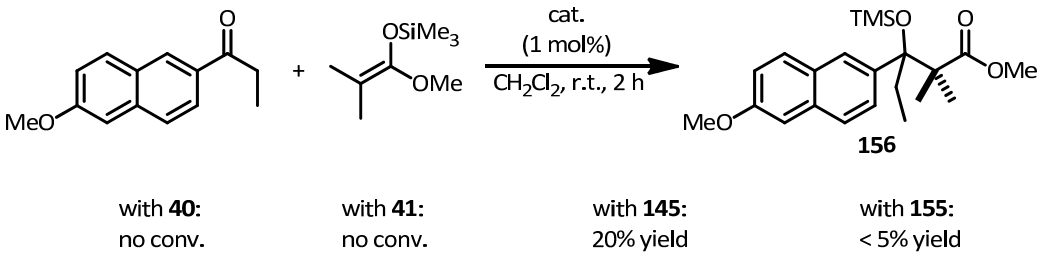


Figure 107. *Catalyst screening for the partial synthesis of Methallenestril.*

To explain this behavior, we analyzed the structure of catalyst **155**. For this purpose we undertook DFT-geometry optimization, following the protocol of Fig. 95. Surprisingly, the hydrogen bond activation apparent for the structure of **145** is lacking in **155**. In the case of

this molecule, only one hydrogen bond points towards a Lewis basic oxygen, furthermore in a distance of 1.922 Å, which indicates a lower co-activation of the catalyst (Fig. 108).

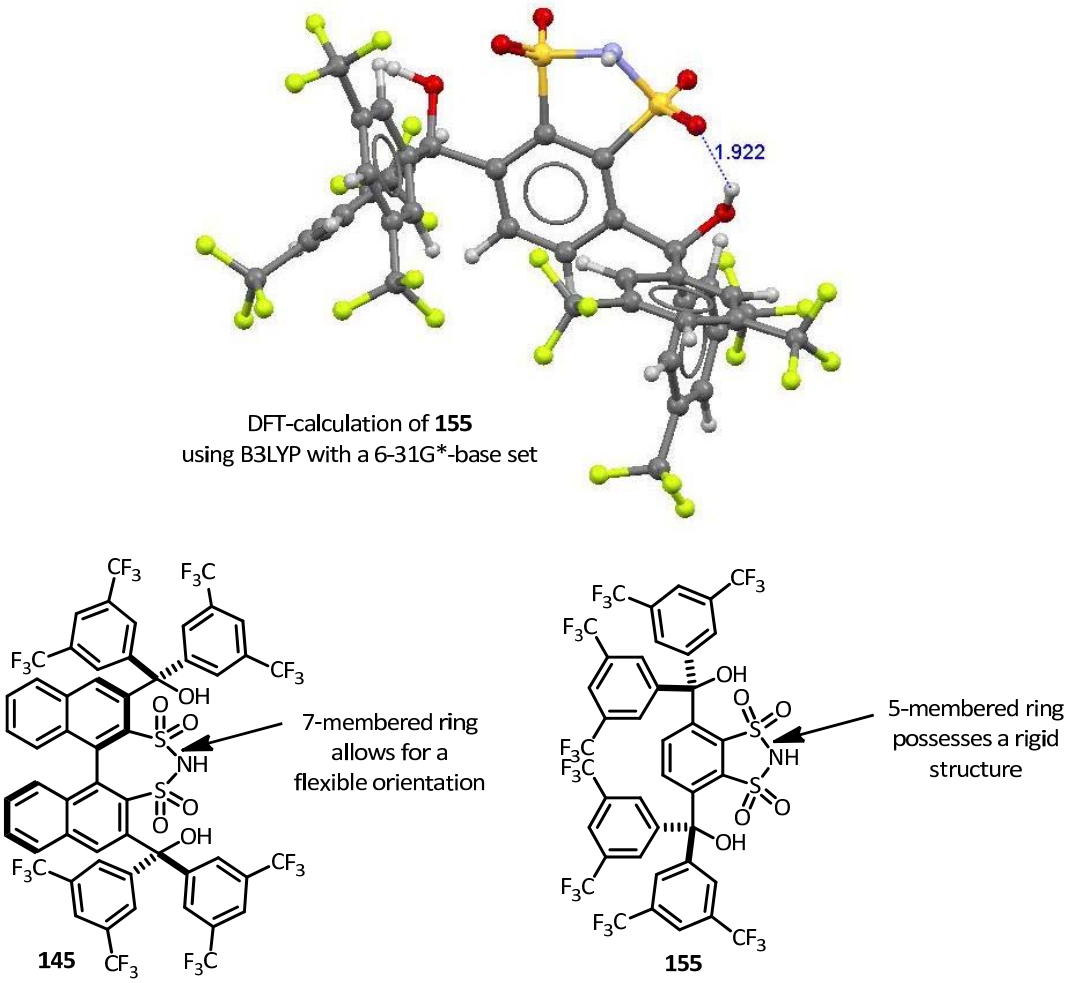


Figure 108. *Analysis of the structures of* ***145*** *and* ***155****.*

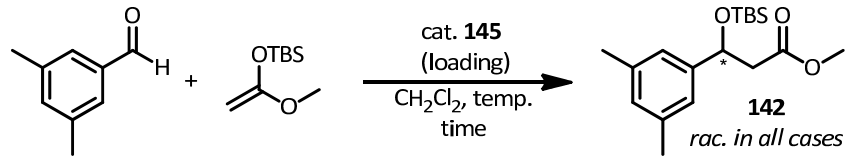
To explain this difference, one can analyze the ring sizes of the corresponding disulfonimide moieties:

Catalyst **145** offers a 7-membered ring, which facilitates a flexible orientation of the Lewis-basic oxygen atoms; catalyst **155** bears a structurally more rigid 5-membered ring, which possesses a strain restricting structural alignment with the hydrogen-bonding moieties on the 3,3'-substituents.

Stimulated by all previous results regarding the exceptional reactivity of **145**, we were interested in the minimization of its catalyst loadings. Therefore we used the reaction which we had already investigated during the ReactIR-screenings (Fig. 96). The lowest catalyst loadings used in metal-free catalysis to date, rank as low as 0.01 mol%,[169] reported by the

group of Rueping in the transfer hydrogenation of benzochalcogenazines and our group in the disulfonimide-**41**-catalyzed Mukaiyama aldol reaction.[129a]

Pleasingly we could decrease the catalyst loading of **145** for the production of **142** dramatically, even without precaution towards the exclusion of water or air (Fig. 109). Nevertheless, the optical purity observed in these reactions followed the previous trends, and the product was racemic. Although the outcome of the Mukaiyama aldol reactions with catalyst **145** was unsatisfying concerning its enantioinduction, the provided reactivity proved to be outstanding, and values of 0.1 mol% or lower (as low as 0.0001 mol%) represent a benchmark which can normally only be reached with triflimide, triflic acid and related catalysts or with especially activated substrates.[119a]



1 mol%, 1 h, 0°C: 92% yield **TON** = 90

0.5 mol%, 1 h, 0°C: 92% yield **TON** = 180

0.1 mol%, 1 h, 0°C: 94% yield **TON** = 920

0.01 mol%, 24 h, 0°C: 48% yield **TON** = 4600 **TOF** = 192

0.001 mol%, 24 h, 0°C: 31% yield **TON** = 29000 **TOF** = 1208

0.0001 mol%, 24 h, 0°C: 7% yield **TON** = 50000 **TOF** = 2083

background reaction, 24 h, r.t.: 2% **TON** = turnover number **TOF** = turnover frequency (per hour)

Figure 109. *Examination of low catalyst loadings with catalyst* ***145****.*

This fact underlines the status that disulfonimides might find in the future: powerful triflimide equivalents, which can offer similar reactivities, in an enantioselective way. Thus the presented catalyst system could open up a new direction for asymmetric Lewis acid catalysis, demonstrating the impact of double activation and cooperative catalysis. Catalyst **145** might find further application in reactions with more complex transition states, allowing for an efficient shielding and high enantioinductions.

5. Summary

The underdeveloped field of organic metal-free Lewis acid-catalysis is a growing area and rapidly closing the gap to the other organocatalytic activation modes: Lewis base-, Brønsted acid- and Brønsted base-catalysis. Our research group significantly contributed to this field by introducing disulfonimides, powerful Brønsted-acidic Lewis acid precursors.[129a] The current PhD-work contributes to this area by disclosing the vinylogous series of Mukaiyama aldol reactions (VMARs) employing these powerful catalysts. Although solutions to vinylogous aldol reactions are not rare, their systematic elaboration from vinylogous reactions towards the unprecedented double vinylogous version was a synthetic challenge yet unmet.

In search of an appropriate catalyst, we identified the candidate **41** bearing electron-withdrawing substituents as very privileged for the solution of VMARs. From an extensive screening of chiral catalysts, **41** emerged as superior in terms of enantioinduction and reactivity (Fig. 110).

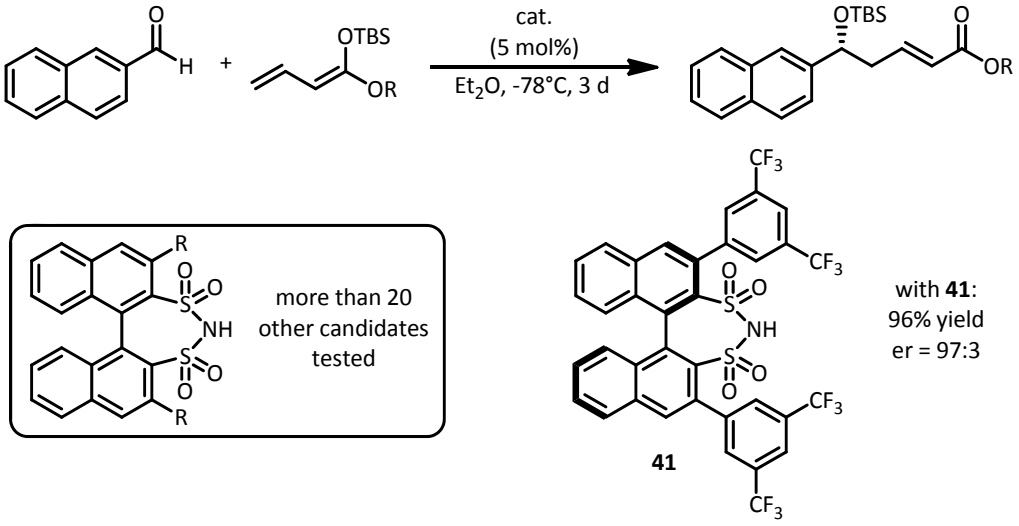


Figure 110. *Identification of catalyst **41** as a superior candidate for the activation of aldehydes towards dienolates.*

The nature of the nucleophile had an influence on the reaction outcome (Fig. 111, eq 1). Nucleophiles with different silyl-protecting groups could be successfully employed. Bulky substituents clearly favoured the γ-addition. Various ester-residues could be introduced, validating that the methyl-ester moiety was the most privileged structure.

Methyl-substitution in the unsaturated moiety was well tolerated, although slightly influencing yields and enantioselectivities.

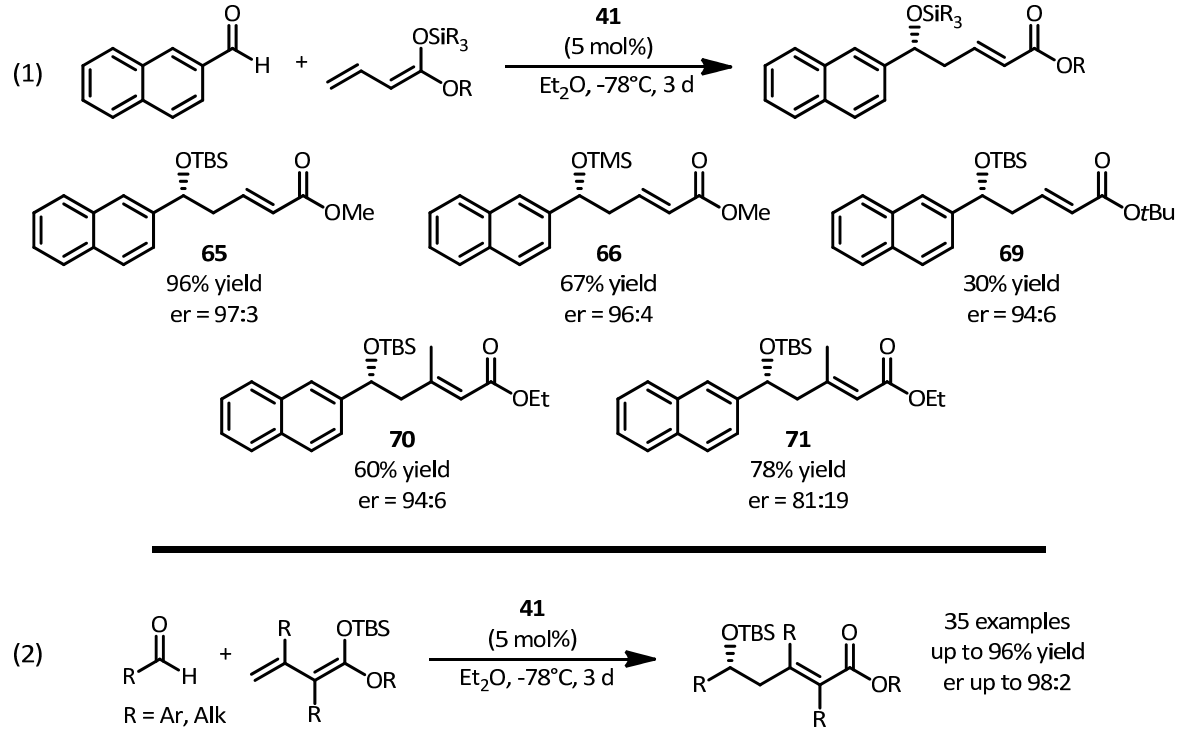


Figure 111. *Selected products of the disulfonimide-**41**-catalyzed vinylogous Mukaiyama aldol reaction.*

The electrophile tolerance proved to be broad, accepting various aromatic and aliphatic aldehydes (Fig. 111, eq 2). Aliphatic aldehydes delivered products in lower optical purities, whereas highest enantioselectivities were observed with aromatic aldehydes. The differences in enantioselectivity suggest a specific structural pattern which is preferably 'accepted' by disulfonimide **41**. Analysis of the respective aldehyde structures led us to propose the need of an α,β-unsaturated moiety for sufficient π-interaction, presumably in combination with a substitution in α- and γ-position.

Since we envisaged a double vinylogous version of the Mukaiyama aldol reaction (DVMAR), we investigated the nucleophilic behavior of potential trienolates by DFT-calculation in a colaboration with Bayer. Strikingly, the nucleophilicities obtained *in silico* encouraged our practical efforts, since they pointed towards the attack from the terminal positions in any case.

Remarkably, we could unveil this expected reactivity for different nucleophiles and electrophiles *in vitro* (Fig. 112, eq 1), representing the first highly enantioselective ε-selective Mukaiyama aldol reactions. This reaction installs 6 carbon-atoms as a doubly unsaturated

ester onto a carbonyl compound. Thus the high complexity offered in a single-step operation is quite remarkable.

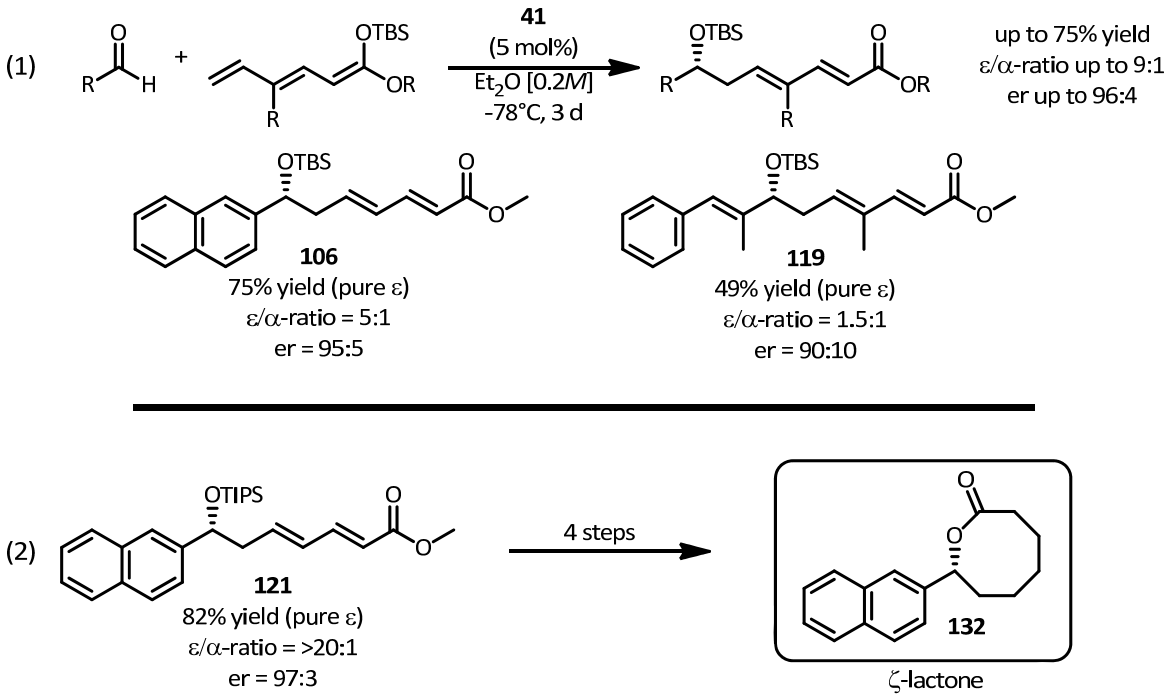


Figure 112. *First enantioselective double vinylogous Mukaiyama aldol reactions and incorporation in a synthetic sequence towards eight-membered ring lactones.*

Facing regioselectivity problems in the beginning, we were able to overcome these issues by installation of a very bulky silyl group (TIPS) on the nucleophile. With these nucleophiles we obtained almost complete desired regioselectivities, retaining high enantioselectivities. Furthermore, we were able to utilize this technique for a straightforward synthesis of eight-membered ring lactones, molecular entities which are difficult to obtain otherwise (Fig. 112, eq 2).

With disulfonimides like **41** as very powerful catalysts for Mukaiyama-type reactions, we envisioned the improvement of these catalysts in two directions: selectivity *and* reactivity. In order to tune the catalyst structure in a more directed way, we carried out investigations on the mechanism.

In these studies it was shown, that the mechanism of the reactions proceeds by Lewis-acid catalysis and not by Brønsted-acid catalysis. Although further studies towards the exact mechanism are required, the key step is suggested as a silyl-transfer event, *i.e.* activating the carbonyl compound towards the nucleophile (Fig. 113).

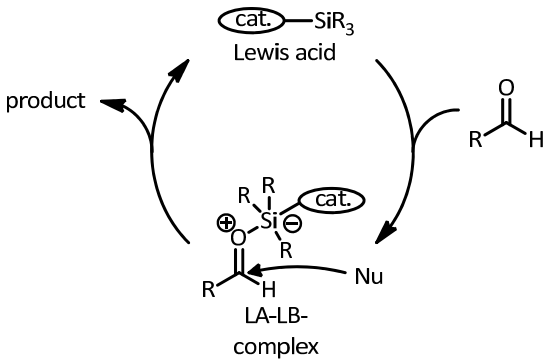


Figure 113. *General reaction mechanism for disulfonimide-catayis.*

Being sure about the crucial role of an operative Lewis acid, we sought to improve the catalyst structure by cooperative effects. With this concept, explored by Yamamoto and others, we were able to tune the reactivity of disulfonimides to unprecedented levels for metal-free catalyzed Mukaiyama aldol reactions. This was achieved by the installation of tertiary alcohol moieties, *i.e.* Brønsted-acidic sites (Fig. 114, eq 1), via a straightforward synthetic route from unsubstituted disulfonimide **44**, capturing the corresponding *o*-lithiated intermediate with benzophenones (Fig. 114, eq 2).

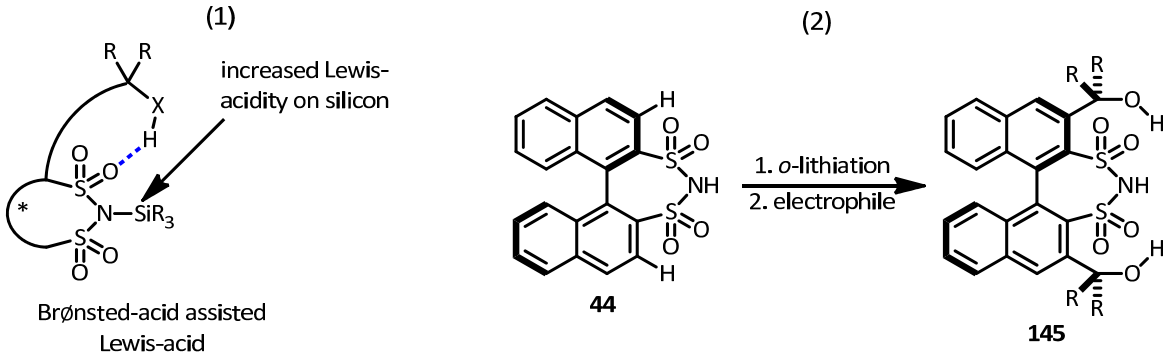


Figure 114. *Double activation strategy and synthetic route to hydroxy-disulfonimides.*

These new catalysts, hydroxy-disulfonimides, showed very interesting behavior in both, their synthesis and their application. Whereas the synthesis of the corresponding salts could be accomplished in differently substituted cases, the subsequent acidification led to decomposition of most hydroxydisulfonimides. Here the special role of electron-poor aryl groups led to stable catalyst **145**, which could be very successfully used in some Mukaiyama aldol type reactions (Fig. 115).

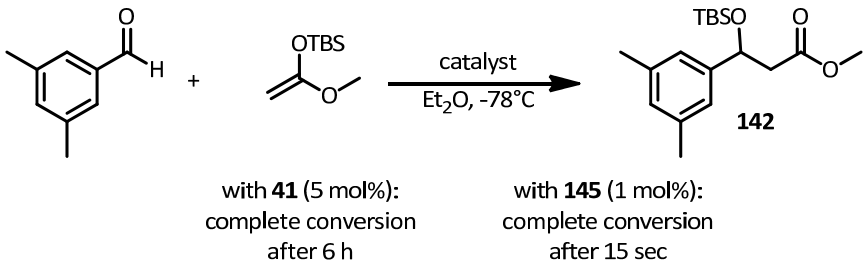


Figure 115. *Comparison of reaction times with catalysts **40**, **41** and **145** for the production of **142**.*

As a remarkable example, we illustrated the outstanding ability to catalyze the generation of **142** with only 1 mol% catalyst loading in seconds, whereas other catalysts needed hours for complete conversion even at higher catalyst loadings.

However, this catalyst only offered very poor enantioinduction for Mukaiyama aldol reactions, probably because the chiral pocket created by the diarylmethanol-residues is more open than in catalyst **41**.

In conclusion, the catalyst **41** provided an efficient and general entry to the complete vinylogous series of Mukaiyama aldol products. Furthermore, we revealed for the first time that double vinylogous versions of these transformations are possible, even in a highly asymmetric manner. With our mechanistic investigations and new catalyst developments reported in the second and third part of this work, we could open up a new route in disulfonimide-catalysis, making use of cooperative effects to improve the catalytic activity. Although these new catalysts are lacking the high setereoselectivity offered by **41**, they could set the cornerstone to a new and superior catalyst generation.

Part of the described work has been published in the following scientific articles:

"*Synthesis of TRIP and Analysis of Phosphate Salt Impurities*": M. Klussmann, L. Ratjen, S. Hoffmann, V. Wakchaure, R. Goddard, B. List, *Synlett* **2010**, 2189-2192.

"*Disulfonimide-Catalyzed Asymmetric Vinylogous and Bisvinylogous Mukaiyama Aldol Reactions*": L. Ratjen, P. García-García, F. Lay, M. E. Beck, B. List, *Angew. Chem. Int. Ed.* **2011**, *50*, 754-758; *Angew. Chem.* **2011**, *123*, 780-784.

6. Outlook

6.1 Possible applications of double vinylogous aldol reactions

The evolution of new synthetic methods, as illustrated here on the example of double vinylogous aldol reactions, is a major share of organic chemistry to life sciences. The rapid assembly of advanced molecular complexity in short reaction sequences is of great interest to the synthetic community. The synthesis and investigation of new molecules as lead structures, as well as the preparation of natural products, is important for medicinal-, crop protection- and materials-chemistry.

The vinylogous Mukaiyama aldol products presented in this work are particularly interesting. With the structural complexity offered by these, one can foresee a total synthetic application towards the previously mentioned Solandelactone A (Fig. 116)

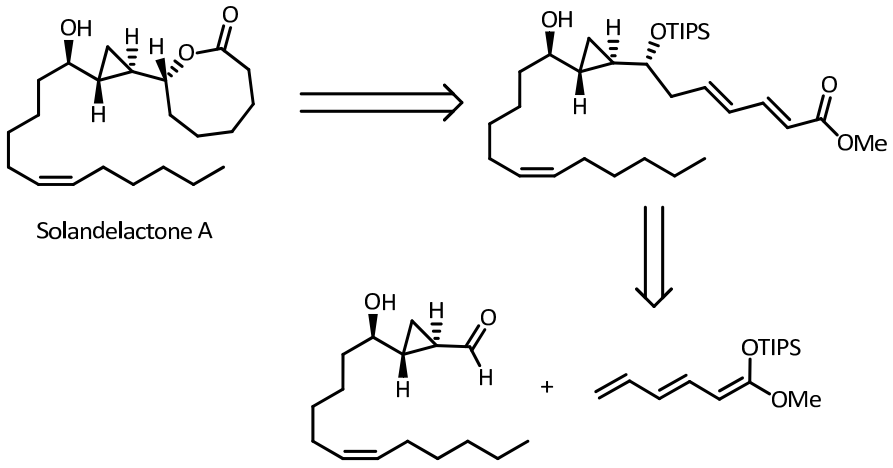


Figure 116. *Potential implementation of methods described in this work in the synthesis of Solandelactone A.*

Featuring a double vinylogous Mukaiyama aldol reaction as a key step, the rapid assembly of the lactone-moiety can be envisioned, starting from a fragment which is structurally significantly less complex.

6.2 Potential developments in disulfonimide-catalysis

Despite the advances made by the development of disulfonimide catalysis, as described in the previous chapters, further improvements remain desirable. Already mentioning the sensitive interplay of catalyst-efficiency and accessibility in the introduction of this thesis, it should be noted that the developments in the field of organocatalysis can play a special role for the future.[170] Although we were not able to identify catalysts for the highly

enantioselective conversion of aliphatic *and* aromatic aldehydes yet, further research concerning this catalyst class might offer great chances. Especially the introduction of new chiral backbones, the installation of better substituents on the backbone or the generation of dimers and oligomers could be promising strategies (see Fig. 117).

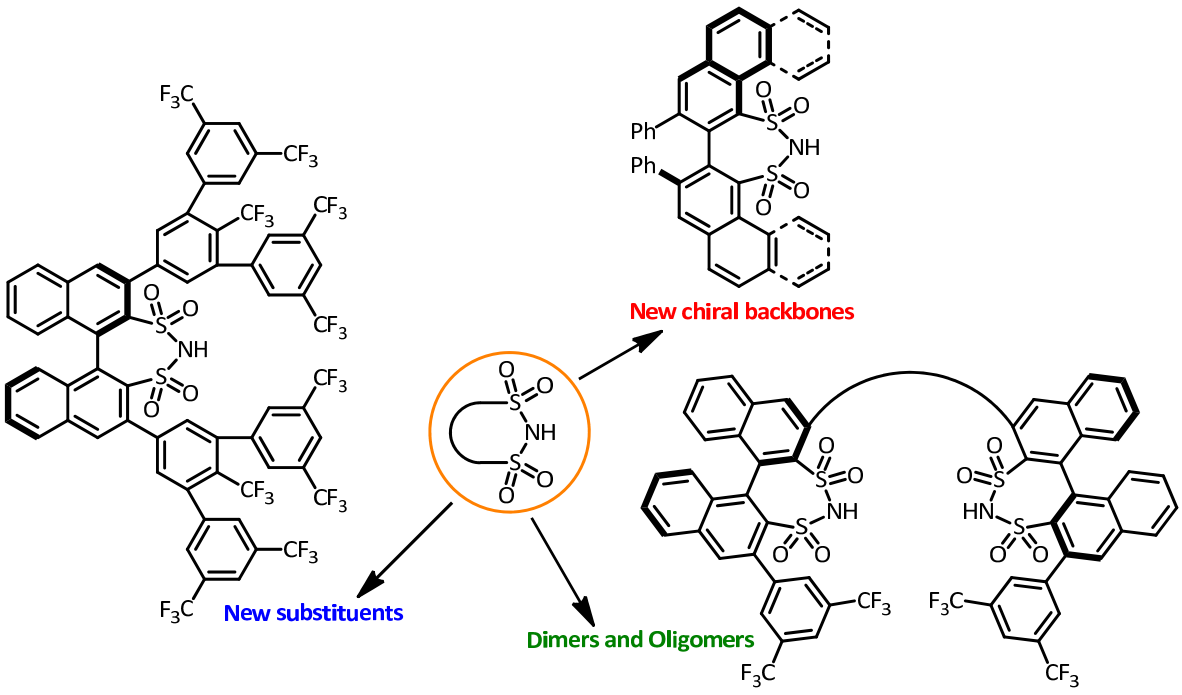


Figure 117. *Possible future developments in disulfonimide-catalysis.*

The exploitation of cooperative effects to tune activity is another area of interest and was already highlighted extensively in the previous chapters. The synthetic approach evaluated for the synthesis of hydroxy-disulfonimides, exhibits remarkable simplicity. This fact possibly allows for the efficient access to various other catalysts (Fig. 118), further exploring the principle of "Brønsted acid assisted Lewis acid catalysis" (BLA). Considering that disulfonimides found application as Brønsted acids recently, could even pave the way to applications as "Brønsted acid assisted Brønsted acids". The installation of electron-poor diarylmethanol- or even dialkylmethanol-rests as substituents allows for different catalysts (Fig. 118, 1 and 2). One great chance might be unsymmetrical ketones as electrophiles, resulting in mono-arylmethanols (Fig. 118, 3). By the installation of these, one adds further stereocenters, raising the chances for the observation of more selective catalysts. The installation of these rests to the *per se* achiral catalyst **40**, should also result in chiral disulfonimides, although their activity might be inferior, as shown previously for **155** (Fig. 118, 4).

One point that has been neglected previously, is the installation of these subunits to phosphoric acids (Fig. 118, 5). By this strategy, one might not only increase the acidity of the parent phosphoric acid, but the second free alcohol moiety could be available for secondary substrate activation. This phosphoric acid **157** was synthesized as part of this work, showing superior reactivity,[XXII] similar to the correspondingly 'tuned' disulfonimide **145**. The reaction behavior of this easily accessible Brønsted acid (synthesized following **GSP 4**) will be studied in our laboratories in the near future.

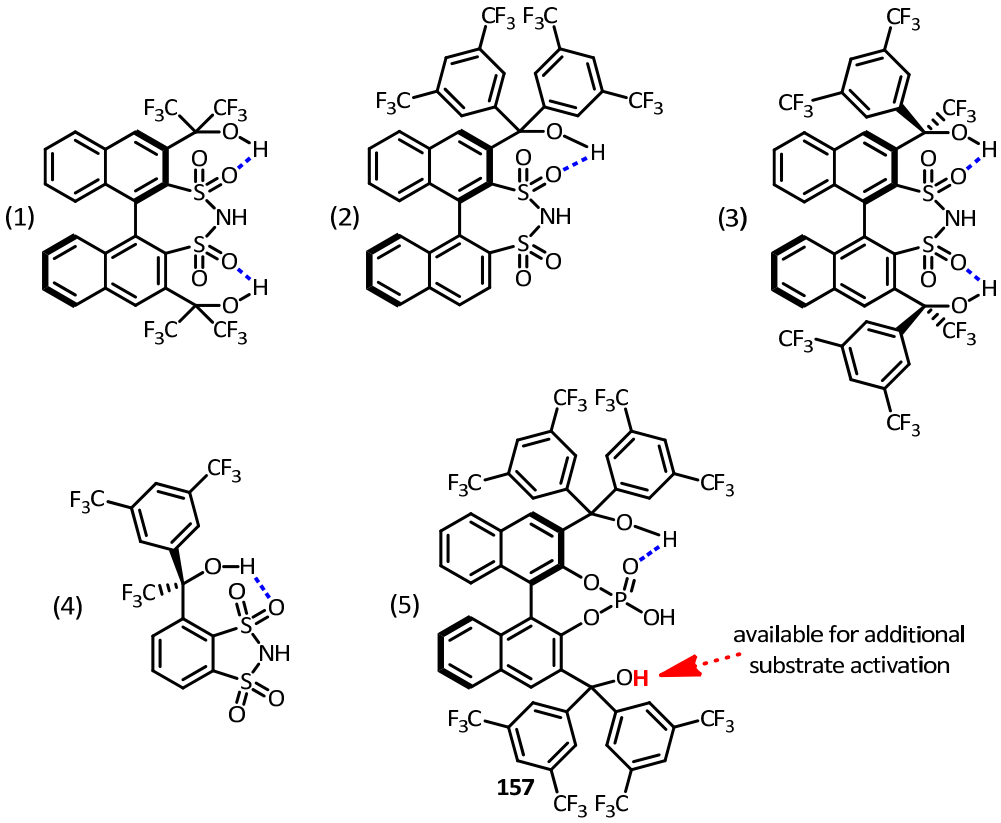


Figure 118. *Potential catalysts using Brønsted acid activation of Lewis acids or Brønsted acids.*

Since the development of phosphoric acids as powerful chiral Brønsted acids by Akiyama and Terada in 2004, these entities found an unprecedented ascent in the catalysis world.[131, 171] If one considers the sheer amount of reactions occurring via silicon Lewis-acid catalysis – like the Mukaiyama aldol reaction –,[172] the true amount of avenues open for disulfonimide-catalysis becomes apparent. The striking feature of disulfonimides is, that they can additionally catalyze reactions under Brønsted acid catalysis.[137] These two factors combined

[XXII] This catalyst was employed to asymmetric protonation reactions by JI-WOONG LEE, resulting in superior conversion in comparison to other phosphoric acid catalysts.

illustrate that the work already conducted in this field only gives a glimpse of what can be expected in the future.

Reports combining aldehydes,[173] ketones,[174] enones,[175] imines,[176] epoxides[177] and aziridines[178] with different silylated nucleophiles like enolates,[179] dienolates,[180] trienolates,[181] phosphonates,[182] azides,[183] dienes,[184] cyanides[185] and allylsilanes[186] display the potential of Lewis acid catalysis, although some of these transformations might as well be catalyzed by Brønsted acids. Imagining the number of electrophiles and nucleophiles meeting in chemical reactions with disulfonimide-catalysts has almost combinatorial character (Fig. 119).

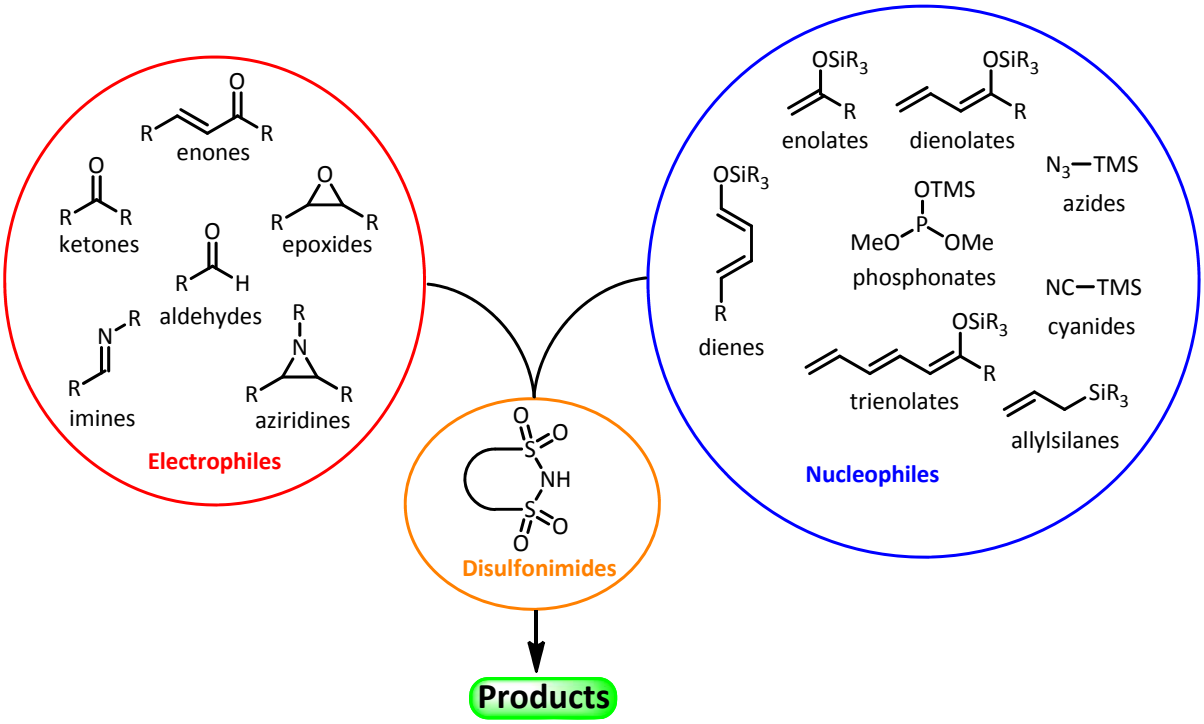


Figure 119. *Manifold of reactions which are imaginable under disulfonimide catalysis.*

Nevertheless it might not be unrealistic to follow this trail in the future, since more and more active catalysts will surely become available.

6.3 The future of metal-free Lewis acid catalysis

Regarding the task of the development of more powerful metal-free Lewis acids, one should consider the intrinsic reactivity offered by the homologous series of triflate, triflimide and triflylmethide. Going back to the reports from Ghosez,[113a] it is only logical to find inspiration in seminal works by Yamamoto[187] and Taguchi,[175] considering carbon-based Brønsted superacids. These catalysts did not only prove extremely acidic and efficient, but also their

potential as pre-Lewis acids was, however rudimentarily, exposed and discussed.[117] Nevertheless, the synthesis of such compounds is not well established.

When envisaging the preparation of chiral carbon based catalysts in the sense of pre-Lewis acidic Brønsted acids, one appealing feature is the existence of three sites for the installation of chiral information (Fig. 120).

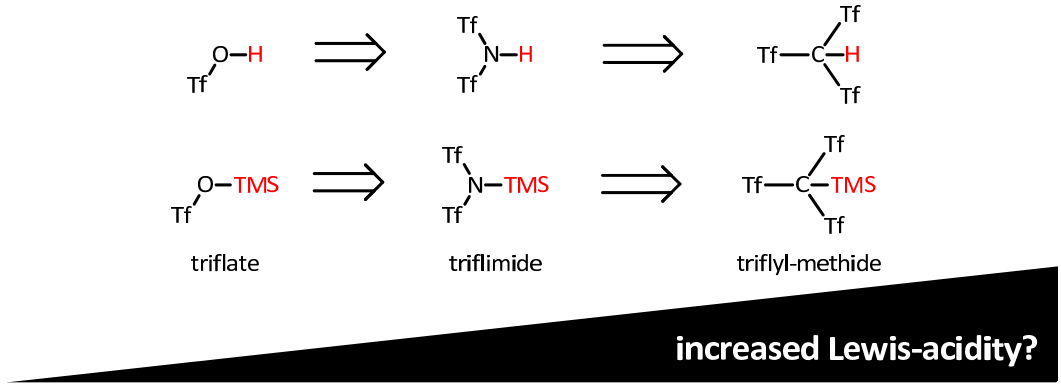


Figure 120. *Categorization of carbon-based Lewis acids.*

This offers some striking possibilities, since the electron-withdrawing character on the reactive center can be kept high with an additional substituent (Fig. 120). First approaches to this new and appealing topic were conducted as part of this work. For this purpose we focused on the rather unusual syntheses of bistriflylmethane **158** and methyl triflone **159** starting from triflylfluoride (Fig. 121, eq 1).[188]

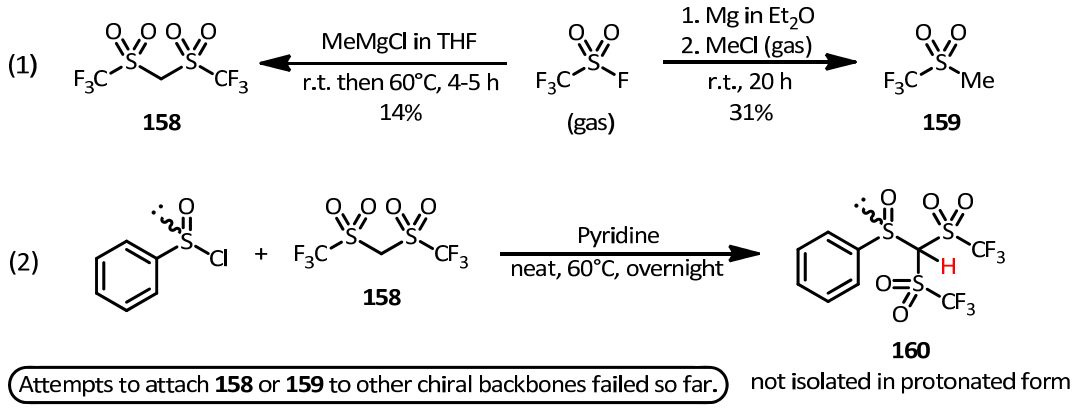


Figure 121. *First approaches towards the synthesis of chiral CH-acids, possible carbon-based silicon Lewis acid precursors.*

The key for a successful synthesis of these very odourous compounds is the solvent effect on the reaction outcome, already described in the original publication. When we treated **158** with benzenesulfinic chloride (Fig. 121, eq 2) in the presence of pyridine, we obtained the

corresponding racemic methide **160** as a salt. With the help of preparative HPLC-techniques we were able to separate the two enantiomers. Nevertheless, the protonated material could not be isolated by any extraction- or ion exchange-technique.

Although not successful in the first trials, we envisage that a careful investigation and optimization of reactions involving **157** and **158** could lead to new and exciting catalysts with superior catalyst performance. As examples, we tried to introduce the CH-acidic center to a sulfonic acid chloride or a phosphoric acid chloride, which would potentially furnish the corresponding phosphonyl-bistriflylmethide **161** or the bissulfonyl-triflylmethide **162** (Fig. 122, eq 1). Other possibilities could be delivered by the utilization of other chiral backbones, such as proline or its derivatives (Fig. 122, eq 2).

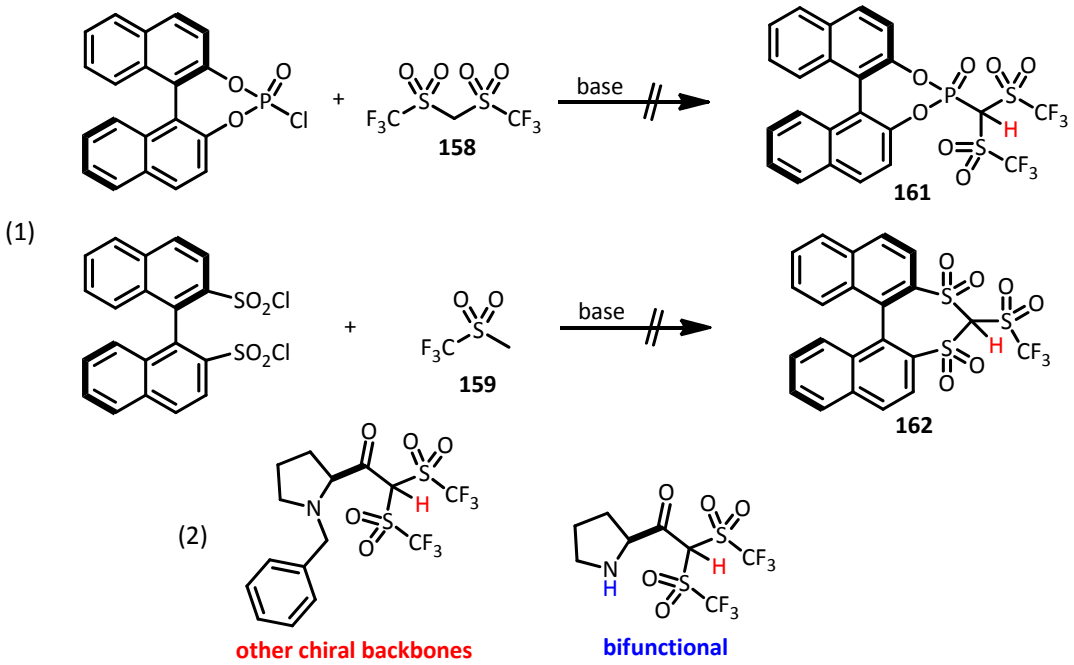


Figure 122. *Potential implementations of CH-acids in chiral backbones.*

One trend which should be reconsidered for future developments, is the orientation towards low molecular weight chiral backbones. This would reduce the complexity of catalysts and represent a development back to the roots of organocatalysis. Furthermore it would bring organocatalysis a step towards the ultimate goal: lower costs and higher atom economy.

7. Experimental part

7.1. General Remarks

- Solvents and Reagents -

Unless otherwise noted, the absolute solvents were purified and distilled following established standard procedures. Diethyl ether (Et_2O), tetrahydrofuran (THF) and toluene were purified by heating over alkaline- or alkaline earth-metal with appropriate indicators, followed by distillation. Acetonitrile (MeCN), dimethylformamide (DMF), chloroform ($CHCl_3$) and dichloromethane (DCM) were distilled from a suspension with CaH_2. Methanol (MeOH) and ethanol (EtOH) were dried by distillation over magnesium. Other solvents were purchased in dried form and stored under Argon.

Commercial reagents were used as purchased unless otherwise stated. Liquid reagents were distilled after purchase and stored under an atmosphere of Argon.

- Inert gas atmosphere -

Air- and moisture-sensitive reagents were stored under Argon in standard Schlenck-equipment. Sensitive reactions were conducted in flame-dried glassware under an atmosphere of Argon. The Argon-supply was delivered with 99.5% pure Argon by *Air Liquide*. In laboratory use, the Argon was additionally dried by passage over a column filled with anhydrous P_2O_5.

- Thin layer chromatography (TLC)/Column chromatography -

Thin layer chromatography was conducted on pre-coated and -shaped silica gel plates supplied by *Macherey-Nagel* (Polygram SilG/UV254, 0.2mm). Visualization was accomplished by UV-light treatment (λ = 254 nm) or staining with standard stain-mixtures (anisaldehyde, phosphomolybdic acid or ninhydrin). Preparative TLC plates were purchased by *Macherey-Nagel* (SIL G-100 UV254, 0.25 mm or 1.0 mm) and the spots were visualized under UV-light (λ = 254 nm).

Column chromatography was conducted on silica gel purchased from *Merck* (60 Å, 230-400 Mesh, 0.040-0.063 mm) utilizing standard solvents as eluent mixtures. The columns were standard glass cylinders and end-capped with glass frits. For flash columns compressed air was used for flow enhancement.

- NMR-spectroscopy (NMR) -

^{1}H-and ^{13}C- and ^{19}F- and ^{31}P-NMR spectra were recorded on *Bruker* AV-500-, AV-400- or DPX-300-spectrometers and the chemical shifts are reported in ppm relative to the abundant natural solvent resonance (for the corresponding data see: H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512-7515). Measurement frequencies are noted at the appropriate positions in this text. The temperatures for measurements were 298 K if not noted otherwise. The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, hept = heptet, sept = septet, m = multiplet, br = broad, or combinations of these. NMR-Data was processed with the *Bruker* TOPSPIN 2.1 software-kit.

- Mass spectrometry (MS) -

Mass spectra (EI-, CI-, ESI- and HRMS) were recorded on *Finnigan* MAT 8200 (70 eV), *Finnigan* MAT 8400 (70 eV), *Finnigan* TSQ 7000, *Finnigan* MAT 95, *Bruker* APEX III FT-MS (7 T magnet) or *Bruker* Esquire instruments. The masses are given in atomic units/elementary charge (m/z) and reported in percentage relative to the basic peak. High resolution masses are given with four decimals. The corresponding ionization-techniques are noted at the appropriate positions in the text.

- IR spectroscopy (IR) -

IR-spectra were recorded on a *Perkin-Elmer* Spectrum 100 FT-IR with *Perkin-Elmer* Universal ATR Sampling Accessory. The wavenumber (v) is given in [cm^{-1}].

ReactIR measurements were conducted on a *Mettler Toledo* ReactIR 15 with flexible diamond probe and the corresponding *Mettler Toledo* ReactIR-software kit.

- X-ray christallography (X-ray) -

Crystal structure measurements were conducted on a *Bruker* AXS Enraf-Nonius KappaCCD (Mo-K_α) with a graphite monochromator and a 0.2 x 2 mm^2 focus rotating anode or alternatively on a *Bruker* AXS X8 Proteum (Cu-K_α) with a focused multilayer optics monochromator and a 0.2 x 2 mm^2 focus rotating anode. The processing software consisted of *Bruker* AXS Datcol, Denzo, Saint, Proteum2 and *Sheldrick* Shelxs-97, Shelxl-97 and *Crystal Impact GbR* Diamond.

- GC/MS-couplings (GC/MS) –

The GC-MS couplings were performed on *Agilent* GC 6890 and MSD 5973 instruments (helium carrier gas) with *HP* 6890 Injector and *Macherey-Nagel* Optima® 5 columns (30m x 0.25 mm x 0.25 mm). The mass spectra were recorded with an *Agilent* 5973 Network MSD.

- High performance liquid chromatography (HPLC) -

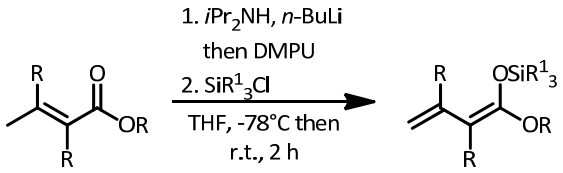
HPLC-measurements were performed on *Shimadzu* LC-2010 C liquid chromatographs or on *Shimadzu* LC-20 series modular equipments, featuring LC-20 AD pump unit, SIL-20 AC auto sampler, CBM-20 A communication module, SPD-M20 A diode array detector and CTO-20 AC column oven. The columns used were purchased from *Daicel* and the solvents were *Sigma-Aldrich* HPLC grade solvents.

- Optical rotation $[\alpha]^D$ -

Optical Rotations were measured on a *Rudolph* RA Autopol IV Automatic Polarimeter using the appropriate 1 mL cell (50 mm) at given temperatures. Concentrations are given in g/100mL.

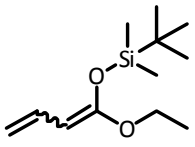
7.2. Vinylogous Mukaiyama aldol reactions (VMAR)

7.2.1 Synthesis of dienolates for VMARs



General synthetic procedure **(GSP 1):** A three-neck round-bottomed flask, equipped with stirring bar, Argon-inlet and septum was flame-dried and set under an atmosphere of Argon. The flask was charged with dry THF and pure diisopropylamine (1.1 equiv). The solution was cooled with an ice/water bath followed by slow addition of a 2.5*M* solution of *n*-butyllithium in hexane (1.1 equiv.). The mixture was stirred for 30 min, prior to cooling to -78°C with an acetone/dry ice bath. Subsequently DMPU (1.2 equiv.) was added and the resulting mixture was stirred for another 30 min after which the mixture turned turbid. Subsequently the corresponding crotonate (1.0 equiv.) was added dropwise and the resulting reaction mixture was stirred for 30 min at -78°C, the turbidity vanished and the corresponding silyl chloride (1.1 equiv.), dissolved in dry THF, was added slowly. After complete addition the cooling was removed and the mixture was stirred for 2 h while reaching room temperature. After this time cold pentane was added to the reaction mixture, causing precipitation of insoluble Li-salts. The liquid was transferred to a separation funnel and washed three times with cold water. The organic layer was dried over $MgSO_4$ and subsequently filtered through a pad of Celite. Removal of the solvents in vacuum (40°C water bath, 10 mbar) gave quantitative amounts of virtually pure products with slight yellow color. For final purification the remainder was distilled in high vacuum (3.0×10^{-2} mbar) and the resulting pure products were directly transferred into Schlenck tubes and stored under Argon at 4°C. Under these conditions the compounds were storable for several weeks without decomposition. The *E*/*Z*-ratio was determined by ^{1}H-NMR-spectroscopy.

• *Compound **47:** tert-Butyl((1-ethoxybuta-1,3-dien-1-yl)oxy)dimethylsilane*



$C_{12}H_{24}O_2Si$
Exact Mass: 228,15
Molecular Weight: 228,40

Following the general synthetic procedure (**GSP 1**), diisopropylamine (6.74 mL, 47.7 mmol, 1.1 equiv) in dry THF (50 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 21.55 mL, 1.1 equiv). DMPU (6.44 mL, 52.0 mmol, 1.2 equiv) was added, followed by ethyl crotonate (5.45 mL, 43.4 mmol, 1 equiv) and TBSCl (7.41 g, 47.7 mmol, 1.1 equiv) dissolved in dry THF (25 mL).

The product **47** was obtained as a colorless liquid (7.18 g, 31.44 mmol, 72% yield) and the geometrical isomers could be resolved by preparative GC.[XXIII]

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.19 major, 0.23 minor (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.96 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$-), 1.25 minor, 1.30 major (t, 3H, ^3J = 7.0 Hz, -OCH$_2$C<u>H</u>$_3$), 3.80 major, 3.95 minor (q, 2H, ^3J = 7.0 Hz, -OC<u>H</u>$_2$CH$_3$), 4.44 major, 4.54 minor (d, 1H, ^3J = 10.5 Hz, -C=C<u>H</u>-), 4.58 (dd, 1H, ^2J = 2.1 Hz, ^3J-*cis* = 10.4 Hz, -CH=C<u>H</u>$_2$), 4.82 (dd, 1H, ^2J = 2.4 Hz, ^3J-*trans* = 17.3 Hz, -CH=C<u>H</u>$_2$), 6.54 (ddd, 1H, ^3J-*cis* = 10.4 Hz, ^3J-*trans* = 17.3 Hz, ^3J = 10.4 Hz, -C<u>H</u>=CH$_2$).

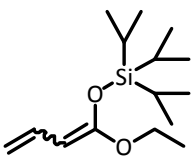
E/*Z*-ratio 5.7:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.90, -4.15, 14.36, 14.84, 18.11, 18.14, 25.54, 25.70, 62.83, 63.26, 80.58, 88.32, 106.30, 107.21, 132.16, 132.57, 154.90, 157.72.

MS (EI) m/z: 228 (27 %), 103 (72 %), 75 (52%), 73 (100 %), 59 (12 %);

HRMS (EI) m/z: calcd. 228.1548, found 228.1546.

• *Compound **48:** ((1-Ethoxybuta-1,3-dien-1-yl)oxy)triisopropylsilane*



$C_{15}H_{30}O_2Si$
Exact Mass: 270,20
Molecular Weight: 270,48

Following the general synthetic procedure (**GSP 1**), diisopropylamine (0.78 mL, 5.5 mmol, 1.1 equiv) in dry THF (6 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 2.19 mL, 1.1 equiv). DMPU (0.72 mL, 6.0 mmol, 1.2 equiv) was added, followed by ethyl

[XXIII] The machine was a custom-made apparatus from the gaschromatographical department of the Max-Planck-Institut für Kohlenforschung.

crotonate (0.62 mL, 5.0 mmol, 1 equiv) and TIPSCl (1.28 mL, 6.0 mmol, 1.1 equiv) dissolved in dry THF (3 mL).

The product **48** was obtained as a colorless liquid (0.90 g, 3.33 mmol, 67% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.08 major, 1.11 minor (d, 18 H, ^3J = 7.3 Hz, -Si(C(C<u>H</u>$_3$)$_2$)$_3$), 1.17-1.25 (m, 3H, -Si(<u>C</u>(CH$_3$)$_2$)$_3$), 1.27 minor, 1.30 major, (t, 3H, ^3J = 7.0 Hz, -OCH$_2$C<u>H</u>$_3$), 3.81 major, 3.99 minor (q, 2H, ^3J = 7.0 Hz, -OC<u>H</u>$_2$CH$_3$), 4.41 (d, 1H, ^3J = 10.4 Hz, -C=C<u>H</u>-), 4.57 (dd, 1H, ^3J-*cis* = 10.4 Hz, ^2J = 2.1 Hz, -CH=C<u>H</u>$_2$), 4.81 (dd, 1H, ^3J-*trans* = 17.2 Hz, ^2J = 2.2 Hz, -CH=C<u>H</u>$_2$), 6.54 minor, 6.61 major (ddd, 1H, ^3J-*trans* = 17.2 Hz, ^3J-*cis* = 10.4 Hz, ^3J = 10.4 Hz, -C<u>H</u>=CH$_2$).

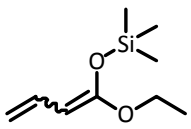
E/*Z*-ratio 5.7:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.61, 12.83, 14.53, 15.06, 17.99, 62.99, 63.40, 79.74, 88.01, 106.02, 106.88, 132.53, 132.95, 155.14, 157.80.

MS (EI) m/z: 270 (71%), 227 (18%), 168 (21%), 156 (57%), 131 (25%), 115 (84%), 73 (73%), 59 (100%).

HRMS (EI) m/z: calcd. 270.2017, found 270.2015.

• *Compound **49:** ((1-Ethoxybuta-1,3-dien-1-yl)oxy)trimethylsilane*



$C_9H_{18}O_2Si$
Exact Mass: 186,11
Molecular Weight: 186,32

Following the general synthetic procedure (**GSP 1**), diisopropylamine (1.55 mL, 11.0 mmol, 1.1 equiv) in dry THF (12 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 4.29 mL, 1.1 equiv). DMPU (1.44 mL, 12.0 mmol, 1.2 equiv) was added, followed by ethyl crotonate (1.24 mL, 10.0 mmol, 1 equiv) and TMSCl (1.52 mL, 12.0 mmol, 1.1 equiv) dissolved in dry THF (6 mL).

The product **49** was obtained as a colorless liquid (0.47 g, 2.52 mmol, 25% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.23 (s, 9H, -Si(C<u>H</u>$_3$)$_3$), 1.30 (t, 3H, ^3J = 7.0 Hz, -OCH$_2$C<u>H</u>$_3$), 3.80 (q, 2H, ^3J = 7.0 Hz, -OC<u>H</u>$_2$CH$_3$), 4.45 (d, 1H, ^3J = 10.4 Hz, -C=C<u>H</u>-), 4.58 (dd, 1H, ^3J-*cis* = 10.5 Hz, ^2J = 2.0 Hz, -CH=C<u>H</u>$_2$), 4.82 (dd, 1H, ^3J-*trans* = 17.0 Hz, ^2J = 2.0 Hz, -CH=C<u>H</u>$_2$), 6.50 (ddd, 1H, ^3J-*trans* = 17.2 Hz, ^3J-*cis* = 10.4 Hz, 10.4 Hz, -C<u>H</u>=CH$_2$).

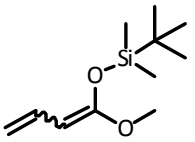
E/*Z*-ratio 99:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 0.53, 14.52, 63.46, 80.91, 106.55, 132.71, 157.77.

MS (EI) m/z: 186 (29%), 103 (16%), 73 (59%), 68 (100%).

HRMS (EI) m/z: calcd. 186.1076, found 186.1076.

• *Compound **50:** tert-Butyl((1-methoxybuta-1,3-dien-1-yl)oxy)dimethylsilane*



$C_{11}H_{22}O_2Si$
Exact Mass: 214,14
Molecular Weight: 214,38

Following the general synthetic procedure (**GSP 1**), diisopropylamine (15.22 mL, 107.6 mmol, 1.1 equiv) in dry THF (90 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 43.10 mL, 1.1 equiv). DMPU (14.54 mL, 120.6 mmol, 1.2 equiv) was added, followed by methyl crotonate (10.60 mL, 92.9 mmol, 1 equiv) and TBSCl (16.74 g, 111.1 mmol, 1.1 equiv) dissolved in dry THF (50 mL).

The product **50** was obtained as a colorless liquid (13.20 g, 61.66 mmol, 57% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.18 major, 0.24 minor (s, 6H, -Si($C\underline{H}_3$)$_2$), 0.95 major, 0.96 minor (s, 9H, -SiC($C\underline{H}_3$)$_3$), 3.57 major, 3.60 minor (s, 3H, -O$C\underline{H}_3$), 4.48 (d, 1H, ^{3}J = 10.4 Hz, -C=C$\underline{H}$-), 4.60 (dd, 1H, ^{2}J = 2.2 Hz, ^{3}J-*cis* = 10.4 Hz, -CH=C$\underline{H}_2$), 4.85 (dd, 1H, ^{2}J = 2.2 Hz, ^{3}J-*trans* = 17.3 Hz, -CH=C$\underline{H}_2$), 6.53 (ddd, 1H, ^{3}J-*cis* = 10.4 Hz, ^{3}J-*trans* = 17.2 Hz, ^{3}J = 10.4 Hz, -C$\underline{H}$=CH_2).

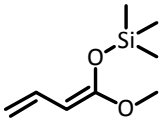
E/*Z*-ratio 5:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.75, -4.12, 18.22, 18.30, 25.58, 25.80, 54.53, 54.91, 80.37, 87.07, 106.85, 107.37, 132.04, 132.54, 155.62, 158.88.

MS (EI) m/z: 214 (25%), 89 (93%), 73 (100%), 68 (29%), 59 (30%).

HRMS (EI) m/z: calcd. 214.1387, found 214.1389.

• *Compound **51:** ((1-Methoxybuta-1,3-dien-1-yl)oxy)trimethylsilane*



$C_8H_{16}O_2Si$
Exact Mass: 172,09
Molecular Weight: 172,30

Following the general synthetic procedure (**GSP 1**), diisopropylamine (17.21 mL, 131.0 mmol, 1.1 equiv) in dry THF (150 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 47.55 mL, 1.1 equiv). DMPU (17.21 mL, 142.8 mmol, 1.2 equiv) was added, followed by

methyl crotonate (12.62 mL, 111.9 mmol, 1 equiv) and TMSCl (14.23 mL, 131.0 mmol, 1.1 equiv) dissolved in dry THF (40 mL).

