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Enantioselective Synthesis of Alkenyl Aziridine Carboxylates and 4-Phenylsulfenyl Prolines

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften der Rheinisch-Westfälischen Technischen Hochschule Aachen zur Erlangung des akademischen Grades eines Doktors der Naturwissenschaften genehmigte Dissertation

vorgelegt von

Vijaya Bhaskara Reddy Iska

aus Indien

Berichter: Universitätsprofessor Dr. H.-J. Gais

Universitätsprofessor Dr. D. Enders

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Diese Dissertation ist auf den Internetseiten der Hochschulbibiliotheck online verfügbar.

Dedicated to my Parents

The work here reported has been carried out at the Institut für Organische Chemie der Fakultät für Mathematik, Informatik und Naturwissenschaften der Rheinisch Westfälischen Technischen Hochschule Aachen under the supervision of Prof. Dr. H.-J. Gais between October 2003 and August 2007.

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Last but not least I would like to express special thanks to my family, especially my wife, aruna, for the support, which helped me many times.

CONTENTS

Anal.	Analysis
aq.	Aqueous
BUS	*tert.*Butyl-sulfonyl
Calcd.	Calculated
d	Doublet
dd	Doublet of doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
de	Diastereomericexcess
DMF	N,N-Dimethylformamide
DMSO	Dimethylsulfoxide
ee	Enantiomericexcess
Et	Ethyl
GC	Gaschromatography
h	Hours
HRMS	High-resolution mass spectrum
Hz	Hertz
IR	Infrared
J	Coupling contant
MeLi	Methyllithium
m	Multiplet
mol	Mole
mg	Milligram
min	Minutes
ml	Milli liter
mmol	Milli mole
mp	Melting point
BuLi	Butyllithium
NMR	Nuclear magnetic resonance
Ph	Phenyl
ppm	Parts per million

Pr	Propyl
q	Quartet
rt	Room temperature
s	Singlet
t	Triplet
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
TMS	Trimethylsilyl
uv	ultraviolet

CHAPTER 1

Sulfoximine Chemistry

1 Sulfoximine Chemistry

1.1 General Introduction

Sulfoximine chemistry started in the late 1940's with the discovery of methionine sulfoximine[1] (Figure 1). Subsequently, many asymmetric reactions using chiral sulfoximines have been developed,[2] and intensive biological and physiological studies of sulfoximines have been performed.[3] Their versatility originates mainly from a unique combination of features of this functional group as for example chirality, carbanion stabilization, nucleofugacity, basicity, nucleophilicity, and a low redox potential. Recent examples where several of these characteristics have been exploited include several asymmetric syntheses of prostacyclin analogs,[4,5] which utilize transition metal mediated cross-coupling reactions of vinylic and allylic sulfoximines with organometallics for the formation of key C-C bonds. The sulfoximines have wider applications as chiral auxiliaries[6] and as catalysts in asymmetric synthesis.[7,8]

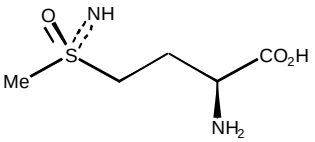


Figure 1.1 Methionine sulfoximine

1.2 Introduction to vinyl and allyl sulfoximines

Among the various sulfoximines '*vinyl sulfoximines*' and '*allyl sulfoximines*' have found many applications in asymmetric synthesis[9,10].

Figure 1.2 Vinyl and allyl sulfoximines

Vinyl sulfoximines have been prepared for the following reasons:

(a) As precursors for allylic sulfoximines to which they can be isomerized[11]

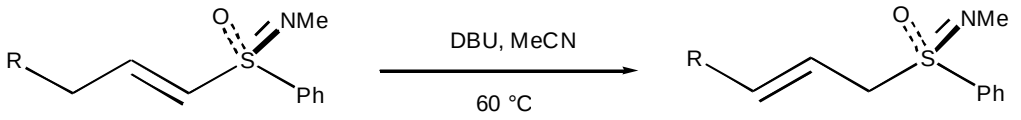


Figure 1.3 Isomerization of vinyl sulfoximines to allyl sulfoximines

(b) As Michael acceptors in conjugate addition reactions[12]

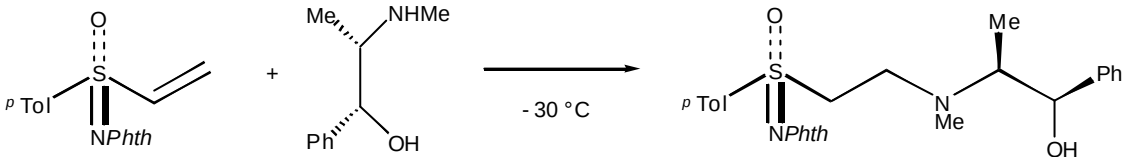


Figure 1.4 Conjugate addition to vinyl sulfoximines

(c) As substrates for Diels-Alder and 1,3-dipolar cycloaddition reactions[13]

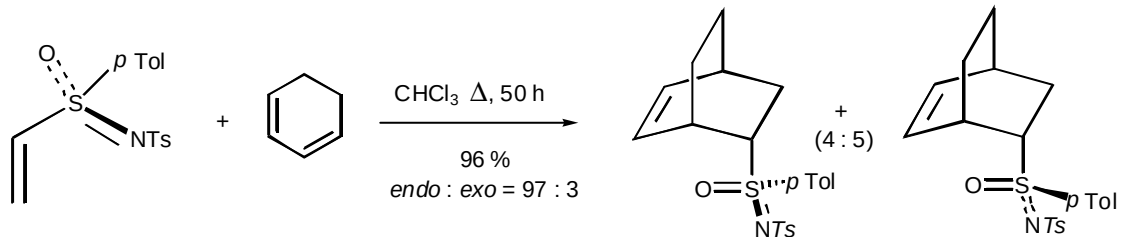


Figure 1.5 Diels-Alder reaction of vinyl sulfoximines

Similarly, allyl sulfoximines have important applications. A [2,3]-sigmatropic rearrangement of allyl sulfoximine gives more stable allyl sulfinamides. In 1994, Gais et al. published a study of the thermal rearrangement of two enantiopure substituted derivatives (Figure 1.6).[14]

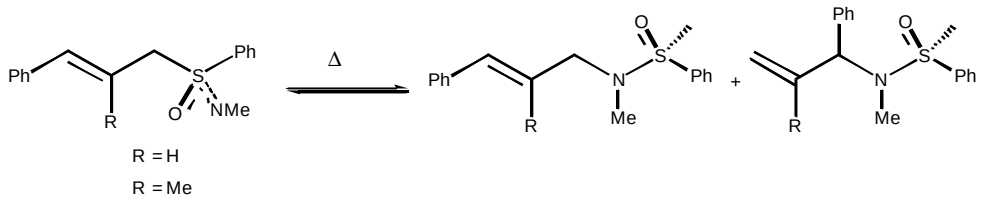


Figure 1.6 [2,3]-sigmatropic rearrangement of allyl sulfoximines[14]

The most important application of allyl sulfoximines is their conversion to chiral allyltitanium complexes followed by a reaction with aldehydes and imines, which yields sulfoximine-substituted homoallylic alcohols[2a,11] and amines[15] respectively. The first allyltitanium complex was synthesized by Reggelin et al. (Figure 1.7).[2a] Later Gais et. al. prepared various allyltitanium complexes with different titanium reagents and also determined their structures[16] in solution and in the crystal.

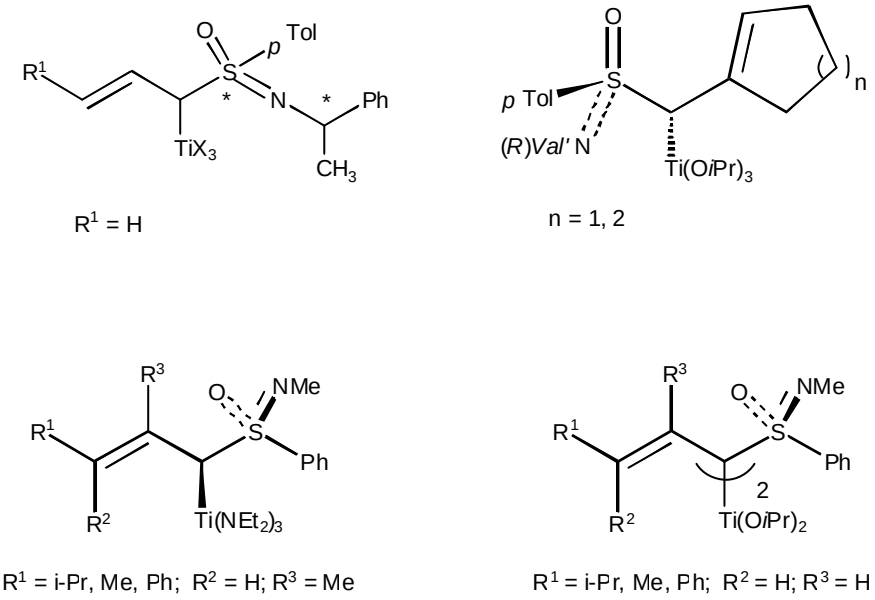


Figure 1.7 Allyltitanium complexes

Noteworthy examples of sulfonimidoyl-substituted allyltitanium(IV) complexes are **II** and **III**[11] (Figure 1.8), which have found application in the asymmetric synthesis of a number of compounds including γ,δ-unsaturated α-amino acids,[15] bicyclic α-amino

acids,[17a,b] γ-hydroxy β-amino acids,[17c] homopropargylic alcohols,[17d] homoallyl alcohols and unsaturated prolines.[18]

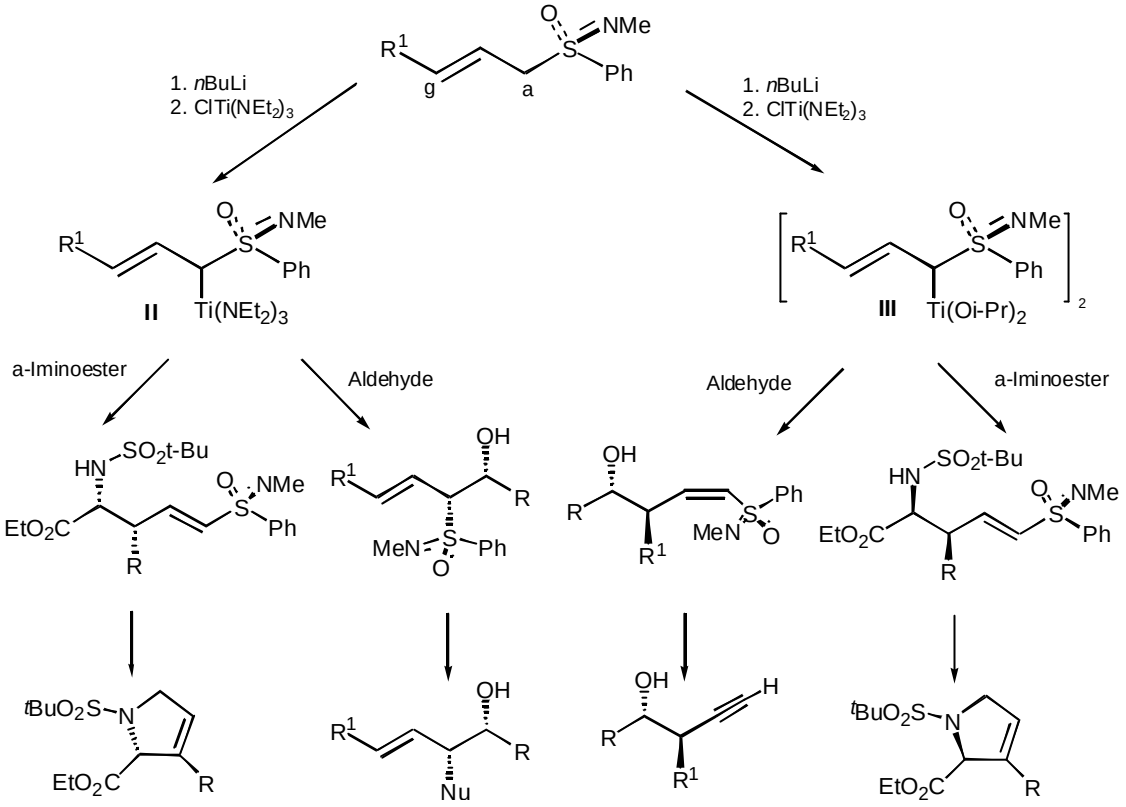


Figure 1.8 Applications of sulfonimidoyl–substituted allyltitanium (IV) complexes.

CHAPTER 2

Asymmetric synthesis of alkenyl aziridine carboxylates via in situ generation of allyl aminosulfoxonium ylides and a-imino ester

2 Asymmetric synthesis of alkenyl aziridine carboxylates via in situ generation of allyl aminosulfoxonium ylides and a-imino ester

2.1 Introduction

2.1.1 Aziridine Chemistry

The synthesis of chiral compounds in optically pure form represents a major challenge in organic chemistry. Much emphasis is placed on the elaboration of naturally occuring starting materials and on the development of techniques for enantioselective transformations of achiral substrates. In this regard, chiral aziridines are an attractive class of compounds.[19,20] Aziridines **I** (Figure 2.1) are saturated three-membered heterocycles containing one nitrogen atom. This class of compounds dates back to 1888, when Gabriel (unwittingly) synthesized the parent member.[21] Since then a variety of methods[22] have been developed for asymmetric synthesis of enantiomerically pure (or highly enriched) aziridine derivatives. The chemistry of aziridines is dominated by ring-opening reactions,[23] the driving force of which is the relief of ring strain. By suitable choice of substituents on the carbon and nitrogen atoms, excellent stereo- and regiocontrol can be attained in ring-opening reactions with a wide variety of nucleophiles, including organometallic reagent.[23b]

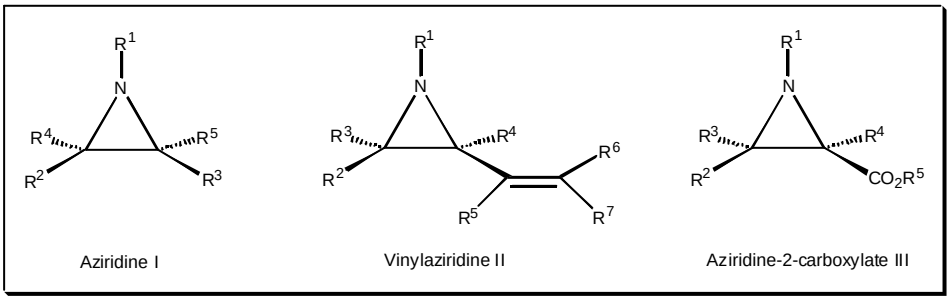


Figure 2.1: Chiral substituted aziridines

Among the variously functionalized aziridines, vinylaziridines[24] **II** and aziridine carboxylates[25] **III** have been increasingly exploited as versatile building blocks for the stereoselective synthesis of biologically and synthetically important compounds.[26] Vinylaziridines have found many synthetic applications because of their high reactivity and ability to undergo a variety of rearrangements[27] (Figure 2.2) and to function as carbon electrophiles. Ring-opening reactions of vinylaziridines can be effected by various carbon and heteroatom nucleophiles to produce a variety of functionalized amines. For example, vinylaziridines upon diborane reduction give allyl amines,[23a] organocopper mediated ring opening gives diastereomerically pure (*E*)-alkene dipeptide isosteres[23b,c], treatment with oxygen nucleophiles gives *vic*-amino alcohols, which is the key step for the synthesis of threo- and erythro-sphingosines[28]. Halogen atoms can be stereoselectively introduced by ring-opening of *g*-aziridinyl-*a*,*b*-enoates. The isomerizarion of vinylaziridines is widely used in organic synthesis. Important isomerizations are shown below.[29]

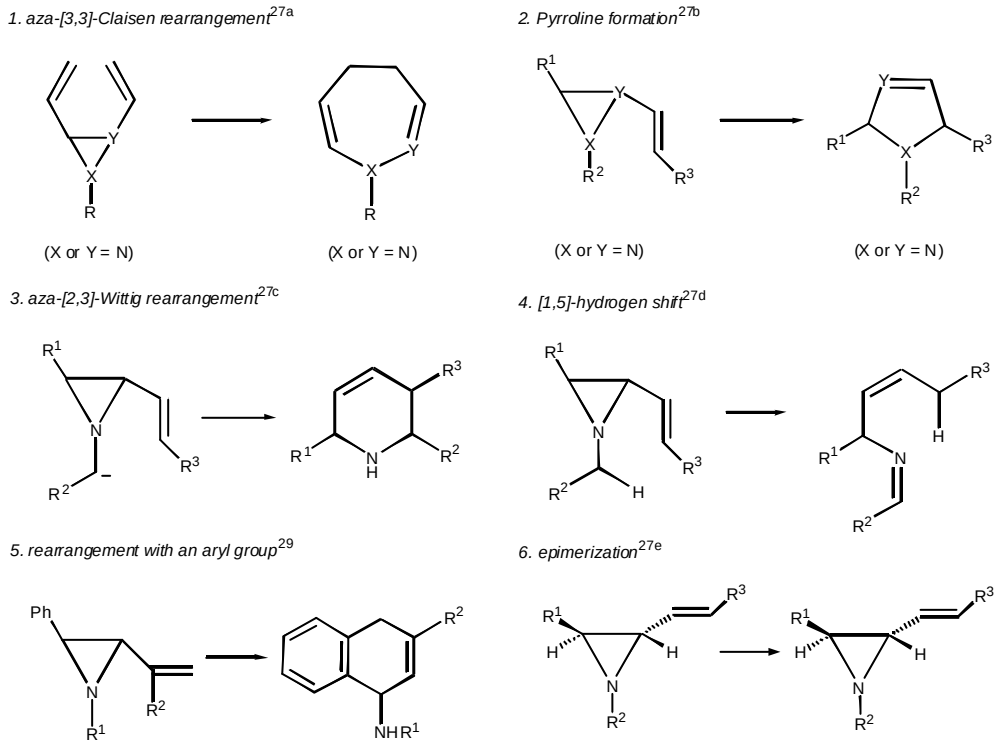


Figure 2.2: Isomerization of vinylaziridines.[27]

Similarly, chiral nonracemic *cis*- and *trans*-aziridine-2-carboxylates[30] are interesting aziridines. In addition to the normally expected reactions at the nitrogen atom and the C-2 carboxylic group, the C-3 and C-2 positions can undergo a variety of nucleophilic ring-opening reactions (Figure 2.3). [31]

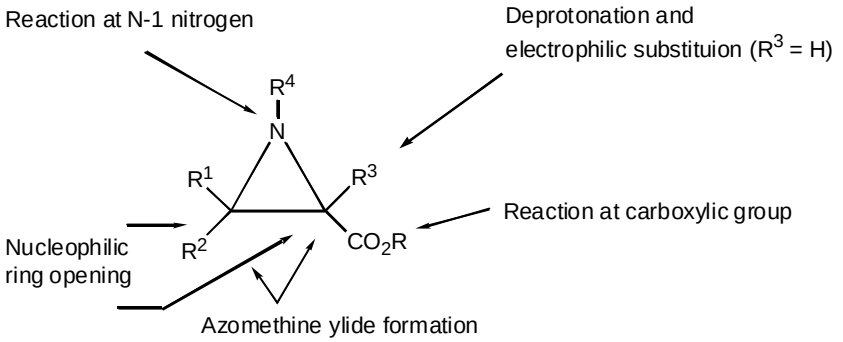


Figure 2.3: Reactions of aziridine carboxylates

The aziridine-2-carboxylates[32] are considered amino acids, not only because of the ease with which they are converted into acyclic *a*- and *b*- amino acids, but also because of the pronounced biological activities resulting from their incorporation into peptides as special amino acid units. In addition, a naturally occuring aziridine-2-carboxylic acid[33] has also been reported.

Chiral alkenyl aziridine carboxylates have also been reported as useful substrates for the synthesis of chiral building blocks in organic synthesis. A few of their applications are described below. In 1995 Davis et al. demonstrated an enantioselective synthesis of (*R*)-(–)-dysidazirine, which is cytotoxic to L1210 cells and inhibits the growth of Gram negative bacteria and yeast, from an enantiomerically pure alkenyl aziridine carboxylate[34] (Figure 2.4).

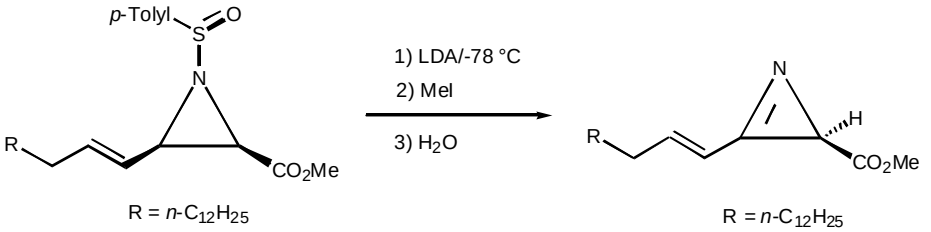


Figure 2.4: Synthesis of (*R*)-(−)-dysidazirine

Alkenyl aziridine carboxylates were found to be useful starting materials for the synthesis of sphingosines. In 2005 Ishikawa et al. reported the synthesis of D-*erythro*-sphingosine from an alkenyl aziridine carboxylate[28] (Figure 2.5).

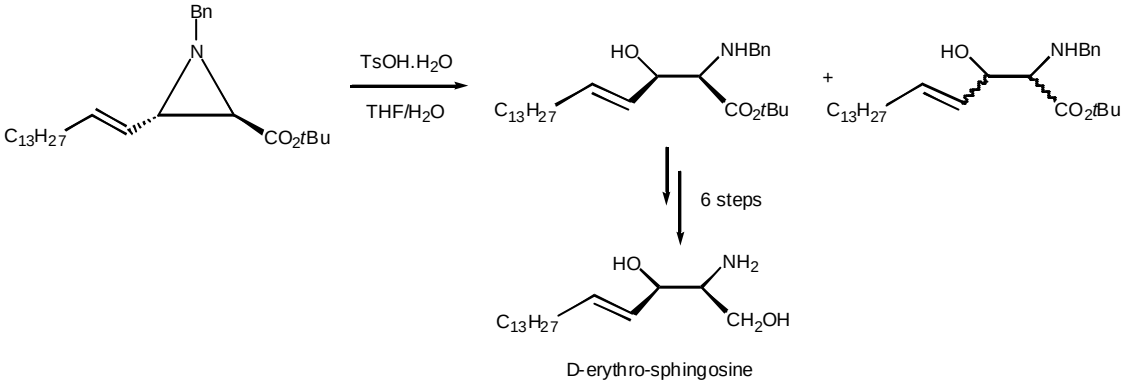


Figure 2.5: Synthesis of D-*erythro*-sphingosine

In 2001 Davis et al. employed alkenyl aziridine carboxylates for the synthesis of quaternary amino acids synthesis, which have important biological activity[35] (Figure 2.6).