The product **51** was obtained as a colorless liquid (8.84 g, 51.31 mmol, 46% yield).

^{1}H-NMR (300 MHz, CD_2Cl_2) δ [ppm]: 0.19 (s, 9H, -Si(C<u>H</u>$_3$)$_3$), 3.53 (s, 3H, -OC<u>H</u>$_3$), 4.46 (d, 1H, ^3J = 10.4 Hz, -C=C<u>H</u>-), 4.53 (dd, 1H, ^2J = 2.3 Hz, ^3J-*cis* = 10.5 Hz, -CH=C<u>H</u>$_2$), 4.78 (dd, 1H, ^2J = 2.2 Hz, ^3J-*trans* = 17.2 Hz, -CH=C<u>H</u>$_2$), 6.41 (ddd, 1H, ^3J-*cis* = 10.4 Hz, ^3J-*trans* = 17.2 Hz, ^3J = 10.4 Hz, -C<u>H</u>=CH$_2$).

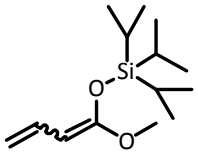
E/*Z*-ratio 99:1.

^{13}C-NMR (75 MHz, CD_2Cl_2) δ [ppm]: 0.01, 54.93, 80.61, 106.54, 132.59, 158.80.

MS (EI) m/z: 172 (22%), 89 (26%), 73 (52%), 68 (100%), 59 (14%).

HRMS (EI) m/z: calcd. 172.0918, found. 172.0920.

• *Compound **52:** Triisopropyl((1-methoxybuta-1,3-dien-1-yl)oxy)silane*



$C_{14}H_{28}O_2Si$
Exact Mass: 256,19
Molecular Weight: 256,46

Following the general synthetic procedure (**GSP 1**), diisopropylamine (7.61 mL, 53.9 mmol, 1.1 equiv) in dry THF (50 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 21.55 mL, 1.1 equiv). DMPU (7.27 mL, 58.8 mmol, 1.2 equiv) was added, followed by methyl crotonate (5.30 mL, 49.0 mmol, 1 equiv) and TIPSCl (11.53 mL, 53.9 mmol, 1.1 equiv) dissolved in dry THF (25 mL).

The product **52** was obtained as a colorless liquid (7.64 g, 29.79 mmol, 61% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 1.06-1.30 (m, 21H, -Si(C<u>H</u>(C<u>H</u>$_3$)$_2$)$_3$), 3.57 major, 3.65 minor (s, 3H, -OC<u>H</u>$_3$), 4.44 major, 4.52 minor (d, 1H, ^3J = 10.6 Hz, -C=C<u>H</u>-), 4.57 minor, 4.59 major (dd, 1H, ^2J = 2.2 Hz, ^3J-*cis* = 10.4 Hz, -CH=C<u>H</u>$_2$), 4.78 minor, 4.84 major (dd, 1H, ^2J = 2.2 Hz, ^3J-*trans* = 17.2 Hz, -CH=C<u>H</u>$_2$), 6.52 minor, 6.60 major (ddd, 1H, ^3J-*cis* = 10.4 Hz, ^3J-*trans* = 17.2 Hz, ^3J = 10.4 Hz, -C<u>H</u>=CH$_2$).

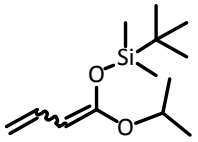
E/*Z*-ratio 4.2:1.

^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 12.56, 12.74, 17.88, 17.92, 54.52, 54.71, 79.33, 86.74, 106.39, 106.89, 132.20, 132.69, 155.63, 158.74.

MS (EI) m/z: 256 (56%), 213 (13%), 156 (38%), 145 (48%), 115 (65%), 87 (51%), 73 (62%), 59 (100%).

HRMS (EI) m/z: calcd. 256.1856, found 256.1859.

• *Compound **53:** tert-Butyl((1-isopropoxybuta-1,3-dien-1-yl)oxy)dimethylsilane*



$C_{13}H_{26}O_2Si$
Exact Mass: 242,17
Molecular Weight: 242,43

Following the general synthetic procedure (**GSP 1**), diisopropylamine (5.94 mL, 42.1 mmol, 1.1 equiv) in dry THF (50 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 16.82 mL, 1.1 equiv). DMPU (5.67 mL, 45.9 mmol, 1.2 equiv) was added, followed by isopropyl crotonate (5.62 mL, 38.2 mmol, 1 equiv) and TBSCl (6.53 g, 42.1 mmol, 1.1 equiv) dissolved in dry THF (25 mL).

The product **53** was obtained as a colorless liquid (6.88 g, 28.38 mmol, 74% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.18 major, 0.23 minor (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.95 (s, 9H, -SiC(C$\underline{H}_3$)$_3$-), 1.22 minor, 1.27 major (d, 6H, ^3J = 6.2 Hz, -OCH(C$\underline{H}_3$)$_2$), 4.26 major, 4.48 minor (sept, 1H, ^3J = 6.1 Hz, -OC$\underline{H}$(CH$_3$)$_2$), 4.43 major, 4.60 minor (d, 1H, ^3J = 10.4 Hz, -C=C$\underline{H}$-), 4.56 major, 4.59 minor (dd, ^2J = 2.2 Hz, ^3J-*cis* = 10.4 Hz, -CH=C$\underline{H}_2$), 4.79 major, 4.81 minor (dd, 1H, ^2J = 2.2 Hz, ^3J-*trans* = 17.3 Hz, -CH=C$\underline{H}_2$), 6.53 minor, 6.56 major (ddd, 1H, ^3J-*cis* = 10.4 Hz, ^3J-*trans* = 17.2 Hz, ^3J = 10.4 Hz, -C$\underline{H}$=CH$_2$).

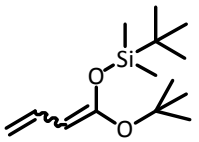
E/*Z*-ratio 5.6:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.77, -3.93, 18.23, 18.26, 21.89, 22.20, 25.69, 25.87, 69.51, 70.19, 81.53, 90.41, 105.95, 107.44, 132.58, 132.96, 154.33, 156.53.

MS (EI) m/z: 242 (41%), 200 (28%), 184 (47%), 142 (53%), 98 (13%), 75 (100%), 73 (95%), 68 (75%).

HRMS (EI) m/z: calcd. 242.1704, found 242.1702.

• *Compound **54:** ((1-(tert-Butoxy)buta-1,3-dien-1-yl)oxy)(tert-butyl)dimethylsilane*



$C_{14}H_{28}O_2Si$
Exact Mass: 256,19
Molecular Weight: 256,46

Following the general synthetic procedure (**GSP 1**), diisopropylamine (5.30 mL, 37.5 mmol, 1.1 equiv) in dry THF (40 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 15.01 mL, 1.1 equiv). DMPU (5.06 mL, 40.9 mmol, 1.2 equiv) was added, followed by *tert*-butyl crotonate (5.00 g, 34.1 mmol, 1 equiv) and TBSCl (5.83 g, 37.5 mmol, 1.1 equiv) dissolved in dry THF (20 mL).

The product **54** was obtained as a colorless liquid (5.34 g, 20.82 mmol, 61% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.18 major, 0.22 minor (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.95 minor, 0.96 major (s, 9H, -SiC(C$\underline{H}_3$)$_3$-), 1.36 minor, 1.37 major (s, 9H, -OC(C$\underline{H}_3$)$_3$), 4.63 (dd, 1H, ^2J = 2.1 Hz, ^3J-*cis* = 10.5 Hz, -CH=C$\underline{H}_2$), 4.72 major, 4.77 minor (d, 1H, ^3J = 10.6 Hz, -C=C$\underline{H}$-), 4.86 (dd, 1H, ^2J = 2.1 Hz, ^3J-*trans* = 17.2 Hz, -CH=C$\underline{H}_2$), 6.50 (ddd, 1H, ^3J-*cis* = 10.5 Hz, ^3J-*trans* = 17.2 Hz, ^3J = 10.4 Hz, -C$\underline{H}$=CH$_2$).

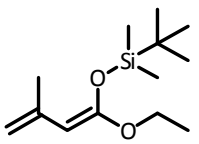
E/*Z*-ratio 5.5:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.56, -4.00, 18.19, 25.84, 28.62, 29.21, 79.68, 79.78, 92.43, 95.41, 108.04, 108.35, 132.95, 133.35, 153.94, 154.34.

MS (EI) m/z: 256 (3%), 200 (32%), 184 (27%), 142 (40%), 75 (100%), 73 (95%), 68 (81%), 57 (50%).

HRMS (EI) m/z: calcd. 256.1860, found 256.1859.

• *Compound **55:** tert-Butyl((1-ethoxy-3-methylbuta-1,3-dien-1-yl)oxy)dimethylsilane*



$C_{13}H_{26}O_2Si$
Exact Mass: 242,17
Molecular Weight: 242,43

Following the general synthetic procedure (**GSP 1**), diisopropylamine (1.55 mL, 11.0 mmol, 1.1 equiv) in dry THF (12 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 4.40 mL, 1.1 equiv). Hexamethylphosphoramide (2.10 mL, 12.0 mmol, 1.2 equiv) was added, followed by ethyl 3-methyl-2-butenoate (1.28 mL, 10.0 mmol, 1 equiv) and TBSCl (1.81 g, 12.0 mmol, 1.1 equiv) dissolved in dry THF (6 mL).

The product **55** was obtained as a colorless liquid (1.08 g, 4.45 mmol, 45% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.21 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.94 (s, 9H, -SiC(C$\underline{H}_3$)$_3$-), 1.30 (t, 3H, ^{3}J = 7.0 Hz, -OCH$_2$C$\underline{H}_3$), 1.95 (s, 3H, -C-C$\underline{H}_3$), 3.78 (q, 2H, ^{3}J = 7.0 Hz, -OC$\underline{H}_2$CH$_3$), 4.20 (s, 1H, -C=C$\underline{H}$-), 4.52 (dd, 1H, ^{2}J = 2.6 Hz, ^{4}J = 1.4 Hz, -C=C$\underline{H}_2$), 4.78 (d, 1 H, ^{3}J = 2.8 Hz, -C=C$\underline{H}_2$).

E/*Z*-ratio 99:1.

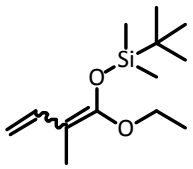
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -3.54, 14.54, 18.30, 24.12, 26.02, 63.59, 80.58, 107.20, 140.64, 156.77.

MS (EI) m/z: 242 (38 %), 171 (45 %), 103 (62 %), 82 (56 %), 75 (55 %), 73 (100 %).

HRMS (EI) m/z: calcd. 242.1700, found 242.1702.

• *Compound **56:** tert-Butyl((1-ethoxy-2-methylbuta-1,3-dien-1-yl)oxy)dimethylsilane*

Following the general synthetic procedure (**GSP 1**), diisopropylamine (6.15 mL, 43.6 mmol, 1.1 equiv) in dry THF (44 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 17.60 mL, 1.1 equiv). DMPU (5.80 mL, 48.1 mmol, 1.2 equiv) was added, followed by ethyl tiglate (5.60 mL, 40.3 mmol, 1 equiv) and TBSCl (6.60 g, 43.6 mmol, 1.2 equiv) dissolved in dry THF (24 mL).



$C_{13}H_{26}O_2Si$
Exact Mass: 242,17
Molecular Weight: 242,43

The product **56** was obtained as a colorless liquid (4.41 g, 18.19 mmol, 45% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.17, 0.18 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.97, 0.98 (s, 9H, -SiC(C$\underline{H}_3$)$_3$-), 1.25 (t, 3H, ^{3}J = 7.1 Hz, -OCH$_2$C$\underline{H}_3$), 1.65, 1.68 (s, 3H, -C-C$\underline{H}_3$), 3.82-3.88 (m, 2H, -OC$\underline{H}_2$CH$_3$), 4.76-4.88 (m, 2H, -CH=C$\underline{H}_2$), 6.70, 6.79 (dd, 1H, ^{3}J-*cis* = 10.8 Hz, ^{3}J-*trans* = 17.5 Hz, -C$\underline{H}$=CH$_2$).

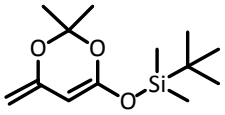
E/*Z*-ratio 1:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.40, -4.33, 10.50, 10.88, 14.88, 14.98, 18.27, 18.31, 25.79, 25.83, 65.34, 66.00, 97.88, 98.41, 107.48, 108.07, 134.71, 134.82, 152.13, 152.52.

MS (EI) m/z: 242 (100%), 227 (27%), 171 (22%), 157 (22%), 103 (40%), 82 (81%).

HRMS (EI) m/z: calcd. 242.1700, found 242.1702.

• *Compound **57:** tert-Butyl((2,2-dimethyl-4-methylene-4H-1,3-dioxin-6-yl)oxy)dimethylsilane*



$C_{13}H_{24}O_3Si$
Exact Mass: 256,15
Molecular Weight: 256,41

Following the general synthetic procedure (**GSP 1**), diisopropylamine (5.47 mL, 38.7 mmol, 1.1 equiv) in dry THF (60 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 15.48 mL, 1.1 equiv). DMPU (5.08 mL, 42.2 mmol, 1.2 equiv) was added, followed by ethyl 2,2,6-trimethyl-4H-1,3-dioxin-4-one (5.67 mL, 35.2 mmol, 1 equiv) and TBSCl (6.36 g, 42.2 mmol, 1.2 equiv) dissolved in dry THF (30 mL).

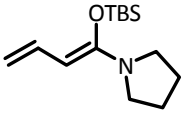
The product **57** was obtained as a yellowish liquid (7.41 g, 28.89 mmol, 82% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.20 (s, 6H, -Si(CH_3)$_2$-), 0.93 (s, 9H, -SiC(CH_3)$_3$-), 1.54 (s, 6H, -C(CH_3)$_2$), 3.86 (d, 1H, ^2J = 0.4 Hz, -C=CH_2), 4.05 (d, 1H, ^2J = 0.6 Hz, -C=CH_2), 4.66 (s, 1H, -C=CH-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.14, 18.16, 24.65, 25.65, 76.80, 84.84, 102.59, 152.07, 153.68.

This data is in accordance with the previously reported.[91]

• *Compound **58:** (Z)-1-(1-((tert-Butyldimethylsilyl)oxy)buta-1,3-dien-1-yl)pyrrolidine*



$C_{14}H_{27}NOSi$
Exact Mass: 253,19
Molecular Weight: 253,46

(*E*)-1-(Pyrrolidin-1-yl)but-2-en-1-one (1.50 g, 11.0 mmol, 1.0 equiv) was dissolved in dry THF (80 mL) in an oven dried three-neck round bottom flask with Argon-Inlet and stirring equipment. The resulting mixture was cooled to -78°C with a dry ice/acetone bath. Subsequently a solution of vacuum-dried KHMDS (2.39 g, 12.1 mmol, 1.1 equiv) in dry THF (25 mL) was added slowly. After complete addition the resulting reaction mixture was stirred for 30 min at -78°C. After this time a solution of vacuum-dried TBSCl (1.82 g, 12.1 mmol, 1.1 equiv) was added slowly. The cooling was subsequently exchanged to an ice bath and the resulting mixture stirred at this temperature for 1 h. After this time the solvent was removed under high-vacuum. The residue was redissolved in pentane and filtered through Celite and the Celite-pad was vigorously washed with pentane. The resulting solution was evaporated and the yellow liquid residue was distilled under high vacuum.

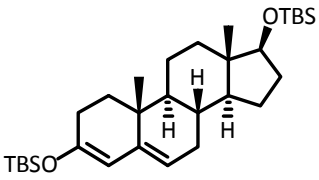
The product **58** was obtained as a yellowish liquid (0.56 g, 2.17 mmol, 20% yield).

^{1}H-NMR (400 MHz, CD_2Cl_2) δ [ppm]: 0.14 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.96 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$-), 1.77-1.80 (m, 4H, -C<u>H</u>$_2$-), 3.02-3.06 (m, 4H, -C<u>H</u>$_2$-), 4.29 (ddd, 1H, ^{2}J = 2.6 Hz, ^{3}J-cis = 10.4 Hz, ^{4}J = 0.4 Hz, -CH=C<u>H</u>$_2$), 4.40 (d, 1H, ^{3}J = 10.8 Hz, -C=C<u>H</u>-), 4.56 (dd, 1H, ^{2}J = 2.5 Hz, ^{3}J-*trans* = 17.0 Hz, -CH=C<u>H</u>$_2$), 6.43 (ddd, ^{3}J-*trans* = 17.0 Hz, ^{3}J = 10.6 Hz, 10.5 Hz, -C<u>H</u>=CH$_2$).

^{13}C-NMR (100 MHz, CD_2Cl_2) δ [ppm]: -4.26, 18.32, 25.04, 25.69, 47.72, 84.99, 101.83, 134.09, 153.09.

This data is in accordance with the previously reported.[147]

• *Compound **59:** (8R,9S,10R,13S,14S,17S)-10,13-dimethyl-2,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthrene-3,17-diol*



$C_{31}H_{56}O_2Si_2$
Exact Mass: 516,38
Molecular Weight: 516,95

A Schlenck tube with a stirring bar was flushed with Argon and charged with testosterone (1.00 g, 3.4 mmol, 1 equiv.) and dry CH_2Cl_2 (17 mL). Subsequently TMEDA (2.00 mL, 13.4 mmol, 2.95 equiv) and TBSOTf (2.70 mL, 11.5 mmol, 3.4 equiv) were added via syringe and the resulting clear solution was stirred for 48 h at r.t. The corresponding mixture was quenched with saturated $NaHCO_3$-solution extracted with CH_2Cl_2, dried over Mg_2SO_4 and the solvent removed in vacuo. The crude product was purified by column chromatography (hexane/ethyl acetate 15:1).

Compound **59** was obtained as a white solid (1.41 g, 2.72 mmol, 80% yield).

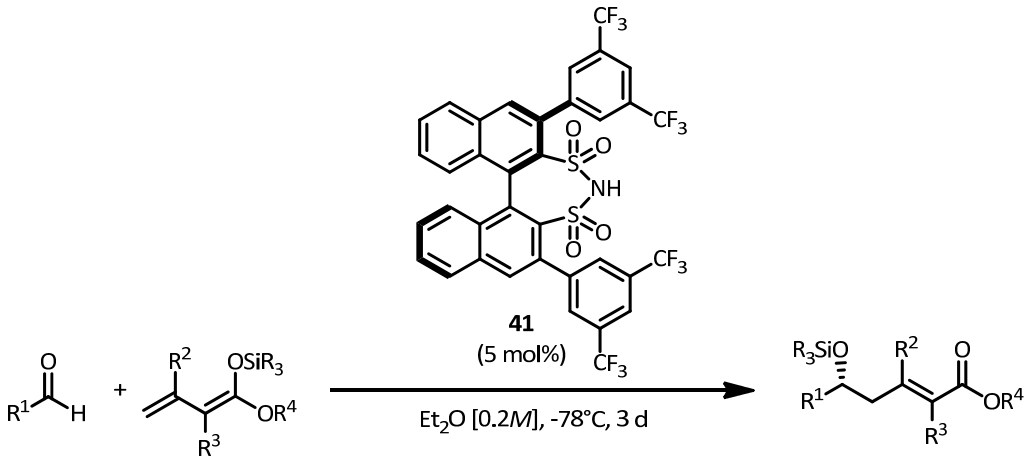
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.00, 0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.14, 0.15 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.73 (s, 3H, -C-C<u>H</u>$_3$), 0.88 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$-), 0.92 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$-), 0.96 (s, 3H, -C-C<u>H</u>$_3$), 0.98-1.08 (m, 2H), 1.20-1.32 (m, 3H), 1.36-1.50 (m, 2H), 1.51-1.67 (m, 4H), 1.75-1.93 (m, 3H), 1.97-2.28 (m, 3H), 3.54-3.58 (m, 1H, -CH$_2$-C<u>H</u>-), 5.16-5.17 (m, 1H, -C=C<u>H</u>-), 5.26 (s, 1H, -C=C<u>H</u>-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.66, -4.35, -4.27, -4.02, 11.47, 18.18, 18.26, 19.14, 21.03 (DEPT 135 negative), 23.67 (DEPT 135 negative), 25.82, 26.01, 27.81 DEPT 135 negative), 31.07 (DEPT 135 negative), 31.61 (DEPT 135 negative), 32.12, 34.29 (DEPT 135 negative), 35.03, 37.19 (DEPT 135 negative), 43.33, 48.61, 51.37, 81.92, 109.02, 118.49, 141.42, 150.71.

MS (EI) m/z: 518 (16 %), 517 (44 %), 516 (100 %), 459 (14 %), 201 (4 %), 73 (20 %).

HRMS (EI) m/z: calcd. 516.3815, found 516.3819.

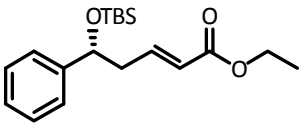
7.2.2 Catalytic asymmetric VMARs



General synthetic procedure **(GSP 2):** A septum-capped vial with a stirring bar was charged with the corresponding aldehyde, disulfonimide (*R*)-**41** (5 mol%), and dry Et_2O [0.2*M*] as solvent. The resulting mixture was cooled to -78°C in an acetone/dry ice-bath, before the nucleophile (1.5 equiv) was added dropwise via syringe. The resulting reaction mixture was stirred at -78°C for 3 d. After this time a saturated $NaHCO_3$-solution was added at -78°C and the reaction mixture was allowed to reach r.t.. Subsequently the reaction was diluted with Et_2O and dried with $MgSO_4$. The solvent was removed in vacuo and the resulting crude material purified by column chromatography on silica gel (hexane/ethyl acetate 8:1), affording the desired products as colorless oily liquids.

• *Compound **60:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-5-phenylpent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing benzaldehyde (21 mg, 1 equiv) and **47** (69 mg, 0.30 mmol) affording the desired product **60** as a colorless liquid (49 mg, 0.15 mmol, 73% yield).



$C_{19}H_{30}O_3Si$
Exact Mass: 334,20
Molecular Weight: 334,53

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.18, -0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.84 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$)), 1.23 (t, 3H, ^3J = 7.2 Hz, -OCH$_2$C<u>H</u>$_3$), 2.44-2.56 (m, 2H, =CH-C<u>H</u>$_2$-), 4.14 (q, 2H, ^3J = 7.2 Hz, -OC<u>H</u>$_2$CH$_3$), 4.71 (dd, 1H, ^3J = 7.7 Hz, 4.7 Hz, -C<u>H</u>-CH$_2$-), 5.77 (d, 1H, ^3J-*trans* = 15.4 Hz, =C<u>H</u>-C=O-), 6.92 (ddd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 7.8 Hz, 7.5 Hz, =C<u>H</u>-CH$_2$-), 7.19-7.29 (m, 5H, -CH$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.91, -4.55, 14.39, 18.33, 25.90, 43.94 (DEPT 135 negative), 60.24 (DEPT 135 negative), 74.24, 123.62, 125.81, 127.42, 128.35, 144.56, 145.73, 166.49.

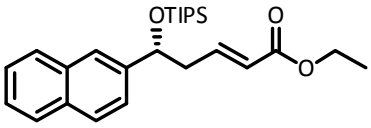
MS (EI) m/z: 277 (58%), 231 (19%), 221 (100%), 171 (28%), 143 (27%), 103 (17%), 73 (64%).

HRMS (ESI-pos) m/z (M+Na): calcd. 357.1860, found 357.1856.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99:1, flow: 1 ml/min, 25°C, absorption at 199 nm, t_{R1} = 4.73 min/ t_{R2} = 5.22 min.

• *Compound **62:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*

The reaction was conducted on a 0.05 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (7.8 mg, 1 equiv) and **48** (18.5 mg, 0.07 mmol) affording the product **62** in 88% yield, as measured by addition of triphenlymethane (12.2 mg, 1 equiv) as an internal standard.



$C_{26}H_{38}O_3Si$
Exact Mass: 426,26
Molecular Weight: 426,66

^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: 0.94, 0.99 (d, 18H, ^{3}J = 6.8 Hz, -SiCH($C\underline{H}_3$)$_3$), 1.01-1.08 (m, 3H, -Si$C\underline{H}$(CH_3)$_3$), 1.17 (t, 3H, ^{3}J = 7.1 Hz, -OCH$_2C\underline{H}_3$), 2.63-2.73 (m, 2H, -CH-$C\underline{H}_2$-), 4.06 (q, 2H, ^{3}J = 7.1 Hz, -O$C\underline{H}_2$CH$_3$), 5.06 (t, 1H, ^{3}J = 6.0 Hz, -$C\underline{H}$-CH$_2$-), 5.70 (d, 1H, ^{3}J-*trans* = 15.4 Hz, =$C\underline{H}$-C=O), 6.86 (ddd, 1H, ^{3}J-*trans* = 15.8 Hz, ^{3}J = 7.8 Hz, 7.5 Hz, -CH$\underline{2}$-$C\underline{H}$=), 7.42-7.47 (m, 3H, -CH_{Ar}), 7.71 (s, 1H, -CH_{Ar}), 7.78-7.80 (m, 3H, -CH_{Ar}).

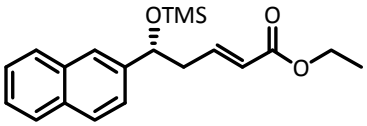
^{13}C-NMR (125 MHz, CD_2Cl_2) δ [ppm]: 12.38, 14.06, 17.79, 17.86, 43.77 (DEPT 135 negative), 60.06 (DEPT 135 negative), 74.37, 123.75, 124.38, 124.65, 125.73, 126.05, 127.67, 127.92, 127.93, 133.00, 133.19, 142.05, 144.65, 166.00.

MS (EI) m/z: 383 (14%), 337 (14%), 313 (100%), 227 (19%), 199 (14%).

HRMS (ESI-pos) m/z (M+Na): calcd. 449.2485, found 449.2482.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 220nm, t_{R1} = 3.34/ t_{R2} = 6.36.

• *Compound **63:** (E)-Ethyl-5-(naphthalen-2-yl)-5-((trimethylsilyl)oxy)pent-2-enoate*



$C_{20}H_{26}O_3Si$
Exact Mass: 342,17
Molecular Weight: 342,50

The reaction was conducted on a 0.10 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (15.6 mg, 1 equiv) and **49** (25.5 mg, 0.13 mmol) affording the product **63** in 86% yield as measured by addition of triphenlymethane (24.4 mg, 1 equiv) as an internal standard.

^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: 0.02 (s, 9H, -Si(CH_3)$_3$), 1.20 (t, 3H, ^3J = 7.1 Hz, -$OCH_2C\underline{H}_3$), 2.56-2.69 (m, 2H, -$C\underline{H}_2$-CH=), 4.09 (q, 2H, ^3J = 7.0 Hz, -$OC\underline{H}_2CH_3$), 4.91 (dd, 1H, ^3J = 7.0 Hz, 5.5 Hz, -$C\underline{H}$-CH_2-), 5.78 (d, 1H, ^3J-*trans* = 15.8 Hz, =$C\underline{H}$-C=O), 6.88 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 7.9 Hz, 7.4 Hz, -CH_2-$C\underline{H}$=), 7.41-7.46 (m, 3H, -$C\underline{H}_{Ar}$), 7.72 (s, 1H, -$C\underline{H}_{Ar}$), 7.78-7.81 (m, 3H, -$C\underline{H}_{Ar}$).

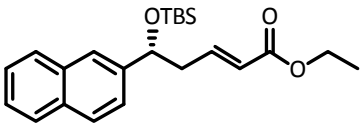
^{13}C-NMR (125 MHz, CD_2Cl_2) δ [ppm]: -0.27, 14.09, 43.18 (DEPT 135 negative), 60.11 (DEPT 135 negative), 73.93, 123.57, 124.14, 124.42, 125.77, 126.09, 127.64, 127.92, 128.00, 132.97, 133.30, 141.85, 145.18, 166.11.

MS (EI) m/z: 229 (100%), 73 (45%).

HRMS (ESI-pos) m/z (M+Na): calcd. 365.1545, found 365.1543.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 5.70 min/ t_{R2} = 6.36 min.

• *Compound **64:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*



$C_{23}H_{32}O_3Si$
Exact Mass: 384,21
Molecular Weight: 384,58

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **47** (69 mg, 0.30 mmol) affording the desired product **64** as a colorless liquid (58 mg, 0.15 mmol, 71% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.12, 0.06 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.90 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 1.27 (t, 3H, ^3J = 7.1 Hz, -$OCH_2C\underline{H}_3$), 2.57-2.69 (m, 2H, -$C\underline{H}_2$-CH=), 4.18 (q, 2H, ^3J = 7.2 Hz, -$OC\underline{H}_2CH_3$), 4.93 (dd, 1H, ^3J = 4.7 Hz, 7.7 Hz, -$C\underline{H}$-CH_2-), 5.84 (d, 1H, ^3J-*trans* = 15.7 Hz, -C=C$\underline{H}$-), 7.00 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.5 Hz, ^3J = 7.5 Hz, -CH_2-$C\underline{H}$=), 7.45-7.50 (m, 3H, -$C\underline{H}_{Ar}$), 7.74 (s, 1H, -$C\underline{H}_{Ar}$), 7.81-7.84 (m, 3H, -$C\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.88, -4.51, 14.38, 18.36, 25.91, 43.87 (DEPT 135 negative), 60.25 (DEPT 135 negative), 74.39, 123.70, 124.13, 124.44, 125.82, 126.15, 127.82, 128.07, 128.20, 133.03, 133.31, 142.05, 145.60, 166.45.

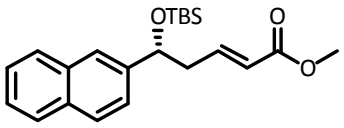
MS (EI) m/z: 327 (10%), 271 (100%), 171 (12%), 143 (14%), 73 (38%).

HRMS (ESI-pos) m/z (M+Na): calcd. 407.2015, found 407.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 227 nm, t_{R1} = 3.84 min/ t_{R2} = 5.34 min.

• *Compound **65:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **65** as a colorless liquid (71 mg, 0.19 mmol, 96% yield).



$C_{22}H_{30}O_3Si$
Exact Mass: 370,20
Molecular Weight: 370,56

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.11, 0.07 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.90 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.59-2.71 (m, 2H, -C<u>H</u>$_2$-CH=), 3.71 (s, 3H, -OC<u>H</u>$_3$), 4.94 (dd, 1H, ^3J = 7.3 Hz, 4.9 Hz, -C<u>H</u>-CH$_2$-), 5.85 (d, 1H, ^3J-*trans* = 15.7 Hz, -C=C<u>H</u>-), 7.00 (ddd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 7.5 Hz, ^3J = 7.5 Hz, -CH$_2$-C<u>H</u>=), 7.45-7.50 (m, 3H, -C<u>H</u>$_{Ar}$), 7.74 (s, 1H, -C<u>H</u>$_{Ar}$), 7.82-7.84 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.87, -4.53, 18.35, 25.90, 43.83 (DEPT 135 negative), 51.52, 74.29, 123.29, 124.12, 124.46, 125.82, 126.16, 127.82, 128.07, 128.21, 133.03, 133.30, 141.94, 145.83, 166.88.

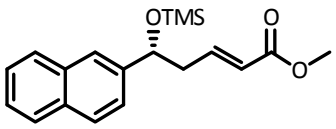
MS (EI) m/z: 313 (4%), 271 (100%), 179 (11%), 157 (25%), 89 (15%), 73 (38%).

HRMS (ESI-pos) m/z (M+Na): calcd. 393.1857, found 393.1856.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 97:3, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 4.74 min/ t_{R2} = 5.98 min.

Optical rotation: $[\alpha]_D^{25}$ = +44.402 (c = 0.207 in $CHCl_3$).

• *Compound **66:** (E)-Methyl-5-(naphthalen-2-yl)-5-((trimethylsilyl)oxy)pent-2-enoate*



$C_{19}H_{24}O_3Si$
Exact Mass: 328,15
Molecular Weight: 328,48

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **51** (52 mg, 0.30 mmol) affording the desired product **66** as a colorless liquid (44 mg, 0.13 mmol, 67% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.06 (s, 9H, -Si(C$\underline{H}_3$)$_3$), 2.60-2.71 (m, 2H, -C$\underline{H}_2$-CH=), 3.71 (s, 3H, -OC$\underline{H}_3$), 4.92 (dd, 1H, ^3J = 7.5 Hz, 5.0 Hz, -C$\underline{H}$-CH$_2$-), 5.85 (d, 1H, ^3J-*trans* = 15.7 Hz, -C=C$\underline{H}$-), 6.98 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.4 Hz, ^3J = 7.7 Hz, -CH$_2$-C$\underline{H}$=), 7.44-7.50 (m, 3H, -C$\underline{H}_{Ar}$), 7.74 (s, 1H, -C$\underline{H}_{Ar}$), 7.81-7.84 (m, 3H, -C$\underline{H}_{Ar}$).

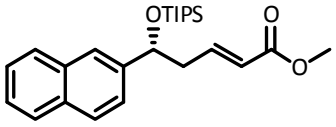
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 0.23, 43.49 (DEPT 135 negative), 51.58, 74.10, 123.24, 124.13, 124.53, 125.90, 126.22, 127.84, 128.11, 128.28, 133.07, 133.35, 141.73, 145.82, 166.95.

MS (EI) m/z: 229 (100%), 178 (4%), 157 (4%), 73 (44%).

HRMS (ESI-pos) m/z (M+Na): calcd. 351.1387, found 351.1387.

HPLC: Daicel Chiralpak AD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 224 nm, t_{R1} = 5.58 min/ t_{R2} = 7.76 min.

• *Compound **67:** (E)-Methyl-5-(naphthalen-2-yl)-5-((triisopropylsilyl)oxy)pent-2-enoate*



$C_{25}H_{36}O_3Si$
Exact Mass: 412,24
Molecular Weight: 412,64

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **52** (77 mg, 0.30 mmol) affording the desired product **67** as a colorless liquid (61 mg, 0.15 mmol, 73% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.98, 1.03 (2d, 18H, ^3J = 7.0 Hz, 6.5 Hz, -Si(CH(C$\underline{H}_3$)$_2$)$_3$), 1.06-1.11 (m, 3H, -Si(C$\underline{H}$(CH$_3$)$_2$)$_3$), 2.67-2.77 (m, 2H, -C$\underline{H}_2$-CH=), 3.68 (s, 3H, -OC$\underline{H}_3$), 5.08 (dd, 1H, ^3J = 6.0 Hz, -C$\underline{H}$-CH$_2$-), 5.77 (d, 1H, ^3J-*trans* = 15.7 Hz, -C=C$\underline{H}$-), 6.93 (ddd, 1H, ^3J-*trans* = 15.6 Hz, ^3J = 7.6 Hz, ^3J = 7.6 Hz, -CH$_2$-C$\underline{H}$=), 7.44-7.49 (m, 3H, -C$\underline{H}_{Ar}$), 7.72 (s, 1H, -C$\underline{H}_{Ar}$), 7.81-7.84 (m, 3H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.41, 18.08, 18.15, 44.04 (DEPT 135 negative), 51.50, 74.40, 123.40, 124.33, 124.70, 125.79, 126.10, 127.83, 128.13, 128.15, 133.06, 133.23, 141.85, 145.20, 166.80.

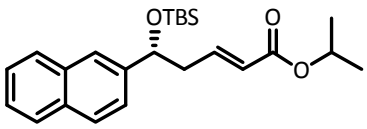
MS (EI) m/z: 369 (12%), 337 (13%), 313 (100%), 215 (42%), 213 (37%), 179 (20%), 145 (29%).

HRMS (ESI-pos) m/z (M+Na): calcd. 435.2323, found 435.2326.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 190 nm, t_{R1} = 3.67 min/ t_{R2} = 5.50 min.

• *Compound **68:** (E)-Isopropyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **53** (73 mg, 0.30 mmol) affording the desired product **68** as a colorless liquid (49 mg, 0.12 mmol, 61% yield).



$C_{24}H_{34}O_3Si$
Exact Mass: 398,23
Molecular Weight: 398,61

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.05 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.90 (s, 9H, -Si(C<u>H</u>$_3$)$_3$), 1.25 (d, 6H, ^3J = 6.3 Hz, -OCH(C<u>H</u>$_3$)$_2$), 2.54-2.67 (m, 2H, -C<u>H</u>$_2$-CH=), 4.91 (dd, 1H, ^3J = 8.0 Hz, 4.5 Hz, -C<u>H</u>-CH$_2$-), 5.06 (sept, 1H, ^3J = 6.3 Hz, -OC<u>H</u>(CH$_3$)$_2$), 5.82 (d, 1H, ^3J-*trans* = 15.7 Hz, -C=C<u>H</u>-), 6.99 (ddd, 1H, ^3J-*trans* = 15.6 Hz, ^3J = 7.5 Hz, ^3J = 7.6Hz, -CH$_2$-C<u>H</u>=), 7.44-7.50 (m, 3H, -C<u>H</u>$_{Ar}$), 7.73 (s, 1H, -C<u>H</u>$_{Ar}$), 7.81-7.84 (m, 3H, -C<u>H</u>$_{Ar}$).

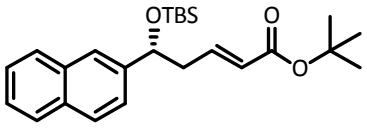
^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: -4.88, -4.48, 18.39, 22.01, 25.93, 43.91, 67.49, 74.48, 124.13, 124.20, 124.43, 125.83, 126.17, 127.83, 128.07, 128.21, 133.04, 133.32, 142.16, 145.38, 165.98.

MS (EI) m/z: 271 (100%), 179 (7%), 143 (26%), 73 (31%).

HRMS (ESI-pos) m/z (M+Na): calcd. 421.2173, found 421.2169.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 190 nm, t_{R1} = 3.77 min/ t_{R2} = 5.69 min.

• *Compound **69:** (E)-tert-Butyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*



$C_{25}H_{36}O_3Si$
Exact Mass: 412,24
Molecular Weight: 412,64

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **54** (77 mg, 0.30 mmol) affording the desired product **69** as a colorless liquid (25 mg, 0.06 mmol, 30% yield, *mixture of rotamers*).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.19, -0.18, 0.00, 0.23 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.85, 0.88 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 1.42, 1.51 (s, 9H, -OC(C$\underline{H}_3$)$_3$), 2.47-2.63 (m, 2H, -C$\underline{H}_2$-CH=), 4.85, 4.88 (dd, 1H, ^3J = 4.4 Hz, 8.1 Hz, -C$\underline{H}$-CH$_2$-), 5.71, 5.76 (d, 1H, ^3J-*trans* = 15.6 Hz, -C=C$\underline{H}$-), 6.85, 6.89 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.5 Hz, ^3J = 7.8 Hz, -CH$_2$-C$\underline{H}$=), 7.40-7.44 (m, 3H, -C$\underline{H}_{Ar}$), 7.68 (s, 1H, -C$\underline{H}_{Ar}$), 7.76-7.79 (m, 3H, -C$\underline{H}_{Ar}$).

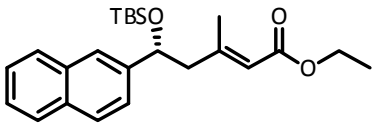
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.87, -4.47, 18.41, 25.95, 28.28, 43.85 (DEPT 135 negative), 74.56, 80.16, 124.16, 124.42, 125.51, 125.81, 126.16, 127.84, 128.08, 128.19, 133.04, 133.33, 142.28, 144.47, 165.86.

MS (EI) m/z: 271 (100%), 143 (16%), 73 (31%).

HRMS (ESI-pos) m/z (M+Na): calcd. 435.2330, found 435.2326.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 226 nm, t_{R1} = 3.80 min/ t_{R2} = 5.26 min.

• *Compound **70:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-3-methyl-5-(naphthalen-2-yl)pent-2-enoate*



$C_{24}H_{34}O_3Si$
Exact Mass: 398,23
Molecular Weight: 398,61

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **55** (73 mg, 0.30 mmol) affording the desired product **70** as a colorless liquid (47 mg, 0.12 mmol, 60% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.19, 0.02 (s, 6H, -Si(C$\underline{H}_3$)$_2$), 0.88 (s, 9H, -Si(C(C$\underline{H}_3$)$_3$), 1.26 (t, 3H, ^3J = 7.1 Hz, -OCH$_2$C$\underline{H}_3$), 2.22 (d, 3H, ^4J = 1.3 Hz, =C-C$\underline{H}_3$), 2.45 (dd, 1H, ^3J = 12.7 Hz, 4.2 Hz, -C$\underline{H}_2$-CH=), 2.58 (dd, 1H, ^3J = 12.9 Hz, 8.5 Hz, -C$\underline{H}_2$-CH=), 4.09-4.20 (m, 2H, -OC$\underline{H}_2$CH$_3$), 4.97 (dd, 1H, ^3J = 8.5 Hz, 4.2 Hz, -C$\underline{H}$-CH$_2$-), 5.71 (d, 1H,

^4J = 1.3 Hz, -C=C<u>H</u>-), 7.43-7.50 (m, 3H, -C<u>H</u>$_{Ar}$), 7.72 (s, 1H, -C<u>H</u>$_{Ar}$), 7.80-7.83 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.01, -4.54, 14.44, 18.29, 19.73, 25.89, 52.62 (DEPT 135 negative), 59.51 (DEPT 135 negative), 74.07, 118.93, 124.21, 124.41, 125.78, 126.13, 127.82, 128.02, 128.17, 133.02, 133.31, 142.48, 155.99, 166.67.

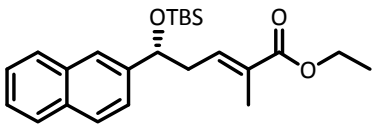
MS (EI) m/z: 341 (4%), 271 (100%), 185 (11%), 157 (9%), 73 (38%).

HRMS (ESI-pos) m/z (M+Na): calcd. 421.2168, found 421.2169.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 225 nm, t_{R1} = 2.99 min/ t_{R2} = 3.78 min.

• *Compound **71:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-2-methyl-5-(naphthalen-2-yl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **56** (73 mg, 0.30 mmol) affording the desired product **71** as a colorless liquid (63 mg, 0.16 mmol, 78% yield).



$C_{24}H_{34}O_3Si$
Exact Mass: 398,23
Molecular Weight: 398,61

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.11, 0.06 (s, 6H, -Si-(C<u>H</u>$_3$)$_2$-), 0.90 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.28 (t, 3H, ^3J = 7.1 Hz, -OCH$_2$C<u>H</u>$_3$), 1.79 (d, 3H, ^4J = 1.3 Hz, =C-C<u>H</u>$_3$), 2.53-2.71 (m, 2H, -CH-C<u>H</u>$_2$-), 4.19 (q, 2H, ^3J = 7.1 Hz, -OC<u>H</u>$_2$CH$_3$), 4.93 (dd, 1H, ^3J = 7.9 Hz, 4.7 Hz, -C<u>H</u>-CH$_2$-), 6.88-6.94 (m, 1H, -CH$_2$-C<u>H</u>=), 7.43-7.51 (m, 3H, -C<u>H</u>$_{Ar}$), 7.75 (s, 1H, -C<u>H</u>$_{Ar}$), 7.81-7.85 (m, 3H, -C<u>H</u>$_{Ar}$).

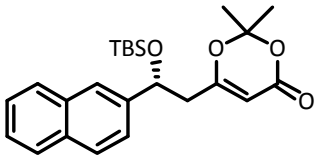
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.88, -4.49, 12.70, 14.42, 18.37, 25.94, 40.49 (DEPT 135 negative), 60.51 (DEPT 135 negative), 74.54, 124.19, 124.40, 125.79, 126.15, 127.85, 128.06, 128.17, 129.42, 133.04, 133.36, 138.65, 142.52, 168.17.

MS (EI) m/z: 295 (4%), 271 (100%), 178 (4%), 73 (34%).

HRMS (ESI-pos) m/z (M+Na): calcd. 421.2168, found 421.2169.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 2.99 min/ t_{R2} = 3.78 min.

• *Compound **72:** 6-(2-((tert-butyldimethylsilyl)oxy)-2-(naphthalen-2-yl)ethyl)-2,2-dimethyl-4H-1,3-dioxin-4-one*



$C_{24}H_{32}O_4Si$
Exact Mass: 412,21
Molecular Weight: 412,59

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **57** (77 mg, 0.30 mmol) affording desired product **72** as a colorless liquid (67 mg, 0.16 mmol, 80% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.19, 0.06 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.89 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 1.62, 1.67 (s, 6H, -C(C$\underline{H}_3$)$_2$), 2.56 (dd, 1H, ^3J = 4.4 Hz, 13.9 Hz, -CH-C$\underline{H}_2$-), 2.70 (dd, 1H, ^3J = 8.4 Hz, 13.9 Hz, -CH-C$\underline{H}_2$-), 5.12 (dd, 1H, ^3J = 4.4 Hz, 8.3 Hz, -C$\underline{H}$-CH$_2$-), 5.26 (s, 1H, -C=C$\underline{H}$-), 7.46-7.51 (m, 3H, -C$\underline{H}_{Ar}$), 7.75 (s, 1H, -C$\underline{H}_{Ar}$), 7.80-7.84 (m, 3H, -C$\underline{H}_{Ar}$).

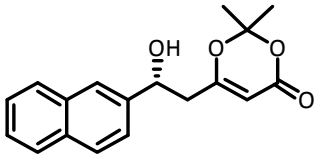
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.99, -4.51, 18.25, 24.55, 25.84, 25.92, 45.55 (DEPT 135 negative), 72.20, 95.65, 106.54, 123.90, 124.70, 126.08, 126.37, 127.87, 127.98, 128.43, 133.15, 133.21, 141.18, 161.18, 168.48.

MS (EI) m/z: 355 (8%), 297 (91%), 271 (100%), 255 (14%), 141 (61%), 99 (55%), 73 (50%).

HRMS (ESI-pos) m/z (M+Na): calcd. 435.1965, found 435.1962.

HPLC: Daicel Chiralpak AD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 224 nm, t_{R1} = 4.85 min/ t_{R2} = 5.28 min.

• *Compound **72a:** (R)-6-(2-Hydroxy-2-(naphthalen-2-yl)ethyl)-2,2-dimethyl-4H-1,3-dioxin-4-one*



To determine the absolute configuration, the optical rotation of the free alcohol was measured. Therefore the product was redissolved in THF and treated with 10% aq. HCl, furnishing the literature known alcohol **72a** cleanly (reaction monitoring by TLC).

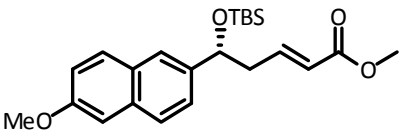
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.66, 1.67 (s, 6H, -C(C$\underline{H}_3$)$_2$), 2.24 (bs, 1H, -O$\underline{H}$), 2.69 (dd, 1H, ^3J = 4.5 Hz, 14.7 Hz, -CH-C$\underline{H}_2$-), 2.77 (dd, 1H, ^3J = 8.8 Hz, 14.7 Hz, -CH-

C<u>H</u>$_2$-), 5.16 (dd, 1H, ^3J = 4.5 Hz, 8.8 Hz, -C<u>H</u>-CH$_2$-), 5.34 (s, 1H, -C=C<u>H</u>-), 7.47-7.52 (m, 3H, -C<u>H</u>$_{Ar}$), 7.82-7.87 (m, 4H, -C<u>H</u>$_{Ar}$).

Optical rotation of deprotected alcohol: $[\alpha]_D^{25}$ = +31.222 (c = 0.442 in $CHCl_3$); literature value: $[\alpha]_D^{25}$ = +46.900 (c = 0.560 in $CHCl_3$) for a sample with e.r. = 96.5:3.5.[14]

• *Compound **73:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(6-methoxynaphthalen-2-yl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale (**GSP 2**), utilizing 6-methoxy-2-naphthaldehyde (37 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **73** as a colorless liquid (64 mg, 0.16 mmol, 80% yield).



$C_{23}H_{32}O_4Si$
Exact Mass: 400,21
Molecular Weight: 400,58

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.05 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.89 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.57-2.70 (m, 2H, =CH-C<u>H</u>$_2$-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 3.92 (s, 3H, -OC<u>H</u>$_3$), 4.90 (dd, 1H, ^3J = 4.9 Hz, 7.4 Hz, -C<u>H</u>-CH$_2$-), 5.84 (d, 1H, ^3J-*trans* = 15.7 Hz, -C<u>H</u>-C=O), 6.99 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.5 Hz, ^3J = 7.5 Hz, -CH$_2$-C<u>H</u>=), 7.14-7.16 (m, 2H, -C<u>H</u>$_{Ar}$), 7.42 (dd, 1H, ^3J = 8.5 Hz, ^4J = 1.6 Hz, -C<u>H</u>$_{Ar}$), 7.65 (s, 1H, -C<u>H</u>$_{Ar}$), 7.71-7.73 (m, 2H, -C<u>H</u>$_{Ar}$).

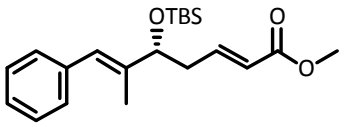
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.96, -4.61, 18.26, 25.81, 43.81 (DEPT 135 negative), 51.42, 55.34, 74.20, 105.71, 118.88, 123.10, 124.27, 124.60, 126.94, 128.62, 129.44, 134.01, 139.63, 145.91, 157.62, 166.82.

MS (EI) m/z: 400 (2%), 301 (100%), 157 (8%), 89 (7%), 73 (31%).

HRMS (ESI-pos) m/z (M+Na): calcd. 423.1959, found 423.1962.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 97:3, flow: 1 ml/min, 25°C, absorption at 232 nm, t_{R1} = 4.90 min/ t_{R2} = 6.59 min.

• *Compound **74:** (2E,6E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-6-methyl-7-phenylhepta-2,6-dienoate*



$C_{21}H_{32}O_3Si$
Exact Mass: 360,21
Molecular Weight: 360,56

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing (*E*)-2-methyl-3-phenylacrylaldehyde (29 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **74** as a colorless liquid (64 mg, 0.18 mmol, 89% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.04, 0.08 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.91 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 1.84 (d, 3H, ^4J = 1.2 Hz, -C-$C\underline{H}_3$), 2.43-2.55 (m, 2H, =CH-$C\underline{H}_2$-), 3.73 (s, 3H, -O$C\underline{H}_3$), 4.24 (dd, 1H, ^3J = 5.1 Hz, 7.1 Hz, -$C\underline{H}$-CH_2-), 5.88 (d, 1H, ^3J-*trans* = 15.8 Hz, -$C\underline{H}$-C=O), 6.46 (s, 1H, -CH_{Ar}-$C\underline{H}$=), 6.98 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 7.5 Hz, ^3J = 7.8 Hz, -CH_2-$C\underline{H}$=), 7.20-7.35 (m, 5H, -$C\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.90, -4.50, 13.42, 18.34, 25.91, 39.84 (DEPT 135 negative), 51.55, 77.66, 122.89, 125.94, 126.56, 128.26, 129.03, 137.68, 139.79, 146.28, 166.95.

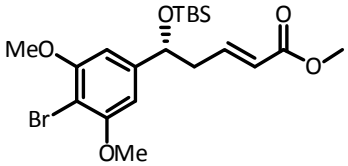
MS (EI) m/z: 261 (100%), 157 (9%), 129 (9%), 89 (10%), 73 (55%).

HRMS (ESI-pos) m/z (M+Na): calcd. 383.2013, found 383.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99:1, flow: 1 ml/min, 25°C, absorption at 200 nm, t_{R1} = 3.81 min/ t_{R2} = 4.15 min.

Optical rotation: $[\alpha]_D^{25}$ = -8.036 (c = 0.224 in $CHCl_3$).

• *Compound **75:** (E)-Methyl-5-(4-bromo-3,5-dimethoxyphenyl)-5-((tert-butyldimethylsilyl)-oxy)pent-2-enoate*



$C_{20}H_{31}BrO_5Si$
Exact Mass: 458,11
Molecular Weight: 459,45

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 4-bromo-3,5-dimethoxybenzaldehyde (49 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **75** as a colorless liquid (62 mg, 0.13 mmol, 67% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.09, 0.04 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.89 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 2.49-2.58 (m, 2H, =CH-$C\underline{H}_2$-), 3.72 (s, 3H, -O$C\underline{H}_3$), 3.88 (s, 6H, -O$C\underline{H}_3$), 4.73

(dd, 1H, ^3J = 5.3 Hz, 6.6 Hz, -C<u>H</u>-CH_2-), 5.81 (d, 1H, ^3J = 15.7 Hz, -C<u>H</u>-C=O), 6.53 (s, 2H, -C<u>H</u>$_{Ar}$), 6.93 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.5 Hz, ^3J = 7.8 Hz, -CH_2-C<u>H</u>=).

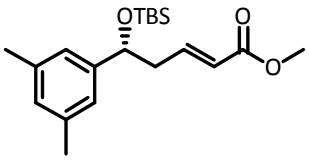
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.00, -4.67, 18.21, 25.72, 43.64 (DEPT 135 negative), 51.48, 56.44, 73.84, 99.20, 101.98, 123.97, 145.20, 145.43, 156.88, 166.60.

MS (EI) m/z: 403, 401 (9%), 361, 359 (78%, 76%), 157 (43%), 89 (46%), 73 (100%).

HRMS (ESI-pos) m/z (M+Na): calcd. 481.1017, found 481.1016.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 97:3, flow: 1 ml/min, 25°C, absorption at 190 nm, t_{R1} = 6.65min/ t_{R2} = 7.53 min.

• *Compound **76:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(3,5-dimethylphenyl)pent-2-enoate*



$C_{20}H_{32}O_3Si$
Exact Mass: 348,21
Molecular Weight: 348,55

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 3,5-dimethylbenzaldehyde (27 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **76** as a colorless liquid (56 mg, 0.16 mmol, 81% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.88 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.30 (s, 6H, -CH_{Ar}-C<u>H</u>$_3$), 2.47-2.59 (m, 2H, =CH-C<u>H</u>$_2$-), 3.72 (s, 3H, -OC<u>H</u>$_3$), 4.68 (dd, 1H, ^3J = 4.8 Hz, 7.7 Hz, -C<u>H</u>-CH_2-), 5.83 (d, 1H, ^3J-*trans* = 15.7 Hz, -C<u>H</u>-C=O), 6.88-6.90 (m, 3H, -C<u>H</u>$_{Ar}$), 6.97 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 7.5 Hz, ^3J = 7.8 Hz, -CH_2-C<u>H</u>=).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.87, -4.51, 18.34, 21.49, 25.91, 44.01 (DEPT 135 negative), 51.51, 74.18, 123.00, 123.59, 128.99, 137.72, 144.50, 146.40, 166.99.

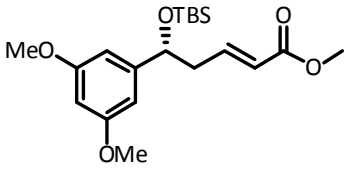
MS (EI) m/z: 291 (37%), 249 (100%), 157 (41 %), 89 (28%), 73 (62%).

HRMS (ESI-pos) m/z (M+Na): calcd. 371.2014, found 371.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.9:0.1, flow: 1 ml/min, 25°C, absorption at 221 nm, t_{R1} = 10.58 min/ t_{R2} = 12.18 min.

Optical rotation: $[\alpha]_D^{25}$ = +46.829 (c = 0.205 in $CHCl_3$).

• *Compound **77:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(3,5-dimethoxyphenyl)pent-2-enoate*



$C_{20}H_{32}O_5Si$
Exact Mass: 380,20
Molecular Weight: 380,55

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 3,5-dimethoxybenzaldehyde (33 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **77** as a colorless liquid (52 mg, 0.14 mmol, 68% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.10, 0.02 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.88 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.47-2.58 (m, 2H, =CH-C$\underline{H}_2$-), 3.71 (s, 3H, -OC$\underline{H}_3$), 3.77 (s, 6H, -OC$\underline{H}_3$), 4.69 (dd, 1H, ^3J = 7.2 Hz, 4.9 Hz, -C$\underline{H}$-CH$_2$-), 5.82 (d, 1H, ^3J-*trans* = 15.8 Hz, -C$\underline{H}$-C=O), 6.33 (t, 1H, ^4J = 2.2 Hz, -C$\underline{H}_{Ar}$), 6.46 (d, 2H, ^4J = 2.2 Hz, -C$\underline{H}_{Ar}$), 6.95 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.8 Hz, 7.5 Hz, -CH$_2$-C$\underline{H}$=).

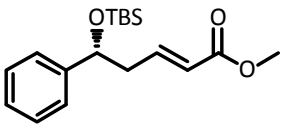
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.92, -4.56, 18.32, 25.89, 43.79 (DEPT 135 negative), 51.53, 55.42, 74.07, 99.32, 103.68, 123.19, 145.93, 147.14, 160.75, 166.90.

MS (EI) m/z: 380 (3%), 323 (64%), 291 (21%), 281 (100%), 255 (15%), 189 (19%), 157 (62%), 89 (63%), 73 (99%).

HRMS (ESI-pos) m/z (M+Na): calcd. 403.1914, found 403.1911.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 97:3, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 3.22 min/ t_{R2} = 3.48 min.

• *Compound **78:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-phenylpent-2-enoate*



$C_{18}H_{28}O_3Si$
Exact Mass: 320,18
Molecular Weight: 320,50

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing benzaldehyde (21 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **78** as a colorless liquid (43 mg, 0.14 mmol, 68% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: -0.18, -0.02 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.84 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.45-2.57 (m, 2H, =CH-C$\underline{H}_2$-), 3.67 (s, 3H, -OC$\underline{H}_3$), 4.72 (dd, 1H, ^3J = 7.4 Hz, 4.9 Hz, -C$\underline{H}$-CH$_2$-), 5.77 (d, 1H, ^3J-*trans* = 15.8 Hz, -C$\underline{H}$-C=O), 6.91 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.9 Hz, 7.5 Hz, -CH$_2$-C$\underline{H}$=), 7.19-7.29 (m, 5H, -C$\underline{H}_{Ar}$).

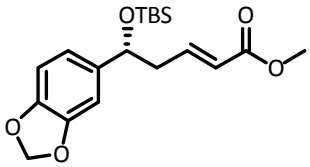
^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: -4.91, -4.58, 18.30, 25.88, 43.90 (DEPT 135 negative), 51.53, 74.13, 123.19, 125.81, 127.42, 128.33, 144.45, 145.96, 166.92.

MS (EI) m/z: 263 (60%), 231 (24%), 221 (100%), 195 (21%), 157 (66%), 129 (11%), 89 (53%), 73 (90%).

HRMS (ESI-pos) m/z (M+Na): calcd. 343.1700, found 343.1700.

HPLC: Daicel Chiralcel OJ-R, MeOH:H_2O = 90:10, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 3.34 min/ t_{R2} = 3.97 min.

• *Compound **79:** (E)-Methyl-5-(benzo[d][1,3]dioxol-5-yl)-5-((tert-butyldimethylsilyl)oxy)pent-2-enoate*



$C_{19}H_{28}O_5Si$
Exact Mass: 364,17
Molecular Weight: 364,51

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing piperonal (30 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **79** as a colorless liquid (53 mg, 0.15 mmol, 73% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.02 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 2.44-2.57 (m, 2H, =CH-$C\underline{H}_2$-), 3.71 (s, 3H, -O$C\underline{H}_3$), 4.66 (dd, 1H, ^3J = 7.3 Hz, 5.0 Hz, -$C\underline{H}$-CH_2-), 5.80 (d, 1H, ^3J-*trans* = 15.8 Hz, -$C\underline{H}$-C=O), 5.94-5.95 (m, 2H, -O-$C\underline{H}_2$-O-), 6.70-6.74 (m, 2H, -$C\underline{H}_{Ar}$), 6.81 (d, 1H, ^4J = 1.3 Hz, -$C\underline{H}_{Ar}$), 6.91 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.8 Hz, 7.5 Hz, -CH_2-$C\underline{H}$=).

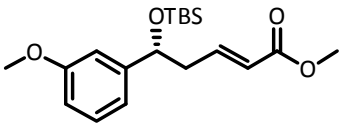
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.92, -4.54, 18.29, 25.89, 44.00 (DEPT 135 negative), 51.55, 73.96, 101.05 (DEPT 135 negative), 106.34, 107.98, 119.03, 123.19, 138.67, 145.83, 146.79, 147.71, 166.91.

MS (EI) m/z: 364 (2%), 265 (100%), 157 (10%), 115 (6%), 89 (11%), 73 (51%).

HRMS (ESI-pos) m/z (M+Na): calcd. 387.1600, found 387.1598.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 205 nm, t_{R1} = 9.85 min/ t_{R2} = 10.79 min.

• *Compound **80:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(3-methoxyphenyl)pent-2-enoate*



$C_{19}H_{30}O_4Si$
Exact Mass: 350,19
Molecular Weight: 350,52

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 3-methoxybenzaldehyde (27 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **80** as a colorless liquid (55 mg, 0.16 mmol, 78% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.11, 0.03 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.88 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.49-2.59 (m, 2H, =CH-C$\underline{H}_2$-), 3.71 (s, 3H, -OC$\underline{H}_3$), 3.80 (s, 3H, -OC$\underline{H}_3$), 4.74 (dd, 1H, ^3J = 7.3 Hz, 4.9 Hz, -C$\underline{H}$-CH$_2$-), 5.81 (d, 1H, ^3J-*trans* = 15.8 Hz, -C$\underline{H}$-C=O), 6.78 (dd, 1H, ^4J = 2.0 Hz, ^3J = 8.2 Hz, -C$\underline{H}_{Ar}$), 6.85-6.88 (m, 2H, -C$\underline{H}_{Ar}$), 6.95 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.8 Hz, 7.5 Hz, -CH$_2$-C$\underline{H}$=), 7.22 (t, 1H, ^3J = 7.9 Hz, -C$\underline{H}_{Ar}$).

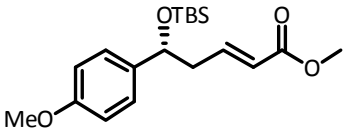
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.90, -4.55, 18.33, 25.90, 43.87 (DEPT 135 negative), 51.54, 55.31, 74.00, 11.21, 112.93, 118.16, 123.21, 129.34, 145.94, 146.23, 159.69, 166.92.

MS (EI) m/z: 293 (41%), 261 (14%), 251 (100%), 225 (18%), 157 (57%), 89 (44%), 73 (75%).

HRMS (ESI-pos) m/z (M+Na): calcd. 373.1806, found 373.1806.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 214 nm, t_{R1} = 10.89 min/ t_{R2} = 16.18 min.