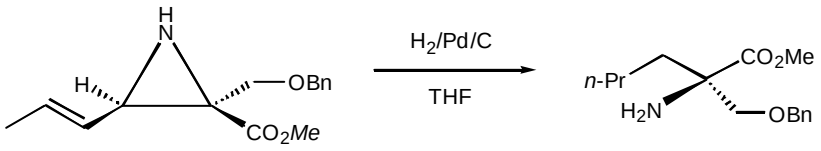


Figure 2.6: Synthesis of quaternary amino acids from alkenyl aziridine carboxylates

2.1.2 Aziridine natural products

Natural products containing an aziridine ring have been found.[36] The best known and first to be discovered are the mitomycin antitumor antibiotics, known to possess an aziridine ring since the 1960s,[37] and several others have been isolated since. There are even few examples of naturally occurring aziridines, where the mode of action of these compounds has been studied in detail. The biochemical reactions used for the formation of the aziridine ring remain a mystery. The important aziridine natural products are mytomycins, azinomycins, ficellomycin, dicarboxyaziridine, miraziridine A, azicemicins, maduropeptin, madurastatins, and (*2S,3S*)-dicarboxyaziridine[29] (Figure 2.7). Where as azinomycin A[38] is an example of a natural product that contains an *'alkenyl aziridine'* analogue, miraziridine and (*2S,3S*)-dicarboxyaziridine[39] are examples for natural products being '*aziridine carboxylate*' analogues.

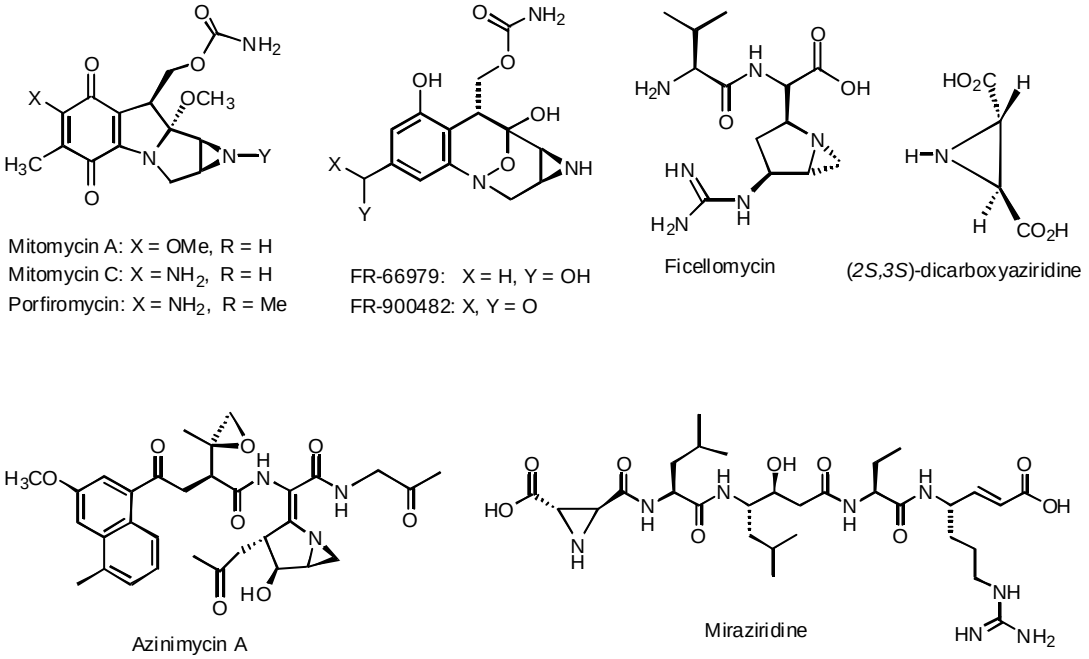


Figure 2.7: Aziridine natural products

It has been proposed that aziridines may be more widespread in biological systems than is generally realized. Many drugs such as ephedrine and pronethalol and endogenous metabolites such as adrenaline contain a *b*-aminoalcohol moiety, which may act as a precursor to an aziridine metabolite that may explain the known carcinogenicity of some compounds such as pronethol.[40]

2.1.3 Synthesis of aziridines

A variety of routes to chiral non–racemic aziridines have been described,[41, 32a] most of which rely either on the availability of enantiomerically pure starting materials from natural sources (amino acids, carbohydrates, hydroxy acids) or on asymmetric transformations of C-C or C-N double bonds (Figure 2.8).[42]

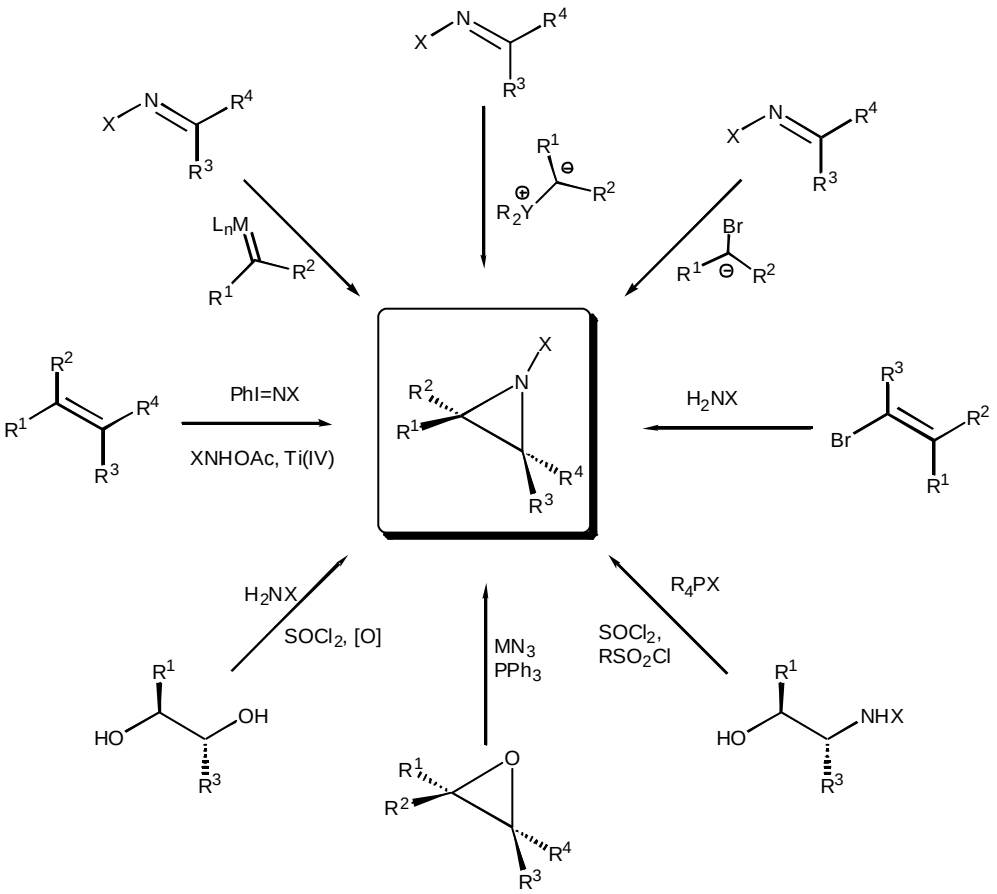


Figure 2.8: Methods for the synthesis of aziridines

The biological significance and chemical versatility of non-racemic aziridines make them one of the most useful synthetic intermediates. Synthetic methodologies for the preparation of aziridines include nitrene addition[43] to olefins, carbene and ylide addition to imines,[44] and cyclization of 1,2-amino alcohols, 1,2-amino halides, and 1,2-azido alcohols[37] (Figure 2.8). Darzens-type reaction[45] and Gabriel-Cromwell reaction[46] are other well-documented reactions for aziridine synthesis.

A few asymmetric syntheses of alkenyl aziridine carboxylates have been reported. Recently Sweeney et al. reported an asymmetric aziridine synthesis by using an aza-Darzens reaction of *N*-diphenylphosphinylimines with chiral enolates (Figure 2.9). Although the method gives high diastereoselectivities in the preparation of alkenyl aziridine carboxylates, the yields were poor in all the cases.[47]

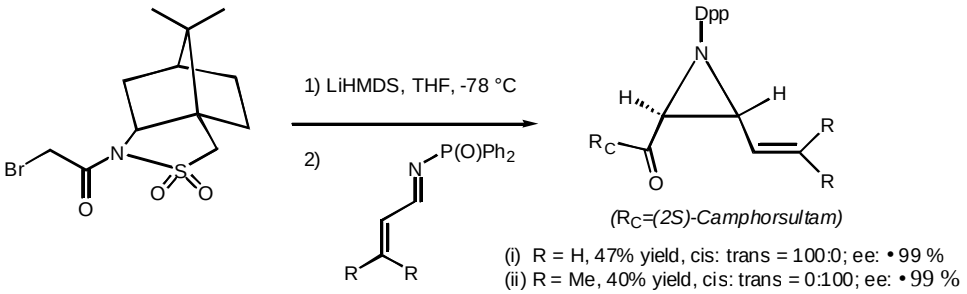


Figure 2.9: Synthesis of alkenyl aziridine carboxylates

Hanessian et al. reported another efficient asymmetric synthesis of alkenyl aziridine carboxylates in 2001.[48] The method is based on the application of a C_2-symmetrical chiral chloroallyl phosphonamide as depicted in Figure 2.10.

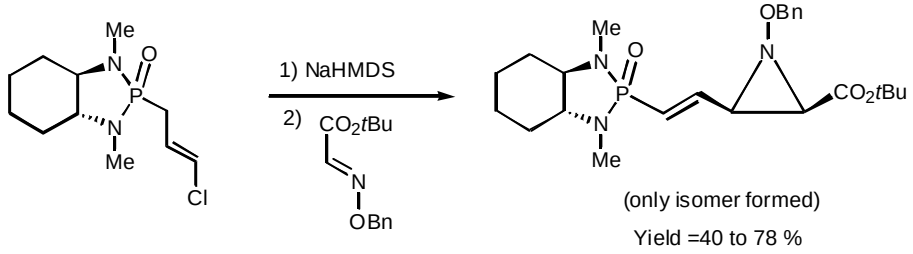


Figure 2.10: Synthesis of alkenyl aziridine carboxylates

In 2001 Ishikawa et al. found that treatment of guanidinium bromides with aryl or alkenyl aryl aldehydes in the presence of a base directly afforded 3-aryl (or alkenyl aryl) aziridine-2-carboxylates in high yields with moderate to excellent *trans* diastereoselectivity[49] (Figure 2.11).