• *Compound **81:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(4-methoxyphenyl)pent-2-enoate*



$C_{19}H_{30}O_4Si$
Exact Mass: 350,19
Molecular Weight: 350,52

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 4-methoxybenzaldehyde (27 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **81** as a colorless liquid (61 mg, 0.17 mmol, 87% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.15, 0.01 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.86 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.46-2.59 (m, 2H, =CH-C$\underline{H}_2$-), 3.71 (s, 3H, -OC$\underline{H}_3$), 3.80 (s, 3H, -OC$\underline{H}_3$), 4.71 (dd, 1H, ^3J = 7.3 Hz, 4.9 Hz, -C$\underline{H}$-CH$_2$-), 5.80 (d, 1H, ^3J-*trans* = 15.4 Hz, -C$\underline{H}$-C=O), 6.84 (d,

2H, ^3J = 8.8 Hz, -C<u>H</u>$_{Ar}$), 6.93 (ddd, 1H, ^3J-*trans* = 15.6 Hz, ^3J = 7.8 Hz, 7.5 Hz, -CH$_2$-C<u>H</u>=), 7.20 (d, 2H, ^3J = 8.6 Hz, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.89, -4.53, 18.32, 25.91, 44.01 (DEPT 135 negative), 51.53, 55.34, 73.77, 113.67, 123.09, 126.98, 136.69, 146.13, 158.90, 166.97.

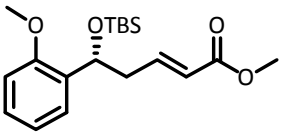
MS (EI) m/z: 251 (100%), 157 (14%), 121 (5%), 89 (11%), 73 (46%).

HRMS (ESI-pos) m/z (M+Na): calcd. 373.1802, found 373.1806.

HPLC: Cellucoat RP, MeCN:H_2O = 60:40, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 8.45 min/ t_{R2} = 9.09 min.

• *Compound **82:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(2-methoxyphenyl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-methoxybenzaldehyde (27 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **82** as a colorless liquid (59 mg, 0.17 mmol, 84% yield).



$C_{19}H_{30}O_4Si$
Exact Mass: 350,19
Molecular Weight: 350,52

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.11, 0.03 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.89 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.45-2.51 (m, 1H, =CH-C<u>H</u>$_2$-), 2.53-2.58 (m, 1H, =CH-C<u>H</u>$_2$-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 3.82 (s, 3H, -OC<u>H</u>$_3$), 5.19 (dd, 1H, ^3J = 7.2 Hz, 4.2 Hz, -C<u>H</u>-CH$_2$-), 5.79 (d, 1H, ^3J-*trans* = 15.8 Hz, -C<u>H</u>-C=O), 6.82 (d, 1H, ^3J = 8.2 Hz, -C<u>H</u>$_{Ar}$), 6.94-7.03 (m, 2H, -C<u>H</u>$_{Ar}$), 7.19-7.23 (m, 1H, -CH$_2$-C<u>H</u>=), 7.47 (dd, 1H, ^4J = 1.5 Hz, ^3J = 7.4 Hz, -C<u>H</u>$_{Ar}$).

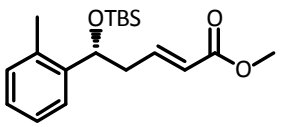
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.93, -4.69, 18.35, 25.95, 42.02 (DEPT 135 negative), 51.46, 55.32, 67.72, 109.94, 120.63, 122.74, 126.81, 128.03, 132.77, 146.96, 155.28, 167.09.

MS (EI) m/z: 293 (30%), 261 (20%), 251 (100%), 225 (11%), 179 (13%), 157 (28%), 89 (26%), 73 (53%).

HRMS (ESI-pos) m/z (M+Na): calcd. 373.1802, found 373.1806.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 3.41 min/ t_{R2} = 3.67 min.

• *Compound **83:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(o-tolyl)pent-2-enoate*



$C_{19}H_{30}O_3Si$
Exact Mass: 334,20
Molecular Weight: 334,53

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 2-methylbenzaldehyde (24 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **83** as a colorless liquid (54 mg, 0.16 mmol, 80% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.16, 0.00 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 2.30 (s, 3H, -CH_{Ar}-$C\underline{H}_3$), 2.42-2.54 (m, 2H, =CH-$C\underline{H}_2$-), 3.73, (s, 3H, -O$C\underline{H}_3$), 4.95 (dd, 1H, ^3J = 4.4 Hz, 7.7 Hz, -$C\underline{H}$-CH_2-), 5.84 (d, 1H, ^3J-*trans* = 15.8 Hz, -$C\underline{H}$-C=O), 7.00 (ddd, 1H, ^3J-*trans* = 15.5 Hz, ^3J = 7.5 Hz, 7.8 Hz, -CH_2-$C\underline{H}$=), 7.09 (d, 1H, ^3J = 7.6 Hz, -$C\underline{H}_{Ar}$), 7.12-7.16 (m, 1H, -$C\underline{H}_{Ar}$), 7.20 (t, 1H, ^3J = 7.3 Hz, -$C\underline{H}_{Ar}$), 7.46 (d, 1H, ^3J = 7.6 Hz, -$C\underline{H}_{Ar}$).

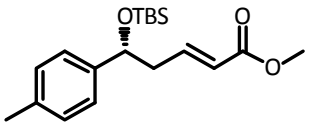
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.97, -4.62, 18.32, 19.15, 25.88, 42.55 (DEPT 135 negative), 51.57, 70.85, 123.10, 126.23, 127.11, 130.26, 133.17, 142.60, 146.38, 166.97.

MS (EI) m/z: 277 (29%), 235 (100%), 157 (62 %), 89 (20%), 73 (43%).

HRMS (ESI-pos) m/z (M+Na): calcd. 357.1858, found 357.1856.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99:1, flow: 1 ml/min, 25°C, absorption at 214 nm, t_{R1} = 3.39 min/ t_{R2} = 3.91 min.

• *Compound **84:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(p-tolyl)pent-2-enoate*



$C_{19}H_{30}O_3Si$
Exact Mass: 334,20
Molecular Weight: 334,53

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 4-methylbenzaldehyde (24 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **84** as a colorless liquid (41 mg, 0.12 mmol, 61% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.14, 0.01 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 2.33 (s, 3H, -CH_{Ar}-$C\underline{H}_3$), 2.46-2.59 (m, 2H, =CH-$C\underline{H}_2$-), 3.71 (s, 3H, -O$C\underline{H}_3$), 4.73 (dd, 1H, ^3J = 4.9 Hz, 7.4 Hz, -$C\underline{H}$-CH_2-), 5.81 (d, 1H, ^3J-*trans* = 15.8 Hz, -$C\underline{H}$-C=O), 6.95 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 7.5 Hz, 7.8 Hz, -CH_2-$C\underline{H}$=), 7.11 (d, 2H, ^3J = 7.9 Hz, -$C\underline{H}_{Ar}$), 7.18 (d, 2H, ^3J = 8.0 Hz, -$C\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.89, -4.53, 18.32, 21.27, 25.91, 43.99 (DEPT 135 negative), 51.53, 74.01, 123.09, 125.74, 129.02, 136.96, 141.52, 146.18, 166.98.

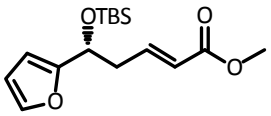
MS (EI) m/z: 277 (18%), 235 (100%), 157 (42 %), 89 (17%), 73 (35%).

HRMS (ESI-pos) m/z (M+Na): calcd. 357.1858, found 357.1856.

HPLC: Daicel Chiralpak IC, *n*-heptane:*i*-PrOH = 99:1, flow: 0.5 ml/min, 25°C, absorption at 215 nm, t_{R1} = 5.25 min/ t_{R2} = 5.70 min.

• *Compound **85:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(furan-2-yl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing furan-2-carbaldehyde (19 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **85** as a colorless liquid (47 mg, 0.15 mmol, 76% yield).



$C_{16}H_{26}O_4Si$
Exact Mass: 310,16
Molecular Weight: 310,46

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.07, 0.05 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.86 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.64-2.75 (m, 2H, =CH-C<u>H</u>$_2$-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 4.79 (dd, 1H, ^3J = 6.0 Hz, 6.8 Hz, -C<u>H</u>-CH$_2$-), 5.86 (d, 1H, ^3J-*trans* = 15.8 Hz, -C<u>H</u>-C=O), 6.18 (d, 1H, ^3J = 3.5 Hz, -C<u>H</u>$_{Ar}$), 6.30 (dd, 1H, ^3J = 1.8 Hz, 3.2 Hz, -C<u>H</u>$_{Ar}$), 6.93 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.5 Hz, 7.3 Hz, -CH$_2$-C<u>H</u>=), 7.34 (dd, 1H, ^3J = 1.7 Hz, ^4J = 0.8 Hz, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.01, -4.82, 18.29, 25.84, 39.94 (DEPT 135 negative), 51.58, 67.59, 106.39, 110.22, 123.38, 141.76, 145.24, 156.10, 166.89.

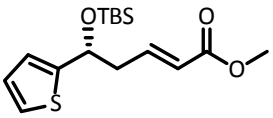
MS (EI) m/z: 253 (37%), 211 (80%), 159 (100 %), 89 (35%), 73 (80%).

HRMS (ESI-pos) m/z (M+Na): calcd. 333.1491, found 333.1493.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 214 nm, t_{R1} = 3.95 min/ t_{R2} = 4.22 min.

• *Compound **86:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(thiophen-2-yl)pent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing thiophene-2-carboxaldehyde (22 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **86** as a colorless liquid (53 mg, 0.16 mmol, 81% yield).



$C_{16}H_{26}O_3SSi$
Exact Mass: 326,14
Molecular Weight: 326,53

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.06, 0.05 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.88 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.59-2.72 (m, 2H, =CH-C<u>H</u>$_2$-), 3.72 (s, 3H, -OC<u>H</u>$_3$), 5.04 (dd, 1H, ^3J = 6.7 Hz, 5.6 Hz, -C<u>H</u>-CH$_2$-), 5.85 (d, 1H, ^3J-*trans* = 15.8 Hz, -C<u>H</u>-C=O), 6.87 (d, 1H, ^3J = 3.5 Hz, -C<u>H</u>$_{Ar}$), 6.91-6.97 (m, 2H, -C<u>H</u>$_{Ar}$ and -CH$_2$-C<u>H</u>=), 7.20 (dd, 1H, ^3J = 5.0 Hz, ^4J = 1.1 Hz, -C<u>H</u>$_{Ar}$).

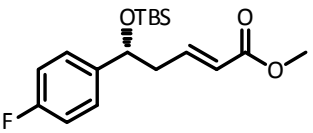
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.88, -4.73, 18.30, 25.83, 44.08 (DEPT 135 negative), 51.59, 70.24, 123.13, 123.57, 124.31, 126.47, 145.15, 148.83, 166.85.

MS (EI) m/z: 269 (14%), 227 (100%), 201 (11%), 157 (40%), 135 (12%), 115 (5%), 89 (20%), 73 (61%).

HRMS (ESI-pos) m/z (M+Na): calcd. 349.1260, found 349.1264.

HPLC: Daicel Chiralpak IC-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 232 nm, t_{R1} = 5.80 min/ t_{R2} = 6.82 min.

• *Compound **87:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(4-fluorophenyl)pent-2-enoate*



$C_{18}H_{27}FO_3Si$
Exact Mass: 338,17
Molecular Weight: 338,49

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 4-fluorobenzaldehyde (25 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **87** as a colorless liquid (50 mg, 0.15 mmol, 73% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.14, 0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.87 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.46-2.58 (m, 2H, =CH-C<u>H</u>$_2$-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 4.74 (dd, 1H, ^3J = 5.1 Hz, 7.1 Hz, -C<u>H</u>-CH$_2$-), 5.79 (d, 1H, ^3J-*trans* = 15.8 Hz, -C<u>H</u>-C=O), 6.91 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.5 Hz, ^3J = 7.8 Hz, -CH$_2$-C<u>H</u>=), 6.97-7.02 (m, 2H, -C<u>H</u>$_{Ar}$), 7.25-7.27 (m, 2H, -C<u>H</u>$_{Ar}$).

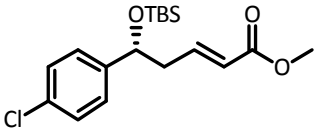
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.90, -4.59, 18.28, 25.86, 43.91 (DEPT 135 negative), 51.58, 73.51, 115.21 (d, $^{C\text{-}F}J$ = 21.2 Hz), 123.40, 127.38 (d, $^{C\text{-}F}J$ = 7.7 Hz), 140.22 (d, $^{C\text{-}F}J$ = 3.2 Hz), 145.50, 162.13 (d, $^{C\text{-}F}J$ = 245.8 Hz), 166.86.

MS (EI) m/z: 282 (12%), 281 (59%), 249 (22%), 240 (19%), 239 (100%), 213 (18%), 159 (30%), 157 (62%), 89 (49%), 73 (87%).

HRMS (ESI-pos) m/z (M+Na): calcd. 361.1605, found 361.1606.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 223 nm, t_{R1} = 4.31 min/ t_{R2} = 5.30 min.

• *Compound **88:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(4-chlorophenyl)pent-2-enoate*



$C_{18}H_{27}ClO_3Si$
Exact Mass: 354,14
Molecular Weight: 354,94

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 4-chloro-benzaldehyde (28 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **88** as a colorless liquid (46 mg, 0.13 mmol, 64% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.02 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.46-2.57 (m, 2H, =CH-C$\underline{H}_2$-), 3.71 (s, 3H, -OC$\underline{H}_3$), 4.74 (dd, 1H, ^3J = 7.0 Hz, 5.2 Hz, -C$\underline{H}$-CH$_2$-), 5.79 (d, 1H, ^3J-*trans* = 16.1 Hz, -C$\underline{H}$-C=O), 6.90 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 7.8 Hz, 7.5 Hz, -CH$_2$-C$\underline{H}$=), 7.22 (d, 2H, ^3J = 8.2 Hz, -C$\underline{H}_{Ar}$), 7.28 (d, 2H, ^3J = 8.4 Hz, -C$\underline{H}_{Ar}$).

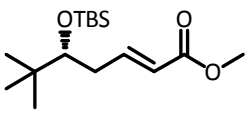
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.90, -4.59, 18.29, 25.86, 43.76 (DEPT 135 negative), 51.59, 73.48, 123.52, 127.20, 128.56, 133.05, 143.97, 145.27, 166.81.

MS (EI) m/z: 297 (47%), 265 (18%), 255 (78%), 229 (15%), 157 (69%), 89 (61%), 73 (100%).

HRMS (ESI-pos) m/z (M+Na): calcd. 377.1310, found 377.1311.

HPLC: Daicel Chiralpak IC-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 2.70 min/ t_{R2} = 3.06 min.

• *Compound **89:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-6,6-dimethylhept-2-enoate*



$C_{16}H_{32}O_3Si$
Exact Mass: 300,21
Molecular Weight: 300,51

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing pivalic aldehyde (17 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **89** as a colorless liquid (37 mg, 0.12 mmol, 62% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.02, 0.03 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 0.90 (s, 9H, -C(C$\underline{H}_3$)$_3$), 2.27-2.33 (m, 1H, =CH-C$\underline{H}_2$-), 2.43-2.49 (m, 1H, =CH-

C$\underline{H}_2$-), 3.42 (dd, 1H, ^3J = 4.4 Hz, 6.5 Hz, -C$\underline{H}$-CH$_2$-), 3.73 (s, 3H, -OC$\underline{H}_3$), 5.81 (d, 1H, ^3J-*trans* = 15.8 Hz, -C$\underline{H}$-C=O), 7.03 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 6.9 Hz, 8.2 Hz, -CH$_2$-C$\underline{H}$=).

^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: -4.03, -3.41, 18.39, 26.17, 26.54, 36.31 (DEPT 135 negative), 36.83, 51.54, 79.35, 121.99, 148.78, 167.08.

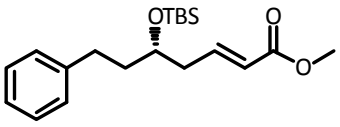
MS (EI) m/z: 285 (6%), 243 (90%), 211 (24%), 201 (100%), 175 (86%), 157 (80%), 115 (9%), 97 (15%), 89 (40%), 73 (58%).

HRMS (ESI-pos) m/z (M+Na): calcd. 323.2013, found 323.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.9:0.1, flow: 1 ml/min, 25°C, absorption at 221 nm, t_{R1} = 5.38 min/ t_{R2} = 5.97 min.

• *Compound **90:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-7-phenylhept-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing hydro-cinnamaldehyde (27 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **90** as a colorless liquid (21 mg, 0.06 mmol, 30% yield).



$C_{20}H_{32}O_3Si$
Exact Mass: 348,21
Molecular Weight: 348,55

^{1}H-NMR (500 MHz, CDCl$_3$) δ [ppm]: 0.03, 0.04 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.89 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 1.71-1.76 (m, 2H, -CH$_2$-C$\underline{H}_2$-), 2.33-2.43 (m, 2H, =CH-C$\underline{H}_2$-), 2.57 (ddd, 1H, ^3J = 14.1 Hz, 8.3 Hz, 8.4 Hz, -C$_{Ar}$-C$\underline{H}_2$-), 2.68 (ddd, 1H, ^3J = 13.7 Hz, 8.4 Hz, 8.4 Hz, -C$_{Ar}$-C$\underline{H}_2$-), 3.71 (s, 3H, -OC$\underline{H}_3$), 3.80-3.85 (m, 1H, -CH$_2$-C$\underline{H}$-CH$_2$-), 5.83 (d, 1H, ^3J-*trans* = 15.7 Hz, -C$\underline{H}$-C=O), 6.95 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.8 Hz, 7.6 Hz, -CH$_2$-C$\underline{H}$=), 7.14-7.17 (m, 3H, -C$\underline{H}_{Ar}$), 7.24-7.27 (m, 2H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: -4.41, -4.31, 18.22, 25.97, 31.88 (DEPT 135 negative), 39.17 (DEPT 135 negative), 40.30 (DEPT 135 negative), 51.57, 70.96, 123.16, 125.95, 128.44, 128.53, 142.26, 146.05, 166.93.

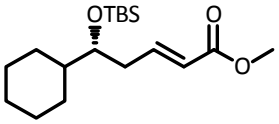
MS (EI) m/z: 291 (44%), 249 (22%), 223 (8%), 193 (6%), 157 (33%), 117 (100%), 89 (33%), 73 (29%).

HRMS (ESI-pos) m/z (M+Na): calcd. 371.2015, found 371.2013.

HPLC: Daicel Chiralpak IC, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 214 nm, t_{R1} = 14.65 min/ t_{R2} = 17.36 min.

• *Compound **91:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-cyclohexylpent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing cyclohexanecarbaldehyde (22 mg, 1 equiv) and **50** (64 mg, 0.30 mmol) affording the desired product **91** as a colorless liquid (25 mg, 0.08 mmol, 38% yield).



$C_{18}H_{34}O_3Si$
Exact Mass: 326,23
Molecular Weight: 326,55

^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 0.03, 0.03 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.88 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 0.91-1.25 (m, 6H, -$C\underline{H}_{2Cy}$), 1.29-1.41 (m, 1H, -$C\underline{H}_{Cy}$), 1.60-1.68 (m, 2H, -$C\underline{H}_{2Cy}$), 1.71-1.76 (m, 2H, -$C\underline{H}_{2Cy}$), 2.32-2.37 (m, 2H, =CH-$C\underline{H}_2$-), 3.50-3.56 (m, 1H, -CH-C$\underline{H}$-CH_2-), 3.73 (s, 3H, -O$C\underline{H}_3$), 5.83 (d, 1H, ^3J-*trans* = 15.7 Hz, -C$\underline{H}$-C=O), 6.98 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 7.9 Hz, 7.5 Hz, -CH_2-C$\underline{H}$=).

^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: -4.41, -4.18, 18.26, 26.03, 26.43 (DEPT 135 negative), 26.49 (DEPT 135 negative), 26.76 (DEPT 135 negative), 28.33 (DEPT 135 negative), 29.00 (DEPT 135 negative), 37.24 (DEPT 135 negative), 43.31, 51.52, 75.52, 122.70, 147.02, 167.06.

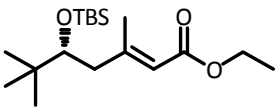
MS (EI) m/z: 269 (68%), 237 (37%), 227 (100%), 201 (68%), 157 (96%), 119 (16%), 95 (79%), 89 (82%), 73 (89%).

HRMS (ESI-pos) m/z (M+Na): calcd. 349.2171, found 349.2169.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 225 nm, t_{R1} = 2.73 min/ t_{R2} = 3.17 min.

• *Compound **92:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-3,6,6-trimethylhept-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing pivalic aldehyde (17 mg, 1 equiv) and **55** (73 mg, 0.30 mmol) affording the desired product **92** as a colorless liquid (43 mg, 0.13 mmol, 65% yield).



$C_{18}H_{36}O_3Si$
Exact Mass: 328,24
Molecular Weight: 328,56

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: -0.07, 0.01 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.88 (s, 18H, -SiC(C$\underline{H}_3$)$_3$ and –C(C$\underline{H}_3$)$_3$), 1.26 (t, 3H, ^{3}J = 7.1, -OCH$_2$C$\underline{H}_3$), 2.10-2.11 (m, 1H, =CH-C$\underline{H}_2$-), 2.17 (d, 3H, ^{4}J = 1.1 Hz, -C-C$\underline{H}_3$), 2.37-2.41 (m, 1H, =CH-C$\underline{H}_2$-), 3.51 (dd, 1H, ^{3}J = 3.2 Hz, 8.0 Hz, -C$\underline{H}$-CH$_2$-), 4.08-4.21 (m, 2H, -OC$\underline{H}_2$CH$_3$), 5.71 (d, 1H, ^{4}J = 0.8 Hz, -C$\underline{H}$-C=O).

^{13}C-NMR (100 MHz, $CDCl_3$) δ [ppm]: -3.83, -3.28, 14.51, 18.50, 19.32, 26.31, 26.52, 36.35, 45.53 (DEPT 135 negative), 59.53 (DEPT 135 negative), 77.99, 118.58, 157.87, 166.72.

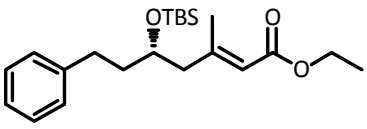
MS (EI) m/z: 271 (57%), 201 (100%), 189 (50%), 185 (44%), 157 (24%), 111 (14%), 73 (36%).

HRMS (ESI-pos) m/z (M+Na): calcd. 351.2326, found 351.2326.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.9:0.1, flow: 1 ml/min, 25°C, absorption at 219 nm, t_{R1} = 3.08 min/ t_{R2} = 3.38 min.

• *Compound **93:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-3-methyl-7-phenylhept-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing 3-phenylpropanal (27 mg, 1 equiv) and **55** (73 mg, 0.30 mmol) affording of the desired product **93** as a colorless liquid (25 mg, 0.07 mmol, 33% yield).



$C_{22}H_{36}O_3Si$
Exact Mass: 376,24
Molecular Weight: 376,60

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.03, 0.06 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.90 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 1.26 (t, 3H, ^{3}J = 7.1 Hz, -OCH$_2$C$\underline{H}_3$), 1.68-1.83 (m, 2H, -CH$_2$-C$\underline{H}_2$-), 2.17 (d, 3H, ^{4}J = 1.3 Hz, -C-C$\underline{H}_3$), 2.27-2.37 (m, 2H, -C$_{Ar}$-C$\underline{H}_2$-), 2.58-2.78 (m, 2H, =C-C$\underline{H}_2$-), 3.88-3.94 (m, 1H, -CH$_2$-C$\underline{H}$-CH$_2$-), 4.10-4.18 (m, 2H, -OC$\underline{H}_2$CH$_3$), 5.68 (d, 1H, ^{4}J = 1.2 Hz, -C$\underline{H}$-C=O), 7.16-7.21 (m, 3H, -C$\underline{H}_{Ar}$), 7.26-7.30 (m, 2H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.35, 14.48, 18.22, 19.54, 26.00, 31.71 (DEPT 135 negative), 39.23 (DEPT 135 negative), 48.95 (DEPT 135 negative), 59.61 (DEPT 135 negative), 70.34, 118.51, 125.95, 128.48, 128.54, 142.36, 156.61, 166.70.

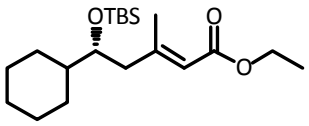
MS (EI) m/z: 319 (66%), 273 (19%), 249 (58%), 193 (39%), 185 (41%), 157 (38%), 117 (100%), 91 (44%), 73 (48%).

HRMS (ESI-pos) m/z (M+Na): calcd. 399.2329, found 399.2326.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.9:0.1, flow: 1 ml/min, 25°C, absorption at 212 nm, t_{R1} = 7.97 min/ t_{R2} = 8.80 min.

• *Compound **94:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-5-cyclohexyl-3-methylpent-2-enoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing cyclohexanecarbaldehyde (22 mg, 1 equiv) and ***55*** (73 mg, 0.30 mmol) affording the desired product **94** as a colorless liquid (32 mg, 0.09 mmol, 47% yield).



$C_{20}H_{38}O_3Si$
Exact Mass: 354,26
Molecular Weight: 354,60

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.02, 0.01 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 1.01-1.38 (m, 6H), 1.26 (t, 3H, ^3J = 7.0 Hz, -$OCH_2C\underline{H}_3$), 1.64-1.75 (m, 5H), 2.15 (d, 3H, ^4J = 1.3 Hz, -C-$C\underline{H}_3$), 2.17-2.27 (m, 2H, -C-$C\underline{H}_2$-), 3.63-3.67 (m, 1H, -$C\underline{H}$-CH_2-), 4.08-4.20 (m, 2H, -$OC\underline{H}_2CH_3$), 5.67 (d, 1H, ^4J = 0.9 Hz, -$C\underline{H}$-C=O).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.34, -4.29, 14.50, 18.27, 19.49, 26.06, 26.64 (DEPT 135 negative), 26.68 (DEPT 135 negative), 26.91 (DEPT 135 negative), 27.79 (DEPT 135 negative), 28.85 (DEPT 135 negative), 43.78, 45.42 (DEPT 135 negative), 59.55 (DEPT 135 negative), 74.71, 118.25, 157.56, 166.82.

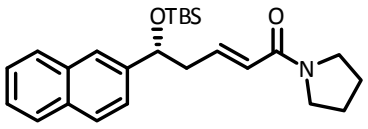
MS (EI) m/z: 297 (39%), 251 (23%), 227 (100%), 215 (44%), 185 (54%), 157 (40%), 95 (37%), 73 (38%).

HRMS (ESI-pos) m/z (M+Na): calcd. 377.2480, found 377.2482.

HPLC: Daicel Chiralpak IC, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 0.5 ml/min, 25°C, absorption at 221 nm, t_{R1} = 9.01 min/ t_{R2} = 9.80 min.

• *Compound **95:** (E)-5-((tert-Butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)-1-(pyrrolidin-1-yl)pent-2-en-1-one*

The reaction was conducted on a 0.51 mmol scale following (**GSP 2**), utilizing 2-naphtaldehyde (80 mg, 1 equiv) and **58** (210 µL, 1.5 equiv) affording desired product **95** as a colorless liquid



$C_{25}H_{35}NO_2Si$
Exact Mass: 409,24
Molecular Weight: 409,64

(118 mg, 0.29 mmol, 56% yield).

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: -0.12, 0.07 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.89 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 1.77-1.89 (m, 4H, -C$\underline{H}_2$-CH$_2$-), 2.58-2.71 (m, 2H, -C$\underline{H}_2$-CH-), 3.31 (dd, 2H, ^{3}J = 7.5 Hz, 6.6 Hz, -C$\underline{H}_2$-CH$_2$-), 3.48 (dd, 2H, ^{3}J = 6.5 Hz, 6.6 Hz, -C$\underline{H}_2$-CH$_2$-), 4.95 (dd, 1H, ^{3}J = 5.8 Hz, 6.3 Hz, -CH$_2$-C$\underline{H}$-), 6.01 (d, 1H, ^{3}J = 15.2 Hz, -C$\underline{H}$-C=O), 6.89 (ddd, 1H, ^{3}J-*trans* = 15.5 Hz, ^{3}J = 7.5 Hz, 7.5 Hz, -CH$_2$-C$\underline{H}$=), 7.42-7.48 (m, 3H, -C$\underline{H}_{Ar}$), 7.72 (s, 1H, -C$\underline{H}_{Ar}$), 7.79-7.82 (m, 3H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (100 MHz, $CDCl_3$) δ [ppm]: -4-73, -4.52, 18.39, 24.41, 25.96, 26.17, 44.13, 45.79, 46.51, 74.46, 124.36, 124.53, 124.62, 125.72, 126.07, 127.78, 128.05, 128.09, 133.00, 141.27, 142.19, 164.68.

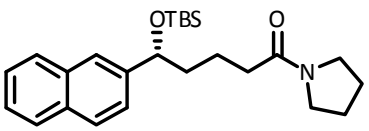
MS (EI) m/z: 394 (2%), 352 (34%), 271 (100%), 196 (23%), 168 (7%), 73 (34%).

HRMS (ESI-pos) m/z (M+Na): calcd. 432.2337, found 432.2329.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 90:10, flow: 1.0 ml/min, 25°C, absorption at 222 nm, t_{R1} = 6.39 min/ t_{R2} = 8.14 min.

• *Compound **96:** 5-((tert-Butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)-1-(pyrrolidin-1-yl)pentan-1-one*

Product **95** (118 mg, 0.29 mmol) was dissolved in MeOH (10 mL) and 10% Pd/C (3.2 mg, 1 mol%) was added. Subsequently the reaction mixture was set under an atmosphere of H_2 and stirred for 30 min at r.t. After this time the reaction mixture was filtered and evaporation gave the desired product **96** quantitatively (119 mg, 0.29 mmol, > 99% yield).



$C_{25}H_{37}NO_2Si$
Exact Mass: 411,26
Molecular Weight: 411,65

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: -0.14, 0.06 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.90 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 1.59-1.70 (m, 1H, -C$\underline{H}_2$-), 1.74-1.91 (m, 7H, -C$\underline{H}_2$-), 2.21-2.24 (m, 2H, -C$\underline{H}_2$-), 3.25-3.34 (m, 2H, -C$\underline{H}_2$-), 3.41 (dd, 2H, ^{3}J = 7.0 Hz, 6.7 Hz, -C$\underline{H}_2$-), 4.84 (dd, 1H, ^{3}J = 6.8 Hz, 6.6 Hz, -CH$_2$-C$\underline{H}$-), 7.40-7.48 (m, 3H, -C$\underline{H}_{Ar}$), 7.71 (s, 1H, -C$\underline{H}_{Ar}$-), 7.77-7.81 (m, 3H, -C$\underline{H}_{Ar}$-).

^{13}C-NMR (100 MHz, $CDCl_3$) δ [ppm]: -5.22, -4.92, 17.91, 20.81 (DEPT 135 negative), 24.00, 25.55 (DEPT 135 negative), 25.71 (DEPT 135 negative), 34.37 (DEPT 135 negative), 40.17 (DEPT 135 negative), 45.20 (DEPT 135 negative), 46.20 (DEPT 135 negative), 74.80, 124.04, 124.07, 125.07, 125.49, 127.29, 127.44, 127.53, 132.42, 132.85, 142.68, 171.15.

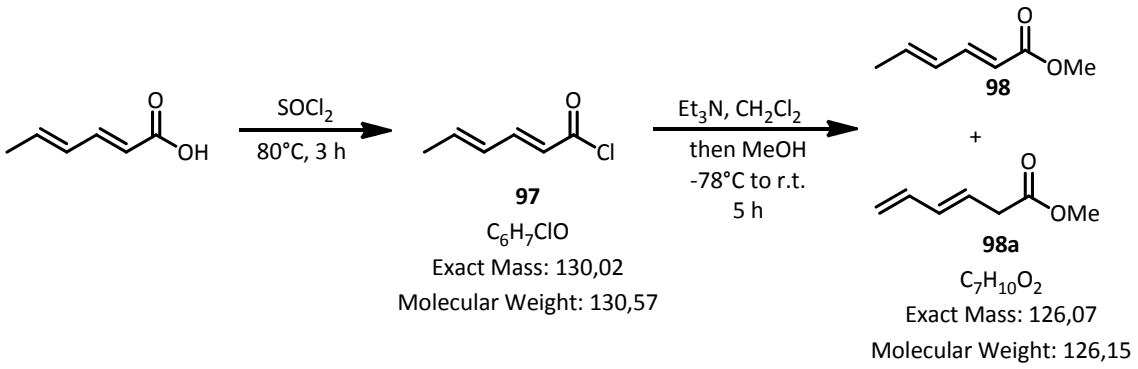
MS (EI) m/z: 411 (8%), 354 (100%), 271 (10%), 167 (21%), 110 (16%), 73 (13%).

HRMS (ESI-pos) m/z (M+Na): calcd. 434.2486, found 434.2486.

7.3 Double vinylogous Mukaiyama aldol reactions (DVMARs)

7.3.1 Synthesis of trienolates for DVMARs

• *Compound **98:** (2E,4E)-Methyl-hexa-2,4-dienoate and **98a**: (E)-Methyl-hexa-3,5-dienoate*



A 100 mL round-bottom flask with reflux condenser, stirring bar and Argon-inlet was charged with sorbic acid (19.80 g, 176.6 mmol, 1.0 equiv). Subsequently thionyl chloride (27.00 ml, 372.0 mmol, 2.1 equiv) was added and the mixture heated to 80°C with an oil bath. After the initially observed evolution of gas ceased, all volatile compounds were removed in vacuo.

Distillation (38°C at 4 mbar) of the resulting crude material afforded sorbic chloride **97** as a colourless liquid as an *E*/*Z*-mixture (14.92 g, 114.2 mmol, 65% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.92 (d, 3H, ^{3}J = 6.7 Hz, -C<u>H</u>$_3$), 5.99 (d, 1H, ^{3}J-*trans* = 14.9 Hz, -C<u>H</u>=CH-), 6.20-6.29 (m, 1H, -C<u>H</u>=CH-), 6.36-6.43 (m, 1H, =C<u>H</u>-C=O), 7.42 (dd, 1H, ^{3}J-*trans* = 14.8 Hz, ^{3}J = 11.0 Hz, -C<u>H</u>=CH-).

E/*Z*-ratio 7.5:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 19.26, 123.19, 129.31, 145.42, 151.46, 166.25.

A 500 mL round-bottomed flask with stirring bar and Argon-inlet was charged with dry CH_2Cl_2 (220 mL) and Et_3N (32.00 mL, 231.0 mmol, 2 equiv). The resulting mixture was cooled to -78°C with a dry ice/acetone bath. Subsequently **97** (14.92 g, 114.2 mmol, 1 equiv) was added slowly and the resulting slurry mixture stirred for 10 min at the same temperature. Dry MeOH (9.50 ml, 234.0 mmol, 2.05 equiv) was added and the reaction mixture was allowed to reach room temperature and stirred for 4 h. After this time the reaction was diluted with CH_2Cl_2, washed with 10% aqueous H_2SO_4, sat. $NaHCO_3$, H_2O and brine, dried over $MgSO_4$ and concentrated in vacuo.

The resulting crude material was distilled (54°-57°C at 10 mbar) to afford (2*E*,4*E*)-methyl hexa-2,4-dienoate **98** as an E/Z-mixture (6.1:1) along with its dehomologized analogue (*E*)-methyl hexa-3,5-dienoate **98a** (ratio 1:3, 10.30 g, 81.65 mmol, 71% yield) as an E/Z-mixture (23.3:1).

•(2*E*,4*E*)-Methyl hexa-2,4-dienoate

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.84 (d, 2H, ^{3}J = 5.7 Hz), 3.73 (s, 3H), 5.74-5.81 (m, 1H), 6.11-6.18 (m, 2H), 7.25 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.1 Hz).

E/*Z*-ratio 6.1:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 18.78, 51.56, 118.66, 129.88, 139.60, 145.32, 167.88.

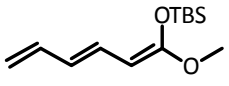
• (*E*)-Methyl hexa-3,5-dienoate

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 3.12 (d, 2H, ^{3}J = 6.9 Hz), 3.68 (s, 3H), 5.06 (d, 1H, ^{3}J-*cis* = 10.1 Hz), 5.16 (d, 1H, ^{3}J-*trans* = 17.0 Hz), 5.75-5.81 (m, 1H), 6.11-6.18 (m, 1H), 6.33 (ddd, 1H, ^{3}J = 17.0 Hz, 10.4 Hz, 10.4 Hz).

E/*Z*-ratio 23.3:1.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 37.88, 52.02, 117.16, 125.62, 134.54, 136.44, 172.04.

• *Compound **99:** tert-Butyl(((1Z,3E)-1-methoxyhexa-1,3,5-trien-1-yl)oxy)dimethylsilane*



$C_{13}H_{24}O_2Si$
Exact Mass: 240,15
Molecular Weight: 240,41

Following the general synthetic procedure (**GSP 1**), diisopropylamine (12.32 mL, 87.0 mmol, 1.1 equiv) in dry THF (110 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 34.80 mL, 1.1 equiv). DMPU (11.46 mL, 95.0 mmol, 1.2 equiv) was added, followed by pure (2*E*,4*E*)-methyl hexa-2,4-dienoate or the above mentioned mixture **98** / **98a** (10.00 g, 79.3 mmol, 1 equiv) and TBSCl (13.11 g, 87.0 mmol, 1.1 equiv) dissolved in dry THF (30 mL).

Distillation (75°C at at $3.1 \cdot 10^{-2}$ mbar) afforded the product **99** as a yellowish liquid (12.22 g, 50.82 mmol, 64% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.18 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.96 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 3.59 (s, 3H, -OC$\underline{H}_3$), 4.48 (d, 2H, ^{3}J = 10.6 Hz, -C$\underline{H}$=C-O), 4.83 (d, 1H, ^{3}J-*cis* = 10.2 Hz, -

CH=C<u>H</u>$_2$), 4.99 (d, 1H, ^3J-*trans* = 16.9 Hz, -CH=C<u>H</u>$_2$), 5.97 (dd, 1H, ^3J = 10.7 Hz, ^3J-*trans* = 15.2 Hz, -CH=C<u>H</u>-), 6.37 (ddd, 1H, ^3J-*cis* = 10.3 Hz, ^3J-*trans* = 16.9 Hz, ^3J = 10.6 Hz, -C<u>H</u>=CH$_2$), 6.42 (dd, 1H, ^3J = 10.7 Hz, ^3J-*trans* = 15.2 Hz, -CH=C<u>H</u>-).

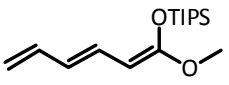
E/*Z*-ratio > 50:1.

^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: -4.09, 18.27, 25.82, 55.07, 79.98, 111.85, 124.19, 129.78, 138.52, 159.39.

MS (EI) m/z: 240 (41%), 94 (66%), 89 (32%), 73 (100%), 66 (37%), 59 (20%).

HRMS (EI) m/z: calcd. 240.1543, found 240.1546.

• *Compound **100:** Triisopropyl(((1Z,3E)-1-methoxyhexa-1,3,5-trien-1-yl)oxy)silane*



$C_{16}H_{30}O_2Si$
Exact Mass: 282,20
Molecular Weight: 282,49

Following the general synthetic procedure (**GSP 1**), diisopropylamine (6.16 mL, 43.5 mmol, 1.1 equiv) in dry THF (60 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 17.40 mL, 1.1 equiv). DMPU (5.73 mL, 47.5 mmol, 1.2 equiv) was added, followed by pure (2*E*,4*E*)-methyl hexa-2,4-dienoate or the above mentioned mixture (5.00 g, 39.7 mmol, 1 equiv) and TIPSCl (9.31 g, 43.5 mmol, 1.1 equiv) dissolved in dry THF (5 mL).

Distillation (103°C at at $2.1 \cdot 10^{-2}$ mbar) afforded the product **100** as a yellowish liquid (7.11 g, 25.17 mmol, 63% yield).

^{1}H-NMR (500 MHz, CDCl$_3$) δ [ppm]: 1.07, 1.08 major, 1.11.1.13 minor (s, 18H, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.16-1.24 (m, 3H, -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 3.59 major, 3.67 minor (s, 3H, -OC<u>H</u>$_3$), 4.45 major, 4.51 minor (d, 1H, ^3J = 10.8 Hz, -C<u>H</u>=C-O), 4.82 (d, 1H, ^3J-*cis* = 10.3 Hz, -CH=C<u>H</u>$_2$), 4.98 (d, 1H, ^3J-*trans* = 16.9 Hz, -CH=C<u>H</u>$_2$), 5.90 minor, 5.96 major (dd, 1H, ^3J = 10.7 Hz, ^3J-*trans* = 15.2 Hz, -CH=C<u>H</u>-), 6.32-6.43 (m, 1H, -C<u>H</u>=CH$_2$), 6.44 minor, 6.50 major (dd, 1H, ^3J = 10.5 Hz, ^3J-*trans* = 15.2 Hz, -CH=C<u>H</u>-).

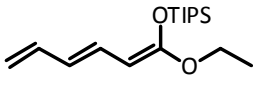
E/*Z*-ratio 5.8:1 (not resolved).

^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: 12.60, 12.77, 17.93, 17.97, 54.48, 54.91, 78.97, 85.91, 111.58 (DEPT 135 negative), 111.90 (DEPT 135 negative), 123.94, 124.11, 129.49, 130.02, 138.44, 138.62, 156.17, 159.28.

MS (EI) m/z: 282 (100%), 157 (22%), 94 (75%), 59 (83%).

HRMS (EI) m/z: calcd. 282.2015, found 282.2015.

• *Compound **101:** (((1Z,3E)-1-Ethoxyhexa-1,3,5-trien-1-yl)oxy)triisopropylsilane*



$C_{17}H_{32}O_2Si$
Exact Mass: 296,22
Molecular Weight: 296,52

Following the general synthetic procedure (**GSP 1**), diisopropylamine (6.16 mL, 43.5 mmol, 1.1 equiv) in dry THF (60 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 17.40 mL, 1.1 equiv). DMPU (5.73 mL, 47.5 mmol, 1.2 equiv) was added, followed by (2E,4E)-ethyl hexa-2,4-dienoate (5.60 g, 39.7 mmol, 1 equiv) and TIPSCl (9.31 g, 43.5 mmol, 1.1 equiv) dissolved in dry THF (5 mL).

Distillation (109°C at at $2.4 \cdot 10^{-2}$ mbar) afforded the product **101** as a yellowish liquid (6.19 g, 20.88 mmol, 53% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.08, 1.10 major, 1.11.1.12 minor (s, 18H, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.18-1.27 (m, 3H, -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 1.31 (t, 3H, ^3J = 7.1 Hz, -OCH$_2$C<u>H</u>$_3$), 3.83 major, 4.01 minor (q, 2H, ^3J = 7.1 Hz, -OC<u>H</u>$_2$CH$_3$), 4.42 major, 4.55 minor (d, 1H, ^3J = 10.8 Hz, -C<u>H</u>=C-O), 4.80-4.83 (m, 1H, -CH=C<u>H</u>$_2$), 4.95-4.99 (m, 1H, -CH=C<u>H</u>$_2$), 5.94 (dd, 1H, ^3J = 10.7 Hz, ^3J-*trans* = 15.2 Hz, -CH=C<u>H</u>-), 6.38 (ddd, 1H, ^3J = 10.7 Hz, 10.1 Hz, ^3J-*trans* = 16.7 Hz, -C<u>H</u>=CH$_2$), 6.51 (dd, 1H, ^3J = 10.1 Hz, ^3J-*trans* = 15.2 Hz, -CH=C<u>H</u>-).

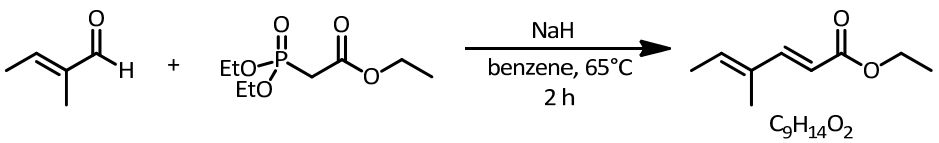
E/*Z*-ratio 9:1 (not resolved).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.59, 12.80, 14.47, 17.95, 62.91, 63.55, 79.38, 87.11, 111.31, 111.83, 123.50, 124.08, 129.69, 130.23, 138.43, 138.64, 155.62, 158.25.

MS (EI) m/z: 296 (100%), 157 (17%), 59 (63%).

HRMS (EI) m/z: calcd. 296.2172, found 296.2172.

• *Compound **102:** (2E,4E)-Ethyl 4-methylhexa-2,4-dienoate*



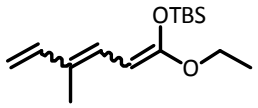
$C_9H_{14}O_2$
Exact Mass: 154,10
Molecular Weight: 154,21

A 100 mL round-bottom flask with stirring bar is charged with NaH / 60%-suspension in mineral oil (1.50 g, 37.5 mmol, 1.4 equiv) and dry benzene (40 mL). Ethyl 2-(diethoxyphosphoryl)acetate (8.85 mL, 44.6 mmol, 1.66 equiv) was added dropwise at r.t. and the resulting mixture was stirred for 1 h. After this time (*E*)-2-methylbut-2-enal (2.58 mL, 26.76 mmol, 1 equiv) was added slowly and the reaction mixture was heated to 65°C for 1 h. After reaching r.t. the reaction was slowly quenched with cold H_2O and subsequently extracted with hexane 3 times. The unified organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The resulting crude material was distilled (70°-74°C at 3 mbar) affording (2*E*,4*E*)-ethyl 4-methylhexa-2,4-dienoate **102** as a colourless liquid (1.72 g, 11.15 mmol, 42% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.29 (t, 3H, ^3J = 7.2 Hz, -$OCH_2C\underline{H}_3$), 1.76 (s, 3H, -C-$C\underline{H}_3$), 1.80 (d, 3H, ^3J = 7.1 Hz, -CH-$C\underline{H}_3$), 4.19 (q, 2H, ^3J = 7.2 Hz, -$OC\underline{H}_2CH_3$), 5.77 (d, 1H, ^3J-trans = 15.8 Hz, =C<u>H</u>-C=O-), 5.97 (q, 1H, ^3J = 7.1 Hz, -C<u>H</u>-CH_3), 7.31 (d, 1H, ^3J-trans = 15.8 Hz, -CH=C<u>H</u>-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 11.89, 14.45, 14.67, 60.25, 115.35, 133.86, 136.45, 149.60, 167.79.

• *Compound **103:** tert-Butyl(((1Z,3E)-1-ethoxy-4-methylhexa-1,3,5-trien-1-yl)oxy)dimethylsilane*



$C_{15}H_{28}O_2Si$
Exact Mass: 268,19
Molecular Weight: 268,47

Following the general synthetic procedure (**GSP 1**), diisopropylamine (2.01 mL, 14.3 mmol, 1.1 equiv) in dry THF (20 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 5.71 mL, 1.1 equiv). DMPU (1.88 mL, 15.6 mmol, 1.2 equiv) was added, followed by (2*E*,4*E*)-ethyl 4-methylhexa-2,4-dienoate **102** (2.00 g, 13.0 mmol, 1 equiv) and TBSCl (2.15 g, 14.3 mmol mmol, 1.1 equiv) dissolved in dry THF (30 mL).

Distillation (85°C at at $3.1 \cdot 10^{-2}$ mbar) afforded the product **103** as a yellowish liquid (1.83 g, 6.82 mmol, 52% yield).

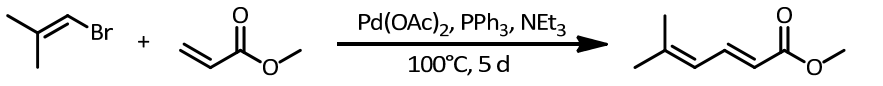
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.20 major, 0.26 minor (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.90 minor, 0.96 major (s, 9H, -Si(C($C\underline{H}_3$)$_3$), 1.27 minor, 1.33 major (t, 3H, ^3J = 7.1 Hz, -$OCH_2C\underline{H}_3$), 1.73 minor, 1.76 major (d, 3H, ^4J = 1.1 Hz, -C-$C\underline{H}_3$), 3.86 major, 3.97 minor

(q, 3H, ^{3}J = 7.1 Hz, -OC<u>H</u>$_2$CH$_3$), 4.55 major, 4.69 minor (d, 1H, ^{3}J = 11.1 Hz, -C<u>H</u>=C=O-), 4.80 (d, 1H, ^{3}J-*cis* = 10.7 Hz, -CH=C<u>H</u>$_2$), 4.95 (d, 1H, ^{3}J-*trans* = 17.4 Hz, -CH=C<u>H</u>$_2$), 6.28 (d, 1H, ^{3}J = 11.0 Hz, =C<u>H</u>-CH=), 6.43 (dd, 1H, ^{3}J-*cis* = 10.7 Hz, ^{3}J-*trans* = 17.3 Hz, -C<u>H</u>=CH$_2$).

Major/Minor 8:1.

^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: -4.01, 11.95, 14.49, 18.28, 25.84, 63.61, 107.63, 126.44, 127.68, 142.39, 158.50.

• *Compound **104:** (E)-Methyl 5-methylhexa-2,4-dienoate*



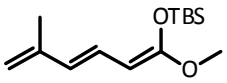
Chemical Formula: $C_8H_{12}O_2$
Exact Mass: 140,08
Molecular Weight: 140,18

A flame-dried, sealable Schlenck tube under Argon is subsequently filled with NEt$_3$ (2.70 mL, 18.8 mmol, 1.25 equiv), methyl acrylate (1.62 mL, 18.8 mmol, 1.25 equiv) and isocrotyl bromide (1.56 mL, 15.0 mmol, 1 equiv), mixed homogeneously and subsequently degassed with an Argon-needle for 5 min. Subsequently Pd(OAc)$_2$ (33.8 mg, 0.15 mmol, 1 mol%) and PPh$_3$ (79.1 mg, 0.30 mmol, 2 mol%) are added and the mixture is degassed with 3 freeze-pum-thaw degassing cycles and set under Argon. The Schlenck tube is sealed and the resulting brownish slurry is heated to 100°C for 5 d. After this time the reaction mixture is allowed to reach room temperature and is diluted with Et$_2$O. The mixture is filtered through a bed of Celite, the solvent evaporated and the resulting crude material subjected to column chromatography (hexane / ethyl acetate 20:1), affording **104** as a colorless liquid (1.06 g, 7.57 mmol, 50% yield).

^{1}H-NMR (500 MHz, CDCl$_3$) δ [ppm]: 1.86, 1.88 (s, 6H, =C-(C<u>H</u>$_3$)$_2$), 3.72 (s, 3H, -OC<u>H</u>$_3$), 5.75 (d, 1H, ^{3}J-*trans* = 15.2 Hz, =C<u>H</u>-C=O-), 5.97 (d, 1H, ^{3}J = 11.7 Hz, -C=C<u>H</u>-), 7.55 (dd, 1H, ^{3}J-*trans* = 15.2 Hz, ^{3}J = 11.7 Hz, -CH=C<u>H</u>-).

^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: 19.05, 26.66, 51.48, 118.17, 123.80, 141.35, 146.59, 168.22.

• *Compound **105:** tert-Butyl(((1Z,3E)-1-ethoxy-4-methylhexa-1,3,5-trien-1-yl)oxy)dimethyl-silane*



Chemical Formula: $C_{14}H_{26}O_2Si$
Exact Mass: 254,17
Molecular Weight: 254,44

Following the general synthetic procedure (**GSP 1**), diisopropylamine (1.12 mL, 7.9 mmol, 1.1 equiv) in dry THF (10 mL) was reacted with *n*-butyllithium in hexane (2.5*M* solution, 3.18 mL, 7.9 mmol, 1.1 equiv). DMPU (1.00 mL, 8.3 mmol, 1.2 equiv) was added, followed by **104** (1.06 g, 7.6 mmol, 1 equiv) in dry THF (5 mL) and TBSCl (1.20 g, 7.9 mmol, 1.1 equiv) dissolved in dry THF (5 mL). Distillation afforded the product **105** as a yellowish liquid (1.04 g, 4.09 mmol, 54% yield).

^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: 0.15 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.93 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.81 (s, 3H, =C-C<u>H</u>$_3$), 3.55 (s, 3H, -OC<u>H</u>$_3$), 4.50 (d, 1H, ^3J = 10.5 Hz, -C<u>H</u>=C-O-), 4.72 (d, 2H, ^3J = 12.7 Hz, -C=C<u>H</u>$_2$), 5.99 (d, 1H, ^3J-*trans* = 15.5 Hz, =C-C<u>H</u>=), 6.38 (dd, 1H, ^3J-*trans* = 15.6 Hz, ^3J = 10.5 Hz, -C<u>H</u>=CH-).

Major/Minor 8.2:1.

^{13}C-NMR (125 MHz, CD_2Cl_2) δ [ppm]: -4.58, 18.03, 18.48, 25.45, 54.98, 80.19, 111.64, 125.70, 125.72, 143.21, 159.24.

7.3.2 Towards the nucleophilicity of silyl enolates, dienolates and trienolates

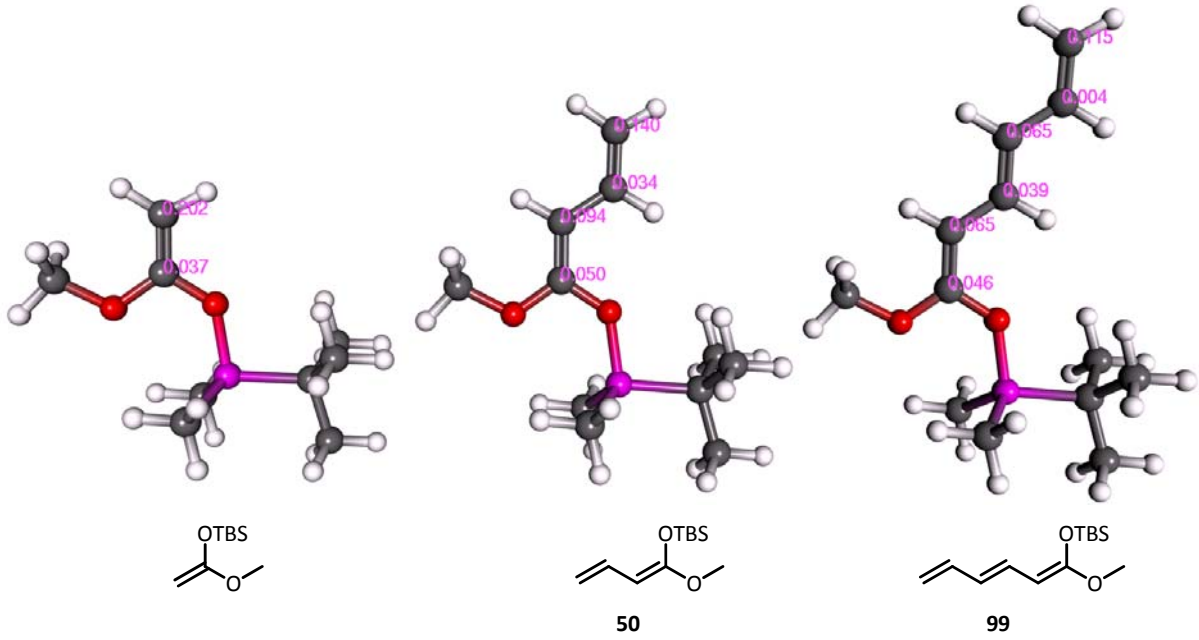


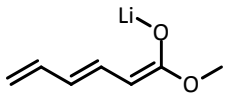
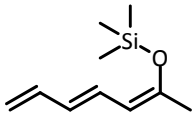
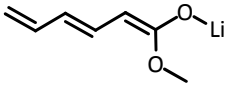
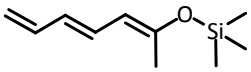
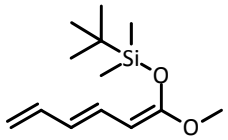
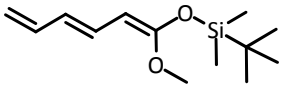
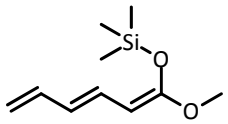
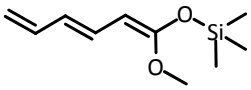
Figure 123.Optimized geometries of silyl enol ethers along with the condensed Fukui functions cff⁻

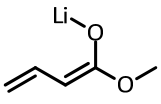
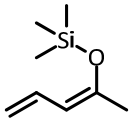
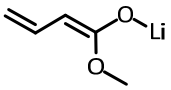
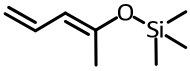
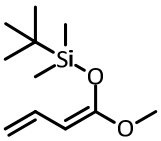
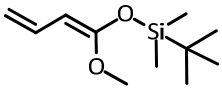
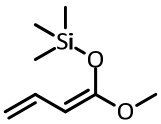
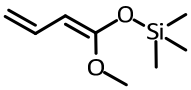
Level of theory:

Molecular structures have been optimized by RI-DFT-gasphase calculations using the BP86 functional and def2-TZVP basis sets as implemented in Turbomole V5.10. Molecular electronic densities and electrostatic potentials were calculated on rectangular grids consisting of 64^3=254016 grid points each, leading to grid spacings of 0.15 - 0.2 atomic length units. Note that the electrostatic potentials were not calculated from atomic charges but from the DFT densities directly. Fukui functions were calculated numerically by finite differences according to the Equation. Here, rho denotes the electron density as function of space r, and N is the number of electrons.

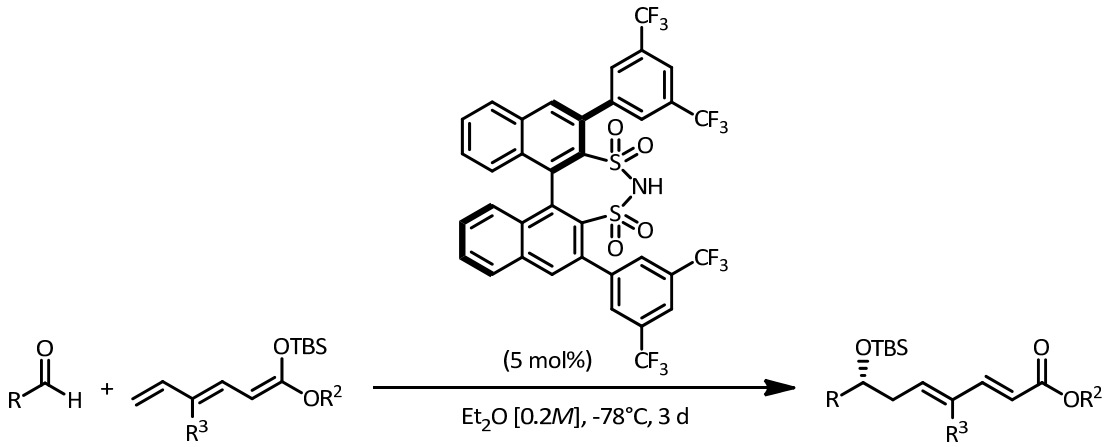
$$f^{+}(\mathbf{r}) \approx \rho(N+1,\mathbf{r}) - \rho(N,\mathbf{r})$$
$$f^{-}(\mathbf{r}) \approx \rho(N,\mathbf{r}) - \rho(N-1,\mathbf{r})$$

Condensed Fukui functions were calculated by finite differences of atomic charges as defined by the Mulliken schema.

molecule	CFF-ε	CFF-δ	CFF-γ	CFF-β	CFF-α	CFF-C1
	0.12	-0.01	0.07	0.03	0.08	0.03
	0.11	0.01	0.06	0.04	0.05	0.06
	0.12	-0.01	0.08	0.00	0.09	0.03
	0.11	0.00	0.07	0.01	0.07	0.05
	0.11	0.00	0.07	0.04	0.07	0.05
	0.11	0.00	0.06	0.04	0.06	0.05
	0.12	0.00	0.06	0.04	0.06	0.05
	0.11	0.00	0.06	0.04	0.07	0.05

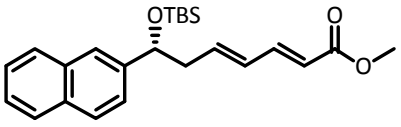
molecule	CFF-γ	CFF-β	CFF-α	CFF-C1
	0.15	0.02	0.12	0.03
	0.21	0.06	0.15	0.10
	0.15	0.02	0.12	0.02
	0.14	0.02	0.09	0.05
	0.14	0.03	0.09	0.05
	0.14	0.03	0.08	0.06
	0.22	0.05	0.18	0.08
	0.14	0.04	0.10	0.05

7.3.3 Catalytic asymmetric DVMARs



General synthetic procedure **(GSP 3):** A septum-capped vial with a stirring bar was charged with the corresponding aldehyde, disulfonimide **41** (5 mol%), and dry Et_2O [0.2*M*] as solvent. The resulting mixture was cooled to -78°C in an acetone/dry ice-bath, before the silyl enolate (1.5 equiv) was added dropwise via syringe. The resulting reaction mixture was stirred at -78°C for 3 d. After this time a saturated $NaHCO_3$-solution was added at -78°C and the reaction mixture was allowed to reach room temperature. Subsequently the reaction was diluted with Et_2O and dried with $MgSO_4$. The solvent was removed in vacuo and the resulting crude material purified by column chromatography on silica gel (hexane/ethyl acetate 8:1), affording the desired products as colorless oily liquids.

• *Compound **106:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(naphthalen-2-yl)hepta-2,4-dienoate*



$C_{24}H_{32}O_3Si$
Exact Mass: 396,21
Molecular Weight: 396,59

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **106** as a colorless liquid (57 mg, 0.14 mmol, 75% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.16, 0.01 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.87 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.51-2.63 (m, 2H, =CH-C$\underline{H}_2$-), 3.70 (s, 3H, -OC$\underline{H}_3$), 4.86 (dd, 1H, ^3J = 4.8 Hz, 7.2 Hz, -C$\underline{H}$-CH$_2$-), 5.75 (d, 1H, ^3J-*trans* = 15.4 Hz, =C$\underline{H}$-C=O), 6.13 (ddd, 1H, ^3J-*trans* = 15.2 Hz, ^3J = 8.1 Hz, 6.6 Hz, -CH$_2$-C$\underline{H}$=), 6.19 (dd, 1H, ^3J-*trans* = 15.1 Hz, ^3J = 10.1 Hz, -

CH=C<u>H</u>-), 7.21 (dd, 1H, ^{3}J-*trans* = 15.5 Hz, ^{3}J = 10.2 Hz, -CH=C<u>H</u>-), 7.41-7.46 (m, 3H, -C<u>H</u>$_{Ar}$), 7.68 (s, 1H, -C<u>H</u>$_{Ar}$), 7.77-7.80 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.78, -4.51, 18.34, 25.92, 44.62 (DEPT 135 negative), 51.58, 74.71, 119.48, 124.21, 124.42, 124.77, 126.13, 127.81, 128.03, 128.09, 130.82, 132.97, 133.28, 140.58, 142.23, 145.03, 167.78.