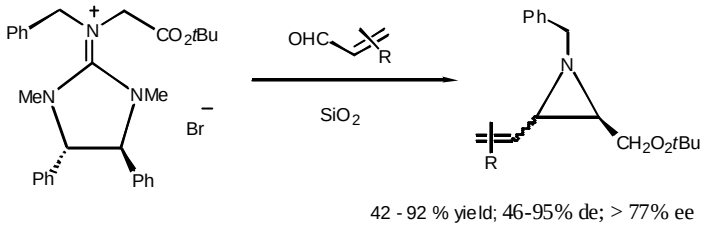


Figure 2.11: Synthesis of alkenyl aziridine carboxylates by Ishikawa et al.[49]

Davis et al. developed an asymmetric synthesis of alkenyl aziridine carboxylates by sulfinimine mediated Darzens-type reaction as shown in the Figure 2.12.[34]

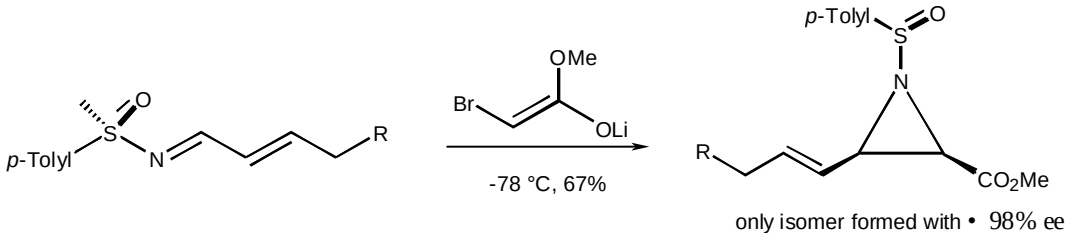


Figure 2.12: Synthesis of alkenyl aziridine carboxylates by Davis et al.[34]

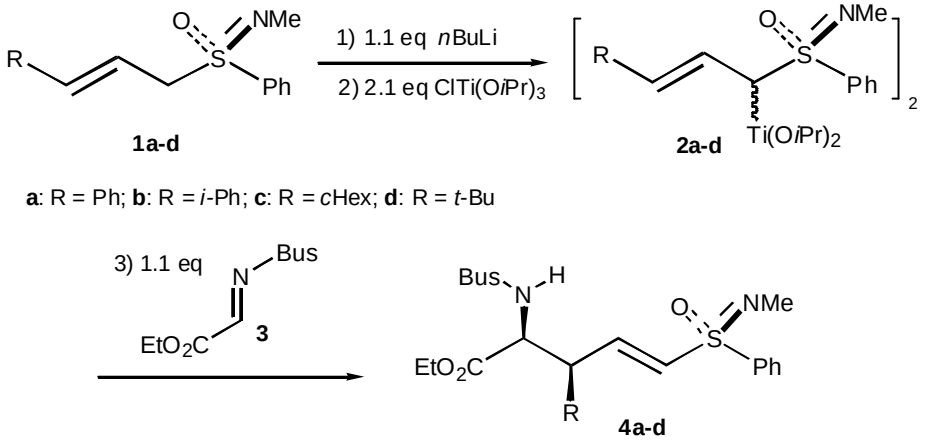
Although a few methods for asymmetric alkenyl aziridine carboxylates synthesis were reported in the literature, the extension of any of those methods to a variety of substituted alkenyl aziridine carboxylates was not successful in terms of yield.

2.2 Present work

2.2.1 Aim

As mentioned in the earlier section, chiral alkenyl aziridine carboxylates have found valuable applications in organic synthesis. Hence the asymmetric synthesis of such

compounds is an interesting task. In 2002, Gais et al. disclosed a method for the highly regio– and diastereoselective aminoalkylation of the allylic sulfoximines **1a-d** with *N*-*tert*-butylsulfonyl (Bus) α-imino ester **3**[50] leading to the formation of the (*syn*,*E*)-configured β-alkyl-γ,δ-unsaturated α-amino acid derivatives **4a-d**.[15] Thus, titanation of the lithiated allylic sulfoximines **1a-d** with $Cl(Ti(OiPr)_3$ afforded the corresponding bis(allyl)titanium complexes **2a-d** which reacted with the *N*-Bus α-imino ester **3** with high regio- and diastereoselectivities, preferentially at the *g*-position, to give the *syn*-configured *b*-alkyl-*g*,*d*-unsaturated α-amino acid derivatives **4a-d** in good yields (Scheme 2.1). Formation of (*S*,*R*,*E*)-configured homoallylic amines **4a-d** entails *Si*,*Re*,*E*–processes of the α-imino ester **3** with the (*R*,*R*)-configured bis(allyl)titanium complexes (*R*,*R*)-**2a-d**.



Scheme 2.1: Aminoalkylation of allylic sulfoximines.

Furthermore, Gais et al. described the synthesis, structure and application of chiral conjugated *N*-titanium allyl aminosulfoxonium ylides of type **I** (R^2 = H, R^3 = $Ti(NEt_2)_3$) (Figure 2.13).[16] The investigations of **I** were supplemented by ab initio calculations of the conjugated allyl aminosulfoxonium ylide **I** (R^1 = Me, R^2 = H, R^3 = Me). The hitherto unknown chiral allyl S ylides of type **I** (R^3 = Me) should be of considerable synthetic interest. A number of highly useful transformations of **I** can be envisioned based on the chemistry of the corresponding alkyl aminosulfoxonium ylides.[2a] Although chiral alkyl S-

ylides are well established reagents,[51] only a few examples of chiral conjugated allyl sulfonium ylides had been described.[52]

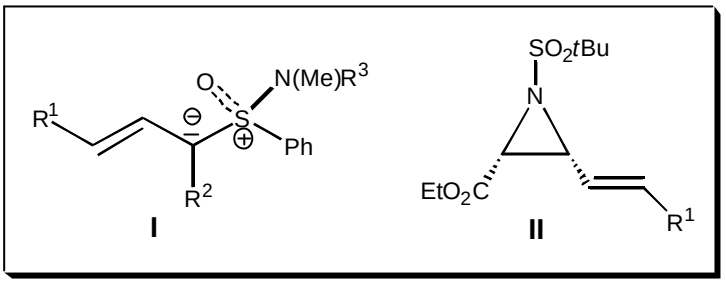
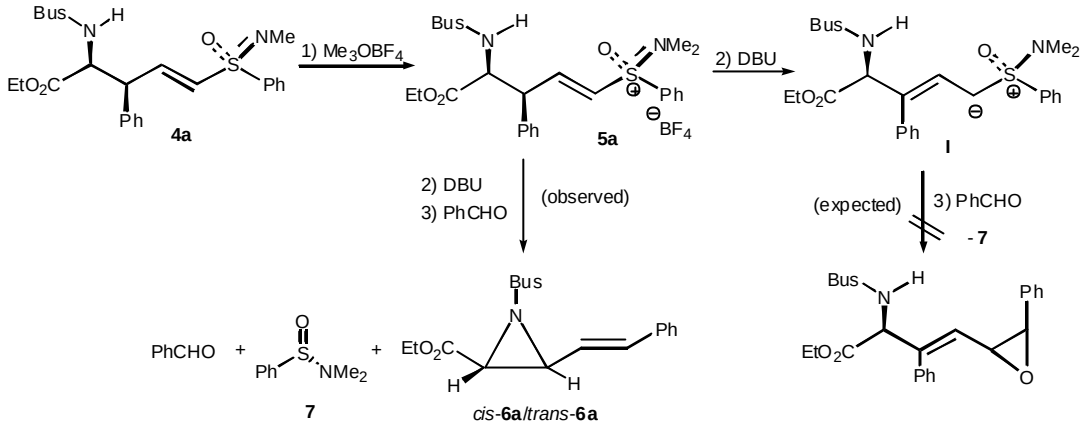


Figure 2.13 Chiral allyl aminosulfoxonium ylides and alkenyl aziridine carboxylates

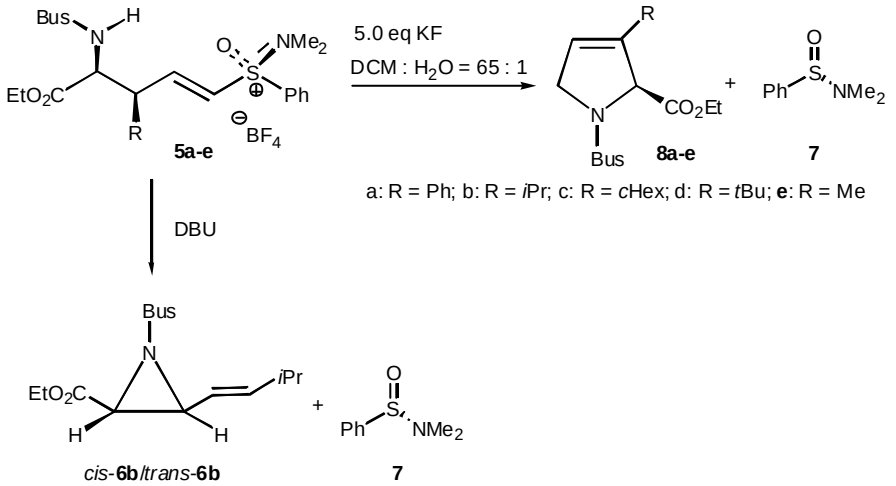
Thus, we have developed an interest in the synthesis of chiral ylides of type **I** and wished to apply them in the synthesis of enantio enriched alkenyl aziridine carboxylates of type **II**, for which only a few enantioselective syntheses had been described[53] as mentioned in the foregoing section.

An attempt was made to synthesize ylides of type **I** by treatment of the amino–substituted sulfoxonium salt **5a** with DBU. It was thought that the resulting ylide would then react with an electrophile, an aldehyde for example. Thus, the amino–substituted sulfoximine **4a** was treated with Meerwein's salt in CH_2Cl_2 at room temperature in order to produce the corresponding sulfoxonium salt **5a**,[16] which was then treated with DBU in the presence of benzaldehyde under the same reaction conditions in the expectation of formation of **I** and its reaction with benzaldehyde, Scheme 2.2. Surprisingly, however the reaction yielded a *cis*/*trans*–mixture of the alkenyl aziridine carboxylates *cis*-**6a**/*trans*-**6a** with good yields and good *cis*-diastereoselectivity. The sulfinamide **7** was isolated in good yield with ≥98% ee.



Scheme 2.2: Reaction of aminosulfoxonium salt **5a** with DBU in the presence of benzaldehyde

At the same time Tiwari, a former coworker of Prof. Gais, independently studied the reaction of the sulfoxonium salts **5a-e** with different bases. He observed that the salts undergo a facile migratory cyclization to afford the 3,4-dehydro prolines **8a-e** upon treatment with KF[54] (Scheme 2.2). He also observed the formation of a *cis*/*trans*–mixture of the alkenyl aziridine carboxylate *cis*-**6b**/*trans*-**6b** upon treatment of the sulfoxonium salt **5b** with DBU in CH_2Cl_2.



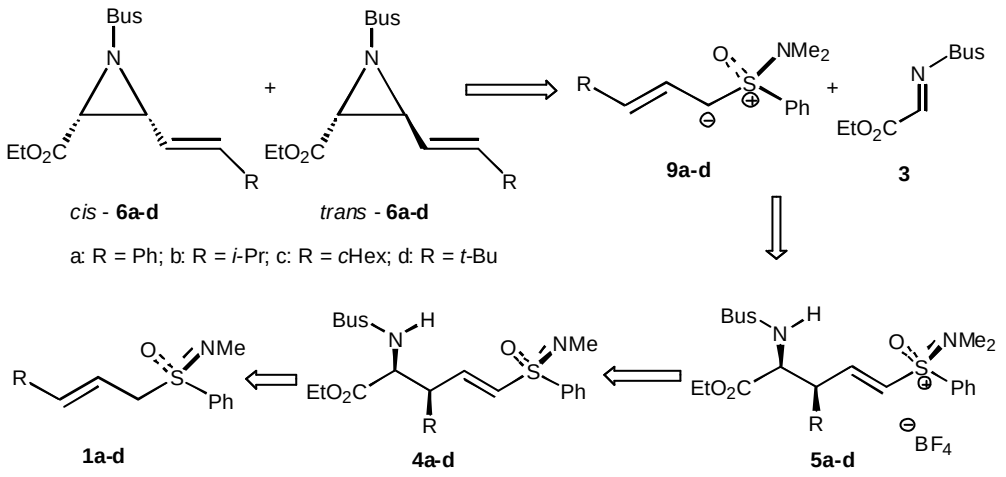
Scheme 2.3: Reactivities of the sulfoxonium salts **5** towards bases

The formation of prolines from the sulfoxonium salts **5a-e** was reported recently by Gais et al.[57] The above mentioned results of intial experiments toward aziridine formation and Tiwari's observation suggested an asymmetric synthesis of alkenyl aziridine carboxylates **6** from amino–substituted sulfoximines **4** with the formation of their corresponding salts **5** followed by treatment with DBU.