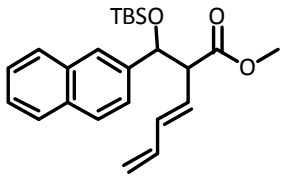
MS (EI) m/z: 339 (2%), 271 (100%), 141 (6%), 89 (6%), 73 (61%).

HRMS (ESI-pos) m/z (M+Na): calcd. 419.2011, found 419.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 219 nm, t_{R1} = 4.02 min/ t_{R2} = 5.78 min.

Optical rotation: $[\alpha]_D^{25}$ = +35.826 (c = 0.642 in $CHCl_3$).

• *Compound **106a:** (E)-Methyl-2-(((tert-butyldimethylsilyl)oxy)(naphthalen-2-yl)methyl)hexa-3,5-dienoate*

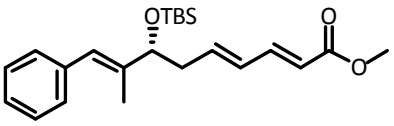


^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.30, 0.03 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.83 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 3.49 (t, 1H, ^{3}J = 9.1 Hz, -CH-C<u>H</u>-), 3.75 (s, 3H, -OC<u>H</u>$_3$), 4.91 (d, 1H, ^{3}J-*cis* = 10.3 Hz, -CH=C<u>H</u>$_2$), 4.95 (d, 1H, ^{3}J-*trans* = 17.0 Hz, -CH=C<u>H</u>$_2$), 5.04 (d, 1H, ^{3}J = 9.5 Hz, -C$_{Ar}$-C<u>H</u>-), 5.44 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 8.9 Hz, -CH-C<u>H</u>=), 5.80 (dd, 1H, ^{3}J-*trans* = 15.3 Hz, ^{3}J = 10.5 Hz, =C<u>H</u>-CH=), 6.09 (ddd, 1H, ^{3}J-*trans* = 17.1 Hz, ^{3}J-*cis* = 10.3 Hz, ^{3}J = 10.3 Hz, -C<u>H</u>=CH$_2$), 7.43-7.49 (m, 3H, -C<u>H</u>$_{Ar}$), 7.66 (s, 1H, -C<u>H</u>$_{Ar}$), 7.79-7.83 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.28, -4.46, 18.11, 25.72, 52.01, 59.23, 117.66 (DEPT 135 negative), 124.97, 125.97, 126.10, 126.29, 127.35, 127.84, 128.06, 128.16, 133.09, 133.27, 134.84, 136.22, 139.42, 173.03.

• *Compound **107:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(naphthalen-2-yl)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing (*E*)-2-methyl-3-phenylacrylaldehyde (29 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **107** as a colorless liquid (50 mg, 0.13 mmol, 65% yield).



$C_{23}H_{34}O_3Si$
Exact Mass: 386,23
Molecular Weight: 386,60

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.03, 0.00 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.84 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.77 (d, 3H, ^4J = 0.9 Hz, =CH-C<u>H</u>$_3$), 2.34-2.45 (m, 2H, =CH-C<u>H</u>$_2$-), 3.68 (s, 3H, -OC<u>H</u>$_3$), 4.13 (dd, 1H, ^3J = 7.1 Hz, 5.5 Hz, -C<u>H</u>-CH$_2$-), 5.75 (d, 1H, ^3J = 15.4 Hz, =C<u>H</u>-C=O), 6.07 (ddd, 1H, ^3J-*trans* = 15.1 Hz, ^3J = 7.3 Hz, ^3J = 7.7 Hz, -CH$_2$-C<u>H</u>=), 6.16 (dd, 1H, ^3J-*trans* = 15.2 Hz, ^3J = 10.8 Hz, -CH=C<u>H</u>-), 6.38 (s, 1H, -C<u>H</u>-), 7.14-7.29 (m, 6H, -C<u>H</u> and -CH=C<u>H</u>-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.81, -4.48, 13.49, 18.34, 25.93, 40.60 (DEPT 135 negative), 51.61, 78.09, 119.36, 125.69, 126.51, 128.25, 129.01, 130.43, 137.75, 140.09, 141.07, 145.16, 167.82.

MS (EI) m/z: 261 (100%), 129 (9%), 73 (64%).

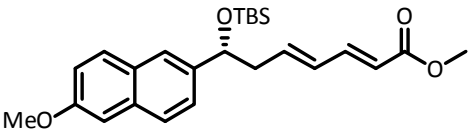
HRMS (ESI-pos) m/z (M+Na): calcd. 409.2168, found 409.2169.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 220 nm, t_{R1} = 3.24 min/ t_{R2} = 3.82 min.

Optical rotation: $[\alpha]_D^{25}$ = -19.000 (c = 0.600 in $CHCl_3$).

• *Compound **108:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(6-methoxy-naphthalen-2-yl)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 6-methoxy-2-naphthaldehyde (37 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **108** as a colorless liquid (46 mg, 0.11 mmol, 54% yield).



$C_{25}H_{34}O_4Si$
Exact Mass: 426,22
Molecular Weight: 426,62

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.19, -0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.84 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.48-2.61 (m, 2H, =CH-C<u>H</u>$_2$-), 3.69 (s, 3H, -OC<u>H</u>$_3$), 3.87 (s, 3H, -OC<u>H</u>$_3$), 4.81 (dd, 1H, ^3J = 7.2 Hz, 5.0 Hz, -C<u>H</u>-CH$_2$-), 5.73 (d, 1H, ^3J = 15.4 Hz, =C<u>H</u>-C=O), 6.04-6.16 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.09-7.11 (m, 2H, -C<u>H</u>$_{Ar}$), 7.19 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 10.2 Hz, -CH=C<u>H</u>-), 7.37 (dd, 1H, ^3J = 8.5 Hz, 1.4 Hz, -C<u>H</u>$_{Ar}$), 7.59 (s, 1H, -C<u>H</u>$_{Ar}$), 7.65-7.68 (m, 2H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.77, -4.48, 18.36, 25.94, 44.71 (DEPT 135 negative), 51.61, 55.45, 74.72, 105.82, 118.95, 119.42, 124.34, 124.80, 126.93, 128.71, 129.51, 130.76, 134.06, 140.02, 140.79, 145.12, 157.69, 167.83.

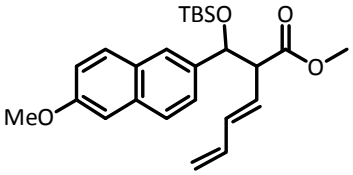
MS (EI) m/z: 301 (100%), 171 (5%), 73 (24%).

HRMS (ESI-pos) m/z (M+Na): calcd. 449.2120, found 449.2119.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 226 nm, t_{R1} = 3.95 min/ t_{R2} = 6.36 min.

Optical rotation: $[\alpha]_D^{25}$ = +27.247 (c = 0.712 in $CHCl_3$).

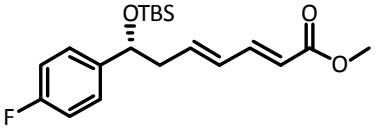
• *Compound **108a:** (E)-Methyl-2-(((tert-butyldimethylsilyl)oxy)(6-methoxynaphthalen-2-yl)methyl)hexa-3,5-dienoate*



^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.31, 0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.82 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 3.48 (t, 1H, ^3J = 9.2 Hz, -CH-C<u>H</u>-), 3.75 (s, 3H, -OC<u>H</u>$_3$), 3.91 (s, 3H, -OC<u>H</u>$_3$), 4.91 (d, 1H, ^3J-*cis* = 10.1 Hz, -CH=C<u>H</u>$_2$), 4.95 (d, 1H, ^3J-*trans* = 17.1 Hz, -CH=C<u>H</u>$_2$), 5.00 (d, 1H, ^3J = 9.5 Hz, -C$_{Ar}$-C<u>H</u>-), 5.43 (dd, 1H, ^3J-*trans* = 15.3 Hz, ^3J = 8.9 Hz, -CH-C<u>H</u>=), 5.80 (dd, 1H, ^3J-*trans* = 15.3 Hz, ^3J = 10.4 Hz, =C<u>H</u>-CH=), 6.08 (ddd, 1H, ^3J-*trans* = 17.0 Hz, ^3J-*cis* = 10.3 Hz, ^3J = 10.3 Hz, -C<u>H</u>=CH$_2$), 7.11-7.15 (m, 2H, -C<u>H</u>$_{Ar}$), 7.39 (dd, 1H, ^3J = 8.5 Hz, 1.4 Hz, -C<u>H</u>$_{Ar}$), 7.58 (s, 1H, -C<u>H</u>$_{Ar}$), 7.68-7.71 (m, 2H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.27, -4.44, 18.12, 25.73, 51.98, 55.44, 59.28, 77.11, 105.82, 117.58 (DEPT 135 negative), 118.92, 125.55, 126.16, 126.89, 127.50, 128.51, 129.64, 134.39, 134.75, 136.28, 137.17, 157.83, 173.09.

• *Compound **109:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(4-fluorophenyl)hepta-2,4-dienoate*



$C_{20}H_{29}FO_3Si$
Exact Mass: 364,19
Molecular Weight: 364,53

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 4-fluorobenzaldehyde (25 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **109** as a

colorless liquid (27 mg, 0.07 mmol, 37% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.15, 0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.86 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.43-2.54 (m, 2H, =CH-C<u>H</u>$_2$-), 3.74 (s, 3H, -OC<u>H</u>$_3$), 4.70 (dd, 1H, ^{3}J = 5.2 Hz, 6.9 Hz, -C<u>H</u>-CH$_2$-), 5.78 (d, 1H, ^{3}J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.05 (ddd, 1H, ^{3}J-*trans* = 15.2 Hz, ^{3}J = 7.2 Hz, ^{3}J = 7.8 Hz, -CH$_2$-C<u>H</u>=), 6.14 (dd, 1H, ^{3}J-trans = 15.3 Hz, ^{3}J = 10.7 Hz, -CH=C<u>H</u>-), 6.97-7.01 (m, 2H, -C<u>H</u>$_{Ar}$), 7.20-7.26 (m, 3H, -C<u>H</u>$_{Ar}$ and -CH=C<u>H</u>-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.81, -4.56, 18.29, 25.89, 44.71 (DEPT 135 negative), 51.66, 73.95, 115.12 (d, $^{C\text{-}F}J$ = 21.6 Hz), 119.61, 127.39 (d, $^{C\text{-}F}J$ = 7.4 Hz), 130.95, 140.25, 140.50 (d, $^{C\text{-}F}J$ = 3.2 Hz), 144.97, 162.07 (d, $^{C\text{-}F}J$ = 244.8 Hz), 167.82.

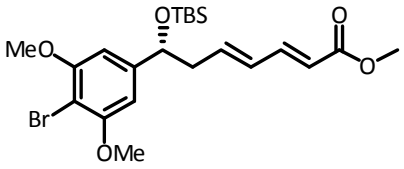
MS (EI) m/z: 307 (11%), 239 (100%), 183 (10%), 153 (8%), 109 (14%), 89 (16%), 73 (89%).

HRMS (ESI-pos) m/z (M+Na): calcd. 387.1762, found 387.1762.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 2.68 min/ t_{R2} = 3.79 min.

• *Compound **110:** (2E,4E)-Methyl-7-(4-bromo-3,5-dimethoxyphenyl)-7-((tert-butyldimethyl-silyl)oxy)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 4-bromo-3,5-dimethoxybenzaldehyde (49 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **110** as a colorless liquid (48 mg, 0.09 mmol, 49% yield).



$C_{22}H_{33}BrO_5Si$
Exact Mass: 484,13
Molecular Weight: 485,48

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.10, 0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.88 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.45-2.54 (m, 2H, =CH-C<u>H</u>$_2$-), 3.73 (s, 3H, -OC<u>H</u>$_3$), 3.87 (s, 6H, -OC<u>H</u>$_3$), 4.69 (dd, 1H, ^{3}J = 6.5 Hz, 5.0 Hz, -C<u>H</u>-CH$_2$-), 5.79 (d, 1H, ^{3}J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.08 (ddd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 7.4 Hz, ^{3}J = 7.4 Hz, -CH$_2$-C<u>H</u>=), 6.17 (dd, 1H, ^{3}J-*trans* = 15.3 Hz, ^{3}J = 10.8 Hz, -CH=C<u>H</u>-), 6.53 (s, 2H, -C<u>H</u>$_{Ar}$), 7.23 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.7 Hz, -CH=C<u>H</u>-).

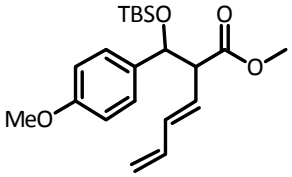
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.81, -4.55, 18.29, 25.84, 44.60 (DEPT 135 negative), 51.64, 56.52, 74.35, 99.17, 102.10, 119.76, 131.07, 140.03, 144.77, 145.91, 156.93, 167.73.

MS (EI) m/z: 361 (100%), 359 (97%), 115 (7%), 89 (7%), 73 (73%).

HRMS (ESI-pos) m/z (M+Na): calcd. 507.1176, found 507.1173.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 6.01 min/ t_{R2} = 7.31 min.

• *Compound **111a:** (E)-Methyl-2-(((tert-butyldimethylsilyl)oxy)(4-methoxyphenyl)methyl)-hexa-3,5-dienoate*



$C_{21}H_{32}O_4Si$
Exact Mass: 376,21
Molecular Weight: 376,56

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.29, -0.02 (s, 6H, -Si($C\underline{H}_3$)$_2$-), 0.81 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 3.34 (t, 1H, ^3J = 9.2 Hz, -CH-C<u>H</u>-), 3.72 (s, 3H, -O$C\underline{H}_3$), 3.79 (s, 3H, -O$C\underline{H}_3$), 4.81 (d, 1H, ^3J = 9.5 Hz, -C_{Ar}-C<u>H</u>-), 4.96 (d, 1H, ^3J-*cis* = 10.2 Hz, -CH=C$\underline{H}_2$), 5.01 (d, 1H, ^3J-*trans* = 17.2 Hz, - CH=C$\underline{H}_2$), 5.39 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 9.0 Hz, -CH-C<u>H</u>=), 5.80 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 10.4 Hz, =C<u>H</u>-CH=), 6.12 (ddd, 1H, ^3J-*trans* = 17.0 Hz, ^3J-*cis* = 10.3 Hz, ^3J = 10.2 Hz, -C<u>H</u>=CH_2), 6.81 (d, 2H, ^3J = 8.7 Hz, -C$\underline{H}_{Ar}$), 7.15 (d, 2H, ^3J = 8.5 Hz, -C$\underline{H}_{Ar}$).

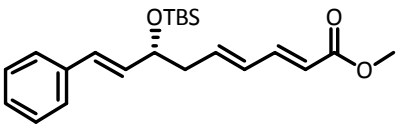
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.32, -4.48, 18.08, 25.71, 51.91, 55.27, 59.44, 76.53, 113.46, 117.48 (DEPT 135 negative), 127.64, 128.28, 134.12, 134.71, 136.38, 159.17, 173.14.

MS (EI) m/z: 319 (11%), 251 (100%), 183 (10%), 121 (5%), 89 (10%), 73 (26%)

HRMS (ESI-pos) m/z (M+Na): calcd. 399.1958, found 399.1962.

• *Compound **112:** (2E,4E,8E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-9-phenylnona-2,4,8-trienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing cinnamaldehyde (26 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **112** as a colorless liquid (34 mg, 0.09 mmol, 46% yield).



$C_{22}H_{32}O_3Si$
Exact Mass: 372,21
Molecular Weight: 372,57

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.05, 0.07 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.91 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.45 (t, 2H, ^3J = 6.6 Hz, =CH-C<u>H</u>$_2$-), 3.74 (s, 3H, -OC<u>H</u>$_3$), 4.34-4.38 (m, 1H, -C<u>H</u>-CH$_2$-), 5.81 (d, 1H, ^3J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.12-6.19 (m, 2H, -CH$_2$-C<u>H</u>= and –C-O-C<u>H</u>=), 6.23 (dd, 1H, ^3J-*trans* = 15.5 Hz, ^3J = 10.8 Hz, -CH=C<u>H</u>-), 6.51 (d, 1H, ^3J-*trans* = 16.1 Hz, -C$_{Ar}$-C<u>H</u>=), 7.22-7.37 (m, 6H, -C<u>H</u>$_{Ar}$ and -CH=C<u>H</u>-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.61, -4.15, 18.37, 25.98, 42.36 (DEPT 135 negative), 51.62, 73.04, 119.49, 126.56, 127.67, 128.71, 129.73, 130.82, 132.46, 136.91, 140.43, 145.10, 167.81.

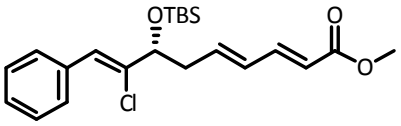
MS (EI) m/z: 315 (2%), 247 (100%), 115 (12%), 91 (8%), 73 (60%).

HRMS (ESI-pos) m/z (M+Na): calcd. 395.2015, found 395.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 3.83 min/ t_{R2} = 5.88 min.

Optical rotation: $[\alpha]_D^{25}$ = +4.110 (c = 0.584 in $CHCl_3$).

• *Compound **113:** (2E,4E,8Z)-Methyl-7-((tert-butyldimethylsilyl)oxy)-8-chloro-9-phenylnona-2,4,8-trienoate*



$C_{22}H_{31}ClO_3Si$
Exact Mass: 406,17
Molecular Weight: 407,02

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing α-chlorocinnamaldehyde (33 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **113** as a colorless liquid (47 mg, 0.12 mmol, 57% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.00, 0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.85 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.48-2.59 (m, 2H, =CH-C<u>H</u>$_2$-), 3.66 (s, 3H, -OC<u>H</u>$_3$), 4.26 (dd, 1H, ^3J = 6.3 Hz, 5.0 Hz, -C<u>H</u>-CH$_2$-), 5.74 (d, 1H, ^3J = 15.4 Hz, =C<u>H</u>-C=O), 6.04 (ddd, 1H, ^3J-*trans* = 15.3 Hz, ^3J = 7.6 Hz, ^3J = 7.4 Hz, -CH$_2$-C<u>H</u>=), 6.17 (dd, 1H, ^3J-*trans* = 15.1 Hz, ^3J = 11.0 Hz, -CH=C<u>H</u>-), 6.70 (s, 1H, -C<u>H</u>=C-Cl), 7.16-7.30 (m, 4H, -C<u>H</u>$_{Ar}$ and -CH=C<u>H</u>-), 7.51-7.53 (m, 2H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.84, -4.61, 18.31, 25.86, 39.91 (DEPT 135 negative), 51.63, 76.21, 119.76, 124.40, 128.06, 128.38, 129.30, 131.29, 134.44, 135.40, 139.40, 144.88, 167.76.

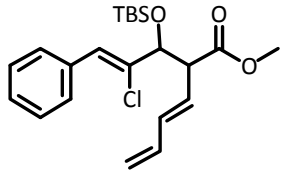
MS (EI) m/z: 349 (3%), 283 (37%), 281 (100%), 115 (8%), 73 (63%).

HRMS (ESI-pos) m/z (M+Na): calcd. 429.1621, found 429.1623.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 2.94 min/ t_{R2} = 3.99 min.

Optical rotation: $[\alpha]_D^{25}$ = +39.566 (c = 0.738 in $CHCl_3$).

• *Compound **113a:** (E)-Methyl-2-((Z)-1-((tert-butyldimethylsilyl)oxy)-2-chloro-3-phenylallyl)-hexa-3,5-dienoate*

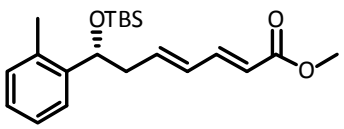


^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.07 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.90 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 3.54-3.60 (m, 1H, -CH-C<u>H</u>-), 3.67 (s, 3H, -OC<u>H</u>$_3$), 4.70 (d, 1H, ^3J = 5.6 Hz, -C$_{Ar}$-C<u>H</u>-), 5.05 (d, 1H, ^3J-*cis* = 10.1 Hz, -CH=C<u>H</u>$_2$), 5.15 (d, 1H, ^3J-*trans* = 17.6 Hz, -CH=C<u>H</u>$_2$), 5.79 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 9.5 Hz, -CH-C<u>H</u>=), 6.10 (dd, 1H, ^3J-*trans* = 15.1 Hz, ^3J = 10.4 Hz, =C<u>H</u>-CH=), 6.34 (ddd, 1H, ^3J-*trans* = 17.0 Hz, ^3J-*cis* = 10.4 Hz, ^3J = 10.3 Hz, -C<u>H</u>=CH$_2$), 6.70 (s, 1H, -C<u>H</u>=C-Cl), 7.28-7.36 (m, 3H, -C<u>H</u>$_{Ar}$), 7.53-7.55 (m, 2H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.11, -4.48, 18.26, 52.19, 54.17, 77.87, 117.49 (DEPT 135 negative), 126.35, 126.95, 128.11, 128.36, 129.25, 133.49, 134.43, 135.77, 136.52, 172.32.

• *Compound **114:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(o-tolyl)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 2-methylbenzaldehyde (24 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **114** as a colorless liquid (30 mg, 0.08 mmol, 42% yield).



$C_{21}H_{32}O_3Si$
Exact Mass: 360,21
Molecular Weight: 360,56

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.17, -0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.86 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.30 (s, 3H, -C$_{Ar}$-C<u>H</u>$_3$), 2.41-2.51 (m, 2H, =CH-C<u>H</u>$_2$-), 3.74 (s, 3H, -OC<u>H</u>$_3$), 4.92 (dd, 1H, ^{3}J = 4.6 Hz, 7.4 Hz, -C<u>H</u>-CH$_2$-), 5.79 (d, 1H, ^{3}J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.10-6.21 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.08 (d, 1H, ^{3}J = 7.3 Hz), -C<u>H</u>$_{Ar}$), 7.12-7.15 (m, 1H, -C<u>H</u>$_{Ar}$), 7.19 (t, 1H, ^{3}J = 7.6 Hz, -C<u>H</u>$_{Ar}$), 7.23-7.28 (m, 1H, -CH=C<u>H</u>-), 7.44 (d, 1H, ^{3}J = 7.3 Hz, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.78, -4.50, 18.43, 19.32, 26.01, 43.40 (DEPT 135 negative), 51.74, 71.30, 119.56, 126.25, 126.37, 127.10, 130.29, 130.79, 133.29, 141.16, 142.95, 145.21, 167.97.

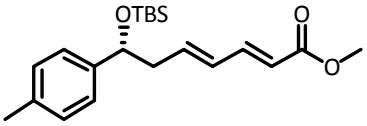
MS (EI) m/z: 303 (5%), 235 (100%), 73 (40%).

HRMS (ESI-pos) m/z (M+Na): calcd. 383.2013, found 383.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99.5:0.5, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 4.77 min/ t_{R2} = 5.13 min.

• *Compound **115:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(p-tolyl)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 4-methylbenzaldehyde (24 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the undesired product **115a** (51 mg, 0.14 mmol, 71% yield) and 8 mg of the desired product **115** (8 mg, 0.02 mmol, 11% yield) as colorless liquids.



$C_{21}H_{32}O_3Si$
Exact Mass: 360,21
Molecular Weight: 360,56

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.15, -0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.86 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.33 (s, 3H, -C$_{Ar}$-C<u>H</u>$_3$), 2.44-2.56 (m, 2H, =CH-C<u>H</u>$_2$-), 3.74 (s, 3H, -OC<u>H</u>$_3$), 4.68 (dd, 1H, ^{3}J = 7.2 Hz, 4.9 Hz, -C<u>H</u>-CH$_2$-), 5.78 (d, 1H, ^{3}J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.05-6.18 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.10 (d, 2H, ^{3}J = 7.9 Hz, -C<u>H</u>$_{Ar}$), 7.16 (d, 2H, ^{3}J = 8.1 Hz, -C<u>H</u>$_{Ar}$), 7.23 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.5 Hz, -CH=C<u>H</u>-).

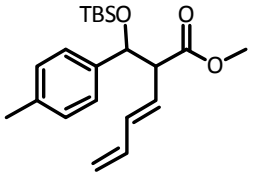
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.79, -4.50, 18.33, 21.28, 25.93, 44.78 (DEPT 135 negative), 51.63, 74.44, 119.34, 125.78, 128.95, 130.66, 136.85, 140.99, 141.81, 145.21, 167.88

MS (EI) m/z: 303 (5%), 235 (100%), 183 (4%), 163 (4%), 105 (4%), 89 (6%), 73 (48%).

HRMS (ESI-pos) m/z (M+Na): calcd. 383.2014, found 383.2013.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 2.50 min/ t_{R2} = 3.20 min.

• *Compound **115a:** (E)-Methyl-2-(((tert-butyldimethylsilyl)oxy)(p-tolyl)methyl)hexa-3,5-dienoate*



$C_{21}H_{32}O_3Si$
Exact Mass: 360,21
Molecular Weight: 360,56

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.29, -0.01 (s, 6H, -Si($C\underline{H}_3$)$_2$), 0.81 (s, 9H, -SiC($C\underline{H}_3$)$_3$), 2.31 (s, 3H, -C_{Ar}-$C\underline{H}_3$), 3.34-3.38 (m, 1H, -CH-C<u>H</u>-), 3.72 (s, 3H, -O$C\underline{H}_3$), 4.82 (d, 1H, ^3J = 9.4 Hz, -C_{Ar}-C<u>H</u>-), 4.96 (d, 1H, ^3J = 10.7 Hz, -CH=C$\underline{H}_2$), 5.01 (d, 1H, ^3J-*trans* = 16.8 Hz, -CH=C$\underline{H}_2$), 5.40 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 8.9 Hz, -CH-C<u>H</u>=), 5.81 (1H, dd, ^3J-*trans* = 15.4 Hz, ^3J = 10.8 Hz, -C<u>H</u>=CH-), 6.12 (ddd, 1H, ^3J-*trans* = 17.0 Hz, ^3J = 10.3 Hz, 10.2 Hz, -C<u>H</u>=CH_2), 7.07 (d, 2H, ^3J = 7.9 Hz, -$C\underline{H}_{Ar}$), 7.12 (d, 2H, ^3J = 8.1 Hz, -$C\underline{H}_{Ar}$).

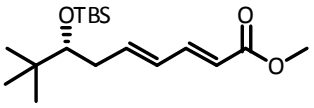
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.32, -4.47, 18.08, 21.33, 25.72, 51.91, 59.34, 76.80, 117.42 (DEPT 135 negative), 127.05, 127.66, 128.80, 134.65, 136.41, 137.39, 138.88, 173.11.

MS (EI) m/z: 303 (28%), 235 (100%), 183 (17%), 163 (5%), 115 (5%), 89 (27%), 73 (52%).

HRMS (ESI-pos) m/z (M+Na): calcd. 383.2012, found 383.2013.

• *Compound **116:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-8,8-dimethylnona-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing pivalic aldehyde (17 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the desired product **116** as a colorless liquid (30 mg, 0.09 mmol, 47% yield).



$C_{18}H_{34}O_3Si$
Exact Mass: 326,23
Molecular Weight: 326,55

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.00, 0.02 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.86 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 0.89 (s, 9H, -C(C$\underline{H}_3$)$_3$), 2.24-2.30 (m, 1H, =CH-C$\underline{H}_2$-), 2.42-2.47 (m, 1H, =CH-C$\underline{H}_2$-), 3.38 (dd, 1H, ^3J = 4.3 Hz, 6.3 Hz, -C$\underline{H}$-CH$_2$-), 3.74 (s, 3H, -OC$\underline{H}_3$), 5.78 (d, 1H, ^3J-*trans* = 15.4 Hz, =C$\underline{H}$-C=O), 6.12-6.23 (m, 2H, -CH$_2$-C$\underline{H}$= and -CH=C$\underline{H}$-), 7.26 (dd, 1H, ^3J = 10.2 Hz, ^3J-*trans* = 15.4 Hz, -CH=C$\underline{H}$-).

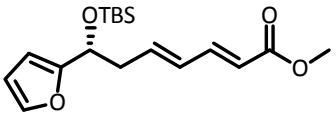
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.02, -3.14, 18.40, 26.19, 26.63, 36.31, 37.54 (DEPT 135 negative), 51.62, 79.70, 118.95, 129.55, 143.58, 145.31, 167.91.

MS (EI) m/z: 269 (34%), 201 (83%), 73 (100%).

HRMS (ESI-pos) m/z (M+Na): calcd. 349.2172, found 349.2169.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 99:1, flow: 1 ml/min, 25°C, absorption at 258 nm, t_{R1} = 2.64 min/ t_{R2} = 3.41 min.

• *Compound **117:** (2E,4E)-Methyl-7-((tert-butyldimethylsilyl)oxy)-7-(furan-2-yl)hepta-2,4-dienoate*



$C_{18}H_{28}O_4Si$
Exact Mass: 336,18
Molecular Weight: 336,50

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing furan-2-carbaldehyde (19 mg, 1 equiv) and **99** (72 mg, 0.30 mmol) affording the undesired product **117a** (37 mg, 0.11 mmol, 55% yield) and trace amounts of the desired product **117** as colorless liquids.

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.07, 0.03 (2s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.86 (s, 9H, -SiC(C$\underline{H}_3$)$_3$), 2.60-2.71 (m, 2H, =CH-C$\underline{H}_2$-), 3.74 (s, 3H, -OC$\underline{H}_3$), 4.74-4.76 (m, 1H, -C$\underline{H}$-CH$_2$-), 5.80 (d, 1H, ^3J-*trans* = 15.4 Hz, =C$\underline{H}$-C=O), 6.05-6.11 (m, 1H, -CH$_2$-C$\underline{H}$=), 6.16 (d, 1H, ^3J = 3.2 Hz, -C$\underline{H}_{Ar}$), 6.18-6.23 (m, 1H, -CH=C$\underline{H}$-), 6.30 (dd, 1H, ^3J = 3.2 Hz, 1.8 Hz, -C$\underline{H}_{Ar}$), 7.23 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 10.9 Hz, -CH=C$\underline{H}$-), 7.34-7.34 (m, 1H, -C$\underline{H}_{Ar}$).

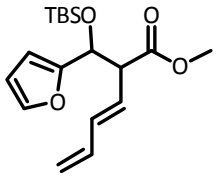
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.92, -4.79, 18.30, 25.87, 40.78 (DEPT 135 negative), 51.64, 68.08, 106.21, 110.18, 119.60, 130.88, 139.97, 141.65, 145.04, 156.47, 167.81.

MS (EI) m/z: 279 (18%), 211 (100%), 155 (5%), 117 (7%), 73 (29%)

HRMS (ESI-pos) m/z (M+Na): calcd. 359.1652, found 359.1649.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 256 nm, t_{R1} = 2.68 min/ t_{R2} = 3.50 min.

• *Compound **117a:** (E)-Methyl-2-(((tert-butyldimethylsilyl)oxy)(furan-2-yl)methyl)hexa-3,5-dienoate*



$C_{18}H_{28}O_4Si$
Exact Mass: 336,18
Molecular Weight: 336,50

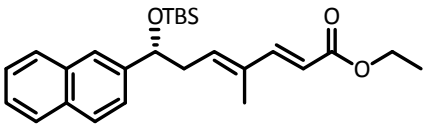
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.20, 0.01 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.80 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 3.64-3.68 (m, 1H, -CH-C<u>H</u>-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 4.93 (d, 1H, ^3J = 9.9 Hz, -C_{Ar}-C<u>H</u>-), 4.99 (d, 1H, ^3J = 10.3 Hz, -CH=C<u>H</u>$_2$), 5.07 (d, 1H, ^3J-*trans* = 17.0 Hz, -CH=C<u>H</u>$_2$), 5.42 (dd, 1H, ^3J-*trans* = 15.2 Hz, ^3J = 9.0 Hz, -CH-C<u>H</u>=), 5.96 (dd, 1H, ^3J-*trans* = 15.5 Hz, ^3J = 10.7 Hz, -C<u>H</u>=CH-), 6.11-6.18 (m, 2H, -C<u>H</u>=CH_2 and -C<u>H</u>$_{Ar}$), 6.27 (dd, 1H, ^3J = 3.2 Hz, 1.8 Hz, -C<u>H</u>$_{Ar}$), 7.34-7.35 (m, 1H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.44, -5.10, 18.06, 25.66, 52.02, 56.31, 69.93, 108.35, 110.12, 117.79 (DEPT 135 negative), 126.83, 134.94, 136.32, 142.14, 153.85, 172.70.

MS (EI) m/z: 321 (3%), 279 (77%), 211 (100%), 183 (18%), 89 (42%), 73 (61%).

HRMS (ESI-pos) m/z (M+Na): calcd. 359.1652, found 359.1649.

• *Compound **118:** (2E,4E)-Ethyl-7-((tert-butyldimethylsilyl)oxy)-4-methyl-7-(naphthalen-2-yl)hepta-2,4-dienoate*



$C_{26}H_{36}O_3Si$
Exact Mass: 424,24
Molecular Weight: 424,65

The reaction was conducted on a 0.10 mmol scale following (**GSP 3**), utilizing 2-naphtaldehyde (16 mg, 1 equiv) and **103** (40 mg, 0.15 mmol) affording the undesired product **118a** (29 mg, 0.07 mmol, 69% yield) and the desired product **118** (8 mg, 0.02 mmol, 18% yield) as colorless liquids.

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.03 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.88 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.29 (t, 3H, ^3J = 7.1 Hz, -OCH_2C<u>H</u>$_3$), 1.68 (s, 3H, =C-C<u>H</u>$_3$), 2.58-2.73 (m, 2H,

=CH-C<u>H</u>$_2$-), 4.20 (q, 2H, ^3J = 7.1 Hz, -OC<u>H</u>$_2$CH$_3$), 4.91 (dd, 1H, ^3J = 5.5 Hz, 6.8 Hz, -C<u>H</u>-CH$_2$-), 5.76 (d, 1H, ^3J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 5.93-5.96 (m, 1H, -CH$_2$-C<u>H</u>=), 7.28 (d, 1H, ^3J-*trans* = 15.4 Hz, =C-C<u>H</u>=), 7.44-7.49 (m, 3H, -C<u>H</u>$_{Ar}$), 7.72 (s, 1H, -C<u>H</u>$_{Ar}$), 7.80-7.83 (m, 3H, -C<u>H</u>$_{Ar}$).

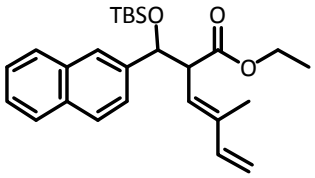
^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: -4.77, -4.52, 12.51, 14.47, 18.36, 25.94, 40.46 (DEPT 135 negative), 53.58, 60.34 (DEPT 135 negative), 74.67, 116.09, 124.28, 124.48, 125.78, 126.14, 127.84, 128.09, 132.99, 133.31, 134.62, 137.84, 142.42, 149.49, 167.77.

MS (EI) m/z: 272 (23%), 271 (100%), 141 (5%), 73 (30%).

HRMS (ESI-pos) m/z (M+Na): calcd. 447.2327, found 447.2326.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 224 nm, t_{R1} = 2.97 min/ t_{R2} = 3.96 min.

• *Compound **118a:** (E)-Ethyl-2-(((tert-butyldimethylsilyl)oxy)(naphthalen-2-yl)methyl)-4-methylhexa-3,5-dienoate*



$C_{26}H_{36}O_3Si$
Exact Mass: 424,24
Molecular Weight: 424,65

^{1}H-NMR (500 MHz, CDCl$_3$) δ [ppm]: -0.30, 0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.84 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.21 (d, 3H, ^4J = 1.2 Hz, =C-C<u>H</u>$_3$), 1.30 (t, 3H, ^3J = 7.2 Hz, -OCH$_2$C<u>H</u>$_3$), 3.76-3.80 (m, 1H, -CH-C<u>H</u>-), 4.16-4.20 (m, 2H, -OC<u>H</u>$_2$CH$_3$), 4.85 (d, 1H, ^3J = 10.8 Hz, -CH=C<u>H</u>$_2$), 4.88 (d, 1H, ^3J-*trans* = 17.5 Hz, -CH=C<u>H</u>$_2$), 5.03 (d, 1H, ^3J = 9.5 Hz, -C$_{Ar}$-C<u>H</u>-), 5.41 (d, 1H, ^3J = 10.2 Hz, =C<u>H</u>-CH), 6.19 (dd, 1H, ^3J-*trans* = 17.5 Hz, ^3J = 10.6 Hz, -C<u>H</u>=CH$_2$), 7.43-7.47 (m, 3H, -C<u>H</u>$_{Ar}$), 7.66 (s, 1H, -C<u>H</u>$_{Ar}$), 7.74-7.81 (m, 3H, -C<u>H</u>$_{Ar}$).

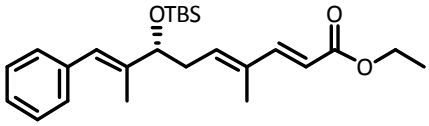
^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: -5.25, -4.43, 11.84, 14.34, 18.16, 25.77, 55.82, 60.92 (DEPT 135 negative), 112.79 (DEPT 135 negative), 125.00, 125.80, 125.87, 126.02, 126.19, 127.79, 127.81, 128.12, 133.07, 133.15, 138.22, 139.63, 140.66, 172.90.

MS (EI) m/z: 367 (13%), 271 (100%), 141 (6%), 73 (40%).

HRMS (ESI-pos) m/z (M+Na): calcd. 447.2327, found 447.2326.

• *Compound **119:** (2E,4E,8E)-Ethyl-7-((tert-butyldimethylsilyl)oxy)-4,8-dimethyl-9-phenylnona-2,4,8-trienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing (*E*)-2-methyl-3-phenylacrylaldehyde (29 mg, 1 equiv) and **103** (80 mg, 0.30 mmol) affording the desired product **119** as a colorless liquid (40 mg, 0.10 mmol, 49% yield).



$C_{25}H_{38}O_3Si$
Exact Mass: 414,26
Molecular Weight: 414,65

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.04, 0.06 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.90 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.30 (t, 3H, ^3J = 7.1 Hz, -OCH$_2$C<u>H</u>$_3$), 1.80 (s, 3H, =C-C<u>H</u>$_3$), 1.85 (d, 3H, ^4J = 1.2 Hz, =C-C<u>H</u>$_3$), 2.43-2.58 (m, 2H, =CH-C<u>H</u>$_2$-), 4.19-4.23 (m, 3H, -OC<u>H</u>$_2$CH$_3$ and -C<u>H</u>-CH$_2$-), 5.81 (d, 1H, ^3J-*trans* = 15.6 Hz, =C<u>H</u>-C=O), 5.94 (t, 1H, ^3J = 7.4 Hz, -CH$_2$-C<u>H</u>=), 6.44 (s, 1H, -C<u>H</u>=C-CH$_3$), 7.20-7.26 (m, 3H, -C<u>H</u>$_{Ar}$ and =C-C<u>H</u>=), 7.31-7.35 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.83, -4.52, 12.60, 13.46, 14.47, 18.32, 25.93, 36.39 (DEPT 135 negative), 60.32 (DEPT 135 negative), 78.08, 115.97, 125.70, 126.50, 128.25, 129.03, 134.21, 137.78, 138.33, 140.19, 149.54, 167.76.

MS (EI) m/z: 357 (7%), 261 (100%), 129 (4%), 73 (30%).

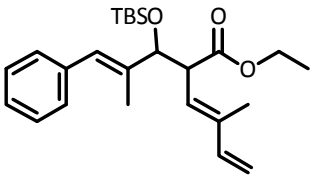
HRMS (ESI-pos) m/z (M+Na): calcd. 437.2483, found 437.2482.

HPLC: Cellucoat RP, Methanol:water= 95:5, flow: 1 ml/min, 25°C, absorption at <u>260</u> nm, t_{R1} = 3.63 min/ t_{R2} = 4.61 min.

Optical rotation: $[\alpha]_D^{25}$ = -19.003 (c = 0.642 in $CHCl_3$).

• *Compound **119a:** (E)-Ethyl-2-((E)-1-((tert-butyldimethylsilyl)oxy)-2-methyl-3-phenylallyl)-4-methylhexa-3,5-dienoate*

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.02, 0.03 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.82 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.23 (t, 3H, ^3J = 7.2 Hz, -OCH$_2$C<u>H</u>$_3$), 1.71 (d, 3H, ^4J = 1.2 Hz, =C-C<u>H</u>$_3$), 1.73 (d, 3H, ^4J = 1.1 Hz, =C-C<u>H</u>$_3$), 3.62 (t, 1H, ^3J = 10.0 Hz, -CH-C<u>H</u>-), 4.06-4.13 (m, 2H, -OC<u>H</u>$_2$CH$_3$), 4.46 (d, 1H, ^3J = 9.7 Hz, -C$_{Ar}$-C<u>H</u>-), 4.94 (d, 1H, ^3J-*cis* = 10.7 Hz, -CH=C<u>H</u>$_2$), 5.08 (d, 1H, ^3J-

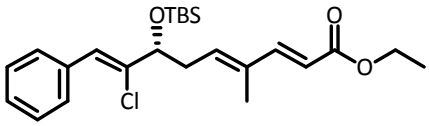


trans = 17.4 Hz, -CH=C<u>H</u>$_2$), 5.30 (d, 1H, ^3J = 10.2 Hz, =C<u>H</u>-CH), 6.27 (dd, 1H, ^3J-*trans* = 17.4 Hz, ^3J-*cis* = 10.8 Hz, -C<u>H</u>=CH$_2$), 6.37 (s, 1H, -C<u>H</u>=C-CH$_3$), 7.12-7.28 (m, 5H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -5.29, -4.45, 12.33, 12.79, 14.31, 18.16, 25.78, 51.85, 60.83 (DEPT 135 negative), 80.86, 112.89 (DEPT 135 negative), 126.47, 126.65, 128.25, 128.47, 128.96, 137.37, 137.53, 137.91, 140.91, 172.81.

• *Compound **120:** (2E,4E,8Z)-Ethyl-7-((tert-butyldimethylsilyl)oxy)-8-chloro-4-methyl-9-phenylnona-2,4,8-trienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing α-chlorocinnamaldehyde (33 mg, 1 equiv) and **103** (72 mg, 0.30 mmol) affording the desired product **120** as a colorless liquid as a mixture with side product (47 mg, 0.11 mmol, 55% uncorrected yield).



$C_{24}H_{35}ClO_3Si$
Exact Mass: 434,20
Molecular Weight: 435,07

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.08, 0.08 (s, 6H, -Si(C<u>H</u>$_3$)$_2$), 0.92 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 1.30 (t, 3H, ^3J = 7.2 Hz, -OCH$_2$C<u>H</u>$_3$), 1.80 (s, 3H, =C-C<u>H</u>$_3$), 2.66-2.68 (m, 2H, =CH-C<u>H</u>$_2$-), 4.21 (q, 2H, ^3J = 7.1 Hz, -OC<u>H</u>$_2$CH$_3$), 4.36 (t, 1H, ^3J = 5.4 Hz, -C<u>H</u>-CH$_2$-), 5.81 (d, 1H, ^3J-*trans* = 15.8 Hz, =C<u>H</u>-C=O), 5.93 (t, 1H, ^3J = 7.5 Hz, -CH$_2$-C<u>H</u>=), 6.78 (s, 1H, -C<u>H</u>=C-Cl), 7.26-7.38 (m, 4H, -C<u>H</u>$_{Ar}$ and =C-C<u>H</u>=), 7.60 (d, 2H, ^3J = 7.4 Hz, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -4.88, -4.65, 12.64, 14.45, 18.29, 25.86, 35.75 (DEPT 135 negative), 60.35 (DEPT 135 negative), 76.25, 116.31, 124.37, 128.04, 128.37, 129.31, 134.48, 135.06, 135.56, 136.72, 149.31, 167.71

MS (EI) m/z: 377 (1%), 283 (37%), 281 (100%), 115 (8%), 73 (52%).

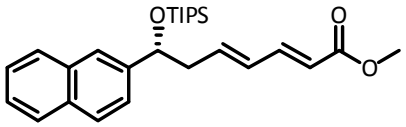
HRMS (ESI-pos) m/z (M+Na): calcd. 457.1938, found 457.1936.

HPLC: Cellucoat RP, Methanol:water= 95:5, flow: 1 ml/min, 25°C, absorption at <u>260</u> nm, t_{R1} = 3.38 min/ t_{R2} = 4.36 min.

Optical rotation: $[\alpha]_D^{25}$ = +35.220 (c = 0.318 in $CHCl_3$).

• *Compound **121:** (2E,4E)-Methyl-7-(naphthalen-2-yl)-7-((triisopropylsilyl)oxy)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 2-naphtaldehyde (31 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the desired product **121** as a colorless liquid (72 mg, 0.16 mmol, 82% yield).



$C_{27}H_{38}O_3Si$
Exact Mass: 438,26
Molecular Weight: 438,67

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.97, 1.03 (d, 18H, ^3J = 6.5 Hz, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.05-1.11 (m, 3H, -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 2.64-2.73 (m, 2H, =CH-C<u>H</u>$_2$-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 5.03-5.06 (m, 1H, -C<u>H</u>-CH$_2$-), 5.73 (d, 1H, ^{3}*J-trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.02-6.14 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.19 (dd, 1H, ^{3}*J-trans* = 15.4 Hz, ^3J = 10.3 Hz, -CH=C<u>H</u>-), 7.44-7.49 (m, 3H, -C<u>H</u>$_{Ar}$), 7.70 (s, 1H, -C<u>H</u>$_{Ar}$), 7.80-7.83 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.42, 18.11, 18.18, 44.73 (DEPT 135 negative), 51.60, 74.78, 119.41, 124.47, 124.67, 125.75, 126.09, 127.84, 128.01, 128.10, 130.90, 133.02, 133.21, 139.99, 142.13, 145.05, 167.81.

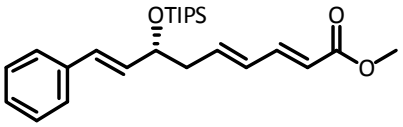
MS (EI) m/z: 395 (5%), 313 (100%), 271 (5%), 205 (5%), 157 (12%), 115 (13%).

HRMS (ESI-pos) m/z (M+Na): calcd. 461.2479, found 461.2482.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 224 nm, t_{R1} = 3.77 min/ t_{R2} = 4.82 min.

• *Compound **122:** (2E,4E,8E)-Methyl-9-phenyl-7-((triisopropylsilyl)oxy)nona-2,4,8-trienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing cinnamaldehyde (26 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the desired product **122** as a colorless liquid (62 mg, 0.15 mmol, 75% yield).



$C_{25}H_{38}O_3Si$
Exact Mass: 414,26
Molecular Weight: 414,65

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 0.99-1.08 (m, 21H, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$ and -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 2.46-2.49 (m, 2H, =CH-C<u>H</u>$_2$-), 3.68 (s, 3H, -OC<u>H</u>$_3$), 4.43-4.47 (m, 1H, -C<u>H</u>-CH$_2$-), 5.75 (d, 1H, ^{3}*J-trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.10-6.21 (m, 3H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>- and -CH=C<u>H</u>-), 6.46 (d, 1H, ^{3}*J-trans* = 15.9 Hz, -C$_{Ar}$-C<u>H</u>=), 7.16-7.32 (m, 6H, -CH=C<u>H</u>- and -C<u>H</u>$_{Ar}$).

^{13}C-NMR (100 MHz, $CDCl_3$) δ [ppm]: 12.51, 18.19, 18.23, 42.68 (DEPT 135 negative), 51.57, 73.23, 119.43, 126.56, 127.64, 128.70, 129.86, 130.83, 132.68, 136.94, 140.11, 145.11, 167.77.

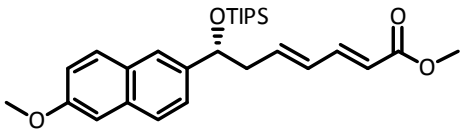
MS (EI) m/z: 371 (3%), 289 (100%), 247 (3%), 157 (12%), 115 (18%).

HRMS (ESI-pos) m/z (M+Na): calcd. 437.2486, found 437.2482.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 3.60 min/ t_{R2} = 4.84 min.

• *Compound **123:** (2E,4E)-Methyl-7-(6-methoxynaphthalen-2-yl)-7-((triisopropylsilyl)oxy)-hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 6-methoxy-naphtaldehyde (37 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the desired product **123** as a colorless liquid (84 mg, 0.18 mmol, 89% yield).



$C_{28}H_{40}O_4Si$
Exact Mass: 468,27
Molecular Weight: 468,70

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.97 (d, 9H, ^{3}J = 6.8 Hz, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.02 (d, 9H, ^{3}J = 6.8 Hz, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.04-1.10 (m, 3H, -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 2.63-2.72 (m, 2H, =CH-C<u>H</u>$_2$-), 3.72 (s, 3H, -OC<u>H</u>$_3$), 3.92 (s, 3H, -OC<u>H</u>$_3$), 4.99-5.01 (m, 1H, -C<u>H</u>-CH$_2$-), 5.73 (d, 1H, ^{3}J-*trans* = 15.1 Hz, =C<u>H</u>-C=O), 6.02-6.14 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.13-7.16 (m, 2H, -C<u>H</u>$_{Ar}$), 7.19 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.2 Hz, -CH=C<u>H</u>-), 7.42-7.44 (m, 1H, -C<u>H</u>$_{Ar}$), 7.62 (s, 1H, -C<u>H</u>$_{Ar}$), 7.69-7.72 (m, 2H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.41, 18.07, 18.14, 44.78 (DEPT 135 negative), 51.51, 55.37, 74.77, 105.84, 118.87, 119.33, 124.54, 124.99, 126.80, 128.61, 129.51, 130.80, 134.08, 139.87, 140.12, 145.04, 157.66, 167.75.

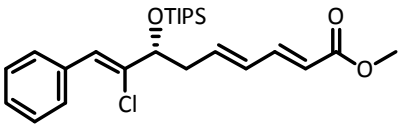
MS (EI) m/z: 425 (1%), 343 (100%), 235 (3%), 171 (8%), 115 (11%).

HRMS (ESI-pos) m/z (M+Na): calcd. 491.2591, found 491.2588.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 3.57 min/ t_{R2} = 4.91 min.

• *Compound **124:** (2E,4E,8Z)-Methyl-8-chloro-9-phenyl-7-((triisopropylsilyl)oxy)nona-2,4,8-trienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing α-chlorocinnamaldehyde (33 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the desired product **125** as a colorless liquid (50 mg, 0.11 mmol, 56% yield).



Chemical Formula: $C_{25}H_{37}ClO_3Si$
Exact Mass: 448,22
Molecular Weight: 449,10

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.99-1.12 (m, 21H, -Si(CH(C$\underline{H}_3$)$_2$)$_3$ and -Si(C$\underline{H}$(CH$_3$)$_2$)$_3$), 2.58-2.67 (m, 2H, =CH-C$\underline{H}_2$-), 3.68 (s, 3H, -OC$\underline{H}_3$), 4.46-4.48 (m, 1H, -C$\underline{H}$-CH$_2$-), 5.75 (d, 1H, ^{3}*J-trans* = 15.4 Hz, =C$\underline{H}$-C=O), 6.05-6.11 (m, 1H, -CH$_2$-C$\underline{H}$=), 6.19 (dd, 1H, ^{3}*J-trans* = 15.3 Hz, ^{3}*J* = 10.9 Hz, -CH=C$\underline{H}$-), 6.74 (s, 1H, -CH=C-Cl), 7.17-7.25 (m, 2H, -CH=C$\underline{H}$- and -C$\underline{H}_{Ar}$), 7.29-7.32 (m, 2H, -C$\underline{H}_{Ar}$), 7.52-7.54 (m, 2H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.45, 18.13, 18.15, 39.66 (DEPT 135 negative), 51.62, 76.18, 119.70, 124.77, 128.03, 128.38, 129.31, 131.31, 134.44, 135.27, 138.79, 144.92, 167.78.

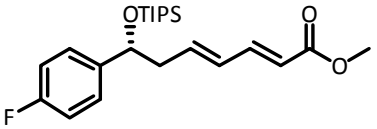
MS (EI) m/z: 405 (6%), 323 (100%), 179 (7%), 157 (37%), 115 (31%), 59 (17%).

HRMS (ESI-pos) m/z (M+Na): calcd. 471.2095, found 471.2093.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 249 nm, t_{R1} = 2.66 min/ t_{R2} = 3.14 min.

• *Compound **125:** (2E,4E)-Methyl-7-(4-fluorophenyl)-7-((triisopropylsilyl)oxy)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 4-fluorobenzaldehyde (25 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the desired product **125** as a colorless liquid (33 mg, 0.08 mmol, 41% yield).



$C_{23}H_{35}FO_3Si$
Exact Mass: 406,23
Molecular Weight: 406,61

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.90 (d, 9H, ^{3}*J* = 6.5 Hz, -Si(CH(C$\underline{H}_3$)$_2$)$_3$), 0.95 (d, 9H, ^{3}*J* = 5.7 Hz, -Si(CH(C$\underline{H}_3$)$_2$)$_3$), 0.96-1.03 (m, 3H, -Si(C$\underline{H}$(CH$_3$)$_2$)$_3$), 2.48-2.56 (m, 2H, =CH-C$\underline{H}_2$-), 3.68 (s, 3H, -OC$\underline{H}_3$), 4.79-4.81 (m, 1H, -C$\underline{H}$-CH$_2$-), 5.70 (d, 1H, ^{3}*J-trans* = 15.4 Hz, =C$\underline{H}$-C=O), 5.91-5.96 (m, 1H, -CH$_2$-C$\underline{H}$=), 6.02 (dd, 1H, ^{3}*J-trans* = 15.3 Hz, ^{3}*J* =

10.7 Hz, -CH=CH-), 6.92-6.95 (m, 2H, -CH_{Ar}), 7.14 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.6 Hz, -CH=CH-), 7.17-7.20 (m, 2H, -CH_{Ar}).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.35, 18.04, 18.12, 44.77 (DEPT 135 negative), 51.63, 74.03, 115.00 (d, ^{C-F}J = 21.2 Hz), 119.55, 127.61 (d, ^{C-F}J = 7.6 Hz), 131.05, 139.59, 140.40 (d, ^{C-F}J = 3.1 Hz), 144.93, 162.07 (d, ^{C-F}J = 244.8 Hz), 167.79.

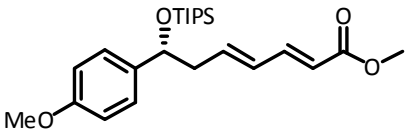
MS (EI) m/z: 363 (18%), 281 (100%), 239 (8%), 157 (25%), 115 (17%), 75 (11%).

HRMS (ESI-pos) m/z (M+Na): calcd. 429.2234, found 429.2232.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 2.55 min/ t_{R2} = 3.35 min.

• *Compound **126:** (2E,4E)-Methyl-7-(4-methoxyphenyl)-7-((triisopropylsilyl)oxy)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 4-methoxybenzaldehyde (27 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the undesired product **126a** (19 mg, 0.05 mmol, 23% yield) and the desired product **126** (45 mg, 0.11 mmol, 54% yield) as colorless liquids.



$C_{24}H_{38}O_4Si$
Exact Mass: 418,25
Molecular Weight: 418,64

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.95 (d, 9H, ^{3}J = 6.5 Hz, -Si(CH(CH_3)$_2$)$_3$), 1.00-1.03 (m, 12H, -Si(CH(CH_3)$_2$)$_3$ and -Si(CH(CH$_3$)$_2$)$_3$), 2.52-2-62 (m, 2H, =CH-CH_2-), 3.72 (s, 3H, -OCH_3), 3.79 (s, 3H, -OCH_3), 4.80-4.82 (m, 1H, -CH-CH_2-), 5.75 (d, 1H, ^{3}J-*trans* = 15.4 Hz, =CH-C=O), 5.95-6.04 (m, 1H, -CH_2-CH=), 6.09 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.7 Hz, -CH=CH-), 6.83 (d, 2H, ^{3}J = 8.5 Hz, -CH_{Ar}), 7.17-7.22 (m, 3H, -CH_{Ar} and -CH=CH-).

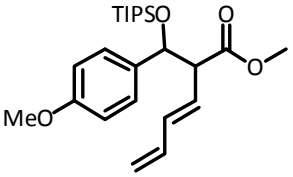
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.38, 18.06, 18.15, 44.89 (DEPT 135 negative), 51.58, 55.30, 74.26, 113.45, 119.26, 127.20, 130.71, 136.89, 140.39, 145.17, 158.80, 167.84.

MS (EI) m/z: 375 (2%), 293 (100%), 213 (3%), 185 (4%), 157 (8%), 115 (13%), 97 (5%).

HRMS (ESI-pos) m/z (M+Na): calcd. 441.2436, found 441.2432.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 3.00 min/ t_{R2} = 3.60 min.

• *Compound **126a:** (E)-Methyl-2-((4-methoxyphenyl)((triisopropylsilyl)oxy)methyl)hexa-3,5-dienoate*



$C_{24}H_{38}O_4Si$
Exact Mass: 418,25
Molecular Weight: 418,64

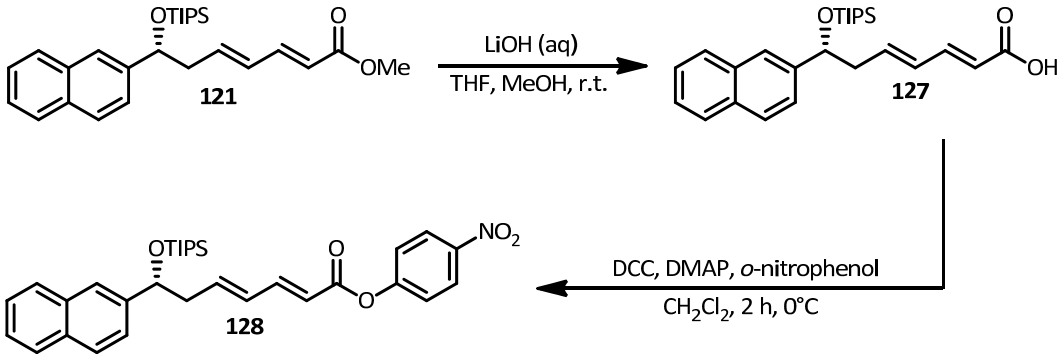
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.91-0.91 (m, 9H, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 0.96-0.97 (m, 9H, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 1.05-1.12 (m, 3H, -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 3.40-3.43 (m, 1H, -CH-C<u>H</u>-), 3.70 (s, 3H, -OC<u>H</u>$_3$), 3.79 (s, 3H, -OC<u>H</u>$_3$), 4.96 (d, 1H, ^3J = 10.3 Hz, -CH=C<u>H</u>$_2$), 5.03 (d, 1H, ^3J-*trans* = 16.9 Hz, -CH=C<u>H</u>$_2$), 5.03 (d, 1H, ^3J = 8.6 Hz, -C$_{Ar}$-C<u>H</u>-), 5.36 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 9.1 Hz, -CH-C<u>H</u>=), 5.85 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 10.6 Hz, -C<u>H</u>=CH-), 6.13 (ddd, 1H, ^3J-*trans* = 17.0 Hz, ^3J = 10.3 Hz, 10.3 Hz, -C<u>H</u>=CH$_2$), 6.81 (d, 2H, ^3J = 8.5 Hz, -C<u>H</u>$_{Ar}$), 7.16 (d, 2H, ^3J = 8.6 Hz, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.54, 17.97, 18.03, 51.90, 55.30, 59.24, 76.46, 113.37, 117.28 (DEPT 135 negative), 127.72, 128.44, 134.23, 134.68, 136.48, 159.22, 173.01.

MS (EI) m/z: 375 (30%), 293 (100%), 145 (12%), 115 (10%), 89 (7%), 59 (10%).

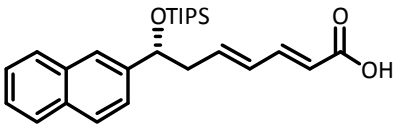
HRMS (ESI-pos) m/z (M+Na): calcd. 441.2435, found 441.2432.

7.3.4 Synthesis of a 4-nitrophenyl-derivative of 121



A sample of **121** (203 mg, 0.46 mmol) is dissolved in MeOH (5 mL) and THF (10 mL), subsequently a solution of LiOH (20 mg, 0.84 mmol) in water (2.5 mL) is added and the resulting mixture is stirred until the starting material is completely consumed by TLC. After complete consumption the pH of the solution is adjusted to 1-2 (10% HCl) and the resulting mixture is extracted with CH_2Cl_2 three times. The resulting organic extracts are dried with $MgSO_4$, evaporated, resulting in the intermediate acid **127** (186 mg, 0.44 mmol, 95% yield).

• *Compound **127:** (2E,4E)-7-(Naphthalen-2-yl)-7-((triisopropylsilyl)oxy)hepta-2,4-dienoic-acid*



$C_{26}H_{36}O_3Si$
Exact Mass: 424,24
Molecular Weight: 424,65

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.88-1.04 (m, 21H, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$ and -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 2.61 (dd, 1H, ^3J = 5.9 Hz, 5.8 Hz, -CH-C<u>H</u>$_2$-), 4.97 (dd, 1H, ^3J = 5.8 Hz, 5.7 Hz, -C<u>H</u>-CH$_2$-), 5.63 (d, 1H, ^{3}*J-trans* = 15.8 Hz, =C<u>H</u>-C=O), 5.98-6.10 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.13-7.22 (m, 1H, =CH-CH$_2$-), 7.34-7.41 (m, 3H, -C<u>H</u>$_{Ar}$), 7.62 (s, 1H, -C<u>H</u>$_{Ar}$), 7.71-7.75 (m, 3H, -C<u>H</u>$_{Ar}$).

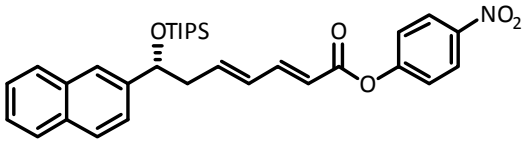
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 12.43, 18.11, 18.18, 44.78, 74.73, 118.98, 124.43, 124.67, 125.78, 126.12, 127.85, 128.05, 128.10, 130.80, 133.04, 133.22, 141.30, 142.05, 147.18, 172.79.

MS (EI) m/z: 363 (3%), 313 (100%), 271 (5%), 225 (5%), 157 (11%), 115 (13%).