2.2.2 Results and Discussion

2.2.2.1 Retrosynthetic analysis

As illustrated in the foregoing section, the asymmetric synthesis of aziridines has been accomplished by several methods. Although some of these methods are very efficient for the synthesis of alkenylaziridines and aziridine carboxylates, they are not so well suited for preparing alkenylaziridine carboxylates **6** in good yields with high enantioselectivity. We therefore focused our interest on the asymmetric synthesis of alkenylaziridine carboxylates by following the retrosynthetic analysis shown in Scheme 2.4.

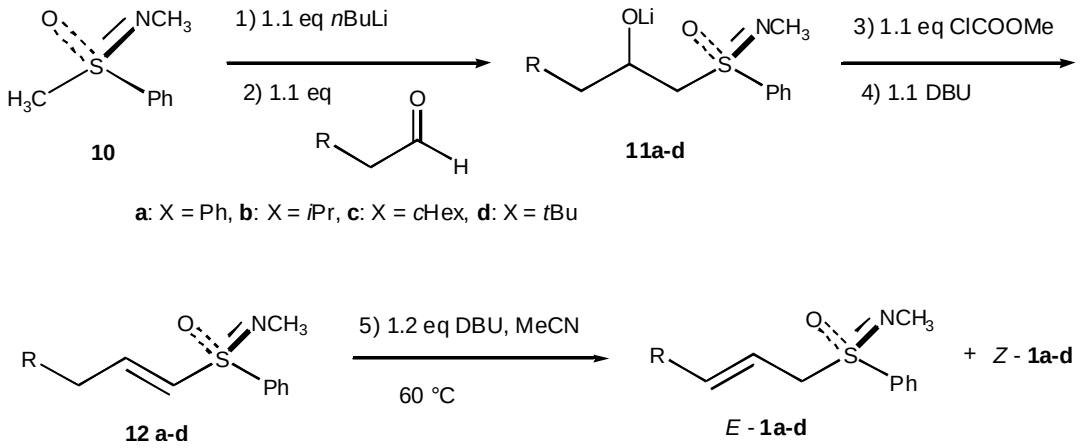


Scheme 2.4: Retrosynthetic analysis of alkenyl aziridine carboxylates

Key to the facile conversion of the vinyl aminosulfoxonium salts **5a-d** via the allyl aminosulfoxonium ylides **9a-d** to vinylaziridines is the ability of the aminosulfoxonium group to act as both a powerful carbanion-stabilizer and an excellent nucleofuge.[55,17d] The *cis*- and *trans*- alkenylaziridine carboxylates **6a-d** were realized from the corresponding vinyl aminosulfoxonium salts **5a-d**, which in turn can be derived from **4a-d** by methylation with Me_3OBF_4. The vinyl aminosulfoximine derivatives **4a-d** can be achieved from the allylic sulfoximines **1a-d**, the synthesis of which has been reported by Gais et al.[11] starting from (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximine **10**.[10b]

2.2.2.2 Asymmetric synthesis of allyl sulfoximines

The synthesis of the vinyl aminosulfoxonium salts **5a-d** commenced with the preparation of allylic sulfoximines **1a-d**. The known allylic sulfoximines **1a-d** were prepared without the isolation of intermediates from the enantiomerically pure (*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximine **10**[56-57] and the corresponding aldehydes by the inverse Peterson-olefination and isomerization as described previously[11] (Scheme 2.5). The lithiomethyl sulfoximine derived from **10** was treated with aldehydes in order to get the hydroxy sulfoximines **11a-d**, which were *in situ* treated with ClCOOMe to form the corresponding chloroformates. Treatment of the chloroformates with DBU gave the vinyl sulfoximines **12a-d** in good yields. The vinyl sulfoximines were then reacted with DBU in MeCN at 60 °C for 5 days to obtain a mixture of the allyl sulfoximines *E*–**1a-d** and *Z*–**1a-d** in good yields.[11] Flash column chromatography gave the pure *E*–allyl sulfoximine **1a-d** in >70% yield along with a mixture of the *E*– and *Z*–allyl sulfoximines, which were separated by preparative HPLC.



Scheme 2.5: Synthesis of allylic sulfoximines

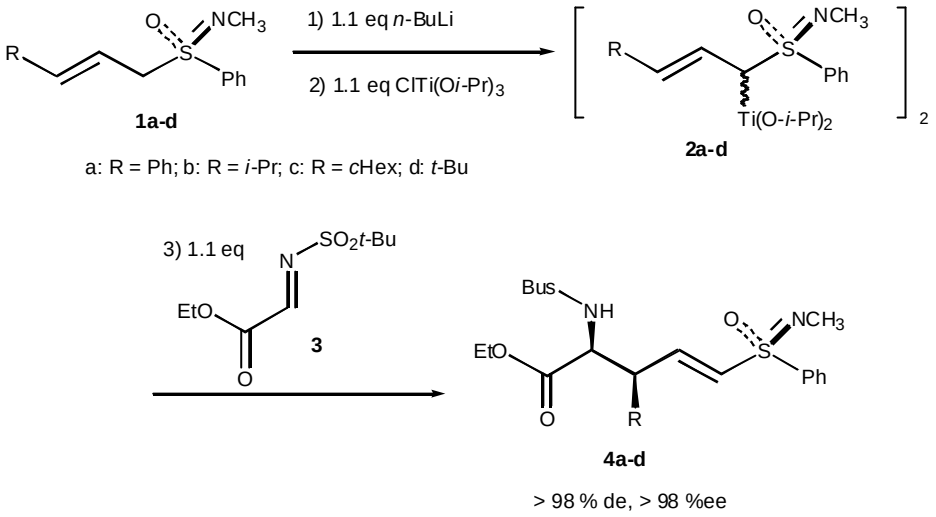
Table 2.1. Synthesis of allyl aminosulfoximines

1	R	Yield of *E*-(**1**)	Total Yield (*E* + *Z*) (%)
a	Ph	71	71
b	*i*Pr	75	90
c	cC_6H_{11}	82	91
d	*t*Bu	86	86

2.2.2.3 γ-Aminoalkylation of allyl sulfoximines

Schleusner investigated the reactivity of the bis(allylsulfoximine)titanium complexes **2a-d** towards imines (Scheme 2.6).[58] Treatment of the allylic sulfoximine **1a-d** in THF at –78 °C with 1.1 equiv of *n*-BuLi resulted in the lithiated sulfoximines which were subsequently transmetalated to the corresponding titanium complexes with 1.2 equiv of $ClTi(OiPr)_3$. The allyltitanium complexes were treated with 1.1 equiv of *N*-Bus α-imino ester **3** at -78 °C in THF following the addition of 1 equiv of $ClTi(OiPr)_3$. The second equiv of $ClTi(OiPr)_3$ was added in order to ensure the completion of the reaction.[15] The

reaction of the bis(allylsulfoximine)titanium complexes **2a-d** with *N*-Bus *a*-imino ester **3** took place with high regio- and diastereoselectivities and in good yields to afford the (*syn*,*E*)-configured *b*-alkyl-*g*,*d*-unsaturated *a*-amino acid derivatives **4a-d**. Formation of the (*S*,*R*,*E*)-configured homoallylic amines **4a-d** entails *Si*,*Re*,*E* processes of *a*-imino ester **3** with the (*R*,*R*)-configured bis-(allyl)titanium complexes (*R*,*R*)-**2a-d** (Table 2.2).



Scheme 2.6: Aminoalkylation of allyl sulfoximines **1a-d**

Table 2.2. Synthesis of amino substituted sulfoximines **4a-d**

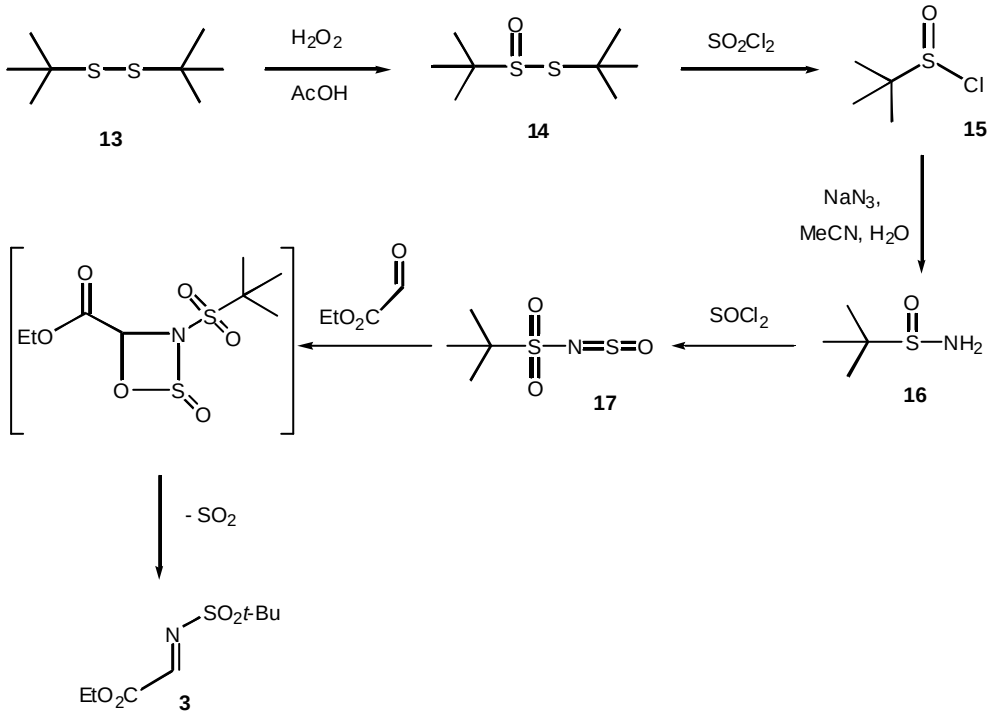
titanium complex	R	amino acid derivative	dr[a]	yield (%)	dr[b]
2a	Ph	**4a**	≥95:5	82	≥98:2
2b	iPr	**4b**	≥95:5	82	≥98:2
2c	cC$_6$H$_{11}$	**4c**	≥95:5	77	≥98:2
2d	*t*Bu	**4d**	≥95:5	84	≥98:2

[a] dr values of the sulfoximines **4a-d** determined from the crude reaction mixture. [b] dr values of the sulfoximines **4a-d** determined after recrystallization.

The *N*-Bus *a*-imino ester **3** is not commercially available. However much efforts have been made towards the optimization of the synthesis of **3**.[50]

2.2.2.4 Synthesis of *N*-Bus *a*-Iminoester 3

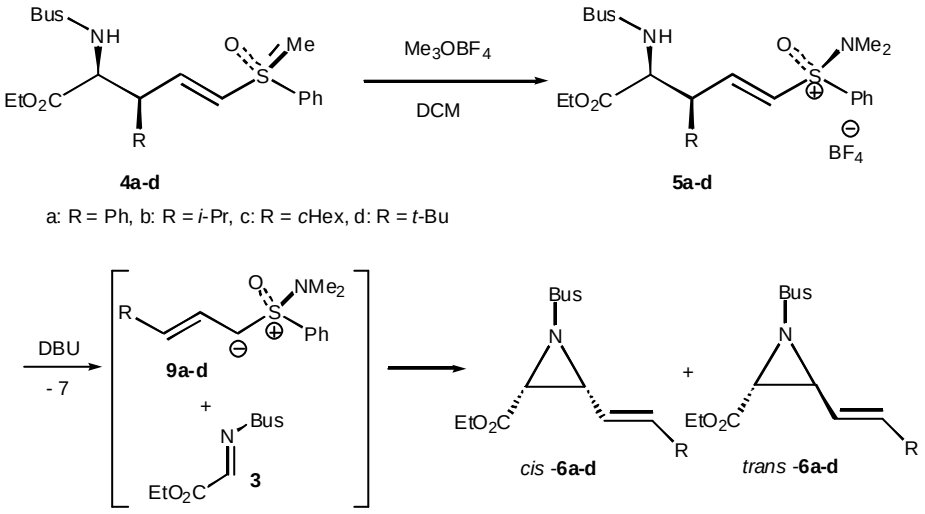
The *N*-*tert*-butylsulfonyl *a*-imino ester **3** was prepared from the commercially available di-*tert*-butyl disulfide **13**. The disulfide was oxidized with H_2O_2 to obtain sulfinate **14** which was not isolated but treated with SO_2Cl_2 to afford the sulfinyl chloride **15** in 92 % yield. Treatment of **15** with NaN_3 in MeCN in the presence of a small amount of H_2O at elevated temperatures by the slow addition of the sulfinyl chloride to a suspension of the azide gave amide **16** in 89% yield.[59] This method was originally described by Kresze for the synthesis of the *N*-tolylsulfonyl imino ester (Scheme 2.7).[59] Then amide **16**[60] was treated with 1.6 equiv of $SOCl_2$ at reflux temperature in toluene for 8-10 h to afford the tert-butylsulfonyl isothiocyanate **17**, which was not isolated but treated with excess of freshly distilled ethyl glyoxylate (2 equiv) at 80 °C and refluxed at 120 °C for 2.5 days. This gave the imino ester **3** as yellow oil in 92% yield based on amide **17**.[50]



Scheme 2.7: Synthesis of *N*-Bus *a*-Iminoester **3**

2.2.3 Asymmetric synthesis of alkenyl aziridine carboxylates from aminosulfoxonium salts 5

In order to generate the allyl aminosulfoxonium ylides the corresponding sulfoximines **4a-d** have to be activated by transforming them into their corresponding salts **5a-d** (Scheme 2.8), the synthesis of which is well established.[17a,61] The vinyl sulfoximines **4a-d** upon treatment with Me_3OBF_4 (1.1 equiv) in CH_2Cl_2 afforded the *N*-dimethylated alkenyl aminosulfoxonium salts **5a-d** in ≥ 95 % yield. The salts thus obtained were subjected to a DBU (1.1 equiv) treatment in dry CH_2Cl_2 at room temperature, which afforded the corresponding alkenyl aziridine carboxylate derivatives **6a-d** (Scheme 2.8) in less than 5 min in high yields, over 90% in all cases, with good diastereoselectivities and medium to high enantioselectivities. The ee–values were determined by chiral HPLC (Table 2.3).



Scheme 2.8: Synthesis of alkenyl aziridine carboxylates **6a-d** from amino alkylated aminosulfoxonium salts **5a-d** via ylides **9a-d**

The *cis*-aziridines **6a-d** were formed as the major isomers and the *trans*-aziridines **6a-d** as the minor isomers. The enantioselectivity of the formation of the *cis*-configured

aziridines is significantly higher than that of their *trans*-configured isomers. A mechanistic rationalization for the diastereo– and enantioselectivities is given later in this chapter.

Table 2.3: Synthesis of alkenyl aziridine carboxylates **6a-d** from amino alkylated aminosulfoxonium salts **5a-d** via ylides **9a-d**

vinyl sulfoximine (**4**)	R	aziridines (**6**) *cis:trans*	yield (%)	*cis*		*trans*		sulfinamide (**7**) yield (%)
				ee[a] (%)	yield (%)	ee[a] (%)	yield (%)	
a	Ph	93:7	94	≥98	82	30	5	96
b	iPr	91:9	91	92	76	26	6	93
c	cC_6H_{11}	90:10	93	71	75	48	9	94
d	tBu	91:9[b]	94	50	–	5	–	94

[a] Determination by HPLC. **6a**: Chiralpack-AD; **6b** and **6d**: Chiracel OD-H; **6c**: Chiralpack-IA.

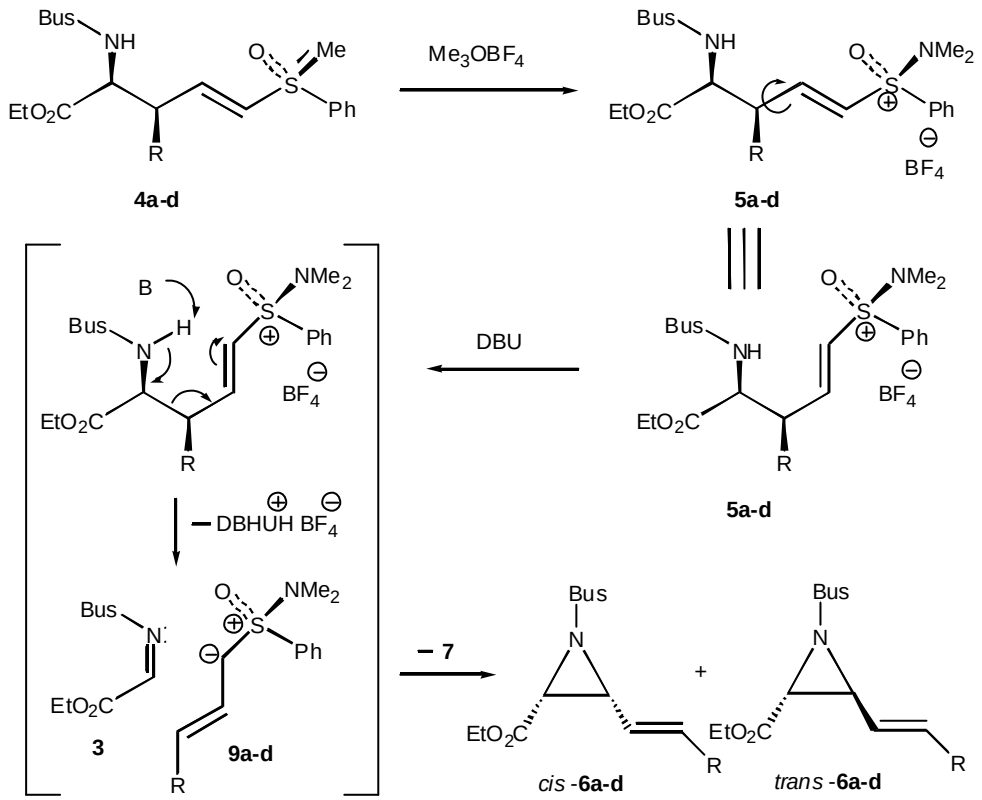
[b] Inseparable mixture.

The *cis*/*trans*-aziridine **6a-d** mixtures were not separable by column chromatography. However, preparative HPLC afforded the pure *cis*- and *trans*- aziridines except in the case of **6d**. It seems noteworthy that both the *cis*- and *trans*-configured aziridines have an *E*-configurated double bond. The conversion of vinyl aminosulfoximines **4a-d** to vinyl aziridines **6a-d**, respectively, has also been carried out with similar results without isolation of **5a-d**. Besides aziridines *cis*-**6a-d** and *trans*-**6a-d**, sulfinamide **7** of ≥98% ee was isolated in each case in high yields. The sulfinamide **7** can be converted to (*S*)-*S*, *N*-dimethyl-*S*-phenyl sulfoximine (**10**) with ≥98%.[17d]

2.2.4 Mechanistic consideration of the aziridine formation from salts 5a-d

The formation of the *E*-configured vinylaziridine carboxylates **6a-d** from the vinyl aminosulfoxoium salts **5a-d** can be rationalized as shown in Scheme 2.9.The vinyl

aminosulfoxonium salts **5a-d** are highly soluble in CH_2Cl_2 and the addition of DBU to this solution causes a deprotonation of the aminosulfoxonium salts **5a-d** at the *N*-atom to which the strong electron with–drawing Bus-group is attached. Deprotonation is followed by a fragmentation to give the conjugated allyl aminosulfoxonium ylides **9a-d** and the *N*-Bus *a*-imino ester **3**. Subsequently ylides **9a-d** combine with the imino ester **3**, in a different manner with formation of the *C–N* and *C–C* bonds to afford the aziridines **6a-d** and sulfinamide **7**.



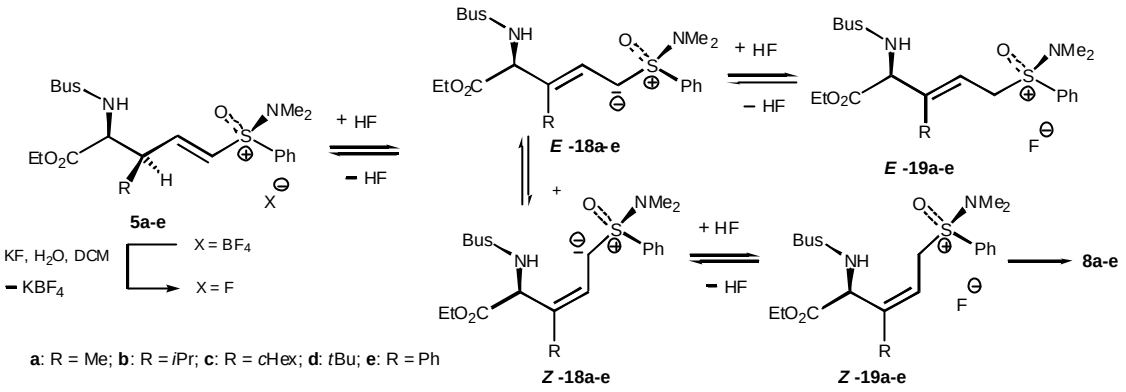
Scheme 2.9: Mechanistic considerations of aziridine formation

It is noteworthy that the reactions of the vinyl aminosulfoxonium salts **5a-d** depend on the nature of the base used. Scheme 2.9 shows the aziridine formation from the salts **5a-d** upon treatment with DBU in CH_2Cl_2. It is very interesting to note that prolines **8a-d** were formed from the same salts **5a-d** upon treatment with KF[54] in CH_2Cl_2-H_2O, as described

by Tiwari and Lindenmaier. The explanation for the base dependence of the reaction course is rationalized below.