HRMS (ESI-pos) m/z (M+Na): calcd. 447.2333, found 447.2326.

The acid **127** (93 mg, 0.22 mmol) and *p*-nitrophenol (1.2 equiv, 37 mg, 0.26 mmol) are dissolved in CH_2Cl_2 (4 mL) under Argon at 0°C. Subsequently a solution of DCC (1.1 equiv, 50 mg, 0.24 mmol) in CH_2Cl_2 (1 mL) and a catalytic amount (spatula tip) DMAP is added. The resulting mixture is stirred for 2 h, evaporated and the residue subjected to column chromatography resulting in the desired product **128** as an off-white solid (91 mg, 0.17 mmol, 76% yield). **128** could be crystallized from a mixture of CH_2Cl_2 and *i*PrOH.

• *Compound **128:** (2E,4E)-4-Nitrophenyl-7-(naphthalen-2-yl)-7-((triisopropylsilyl)oxy)hepta-2,4-dienoate*



$C_{32}H_{39}NO_5Si$
Exact Mass: 545,26
Molecular Weight: 545,74

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 0.91 (d, 9H, ^3J = 6.6 Hz, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 0.96 (d, 9H, ^3J = 6.1 Hz, -Si(CH(C<u>H</u>$_3$)$_2$)$_3$), 0.98-1.05 (m, 3H, -Si(C<u>H</u>(CH$_3$)$_2$)$_3$), 2.67 (dd, 2H, ^3J = 5.8 Hz, 5.8 Hz, -CH-C<u>H</u>$_2$-), 5.02 (dd, 1H, ^3J = 5.7 Hz, 5.6 Hz, -C<u>H</u>-CH$_2$-), 5.81 (d, 1H, ^3J-*trans* = 15.2 Hz, =C<u>H</u>-C=O), 6.10-6.13 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.20 (d, 2H, ^3J = 9.2 Hz, -C<u>H</u>$_{Ar}$), 7.27-7.34 (m, 1H, =CH-CH$_2$-), 7.35-7.42 (m, 3H, -C<u>H</u>$_{Ar}$), 7.64 (s, 1H, -C<u>H</u>$_{Ar}$), 7.72-7.75 (m, 3H, -C<u>H</u>$_{Ar}$), 8.16 (d, 2H, ^3J = 9.2 Hz, -C<u>H</u>$_{Ar}$).

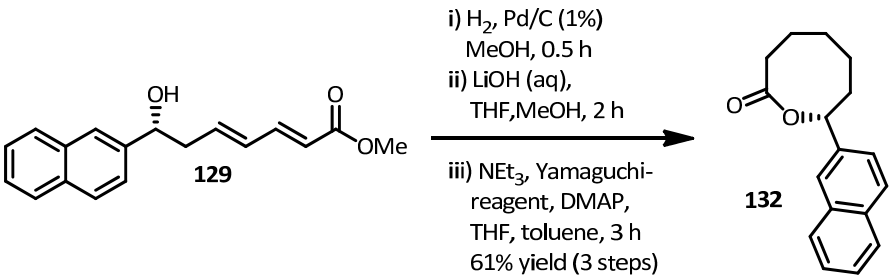
^{13}C-NMR (100 MHz, $CDCl_3$) δ [ppm]: 12.43, 18.10, 18.17, 44.75 (DEPT 135 negative), 74.60, 117.73, 122.55, 124.37, 124.68, 125.24, 125.82, 126.15, 127.85, 128.08, 130.67, 133.04, 133.21, 141.90, 142.43, 145.26, 148.10, 155.79, 164.59.

MS (EI) m/z: 502 (2%), 313 (100%), 252 (17%), 205 (6%), 141 (7%), 115 (10%).

HRMS (ESI-pos) m/z (M+Na): calcd. 568.2498, found 568.2490.

7.3.5 The synthesis of ζ-Lactones from DVMAR-products

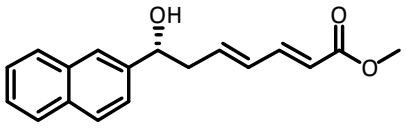
7.3.5.1 Synthesis of lactone 132: 8-(Naphthalen-2-yl)oxoctan-2-one



A crude sample of **106** (er = 95:5) was evaporated and redissolved in THF (10 mL) and stirred with 10% aqueous HCl (3 mL) until complete consumption of starting material was indicated by TLC. The mixture was diluted with CH_2Cl_2 and washed with water. The organic extracts were dried with $MgSO_4$, filtered and evaporated, prior to column chromatography (hexane / ethyl acetate 4:1), affording 51 mg (0.18 mmol) of the deprotected product **129**.

129 was dissolved in MeOH (2.5 mL) in a 5 mL round bottom flask and stirred with 7 mg Pd/C (10% Pd on charcoal, corresponding to 1 mol% Pd with respect to the starting material), under an atmosphere of H_2. After 10 min the starting material was completely consumed and the mixture was filtered through a pad of cotton via a syringe filter, followed by evaporation of the solvent and purity control of the product **130** by NMR. The product **130** was redissolved in THF (2.5 mL) and MeOH (1.25 mL) and treated with a solution of 10 mg LiOH in H_2O (1.25 mL). The resulting mixture was stirred for 2 h, acidified with 1*M* HCl and extracted with EtOAc (5 x 10 mL). The organic extracts were dried over $MgSO_4$, filtered, and the solvent was evaporated and the purity of product **131** controlled by NMR. The product **131** was mixed with THF (2.5 mL) and treated with NEt_3 (0.30 mmol) and 2,4,6-trichlorobenzoyl chloride (0.26 mmol), after stirring for 2 h at r.t. a white precipitate was formed. The resulting mixture was slowly added to a solution of DMAP (3.00 mmol) in toluene (15 mL) at 70°C. After stirring for 1 h the solvents were removed and column chromatography of the residue (hexane / ethyl acetate 5:1) gave the desired lactone **132** (28 mg, 0.11 mmol, 61% yield over 3 steps).

• *Compound **129:** (2E,4E)-Methyl-7-hydroxy-7-(naphthalen-2-yl)hepta-2,4-dienoate*



$C_{18}H_{18}O_3$
Exact Mass: 282,13
Molecular Weight: 282,33

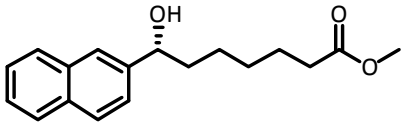
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 2.48 (bs, 1H, -O<u>H</u>), 2.63-2.73 (m, 2H, -CH-C<u>H</u>$_2$-), 3.71 (s, 3H, -OC<u>H</u>$_3$), 4.91 (dd, 1H, ^3J = 7.1 Hz, 5.7 Hz, -CH-C<u>H</u>$_2$-), 5.77 (d, 1H, ^3J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.08 (ddd, 1H, ^3J-*trans* = 15.2 Hz, ^3J = 7.3 Hz, 7.7 Hz, -CH$_2$-C<u>H</u>=), 6.22 (dd, 1H, ^3J-*trans* = 15.1 Hz, ^3J = 10.9 Hz, -CH=C<u>H</u>-), 7.21 (dd, 1H, ^3J-*trans* = 15.4 Hz, ^3J = 10.9 Hz, -CH=C<u>H</u>-), 7.44 (m, 3H, -C<u>H</u>$_{Ar}$), 7.76 (s, 1H, -C<u>H</u>$_{Ar}$), 7.80-7.83 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 42.70, 51.59, 73.65, 119.88, 123.91, 124.60, 126.05, 126.33, 127.78, 128.05, 128.45, 131.18, 133.10, 133.30, 139.60, 141.15, 144.74, 167.68.

MS (EI) m/z: 282 (3%), 157 (100%), 129 (93%), 126 (80%), 111 (13%), 94 (8%), 67 (21%).

HRMS (ESI-pos) m/z (M+Na): calcd. 305.1147, found 305.1148.

• *Compound **130:** Methyl 7-hydroxy-7-(naphthalen-2-yl)heptanoate*



$C_{18}H_{22}O_3$
Exact Mass: 286,16
Molecular Weight: 286,37

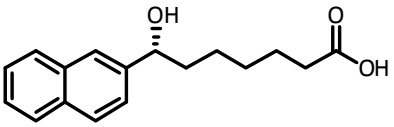
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.28-1.92 (m, 8H, -C<u>H</u>$_2$-), 2.28 (t, 2H, ^3J = 7.5 Hz, -C<u>H</u>$_2$), 3.64 (s, 3H, -OC<u>H</u>$_3$), 4.83 (dd, 1H, ^3J = 6.1 Hz, 6.9 Hz, -C$_{Ar}$-C<u>H</u>-), 7.45-7.50 (m, 3H, -C<u>H</u>$_{Ar}$), 7.77 (s, 1H, -C<u>H</u>$_{Ar}$), 7.82-7.84 (m, 3H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 24.93, 25.57, 29.12, 34.10, 38.83, 51.60, 74.77, 124.17, 124.70, 125.93, 126.27, 127.80, 128.04, 128.42, 133.10, 142.26, 174.35.

MS (EI) m/z: 286 (17%), 157 (100%), 141 (7%), 129 (45%), 87 (9%).

HRMS (ESI-pos) m/z (M+Na): calcd. 309.1462, found 309.1461.

• *Compound **131:** 7-Hydroxy-7-(naphthalen-2-yl)heptanoic-acid*

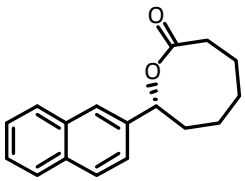


$C_{17}H_{20}O_3$
Exact Mass: 272,14
Molecular Weight: 272,34

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.29-1.41 (m, 3H, -C<u>H</u>$_2$-), 1.42-1.50 (m, 1H, -C<u>H</u>$_2$-), 1.59-1.65 (m, 2H, -C<u>H</u>$_2$-), 1.76-1.83 (m, 1H, -C<u>H</u>$_2$-), 1.85-1.92 (m, 1H, -C<u>H</u>$_2$-), 2.32 (t, 2H, ^3J = 7.5 Hz, -C<u>H</u>$_2$-), 4.40 (bs, 1H, -O<u>H</u>), 4.81-4.85 (m, 1H, -C<u>H</u>-CH$_2$-), 7.45-7.50 (m, 3H, -CH$_{Ar}$), 7.76 (s, 1H, -CH$_{Ar}$), 7.82-7.84 (m, 3H, -CH$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 24.67, 25.58, 29.02, 33.91, 38.77, 74.81, 124.16, 124.74, 125.96, 126.29, 127.82, 128.06, 128.46, 133.12, 133.39, 142.16, 179.18.

• *Compound **132:** 8-(Naphthalen-2-yl)oxoctan-2-one*



$C_{17}H_{18}O_2$
Exact Mass: 254,13
Molecular Weight: 254,32

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 1.67-1.78 (m, 3H, -CH$_2$-), 1.85-1.91 (m, 1H, -CH$_2$-), 1.96-2.14 (m, 4H, -CH$_2$-), 2.58-2.70 (m, 2H, -CH$_2$-), 5.85 (dd, 1H, ^3J = 10.5 Hz, 3.8 Hz, -C<u>H</u>-CH$_2$-), 7.47-7.52 (m, 3H, -C<u>H</u>$_{Ar}$), 7.83-7.88 (m, 4H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 24.63 (DEPT 135 negative), 26.86 (DEPT 135 negative), 29.59 (DEPT 135 negative), 33.28 (DEPT 135 negative), 40.03 (DEPT 135 negative), 80.04, 124.13, 124.80, 126.26, 126.45, 127.81, 128.16, 128.46, 133.10, 133.30, 137.86, 176.60.

MS (EI) m/z: 254 (31%), 194 (13%), 167 (14%), 156 (100%), 55 (10%).

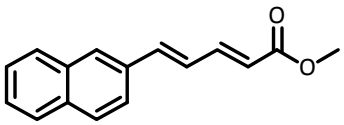
HRMS (EI) m/z: calcd. 254.1304, found 254.1307.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 95:5, flow: 1 ml/min, 25°C, absorption at 225 nm, t_{R1} = 6.82 min/ t_{R2} = 8.14 min, detected e.r. = 94:6.

• *Compound **133:** (2E,4E)-Methyl-5-(naphthalen-2-yl)penta-2,4-dienoate*

^{1}H-NMR (300 MHz, $CDCl_3$) δ [ppm]: 3.96 (s, 3H, -OC<u>H</u>$_3$), 5.94 (d, 1H, ^3J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.83-6.97 (m, 2H), 7.35-7.45 (m, 3H), 7.53 (dd, 1H, ^3J = 8.7 Hz, 1.5 Hz), 7.69-7.75 (m, 4H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ [ppm]: 51.69, 120.91, 123.45, 126.56, 126.69, 126.79, 127.84, 128.33, 128.39, 128.62, 133.56, 133.59, 133.74, 140.74, 144.97, 167.60.

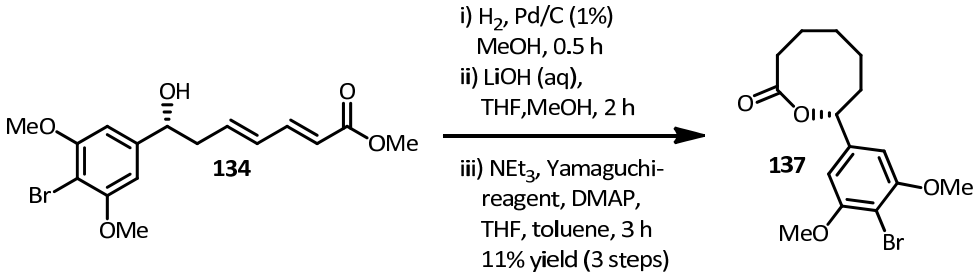


$C_{16}H_{14}O_2$
Exact Mass: 238,10
Molecular Weight: 238,28

MS (EI) m/z: 238 (27%), 179 (100%), 178 (55%), 152 (7%), 104 (9%), 89 (30%), 76 (12%).

HRMS (ESI-pos) m/z (M+Na): calcd. 261.0885, found 261.0886.

7.3.5.2 Synthesis of lactone 137: 8-(4-Bromo-3,5-dimethoxyphenyl)oxocan-2-one



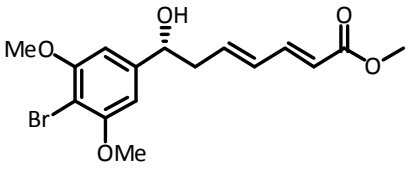
A crude sample of **110** was evaporated and redissolved in THF (10 mL) and stirred with 10% aqueous HCl (3 mL) until complete consumption of starting material was indicated by TLC. The mixture was diluted with CH_2Cl_2 and washed with water. The organic extracts were dried with $MgSO_4$, filtered and evaporated, prior to column chromatography (hexane / ethyl acetate mixtures), affording 174 mg (0.47 mmol) of the deprotected product **134**.

134 was dissolved in MeOH (5 mL) in a 10 mL round bottom flask and stirred with 5 mg Pd/C (10% Pd on charcoal), under an atmosphere of H_2. After the starting material was completely consumed and the mixture was filtered through a pad of cotton via a syringe filter, followed by evaporation of the solvent and purity control of product **135** by NMR. The product **135** was redissolved in THF (5 mL) and MeOH (2.5 mL) and treated with a solution of 25 mg LiOH in H_2O (2.5 mL). The resulting mixture was stirred for 2 h, acidified with 1*M* HCl and extracted with EtOAc (5 x 10 mL). The organic extracts were dried over $MgSO_4$, filtered, and the solvent was evaporated and the purity of product **136** controlled. The product **137** was mixed with THF (5.5 mL) and treated with NEt_3 (0.70 mmol) and 2,4,6-trichlorobenzoyl chloride (0.61 mmol), after stirring for 2 h at r.t. a white precipitate formed. The mixture was slowly added to a solution of DMAP (7.00 mmol) in toluene (35 mL) at 70°C. After stirring for 1 h the solvents were removed and column chromatography (hexane / ethyl acetate 4:1) gave the desired lactone **138** (17 mg, 0.05 mmol, 11% yield over 3 steps).

• *Compound **134:** (2E,4E)-Methyl-7-(4-bromo-3,5-dimethoxyphenyl)-7-hydroxyhepta-2,4-dienoate*

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 2.54-2.57 (m, 2H, -CH-C$\underline{H}_2$-), 2.65 (bs, 1H, -O$\underline{H}$), 3.69 (s, 3H, -OC$\underline{H}_3$), 3.85 (s, 6H, -OC$\underline{H}_3$), 4.70-4.72 (m, 1H, -CH-C$\underline{H}_2$-), 5.77 (d, 1H, ^{3}*J-trans* = 15.4 Hz, =C$\underline{H}$-C=O), 6.07 (ddd, 1H, ^{3}J-trans = 15.1 Hz, ^{3}J = 7.6 Hz, 7.2 Hz, -CH_2-

C<u>H</u>=), 6.21 (dd, 1H, ^{3}J-*trans* = 15.2 Hz, ^{3}J = 11.0 Hz, -CH=C<u>H</u>-), 6.52 (s, 2H, -C<u>H</u>$_{Ar}$), 7.19 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.9 Hz, -CH=C<u>H</u>-).



$C_{16}H_{19}BrO_5$
Exact Mass: 370,04
Molecular Weight: 371,22

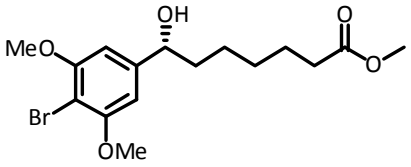
^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: 42.83, 51.63, 56.50, 73.41, 99.65, 102.08, 120.01, 131.27, 139.29, 144.55, 144.90, 156.99, 167.64.

MS (EI) m/z: 247 (25%), 245 (27%), 217 (8%), 166 (6%), 138 (61%), 126 (100%).

HRMS (ESI-pos) m/z (M+Na): calcd. 393.0311, found 393.0308.

• *Compound **135:** Methyl-7-(4-bromo-3,5-dimethoxyphenyl)-7-hydroxyheptanoate*

^{1}H-NMR (500 MHz, CDCl$_3$) δ [ppm]: 1.27-1.39 (m, 3H, -C<u>H</u>$_2$-), 1.40-1.47 (m, 1H, -C<u>H</u>$_2$-), 1.58-1.64 (m, 2H, -C<u>H</u>$_2$-), 1.65-1.70 (m, 1H, -C<u>H</u>$_2$-), 1.72-1.80 (m, 1H, -C<u>H</u>$_2$-), 2.08 (bs, 1H, -OH), 2.29 (t, 2H, ^{3}J = 7.5 Hz, -CH$_2$-C<u>H</u>-), 3.65 (s, 3H, -OC<u>H</u>$_3$), 3.89 (s, 6H), 4.62 (dd, 1H, ^{3}J = 7.6 Hz, 5.5 Hz, -C<u>H</u>$_2$-CH-), 6.55 (s, 2H, -C<u>H</u>$_{Ar}$).



$C_{16}H_{23}BrO_5$
Exact Mass: 374,07
Molecular Weight: 375,25

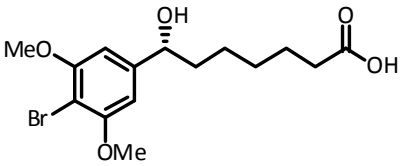
^{13}C-NMR (125 MHz, CDCl$_3$) δ [ppm]: 24.89, 25.55, 29.04, 34.04, 39.05, 51.62, 56.57, 74.61, 99.53, 102.23, 146.04, 157.09, 174.31.

MS (EI) m/z: 376 (33%), 374 (33%), 295 (5%), 263 (32%), 245 (89%), 217 (62%), 138 (100%), 101 (15%), 87 (52%).

HRMS (ESI-pos) m/z (M+Na): calcd. 397.0621, found 397.0621.

• *Compound **136:** 7-(4-Bromo-3,5-dimethoxyphenyl)-7-hydroxyheptanoic-acid*

^{1}H-NMR (500 MHz, CDCl$_3$) δ [ppm]: 1.26-1.44 (m, 4H, -C<u>H</u>$_2$-), 1.56-1.68 (m, 3H, -C<u>H</u>$_2$-), 1.70-1.78 (m, 1H, -C<u>H</u>$_2$-), 2.06 (s, 1H, -OH), 2.30 (t, 2H, ^{3}J = 7.5 Hz, -CH-C<u>H</u>$_2$-), 3.86 (s, 6H, -OC<u>H</u>$_3$), 4.59 (dd, 1H, ^{3}J = 7.3 Hz, 5.9 Hz, -C<u>H</u>-CH$_2$-), 6.51 (s, 2H, -C<u>H</u>$_{Ar}$), 8.12 (bs, 1H, -COO<u>H</u>).



$C_{15}H_{21}BrO_5$
Exact Mass: 360,06
Molecular Weight: 361,23

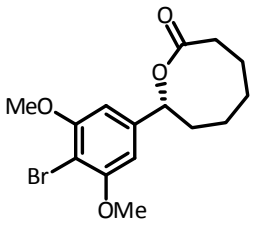
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 24.55, 25.43, 28.86, 33.96, 38.80, 56.49, 74.62, 99.47, 102.22, 145.71, 156.97, 179.88.

MS (ESI-pos) m/z: 360.

HRMS (ESI-pos) m/z (M+Na): calcd. 383.0461, found 383.0465.

- *Compound **137:** 8-(4-Bromo-3,5-dimethoxyphenyl)oxocan-2-one*

^{1}H-NMR (300 MHz, CD_2Cl_2) δ [ppm]: 1.54-1.94 (m, 8H, -C<u>H</u>$_2$-), 2.45-2.63 (m, 2H, -C<u>H</u>$_2$-), 3.86 (s, 6H, -OC<u>H</u>$_3$), 5.56 (dd, 1H, ^{3}J = 7.7 Hz, 6.7 Hz, -C<u>H</u>-CH$_2$-), 6.59 (s, 2H, -C<u>H</u>$_{Ar}$).



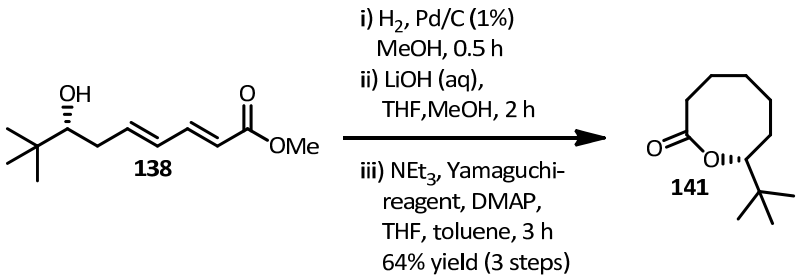
$C_{15}H_{19}BrO_4$
Exact Mass: 342,05
Molecular Weight: 343,21

^{13}C-NMR (75 MHz, CD_2Cl_2) δ [ppm]: 24.51 (DEPT 135 negative), 26.61 (DEPT 135 negative), 29.43 (DEPT 135 negative), 33.00 (DEPT 135 negative), 40.04 (DEPT 135 negative), 56.53, 79.53, 99.83, 102.41, 141.75, 157.19, 175.78.

MS (EI) m/z: 344 (41%), 342 (41%), 260 (21%), 258 (21%), 246 (99%), 244 (100%), 55 (24%).

HRMS (ESI-pos) m/z (M+Na): calcd. 365.0357, found 365.0359.

7.3.5.3 Synthesis of lactone 141: 8-(tert-Butyl)oxocan-2-one



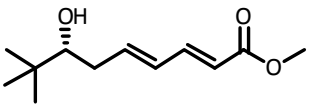
A crude sample of **116** was evaporated and redissolved in THF (10 mL) and stirred with 10% aqueous HCl (3 mL) until complete consumption of starting material was indicated by TLC. The mixture was diluted with CH_2Cl_2 and washed with water. The organic extracts were dried with $MgSO_4$, filtered and evaporated, prior to column chromatography (hexane / ethyl acetate mixtures), affording 57 mg (0.27 mmol) of the deprotected product **138**.

138 was dissolved in MeOH (3 mL) in a 10 mL round bottomed flask and stirred with 3 mg Pd/C (10% Pd on charcoal), under an atmosphere of H_2. After the starting material was completely consumed and the mixture was filtered through a pad of cotton via a syringe filter, followed by evaporation of the solvent and purity of **139** controlled by NMR. The product **139** was redissolved in THF (5 mL) and MeOH (2.5 mL) and treated with a solution of 20 mg LiOH in H_2O (2.5 mL). The resulting mixture was stirred for 2 h, acidified with 1*M* HCl and extracted with EtOAc (5 x 10 mL). The organic extracts were dried over $MgSO_4$, filtered, and the solvent was evaporated and the purity of product **140** controlled by NMR. The residue was mixed with THF (3 mL) and treated with NEt_3 (0.40 mmol) and 2,4,6-trichlorobenzoyl chloride (0.35 mmol), after stirring for 2 h at r.t. a white precipitate was formed. The resulting mixture was slowly added to a solution of DMAP (4.02 mmol) in toluene (20 mL) at 70°C. After stirring for 1 h the solvents were removed and column chromatography of the residue (hexane / ethyl acetate 4:1) gave the desired lactone **141** (32 mg, 0.17 mmol, 64% yield over 3 steps).

• *Compound **138:** (2E,4E)-Methyl-7-hydroxy-8,8-dimethylnona-2,4-dienoate*

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.90 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.71 (bs, 1H, -O<u>H</u>), 2.10-2.16 (m, 1H, -CH-C<u>H</u>$_2$-), 2.39-2.43 (m, 1H, -CH-C<u>H</u>$_2$-), 3.29-3.31 (m, 1H, -C<u>H</u>-CH$_2$-), 3.72 (s, 3H, -OC<u>H</u>$_3$), 5.80 (d, 1H, ^{3}*J-trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.16-6.22 (m, 1H, -CH$_2$-C<u>H</u>=),

6.25 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.3 Hz, -CH=CH-), 7.26 (dd, 1H, ^{3}J-*trans* = 15.4 Hz, ^{3}J = 10.2 Hz, -CH=CH-).



$C_{12}H_{20}O_3$
Exact Mass: 212,14
Molecular Weight: 212,29

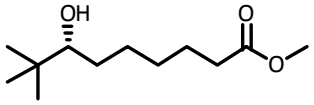
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 25.76, 35.06, 35.70, 51.61, 78.77, 119.49, 130.61, 142.27, 144.94, 167.75.

MS (EI) m/z: 181 (6%), 165 (5%), 126 (100%), 111 (45%), 94 (21%), 87 (47%), 67 (54%), 41 (34%).

HRMS (ESI-pos) m/z (M+Na): calcd. 235.1305, found 235.1305.

• *Compound **139:** Methyl-7-hydroxy-8,8-dimethylnonanoate*

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.86 (s, 9H, -C(CH$_3$)$_3$), 1.18-1.40 (m, 4H, -CH$_2$-), 1.45-1.65 (m, 5H, -CH-CH$_2$- and -CH$_2$- and -OH), 2.29 (t, 2H, ^{3}J = 7.6 Hz, -CH$_2$-), 3.13-3.16 (dd, 1H, ^{3}J = 10.5 Hz, 1.4 Hz, -CH$_2$-CH-), 3.64 (s, 3H, -OCH$_3$).



$C_{12}H_{24}O_3$
Exact Mass: 216,17
Molecular Weight: 216,32

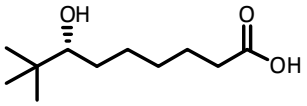
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 25.03, 25.79, 26.84, 29.31, 31.36, 34.15, 35.04, 51.58, 79.95, 174.41.

MS (EI) m/z: 185 (2%), 159 (44%), 127 (100%), 87 (17%), 81 (58%), 57 (19%), 41 (16%).

HRMS (ESI-pos) m/z (M+Na): calcd. 239.1616, found 239.1618.

• *Compound **140:** 7-Hydroxy-8,8-dimethylnonanoic acid*

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.87 (s, 9H, -C(CH$_3$)$_3$), 1.21-1.43 (m, 4H, -CH$_2$-), 1.46-1.66 (m, 4H, -CH$_2$-), 2.07 (s, 1H, -OH), 2.33 (t, 2H, ^{3}J = 7.5 Hz, -CH$_2$-), 3.17-3.20 (m, 1H, -CH$_2$-CH-), 7.60 (bs, 1H, -COOH).



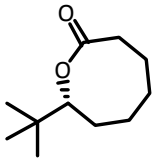
$C_{11}H_{22}O_3$
Exact Mass: 202,16
Molecular Weight: 202,29

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 24.76, 25.79, 26.73, 29.18, 31.18, 34.12, 35.03, 80.31, 179.72.

MS (EI) m/z: 145 (13%), 127 (100%), 87 (10%), 87 (56%), 57 (30%), 41 (21%).

HRMS (ESI-neg) m/z (M-H): calcd. 201.1497, found 201.1496.

- *Compound **141:** 8-(tert-Butyl)oxocan-2-one*



$C_{11}H_{20}O_2$
Exact Mass: 184,15
Molecular Weight: 184,28

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.94 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.43-1.58 (m, 3H, -C<u>H</u>$_2$-), 1.60-1.66 (m, 1H, -C<u>H</u>$_2$-), 1.67-1.74 (m, 2H, -C<u>H</u>$_2$-), 1.77-1.93 (m, 2H, -C<u>H</u>$_2$-), 2.41-2.46 (m, 1H, -C<u>H</u>$_2$-), 2.48-2.53 (m, 1H, -C<u>H</u>$_2$-), 4.26 (dd, 1H, ^3J = 11.7 Hz, 3.2 Hz, -C<u>H</u>-CH$_2$-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 24.21 (DEPT 135 negative), 26.09, 26.72 (DEPT 135 negative), 29.42 (DEPT 135 negative), 31.41 (DEPT 135 negative), 32.98 (DEPT 135 negative), 34.31, 86.10, 177.27.

MS (EI) m/z: 184 (3%), 127 (70%), 99 (100%), 81 (91%), 69 (27%), 55 (58%), 41 (39%).

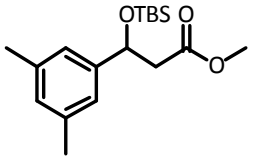
HRMS (CI-FE, *iso*-butane) m/z (M+H): calcd. 185.1540, found 185.1542.

7.4 NMR-, and scrambling-experiments

7.4.1 Experiments corresponding to Fig. 87

The following data correspond to separately synthesized material for compound **142** and **143** discussed in.

• *Compound **142:** Methyl-3-((tert-butyldimethylsilyl)oxy)-3-(3,5-dimethylphenyl)propanoate*



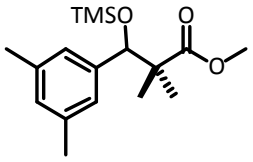
$C_{18}H_{30}O_3S_i$
Exact Mass: 322,20
Molecular Weight: 322,51

^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: -0.20, -0.04 (s, 6H, -Si(C$\underline{H}_3$)$_2$-), 0.80 (s, 9H, -Si(C(C$\underline{H}_3$)$_3$), 2.25 (s, 6H, -CH$_{Ar}$-C$\underline{H}_3$), 2.47 (dd, 1H, ^3J = 14.5 Hz, 4.0 Hz, -C$\underline{H}_2$-), 2.61 (dd, 1H, ^3J = 14.5 Hz, 9.4 Hz, -C$\underline{H}_2$-), 3.61 (s, 3H, -OC$\underline{H}_3$), 5.02 (dd, 1H, ^3J = 9.4 Hz, 4.0 Hz), 6.85 (s, 1H, -C$\underline{H}_{Ar}$), 6.90 (s, 2H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, CD_2Cl_2) δ [ppm]: -5.55, -4.95, 17.99, 21.07, 25.46, 46.35 (DEPT 135 negative), 51.39, 72.28, 123.61, 128.94, 137.80, 144.12, 171.40.

HPLC: Daicel Chiralpak OD-3, *n*-heptane:*i*-PrOH = 98:2, flow: 1 ml/min, 25°C, absorption at 200 nm, t_{R1} = 2.12 min/ t_{R2} = 2.66 min.

• *Compound **143:** Methyl-3-(3,5-dimethylphenyl)-2,2-dimethyl-3-((trimethylsilyl)oxy)-propanoate*



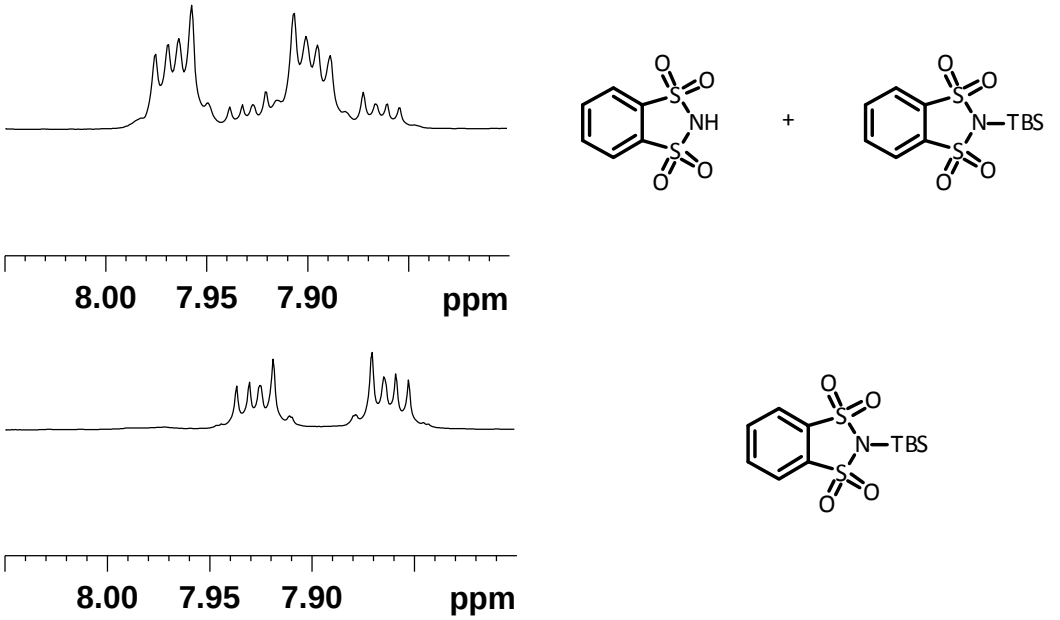
$C_{17}H_{28}O_3Si$
Exact Mass: 308,18
Molecular Weight: 308,49

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.04 (s, 9H), 0.98 (s, 3H), 1.11 (s, 3H), 2.29 (s, 6H), 3.67 (s, 3H), 4.89 (s, 1H), 6.85 (s, 2H), 6.87 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 0.2, 19.3, 21.5, 21.9, 49.2, 51.7, 79.3, 125.8, 129.0, 136.7, 140.8, 177.6.[129a]

NMR-Experiment (Fig. 87, eq 1): An NMR-tube was filled with **40** (21.9 mg, 0.10 mmol, 1 equiv), dried under vacuum and flushed with Argon at r.t. Subsequently CD_2Cl_2 (0.5 mL) was added, followed by ((1-methoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane (1.0 equiv), the mixture is controlled by ^{1}H-NMR-spectroscopy, and ((1-methoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane is added in small portions, until a complete shift of the signal set of

compound **40** to a new species is observed, usually between 1 and 2 equivs. (exemplarily shown for a mixture of **40** with nucleophile **99** in CD_2Cl_2):



After the complete formation of the active species, the solution is added to a vial containing 3,5-dimethylbenzaldehyde (13.5 µl, 1 equiv) and *tert*-butyl((1-methoxyvinyl)oxy)dimethylsilane (18.8 mg, 1 equiv). The resulting reaction mixture is stirred for 1h, after which a solution of $NaHCO_3$ is added, the organic layer separated, dried, evaporated and the product distribution examined by NMR-spectroscopy:

The mainly observed product was **142** (> 20:1).

NMR-Experiment (Fig. 87, eq 2): An NMR-tube was filled with **40** (21.9 mg, 0.10 mmol, 1 equiv), dried under vacuum and flushed with Argon at r.t. Subsequently CD_2Cl_2 (0.5 mL) was added, followed by tert-butyl((1-methoxyvinyl)oxy)dimethylsilane (1.0 equiv), the mixture is controlled by ^{1}H-NMR-spectroscopy, and tert-butyl((1-methoxyvinyl)oxy)dimethylsilane is added in small portions, until a complete shift of the signal set of compound **40** to a new species is observed, usually between 1 and 2 equivs. After the complete formation of the active species, the solution is added to a vial containing 3,5-dimethylbenzaldehyde (13.5 µl, 1 equiv) and ((1-methoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane (17.4 mg, 1 equiv). The resulting reaction mixture is stirred for 1h, after which a solution of $NaHCO_3$ is added, the organic layer separated, dried, evaporated and the product distribution examined by NMR-spectroscopy.

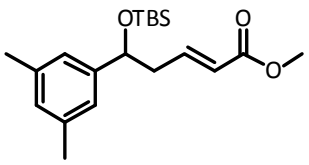
The mainly observed product was product **143** (> 20:1).

7.4.2. Experiments corresponding to Fig. 88

The following data correspond to separately synthesized material for compound **76** and **144** according to.

• *Compound **76:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(3,5-dimethylphenyl)pent-2-enoate*

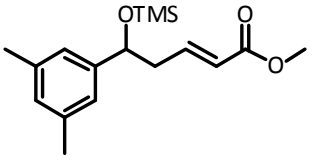
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.13, 0.02 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.88 (s, 9H, -SiC(C<u>H</u>$_3$)$_3$), 2.30 (s, 6H, -CH$_{Ar}$-C<u>H</u>$_3$), 2.47-2.59 (m, 2H, =CH-C<u>H</u>$_2$-), 3.72 (s, 3H, -OC<u>H</u>$_3$), 4.68 (dd, 1H, ^3J = 4.8 Hz, 7.7 Hz, -C<u>H</u>-CH$_2$-), 5.83 (d, 1H, ^3J-*trans* = 15.7 Hz, -C<u>H</u>-C=O), 6.88-6.90 (m, 3H, -C<u>H</u>$_{Ar}$), 6.97 (ddd, 1H, ^3J-*trans* = 15.8 Hz, ^3J = 7.5 Hz, ^3J = 7.8 Hz, -CH$_2$-C<u>H</u>=).



$C_{20}H_{32}O_3Si$
Exact Mass: 348,21
Molecular Weight: 348,55

• *Compound **144:** (E)-Methyl-5-(3,5-dimethylphenyl)-5-((trimethylsilyl)oxy)pent-2-enoate*

^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: -0.01 (s, 9H, -Si(C<u>H</u>$_3$)$_3$), 2.26 (s, 6H, -CH$_{Ar}$-C<u>H</u>$_3$), 2.45-2.55 (m, 2H, =CH-C<u>H</u>$_2$-), 3.64 (s, 3H, -OC<u>H</u>$_3$), 4.66 (dd, 1H, ^3J = 7.1 Hz, 5.4 Hz, -C<u>H</u>-CH$_2$-), 5.77 (d, 1H, ^3J-*trans* = 15.8 Hz, -C<u>H</u>-C=O), 6.81-6.87 (m, 4H, CH$_2$-C<u>H</u>=, -C<u>H</u>$_{Ar}$).



$C_{17}H_{26}O_3Si$
Exact Mass: 306,17
Molecular Weight: 306,47

NMR-Experiment (Fig. 88, eq 1): An NMR-tube was filled with **40** or **41** (1 equiv), dried under vacuum and flushed with Argon at r.t. Subsequently CD_2Cl_2 (0.5 mL) was added, followed by **51** (1.0 equiv), the mixture is controlled by ^{1}H-NMR-spectroscopy, and **51** is added in small portions, until a complete shift of the signal set of compound **40** or **41** to a new species is observed, usually between 1 and 2 equivs. After the complete formation of the active species, the solution is added to a vial containing 3,5-dimethylbenzaldehyde (13.5 µl, 1 equiv) and **50** (1 equiv). The resulting reaction mixture is stirred for 1h, after which a solution of $NaHCO_3$ is added, the organic layer separated, dried, evaporated and the product distribution examined by NMR-spectroscopy:

The mainly observed product was product **76** (13:1) with catalyst **40**.

The mainly observed product was product **76** (2:1) with catalyst **41**.

NMR-Experiment (Fig. 88, eq 2): An NMR-tube was filled with **40** or **41** (1 equiv), dried under vacuum and flushed with Argon at r.t. Subsequently CD_2Cl_2 (0.5 mL) was added, followed by **50** (1.0 equiv), the mixture is controlled by ^{1}H-NMR-spectroscopy, and **50** is added in small portions, until a complete shift of the signal set of compound **40** or **41** to a new species is observed, usually between 1 and 2 equivs. After the complete formation of the active species, the solution is added to a vial containing 3,5-dimethylbenzaldehyde (13.5 µl, 1 equiv) and **51** (1 equiv). The resulting reaction mixture is stirred for 1h, after which a solution of $NaHCO_3$ is added, the organic layer separated, dried, evaporated and the product distribution examined by NMR-spectroscopy:

The mainly observed product was product **76** (3:1) with catalyst **40**.

The mainly observed product was product **76** (2:1) with catalyst **41**.

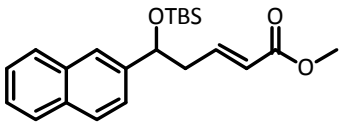
7.4.3 Experiments corresponding to Fig. 89 and Fig. 90

The product distribution was analyzed by GC-MS, resulting in the corresponding peaks which could be assigned by their fragmentation pattern. The fragmentation was compared with separately synthesized material.

• *Compound **I:** (E)-Methyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*

MS (EI) m/z: 313 (4%), 281 (5%), 271 (100%), 245 (5%), 199 (5%), 179 (11%), 157 (25%), 141 (4%), 115 (3%), 89 (15%), 73 (38%).

GC-MS elution peak: 17.36 min.

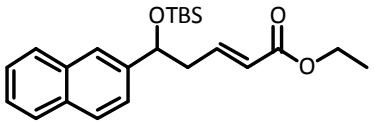


$C_{22}H_{30}O_3Si$
Exact Mass: 370,20
Molecular Weight: 370,56

• *Compound **II:** (E)-Ethyl-5-((tert-butyldimethylsilyl)oxy)-5-(naphthalen-2-yl)pent-2-enoate*

MS (EI) m/z: 327 (10%), 281 (8%), 271 (100%), 215 (6%), 199 (4%), 171 (10%), 143 (12%), 103 (8%), 73 (36%).

GC-MS elution peak: 17.71 min.

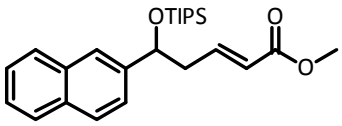


$C_{23}H_{32}O_3Si$
Exact Mass: 384,21
Molecular Weight: 384,58

• *Compound **III:** (E)-Methyl-5-(naphthalen-2-yl)-5-((triisopropylsilyl)oxy)pent-2-enoate*

MS (EI) m/z: 369 (12%), 337 (13%), 313 (100%), 301 (13%), 271 (3%), 215 (42%), 179 (20%), 157 (11%), 145 (29%), 115 (14%), 75 (17%).

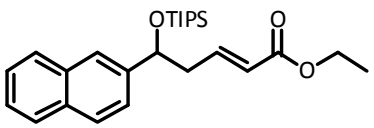
GC-MS elution peak: 18.90 min.



$C_{25}H_{36}O_3Si$
Exact Mass: 412,24
Molecular Weight: 412,64

• *Compound **IV:** (E)-Ethyl-5-(naphthalen-2-yl)-5-((triisopropylsilyl)oxy)pent-2-enoate*

MS (EI) m/z: 383 (14%), 337 (14%), 313 (100%), 271 (6%), 227 (19%), 199 (14%), 179 (10%), 159 (11%), 115 (10%), 75 (9%).



$C_{26}H_{38}O_3Si$
Exact Mass: 426,26
Molecular Weight: 426,66

GC-MS elution peak: 19.24 min.

GC/MS-Experiment (Fig. 89): A sealable vial with septum was charged with **40** or **41** (1 equiv) and 2-naphtaldehyde (1 equiv) and the solids were dissolved in CH_2Cl_2 (1 mL). The vial was either stirred at r.t. or installed in a dry ice/acetone bath. A mixture of **47** and **52** (1:1 mixture; 3 equivs in total with respect to the aldehyde) was added via syringe and the resulting mixture stirred for 30 min before quenching with $NaHCO_3$-solution. The organic layer was separated, dried, evaporated and the product distribution examined by GC-MS:

Distribution (**I** to **II** to **III** to **IV**) with **40** at r.t.: 1 : 1 : 0.8 : 0.8.

Distribution (**I** to **II** to **III** to **IV**) with **40** at -78°C: 0.9 : 1 : 0.6 : 0.7.

Distribution (**I** to **II** to **III** to **IV**) with **41** at r.t.: 1 : 0.9 : 0.9 : 0.8.

Distribution (**I** to **II** to **III** to **IV**) with **41** at -78°C: 1 : 1 : 0.7 : 0.8.

GC/MS-Experiment (Fig. 90): An NMR-tube was filled with **40** (1 equiv), dried under vacuum and flushed with Argon at r.t. Subsequently CD_2Cl_2 or Et_2O-d10 (0.5 mL) was added, followed by the corresponding TMS-source (1.0 equiv), the mixture is controlled by ^{1}H-NMR-spectroscopy, and TMS-source is added in small portions, until a complete shift of the signal set of compound is observed. After the complete formation of the active species, the solution is added to a vial containing the aldehyde (1 equiv) and a mixture of **47** and **52** (1:1 mixture; 2 equivs in total with respect to the aldehyde) at the respective temperature. The resulting reaction mixture is stirred for 30 min, after which a solution of $NaHCO_3$ is added, the organic layer separated, dried, evaporated and the product distribution examined by GC-MS:

Distribution (**I** to **II** to **III** to **IV**) at r.t. with TMS-dienolate in Et_2O-d10: 1 : 1 : 0.8 : 0.8.

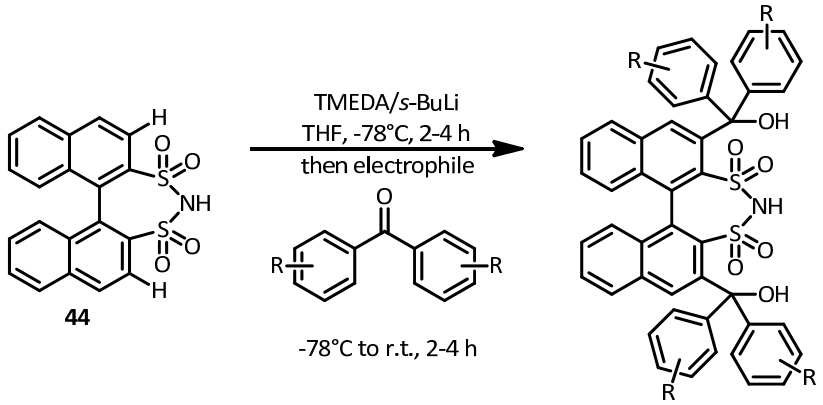
Distribution (**I** to **II** to **III** to **IV**) at -78°C with TMS-dienolate in Et_2O-d10: 0.9 : 1 : 0.2 : 0.2

Distribution (**I** to **II** to **III** to **IV**) at r.t. with TMS-enolate in Et_2O-d10: 1 : 0.6 : 0.6 : 0.2.

Distribution (**I** to **II** to **III** to **IV**) at r.t. with TMS-enolate in CD_2Cl_2: 0.9 : 1 : 0.4 : 0.4.

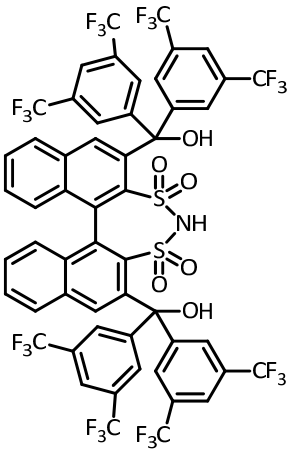
7.5 Synthesis of new catalysts

7.5.1 Preparation of hydroxy-disulfonimides:

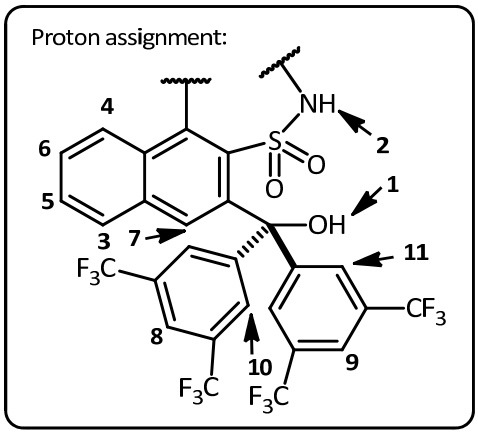


General synthetic procedure (GSP 4): A flame dried two neck-flask with stirring equipment, Argon-inlet and rubber septum is charged with **44** (1.0 equiv). Subsequently the solid is dissolved in dry THF [0.1*M*] followed by dry TMEDA (3.5 equiv). After complete addition the solution turns turbid and is stirred for 0.5 h. Subsequently the reaction mixture is cooled to -78°C. At this temperature *sec*-butyllithium (1.4*M* solution in cyclohexane, 3.5 equiv) is added slowly, upon which the reaction mixture turns green. After complete addition, the reaction is stirred for 2-4 h at -78°C. At this time the solution should turn dark green / black. Subsequently a solution of the electrophile (4 equiv) in dry THF (least amount possible) is added dropwise at -78°C. After complete addition the cooling is removed and the resulting mixture is allowed to reach room temperature and stirred for 2 h. The reaction is quenched by careful addition of H_2O. Subsequently the mixture is transferred to a separation funnel and extracted with CH_2Cl_2 (two times). The united organic layers are dried with $MgSO_4$, filtered and the solvent evaporated. The residue is subjected to column chromatography (ethyl acetate / *i*PrOH 20:1) giving the resulting hydroxy-disulfonimide as salt. Acidification can be accomplished by subsequently dissolving in dichloromethane and thorough shaking with 4*M* HCl solution. The resulting organic layer is then evaporated and dried carefully in high vacuum.

• *Compound **145:** 2,6-Bis(bis(3,5-bis(trifluoromethyl)phenyl)(hydroxy)-methyl)dinaphtho-[2,1-d:1',2'-f][1,3,2]dithiazepine 3,3,5,5-tetraoxide*

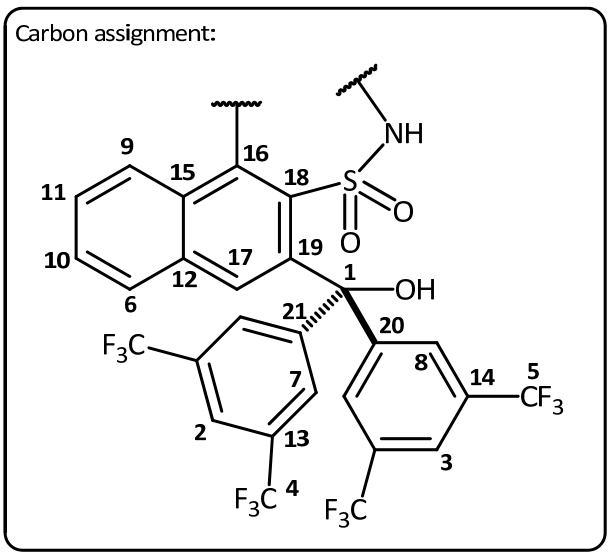


$C_{54}H_{25}F_{24}NO_6S_2$
Exact Mass: 1303,07
Molecular Weight: 1303,87



The reaction was conducted on a 1.27 mmol scale following (**GSP 4**), affording the desired product **145** as a yellow-brownish solid (571 mg, 0.44 mmol, 35% yield).

^{1}H-NMR (500 MHz, C_6D_6, 60°C) δ [ppm]: 6.17 (bs, 2H, -OH **1**), 6.35 (bs, 1H, -NH **2**), 6.76 (dd, 2H, ^{3}J = 8.4 Hz, ^{4}J = 1.3 Hz, -CH_{Ar} **3**), 6.81 (d, 2H, ^{3}J = 8.0 Hz, -CH_{Ar} **4**), 6.84 (ddd, 2H, ^{3}J = 8.5 Hz, ^{3}J = 6.8 Hz, ^{4}J = 1.4 Hz, -CH_{Ar} **5**), 6.89 (ddd, 2H, ^{3}J = 8.0 Hz, ^{3}J = 6.8 Hz, ^{4}J = 1.3 Hz, -CH_{Ar} **6**), 7.23 (s, 2H, -CH_{Ar} **7**), 7.71 (s, 2H, -CH_{Ar} **8**), 7.79 (s, 2H, -CH_{Ar} **9**), 7.99 (bs, 4H, -CH_{Ar} **10**), 8.07 (bs, 4H, -CH_{Ar} **11**).



^{13}C-NMR (125 MHz, C_6D_6, 60°C) δ [ppm]: 82.0 (C **1**), 122.6, 122.6 (C **2**, **3**, 2d, $^{C\text{-}F}J$ = 3.5 Hz), 123.5, 123.5 (C **4**, **5**, 2q, $^{C\text{-}F}J$ = 273 Hz), 127.6 (C **6**), 128.0 (C **7**), 128.1 (C **8**), 129.3 (C **9**), 130.2

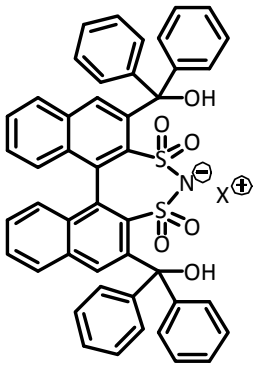
(C **10**), 131.1 (C **11**), 132.6 (C **12**), 132.7, 132.8 (C **13**, **14**, 2q, $^{C\text{-}F}J$ = 34.1 Hz), 133.4 (C **15**), 133.5 (C **16**), 134.2 (C **17**), 137.5 (C **18**), 142.5 (C **19**), 148.5 (C **20**), 150.1 (C **21**).

^{19}F-NMR (470 MHz, C_6D_6) δ [ppm]: -62.97, -62.81.

MS (ESI-neg) m/z: 1303 (100%).

HRMS (ESI-neg) m/z (M-H): calcd. 1302.0666, found 1302.0667.

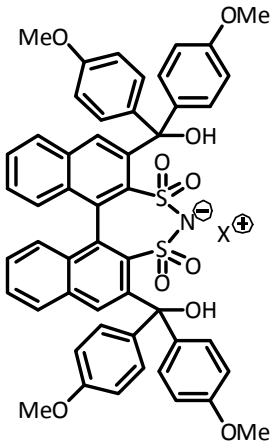
• *Compound **146:** 2,6-Bis(hydroxydiphenylmethyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dithiazepine 3,3,5,5-tetraoxide (salt-form)*



^{1}H-NMR (500 MHz, MeOD) δ [ppm]: 6.79 (d, 2H, ^{3}J = 8.5 Hz, -C$\underline{H}_{Ar}$), 7.19-7.30 (m, 22H, -C$\underline{H}_{Ar}$), 7.39-7.42 (m, 2H, -C$\underline{H}_{Ar}$), 7.47 (d, 2H, ^{3}J = 8.1 Hz, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, MeOD) δ [ppm]: 84.30, 127.99, 128.08, 128.46, 128.66, 128.84, 129.07, 129.29, 129.37, 129.48, 133.40, 133.46, 133.94, 140.50, 141.25, 141.54, 148.45, 150.33.

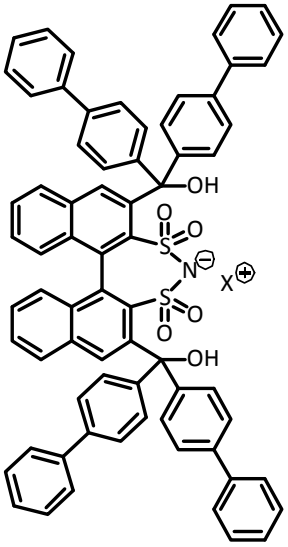
• *Compound **147:** 2,6-bis(hydroxybis(4-methoxyphenyl)methyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dithiazepine 3,3,5,5-tetraoxide (salt-form)*



^{1}H-NMR (500 MHz, MeOD) δ [ppm]: 3.78 (s, 6H, -OC$\underline{H}_3$), 3.79 (s, 6H, -OC$\underline{H}_3$), 6.77 (d, 2H, ^{3}J = 9.0 Hz, -C$\underline{H}_{Ar}$), 6.83-6.86 (m, 8H, -C$\underline{H}_{Ar}$), 7.16-7.21 (m, 8H, -C$\underline{H}_{Ar}$), 7.23 (s, 2H, -C$\underline{H}_{Ar}$), 7.39-7.42 (m, 2H, -C$\underline{H}_{Ar}$), 7.50 (d, 2H, ^{3}J = 8.5 Hz).

^{13}C-NMR (125 MHz, MeOD) δ [ppm]: 55.60, 55.66, 83.95, 113.93, 128.35, 128.89, 129.02, 129.33, 130.49, 130.67, 133.33, 133.45, 133.98, 140.63, 140.81, 141.30, 142.16, 142.71, 160.03, 160.07.

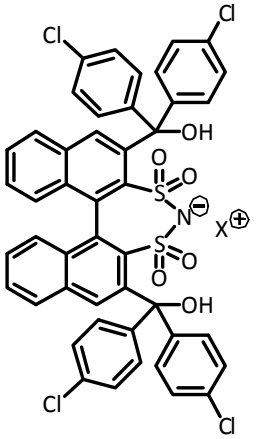
• *Compound **148:** 2,6-bis(di([1,1'-biphenyl]-4-yl)(hydroxy)methyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dithiazepine 3,3,5,5-tetraoxide (salt-form)*



^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: 1.25 (bs), 1.79 (bs), 6.85 (d, 2H, ^{3}J = 8.7 Hz, -C$\underline{H}_{Ar}$), 7.24-7.46 (m, 26H, -C$\underline{H}_{Ar}$), 7.54-7.61 (m, 18H, , -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, CD_2Cl_2) δ [ppm]: 82.43, 126.33, 126.43, 126.90, 126.97, 127.33, 127.42, 127.58, 127.92, 128.34, 128.44, 128.66, 128.78, 128.86, 132.31, 132.66, 132.77, 138.41, 139.51, 139.55, 139.68, 139.87, 140.35, 140.49, 146.37, 147.97.

• *Compound **149:** 2,6-bis(bis(4-chlorophenyl)(hydroxy)methyl)dinaphtho[2,1-d:1',2'-f][1,3,2]dithiazepine 3,3,5,5-tetraoxide (salt-form)*



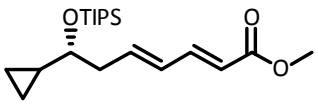
^{1}H-NMR (500 MHz, MeOD) δ [ppm]: 6.84 (d, 2H, ^{3}J = 8.6 Hz, -C$\underline{H}_{Ar}$), 7.22-7.25 (m, 2H, -C$\underline{H}_{Ar}$), 7.27 (s, 2H, -C$\underline{H}_{Ar}$), 7.30-7.37 (m, 16H, -C$\underline{H}_{Ar}$), 7.44-7.47 (m, 2H, -C$\underline{H}_{Ar}$), 7.58 (d, 2H, ^{3}J = 9.0 Hz, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, MeOD) δ [ppm]: 83.37, 128.73, 128.79, 128.85, 129.33, 129.40, 130.81, 131.03, 133.20, 133.41, 133.93, 133.98, 134.09, 140.09, 140.68, 141.44, 147.06, 148.70.

7.5.2 Synthesis of challenging VMAR and DVMAR-products

• *Compound **150:** (2E,4E)-Methyl-7-cyclopropyl-7-((triisopropylsilyl)oxy)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing cyclopropanecarbaldehyde (15 mg, 1 equiv) and **100** (85 mg, 0.30 mmol) affording the desired product **150** as a colorless liquid (31 mg, 0.09 mmol, 44% yield).



$C_{20}H_{36}O_3Si$
Exact Mass: 352,24
Molecular Weight: 352,58

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.13-0.18 (m, 1H, -C<u>H</u>$_2$-), 0.31-0.35 (m, 1H, -C<u>H</u>$_2$-), 0.42-0.50 (m, 2H, -C<u>H</u>$_2$-), 0.86-0.94 (m, 1H, -C<u>H</u>-), 1.04-1.06 (m, 22H, -Si(C<u>H</u>(C<u>H</u>$_3$)$_2$)$_3$), 2.42-2.51 (m, 2H, -C<u>H</u>$_2$-CH=), 3.30-3.33 (m, 1H, -C<u>H</u>-O-), 3.74 (s, 3H, -OC<u>H</u>$_3$), 5.79 (d, 1H, ^3J-*trans* = 15.4 Hz, =C<u>H</u>-C=O), 6.19-6.30 (m, 2H, -CH$_2$-C<u>H</u>= and -CH=C<u>H</u>-), 7.28 (dd, 1H, ^3J-*trans* = 15.1 Hz, ^3J = 10.1 Hz, -CH=C<u>H</u>-).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 2.35 (DEPT 135 negative), 4.04 (DEPT 135 negative), 12.88, 17.58, 18.34, 18.38, 42.49 (DEPT 135 negative), 51.61, 75.86, 119.04, 130.29, 141.36, 145.38, 167.91.

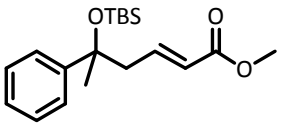
MS (EI) m/z: 309 (44%), 227 (100%), 157 (18%), 145 (15%), 115 (14%), 75 (23%), 59 (16%).

HRMS (ESI-pos) m/z (M+Na): calcd. 375.2327, found 375.2326.

HPLC: Daicel Chiralpak OD-H, *n*-heptane:*i*-PrOH = 98:2, flow: 0.5 ml/min, 25°C, absorption at 254 nm, t_{R1} = 2.45 min/ t_{R2} = 3.03 min.

• *Compound **151:** (2E,4E)-Methyl-7-cyclopropyl-7-((triisopropylsilyl)oxy)hepta-2,4-dienoate*

The reaction was conducted on a 0.20 mmol scale following (**GSP 2**), utilizing acetophenone (23 mg, 1 equiv) and **50** (85 mg, 0.30 mmol) affording the desired product **151** as a colorless liquid (4 mg, 0.01 mmol, 6% yield).