2.2.4.1 Effect of base on the reactivity of vinyl aminosulfoxonium salts 5a-d

The formation of the proline derivatives **8a-d** from the corresponding vinyl aminosulfoxonium salts **5a-d** can be explained as follows (Scheme 2.10). The vinyl aminosulfoxonium salts **5a-d** are highly soluble in CH_2Cl_2. Thus solid KF, water and CH_2Cl_2 form a three-phase system and it is assumed that an anion exchange between **5a-d** and KF occurs. That means F^- displaces the counter ion BF_4^- from the salts **5a-d**.[62] The F^- ion could then cause a deprotonation of the aminosulfoxonium salts **5a-d** at the *g*-position (the allylic proton is the most acidic proton in the molecule) with formation of the corresponding allyl aminosulfoxonium ylides *Z*-**18a-d**.[16] The ylides Z-**18a-d** will be protonated at the *a*-position to form the thermodynamically more stable allyl aminosulfoxonium salts *Z*-**19a-d**. Then because of the high nucleofugacity of the allylic aminosulfoxonium group,[17a] salts *Z*-**19a-d** could undergo a cyclization following a deprotonation of the sulfonamide group by the F^- ion with formation of the corresponding prolines **8a-d** and sulfinamide **7**. There is evidence suggesting that the reaction of **5a-d** with the KF could also give to small amount of the isomeric allyl aminosulfoxonium ylides *E*-**18a-d** and subsequently the allyl aminosulfoxonium salts *E*-**19a-e**. Salts *E*-**19a-e**, which cannot cyclize, may however be, in equilibrium with *Z*-**19a-e**.[52]



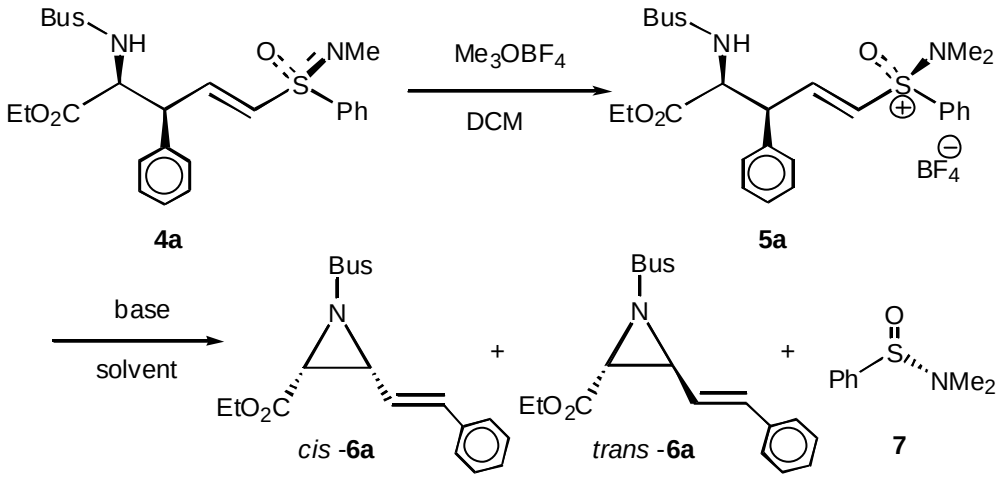
Scheme 2.10: Rationalization of the formation of the 3,4-dehydro prolines

The above mechanism implies that the allylic proton is the most acidic proton in the vinyl aminosulfoxonium salts **5a-e** due to the presence of the sulfoxonium group. Hence the F^- ion can easily deprotonate the allylic position of the sulfoxoium salt **5a-e**. Successive transformations then afford prolines as shown in scheme 2.10. Whereas the same vinyl aminosulfoxonium salts when treated with DBU undergoes a different reaction sequence from the Scheme 2.10, but follows a different reaction pathway as shown in Scheme 2.9 resulting in alkenyl aziridine carboxylates **6a-d** formation.

Decisive for the product formation, aziridine or proline, is the position of the deprotonation of salts **5a-d** upon treatment with base. It is understandable that the allylic proton is the most acidic proton of the salts **5a-d** due to the activation by the amino sulfoxonium group. Hence one can assume that bases will first tend to deprotonate at the allylic position. But another important factor is the size and basicity of the base. The allylic proton of the salts **5a-d** is not only the most acidic but also the most hindered proton. Hence only a small base like F^- can attack on this proton, where as the bulky base DBU cannot attack on this proton. So DBU attacks the salts at the sterically less hindered amino group, which will lead to a fragmentation followed by the formation of alkenyl aziridines **6** as shown in scheme 2.9. To strengthen this argument, the salt **5a** was treated with another bulky base, di-isopropyl ethylamine (DIEPA). The aziridines *cis*-**6a** and *trans*-**6a** were isolated with similar de values and in good yields.

2.2.5 Aziridine formation from aminosulfoxonium salts 5 under different conditions

After having observed the formation of *cis*/*trans*-mixtures of aziridines from the vinyl aminosulfoxonimium salts **5a-d** by treatment with DBU in CH_2Cl_2 at room temperature, it was of interest to increase the diastereoselectivity by carrying out the aziridination under different reaction conditions. The vinyl sulfoximine **4a** was taken as the substrate. The sulfoximine **4a** was first activated by methylation with Me_3OBF_4, which resulted in the quantitative formation of salt **5a**. Salt **5a** was then treated with DBU and diisopropyl ethyl amine (DIPEA) in different solvents and at different temperatures (Scheme 2.11). Similar results were observed under various conditions as shown in the Table 2.3.



Scheme 2.11: Aziridination under different reaction conditions

Table 2.4. Aziridination with **4a** under different reaction conditions

entry	solvent	base	temp	*cis*–**4a**/ *trans*–**4a**	yield (%)	Remarks
1	DCM	DBU	rt	93:7	94	–
2	DCM	DBU	0° C	92:8	92	–
3	CCl_4	DBU	rt	93:7	93	–
4	CCl_4	DIEPA	rt	93:7	94	–
5	CCl_4	DIEPA	0° C	91:9	93	–
6	DCM	DBU	-78° C	92:8	–	Reaction was not complete
7	DCM	DBU	50° C	–	–	Decomposition of products was observed

Therefore, it is approved that treatment of the salts **5** with a bulky base will lead to aziridine formation and furthermore that solvent and temperature show only minor effects on the stereoselectivity of aziridine formation.

2.2.6 Determination of the relative configuration of the alkenyl aziridine caboxylates

The absolute configuration of the chiral centers of the vinyl aminosulfoximines **4a-d** is known but that of the aziriridines **6a-d** is not known and predictions are difficult to make. None of the aziridines was crystalline. Thus it was desided to determine the absolute configuration of the *cis*- and *trans*- aziridines *cis*-**6a** and *trans*-**6a** by chemical correlation. First the relative configuration of the *cis*- and *trans*-aziridines **6a-d** was determined based on their NMR spectra. ^{1}H NMR spectroscopy confirmed that the double bond of both the *cis*- and *trans*- airidines **6a-d** had the *E*-configuration since it showed coupling constants (*J*) above 15 Hz in all the cases. Furthermore the 2,3-*cis*-aziridines *cis*-**6a-d** showed $J(H_a,H_b)$ values of ~ 7.14 Hz which are larger than the

$J(H_a,H_b)$ values (J ~ 3.84 Hz) of the 2,3-*trans*-isomers *trans*-**6a-d**. This is in accordance with literature observation.[63] Besides that NoE measurements confirmed that *cis*–**6a-d** have the *cis*- and *trans*–**6a-d** the *trans*–configuration (Figure 2.14).

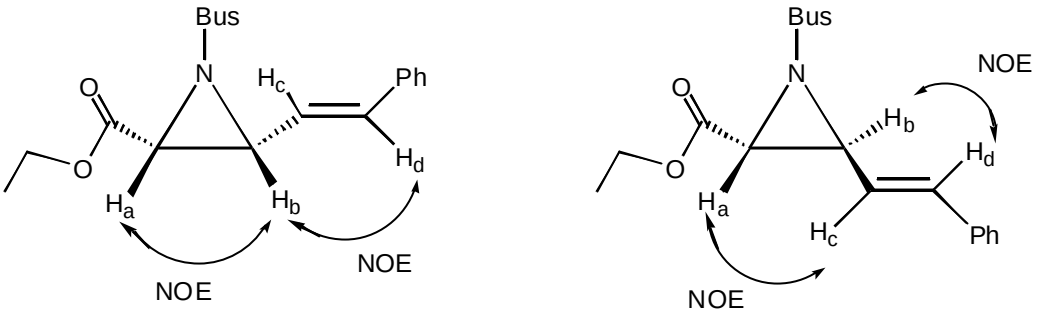


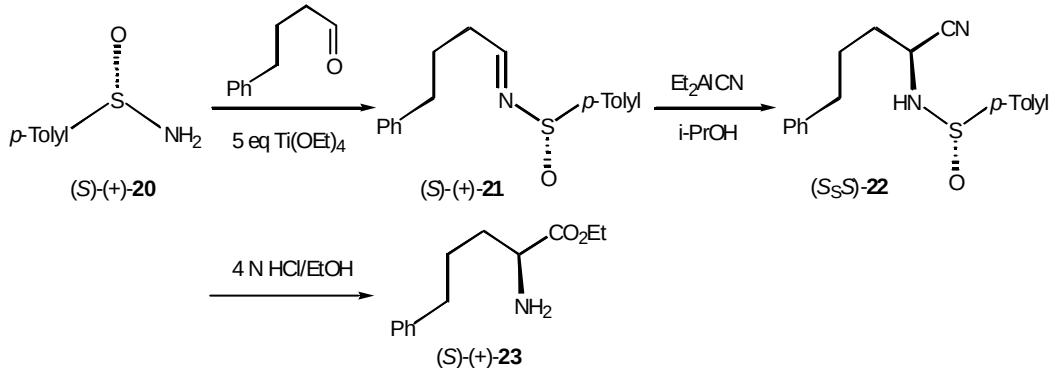
Figure 2.14: NoE measurements of *cis*-**6a** and *trans*-**6a**

In the case of the major isomer *cis*–**6a**, an NoE was observed between H_a and H_b meaning that they are *cis* to each other. In addition an Noe was observed between H_b and H_d, which proves the *E*-configuration of the double bond. However no NoE was observed between H_c and H_d, as they are *trans* to each other. Similarly, in the case of the minor isomer, no NoE was observed between H_a and H_b but a strong NoE was observed between H_a and H_c, which means that the minor isomer has the 2,3-*trans*-configuration.

2.2.6.1 Determination of the absolute configuration of alkenyl aziridine carboxylates

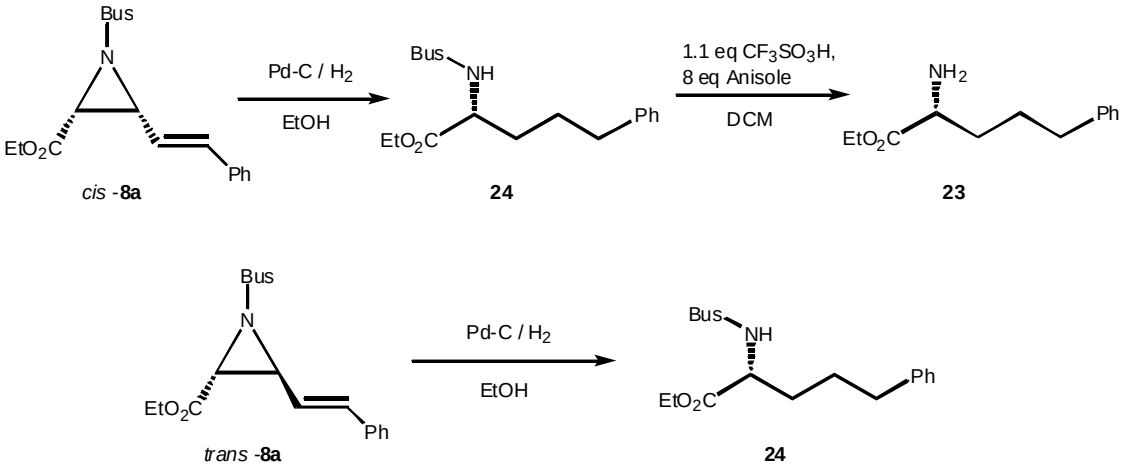
The absolute configuration of *cis*-**6a** and *trans*-**6a** was determined by converting them into the known *a*-amino acid **23**.[64] The *a*-amino acid **23** was originally synthesized by Davis et al. by a sulfinimine-mediated asymmetric Strecker reaction[65] as shown in Scheme 2.12. 4-Phenylbutaraldehyde was condensed with commercially available (*S*)-(+)-*p*-toluenesulfinamide (**20**) and $Ti(OEt)_4$ to give sulfinimine (*S*)-(+)-**21**. Next, the sulfinimine was treated with EtAl(O-*i*Pr)CN, generated *in situ* by addition of 1.0 equiv of

i-PrOH to 1.5 equiv of diethylaluminum cyanide (Et_2AlCN), to give the amino nitrile **22** with 70% de. Since the sulfinyl group controls the stereoselective *Re*-face addition of CN, (S_S,*S*)-(+)-**22** was obtained as the major diastereoisomer.[66] The diastereomeric aminonitriles were separated by flash chromatography and the major diastereomer was treated with 4 N HCl-EtOH. This treatment not only removed the sulfinyl group, but also hydrolyzed the nitrile and gave the *a*-amino acid ((*S*)-(+)-**23**.