$C_{19}H_{30}O_3Si$
Exact Mass: 334,20
Molecular Weight: 334,53

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: -0.08, 0.08 (s, 6H, -Si(C<u>H</u>$_3$)$_2$-), 0.94 (s, 9H, -Si(C(C<u>H</u>$_3$)$_3$), 1.64 (s, 3H, -C-C<u>H</u>$_3$), 2.59 (ddd, 1H, ^4J = 1.3 Hz, ^3J = 14.3 Hz, 7.7 Hz, -C<u>H</u>$_2$-CH=), 2.69 (ddd, 1H, ^4J = 1.4 Hz, ^3J = 14.2 Hz, 7.3 Hz, -C<u>H</u>$_2$-CH=), 3.68 (s, 3H, -OC<u>H</u>$_3$), 5.73 (d, 1H, ^3J-*trans* = 15.7 Hz, =C<u>H</u>-C=O), 6.82 (ddd, 1H, ^3J-*trans* = 15.7 Hz, ^3J = 8.0 Hz,

7.4 Hz, -CH=C<u>H</u>-), 7.21-7.24 (m, 1H, -C<u>H</u>$_{Ar}$), 7.30-7.33 (m, 2H, -C<u>H</u>$_{Ar}$), 7.40-7.42 (m, 2H, -C<u>H</u>$_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: -2.21, -1.74, 18.63, 26.20, 29.02, 49.13 (DEPT 135 negative), 51.52, 76.71, 123.41, 125.35, 126.91, 128.12, 145.72, 147.65, 167.52.

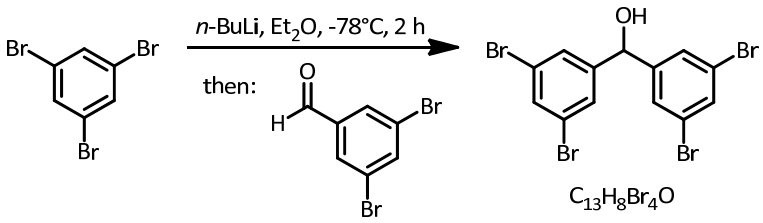
MS (EI) m/z: 319 (1%), 277 (23%), 235 (100%), 209 (10%), 177 (15%), 157 (58%), 89 (17%), 73 (45%).

HRMS (ESI-pos) m/z (M+Na): calcd. 357.1855, found 357.1856.

HPLC: Daicel Chiralpak OD-H, *n*-heptane:*i*-PrOH = 98:2, flow: 0.5 ml/min, 25°C, absorption at 220 nm, t_{R1} = 9.42 min/ t_{R2} = 14.02 min.

7.5.3 Synthesis of an electron-poor ketone substituent for hydroxy-disulfonimides

• *Compound **152:** Bis(3,5-dibromophenyl)methanol*



$C_{13}H_8Br_4O$
Exact Mass: 495,73
Molecular Weight: 499,82

A 250 mL three-necked round bottom flask with stirring bar, Argon-inlet and septum was charged with 2.60 g (8.3 mmol, 1 equiv) set under Argon and filled with dry Et_2O (150 mL). The resulting mixture was stirred and cooled to -78°C. Subsequently *n*-butyllithium (2.5*M* in hexane, 3.32 mL, 8.3 mmol, 1 equiv) was added slowly via syringe over 60 min and the resulting mixture stirred for 2 h at -78°C. After this time a solution of 3,5-dibromobenzaldehyde (2.40 g, 9.1 mmol, 1.1 equiv.) in dry Et_2O (30 mL) was added over 5 min. The resulting reaction mixture was stirred for 2 additional hours at -78°C, then allowed to reach room temperature and quenched with MeOH (100 mL). The reaction mixture was transferred to a separation funnel, washed with H_2O (200 mL), the organic layer dried with $MgSO_4$, filtered and evaporated. The resulting crude material was subjected to column chromatography (hexane/ethyl acetate 8:1) furnishing **152** as a slightly orange solid (2.56 g, 5.1 mmol, 62% yield).

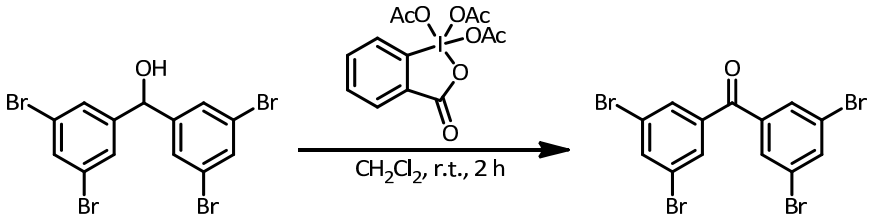
^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: 2.34 (bs, 1H), 5.67 (s, 1H), 7.43 (dd, 4H, ^4J = 1.7 Hz, 0.5 Hz), 7.60 (t, 2H, ^4J = 1.7 Hz).

^{13}C-NMR (125 MHz, CD_2Cl_2) δ [ppm]: 74.01, 123.52, 128.41, 133.96, 146.28.

MS (EI) m/z: 500 (34%), 419 (15%), 263 (100%), 237 (16%), 183 (11%), 156 (29%), 75 (35%).

HRMS (ESI-pos) m/z (M+Na): calcd. 518.7199, found 518.7201.

• *Compound **153:** Bis(3,5-dibromophenyl)methanone*



$C_{13}H_6Br_4O$
Exact Mass: 493,72
Molecular Weight: 497,80

A 50 mL round bottom flask was charged with bis(3,5-dibromophenyl)methanol (1.00 g, 2.0 mmol, 1 equiv.) and CH_2Cl_2 (25 mL). To the resulting solution was added Dess-Martin periodinane (1.00 g, 2.4 mmol, 1.2 equiv.) as a solid and the resulting mixture was stirred until TLC-control showed complete consumption. After the completion of the reaction the solvent was evaporated and the crude reaction product was absorbed on silica gel. Subsequent column chromatography (hexane/ethyl acetate mixtures) provided **153** as a slightly orange solid (0.71 g, 1.43 mmol, 71% yield).

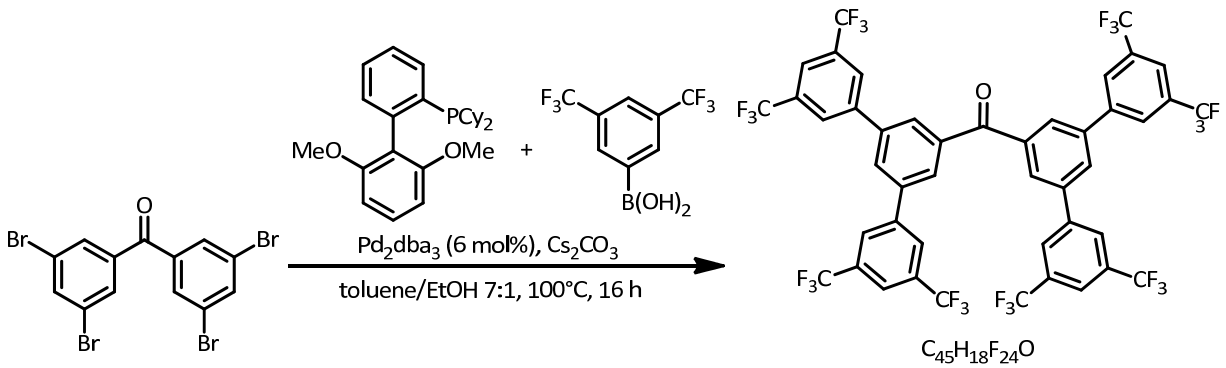
^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 7.78 (d, 4H, ^4J = 1.8 Hz), 7.91 (t, 2H, ^4J = 1.7 Hz).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 123.36, 131.38, 138.36, 139.54, 190.83.

MS (EI) m/z: 498 (52%), 417 (4%), 263 (100%), 235 (37%), 154 (14%), 75 (44%).

HRMS (ESI-pos) m/z (M+Na): calcd. 516.7045, found 516.7045.

• *Compound **154:** Bis(3,3'',5,5''-tetrakis(trifluoromethyl)-[1,1':3',1''-terphenyl]-5'-yl)methanone*



$C_{45}H_{18}F_{24}O$
Exact Mass: 1030,10
Molecular Weight: 1030,59

A dry 25 mL Schlenck tube was charged with bis(3,5-dibromophenyl)methanone (0.50 g, 1.0

mmol, 1 equiv.) set under Argon and subsequently filled with dry toluene (11 mL) and EtOH (1.5 mL). The resulting slurry was thoroughly degassed with a stream of Argon for 10 min. A dry 50 mL Schlenck-tube was charged with (3,5-bis(trifluoromethyl)phenyl)boronic acid (1.56 g, 6.0 mmol, 6 equiv.), Pd_2dba_3 (55 mg, 0.06 mmol, 6 mol%), S-Phos (62 mg, 0.15 mmol, 15 mol%) and Cs_2CO_3 (3.26 g, 10.0 mmol, 10 equiv.) and set under Argon. The solution of bis(3,5-dibromophenyl)methanone in toluene/EtOH was added, the resulting red mixture degassed with a stream of Argon for 1 min, the Schlenck-tube sealed with a stopper and heated and stirred for 16 h at 100°C. The mixture was allowed to reach r.t, diluted with ethyl acetate (20 mL), filtered through a pad of silica gel and Celite, evaporated to dryness and subjected to column chromatography (hexane/ethyl acetate 35:1). The product **154** was obtained as a white solid (970 mg, 0.94 mmol, 94% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 7.96 (bs, 4H), 8.06-8.07 (m, 10H), 8.13-8.13 (m, 4H).

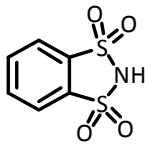
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 122.39 (m), 123.24 (q, ^{C-F}J = 272.7 Hz), 127.70 (d, ^{C-F}J = 2.3 Hz), 129.12, 130.75, 132.87 (q, ^{C-F}J = 33.6 Hz), 139.24, 140.56, 141.62, 194.54.

MS (EI) m/z: 1030 (59%), 529 (100%), 481 (16%), 432 (11%).

HRMS (EI) m/z: calcd. 1030.0981, found 1030.0975.

7.5.4 Synthesis of an achiral hydroxy-disulfonimide

• *Compound **40:** Benzo[d][1,3,2]dithiazole 1,1,3,3-tetraoxide*



$C_6H_5NO_4S_2$
Exact Mass: 218,97
Molecular Weight: 219,24

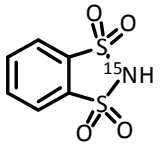
Benzene-1,2-disulfonyl dichloride (1.00 g, 3.63 mmol, 1.0 equiv) are dissolved in toluene (35 mL) at r.t. Subsequently NH_3-solution (7*M* in MeOH, 5.20 mL) is added in one shot and the resulting mixture stirred overnight. After this time a white precipitate formed. The solvents are removed in vacuo and the resulting crude material subjectd to a column chromatography with Amberlite IR120 (hydrogen form). For this purpose a standard glass column is charged with the resin and washed with water until the pH of the eluent water appears to be neutral. Subsequently the column is charged with a solution of the crude material in water and eluted with water. The fractions with a pH of 1 are collected and the water evaporated, giving a solid product which is thoroughly dried under vacuum giving the desired product **40** (712 mg, 3.24 mmol, 89% yield) as a white solid.

^{1}H-NMR (500 MHz, MeOH) δ [ppm]: 7.79-7.82 (m, 2H, -C$\underline{H}_{Ar}$), 7.85-7.89 (m, 2H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, MeOH) δ [ppm]: 122.31, 134.34, 142.68.

MS (EI) m/z: 219 (100%), 156 (74%), 108 (22%), 91 (47%), 76 (50%), 64 (51%), 50 (59%).

HRMS (ESI-neg) m/z (M-H): calcd. 217.9589, found 217.9587.



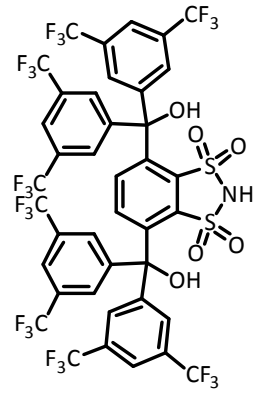
$C_6H_5{}^{15}NO_4S_2$
Exact Mass: 219,96
Molecular Weight: 220,23

A two necked flask with stirring equipment, a rubber septum and a solution of benzene-1,2-disulfonyl dichloride in a mixture of toluene / EtOH (4:1) is capped with a reflux condenser with Argon-inlet. The reflux condenser is connected to cryostatic equipment and cooled to -70°C. Following, a gas bottle with $^{15}NH_3$-gas is connected with a rubber tube with a needle and the gas injected directly into the solution and the mixture refluxed. The conversion of the starting material is controlled by TLC and the cooling equipment removed upon maximum conversion. The reaction is processed further like for the non-marked material.

MS (EI) m/z: 220 (100%), 156 (95%), 140 (9%), 108 (33%), 92 (64%), 80 (23%), 76 (40%), 64 (43%), 50 (40%).

HRMS (EI) m/z: calcd. 219.9631, found 219.9630.

• *Compound **155:** 4,7-Bis(bis(3,5-bis(trifluoromethyl)phenyl)(hydroxy)methyl)benzo[d]-[1,3,2]dithiazole-1,1,3,3-tetraoxide*



$C_{40}H_{17}F_{24}NO_6S_2$
Exact Mass: 1127,01
Molecular Weight: 1127,66

The reaction was conducted on a 1.14 mmol scale following (**GSP 4**) in 10-fold dilution, affording the desired product **155** as a yellow solid (571 mg, 0.51 mmol, 44% yield).

^{1}H-NMR (500 MHz, CD_2Cl_2) δ [ppm]: 4.65 (bs, 2H, -OH), 4.99 (bs, 1H, -NH), 7.22 (s, 2H, -C$\underline{H}_{Ar}$), 7.73 (s, 8H, -C$\underline{H}_{Ar}$), 7.95 (s, 4H, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, MeOH) δ [ppm]: 81.81, 123.21 (t, $^{C\text{-}F}J$ = 4.3 Hz), 124.66 (q, $^{C\text{-}F}J$ = 271.54 Hz), 129.59 (d, $^{C\text{-}F}J$ = 3.0 Hz), 132.72 (q, $^{C\text{-}F}J$ = 32.8 Hz), 134.42, 143.18, 145.32, 148.50.

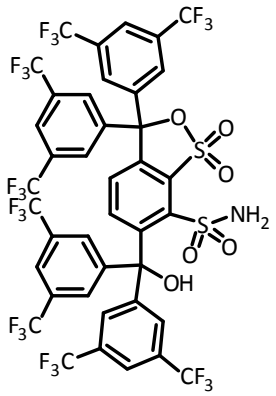
^{19}F-NMR (376 MHz, CD_2Cl_2) δ [ppm]: -63.34.

IR (ATR Diamond bridge) [cm^{-1}]: 681, 708, 799, 845, 899, 1120, 1275, 1372, 1626, 1701.

MS (ESI-neg) m/z (M-Na): 1149.

HRMS (ESI-pos) m/z (M+Na+Na): calcd. 1171.9837, found 1171.9826.

• *Compound **155a:** 6-(Bis(3,5-bis(trifluoromethyl)phenyl)(hydroxy)methyl)-3,3-bis(3,5-bis(trifluoromethyl)phenyl)-3H-benzo[c][1,2]oxathiole-7-sulfonamide-1,1-dioxide*



Chemical Formula: $C_{40}H_{17}F_{24}NO_6S_2$
Exact Mass: 1127,01
Molecular Weight: 1127,66

Compound **155a** was occasionally obtained during the workup process of **155**, e.g. after prolonged exposure to acid solutions.

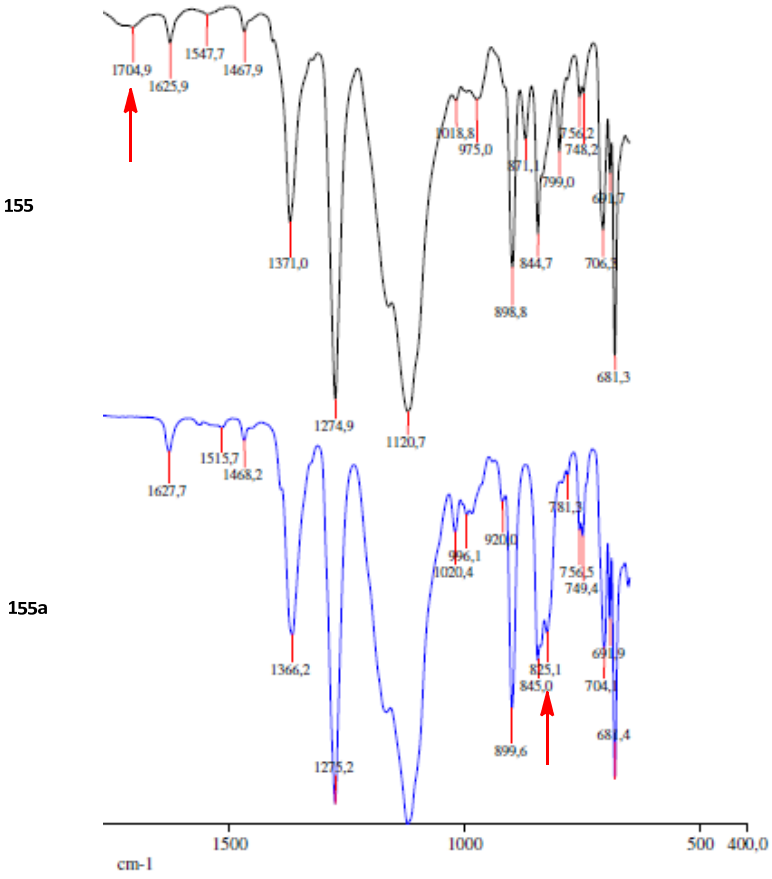
^{1}H-NMR (400 MHz, MeOH) δ [ppm]: 5.86 (d, 1H, ^{3}J = 8.4 Hz), 6.19 (s, 4H), 6.26 (d, 1H, ^{3}J = 8.4 Hz), 6.34 (s, 4H), 6.49 (s, 2H), 6.63 (s, 2H).

^{13}C-NMR (125 MHz, MeOH) δ [ppm]: 84.59, 89.43,

124.23 (q, $^{C\text{-}F}J$ = 272.3 Hz), 124.54 (q, $^{C\text{-}F}J$ = 272.3 Hz), 129.33 (t, broad), 130.30, 132.97 (q, $^{C\text{-}F}J$ = 32.8 Hz), 133.76 (q, $^{C\text{-}F}J$ = 33.9 Hz), 136.29, 140.01, 142.35, 142.80, 142.88, 147.65, 149.77.

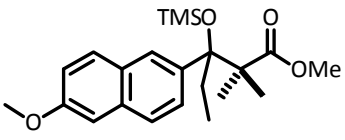
^{19}F-NMR (376 MHz, MeOH) δ [ppm]: -66.02, -66.01.

IR (ATR Diamond bridge) [cm^{-1}]: 681, 704, 750, 826, 845, 899, 1020, 1120, 1275, 1366, 1627.



7.5.5 Preparation of the precursor for Methallenestril

• *Compound **156:** Methyl-3-(6-methoxynaphthalen-2-yl)-2,2-dimethyl-3-((trimethylsilyl)-oxy)pentanoate*



$C_{22}H_{32}O_4Si$
Exact Mass: 388,21
Molecular Weight: 388,57

The reaction was conducted on a 0.20 mmol scale following (**GSP 3**), utilizing 1-(6-methoxynaphthalen-2-yl)propan-1-one (43 mg, 1 equiv) and ((1-methoxy-2-methylprop-1-en-1-yl)oxy)trimethylsilane (61 µl, 1.5 equiv). The corresponding yield of product **156** was measured by addition of triphenlymethane (1 equiv) as an internal standard.

^{1}H-NMR (500 MHz, $CDCl_3$) δ [ppm]: 0.23 (s, 9H, -SiC$\underline{H}_3$)$_3$), 0.72 (t, 3H, ^3J = 7.3 Hz, -CH_2-C$\underline{H}_3$), 1.08, 1.17 (s, 6H, -C(C$\underline{H}_3$)$_2$), 1.99-2.07 (m, 1H, -C$\underline{H}_2$-CH_3), 2.53-2.61 (m, 1H, -C$\underline{H}_2$-CH_3), 3.56 (s, 3H, -OC$\underline{H}_3$), 3.92 (s, 3H, -OC$\underline{H}_3$), 7.13-7.15 (m, 2H, -C$\underline{H}_{Ar}$), 7.31 (dd, 1H, ^3J = 8.4 Hz, ^4J = 1.5 Hz, -C$\underline{H}_{Ar}$), 7.63-7.66 (m, 2H, -C$\underline{H}_{Ar}$), 7.73 (d, 1H, ^3J = 8.6, -C$\underline{H}_{Ar}$).

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 2.73, 9.67, 22.11, 22.21, 27.23 (DEPT 135 negative), 51.56, 53.17, 55.47, 85.72, 105.42, 118.68, 125.18, 126.62, 126.69, 128.30, 129.87, 133.34, 137.67, 157.72, 177.07.

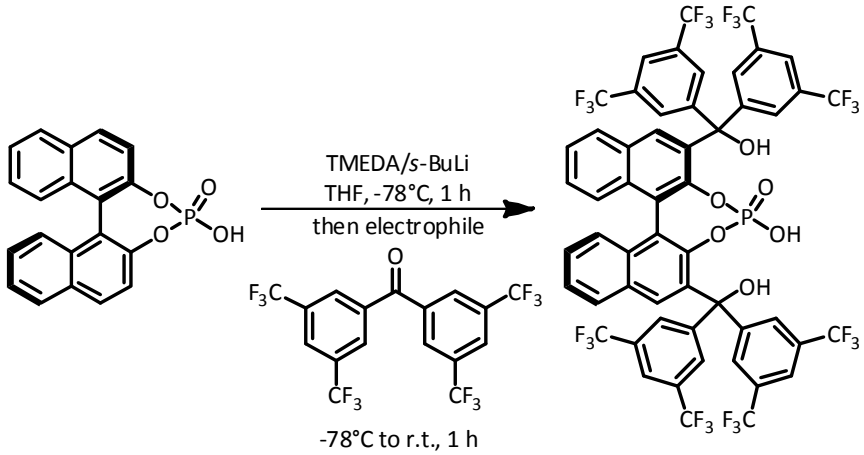
MS (EI) m/z: 373 (1%), 287 (100%), 271 (3%), 185 (4%), 89 (4%), 73 (31%)

HRMS (ESI-pos) m/z (M+Na): calcd. 411.1965, found 411.1962.

HPLC: no separation method found.

7.5.6 Synthesis of a hydroxy-phosphoric acid

• *Compound **157:** 2,6-bis(bis(3,5-bis(trifluoromethyl)phenyl)(hydroxy)methyl)-4-hydroxy-dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine 4-oxide*



$C_{54}H_{25}F_{24}O_6P$
Exact Mass: 1256,10
Molecular Weight: 1256,71

The reaction was conducted on a 0.72 mmol scale following (**GSP 4**) in 10-fold dilution, affording the desired product **157** as a yellow solid (379 mg, 0.30 mmol, 42% yield).

^{1}H-NMR (500 MHz, CH_2Cl_2) δ [ppm]: 7.19 (d, 2H, ^{3}J = 8.6 Hz, -C$\underline{H}_{Ar}$), 7.29 (s, 2H, -C$\underline{H}_{Ar}$), 7.32 (bs, 3H, -O$\underline{H}$), 7.39 (dd, 2H, ^{3}J = 8.0 Hz, 7.5 Hz, -C$\underline{H}_{Ar}$), 7.51 (dd, 2H, ^{3}J = 7.9 Hz, 7.5 Hz, -C$\underline{H}_{Ar}$), 7.72 (s, 2H, -C$\underline{H}_{Ar}$), 7.76 (d, 2H, ^{3}J = 8.3 Hz, -C$\underline{H}_{Ar}$), 7.90 (s, 4H, -C$\underline{H}_{Ar}$), 7.91 (s, 2H, -C$\underline{H}_{Ar}$), 7.98 (s, 4H, -C$\underline{H}_{Ar}$).

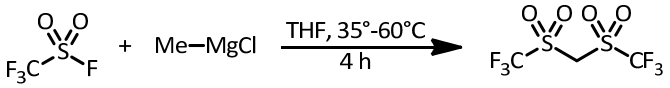
^{13}C-NMR (125 MHz, CH_2Cl_2) δ [ppm]: 80.14, 121.83 (broad), 122.44 (broad), 123.19 (q, ^{C-F}J = 272.5 Hz), 123.28 (q, ^{C-F}J = 272.5 Hz), 124.03 (d, ^{C-P}J = 1.9 Hz), 126.19, 126.47 (broad), 127.31, 128.21 (broad), 128.69, 129.22, 130.70, 131.73 (q, ^{C-F}J = 32.9 Hz), 131.79 (q, ^{C-F}J = 33.2 Hz), 132.84, 133.85 (d, ^{C-P}J = 2.1 Hz), 144.44, 144.52, 146.05, 149.08.

^{31}P-NMR (202 MHz, CH_2Cl_2) δ [ppm]: 2.60.

MS (ESI-neg) m/z (M-H): 1255.

7.5.7 Preparation of carbon-based Brønsted-acid-precursors and -catalysts

• *Compound **158:** Bis((trifluoromethyl)sulfonyl)methane*



$C_3H_2F_6O_4S_2$
Exact Mass: 279,93
Molecular Weight: 280,17

A flame dried 250 mL three-necked flask with stirring bar, septum, thermometer and a reflux condenser with an Argon-inlet was charged with a commercial 3*M* MeMgCl-solution in THF (99.00 mL, 296.00 mmol, 3 equiv). The reflux condenser was connected to cryogenic cooling equipment and equilibrated at -70°C. The solution was stirred and trifluoromethanesulfonyl fluoride (15.00 g, 99.00 mmol, 1 equiv) was added via syringe over a period of 1 h.[XXIV] The reaction heat was removed with an ice-water bath and the mixture kept in a temperature-range of 35°-50°C (highly exothermic reaction!!!). After the complete gas addition, the septum was exchanged by a glas-stopper, and the mixture heated to 60°C. After this time the reaction was cooled with an ice bath and carefully (!!!) quenched with a 1*M* HCl-soln. until the exothermic reaction ceased. The resulting organic phase was separated and the THF distilled off. The residue was stirred with a 1*M* HCl-soln. and extracted with Et_2O (3 times). The residue was distilled and afforded 4.00 g (14.30 mmol, 14% yield) of the reaction product **158** which solidified upon distillation.

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 4.88.

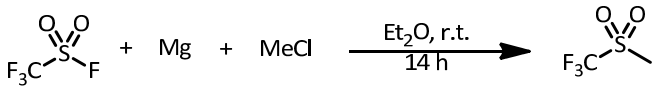
^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 63.90, 118.43 (q).

MS (EI) m/z: 216 (2%), 211 (4%), 147 (4%), 131 (14%), 117 (5%), 99 (3%), 69 (100%), 62 (6%), 48 (4%).

HRMS (CI) m/z (M+H): calcd. 280.9375, found 280.9377.

[XXIV] The gas bottle was connected to a PVC-tube and a long syringe, the addition of the correct amount of reactant was controlled with a gas-balance.

• *Compound **159:** Trifluoro(methylsulfonyl)methane*



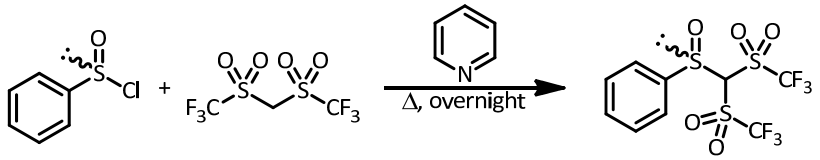
$C_2H_3F_3O_2S$
Exact Mass: 147,98
Molecular Weight: 148,10

A flame dried 1000 mL three-necked flask with stirring bar, septum, thermometer and a reflux condenser with an Argon-inlet was charged with Mg-turnings (11.99 g, 493.00 mmol, 3 equiv) and dry Et_2O (329 mL). The reflux condenser was connected to cryogenic cooling equipment and equilibrated at -70°C. The mixture was efficiently stirred and methyl chloride (24.90 g, 493.00 mmol, 3 equiv) were added during 2 h (gas-balance) The mixture turned cloudy and grey, and the Mg was completely consumed. After all the Mg reacted, the mixture was stirred for another 30 min, before trifluoromethanesulfonyl fluoride (25.00 g, 164.00 mmol, 1 equiv) was added via syringe over a period of 1-2 h (gas-balance). After complete addition, the reaction was stirred overnight. Since the reaction mixture became very viscous, the reaction mixture was diluted with Et_2O and subsequently quenched with 100 mL of a 3*M* HCl, upon which a strong (!!!) exothermic reaction occurred. After the temperature reached r.t. again, the reaction mixture was extracted with Et_2O (three times) and the organic layer dried with $MgSO_4$, and evaporated. The resulting residue was treated with 1M HCl-soln. (90 mL) and subsequently extracted with ether (three times). The organic layers were united, dried and evaporated, and the resulting residue purified by distillation. The reaction product **159** was obtained as a yellowish liquid (7.48 g, 50.51 mmol, 31% yield).

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 3.17.

^{13}C-NMR (125 MHz, $CDCl_3$) δ [ppm]: 36.51, 119.17 (q).

• *Compound **160:** ((Bis((trifluoromethyl)sulfonyl)methyl)sulfinyl)benzene*



$C_9H_6F_6O_5S_3$
Exact Mass: 403,93
Molecular Weight: 404,33

A flame dried 50 mL two-necked flask with stirring bar, septum and a reflux condenser with an Argon-inlet was charged with **158** (2.51 g, 8.96 mmol, 1.2 equiv) and pyridine (30 mL) was added slowly under stirring. After complete addition of pyridine benzenesulfinic chloride (1.20 g, 7.47 mmol, 1 equiv) was added via syringe. Subsequently the septum was exchanged by a glass stopper and the mixture was stirred overnight at 60°C. The resulting reaction mixture is quenched with water, extracted with CH_2Cl_2 (three times), the organic layers dried over $MgSO_4$ and the solvent evaporated. The residue is subjected to column chromatography (CH_2Cl_2 / MeOH 10:1), affording the product **160** as a white solid (2.05 g, 4.91 mmol, 66% yield). The product was further purified (racemate separation possible by HPLC).

^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.43-7.50 (m, 3H, -C$\underline{H}_{Ar}$), 7.65 (d, 2H, ^3J = 7.3 Hz).

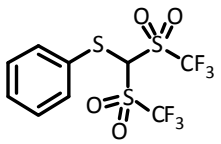
MS (ESI-pos) m/z (M-H+Na+Na): 449.

HRMS (ESI-pos) m/z (M+Na): calcd. 426.9179, found 426.9174.

HPLC: Daicel Chiralpak QN-AX, MeOH : AcOH : NH_4Ac = 98:2: 0.5 (v/v/w), flow: 1 ml/min, 25°C, absorption at 254 nm, t_{R1} = 4.97 min/ t_{R2} = 5.67 min. Side product (sulfanylmethide **160a**) t_R = 6.71 min.

• *Compound **160a:** (Bis((trifluoromethyl)sulfonyl)methyl)(phenyl)sulfane*

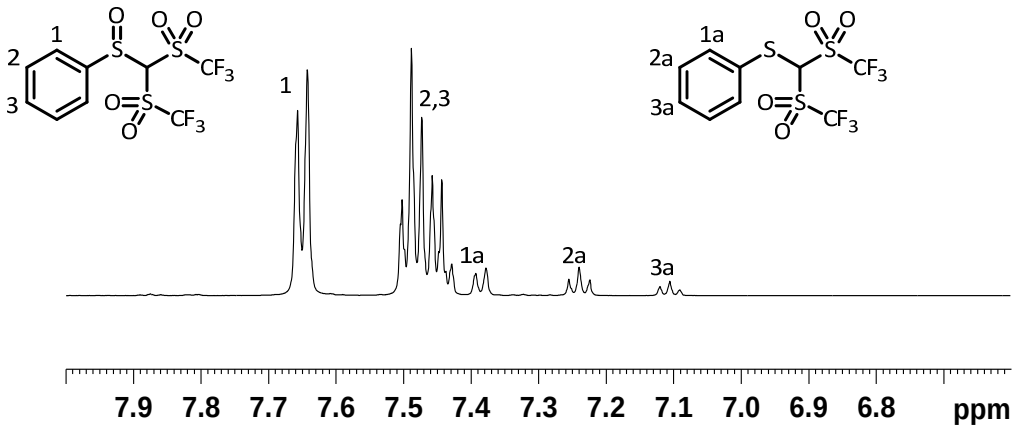
^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.09-7.12 (m, 1H, -C$\underline{H}_{Ar}$), 7.22-7.26 (m, 2H, -C$\underline{H}_{Ar}$), 7.39 (d, 2H, ^3J = 7.6 Hz).



Chemical Formula: $C_9H_6F_6O_4S_3$
Exact Mass: 387,93
Molecular Weight: 388,33

HPLC: Daicel Chiralpak QN-AX, MeOH : AcOH : NH_4Ac = 98:2: 0.5 (v/v/w), flow: 1 ml/min, 25°C, absorption at 254 nm, t_R = 6.71 min.

Illustration of a crude ^{1}H-NMR spectrum of **160** and **160a** and presumable signal assignments:


1
2
3
1a
2a
3a
2,3
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
ppm

8. Bibliography

[1] E. Fischer, *Chem. Ber.* **1894**, *27*, 2985.

[2] E. Fischer, *Chem. Ber.* **1894**, *27*, 3189.

[3] I. Ojima, *Catalytic Asymmetric Synthesis* **2000**, *2nd ed., Wiley-VCH, Weinheim*.

[4] E. J. Corey, L. Kürti, *Enantioselective Chemical Synthesis, Direct Book Publishing LLC, Dallas, USA* **2010**.

[5] L. Pasteur, *Ann. Chim. Phys.* **1848**, *24*, 442.

[6] W. Marckwald, *Chem. Ber.* **1904**, *37*, 349.

[7] W. Marckwald, *Chem. Ber.* **1904**, *37*, 1368.

[8] W. S. Knowles, *Angew. Chem. Int. Ed.* **2002**, *41*, 1998.

[9] M. Kitamura, M. Tokunaga, T. Ohkuma, R. Noyori, *Org. Synth. Coll. Vol. 9, p. 589 (1998)* **1993**, *71*, 1.

[10] a) T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 5974; b) E. N. Jacobsen, I. Marko, W. S. Mungall, G. Schroeder, K. B. Sharpless, *J. Am. Chem. Soc.* **1988**, *110*, 1968.

[11] a) B. List, R. A. Lerner, C. F. Barbas, *J. Am. Chem. Soc.* **2000**, *122*, 2395; b) K. A. Ahrendt, C. J. Borths, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2000**, *122*, 4243.

[12] a) B. List, *Tetrahedron* **2002**, *58*, 5573; b) M. T. Reetz, B. List, S. Jaroch, H. Weinmann, *Organocatalysis (Ernst Schering Foundation Symposium Proceedings)* **2008**, *1st ed., Springer Verlag, Berlin / Heidelberg*; c) M. J. Gaunt, C. C. C. Johansson, A. McNally, N. T. Vo, *Drug Discov. Today* **2007**, *12*, 8; d) P. I. Dalko, *Enantioselective Organocatalysis: Reactions and Experimental Procedures* **2007**, *1st ed., Wiley-VCH, Weinheim*; e) S. Bertelsen, K. A. Jorgensen, *Chem. Soc. Rev.* **2009**, *38*, 2178.

[13] J. Seayad, B. List, *Org. Biomol. Chem.* **2005**, *3*, 719.

[14] S. A. Arrhenius, in *PhD-Thesis*, P. A. Norstedt, Stockholm, **1884**.

[15] a) T. M. Lowry, *J. Soc. Chem. Ind.* **1923**, *42*, 1048; b) J. N. Brönsted, *Recl. Trav. Chim. Pay. B.* **1923**, *42*, 718.

[16] a) G. N. Lewis, *Journal of the Franklin Institute* **1938**, *226*, 293; b) G. N. Lewis, G. T. Seaborg, *J. Am. Chem. Soc.* **1939**, *61*, 1886.

[17] R. G. Pearson, *J. Am. Chem. Soc.* **1963**, *85*, 3533.

[18] J. B. F. N. Engberts, B. L. Feringa, E. Keller, S. Otto, *Recl. Trav. Chim. Pay. B.* **1996**, *115*, 457.

[19] Y. Yamamoto, *J. Org. Chem.* **2007**, *72*, 7817.

[20] O. Helmboldt, L. Keith Hudson, C. Misra, K. Wefers, W. Heck, H. Stark, M. Danner, N. Rösch, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, **2000**.

[21] C. Friedel, J. M. Crafts, *C. R. Hebd. Séances Acad. Sci.* **1887**, *84*, 1392.

[22] T. B. Poulsen, K. A. Jørgensen, *Chem. Rev.* **2008**, *108*, 2903.

[23] a) K. B. Jensen, J. Thorhauge, R. G. Hazell, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2001**, *40*, 160; b) R. Rasappan, M. Hager, A. Gissibl, O. Reiser, *Org. Lett.* **2006**, *8*, 6099.

[24] E. J. Corey, R. K. Bakshi, S. Shibata, *J. Am. Chem. Soc.* **1987**, *109*, 5551.

[25] A. Hirao, S. Itsuno, S. Nakahama, N. Yamazaki, *J. Chem. Soc., Chem. Commun.* **1981**, 315.

[26] O. Diels, K. Alder, *Liebigs Ann. Chem.* **1928**, *460*, 98.

[27] Y. Apeloig, E. Matzner, *J. Am. Chem. Soc.* **1995**, *117*, 5375.

[28] K. C. Nicolaou, S. A. Snyder, T. Montagnon, G. Vassilikogiannakis, *Angew. Chem. Int. Ed.* **2002**, *41*, 1668.

[29] E. J. Corey, R. Imwinkelried, S. Pikul, Y. B. Xiang, *J. Am. Chem. Soc.* **1989**, *111*, 5493.

[30] P. Li, H. Yamamoto, *J. Am. Chem. Soc.* **2009**, *131*, 16628.

[31] a) K. Ziegler, E. Holzkamp, H. Breil, H. Martin, *Angew. Chem.* **1955**, *67*, 541; b) G. Natta, *Angew. Chem.* **1964**, *76*, 553.

[32] a) G. Allegra, *Makromol. Chem.* **1971**, *145*, 235; b) P. Cossee, *J. Catal.* **1964**, *3*, 80.

[33] A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410.

[34] Y. Ito, M. Sawamura, T. Hayashi, *J. Am. Chem. Soc.* **1986**, *108*, 6405.

[35] M. P. Muñoz, J. Adrio, J. C. Carretero, A. M. Echavarren, *Organometallics* **2005**, *24*, 1293.

[36] a) G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, *Science* **2007**, *317*, 496; b) S. Mayer, B. List, *Angew. Chem. Int. Ed.* **2006**, *45*, 4193; c) S. Mukherjee, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 11336.

[37] H. Yamamoto, K. Futatsugi, *Angew. Chem. Int. Ed.* **2005**, *44*, 1924.

[38] a) H. Ishitani, S. Komiyama, Y. Hasegawa, S. Kobayashi, *J. Am. Chem. Soc.* **2000**, *122*, 762; b) H. Ishitani, S. Komiyama, S. Kobayashi, *Angew. Chem. Int. Ed.* **1998**, *37*, 3186.

[39] M. Oishi, S. Aratake, H. Yamamoto, *J. Am. Chem. Soc.* **1998**, *120*, 8271.

[40] K. Ishihara, H. Yamamoto, *J. Am. Chem. Soc.* **1994**, *116*, 1561.

[41] D. H. Ryu, E. J. Corey, *J. Am. Chem. Soc.* **2003**, *125*, 6388.

[42] W.-D. Fessner, *in Modern Aldol reactions (Vol. 1)* **2004**, *1st ed. (Ed.: R. Mahrwald), Wiley-VCH, Weinheim*, 201.

[43] F. Tanaka, C. F. Barbas, *in Modern Aldol reactions (Vol. 1)* **2004**, *1st ed. (Ed.: R. Mahrwald), Wiley-VCH, Weinheim*, 273.

[44] a) A. Borodin, *J. Prakt. Chem.* **1864**, *93*, 413; b) A. Wurtz, *J. Prakt. Chem.* **1872**, *5*, 457.

[45] a) J.-E. Dubois, M. Dubois, *Tetrahedron Lett.* **1967**, *8*, 4215; b) W. A. Kleschick, C. T. Buse, C. H. Heathcock, *J. Am. Chem. Soc.* **1977**, *99*, 247.

[46] a) D. A. Evans, J. Bartroli, T. L. Shih, *J. Am. Chem. Soc.* **1981**, *103*, 2127; b) D. A. Evans, J. S. Clark, R. Metternich, V. J. Novack, G. S. Sheppard, *J. Am. Chem. Soc.* **1990**, *112*, 866; c) D. A. Evans, J. V. Nelson, E. Vogel, T. R. Taber, *J. Am. Chem. Soc.* **1981**, *103*,

3099; d) D. A. Evans, D. L. Rieger, M. T. Bilodeau, F. Urpi, *J. Am. Chem. Soc.* **1991**, *113*, 1047; e) D. A. Evans, E. Vogel, J. V. Nelson, *J. Am. Chem. Soc.* **1979**, *101*, 6120.

[47] M. T. Reetz, F. Kunisch, P. Heitmann, *Tetrahedron Lett.* **1986**, *27*, 4721.

[48] a) U. Eder, G. Sauer, R. Wiechert, *Angew. Chem. Int. Ed.* **1971**, *10*, 496; b) Z. G. Hajos, D. R. Parrish, *J. Org. Chem.* **1974**, *39*, 1615.

[49] a) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, R. Terrell, *J. Am. Chem. Soc.* **1963**, *85*, 207; b) G. Stork, S. R. Dowd, *J. Am. Chem. Soc.* **1963**, *85*, 2178.

[50] a) A. B. Northrup, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 6798; b) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471; c) A. Erkkilä, I. Majander, P. M. Pihko, *Chem. Rev.* **2007**, *107*, 5416.

[51] P. Krattiger, R. Kovasy, J. D. Revell, S. Ivan, H. Wennemers, *Org. Lett.* **2005**, *7*, 1101.

[52] a) N. Yoshikawa, Y. M. A. Yamada, J. Das, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc.* **1999**, *121*, 4168; b) B. M. Trost, H. Ito, *J. Am. Chem. Soc.* **2000**, *122*, 12003; c) B. M. Trost, E. R. Silcoff, H. Ito, *Org. Lett.* **2001**, *3*, 2497.

[53] K. Mori, T. Katoh, T. Suzuki, T. Noji, M. Yamanaka, T. Akiyama, *Angew. Chem. Int. Ed.* **2009**, *48*, 9652.

[54] G. Pousse, F. L. Cavelier, L. Humphreys, J. Rouden, J. Blanchet, *Org. Lett.* **2010**, *12*, 3582.

[55] a) S. G. Nelson, *Tetrahedron: Asymmetry* **1998**, *9*, 357; b) R. Mahrwald, *Chem. Rev.* **1999**, *99*, 1095.

[56] a) T. Mukaiyama, K. Banno, K. Narasaka, *J. Am. Chem. Soc.* **1974**, *96*, 7503; b) T. Mukaiyama, K. Narasaka, K. Banno, *Chem. Lett.* **1973**, 1011; c) K. Saigo, M. Osaki, T. Mukaiyama, *Chem. Lett.* **1975**, 989.

[57] T. Mukaiyama, S. Kobayashi, M. Murakami, *Chem. Lett.* **1985**, 447.

[58] S. Murata, M. Suzuki, R. Noyori, *J. Am. Chem. Soc.* **1980**, *102*, 3248.

[59] S. Kobayashi, M. Murakami, T. Mukaiyama, *Chem. Lett.* **1985**, 1535.

[60] a) G. Helmchen, U. Leikauf, I. Taufer-Knöpfel, *Angew. Chem. Int. Ed.* **1985**, *24*, 874; b) C. Gennari, A. Bernardi, L. Colombo, C. Scolastico, *J. Am. Chem. Soc.* **1985**, *107*, 5812.

[61] M. T. Reetz, S.-H. Kyung, C. Bolm, T. Zierke, *Chem. Ind. (London, U.K.)* **1986**, 824.

[62] a) N. Iwasama, T. Mukaiyama, *Chem. Lett.* **1987**, 463; b) S. Kobayashi, H. Uchiro, Y. Fujishita, I. Shiina, T. Mukaiyama, *J. Am. Chem. Soc.* **1991**, *113*, 4247.

[63] T. Mukaiyama, S. Kobayashi, H. Uchiro, I. Shiina, *Chem. Lett.* **1990**, 129.

[64] S. Kobayashi, H. Uchiro, I. Shiina, T. Mukaiyama, *Tetrahedron* **1993**, *49*, 1761.

[65] K. Furuta, Y. Miwa, K. Iwanaga, H. Yamamoto, *J. Am. Chem. Soc.* **1988**, *110*, 6254.

[66] K. Furuta, T. Maruyama, H. Yamamoto, *J. Am. Chem. Soc.* **1991**, *113*, 1041.

[67] E. J. Corey, C. L. Cywin, T. D. Roper, *Tetrahedron Lett.* **1992**, *33*, 6907.

[68] S. Kiyooka, Y. Kaneko, M. Komura, H. Matsuo, M. Nakano, *J. Org. Chem.* **1991**, *56*, 2276.

[69] E. R. Parmee, O. Tempkin, S. Masamune, A. Abiko, *J. Am. Chem. Soc.* **1991**, *113*, 9365.

[70] S.-i. Kiyooka, Y. Kaneko, K.-i. Kume, *Tetrahedron Lett.* **1992**, *33*, 4927.

[71] K. Mikami, S. Matsukawa, *J. Am. Chem. Soc.* **1993**, *115*, 7039.

[72] H. Shoda, T. Nakamura, K. Tanino, I. Kuwajima, *Tetrahedron Lett.* **1993**, *34*, 6281.

[73] S. Matsukawa, K. Mikami, *Tetrahedron: Asymmetry* **1995**, *6*, 2571.

[74] E. M. Carreira, R. A. Singer, W. Lee, *J. Am. Chem. Soc.* **1994**, *116*, 8837.

[75] E. M. Carreira, R. A. Singer, *Tetrahedron Lett.* **1994**, *35*, 4323.

[76] M. T. Reetz, A. E. Vougioukas, *Tetrahedron Lett.* **1987**, *28*, 793.

[77] T. Mukaiyama, T. Takashima, H. Kusaka, T. Shimpuku, *Chem. Lett.* **1990**, 1777.

[78] K. Uotsu, H. Sasai, M. Shibasaki, *Tetrahedron: Asymmetry* **1995**, *6*, 71.

[79] D. A. Evans, J. A. Murry, M. C. Kozlowski, *J. Am. Chem. Soc.* **1996**, *118*, 5814.

[80] D. A. Evans, D. W. C. MacMillan, K. R. Campos, *J. Am. Chem. Soc.* **1997**, *119*, 10859.

[81] Y. Mei, P. Dissanayake, M. J. Allen, *J. Am. Chem. Soc.* **2010**, *132*, 12871.

[82] S. Adachi, T. Harada, *Org. Lett.* **2008**, *10*, 4999.

[83] T. Mukaiyama, A. Ishida, *Chem. Lett.* **1975**, 319.

[84] R. C. Fuson, *Chem. Rev.* **1935**, *16*, 1.

[85] a) M. W. Rathke, D. Sullivan, *Tetrahedron Lett.* **1972**, *13*, 4249; b) J. L. Herrmann, G. R. Kieczykowski, R. H. Schlessinger, *Tetrahedron Lett.* **1973**, *14*, 2433.

[86] S. E. Denmark, J. R. Heemstra, G. L. Beutner, *Angew. Chem. Int. Ed.* **2005**, *44*, 4682.

[87] a) G. Casiraghi, F. Zanardi, G. Appendino, G. Rassu, *Chem. Rev.* **2000**, *100*, 1929; b) G. Casiraghi, L. Battistini, C. Curti, G. Rassu, F. Zanardi, *Chem. Rev.* **2011**, *111*, 3076.

[88] M. Sato, S. Sunami, Y. Sugita, C. Kaneko, *Chem. Pharm. Bull.* **1994**, *42*, 839.

[89] M. Sato, S. Sunami, Y. Sugita, C. Kaneko, *Heterocycles* **1995**, *41*, 1435.

[90] a) M. De Rosa, M. R. Acocella, R. Villano, A. Soriente, A. Scettri, *Tetrahedron: Asymmetry* **2003**, *14*, 2499; b) R. Villano, M. R. Acocella, M. De Rosa, A. Soriente, A. Scettri, *Tetrahedron: Asymmetry* **2004**, *15*, 2421.

[91] R. A. Singer, E. M. Carreira, *J. Am. Chem. Soc.* **1995**, *117*, 12360.

[92] Y. Kim, R. A. Singer, E. M. Carreira, *Angew. Chem. Int. Ed.* **1998**, *37*, 1261.

[93] D. A. Evans, D. M. Fitch, T. E. Smith, V. J. Cee, *J. Am. Chem. Soc.* **2000**, *122*, 10033.

[94] J. Krüger, E. M. Carreira, *J. Am. Chem. Soc.* **1998**, *120*, 837.

[95] B. L. Pagenkopf, J. Krüger, A. Stojanovic, E. M. Carreira, *Angew. Chem. Int. Ed.* **1998**, *37*, 3124.

[96] a) G. Bluet, J.-M. Campagne, *J. Org. Chem.* **2001**, *66*, 4293; b) G. Bluet, B. Bazán-Tejeda, J.-M. Campagne, *Org. Lett.* **2001**, *3*, 3807.

[97] a) M. Christmann, M. Kalesse, *Tetrahedron Lett.* **2001**, *42*, 1269; b) S. Simsek, M. Horzella, M. Kalesse, *Org. Lett.* **2007**, *9*, 5637.

[98] M. T. Gieseler, M. Kalesse, *Org. Lett.* **2011**, *13*, 2430.

[99] S. Onitsuka, Y. Matsuoka, R. Irie, T. Katsuki, *Chem. Lett.* **2003**, *32*, 974.

[100] Y. Shimada, Y. Matsuoka, R. Irie, T. Katsuki, *Synlett* **2004**, 57.

[101] a) J. Burfeindt, M. Patz, M. Müller, H. Mayr, *J. Am. Chem. Soc.* **1998**, *120*, 3629; b) A. D. Dilman, H. Mayr, *Eur. J. Org. Chem.* **2005**, 1760.

[102] V. B. Gondi, M. Gravel, V. H. Rawal, *Org. Lett.* **2005**, *7*, 5657.

[103] a) R. Villano, M. R. Acocella, A. Massa, L. Palombi, A. Scettri, *Tetrahedron Lett.* **2007**, *48*, 891; b) M. De Rosa, L. Citro, A. Soriente, *Tetrahedron Lett.* **2006**, *47*, 8507; c) R. Villano, M. R. Acocella, A. Massa, L. Palombi, A. Scettri, *Tetrahedron* **2009**, *65*, 5571; d) M. De Rosa, C. Talotta, A. Soriente, *Lett. Org. Chem.* **2009**, *6*, 301.

[104] N. Zhu, B.-C. Ma, Y. Zhang, W. Wang, *Adv. Synth. Catal.* **2010**, *352*, 1291.

[105] Y. Yang, K. Zheng, J. Zhao, J. Shi, L. Lin, X. Liu, X. Feng, *J. Org. Chem.* **2010**, *75*, 5382.

[106] H. Ube, N. Shimada, M. Terada, *Angew. Chem. Int. Ed.* **2010**, *49*, 1858.

[107] A. D. Dilman, S. L. Ioffe, *Chem. Rev.* **2003**, *103*, 733.

[108] T. K. Hollis, B. Bosnich, *J. Am. Chem. Soc.* **1995**, *117*, 4570.

[109] J. P. Guthrie, *Can. J. Chem.* **1978**, *56*, 2342.

[110] S. Murata, M. Suzuki, R. Noyori, *Tetrahedron* **1988**, *44*, 4259.

[111] J. Foropoulos, D. D. DesMarteau, *Inorg. Chem.* **1984**, *23*, 3720.

[112] I. A. Koppel, R. W. Taft, F. Anvia, S.-Z. Zhu, L.-Q. Hu, K.-S. Sung, D. D. DesMarteau, L. M. Yagupolskii, Y. L. Yagupolskii, *J. Am. Chem. Soc.* **1994**, *116*, 3047.

[113] a) B. Mathieu, L. Ghosez, *Tetrahedron Lett.* **1997**, *38*, 5497; b) A. Ishii, O. Kotera, T. Saeki, K. Mikami, *Synlett* **1997**, 1145.

[114] N. Kuhnert, J. Peverley, J. Robertson, *Tetrahedron Lett.* **1998**, *39*, 3215.

[115] J. Cossy, F. Lutz, V. Alauze, C. Meyer, *Synlett* **2002**, 45.

[116] K. Ishihara, Y. Hiraiwa, H. Yamamoto, *Chem. Commun.* **2002**, 1564.

[117] Y. Hiraiwa, K. Ishihara, H. Yamamoto, *Eur. J. Org. Chem.* **2006**, 1837.

[118] K. Ishihara, A. Hasegawa, H. Yamamoto, *Angew. Chem. Int. Ed.* **2001**, *40*, 4077.

[119] a) A. Takahashi, H. Yanai, M. Zhang, T. Sonoda, M. Mishima, T. Taguchi, *J. Org. Chem.* **2010**, *75*, 1259; b) A. Hasegawa, K. Ishihara, H. Yamamoto, *Angew. Chem. Int. Ed.* **2003**, *42*, 5731.

[120] S. E. Denmark, G. L. Beutner, T. Wynn, M. D. Eastgate, *J. Am. Chem. Soc.* **2005**, *127*, 3774.

[121] a) S. E. Denmark, S. B. D. Winter, X. Su, K.-T. Wong, *J. Am. Chem. Soc.* **1996**, *118*, 7404; b) S. E. Denmark, K.-T. Wong, R. A. Stavenger, *J. Am. Chem. Soc.* **1997**, *119*, 2333; c) S. E. Denmark, R. A. Stavenger, K.-T. Wong, *J. Org. Chem.* **1998**, *63*, 918.

[122] a) S. E. Denmark, T. Wynn, G. L. Beutner, *J. Am. Chem. Soc.* **2002**, *124*, 13405; b) S. E. Denmark, J. R. Heemstra, *Org. Lett.* **2003**, *5*, 2303; c) S. E. Denmark, W.-j. Chung, *Angew. Chem. Int. Ed.* **2008**, *47*, 1890.

[123] a) S. E. Denmark, G. L. Beutner, *J. Am. Chem. Soc.* **2003**, *125*, 7800; b) S. E. Denmark, J. R. Heemstra, *Synlett* **2004**, 2411.

[124] W. R. H. Hurtley, S. Smiles, *J. Chem. Soc.* **1926**, 1821.

[125] a) A. Blaschette, P. G. Jones, T. Hammann, M. Näveke, D. Schomburg, H. K. Cammenga, M. Epple, I. Steppuhn, *Z. Anorg. Allg. Chem.* **1993**, *619*, 912; b) T. Hamann, A. Blaschette, P. G. Jones, *Z. Anorg. Allg. Chem.* **1998**, *624*, 147.

[126] G. Simchen, S. Jonas, *J. Prakt. Chem./Chemiker-Zeitung* **1998**, *340*, 506.

[127] M. Barbero, S. Cadamuro, S. Dughera, P. Venturello, *Synlett* **2007**, 2209.

[128] a) M. Barbero, S. Bazzi, S. Cadamuro, S. Dughera, C. Piccinini, *Synthesis* **2010**, 315; b) M. Barbero, S. Bazzi, S. Cadamuro, S. Dughera, C. Magistris, A. Smarra, P. Venturello, *Org. Biomol. Chem.* **2011**, *9*, 2192.

[129] a) P. García-García, F. Lay, P. García-García, C. Rabalakos, B. List, *Angew. Chem. Int. Ed.* **2009**, *48*, 4363; b) Y. Zhang, F. Lay, P. García-García, B. List, E. Y. X. Chen, *Chem. Eur. J.* **2010**, *16*, 10462.

[130] T. R. Wu, L. Shen, J. M. Chong, *Org. Lett.* **2004**, *6*, 2701.

[131] a) D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356; b) T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566.

[132] D. Nakashima, H. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 9626.

[133] a) D. Kampen, A. Ladépêche, G. Claßen, B. List, *Adv. Synth. Catal.* **2008**, *350*, 962; b) S. C. Pan, B. List, *Chem. Asian J.* **2008**, *3*, 430.

[134] M. Treskow, J. Neudörfl, R. Giernoth, *Eur. J. Org. Chem.* **2009**, 3693.

[135] H. He, L.-Y. Chen, W.-Y. Wong, W.-H. Chan, A. W. M. Lee, *Eur. J. Org. Chem.* **2010**, 4181.

[136] A. Berkessel, P. Christ, N. Leconte, J.-M. Neudörfl, M. Schäfer, *Eur. J. Org. Chem.* **2010**, 5165.

[137] L.-Y. Chen, H. He, W.-H. Chan, A. W. M. Lee, *J. Org. Chem.* **2011**, *76*, 7141.

[138] S. Schenker, A. Zamfir, M. Freund, S. B. Tsogoeva, *Eur. J. Org. Chem.* **2011**, 2209.

[139] a) C. Palomo, M. Oiarbide, J. M. García, *Chem. Eur. J.* **2002**, *8*, 36; b) B. Schetter, R. Mahrwald, *Angew. Chem. Int. Ed.* **2006**, *45*, 7506.

[140] M. Kalesse, J. Hassfeld, *in Asymmetric Synthesis - The Essentials* **2007**, *1st ed. (Eds.: M. Christmann, S. Bräse), Wiley-VCH, Weinheim*, 105.

[141] S. V. Pansare, E. K. Paul, *Chem. Eur. J.* **2011**, *17*, 8770.

[142] B. W. Domagalska, L. Syper, K. A. Wilk, *Synthesis* **2001**, 2463.

[143] B. Schetter, R. Mahrwald, *in Quaternary Stereocenters* **2005**, *1st ed. (Eds.: J. Christoffers, A. Baro), Wiley-VCH, Weinheim*, 51.

[144] a) N. J. A. Martin, B. List, *J. Am. Chem. Soc.* **2006**, *128*, 13368; b) X. Wang, B. List, *Angew. Chem.* **2008**, *120*, 1135; c) J. Lacour, V. Hebbe-Viton, *Chem. Soc. Rev.* **2003**, *32*, 373; d) C. Carter, S. Fletcher, A. Nelson, *Tetrahedron: Asymmetry* **2003**, *14*, 1995; e) D. B. Llewellyn, B. A. Arndtsen, *Tetrahedron: Asymmetry* **2005**, *16*, 1789.

[145] S. S. So, J. A. Burkett, A. E. Mattson, *Org. Lett.* **2011**, *13*, 716.

[146] T. Mukhopadhyay, D. Seebach, *Helv. Chim. Acta* **1982**, *65*, 385.

[147] S. E. Denmark, J. R. Heemstra, *J. Org. Chem.* **2007**, *72*, 5668.

[148] A. Leonardi, C. Riva, P. Tavecchia, G. Sironi, *Patent: WO 2007025780* **2007**.

[149] G. T. Notte, J. L. Leighton, *J. Am. Chem. Soc.* **2008**, *130*, 6676.

[150] M. Klussmann, L. Ratjen, S. Hoffmann, V. Wakchaure, R. Goddard, B. List, *Synlett* **2010**, 2189.

[151] S. E. Denmark, T. Kobayashi, C. S. Regens, *Tetrahedron* **2010**, *66*, 4745.

[152] E. Lück, M. Jager, N. Raczek, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, **2000**.

[153] T. R. Hoye, A. S. Magee, W. S. Trumper, *Synth. Commun.* **1982**, *12*, 183

[154] A. A. Vasil'ev, L. Engman, E. P. Serebryakov, *J. Chem. Soc., Perkin Trans.* **2000**, 2211.

[155] B. DeBoef, W. R. Counts, S. R. Gilbertson, *J. Org. Chem.* **2007**, *72*, 799.

[156] U. Bhatt, M. Christmann, M. Quitschalle, E. Claus, M. Kalesse, *J. Org. Chem.* **2001**, *66*, 1885.

[157] S. E. Denmark, S. Fujimori, *J. Am. Chem. Soc.* **2005**, *127*, 8971.

[158] A. K. Ghosh, G. Gong, *Org. Lett.* **2007**, *9*, 1437.

[159] J. D. White, C. M. Lincoln, J. Yang, W. H. C. Martin, D. B. Chan, *J. Org. Chem.* **2008**, *73*, 4139.

[160] G. V. Reddy, R. S. C. Kumar, E. Sreedhar, K. S. Babu, J. M. Rao, *Tetrahedron Lett.* **2010**, *51*, 1723.

[161] K. R. Buszek, N. Sato, Y. Jeong, *J. Am. Chem. Soc.* **1994**, *116*, 5511.

[162] J. Pietruszka, A. C. M. Rieche, *Adv. Synth. Catal.* **2008**, *350*, 1407.

[163] M. J. Aurell, I. Carne, J. E. Clar, S. Gil, R. Mestres, M. Parra, A. Tortajada, *Tetrahedron* **1993**, *49*, 6089.

[164] S. E. Denmark, C.-T. Chen, *Tetrahedron Lett.* **1994**, *35*, 4327.

[165] R. He, S. Shirakawa, K. Maruoka, *J. Am. Chem. Soc.* **2009**, *131*, 16620.

[166] L. Wang, S. Shirakawa, K. Maruoka, *Angew. Chem. Int. Ed.* **2011**, *50*, 5327.

[167] A. F. Goldfarb, E. E. Napp, *J. Am. Med. Assoc.* **1956**, *161*, 616.

[168] a) A. Horeau, J. Jacques, *C. R. Hebd. Séances Acad. Sci.* **1947**, *224*, 862; b) J. Jacques, A. Horeau, *Bull. Soc. Chim. Fr.* **1948**, 711.

[169] a) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem. Int. Ed.* **2006**, *45*, 6751; b) M. Terada, K. Machioka, K. Sorimachi, *Angew. Chem. Int. Ed.* **2006**, *45*, 2254.

[170] a) P. I. Dalko, L. Moisan, *Angew. Chem. Int. Ed.* **2001**, *40*, 3726; b) P. I. Dalko, L. Moisan, *Angew. Chem. Int. Ed.* **2004**, *43*, 5138.

[171] D. Kampen, C. Reisinger, B. List*, Vol. 291* (Ed.: B. List), Springer Berlin / Heidelberg, **2009**, pp. 395.

[172] O. Sereda, S. Tabassum, R. Wilhelm*, Vol. 291* (Ed.: B. List), Springer Berlin / Heidelberg, **2009**, pp. 86.

[173] S. Kobayashi, T. Ogino, H. Shimizu, S. Ishikawa, T. Hamada, K. Manabe, *Org. Lett.* **2005**, *7*, 4729.

[174] K. Hara, R. Akiyama, M. Sawamura, *Org. Lett.* **2005**, *7*, 5621.

[175] A. Takahashi, H. Yanai, T. Taguchi, *Chem. Commun.* **2008**, 2385.

[176] S. Yamasaki, K. Fujii, R. Wada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2002**, *124*, 6536.

[177] E. N. Jacobsen, *Acc. Chem. Res.* **2000**, *33*, 421.

[178] S. Nakamura, M. Hayashi, Y. Kamada, R. Sasaki, Y. Hiramatsu, N. Shibata, T. Toru, *Tetrahedron Lett.* **2010**, *51*, 3820.

[179] V. R. Chintareddy, K. Wadhwa, J. G. Verkade, *J. Org. Chem.* **2009**, *74*, 8118.

[180] D. A. Evans, E. Hu, J. D. Burch, G. Jaeschke, *J. Am. Chem. Soc.* **2002**, *124*, 5654.

[181] L. Ratjen, P. García-García, F. Lay, M. E. Beck, B. List, *Angew. Chem. Int. Ed.* **2011**, *50*, 754.

[182] D. Liotta, U. Sunay, S. Ginsberg, *J. Org. Chem.* **1982**, *47*, 2227.

[183] Z. Pakulski, K. M. Pietrusiewicz, *Tetrahedron: Asymmetry* **2004**, *15*, 41.

[184] M. Johannsen, K. A. Jørgensen, G. Helmchen, *J. Am. Chem. Soc.* **1998**, *120*, 7637.

[185] Y. N. Belokon, D. Chusov, A. S. Peregudov, L. V. Yashkina, G. I. Timofeeva, V. I. Maleev, M. North, H. B. Kagan, *Adv. Synth. Catal.* **2009**, *351*, 3157.

[186] P. J. Jervis, B. M. Kariuki, L. R. Cox, *Org. Lett.* **2006**, *8*, 4649.

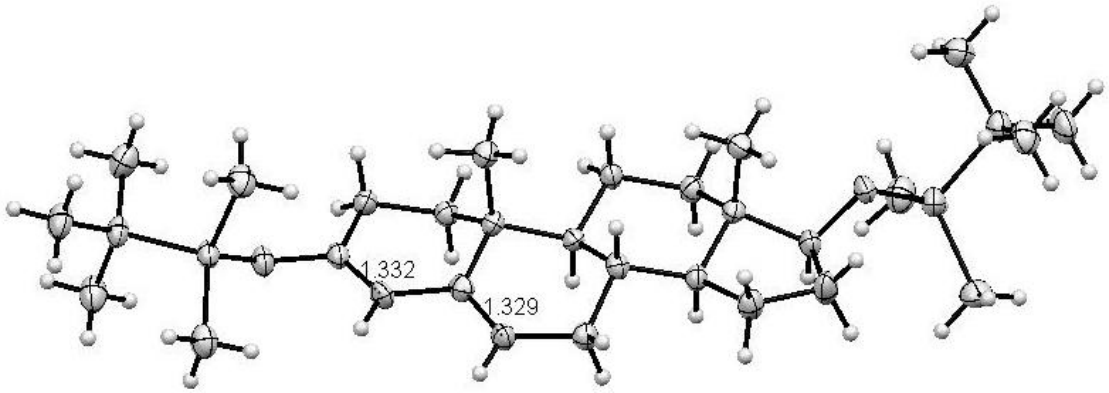
[187] A. Hasegawa, Y. Naganawa, M. Fushimi, K. Ishihara, H. Yamamoto, *Org. Lett.* **2006**, *8*, 3175.

[188] a) R. J. Koshar, R. A. Mitsch, *J. Org. Chem.* **1973**, *38*, 3358; b) S. O. Nwaukwa, S. Lee, P. M. Keehn, *Synth. Commun.* **1986**, *16*, 309.

9. Appendix

9.1 Crystallographic data

• *Compound* ***59***



Empirical formula:	$C_{31}H_{56}O_2Si_2$	
Color:	colourless	
Formula weight :	516.94 g · mol^{-1}	
Temperature:	100 K	
Wavelength:	0.71073 Å	
Crystal system:	monoclinic	
Space group:	C2, (no. 5)	
Unit cell dimensions:	a = 42.7500(17) Å	α= 90°.
	b = 7.1575(3) Å	β= 99.0560(10)°.
	c = 21.4045(8) Å	γ = 90°.
Volume:	6467.8(4) Å^3	
Z:	8	
Density (calculated):	1.062 Mg · m^{-3}	
Absorption coefficient:	0.133 mm^{-1}	
F(000):	2288 e	
Crystal size:	0.22 x 0.09 x 0.07 mm^3	
θ range for data collection:	2.90 to 30.00°.	
Index ranges:	-60 ≤ h ≤ 60, -10 ≤ k ≤ 10, -30 ≤ 1 ≤ 30	

Reflections collected:	95525
Independent reflections:	18661 [R_{int} = 0.1376]
Reflections with I>2σ(I):	10738
Completeness to θ = 30.00°:	99.7 %
Absorption correction:	Gaussian
Max. and min. transmission:	0.99 and 0.98
Refinement method:	Full-matrix least-squares on F^2
Data / restraints / parameters:	18661 / 34 / 656
Goodness-of-fit on F^2:	1.020
Final R indices [I>2σ(I)]:	R_1 = 0.0658 wR^2 = 0.1226
R indices (all data):	R_1 = 0.1488 wR^2 = 0.1530
Absolute structure parameter.	0.05(10)
Largest diff. peak and hole:	0.603 and -0.433 e $Å^{-3}$

Table 1. Atomic coordinates and equivalent isotropic displacement parameters (Å^2).
U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(1)	0.8814(1)	0.0944(5)	0.8428(1)	0.024(1)
C(2)	0.8652(1)	-0.0642(5)	0.8692(1)	0.026(1)
C(3)	0.8292(1)	-0.0437(4)	0.8556(1)	0.023(1)
C(4)	0.8175(1)	0.1547(4)	0.8688(1)	0.022(1)
C(5)	0.7809(1)	0.1675(5)	0.8496(1)	0.021(1)
C(6)	0.7626(1)	0.0404(5)	0.8898(1)	0.025(1)
C(7)	0.7262(1)	0.0585(4)	0.8732(2)	0.025(1)
C(8)	0.7161(1)	0.2624(4)	0.8766(1)	0.023(1)
C(9)	0.6818(1)	0.3063(5)	0.8465(2)	0.026(1)
C(10)	0.6819(1)	0.5168(5)	0.8312(2)	0.037(1)
C(11)	0.7168(1)	0.5681(5)	0.8285(2)	0.030(1)
C(12)	0.7335(1)	0.3773(4)	0.8321(1)	0.023(1)
C(13)	0.7695(1)	0.3713(4)	0.8486(1)	0.022(1)
C(14)	0.7845(1)	0.4865(4)	0.8006(1)	0.026(1)
C(15)	0.8187(1)	0.4382(5)	0.7999(1)	0.026(1)
C(16)	0.8335(1)	0.2916(5)	0.8290(1)	0.025(1)
C(17)	0.8668(1)	0.2534(5)	0.8237(2)	0.027(1)
C(18)	0.9397(1)	0.2887(5)	0.9438(2)	0.036(1)
C(19)	0.9494(1)	0.3849(5)	0.8108(2)	0.035(1)
C(20)	0.9778(1)	0.0151(5)	0.8708(2)	0.028(1)
C(21)	0.9723(1)	-0.1459(5)	0.9152(2)	0.039(1)
C(22)	1.0092(1)	0.1125(5)	0.8975(2)	0.038(1)

C(23)	0.9801(1)	-0.0654(6)	0.8048(2)	0.040(1)
C(24)	0.6259(1)	-0.0709(6)	0.8359(2)	0.042(1)
C(25)	0.6046(1)	0.3185(6)	0.7895(2)	0.038(1)
C(26)	0.6011(1)	0.2060(5)	0.9279(2)	0.030(1)
C(27)	0.6195(1)	0.1066(5)	0.9863(2)	0.039(1)
C(28)	0.5678(1)	0.1199(6)	0.9121(2)	0.041(1)
C(29)	0.5986(1)	0.4151(5)	0.9426(2)	0.036(1)
C(30)	0.8282(1)	0.1993(5)	0.9393(1)	0.029(1)
C(31)	0.7217(1)	0.3328(5)	0.9452(1)	0.031(1)
C(32)	0.6196(1)	0.9451(5)	0.6566(1)	0.025(1)
C(33)	0.6379(1)	0.7678(5)	0.6689(2)	0.028(1)
C(34)	0.6735(1)	0.8062(5)	0.6823(1)	0.026(1)
C(35)	0.6850(1)	0.9384(4)	0.6340(1)	0.021(1)
C(36)	0.7211(1)	0.9796(4)	0.6527(1)	0.021(1)
C(37)	0.7421(1)	0.8047(4)	0.6523(2)	0.026(1)
C(38)	0.7779(1)	0.8464(5)	0.6667(2)	0.026(1)
C(39)	0.7871(1)	0.9958(4)	0.6223(1)	0.024(1)
C(40)	0.8209(1)	1.0757(5)	0.6396(2)	0.028(1)
C(41)	0.8192(1)	1.2772(5)	0.6136(2)	0.034(1)
C(42)	0.7835(1)	1.3265(5)	0.5979(2)	0.032(1)
C(43)	0.7674(1)	1.1724(5)	0.6308(1)	0.024(1)
C(44)	0.7317(1)	1.1428(4)	0.6140(1)	0.024(1)
C(45)	0.7137(1)	1.3215(4)	0.6246(2)	0.026(1)
C(46)	0.6792(1)	1.2872(4)	0.6282(1)	0.027(1)
C(47)	0.6662(1)	1.1204(4)	0.6337(1)	0.022(1)
C(48)	0.6326(1)	1.1037(5)	0.6408(1)	0.026(1)
C(49)	0.5511(1)	0.9043(8)	0.5438(2)	0.066(1)
C(50)	0.5629(1)	0.5724(6)	0.6317(2)	0.054(1)
C(51)	0.5239(1)	0.9036(6)	0.6696(2)	0.041(1)
C(52)	0.5327(1)	0.8618(7)	0.7402(2)	0.058(1)
C(53)	0.4933(1)	0.7958(7)	0.6427(2)	0.051(1)
C(54)	0.5180(1)	1.1132(6)	0.6622(2)	0.064(1)
C(55)	0.8817(1)	0.7550(6)	0.7094(2)	0.057(1)
C(56)	0.9014(1)	1.1406(5)	0.6698(2)	0.036(1)
C(57)	0.8974(1)	0.8160(5)	0.5748(2)	0.038(1)
C(58A)	0.8769(2)	0.6542(10)	0.5440(4)	0.031(2)
C(59A)	0.9311(1)	0.7330(12)	0.6062(4)	0.038(2)
C(60A)	0.9016(2)	0.9520(10)	0.5253(4)	0.047(2)
C(58B)	0.8813(2)	0.6238(12)	0.5585(6)	0.034(3)
C(59B)	0.9328(2)	0.7978(19)	0.5848(6)	0.053(3)
C(60B)	0.8877(3)	0.9574(14)	0.5163(5)	0.050(3)
C(61)	0.6775(1)	0.8494(5)	0.5675(1)	0.027(1)
C(62)	0.7826(1)	0.9261(5)	0.5538(1)	0.033(1)
O(1)	0.9128(1)	0.0588(3)	0.8385(1)	0.028(1)
O(2)	0.6590(1)	0.2594(3)	0.8864(1)	0.028(1)
O(3)	0.5884(1)	0.9418(3)	0.6662(1)	0.031(1)
O(4)	0.8433(1)	0.9622(3)	0.6134(1)	0.034(1)
Si(1)	0.9443(1)	0.1889(1)	0.8655(1)	0.025(1)

Si(2)	0.6233(1)	0.1782(1)	0.8592(1)	0.029(1)
Si(3)	0.5572(1)	0.8305(2)	0.6276(1)	0.032(1)
Si(4)	0.8804(1)	0.9211(1)	0.6424(1)	0.026(1)

Table 2. Bond lengths [Å] and angles [°].

C(1)-C(17)	1.332(4)	C(1)-O(1)	1.384(3)
C(1)-C(2)	1.488(4)	C(2)-C(3)	1.525(4)
C(3)-C(4)	1.547(4)	C(4)-C(16)	1.529(4)
C(4)-C(30)	1.540(4)	C(4)-C(5)	1.556(4)
C(5)-C(13)	1.538(4)	C(5)-C(6)	1.547(4)
C(6)-C(7)	1.545(4)	C(7)-C(8)	1.528(4)
C(8)-C(31)	1.534(4)	C(8)-C(12)	1.537(4)
C(8)-C(9)	1.538(4)	C(9)-O(2)	1.432(3)
C(9)-C(10)	1.542(5)	C(10)-C(11)	1.549(4)
C(11)-C(12)	1.537(4)	C(12)-C(13)	1.522(4)
C(13)-C(14)	1.533(4)	C(14)-C(15)	1.507(4)
C(15)-C(16)	1.329(4)	C(16)-C(17)	1.468(4)
C(18)-Si(1)	1.860(3)	C(19)-Si(1)	1.862(3)
C(20)-C(21)	1.534(5)	C(20)-C(23)	1.542(4)
C(20)-C(22)	1.544(4)	C(20)-Si(1)	1.885(3)
C(24)-Si(2)	1.860(4)	C(25)-Si(2)	1.869(3)
C(26)-C(29)	1.536(5)	C(26)-C(28)	1.538(4)
C(26)-C(27)	1.544(5)	C(26)-Si(2)	1.881(3)
C(32)-C(48)	1.329(5)	C(32)-O(3)	1.381(3)
C(32)-C(33)	1.493(4)	C(33)-C(34)	1.527(4)
C(34)-C(35)	1.538(4)	C(35)-C(47)	1.529(4)
C(35)-C(61)	1.548(4)	C(35)-C(36)	1.561(4)
C(36)-C(37)	1.541(4)	C(36)-C(44)	1.541(4)
C(37)-C(38)	1.539(4)	C(38)-C(39)	1.524(4)
C(39)-C(62)	1.531(4)	C(39)-C(40)	1.544(4)
C(39)-C(43)	1.546(4)	C(40)-O(4)	1.433(4)
C(40)-C(41)	1.544(5)	C(41)-C(42)	1.551(4)
C(42)-C(43)	1.528(4)	C(43)-C(44)	1.526(4)
C(44)-C(45)	1.529(4)	C(45)-C(46)	1.510(4)
C(46)-C(47)	1.328(4)	C(47)-C(48)	1.476(4)
C(49)-Si(3)	1.848(4)	C(50)-Si(3)	1.864(4)
C(51)-C(54)	1.525(6)	C(51)-C(52)	1.528(5)
C(51)-C(53)	1.549(5)	C(51)-Si(3)	1.874(4)
C(55)-Si(4)	1.857(4)	C(56)-Si(4)	1.859(3)
C(57)-C(60A)	1.468(7)	C(57)-C(59B)	1.499(8)
C(57)-C(58A)	1.537(7)	C(57)-C(58B)	1.553(8)
C(57)-C(59A)	1.606(6)	C(57)-C(60B)	1.612(8)
C(57)-Si(4)	1.877(3)	O(1)-Si(1)	1.664(2)
O(2)-Si(2)	1.654(2)	O(3)-Si(3)	1.659(2)
O(4)-Si(4)	1.636(2)		

C(17)-C(1)-O(1)	123.4(3)	C(17)-C(1)-C(2)	122.9(3)
O(1)-C(1)-C(2)	113.6(3)	C(1)-C(2)-C(3)	111.7(3)
C(2)-C(3)-C(4)	113.6(3)	C(16)-C(4)-C(30)	108.8(3)
C(16)-C(4)-C(3)	107.4(2)	C(30)-C(4)-C(3)	108.3(3)
C(16)-C(4)-C(5)	109.6(2)	C(30)-C(4)-C(5)	112.3(2)
C(3)-C(4)-C(5)	110.3(2)	C(13)-C(5)-C(6)	112.2(2)
C(13)-C(5)-C(4)	111.3(3)	C(6)-C(5)-C(4)	113.2(2)
C(7)-C(6)-C(5)	113.7(2)	C(8)-C(7)-C(6)	110.6(3)
C(7)-C(8)-C(31)	110.9(3)	C(7)-C(8)-C(12)	108.2(2)
C(31)-C(8)-C(12)	113.6(3)	C(7)-C(8)-C(9)	115.7(3)
C(31)-C(8)-C(9)	109.2(2)	C(12)-C(8)-C(9)	98.8(2)
O(2)-C(9)-C(8)	113.2(2)	O(2)-C(9)-C(10)	112.3(3)
C(8)-C(9)-C(10)	104.7(3)	C(9)-C(10)-C(11)	105.9(3)
C(12)-C(11)-C(10)	103.3(3)	C(13)-C(12)-C(8)	114.3(2)
C(13)-C(12)-C(11)	118.7(3)	C(8)-C(12)-C(11)	103.9(2)
C(12)-C(13)-C(14)	110.0(2)	C(12)-C(13)-C(5)	109.7(2)
C(14)-C(13)-C(5)	110.7(2)	C(15)-C(14)-C(13)	113.1(3)
C(16)-C(15)-C(14)	124.7(3)	C(15)-C(16)-C(17)	120.4(3)
C(15)-C(16)-C(4)	122.9(3)	C(17)-C(16)-C(4)	116.6(3)
C(1)-C(17)-C(16)	123.3(3)	C(21)-C(20)-C(23)	108.9(3)
C(21)-C(20)-C(22)	108.5(3)	C(23)-C(20)-C(22)	109.3(3)
C(21)-C(20)-Si(1)	110.2(2)	C(23)-C(20)-Si(1)	110.5(2)
C(22)-C(20)-Si(1)	109.4(2)	C(29)-C(26)-C(28)	110.1(3)
C(29)-C(26)-C(27)	109.0(3)	C(28)-C(26)-C(27)	109.3(3)
C(29)-C(26)-Si(2)	108.8(2)	C(28)-C(26)-Si(2)	110.4(2)
C(27)-C(26)-Si(2)	109.3(2)	C(48)-C(32)-O(3)	120.2(3)
C(48)-C(32)-C(33)	122.9(3)	O(3)-C(32)-C(33)	116.8(3)
C(32)-C(33)-C(34)	111.1(3)	C(33)-C(34)-C(35)	113.5(2)
C(47)-C(35)-C(34)	107.7(2)	C(47)-C(35)-C(61)	108.3(2)
C(34)-C(35)-C(61)	108.9(3)	C(47)-C(35)-C(36)	109.7(2)
C(34)-C(35)-C(36)	110.6(2)	C(61)-C(35)-C(36)	111.5(2)
C(37)-C(36)-C(44)	113.1(2)	C(37)-C(36)-C(35)	113.5(2)
C(44)-C(36)-C(35)	111.6(2)	C(38)-C(37)-C(36)	113.7(3)
C(39)-C(38)-C(37)	111.0(2)	C(38)-C(39)-C(62)	111.3(3)
C(38)-C(39)-C(40)	115.8(3)	C(62)-C(39)-C(40)	108.9(2)
C(38)-C(39)-C(43)	107.5(2)	C(62)-C(39)-C(43)	112.9(3)
C(40)-C(39)-C(43)	100.1(2)	O(4)-C(40)-C(41)	112.7(3)
O(4)-C(40)-C(39)	110.6(2)	C(41)-C(40)-C(39)	105.6(3)
C(40)-C(41)-C(42)	106.3(3)	C(43)-C(42)-C(41)	103.6(3)
C(44)-C(43)-C(42)	119.8(3)	C(44)-C(43)-C(39)	113.7(3)
C(42)-C(43)-C(39)	104.1(2)	C(43)-C(44)-C(45)	111.0(3)
C(43)-C(44)-C(36)	110.3(2)	C(45)-C(44)-C(36)	110.9(2)
C(46)-C(45)-C(44)	113.0(3)	C(47)-C(46)-C(45)	125.1(3)
C(46)-C(47)-C(48)	120.6(3)	C(46)-C(47)-C(35)	122.7(3)
C(48)-C(47)-C(35)	116.7(3)	C(32)-C(48)-C(47)	123.2(3)
C(54)-C(51)-C(52)	107.8(4)	C(54)-C(51)-C(53)	109.6(3)
C(52)-C(51)-C(53)	109.4(3)	C(54)-C(51)-Si(3)	110.5(3)
C(52)-C(51)-Si(3)	109.5(3)	C(53)-C(51)-Si(3)	110.1(3)

C(60A)-C(57)-C(59B)	85.8(5)	C(60A)-C(57)-C(58A)	108.4(4)
C(59B)-C(57)-C(58A)	119.4(6)	C(60A)-C(57)-C(58B)	121.7(5)
C(59B)-C(57)-C(58B)	110.9(6)	C(58A)-C(57)-C(58B)	14.9(4)
C(60A)-C(57)-C(59A)	110.2(4)	C(59B)-C(57)-C(59A)	24.4(4)
C(58A)-C(57)-C(59A)	108.4(4)	C(58B)-C(57)-C(59A)	95.9(5)
C(60A)-C(57)-C(60B)	21.7(4)	C(59B)-C(57)-C(60B)	107.3(5)
C(58A)-C(57)-C(60B)	94.6(5)	C(58B)-C(57)-C(60B)	109.3(5)
C(59A)-C(57)-C(60B)	131.6(5)	C(60A)-C(57)-Si(4)	113.3(4)
C(59B)-C(57)-Si(4)	115.5(5)	C(58A)-C(57)-Si(4)	111.5(3)
C(58B)-C(57)-Si(4)	108.4(4)	C(59A)-C(57)-Si(4)	104.9(3)
C(60B)-C(57)-Si(4)	105.2(5)	C(1)-O(1)-Si(1)	127.9(2)
C(9)-O(2)-Si(2)	123.38(19)	C(32)-O(3)-Si(3)	130.9(2)
C(40)-O(4)-Si(4)	128.30(19)	O(1)-Si(1)-C(18)	109.50(14)
O(1)-Si(1)-C(19)	111.80(13)	C(18)-Si(1)-C(19)	108.41(17)
O(1)-Si(1)-C(20)	102.48(13)	C(18)-Si(1)-C(20)	112.74(15)
C(19)-Si(1)-C(20)	111.86(15)	O(2)-Si(2)-C(24)	109.81(15)
O(2)-Si(2)-C(25)	110.33(14)	C(24)-Si(2)-C(25)	109.69(17)
O(2)-Si(2)-C(26)	103.85(13)	C(24)-Si(2)-C(26)	111.76(17)
C(25)-Si(2)-C(26)	111.27(15)	O(3)-Si(3)-C(49)	109.00(17)
O(3)-Si(3)-C(50)	111.30(16)	C(49)-Si(3)-C(50)	109.1(2)
O(3)-Si(3)-C(51)	103.87(14)	C(49)-Si(3)-C(51)	112.61(19)
C(50)-Si(3)-C(51)	110.89(19)	O(4)-Si(4)-C(55)	108.53(17)
O(4)-Si(4)-C(56)	111.03(15)	C(55)-Si(4)-C(56)	110.00(17)
O(4)-Si(4)-C(57)	104.57(13)	C(55)-Si(4)-C(57)	111.74(19)
C(56)-Si(4)-C(57)	110.84(16)		

Table 3. Anisotropic displacement parameters (Å^2).

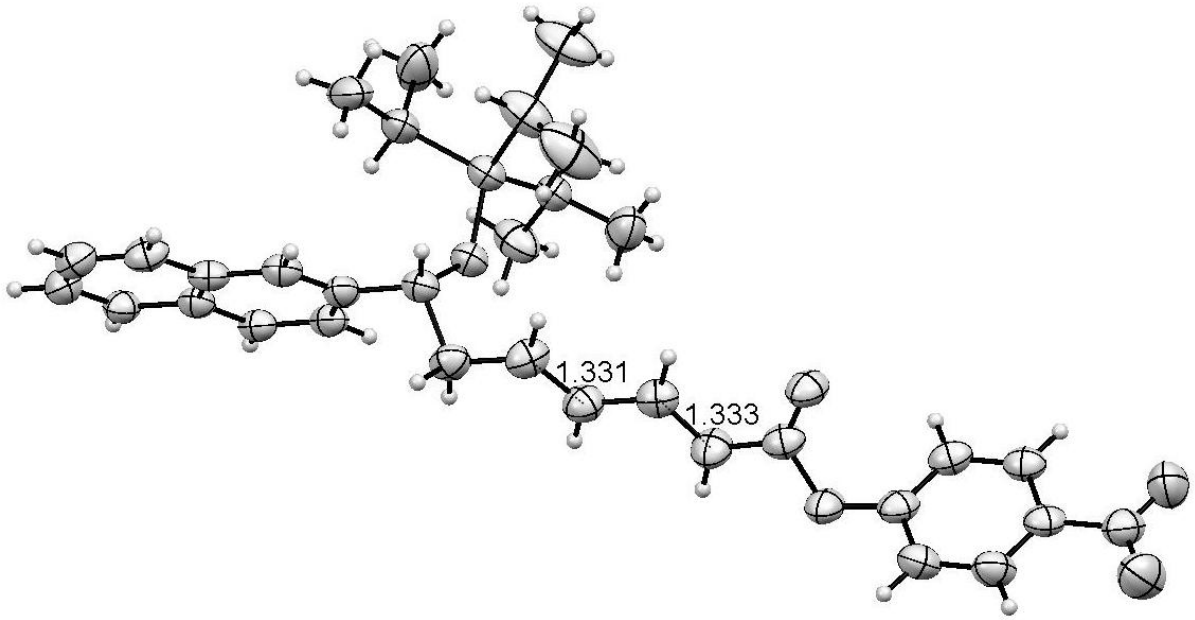
The anisotropic displacement factor exponent takes the form:

$-2\pi^2[h^2a^{*2}U_{11} + ... + 2\ h\ k\ a^*\ b^*\ U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.017(2)	0.032(2)	0.024(2)	-0.002(1)	0.004(1)	0.000(1)
C(2)	0.021(2)	0.030(2)	0.027(2)	0.006(2)	0.003(1)	0.001(1)
C(3)	0.020(2)	0.024(2)	0.026(2)	0.003(1)	0.004(1)	-0.001(1)
C(4)	0.018(1)	0.026(2)	0.021(2)	0.001(1)	0.001(1)	0.001(1)
C(5)	0.018(1)	0.027(2)	0.019(1)	0.002(1)	0.003(1)	-0.001(1)
C(6)	0.020(2)	0.026(2)	0.031(2)	0.003(1)	0.007(1)	0.001(1)
C(7)	0.022(2)	0.025(2)	0.029(2)	0.003(1)	0.004(1)	-0.002(1)
C(8)	0.020(2)	0.028(2)	0.021(2)	-0.001(1)	0.003(1)	0.002(1)
C(9)	0.017(1)	0.032(2)	0.030(2)	0.005(2)	0.006(1)	0.001(1)
C(10)	0.025(2)	0.035(2)	0.053(2)	0.016(2)	0.013(2)	0.009(2)
C(11)	0.027(2)	0.024(2)	0.041(2)	0.005(2)	0.009(2)	0.003(1)
C(12)	0.017(1)	0.026(2)	0.027(2)	0.001(1)	0.004(1)	0.001(1)
C(13)	0.020(2)	0.022(2)	0.026(2)	-0.002(1)	0.005(1)	-0.001(1)
C(14)	0.023(2)	0.025(2)	0.030(2)	0.002(1)	0.005(1)	0.000(1)
C(15)	0.021(2)	0.027(2)	0.031(2)	0.004(1)	0.007(1)	0.000(1)
C(16)	0.021(2)	0.029(2)	0.025(2)	-0.001(1)	0.003(1)	-0.005(1)
C(17)	0.020(2)	0.032(2)	0.029(2)	0.003(1)	0.008(1)	-0.006(1)

C(18)	0.032(2)	0.042(2)	0.034(2)	-0.007(2)	0.004(2)	0.003(2)
C(19)	0.026(2)	0.038(2)	0.041(2)	-0.002(2)	0.005(2)	-0.003(2)
C(20)	0.017(2)	0.034(2)	0.032(2)	-0.004(2)	0.000(1)	0.002(1)
C(21)	0.032(2)	0.038(2)	0.045(2)	0.003(2)	-0.001(2)	0.006(2)
C(22)	0.022(2)	0.047(2)	0.044(2)	-0.006(2)	-0.001(2)	0.001(2)
C(23)	0.028(2)	0.047(2)	0.044(2)	-0.010(2)	0.006(2)	0.004(2)
C(24)	0.037(2)	0.042(2)	0.047(2)	-0.006(2)	0.005(2)	0.006(2)
C(25)	0.035(2)	0.053(2)	0.026(2)	0.001(2)	0.001(1)	-0.001(2)
C(26)	0.022(2)	0.033(2)	0.034(2)	0.000(2)	0.005(1)	-0.001(2)
C(27)	0.036(2)	0.047(2)	0.032(2)	0.007(2)	0.006(2)	-0.003(2)
C(28)	0.023(2)	0.055(3)	0.046(2)	-0.001(2)	0.011(2)	-0.008(2)
C(29)	0.033(2)	0.038(2)	0.038(2)	-0.007(2)	0.010(2)	0.005(2)
C(30)	0.024(2)	0.037(2)	0.026(2)	0.000(2)	0.003(1)	0.000(2)
C(31)	0.030(2)	0.038(2)	0.026(2)	-0.001(2)	0.008(1)	-0.003(2)
C(32)	0.018(2)	0.031(2)	0.027(2)	-0.005(1)	0.007(1)	0.000(1)
C(33)	0.022(2)	0.029(2)	0.033(2)	0.003(1)	0.004(1)	-0.001(1)
C(34)	0.024(2)	0.022(2)	0.032(2)	0.005(1)	0.006(1)	0.000(1)
C(35)	0.020(2)	0.019(2)	0.025(2)	0.000(1)	0.003(1)	-0.002(1)
C(36)	0.020(2)	0.021(2)	0.023(2)	0.002(1)	0.002(1)	0.000(1)
C(37)	0.023(2)	0.023(2)	0.032(2)	0.000(1)	0.005(1)	0.001(1)
C(38)	0.021(2)	0.027(2)	0.031(2)	-0.002(1)	0.004(1)	0.000(1)
C(39)	0.019(2)	0.027(2)	0.023(2)	-0.002(1)	0.002(1)	-0.001(1)
C(40)	0.020(2)	0.035(2)	0.029(2)	-0.007(2)	0.003(1)	-0.003(1)
C(41)	0.027(2)	0.037(2)	0.038(2)	0.005(2)	0.003(1)	-0.008(2)
C(42)	0.025(2)	0.031(2)	0.040(2)	0.003(2)	0.005(1)	-0.003(2)
C(43)	0.023(2)	0.024(2)	0.024(2)	-0.001(1)	0.004(1)	-0.005(1)
C(44)	0.020(2)	0.026(2)	0.025(2)	0.000(1)	0.005(1)	-0.003(1)
C(45)	0.025(2)	0.020(2)	0.034(2)	0.004(1)	0.007(1)	0.001(1)
C(46)	0.024(2)	0.023(2)	0.033(2)	0.002(1)	0.003(1)	0.007(1)
C(47)	0.022(2)	0.025(2)	0.019(2)	-0.001(1)	0.002(1)	0.002(1)
C(48)	0.021(2)	0.028(2)	0.029(2)	-0.001(1)	0.006(1)	0.002(1)
C(49)	0.047(3)	0.112(4)	0.039(2)	0.014(3)	0.009(2)	-0.011(3)
C(50)	0.045(2)	0.051(3)	0.066(3)	-0.008(2)	0.007(2)	-0.011(2)
C(51)	0.024(2)	0.058(3)	0.040(2)	-0.002(2)	0.007(2)	-0.008(2)
C(52)	0.033(2)	0.106(4)	0.038(2)	-0.005(2)	0.014(2)	-0.012(2)
C(53)	0.028(2)	0.081(3)	0.045(2)	-0.005(2)	0.006(2)	-0.016(2)
C(54)	0.034(2)	0.063(3)	0.095(4)	-0.007(3)	0.013(2)	0.008(2)
C(55)	0.077(3)	0.048(3)	0.043(2)	0.006(2)	-0.001(2)	-0.016(2)
C(56)	0.026(2)	0.042(2)	0.040(2)	-0.005(2)	0.005(2)	-0.002(2)
C(57)	0.024(2)	0.045(2)	0.045(2)	-0.013(2)	0.010(2)	-0.002(2)
C(61)	0.024(2)	0.029(2)	0.028(2)	-0.002(1)	0.004(1)	0.000(1)
C(62)	0.024(2)	0.044(2)	0.032(2)	-0.008(2)	0.004(1)	-0.003(2)
O(1)	0.018(1)	0.034(1)	0.033(1)	-0.002(1)	0.005(1)	0.001(1)
O(2)	0.018(1)	0.041(1)	0.027(1)	0.002(1)	0.007(1)	0.000(1)
O(3)	0.019(1)	0.038(1)	0.037(1)	-0.005(1)	0.008(1)	-0.001(1)
O(4)	0.018(1)	0.045(2)	0.037(1)	-0.014(1)	0.002(1)	0.002(1)
Si(1)	0.018(1)	0.031(1)	0.026(1)	-0.003(1)	0.004(1)	0.001(1)
Si(2)	0.022(1)	0.035(1)	0.030(1)	0.001(1)	0.005(1)	0.003(1)
Si(3)	0.022(1)	0.044(1)	0.030(1)	0.001(1)	0.004(1)	-0.005(1)
Si(4)	0.020(1)	0.032(1)	0.027(1)	-0.002(1)	0.003(1)	-0.002(1)

•*Compound **128***



Empirical formula:	$C_{32}H_{39}NO_5Si$
Color:	colourless
Formula weight:	545.73 $g \cdot mol^{-1}$
Temperature :	100 K
Wavelength :	1.54184 Å
Crystal system:	TRICLINIC
Space group:	**P 1, (no. 1)**
Unit cell dimensions:	a = 8.1694(7) Å α= 82.774(4)°.
	b = 13.1020(11) Å β= 78.658(4)°.
	c = 14.4234(12) Å γ = 89.015(4)°.
Volume:	1501.6(2) $Å^3$
Z:	2
Density (calculated):	1.207 $Mg \cdot m^{-3}$
Absorption coefficient:	1.008 mm^{-1}
F(000):	584 e
Crystal size:	0.53 x 0.07 x 0.08 mm^3
θ range for data collection:	3.15 to 67.23°.
Index ranges:	$-9 \le h \le 9, -15 \le k \le 15, -17 \le 1 \le 17$
Reflections collected:	64177
Independent reflections:	8742 [R_{int} = 0.0895]

Reflections with I>2σ(I):	7045
Completeness to θ = 67.23°:	96.3 %
Absorption correction:	Gaussian
Max. and min. transmission.	0.95 and 0.67
Refinement method:	Full-matrix least-squares on F^2
Data / restraints / parameters:	8742 / 3 / 715
Goodness-of-fit on F^2:	1.022
Final R indices [I>2σ(I)]:	R_1 = 0.0556 wR^2 = 0.1334
R indices (all data):	R_1 = 0.0739 wR^2 = 0.1480
Absolute structure parameter:	-0.01(3)
Largest diff. peak and hole:	0.521 and -0.252 e · $Å^{-3}$

Table 1. Atomic coordinates and equivalent isotropic displacement parameters (Å^2).
U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
Si(1)	1.0413(1)	0.0594(1)	0.3577(1)	0.046(1)
Si(2)	0.1026(1)	0.4212(1)	0.6465(1)	0.049(1)
O(1)	0.9040(3)	0.0541(2)	0.2868(2)	0.047(1)
O(2)	0.7183(4)	0.5872(2)	-0.0323(2)	0.059(1)
O(3)	0.9832(4)	0.5367(2)	-0.0295(2)	0.058(1)
O(4)	0.8387(5)	1.0302(3)	-0.2525(3)	0.086(1)
O(5)	0.9380(6)	1.0490(3)	-0.1286(3)	0.082(1)
O(6)	0.1774(4)	0.4374(2)	0.7411(2)	0.061(1)
O(7)	0.4699(4)	-0.1190(3)	1.0376(2)	0.064(1)
O(8)	0.2088(4)	-0.0727(3)	1.0189(2)	0.061(1)
O(9)	0.3218(6)	-0.5600(4)	1.2524(3)	0.102(2)
O(10)	0.2322(8)	-0.5777(4)	1.1265(4)	0.113(2)
N(1)	0.8741(5)	0.9967(3)	-0.1762(3)	0.060(1)
N(2)	0.2978(5)	-0.5272(4)	1.1740(3)	0.070(1)
C(1)	0.9016(5)	-0.0087(3)	0.2132(3)	0.045(1)
C(2)	0.7947(6)	0.0472(4)	0.1459(3)	0.052(1)
C(3)	0.8630(6)	0.1510(4)	0.1030(3)	0.054(1)
C(4)	0.7755(6)	0.2375(4)	0.0986(3)	0.055(1)
C(5)	0.8467(6)	0.3365(3)	0.0542(3)	0.052(1)
C(6)	0.7588(6)	0.4213(4)	0.0380(3)	0.060(1)
C(7)	0.8372(6)	0.5170(4)	-0.0098(3)	0.051(1)
C(8)	0.8298(5)	-0.1142(3)	0.2550(3)	0.045(1)
C(9)	0.6889(5)	-0.1232(3)	0.3305(3)	0.046(1)
C(10)	0.6224(5)	-0.2183(3)	0.3708(3)	0.044(1)
C(11)	0.6950(5)	-0.3080(3)	0.3356(3)	0.042(1)
C(12)	0.6303(5)	-0.4081(3)	0.3748(3)	0.045(1)
C(13)	0.6991(5)	-0.4938(3)	0.3383(3)	0.051(1)
C(14)	0.8356(6)	-0.4842(4)	0.2612(3)	0.054(1)
C(15)	0.9018(5)	-0.3904(3)	0.2232(3)	0.052(1)
C(16)	0.8328(5)	-0.2993(3)	0.2587(3)	0.044(1)

C(17)	0.8990(5)	-0.2013(3)	0.2200(3)	0.045(1)
C(18)	0.7700(5)	0.6870(3)	-0.0698(3)	0.051(1)
C(19)	0.7273(6)	0.7259(4)	-0.1546(3)	0.058(1)
C(20)	0.7601(6)	0.8286(4)	-0.1893(3)	0.059(1)
C(21)	0.8373(5)	0.8883(3)	-0.1394(3)	0.050(1)
C(22)	0.8823(5)	0.8501(3)	-0.0540(3)	0.049(1)
C(23)	0.8466(5)	0.7483(4)	-0.0191(3)	0.051(1)
C(24)	1.2531(7)	0.0985(5)	0.2869(4)	0.079(2)
C(25)	1.2632(10)	0.1641(7)	0.1979(5)	0.112(3)
C(26)	1.3662(7)	0.1389(6)	0.3501(5)	0.092(2)
C(27)	0.9386(5)	0.1576(3)	0.4331(3)	0.049(1)
C(28)	0.9257(8)	0.2628(4)	0.3756(4)	0.075(2)
C(29)	0.7669(6)	0.1190(5)	0.4886(4)	0.070(1)
C(30)	1.0567(6)	-0.0671(4)	0.4338(4)	0.058(1)
C(31)	1.1070(10)	-0.0547(4)	0.5297(4)	0.089(2)
C(32)	1.1706(7)	-0.1447(4)	0.3825(5)	0.075(2)
C(41)	0.3421(5)	0.4533(3)	0.7521(3)	0.058(1)
C(42)	0.3592(6)	0.4174(4)	0.8534(3)	0.059(1)
C(43)	0.3080(6)	0.3094(4)	0.8847(3)	0.058(1)
C(44)	0.3986(6)	0.2322(4)	0.9146(4)	0.063(1)
C(45)	0.3408(5)	0.1291(4)	0.9440(3)	0.054(1)
C(46)	0.4300(6)	0.0501(4)	0.9769(4)	0.062(1)
C(47)	0.3529(6)	-0.0499(4)	1.0110(3)	0.055(1)
C(48)	0.3925(6)	0.5655(3)	0.7224(3)	0.055(1)
C(49)	0.5266(5)	0.5899(3)	0.6463(3)	0.051(1)
C(50)	0.5746(5)	0.6880(3)	0.6131(3)	0.049(1)
C(51)	0.4899(5)	0.7726(3)	0.6542(3)	0.045(1)
C(52)	0.5361(6)	0.8767(4)	0.6210(3)	0.052(1)
C(53)	0.4547(6)	0.9547(4)	0.6642(3)	0.058(1)
C(54)	0.3215(6)	0.9332(4)	0.7430(3)	0.068(1)
C(55)	0.2743(6)	0.8329(4)	0.7749(3)	0.065(1)
C(56)	0.3570(5)	0.7507(4)	0.7325(3)	0.051(1)
C(57)	0.3106(5)	0.6444(4)	0.7644(3)	0.057(1)
C(58)	0.4170(5)	-0.2201(3)	1.0712(3)	0.053(1)
C(59)	0.3492(6)	-0.2802(4)	1.0160(3)	0.058(1)
C(60)	0.3108(6)	-0.3809(4)	1.0495(3)	0.059(1)
C(61)	0.3403(5)	-0.4192(4)	1.1380(3)	0.054(1)
C(62)	0.4075(7)	-0.3605(4)	1.1932(4)	0.069(1)
C(63)	0.4473(6)	-0.2599(4)	1.1585(4)	0.066(1)
C(64)	-0.1191(6)	0.3821(4)	0.7031(4)	0.061(1)
C(65)	-0.1346(9)	0.3220(6)	0.8035(5)	0.097(2)
C(66)	-0.2042(7)	0.3217(5)	0.6458(4)	0.074(1)
C(67)	0.2143(5)	0.3207(3)	0.5760(3)	0.050(1)
C(68)	0.2381(6)	0.2191(4)	0.6372(4)	0.065(1)
C(69)	0.3811(6)	0.3583(4)	0.5126(3)	0.060(1)
C(70)	0.1064(6)	0.5469(4)	0.5674(4)	0.056(1)
C(71)	0.0114(7)	0.6312(4)	0.6195(4)	0.071(1)
C(72)	0.0391(8)	0.5373(4)	0.4763(4)	0.079(2)

Table 2. Bond lengths [Å] and angles [°].

Si(1)-C(30)	1.886(5)	Si(1)-C(24)	1.872(6)
Si(1)-O(1)	1.668(3)	Si(1)-C(27)	1.870(4)
Si(2)-C(67)	1.879(4)	Si(2)-C(70)	1.878(5)
Si(2)-O(6)	1.638(3)	Si(2)-C(64)	1.885(5)

O(2)-C(7)	1.383(5)	O(2)-C(18)	1.390(6)
O(3)-C(7)	1.196(6)	O(8)-C(47)	1.200(6)
O(5)-N(1)	1.219(6)	C(52)-C(51)	1.420(7)
C(52)-C(53)	1.359(6)	C(7)-C(6)	1.447(7)
O(4)-N(1)	1.220(5)	N(1)-C(21)	1.467(6)
C(3)-C(2)	1.492(7)	C(3)-C(4)	1.331(6)
C(30)-C(31)	1.546(7)	C(30)-C(32)	1.526(7)
C(59)-C(60)	1.366(7)	C(59)-C(58)	1.381(7)
C(12)-C(11)	1.427(6)	C(12)-C(13)	1.366(6)
C(51)-C(50)	1.427(6)	C(51)-C(56)	1.409(6)
C(21)-C(20)	1.365(6)	C(21)-C(22)	1.385(6)
C(6)-C(5)	1.334(6)	C(11)-C(10)	1.413(5)
C(11)-C(16)	1.411(5)	C(53)-C(54)	1.413(7)
C(45)-C(46)	1.346(6)	C(45)-C(44)	1.424(7)
C(50)-C(49)	1.350(6)	C(10)-C(9)	1.380(6)
N(2)-O(9)	1.211(6)	N(2)-C(61)	1.467(7)
N(2)-O(10)	1.210(6)	C(56)-C(57)	1.443(7)
C(56)-C(55)	1.402(6)	C(9)-C(8)	1.416(6)
C(18)-C(19)	1.373(6)	C(18)-C(23)	1.384(6)
C(57)-C(48)	1.364(7)	C(20)-C(19)	1.387(7)
C(2)-C(1)	1.540(5)	C(17)-C(8)	1.374(5)
C(17)-C(16)	1.406(6)	C(8)-C(1)	1.516(5)
C(67)-C(69)	1.535(7)	C(67)-C(68)	1.534(7)
C(1)-O(1)	1.425(4)	C(4)-C(5)	1.449(7)
C(14)-C(13)	1.407(6)	C(14)-C(15)	1.356(7)
C(61)-C(60)	1.378(7)	C(61)-C(62)	1.367(7)
C(54)-C(55)	1.372(8)	C(70)-C(71)	1.529(7)
C(70)-C(72)	1.541(7)	C(22)-C(23)	1.380(7)
C(16)-C(15)	1.422(5)	C(62)-C(63)	1.370(8)
C(43)-C(42)	1.471(7)	C(43)-C(44)	1.322(6)
O(6)-C(41)	1.408(5)	C(64)-C(66)	1.485(8)
C(64)-C(65)	1.542(9)	C(24)-C(26)	1.560(8)
C(24)-C(25)	1.441(10)	C(48)-C(49)	1.399(6)
C(48)-C(41)	1.519(6)	C(27)-C(29)	1.532(7)
C(27)-C(28)	1.530(7)	C(46)-C(47)	1.450(7)
C(42)-C(41)	1.510(6)	C(58)-C(63)	1.369(7)
C(58)-O(7)	1.397(6)	C(47)-O(7)	1.381(5)

C(24)-Si(1)-C(30)	109.3(3)	O(1)-Si(1)-C(30)	112.04(18)
O(1)-Si(1)-C(24)	111.1(2)	O(1)-Si(1)-C(27)	99.82(17)
C(27)-Si(1)-C(30)	110.3(2)	C(27)-Si(1)-C(24)	114.1(2)
C(67)-Si(2)-C(64)	112.1(2)	C(70)-Si(2)-C(67)	109.6(2)
C(70)-Si(2)-C(64)	110.3(2)	O(6)-Si(2)-C(67)	113.92(18)
O(6)-Si(2)-C(70)	109.92(19)	O(6)-Si(2)-C(64)	100.6(2)
C(7)-O(2)-C(18)	118.4(4)	C(53)-C(52)-C(51)	120.8(4)
O(2)-C(7)-C(6)	110.6(4)	O(3)-C(7)-O(2)	122.1(4)
O(3)-C(7)-C(6)	127.3(4)	O(5)-N(1)-O(4)	123.2(4)
O(5)-N(1)-C(21)	118.3(4)	O(4)-N(1)-C(21)	118.6(4)

C(4)-C(3)-C(2)	125.7(4)	C(31)-C(30)-Si(1)	113.1(3)
C(32)-C(30)-Si(1)	113.7(4)	C(32)-C(30)-C(31)	110.0(4)
C(60)-C(59)-C(58)	119.4(4)	C(13)-C(12)-C(11)	120.8(4)
C(52)-C(51)-C(50)	122.9(4)	C(56)-C(51)-C(52)	119.1(4)
C(56)-C(51)-C(50)	117.9(4)	C(20)-C(21)-N(1)	119.6(4)
C(20)-C(21)-C(22)	122.2(4)	C(22)-C(21)-N(1)	118.2(4)
C(5)-C(6)-C(7)	122.1(4)	C(10)-C(11)-C(12)	121.6(4)
C(16)-C(11)-C(12)	118.7(3)	C(16)-C(11)-C(10)	119.7(4)
C(52)-C(53)-C(54)	120.3(5)	C(46)-C(45)-C(44)	126.0(5)
C(49)-C(50)-C(51)	121.3(4)	C(9)-C(10)-C(11)	119.6(4)
O(9)-N(2)-C(61)	118.2(5)	O(10)-N(2)-O(9)	122.9(5)
O(10)-N(2)-C(61)	118.8(5)	C(51)-C(56)-C(57)	118.2(4)
C(55)-C(56)-C(51)	118.7(4)	C(55)-C(56)-C(57)	123.1(4)
C(10)-C(9)-C(8)	120.9(3)	C(19)-C(18)-O(2)	117.4(4)
C(19)-C(18)-C(23)	121.1(4)	C(23)-C(18)-O(2)	121.2(4)
C(48)-C(57)-C(56)	122.3(4)	C(21)-C(20)-C(19)	119.3(4)
C(3)-C(2)-C(1)	112.4(4)	C(8)-C(17)-C(16)	120.9(4)
C(9)-C(8)-C(1)	119.7(3)	C(17)-C(8)-C(9)	119.5(4)
C(17)-C(8)-C(1)	120.8(4)	C(69)-C(67)-Si(2)	113.6(3)
C(68)-C(67)-Si(2)	113.6(3)	C(68)-C(67)-C(69)	110.3(4)
C(8)-C(1)-C(2)	111.0(3)	O(1)-C(1)-C(2)	107.1(3)
O(1)-C(1)-C(8)	110.6(3)	C(3)-C(4)-C(5)	123.7(4)
C(6)-C(5)-C(4)	124.9(5)	C(15)-C(14)-C(13)	120.7(4)
C(60)-C(61)-N(2)	118.5(4)	C(62)-C(61)-N(2)	119.1(4)
C(62)-C(61)-C(60)	122.4(5)	C(12)-C(13)-C(14)	120.0(4)
C(55)-C(54)-C(53)	119.3(4)	C(71)-C(70)-Si(2)	112.4(4)
C(71)-C(70)-C(72)	109.4(4)	C(72)-C(70)-Si(2)	112.8(3)
C(23)-C(22)-C(21)	118.2(4)	C(11)-C(16)-C(15)	118.8(4)
C(17)-C(16)-C(11)	119.4(3)	C(17)-C(16)-C(15)	121.9(4)
C(59)-C(60)-C(61)	118.7(5)	C(54)-C(55)-C(56)	121.7(4)
C(61)-C(62)-C(63)	118.5(5)	C(44)-C(43)-C(42)	128.2(5)
C(18)-C(19)-C(20)	119.2(5)	C(41)-O(6)-Si(2)	130.9(3)
C(66)-C(64)-Si(2)	114.9(4)	C(66)-C(64)-C(65)	108.2(5)
C(65)-C(64)-Si(2)	112.9(4)	C(26)-C(24)-Si(1)	111.7(4)
C(25)-C(24)-Si(1)	118.2(5)	C(25)-C(24)-C(26)	111.7(6)
C(14)-C(15)-C(16)	121.0(4)	C(1)-O(1)-Si(1)	130.2(2)
C(57)-C(48)-C(49)	117.9(4)	C(57)-C(48)-C(41)	123.3(4)
C(49)-C(48)-C(41)	118.7(4)	C(29)-C(27)-Si(1)	110.5(3)
C(28)-C(27)-Si(1)	112.8(3)	C(28)-C(27)-C(29)	111.1(4)
C(45)-C(46)-C(47)	120.7(5)	C(50)-C(49)-C(48)	122.3(4)
C(43)-C(42)-C(41)	113.1(4)	C(43)-C(44)-C(45)	125.2(5)
C(22)-C(23)-C(18)	120.0(4)	C(59)-C(58)-O(7)	121.8(4)
C(63)-C(58)-C(59)	121.1(5)	C(63)-C(58)-O(7)	116.9(4)
C(58)-C(63)-C(62)	119.9(5)	O(8)-C(47)-C(46)	127.3(4)
O(8)-C(47)-O(7)	122.6(4)	O(7)-C(47)-C(46)	110.1(4)
C(47)-O(7)-C(58)	117.7(4)	O(6)-C(41)-C(48)	110.4(3)
O(6)-C(41)-C(42)	110.1(4)	C(42)-C(41)-C(48)	111.9(4)

Table 3. Anisotropic displacement parameters (Å^2).

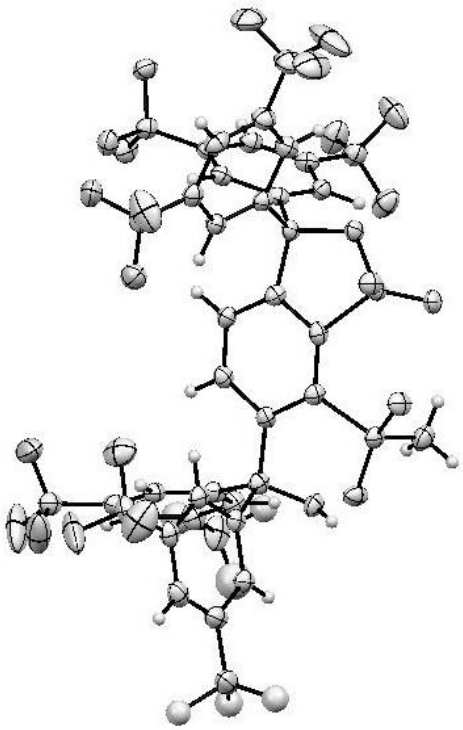
The anisotropic displacement factor exponent takes the form:

$-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Si(1)	0.041(1)	0.050(1)	0.049(1)	-0.008(1)	-0.011(1)	-0.004(1)
Si(2)	0.046(1)	0.051(1)	0.053(1)	-0.008(1)	-0.016(1)	-0.003(1)
N(1)	0.049(2)	0.064(2)	0.064(2)	0.005(2)	-0.015(2)	-0.001(2)
N(2)	0.058(3)	0.076(3)	0.078(3)	0.001(2)	-0.023(2)	-0.001(2)
O(1)	0.047(2)	0.048(1)	0.049(1)	-0.007(1)	-0.016(1)	-0.002(1)
O(2)	0.036(2)	0.053(2)	0.083(2)	0.004(2)	-0.012(1)	0.002(1)
O(3)	0.040(2)	0.062(2)	0.066(2)	0.003(1)	-0.005(1)	0.006(1)
O(4)	0.093(3)	0.085(3)	0.078(2)	0.019(2)	-0.032(2)	-0.017(2)
O(5)	0.093(3)	0.061(2)	0.097(3)	0.001(2)	-0.038(2)	-0.012(2)
O(6)	0.057(2)	0.064(2)	0.066(2)	-0.005(1)	-0.023(1)	-0.005(1)
O(7)	0.039(2)	0.068(2)	0.082(2)	0.000(2)	-0.012(2)	0.006(1)
O(8)	0.035(2)	0.077(2)	0.068(2)	0.007(2)	-0.011(1)	0.003(1)
O(9)	0.124(4)	0.090(3)	0.096(3)	0.029(3)	-0.054(3)	-0.025(3)
O(10)	0.166(5)	0.076(3)	0.117(4)	-0.010(3)	-0.075(4)	-0.023(3)
C(1)	0.039(2)	0.051(2)	0.046(2)	-0.009(2)	-0.013(2)	0.001(2)
C(2)	0.057(3)	0.058(2)	0.046(2)	-0.010(2)	-0.019(2)	0.008(2)
C(3)	0.052(3)	0.064(3)	0.044(2)	0.000(2)	-0.005(2)	0.006(2)
C(4)	0.046(2)	0.059(3)	0.059(2)	-0.008(2)	-0.007(2)	0.006(2)
C(5)	0.051(3)	0.061(2)	0.043(2)	-0.008(2)	-0.008(2)	0.004(2)
C(6)	0.042(2)	0.057(3)	0.074(3)	-0.004(2)	0.000(2)	0.006(2)
C(7)	0.043(3)	0.061(3)	0.048(2)	-0.009(2)	-0.007(2)	0.010(2)
C(8)	0.044(2)	0.048(2)	0.046(2)	0.000(2)	-0.019(2)	-0.002(2)
C(9)	0.042(2)	0.051(2)	0.049(2)	-0.015(2)	-0.017(2)	0.009(2)
C(10)	0.038(2)	0.052(2)	0.044(2)	-0.010(2)	-0.013(2)	0.007(2)
C(11)	0.039(2)	0.049(2)	0.041(2)	-0.008(2)	-0.014(2)	0.001(2)
C(12)	0.035(2)	0.050(2)	0.049(2)	-0.001(2)	-0.010(2)	0.000(2)
C(13)	0.049(2)	0.049(2)	0.055(2)	-0.006(2)	-0.015(2)	0.004(2)
C(14)	0.055(3)	0.056(2)	0.052(2)	-0.009(2)	-0.015(2)	0.014(2)
C(15)	0.044(2)	0.066(3)	0.046(2)	-0.009(2)	-0.006(2)	0.014(2)
C(16)	0.033(2)	0.059(2)	0.040(2)	-0.007(2)	-0.010(2)	0.005(2)
C(17)	0.040(2)	0.056(2)	0.042(2)	-0.008(2)	-0.012(2)	0.003(2)
C(18)	0.035(2)	0.060(3)	0.056(2)	-0.001(2)	-0.008(2)	0.006(2)
C(19)	0.046(3)	0.068(3)	0.063(3)	-0.009(2)	-0.019(2)	-0.004(2)
C(20)	0.053(3)	0.070(3)	0.055(2)	0.001(2)	-0.021(2)	-0.004(2)
C(21)	0.032(2)	0.062(3)	0.054(2)	-0.005(2)	-0.008(2)	0.004(2)
C(22)	0.039(2)	0.061(3)	0.047(2)	-0.011(2)	-0.008(2)	0.006(2)
C(23)	0.045(2)	0.063(3)	0.044(2)	-0.006(2)	-0.008(2)	0.011(2)
C(24)	0.062(3)	0.112(4)	0.064(3)	-0.025(3)	-0.003(2)	-0.025(3)
C(25)	0.097(5)	0.152(7)	0.077(4)	0.012(4)	-0.005(3)	-0.062(5)
C(26)	0.048(3)	0.148(6)	0.082(4)	-0.037(4)	-0.001(3)	-0.023(3)
C(27)	0.046(2)	0.045(2)	0.058(2)	-0.006(2)	-0.017(2)	-0.002(2)
C(28)	0.099(4)	0.053(3)	0.083(3)	-0.015(3)	-0.039(3)	0.011(3)
C(29)	0.047(3)	0.081(3)	0.086(3)	-0.034(3)	-0.007(2)	-0.006(2)
C(30)	0.058(3)	0.052(3)	0.072(3)	-0.012(2)	-0.033(2)	0.001(2)
C(31)	0.135(6)	0.057(3)	0.089(4)	0.002(3)	-0.062(4)	0.002(3)
C(32)	0.061(3)	0.072(3)	0.110(4)	-0.028(3)	-0.048(3)	0.019(2)
C(41)	0.045(3)	0.064(2)	0.064(2)	0.001(2)	-0.014(2)	-0.005(2)
C(42)	0.066(3)	0.061(3)	0.055(2)	-0.010(2)	-0.024(2)	0.008(2)
C(43)	0.047(3)	0.070(3)	0.053(2)	-0.003(2)	-0.007(2)	0.008(2)
C(44)	0.044(3)	0.068(3)	0.073(3)	-0.006(2)	-0.009(2)	0.004(2)

C(45)	0.037(2)	0.073(3)	0.048(2)	-0.005(2)	0.000(2)	0.003(2)
C(46)	0.039(3)	0.067(3)	0.077(3)	-0.004(2)	-0.007(2)	0.006(2)
C(47)	0.037(3)	0.068(3)	0.055(2)	-0.003(2)	-0.001(2)	0.006(2)
C(48)	0.051(3)	0.065(3)	0.054(2)	-0.007(2)	-0.025(2)	-0.005(2)
C(49)	0.050(2)	0.056(2)	0.049(2)	-0.004(2)	-0.019(2)	-0.003(2)
C(50)	0.038(2)	0.062(2)	0.049(2)	-0.007(2)	-0.010(2)	0.003(2)
C(51)	0.030(2)	0.064(3)	0.040(2)	-0.004(2)	-0.010(2)	0.001(2)
C(52)	0.043(2)	0.066(3)	0.049(2)	-0.013(2)	-0.013(2)	0.007(2)
C(53)	0.053(3)	0.059(3)	0.064(3)	-0.008(2)	-0.020(2)	0.011(2)
C(54)	0.055(3)	0.090(4)	0.064(3)	-0.028(3)	-0.017(2)	0.031(3)
C(55)	0.043(3)	0.096(4)	0.052(2)	-0.001(2)	-0.008(2)	0.013(2)
C(56)	0.033(2)	0.075(3)	0.046(2)	-0.010(2)	-0.013(2)	0.004(2)
C(57)	0.036(2)	0.082(3)	0.052(2)	0.010(2)	-0.017(2)	-0.013(2)
C(58)	0.026(2)	0.058(3)	0.070(3)	-0.005(2)	-0.002(2)	0.003(2)
C(59)	0.055(3)	0.074(3)	0.046(2)	-0.011(2)	-0.008(2)	0.010(2)
C(60)	0.055(3)	0.071(3)	0.052(2)	-0.014(2)	-0.011(2)	0.003(2)
C(61)	0.042(2)	0.065(3)	0.054(2)	-0.004(2)	-0.012(2)	0.002(2)
C(62)	0.063(3)	0.083(4)	0.065(3)	0.002(3)	-0.030(2)	-0.006(3)
C(63)	0.058(3)	0.078(3)	0.071(3)	-0.008(3)	-0.035(2)	-0.003(2)
C(64)	0.051(3)	0.058(3)	0.071(3)	-0.011(2)	-0.004(2)	0.003(2)
C(65)	0.080(4)	0.131(6)	0.074(4)	-0.009(4)	0.002(3)	-0.019(4)
C(66)	0.044(3)	0.085(3)	0.094(4)	-0.016(3)	-0.012(2)	-0.003(2)
C(67)	0.039(2)	0.055(2)	0.059(2)	-0.010(2)	-0.014(2)	-0.004(2)
C(68)	0.056(3)	0.055(3)	0.082(3)	-0.002(2)	-0.012(2)	0.006(2)
C(69)	0.053(3)	0.070(3)	0.060(3)	-0.021(2)	-0.007(2)	-0.008(2)
C(70)	0.052(3)	0.053(2)	0.068(3)	-0.006(2)	-0.026(2)	-0.002(2)
C(71)	0.060(3)	0.060(3)	0.103(4)	-0.011(3)	-0.038(3)	0.009(2)
C(72)	0.105(5)	0.066(3)	0.081(4)	-0.001(3)	-0.059(3)	-0.007(3)

- *Compound **155a***



Temperature	100 K	
Wavelength	1.54184 Å	
Crystal system	MONOCLINIC	
Space group	**$P2_1/n$, (no. 14)**	
Unit cell dimensions	a = 13.6797(4) Å	α= 90°.
	b = 22.9157(6) Å	β= 97.6410(10)°.
	c = 28.9530(8) Å	γ = 90°.
Volume	8995.6(4) $Å^3$	
Z	8	
Density (calculated)	1.792 $Mg \cdot m^{-3}$	
Absorption coefficient	3.563 mm^{-1}	
F(000)	4824 e	
Crystal size	0.34 x 0.20 x 0.11 mm^3	
θ range for data collection	2.47 to 67.04°.	
Index ranges	$-16 \leq h \leq 16$, $-27 \leq k \leq 27$, $-34 \leq l \leq 33$	
Reflections collected	197675	
Independent reflections	15549 [R_{int} = 0.0789]	
Reflections with $I>2\sigma(I)$	12936	

Completeness to θ = 67.04°	96.8 %
Absorption correction	Gaussian
Max. and min. transmission	0.78 and 0.53
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	15549 / 0 / 1354
Goodness-of-fit on F^2	1.021
Final R indices [I>2σ(I)]	R_1 = 0.0672 wR^2 = 0.1644
R indices (all data)	R_1 = 0.0808 wR^2 = 0.1757
Largest diff. peak and hole	1.571 and -0.992 e · Å^{-3}

Table 1. Atomic coordinates and equivalent isotropic displacement parameters (Å^2).

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
Cl(1)	0.1895(1)	0.4419(1)	0.5590(1)	0.063(1)
Cl(2)	0.1258(1)	0.3471(1)	0.4955(1)	0.057(1)
Cl(3)	0.1479(1)	0.4113(1)	0.7832(1)	0.053(1)
Cl(4)	0.2609(1)	0.3819(1)	0.8721(1)	0.060(1)
S(1)	0.8941(1)	0.2516(1)	0.4482(1)	0.024(1)
S(2)	0.8125(1)	0.3887(1)	0.4572(1)	0.026(1)
S(3)	0.4717(1)	0.7763(1)	0.7787(1)	0.022(1)
S(4)	0.2677(1)	0.8010(1)	0.8276(1)	0.025(1)
F(1A)	0.5455(5)	0.5955(3)	0.5218(2)	0.041(1)
F(1B)	0.4994(5)	0.5824(3)	0.5217(2)	0.047(2)
F(2A)	0.4828(5)	0.5867(3)	0.5885(2)	0.035(2)
F(2B)	0.5169(6)	0.5967(3)	0.5948(2)	0.046(2)
F(3A)	0.6352(4)	0.6152(3)	0.5844(2)	0.044(1)
F(3B)	0.6346(6)	0.6150(4)	0.5595(3)	0.075(2)
F(4)	0.5295(2)	0.3164(1)	0.5982(1)	0.052(1)
F(5)	0.4110(2)	0.3652(2)	0.5645(1)	0.069(1)
F(6)	0.4643(4)	0.3823(2)	0.6356(1)	0.085(1)
F(7)	0.8275(3)	0.3711(1)	0.7506(1)	0.060(1)
F(8)	0.7195(2)	0.4350(2)	0.7310(1)	0.070(1)
F(9)	0.8431(3)	0.4555(2)	0.7795(1)	0.078(1)
F(10A)	1.0775(8)	0.5844(5)	0.6712(4)	0.077(3)
F(10B)	1.0585(6)	0.5934(3)	0.6598(3)	0.041(2)
F(11A)	1.1432(6)	0.5270(4)	0.7230(3)	0.060(2)
F(11B)	1.1168(4)	0.5506(3)	0.7236(2)	0.035(1)
F(12A)	1.1564(5)	0.5286(3)	0.6528(2)	0.041(2)
F(12B)	1.1640(6)	0.5100(4)	0.6575(3)	0.050(2)
F(13)	1.0398(2)	0.1013(1)	0.6801(1)	0.033(1)
F(14)	1.1802(2)	0.1419(1)	0.7031(1)	0.032(1)
F(15)	1.1748(2)	0.0577(1)	0.6701(1)	0.033(1)
F(16)	1.3925(2)	0.1966(1)	0.5827(1)	0.044(1)
F(17)	1.3121(2)	0.2535(1)	0.5324(1)	0.043(1)
F(18)	1.3368(2)	0.1646(2)	0.5146(1)	0.054(1)
F(19)	0.9316(3)	-0.0077(2)	0.4475(2)	0.087(1)
F(20)	0.7766(3)	-0.0175(1)	0.4279(1)	0.066(1)

F(21)	0.8475(3)	-0.0566(1)	0.4898(1)	0.058(1)
F(22)	0.5567(2)	0.0710(2)	0.5369(1)	0.062(1)
F(23)	0.6056(2)	0.1495(1)	0.5723(1)	0.041(1)
F(24)	0.6495(2)	0.0668(1)	0.6026(1)	0.049(1)
F(25)	0.0546(2)	0.5869(1)	0.8702(1)	0.039(1)
F(26)	0.1236(2)	0.5800(1)	0.8084(1)	0.043(1)
F(27)	-0.0261(2)	0.5500(1)	0.8085(1)	0.039(1)
F(28A)	-0.2194(8)	0.7682(5)	0.8607(4)	0.109(3)
F(28B)	-0.2243(4)	0.7960(2)	0.8415(2)	0.031(1)
F(29A)	-0.2785(5)	0.6913(3)	0.8363(3)	0.048(2)
F(29B)	-0.2614(5)	0.7087(3)	0.8526(2)	0.043(2)
F(30A)	-0.2846(7)	0.7639(5)	0.7903(3)	0.076(3)
F(30B)	-0.2919(4)	0.7454(3)	0.7824(2)	0.026(1)
F(31)	-0.1562(2)	0.6903(1)	0.6133(1)	0.046(1)
F(32)	-0.2783(2)	0.7435(2)	0.6271(1)	0.052(1)
F(33)	-0.2097(2)	0.7587(2)	0.5657(1)	0.054(1)
F(34A)	-0.0902(5)	0.9524(3)	0.5871(3)	0.053(2)
F(34B)	-0.1179(5)	0.9635(3)	0.5995(3)	0.051(2)
F(35A)	-0.1424(8)	0.9734(4)	0.6545(4)	0.081(3)
F(35B)	-0.1146(7)	0.9817(4)	0.6709(3)	0.070(2)
F(36A)	0.0076(5)	0.9782(3)	0.6515(2)	0.043(2)
F(36B)	0.0277(6)	0.9708(3)	0.6376(3)	0.052(2)
F(37)	0.3876(2)	0.6776(1)	0.5250(1)	0.041(1)
F(38)	0.4957(2)	0.7267(2)	0.4955(1)	0.067(1)
F(39)	0.3479(2)	0.7580(1)	0.4922(1)	0.052(1)
F(41A)	0.5311(8)	0.9454(4)	0.6319(3)	0.067(3)
F(41B)	0.4957(8)	0.9487(4)	0.6263(3)	0.070(3)
F(42A)	0.6568(6)	0.9099(3)	0.6237(3)	0.051(2)
F(42B)	0.6273(12)	0.9185(6)	0.6085(5)	0.126(5)
F(43)	0.8016(2)	0.6587(1)	0.7084(1)	0.038(1)
F(43A)	0.5755(5)	0.9261(3)	0.5601(2)	0.051(2)
F(43B)	0.5153(7)	0.9383(4)	0.5608(3)	0.073(2)
F(44)	0.7763(2)	0.5805(1)	0.6673(1)	0.050(1)
F(45)	0.7901(2)	0.5760(1)	0.7420(1)	0.049(1)
F(46A)	0.4692(5)	0.4775(3)	0.7346(3)	0.058(2)
F(46B)	0.4733(4)	0.4706(3)	0.7134(2)	0.042(1)
F(47A)	0.3884(5)	0.4961(3)	0.6696(3)	0.049(2)
F(47B)	0.3671(5)	0.5109(3)	0.6601(2)	0.034(2)
F(48A)	0.3602(6)	0.5230(3)	0.7354(3)	0.041(2)
F(48B)	0.3365(5)	0.5325(3)	0.7277(2)	0.034(2)
O(1)	0.9663(2)	0.2033(1)	0.4740(1)	0.025(1)
O(2)	0.8047(2)	0.2246(1)	0.4288(1)	0.028(1)
O(3)	0.9520(2)	0.2827(1)	0.4191(1)	0.029(1)
O(4)	0.7767(2)	0.3485(1)	0.4212(1)	0.032(1)
O(5)	0.7494(2)	0.4347(1)	0.4685(1)	0.030(1)
O(6)	0.8816(2)	0.4696(1)	0.5393(1)	0.027(1)
O(7)	0.5163(2)	0.7742(1)	0.7305(1)	0.023(1)
O(8)	0.5081(2)	0.7277(1)	0.8064(1)	0.025(1)
O(9)	0.4888(2)	0.8341(1)	0.7960(1)	0.027(1)
O(10)	0.3584(2)	0.7779(1)	0.8503(1)	0.028(1)
O(11)	0.1788(2)	0.7860(1)	0.8459(1)	0.029(1)
O(12)	0.0802(2)	0.8442(1)	0.7746(1)	0.029(1)
N(1)	0.9129(3)	0.4166(2)	0.4433(1)	0.034(1)
N(2)	0.2791(3)	0.8711(2)	0.8283(1)	0.034(1)
C(1)	0.8567(3)	0.3666(2)	0.5551(1)	0.023(1)
C(2)	0.8881(3)	0.3267(2)	0.5908(1)	0.024(1)
C(3)	0.9129(3)	0.2694(2)	0.5828(1)	0.024(1)
C(4)	0.9097(3)	0.2505(2)	0.5372(1)	0.023(1)
C(5)	0.8791(3)	0.2886(2)	0.5013(1)	0.023(1)

C(6)	0.8497(3)	0.3458(2)	0.5086(1)	0.023(1)
C(7)	0.8351(3)	0.4305(2)	0.5682(1)	0.025(1)
C(8)	0.7249(3)	0.4434(2)	0.5662(1)	0.023(1)
C(9)	0.6938(3)	0.5010(2)	0.5633(1)	0.027(1)
C(10)	0.5967(3)	0.5152(2)	0.5683(2)	0.032(1)
C(11)	0.5306(3)	0.4722(2)	0.5779(2)	0.032(1)
C(12)	0.5620(3)	0.4150(2)	0.5814(1)	0.028(1)
C(13)	0.6578(3)	0.3998(2)	0.5747(1)	0.027(1)
C(14)	0.5631(4)	0.5772(2)	0.5634(2)	0.039(1)
C(15)	0.4922(3)	0.3698(2)	0.5945(2)	0.034(1)
C(16)	0.8802(3)	0.4455(2)	0.6187(1)	0.024(1)
C(17)	0.8329(3)	0.4296(2)	0.6565(1)	0.026(1)
C(18)	0.8699(3)	0.4458(2)	0.7014(1)	0.026(1)
C(19)	0.9545(3)	0.4795(2)	0.7097(2)	0.032(1)
C(20)	1.0016(3)	0.4960(2)	0.6723(2)	0.033(1)
C(21)	0.9662(3)	0.4784(2)	0.6270(2)	0.029(1)
C(22)	0.8164(3)	0.4269(2)	0.7408(2)	0.031(1)
C(23)	1.0898(4)	0.5351(3)	0.6793(2)	0.045(1)
C(24)	0.9456(3)	0.1915(2)	0.5214(1)	0.023(1)
C(25)	1.0438(3)	0.1758(2)	0.5505(1)	0.023(1)
C(26)	1.0425(3)	0.1482(2)	0.5932(1)	0.023(1)
C(27)	1.1295(3)	0.1387(2)	0.6222(1)	0.024(1)
C(28)	1.2195(3)	0.1554(2)	0.6083(2)	0.027(1)
C(29)	1.2204(3)	0.1818(2)	0.5657(2)	0.026(1)
C(30)	1.1326(3)	0.1929(2)	0.5367(2)	0.025(1)
C(31)	1.1304(3)	0.1100(2)	0.6685(2)	0.026(1)
C(32)	1.3157(3)	0.1992(2)	0.5492(2)	0.032(1)
C(33)	0.8716(3)	0.1412(2)	0.5194(1)	0.023(1)
C(34)	0.7881(3)	0.1429(2)	0.5413(1)	0.024(1)
C(35)	0.7237(3)	0.0956(2)	0.5377(1)	0.026(1)
C(36)	0.7426(3)	0.0466(2)	0.5128(2)	0.032(1)
C(37)	0.8270(3)	0.0449(2)	0.4910(2)	0.032(1)
C(38)	0.8911(3)	0.0915(2)	0.4940(2)	0.030(1)
C(39)	0.8455(4)	-0.0087(2)	0.4640(2)	0.042(1)
C(40)	0.6334(3)	0.0961(2)	0.5622(2)	0.033(1)
C(41)	0.1710(3)	0.7711(2)	0.7370(1)	0.023(1)
C(42)	0.1777(3)	0.7468(2)	0.6932(1)	0.024(1)
C(43)	0.2665(3)	0.7326(2)	0.6779(1)	0.024(1)
C(44)	0.3529(3)	0.7445(2)	0.7069(1)	0.022(1)
C(45)	0.3482(3)	0.7652(2)	0.7512(1)	0.021(1)
C(46)	0.2590(3)	0.7776(2)	0.7680(1)	0.022(1)
C(47)	0.0685(3)	0.7914(2)	0.7477(2)	0.025(1)
C(48)	0.0152(3)	0.7455(2)	0.7737(1)	0.024(1)
C(49)	0.0524(3)	0.6901(2)	0.7850(1)	0.025(1)
C(50)	-0.0006(3)	0.6515(2)	0.8089(1)	0.026(1)
C(51)	-0.0916(3)	0.6673(2)	0.8213(2)	0.031(1)
C(52)	-0.1277(3)	0.7225(2)	0.8106(2)	0.031(1)
C(53)	-0.0753(3)	0.7616(2)	0.7869(1)	0.029(1)
C(54)	0.0376(3)	0.5923(2)	0.8236(2)	0.031(1)
C(55)	-0.2264(4)	0.7401(2)	0.8227(2)	0.040(1)
C(56)	0.0015(3)	0.8094(2)	0.7026(1)	0.025(1)
C(57)	-0.0596(3)	0.7693(2)	0.6769(1)	0.027(1)
C(58)	-0.1217(3)	0.7875(2)	0.6373(2)	0.030(1)
C(59)	-0.1247(3)	0.8455(2)	0.6241(2)	0.038(1)
C(60)	-0.0643(3)	0.8854(2)	0.6497(2)	0.039(1)
C(61)	-0.0007(3)	0.8671(2)	0.6889(2)	0.033(1)
C(62)	-0.1901(3)	0.7448(2)	0.6110(2)	0.036(1)
C(63)	-0.0696(5)	0.9493(3)	0.6380(2)	0.062(2)
C(64)	0.4578(3)	0.7387(2)	0.6946(1)	0.021(1)

C(65)	0.4689(3)	0.7681(2)	0.6481(1)	0.023(1)
C(66)	0.5035(3)	0.8241(2)	0.6460(2)	0.031(1)
C(67)	0.5118(4)	0.8504(2)	0.6030(2)	0.040(1)
C(68)	0.4838(4)	0.8195(2)	0.5622(2)	0.034(1)
C(69)	0.4491(3)	0.7634(2)	0.5645(1)	0.025(1)
C(70)	0.4418(3)	0.7370(2)	0.6069(1)	0.022(1)
C(71)	0.4208(3)	0.7315(2)	0.5194(2)	0.029(1)
C(72A)	0.5605(9)	0.9078(4)	0.6010(3)	0.023(2)
C(72B)	0.5265(12)	0.9175(7)	0.6015(5)	0.056(4)
C(73)	0.4987(3)	0.6771(2)	0.6979(1)	0.022(1)
C(74)	0.6007(3)	0.6704(2)	0.6990(1)	0.025(1)
C(75)	0.6431(3)	0.6158(2)	0.7032(1)	0.026(1)
C(76)	0.5854(3)	0.5663(2)	0.7060(2)	0.030(1)
C(77)	0.4845(3)	0.5726(2)	0.7043(2)	0.029(1)
C(78)	0.4409(3)	0.6278(2)	0.7003(1)	0.025(1)
C(79)	0.7528(3)	0.6084(2)	0.7051(2)	0.035(1)
C(80)	0.4217(4)	0.5199(2)	0.7064(2)	0.037(1)
C(99)	0.1664(4)	0.3668(2)	0.5536(2)	0.043(1)
C(100)	0.2225(5)	0.4384(2)	0.8327(2)	0.063(2)

Table 2. Bond lengths [Å] and angles [°].

Cl(1)-C(99)	1.754(5)	Cl(2)-C(99)	1.760(5)
Cl(3)-C(100)	1.759(6)	Cl(4)-C(100)	1.759(6)
S(1)-O(1)	1.600(3)	S(1)-O(2)	1.418(3)
S(1)-O(3)	1.423(3)	S(1)-C(5)	1.788(4)
S(2)-O(4)	1.427(3)	S(2)-O(5)	1.429(3)
S(2)-N(1)	1.614(4)	S(2)-C(6)	1.799(4)
S(3)-O(7)	1.596(3)	S(3)-O(8)	1.423(3)
S(3)-O(9)	1.426(3)	S(3)-C(45)	1.787(4)
S(4)-O(10)	1.426(3)	S(4)-O(11)	1.431(3)
S(4)-N(2)	1.615(4)	S(4)-C(46)	1.798(4)
F(1A)-C(14)	1.270(7)	F(1B)-C(14)	1.398(8)
F(2A)-C(14)	1.411(8)	F(2B)-C(14)	1.254(8)
F(3A)-C(14)	1.394(8)	F(3B)-C(14)	1.324(10)
F(4)-C(15)	1.326(6)	F(5)-C(15)	1.321(6)
F(6)-C(15)	1.328(5)	F(7)-C(22)	1.313(5)
F(8)-C(22)	1.330(6)	F(9)-C(22)	1.310(5)
F(10A)-C(23)	1.163(12)	F(10B)-C(23)	1.491(10)
F(11A)-C(23)	1.386(9)	F(11B)-C(23)	1.333(7)
F(12A)-C(23)	1.276(9)	F(12B)-C(23)	1.390(10)
F(13)-C(31)	1.341(5)	F(14)-C(31)	1.348(5)
F(15)-C(31)	1.341(5)	F(16)-C(32)	1.332(5)
F(17)-C(32)	1.335(5)	F(18)-C(32)	1.338(5)
F(19)-C(39)	1.330(6)	F(20)-C(39)	1.326(6)
F(21)-C(39)	1.327(6)	F(22)-C(40)	1.328(5)
F(23)-C(40)	1.327(5)	F(24)-C(40)	1.340(5)
F(25)-C(54)	1.342(5)	F(26)-C(54)	1.341(5)
F(27)-C(54)	1.338(5)	F(28A)-C(55)	1.269(12)
F(28B)-C(55)	1.392(8)	F(29A)-C(55)	1.411(9)
F(29B)-C(55)	1.269(8)	F(30A)-C(55)	1.270(11)

F(30B)-C(55)	1.378(8)	F(31)-C(62)	1.331(6)
F(32)-C(62)	1.351(5)	F(33)-C(62)	1.341(5)
F(34A)-C(63)	1.464(10)	F(34B)-C(63)	1.261(9)
F(35A)-C(63)	1.286(12)	F(35B)-C(63)	1.411(12)
F(36A)-C(63)	1.264(9)	F(36B)-C(63)	1.421(10)
F(37)-C(71)	1.332(5)	F(38)-C(71)	1.315(5)
F(39)-C(71)	1.334(5)	F(41A)-C(72A)	1.341(14)
F(41B)-C(72B)	1.134(18)	F(42A)-C(72A)	1.392(15)
F(42B)-C(72B)	1.37(2)	F(43)-C(79)	1.330(5)
F(43A)-C(72A)	1.297(11)	F(43B)-C(72B)	1.260(15)
F(44)-C(79)	1.342(6)	F(45)-C(79)	1.345(5)
F(46A)-C(80)	1.376(9)	F(46B)-C(80)	1.334(8)
F(47A)-C(80)	1.228(9)	F(47B)-C(80)	1.460(8)
F(48A)-C(80)	1.266(9)	F(48B)-C(80)	1.418(8)
O(1)-C(24)	1.465(5)	O(6)-C(7)	1.432(5)
O(7)-C(64)	1.470(4)	O(12)-C(47)	1.435(5)
C(1)-C(2)	1.404(6)	C(1)-C(6)	1.419(6)
C(1)-C(7)	1.552(6)	C(2)-C(3)	1.383(6)
C(3)-C(4)	1.383(6)	C(4)-C(5)	1.381(6)
C(4)-C(24)	1.529(6)	C(5)-C(6)	1.396(6)
C(7)-C(8)	1.530(6)	C(7)-C(16)	1.548(6)
C(8)-C(9)	1.386(6)	C(8)-C(13)	1.399(6)
C(9)-C(10)	1.395(6)	C(10)-C(11)	1.390(7)
C(10)-C(14)	1.493(7)	C(11)-C(12)	1.380(6)
C(12)-C(13)	1.393(6)	C(12)-C(15)	1.492(6)
C(16)-C(17)	1.392(6)	C(16)-C(21)	1.391(6)
C(17)-C(18)	1.382(6)	C(18)-C(19)	1.384(6)
C(18)-C(22)	1.498(6)	C(19)-C(20)	1.385(7)
C(20)-C(21)	1.396(6)	C(20)-C(23)	1.495(7)
C(24)-C(25)	1.529(5)	C(24)-C(33)	1.530(6)
C(25)-C(26)	1.391(6)	C(25)-C(30)	1.386(6)
C(26)-C(27)	1.379(6)	C(27)-C(28)	1.399(6)
C(27)-C(31)	1.493(6)	C(28)-C(29)	1.373(6)
C(29)-C(30)	1.395(6)	C(29)-C(32)	1.500(6)
C(33)-C(34)	1.379(6)	C(33)-C(38)	1.400(6)
C(34)-C(35)	1.392(6)	C(35)-C(36)	1.376(6)
C(35)-C(40)	1.504(6)	C(36)-C(37)	1.388(7)
C(37)-C(38)	1.377(6)	C(37)-C(39)	1.496(6)
C(41)-C(42)	1.399(6)	C(41)-C(46)	1.410(6)
C(41)-C(47)	1.549(6)	C(42)-C(43)	1.386(6)
C(43)-C(44)	1.383(6)	C(44)-C(45)	1.377(6)
C(44)-C(64)	1.529(5)	C(45)-C(46)	1.401(6)
C(47)-C(48)	1.533(6)	C(47)-C(56)	1.549(6)
C(48)-C(49)	1.390(6)	C(48)-C(53)	1.394(6)
C(49)-C(50)	1.385(6)	C(50)-C(51)	1.386(6)
C(50)-C(54)	1.497(6)	C(51)-C(52)	1.379(7)
C(52)-C(53)	1.385(6)	C(52)-C(55)	1.494(6)
C(56)-C(57)	1.389(6)	C(56)-C(61)	1.380(6)

C(57)-C(58)	1.396(6)	C(58)-C(59)	1.381(7)
C(58)-C(62)	1.492(6)	C(59)-C(60)	1.381(7)
C(60)-C(61)	1.399(7)	C(60)-C(63)	1.503(8)
C(64)-C(65)	1.532(5)	C(64)-C(73)	1.515(5)
C(65)-C(66)	1.373(6)	C(65)-C(70)	1.396(6)
C(66)-C(67)	1.403(6)	C(67)-C(68)	1.388(7)
C(67)-C(72A)	1.478(10)	C(67)-C(72B)	1.551(16)
C(68)-C(69)	1.373(6)	C(69)-C(70)	1.383(6)
C(69)-C(71)	1.503(6)	C(73)-C(74)	1.400(6)
C(73)-C(78)	1.386(6)	C(74)-C(75)	1.379(6)
C(75)-C(76)	1.390(6)	C(75)-C(79)	1.504(6)
C(76)-C(77)	1.382(6)	C(77)-C(78)	1.397(6)
C(77)-C(80)	1.488(6)		

O(1)-S(1)-C(5)	93.54(17)	O(2)-S(1)-O(1)	109.18(17)
O(2)-S(1)-O(3)	120.13(18)	O(2)-S(1)-C(5)	110.85(18)
O(3)-S(1)-O(1)	105.35(17)	O(3)-S(1)-C(5)	114.11(18)
O(4)-S(2)-O(5)	119.04(18)	O(4)-S(2)-N(1)	107.2(2)
O(4)-S(2)-C(6)	106.53(18)	O(5)-S(2)-N(1)	108.9(2)
O(5)-S(2)-C(6)	109.01(18)	N(1)-S(2)-C(6)	105.38(19)
O(7)-S(3)-C(45)	93.16(16)	O(8)-S(3)-O(7)	108.92(16)
O(8)-S(3)-O(9)	120.01(17)	O(8)-S(3)-C(45)	112.28(18)
O(9)-S(3)-O(7)	105.67(16)	O(9)-S(3)-C(45)	113.00(18)
O(10)-S(4)-O(11)	118.19(18)	O(10)-S(4)-N(2)	106.6(2)
O(10)-S(4)-C(46)	105.90(18)	O(11)-S(4)-N(2)	108.6(2)
O(11)-S(4)-C(46)	109.43(18)	N(2)-S(4)-C(46)	107.60(19)
C(24)-O(1)-S(1)	112.4(2)	C(64)-O(7)-S(3)	113.5(2)
C(2)-C(1)-C(6)	117.1(4)	C(2)-C(1)-C(7)	118.9(3)
C(6)-C(1)-C(7)	124.0(4)	C(3)-C(2)-C(1)	123.5(4)
C(2)-C(3)-C(4)	118.7(4)	C(3)-C(4)-C(24)	126.3(4)
C(5)-C(4)-C(3)	119.3(4)	C(5)-C(4)-C(24)	114.2(3)
C(4)-C(5)-S(1)	106.9(3)	C(4)-C(5)-C(6)	123.0(4)
C(6)-C(5)-S(1)	130.0(3)	C(1)-C(6)-S(2)	125.3(3)
C(5)-C(6)-S(2)	116.3(3)	C(5)-C(6)-C(1)	118.3(4)
O(6)-C(7)-C(1)	109.5(3)	O(6)-C(7)-C(8)	111.6(3)
O(6)-C(7)-C(16)	105.2(3)	C(8)-C(7)-C(1)	113.0(3)
C(8)-C(7)-C(16)	105.0(3)	C(16)-C(7)-C(1)	112.2(3)
C(9)-C(8)-C(7)	118.6(4)	C(9)-C(8)-C(13)	119.2(4)
C(13)-C(8)-C(7)	121.4(4)	C(8)-C(9)-C(10)	120.3(4)
C(9)-C(10)-C(14)	119.9(4)	C(11)-C(10)-C(9)	120.6(4)
C(11)-C(10)-C(14)	119.5(4)	C(12)-C(11)-C(10)	119.0(4)
C(11)-C(12)-C(13)	121.1(4)	C(11)-C(12)-C(15)	118.3(4)
C(13)-C(12)-C(15)	120.6(4)	C(12)-C(13)-C(8)	119.8(4)
F(1A)-C(14)-F(1B)	29.8(3)	F(1A)-C(14)-F(2A)	112.1(5)
F(1A)-C(14)-F(3A)	103.9(6)	F(1A)-C(14)-F(3B)	75.5(6)
F(1A)-C(14)-C(10)	114.9(5)	F(1B)-C(14)-F(2A)	89.7(5)
F(1B)-C(14)-C(10)	108.1(5)	F(2A)-C(14)-C(10)	110.4(5)
F(2B)-C(14)-F(1A)	121.3(6)	F(2B)-C(14)-F(1B)	106.2(6)

F(2B)-C(14)-F(2A)	21.9(4)	F(2B)-C(14)-F(3A)	81.8(5)
F(2B)-C(14)-F(3B)	106.2(7)	F(2B)-C(14)-C(10)	116.7(5)
F(3A)-C(14)-F(1B)	130.2(5)	F(3A)-C(14)-F(2A)	103.5(5)
F(3A)-C(14)-C(10)	111.3(4)	F(3B)-C(14)-F(1B)	104.6(6)
F(3B)-C(14)-F(2A)	125.3(6)	F(3B)-C(14)-F(3A)	30.6(4)
F(3B)-C(14)-C(10)	114.1(5)	F(4)-C(15)-F(6)	106.2(4)
F(4)-C(15)-C(12)	114.1(4)	F(5)-C(15)-F(4)	105.1(4)
F(5)-C(15)-F(6)	106.9(4)	F(5)-C(15)-C(12)	113.5(4)
F(6)-C(15)-C(12)	110.4(4)	C(17)-C(16)-C(7)	121.1(4)
C(21)-C(16)-C(7)	120.2(4)	C(21)-C(16)-C(17)	118.6(4)
C(18)-C(17)-C(16)	121.2(4)	C(17)-C(18)-C(19)	120.4(4)
C(17)-C(18)-C(22)	118.8(4)	C(19)-C(18)-C(22)	120.8(4)
C(18)-C(19)-C(20)	118.7(4)	C(19)-C(20)-C(21)	121.2(4)
C(19)-C(20)-C(23)	120.5(4)	C(21)-C(20)-C(23)	118.3(4)
C(16)-C(21)-C(20)	119.8(4)	F(7)-C(22)-F(8)	105.4(4)
F(7)-C(22)-C(18)	113.0(4)	F(8)-C(22)-C(18)	111.9(4)
F(9)-C(22)-F(7)	106.9(4)	F(9)-C(22)-F(8)	105.6(4)
F(9)-C(22)-C(18)	113.4(4)	F(10A)-C(23)-F(10B)	12.9(7)
F(10A)-C(23)-F(11A)	111.0(8)	F(10A)-C(23)-F(11B)	87.1(7)
F(10A)-C(23)-F(12A)	95.0(8)	F(10A)-C(23)-F(12B)	113.9(8)
F(10A)-C(23)-C(20)	117.5(7)	F(10B)-C(23)-C(20)	107.4(5)
F(11A)-C(23)-F(10B)	123.7(6)	F(11A)-C(23)-F(12B)	91.9(6)
F(11A)-C(23)-C(20)	111.3(5)	F(11B)-C(23)-F(10B)	98.9(6)
F(11B)-C(23)-F(11A)	27.6(3)	F(11B)-C(23)-F(12B)	115.0(6)
F(11B)-C(23)-C(20)	114.0(5)	F(12A)-C(23)-F(10B)	93.9(6)
F(12A)-C(23)-F(11A)	101.7(6)	F(12A)-C(23)-F(11B)	118.7(6)
F(12A)-C(23)-F(12B)	19.0(4)	F(12A)-C(23)-C(20)	118.4(5)
F(12B)-C(23)-F(10B)	112.8(6)	F(12B)-C(23)-C(20)	108.4(5)
O(1)-C(24)-C(4)	103.1(3)	O(1)-C(24)-C(25)	107.1(3)
O(1)-C(24)-C(33)	108.2(3)	C(4)-C(24)-C(33)	116.1(3)
C(25)-C(24)-C(4)	109.7(3)	C(25)-C(24)-C(33)	111.9(3)
C(26)-C(25)-C(24)	118.8(4)	C(30)-C(25)-C(24)	121.0(4)
C(30)-C(25)-C(26)	120.0(4)	C(27)-C(26)-C(25)	120.0(4)
C(26)-C(27)-C(28)	120.2(4)	C(26)-C(27)-C(31)	121.3(4)
C(28)-C(27)-C(31)	118.5(4)	C(29)-C(28)-C(27)	119.4(4)
C(28)-C(29)-C(30)	120.8(4)	C(28)-C(29)-C(32)	120.9(4)
C(30)-C(29)-C(32)	118.3(4)	C(25)-C(30)-C(29)	119.4(4)
F(13)-C(31)-F(14)	106.8(3)	F(13)-C(31)-F(15)	106.8(3)
F(13)-C(31)-C(27)	113.1(3)	F(14)-C(31)-C(27)	111.9(3)
F(15)-C(31)-F(14)	106.1(3)	F(15)-C(31)-C(27)	111.8(3)
F(16)-C(32)-F(17)	107.0(4)	F(16)-C(32)-F(18)	106.8(4)
F(16)-C(32)-C(29)	113.1(4)	F(17)-C(32)-F(18)	106.2(4)
F(17)-C(32)-C(29)	111.9(4)	F(18)-C(32)-C(29)	111.4(4)
C(34)-C(33)-C(24)	123.1(4)	C(34)-C(33)-C(38)	119.4(4)
C(38)-C(33)-C(24)	117.5(4)	C(33)-C(34)-C(35)	119.9(4)
C(34)-C(35)-C(40)	120.6(4)	C(36)-C(35)-C(34)	120.9(4)
C(36)-C(35)-C(40)	118.5(4)	C(35)-C(36)-C(37)	119.1(4)
C(36)-C(37)-C(39)	118.0(4)	C(38)-C(37)-C(36)	120.7(4)

C(38)-C(37)-C(39)	121.3(4)	C(37)-C(38)-C(33)	119.9(4)
F(19)-C(39)-C(37)	113.2(4)	F(20)-C(39)-F(19)	106.9(5)
F(20)-C(39)-F(21)	106.2(4)	F(20)-C(39)-C(37)	112.6(4)
F(21)-C(39)-F(19)	105.3(5)	F(21)-C(39)-C(37)	112.1(4)
F(22)-C(40)-F(24)	106.9(4)	F(22)-C(40)-C(35)	112.0(4)
F(23)-C(40)-F(22)	107.1(4)	F(23)-C(40)-F(24)	106.7(4)
F(23)-C(40)-C(35)	112.9(4)	F(24)-C(40)-C(35)	111.0(4)
C(42)-C(41)-C(46)	117.7(4)	C(42)-C(41)-C(47)	118.2(3)
C(46)-C(41)-C(47)	124.0(4)	C(43)-C(42)-C(41)	123.3(4)
C(44)-C(43)-C(42)	118.3(4)	C(43)-C(44)-C(64)	126.5(4)
C(45)-C(44)-C(43)	119.4(4)	C(45)-C(44)-C(64)	114.0(3)
C(44)-C(45)-S(3)	107.8(3)	C(44)-C(45)-C(46)	122.9(4)
C(46)-C(45)-S(3)	129.2(3)	C(41)-C(46)-S(4)	125.8(3)
C(45)-C(46)-S(4)	116.4(3)	C(45)-C(46)-C(41)	117.9(4)
O(12)-C(47)-C(41)	108.9(3)	O(12)-C(47)-C(48)	109.8(3)
O(12)-C(47)-C(56)	104.2(3)	C(41)-C(47)-C(56)	111.1(3)
C(48)-C(47)-C(41)	113.2(3)	C(48)-C(47)-C(56)	109.3(3)
C(49)-C(48)-C(47)	124.1(4)	C(49)-C(48)-C(53)	119.2(4)
C(53)-C(48)-C(47)	116.7(4)	C(50)-C(49)-C(48)	120.1(4)
C(49)-C(50)-C(51)	120.7(4)	C(49)-C(50)-C(54)	122.3(4)
C(51)-C(50)-C(54)	117.0(4)	C(52)-C(51)-C(50)	119.2(4)
C(51)-C(52)-C(53)	120.8(4)	C(51)-C(52)-C(55)	120.3(4)
C(53)-C(52)-C(55)	118.9(4)	C(52)-C(53)-C(48)	120.1(4)
F(25)-C(54)-C(50)	112.1(4)	F(26)-C(54)-F(25)	105.6(4)
F(26)-C(54)-C(50)	112.6(4)	F(27)-C(54)-F(25)	106.2(3)
F(27)-C(54)-F(26)	107.7(4)	F(27)-C(54)-C(50)	112.1(4)
F(28A)-C(55)-F(28B)	36.6(5)	F(28A)-C(55)-F(29A)	98.2(7)
F(28A)-C(55)-F(30A)	113.0(8)	F(28A)-C(55)-F(30B)	131.0(7)
F(28A)-C(55)-C(52)	112.0(6)	F(28B)-C(55)-F(29A)	127.2(5)
F(28B)-C(55)-C(52)	111.7(4)	F(29A)-C(55)-C(52)	110.9(5)
F(29B)-C(55)-F(28A)	71.7(7)	F(29B)-C(55)-F(28B)	104.1(5)
F(29B)-C(55)-F(29A)	26.9(4)	F(29B)-C(55)-F(30A)	119.5(7)
F(29B)-C(55)-F(30B)	111.5(5)	F(29B)-C(55)-C(52)	116.2(5)
F(30A)-C(55)-F(28B)	82.6(6)	F(30A)-C(55)-F(29A)	104.9(6)
F(30A)-C(55)-F(30B)	20.6(5)	F(30A)-C(55)-C(52)	116.1(6)
F(30B)-C(55)-F(28B)	103.2(5)	F(30B)-C(55)-F(29A)	90.6(5)
F(30B)-C(55)-C(52)	109.3(4)	C(57)-C(56)-C(47)	121.5(4)
C(61)-C(56)-C(47)	118.9(4)	C(61)-C(56)-C(57)	119.5(4)
C(56)-C(57)-C(58)	119.9(4)	C(57)-C(58)-C(62)	119.7(4)
C(59)-C(58)-C(57)	120.5(4)	C(59)-C(58)-C(62)	119.7(4)
C(60)-C(59)-C(58)	119.6(4)	C(59)-C(60)-C(61)	120.1(5)
C(59)-C(60)-C(63)	121.0(4)	C(61)-C(60)-C(63)	118.8(5)
C(56)-C(61)-C(60)	120.4(4)	F(31)-C(62)-F(32)	106.4(4)
F(31)-C(62)-F(33)	107.3(4)	F(31)-C(62)-C(58)	113.5(4)
F(32)-C(62)-C(58)	111.4(4)	F(33)-C(62)-F(32)	105.8(4)
F(33)-C(62)-C(58)	112.0(4)	F(34A)-C(63)-C(60)	105.8(6)
F(34B)-C(63)-F(34A)	24.5(4)	F(34B)-C(63)-F(35A)	82.9(7)
F(34B)-C(63)-F(35B)	103.6(7)	F(34B)-C(63)-F(36A)	117.1(6)

F(34B)-C(63)-F(36B)	106.5(6)	F(34B)-C(63)-C(60)	117.2(6)
F(35A)-C(63)-F(34A)	107.3(7)	F(35A)-C(63)-F(35B)	25.1(6)
F(35A)-C(63)-F(36B)	128.8(8)	F(35A)-C(63)-C(60)	110.6(7)
F(35B)-C(63)-F(34A)	127.6(7)	F(35B)-C(63)-F(36B)	108.4(7)
F(35B)-C(63)-C(60)	111.9(6)	F(36A)-C(63)-F(34A)	109.1(6)
F(36A)-C(63)-F(35A)	108.5(8)	F(36A)-C(63)-F(35B)	86.4(7)
F(36A)-C(63)-F(36B)	22.4(4)	F(36A)-C(63)-C(60)	115.3(5)
F(36B)-C(63)-F(34A)	91.7(6)	F(36B)-C(63)-C(60)	108.8(5)
O(7)-C(64)-C(44)	103.2(3)	O(7)-C(64)-C(65)	105.6(3)
O(7)-C(64)-C(73)	108.1(3)	C(44)-C(64)-C(65)	111.8(3)
C(73)-C(64)-C(44)	114.6(3)	C(73)-C(64)-C(65)	112.6(3)
C(66)-C(65)-C(64)	121.6(4)	C(66)-C(65)-C(70)	119.5(4)
C(70)-C(65)-C(64)	118.8(4)	C(65)-C(66)-C(67)	120.6(4)
C(66)-C(67)-C(72A)	120.4(5)	C(66)-C(67)-C(72B)	118.5(7)
C(68)-C(67)-C(66)	119.5(4)	C(68)-C(67)-C(72A)	119.7(5)
C(68)-C(67)-C(72B)	120.3(7)	C(72A)-C(67)-C(72B)	19.4(6)
C(69)-C(68)-C(67)	119.5(4)	C(68)-C(69)-C(70)	121.3(4)
C(68)-C(69)-C(71)	117.6(4)	C(70)-C(69)-C(71)	121.1(4)
C(69)-C(70)-C(65)	119.6(4)	F(37)-C(71)-F(39)	104.7(4)
F(37)-C(71)-C(69)	113.4(3)	F(38)-C(71)-F(37)	106.8(4)
F(38)-C(71)-F(39)	107.5(4)	F(38)-C(71)-C(69)	111.7(4)
F(39)-C(71)-C(69)	112.2(4)	F(41A)-C(72A)-F(42A)	90.7(8)
F(41A)-C(72A)-C(67)	111.7(8)	F(42A)-C(72A)-C(67)	114.6(8)
F(43A)-C(72A)-F(41A)	119.8(9)	F(43A)-C(72A)-F(42A)	99.5(9)
F(43A)-C(72A)-C(67)	116.8(7)	F(41B)-C(72B)-F(42B)	110.3(14)
F(41B)-C(72B)-F(43B)	110.0(15)	F(41B)-C(72B)-C(67)	123.1(13)
F(42B)-C(72B)-C(67)	98.4(13)	F(43B)-C(72B)-F(42B)	97.4(12)
F(43B)-C(72B)-C(67)	113.7(11)	C(74)-C(73)-C(64)	117.5(4)
C(78)-C(73)-C(64)	123.7(4)	C(78)-C(73)-C(74)	118.8(4)
C(75)-C(74)-C(73)	120.6(4)	C(74)-C(75)-C(76)	120.7(4)
C(74)-C(75)-C(79)	120.8(4)	C(76)-C(75)-C(79)	118.5(4)
C(77)-C(76)-C(75)	119.0(4)	C(76)-C(77)-C(78)	120.7(4)
C(76)-C(77)-C(80)	119.6(4)	C(78)-C(77)-C(80)	119.7(4)
C(73)-C(78)-C(77)	120.2(4)	F(43)-C(79)-F(44)	107.3(4)
F(43)-C(79)-F(45)	106.8(4)	F(43)-C(79)-C(75)	113.3(4)
F(44)-C(79)-F(45)	106.1(4)	F(44)-C(79)-C(75)	111.7(4)
F(45)-C(79)-C(75)	111.3(4)	F(46A)-C(80)-F(47B)	126.0(6)
F(46A)-C(80)-F(48B)	103.7(6)	F(46A)-C(80)-C(77)	111.5(5)
F(46B)-C(80)-F(46A)	27.4(4)	F(46B)-C(80)-F(47B)	102.4(5)
F(46B)-C(80)-F(48B)	123.7(6)	F(46B)-C(80)-C(77)	113.3(5)
F(47A)-C(80)-F(46A)	106.9(6)	F(47A)-C(80)-F(46B)	83.3(6)
F(47A)-C(80)-F(47B)	19.2(4)	F(47A)-C(80)-F(48A)	113.4(6)
F(47A)-C(80)-F(48B)	103.6(5)	F(47A)-C(80)-C(77)	118.3(5)
F(47B)-C(80)-C(77)	107.8(4)	F(48A)-C(80)-F(46A)	87.1(6)
F(48A)-C(80)-F(46B)	109.4(6)	F(48A)-C(80)-F(47B)	108.2(5)
F(48A)-C(80)-F(48B)	17.2(4)	F(48A)-C(80)-C(77)	114.8(5)
F(48B)-C(80)-F(47B)	94.5(5)	F(48B)-C(80)-C(77)	111.5(4)
Cl(1)-C(99)-Cl(2)	111.5(3)	Cl(3)-C(100)-Cl(4)	111.1(3)

Table 3. Anisotropic displacement parameters (Å^2).

The anisotropic displacement factor exponent takes the form:
$-2\pi^2[h^2 a^{*2}U_{11} + ... + 2 h k a^* b^* U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl(1)	0.107(1)	0.033(1)	0.042(1)	0.000(1)	-0.013(1)	0.005(1)
Cl(2)	0.064(1)	0.049(1)	0.050(1)	-0.006(1)	-0.020(1)	0.005(1)
Cl(3)	0.064(1)	0.045(1)	0.045(1)	-0.004(1)	-0.010(1)	-0.002(1)
Cl(4)	0.070(1)	0.037(1)	0.062(1)	0.005(1)	-0.025(1)	0.001(1)
S(1)	0.027(1)	0.026(1)	0.017(1)	-0.001(1)	-0.001(1)	0.002(1)
S(2)	0.032(1)	0.027(1)	0.017(1)	0.001(1)	-0.003(1)	0.002(1)
S(3)	0.019(1)	0.027(1)	0.017(1)	-0.001(1)	-0.002(1)	-0.001(1)
S(4)	0.024(1)	0.031(1)	0.018(1)	-0.003(1)	0.000(1)	0.001(1)
F(4)	0.044(2)	0.040(2)	0.072(2)	0.004(2)	0.010(2)	-0.008(1)
F(5)	0.036(2)	0.087(3)	0.079(3)	0.024(2)	-0.010(2)	-0.019(2)
F(6)	0.145(4)	0.064(2)	0.062(2)	-0.024(2)	0.072(3)	-0.045(2)
F(7)	0.078(2)	0.036(2)	0.073(2)	0.018(2)	0.041(2)	0.015(2)
F(8)	0.044(2)	0.121(3)	0.049(2)	0.034(2)	0.018(2)	0.030(2)
F(9)	0.122(3)	0.091(3)	0.026(2)	-0.019(2)	0.024(2)	-0.057(2)
F(13)	0.030(1)	0.041(2)	0.028(1)	0.007(1)	0.005(1)	0.002(1)
F(14)	0.038(1)	0.035(1)	0.023(1)	-0.001(1)	-0.005(1)	-0.001(1)
F(15)	0.039(1)	0.027(1)	0.032(1)	0.004(1)	0.001(1)	0.007(1)
F(16)	0.022(1)	0.063(2)	0.047(2)	0.018(1)	-0.004(1)	-0.001(1)
F(17)	0.030(1)	0.045(2)	0.056(2)	0.019(1)	0.006(1)	-0.001(1)
F(18)	0.045(2)	0.064(2)	0.057(2)	-0.019(2)	0.026(2)	-0.007(2)
F(19)	0.087(3)	0.052(2)	0.136(4)	-0.050(2)	0.069(3)	-0.018(2)
F(20)	0.100(3)	0.046(2)	0.047(2)	-0.021(2)	-0.010(2)	0.009(2)
F(21)	0.084(2)	0.027(2)	0.061(2)	-0.007(1)	0.007(2)	0.008(2)
F(22)	0.036(2)	0.093(3)	0.059(2)	-0.026(2)	0.013(2)	-0.027(2)
F(23)	0.036(1)	0.040(2)	0.049(2)	0.006(1)	0.014(1)	0.007(1)
F(24)	0.065(2)	0.047(2)	0.039(2)	0.014(1)	0.024(2)	0.013(2)
F(25)	0.046(2)	0.039(2)	0.029(2)	0.004(1)	-0.007(1)	-0.003(1)
F(26)	0.036(2)	0.036(2)	0.059(2)	0.007(1)	0.015(1)	0.008(1)
F(27)	0.040(2)	0.034(1)	0.041(2)	-0.005(1)	-0.004(1)	-0.010(1)
F(31)	0.045(2)	0.055(2)	0.036(2)	-0.007(1)	-0.004(1)	-0.014(1)
F(32)	0.026(1)	0.083(2)	0.044(2)	-0.002(2)	-0.001(1)	-0.016(1)
F(33)	0.055(2)	0.079(2)	0.024(2)	0.004(1)	-0.009(1)	-0.016(2)
F(37)	0.061(2)	0.033(1)	0.025(1)	-0.003(1)	-0.004(1)	-0.004(1)
F(38)	0.053(2)	0.103(3)	0.050(2)	-0.042(2)	0.031(2)	-0.027(2)
F(39)	0.071(2)	0.043(2)	0.034(2)	0.000(1)	-0.022(2)	0.013(2)
F(43)	0.023(1)	0.039(2)	0.052(2)	0.001(1)	0.001(1)	0.002(1)
F(44)	0.034(2)	0.057(2)	0.058(2)	-0.018(2)	0.008(1)	0.011(1)
F(45)	0.034(2)	0.049(2)	0.059(2)	0.016(1)	-0.010(1)	0.009(1)
O(1)	0.028(2)	0.029(2)	0.018(1)	0.000(1)	0.001(1)	0.005(1)
O(2)	0.029(2)	0.030(2)	0.023(2)	-0.003(1)	-0.005(1)	0.001(1)
O(3)	0.037(2)	0.031(2)	0.019(2)	0.001(1)	0.005(1)	0.003(1)
O(4)	0.041(2)	0.032(2)	0.018(2)	-0.005(1)	-0.006(1)	0.005(1)
O(5)	0.037(2)	0.027(2)	0.024(2)	-0.001(1)	-0.004(1)	0.009(1)
O(6)	0.032(2)	0.029(2)	0.020(2)	0.004(1)	0.001(1)	0.000(1)
O(7)	0.020(1)	0.028(2)	0.019(1)	-0.003(1)	-0.003(1)	-0.002(1)
O(8)	0.022(1)	0.032(2)	0.021(2)	0.004(1)	-0.003(1)	0.001(1)
O(9)	0.025(1)	0.030(2)	0.024(2)	-0.005(1)	-0.001(1)	-0.003(1)
O(10)	0.025(2)	0.038(2)	0.020(2)	-0.002(1)	-0.001(1)	0.000(1)
O(11)	0.023(1)	0.042(2)	0.021(2)	-0.001(1)	0.005(1)	0.000(1)

O(12)	0.031(2)	0.031(2)	0.025(2)	-0.007(1)	0.000(1)	0.005(1)
N(1)	0.041(2)	0.035(2)	0.026(2)	0.008(2)	0.003(2)	0.000(2)
N(2)	0.041(2)	0.037(2)	0.021(2)	-0.008(2)	-0.001(2)	-0.003(2)
C(1)	0.020(2)	0.027(2)	0.021(2)	0.000(2)	0.000(2)	0.001(2)
C(2)	0.023(2)	0.030(2)	0.018(2)	-0.002(2)	-0.001(2)	0.001(2)
C(3)	0.025(2)	0.026(2)	0.020(2)	0.003(2)	0.000(2)	0.001(2)
C(4)	0.021(2)	0.023(2)	0.022(2)	0.000(2)	-0.002(2)	-0.001(2)
C(5)	0.021(2)	0.030(2)	0.018(2)	-0.002(2)	0.000(2)	-0.002(2)
C(6)	0.022(2)	0.025(2)	0.021(2)	0.000(2)	-0.002(2)	0.000(2)
C(7)	0.027(2)	0.027(2)	0.020(2)	-0.001(2)	-0.001(2)	-0.001(2)
C(8)	0.025(2)	0.028(2)	0.015(2)	-0.001(2)	-0.003(2)	0.000(2)
C(9)	0.030(2)	0.028(2)	0.021(2)	0.000(2)	-0.001(2)	0.002(2)
C(10)	0.036(2)	0.034(2)	0.023(2)	-0.001(2)	-0.002(2)	0.010(2)
C(11)	0.030(2)	0.044(3)	0.022(2)	-0.001(2)	0.001(2)	0.007(2)
C(12)	0.028(2)	0.038(2)	0.016(2)	-0.001(2)	-0.001(2)	-0.001(2)
C(13)	0.036(2)	0.028(2)	0.016(2)	-0.001(2)	-0.001(2)	0.001(2)
C(14)	0.045(3)	0.044(3)	0.027(3)	0.005(2)	0.004(2)	0.015(2)
C(15)	0.036(2)	0.044(3)	0.024(2)	-0.003(2)	0.006(2)	-0.002(2)
C(16)	0.028(2)	0.026(2)	0.018(2)	-0.003(2)	-0.004(2)	0.005(2)
C(17)	0.029(2)	0.022(2)	0.024(2)	-0.001(2)	-0.001(2)	0.003(2)
C(18)	0.031(2)	0.025(2)	0.022(2)	-0.001(2)	0.000(2)	0.005(2)
C(19)	0.036(2)	0.036(2)	0.022(2)	-0.005(2)	-0.005(2)	0.005(2)
C(20)	0.031(2)	0.039(3)	0.027(2)	-0.003(2)	-0.002(2)	-0.002(2)
C(21)	0.028(2)	0.034(2)	0.025(2)	-0.002(2)	-0.002(2)	-0.001(2)
C(22)	0.036(2)	0.031(2)	0.023(2)	-0.003(2)	-0.002(2)	0.005(2)
C(23)	0.053(3)	0.058(4)	0.022(3)	-0.006(2)	-0.006(2)	-0.016(3)
C(24)	0.026(2)	0.026(2)	0.015(2)	-0.001(2)	0.000(2)	0.003(2)
C(25)	0.023(2)	0.022(2)	0.024(2)	-0.004(2)	0.001(2)	0.002(2)
C(26)	0.022(2)	0.024(2)	0.024(2)	-0.002(2)	0.002(2)	0.002(2)
C(27)	0.024(2)	0.023(2)	0.023(2)	-0.002(2)	0.001(2)	0.002(2)
C(28)	0.025(2)	0.028(2)	0.026(2)	0.000(2)	-0.001(2)	0.004(2)
C(29)	0.024(2)	0.023(2)	0.030(2)	-0.002(2)	0.002(2)	0.002(2)
C(30)	0.028(2)	0.023(2)	0.023(2)	0.002(2)	0.003(2)	0.002(2)
C(31)	0.024(2)	0.027(2)	0.025(2)	0.000(2)	-0.002(2)	0.002(2)
C(32)	0.027(2)	0.034(2)	0.034(3)	0.004(2)	0.003(2)	0.002(2)
C(33)	0.025(2)	0.024(2)	0.020(2)	0.001(2)	-0.001(2)	0.002(2)
C(34)	0.026(2)	0.025(2)	0.020(2)	0.000(2)	0.000(2)	0.003(2)
C(35)	0.026(2)	0.031(2)	0.021(2)	0.003(2)	-0.002(2)	0.001(2)
C(36)	0.035(2)	0.027(2)	0.032(2)	0.002(2)	-0.003(2)	-0.004(2)
C(37)	0.036(2)	0.028(2)	0.030(2)	-0.004(2)	0.003(2)	0.001(2)
C(38)	0.029(2)	0.030(2)	0.030(2)	-0.002(2)	0.003(2)	0.003(2)
C(39)	0.051(3)	0.030(3)	0.047(3)	-0.011(2)	0.011(3)	-0.004(2)
C(40)	0.034(2)	0.035(3)	0.030(3)	-0.001(2)	0.004(2)	-0.005(2)
C(41)	0.022(2)	0.022(2)	0.025(2)	0.003(2)	0.001(2)	0.002(2)
C(42)	0.023(2)	0.030(2)	0.020(2)	0.000(2)	-0.004(2)	-0.001(2)
C(43)	0.023(2)	0.028(2)	0.018(2)	-0.001(2)	-0.001(2)	0.001(2)
C(44)	0.020(2)	0.022(2)	0.022(2)	0.001(2)	0.000(2)	0.001(2)
C(45)	0.017(2)	0.024(2)	0.020(2)	0.002(2)	-0.002(2)	0.000(2)
C(46)	0.025(2)	0.022(2)	0.018(2)	-0.002(2)	-0.001(2)	0.000(2)
C(47)	0.024(2)	0.026(2)	0.025(2)	-0.002(2)	0.000(2)	0.002(2)
C(48)	0.021(2)	0.033(2)	0.016(2)	-0.002(2)	-0.002(2)	0.000(2)
C(49)	0.020(2)	0.036(2)	0.020(2)	-0.004(2)	-0.002(2)	0.001(2)
C(50)	0.022(2)	0.034(2)	0.022(2)	-0.002(2)	-0.003(2)	-0.002(2)
C(51)	0.022(2)	0.046(3)	0.024(2)	0.002(2)	0.002(2)	-0.004(2)
C(52)	0.023(2)	0.045(3)	0.023(2)	0.000(2)	0.001(2)	0.001(2)
C(53)	0.025(2)	0.039(2)	0.021(2)	0.001(2)	0.001(2)	0.006(2)
C(54)	0.025(2)	0.033(2)	0.033(3)	-0.002(2)	0.003(2)	-0.005(2)
C(55)	0.030(2)	0.062(3)	0.027(3)	0.005(2)	0.004(2)	0.007(2)
C(56)	0.020(2)	0.033(2)	0.021(2)	-0.001(2)	0.001(2)	0.004(2)

C(57) 0.023(2)	0.035(2)	0.022(2)	0.001(2)	0.002(2)	0.001(2)
C(58) 0.020(2)	0.047(3)	0.020(2)	0.002(2)	-0.001(2)	-0.002(2)
C(59) 0.027(2)	0.055(3)	0.030(3)	0.013(2)	-0.004(2)	0.002(2)
C(60) 0.032(2)	0.042(3)	0.041(3)	0.011(2)	-0.003(2)	0.003(2)
C(61) 0.029(2)	0.035(2)	0.033(3)	0.004(2)	-0.002(2)	0.000(2)
C(62) 0.030(2)	0.055(3)	0.022(2)	0.004(2)	0.000(2)	-0.006(2)
C(63) 0.053(4)	0.071(4)	0.054(4)	0.031(3)	-0.018(3)	-0.005(3)
C(64) 0.018(2)	0.024(2)	0.019(2)	-0.003(2)	-0.002(2)	-0.002(2)
C(65) 0.022(2)	0.027(2)	0.020(2)	0.002(2)	0.003(2)	0.003(2)
C(66) 0.038(2)	0.031(2)	0.024(2)	-0.002(2)	0.001(2)	-0.002(2)
C(67) 0.059(3)	0.032(3)	0.028(3)	0.001(2)	0.003(2)	-0.009(2)
C(68) 0.045(3)	0.036(3)	0.021(2)	0.004(2)	0.002(2)	-0.002(2)
C(69) 0.023(2)	0.030(2)	0.021(2)	-0.002(2)	0.002(2)	0.003(2)
C(70) 0.018(2)	0.025(2)	0.023(2)	-0.002(2)	0.001(2)	0.003(2)
C(71) 0.032(2)	0.033(2)	0.021(2)	0.000(2)	0.002(2)	0.002(2)
C(73) 0.023(2)	0.026(2)	0.016(2)	0.000(2)	-0.001(2)	0.002(2)
C(74) 0.027(2)	0.028(2)	0.019(2)	0.001(2)	0.000(2)	0.001(2)
C(75) 0.023(2)	0.031(2)	0.021(2)	-0.001(2)	-0.001(2)	0.003(2)
C(76) 0.036(2)	0.029(2)	0.024(2)	-0.001(2)	-0.002(2)	0.005(2)
C(77) 0.029(2)	0.030(2)	0.026(2)	0.000(2)	-0.002(2)	-0.002(2)
C(78) 0.023(2)	0.030(2)	0.021(2)	0.000(2)	-0.001(2)	-0.001(2)
C(79) 0.031(2)	0.034(3)	0.038(3)	0.000(2)	-0.002(2)	0.007(2)
C(80) 0.037(3)	0.031(2)	0.044(3)	-0.003(2)	0.005(2)	-0.001(2)
C(99) 0.050(3)	0.039(3)	0.039(3)	0.005(2)	-0.002(2)	0.000(2)
C(100)0.083(4)	0.028(3)	0.065(4)	0.002(3)	-0.035(3)	-0.002(3)

9.2 Abstract / Kurzzusammenfassung

• This thesis delineates the development of efficient disulfonimide-catalyzed enantioselective vinylogous Mukaiyama aldol reactions and their extensions towards double vinlyogous versions. The disulfonimides proved to be very general, tolerating aromatic and aliphatic aldehydes as electrophiles. Focusing on open chain nucleophiles, we investigated differently substituted crotonates and sorbates. The unprecedented double vinylogous Mukaiyama aldol reactions, additions of six carbon atoms to carbonyl compounds, offered a rapid access to eight-membered ring lactones (ζ-lactones). Our endeavors towards the improvement of the disulfonimide-catalysts, led us to the exploitation of cooperative effects. This strategy found its successful embodiment in diarylmethanol-substituted hydroxy-disulfonimides, catalysts bearing a tertiary alcohol moiety in the substituents. With these catalysts we were able to efficiently convert very unreactive electrophiles in Mukaiyama aldol processes. Based on mechanistic studies, indicating a Lewis acid mechanism as operative, we presume that hydroxy-disulfonimides are Brønsted acid assisted Lewis acids. First results with these catalysts allowed for catalyst loadings unprecedented in metal-free catalysis (as low as 0.0001 mol%).

• Die vorliegende Arbeit beschreibt die Entwicklung von effizienten disulfonimid-katalysierten, enantioselektiven vinylogen Mukaiyama Aldolreaktionen und ihrer Erweiterung hinsichtlich doppelt vinyloger Versionen. Die Disulfonimde zeigten sich als generell anwendbar und tolerierten aromatische und aliphatische Aldehyde. Auf offenkettige Nukleophile fokussierend, untersuchten wir verschiedenartig substituierte Crotonate und Sorbate. Die bisher unbekannten doppelt vinylogen Mukaiyama Aldolreaktionen, Additionen von sechs Kohlenstoffatomen an Carbonylverbindungen, eröffneten einen schnellen Aufbau von Achtringlactonen (ζ-Lactone). Das Interesse zur Verbesserung der Katalysatoren brachte uns zum Konzept der kooperativen Effekte. Diese Strategie zeigte sich in elektronenarm substituierten Hydroxydisulfonimiden erfolgreich, Molekülen mit einer tertiären Alkoholfunktion im Substituenten. Mit diesen Katalysatoren konnten wir erfolgreich auch unreaktive Elektrophile in Mukaiyama Aldolreaktionen umsetzen. Basierend auf mechanistischen Studien welche auf Lewis-Säurekatalyse hinweisen, nehmen wir an, dass Hydroxydisulfonimide Brønstedsäure-aktivierte Lewissäuren sind. Erste Ergebnisse mit diesen Katalysatoren erlaubten Katalysatorbeladungen welche bisher einzigartig für metallfreie Katalyse sind (bis zu 0.0001 mol%).

9.3 Erklärung

“Ich versichere, dass ich die von mir vorgelegte Dissertation selbständig angefertigt, die benutzten Quellen und Hilfsmittel vollständig angegeben und die Stellen der Arbeit - einschließlich Tabellen, Karten und Abbildungen - die anderen Werken im Wortlaut oder dem Sinn nach entnommen sind, in jedem Einzelfall als Entlehnung kenntlich gemacht habe; dass diese Dissertation noch keiner anderen Fakultät oder Universität zur Prüfung vorgelegen hat; dass sie noch nicht veröffentlicht worden ist, sowie, dass ich eine solche Veröffentlichung vor Abschluss des Promotionsverfahrens nicht vornehmen werde. Die Bestimmungen der Promotionsordnung sind mir bekannt. Die von mir vorgelegte Dissertation ist von Herrn Professor Dr. Benjamin List betreut worden.”

Mülheim an der Ruhr, 01. Dezember 2011

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(Lars Ratjen)

9.4 Lebenslauf

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