Scheme 2.12: Synthesis of the *a*-amino acid (*S*)-(+)-**23** by Davis et al.

We envisioned a conversion of aziridines *cis*-**6a** and *trans*-**6a** to the *a*-amino acid (*S*)-(+)-**23**. It has been reported that vinyl aziridines readily undergo hydrogenolysis with H_2/Pd(0).[67] The ring-opening takes place at the C-atom bearing the vinyl group without disturbing the other aziridine ring C-atom. Hence the aziridine *cis*–**6a** was subjected to a hydrogenolysis with H_2/Pd/C, which gave the *N*-Bus protected *a*-amino acid **24**. Finally, treatment of **24** with CF_3SO_3H afforded the *N*-Bus deprotected *a*-amino acid **23** in 91% yield. Thus aziridine *cis*-**6a** was transformed into the saturated *a*-amino acid **23** in > 90% yield.



Scheme 2.13: Transformation of aziridines *cis*-**8a** and *trans*-**8a** to amino acid derivatives **23** and **24**

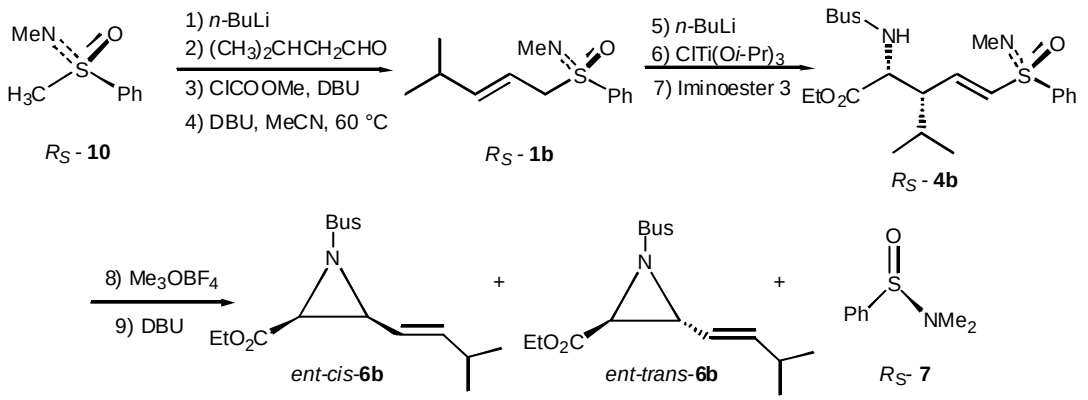
The *a*-amino acid derivative **23**, obtained from *cis*-**8a** of =98% ee, showed an optical rotation value of $[\alpha]_D^{23}$ = –13.6°, similar in magnitude to that of the reported value of $[\alpha]_D^{20}$ = +14.5° by Davis et al[64] for (*S*)–23, but with the opposite sign of rotation. This confirms that our *a*-amino acid **23** is *R*-configurated at the *a*-position. That means that the *cis*-aziridine **6a** has the (*R*,*R*)– configuration. In the same way aziridine *trans*-**6a** was transformed to the *N*-Bus *a*-amino acid **24** in 93% yield. It showed a similar optical rotation, $[\alpha]_D^{23}$ = + 4.7°, as the *N*-Bus *a*-amino acid **24**, $[\alpha]_D^{23}$ = + 5.1°, synthesized from aziridine *cis*-**6a**. Thus both the *cis*- and the *trans*-aziridines have the same configuration (*R*-) at the C-2 position. Hence the absolute configuration of the *trans*-aziridine **6a** is 2*R*,3*S*.

2.2.7 Synthesis of the enantiomeric alkenylaziridine carboxylates

In order to complete the aziridine synthesis, the enantiomeric aziridine derivatives *ent-cis*-**6b** and *ent-trans*-**6b** were prepared from the (*R*)-*S*,*N*-dimethyl-*S*-phenyl sulfoximine

(**10**). As described in the section **2.2.2.2** the corresponding (R_S)-configured allyl sulfoximine (R_S)-**1b** was synthesized by addition-elimination-isomerisation route.[7] From

(R_S)-**1b** the bis(allyl)titanium complex (R_S)-**2b** was prepared, followed by *g*-amino alkylation with the *N*-Bus *a*-amino acid **3**, which gave (*R*,*S*,*E*,*R*S)-vinyl sulfoximine derivative **4b**. The vinyl sulfoximine derivative was methylated with Me_3OBF_4 and treated with DBU, in a one pot transformation, to afford the *cis*/*trans*-aziridine mixture (*ent*-cis-**6b**/*ent*-trans-**6b**) in >90 % yield with 92:8 diastereoselectivity. The *ee* values were determined by chiral-HPLC (Chirasildex CB) and observed (*cis*: 89% *ee*; *trans*: 85% *ee*) from that of the aziridines synthesized from the (*S*)-sullfoximine (R_S-**10**).

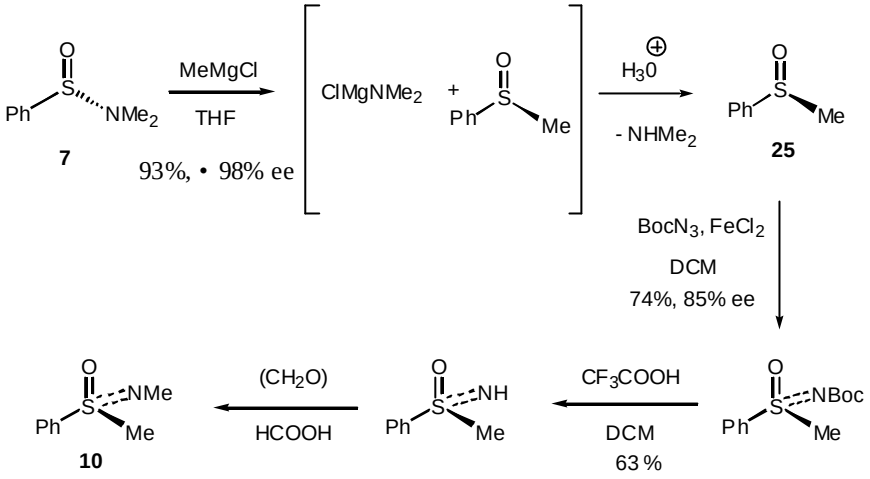


R_S - **10** R_S - **1b** R_S - **4b** R_S- **7**

Scheme 2.14: Synthesis of vinyl aziridine carboxylate ent-*cis*/*trans*-**6b** from (R_S)-**10**

2.2.8 Recycling of sulfinamide

The alkenyl aziridine carboxylates *cis*-**6a-d** and *trans*-**6a-d** as well as sulfinamide **7** of ≥ 98 % ee were isolated in high yields. Thus a conversion of **7** to the sulfoximine **10**, the starting material for the synthesis of allylic sulfoximines **1a-d**, was desirable. Gais et al. had previously shown that treatment of sulfinamide **7** with MeMgCl gives sulfoxide **25**[17d] with inversion of configuration, and it was isolated with ≥ 98 % ee in 93 % yield (Scheme 2.15). Bach et al. have described the conversion of **25** to sulfoximine **10**[68] as shown in the scheme 15.

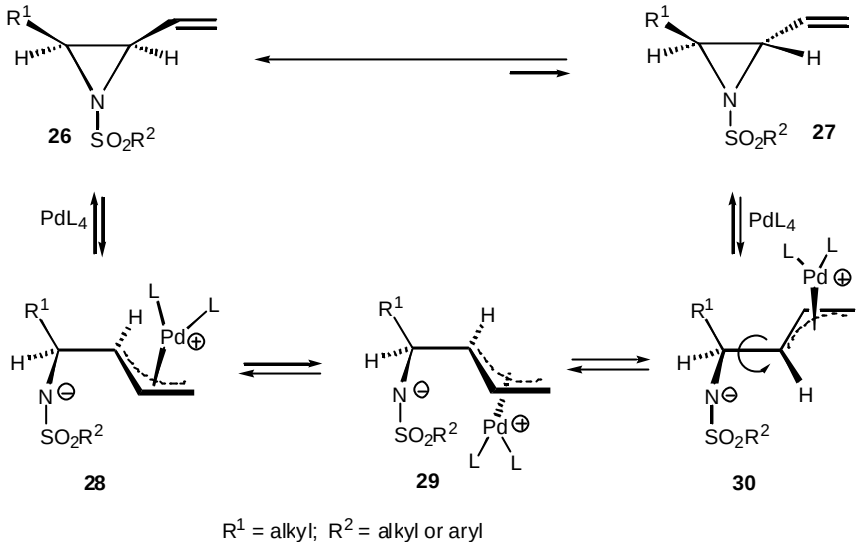


Scheme 2.15: Recycling of sulfinamide **7**

2.3 Stereoselective synthesis of *cis*-alkenyl aziridine methanol derivatives by Pd(0) catalyzed isomerization

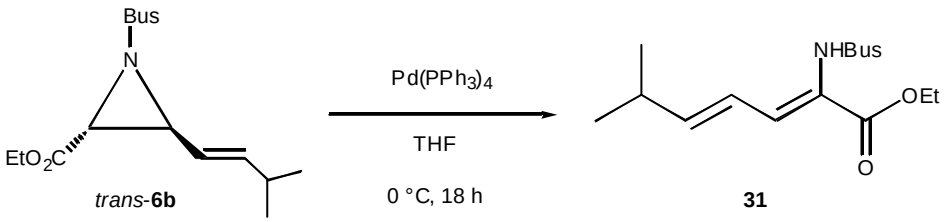
Because of the formation of mixtures of *cis*- and *trans*-aziridines **6a-d**, both having the same configuration at C-2, a convergent conversion of the *cis*/*trans*-mixtures of the aziridines to the *cis*-configured aziridines was sought.[27d]

In 1996 Ibuka et al. determined the thermodynamic stabilities of 2,3–*cis*– and 2,3–*trans*–*N*–methanesulfonyl– or *N*–(arenesulfonyl)–3–alkyl–2–vinylaziridines using *ab initio* calculations.[69,70] Since the energy difference in the gas phase was calculated to give an equilibrium ratio of 94:6 (2,3–*cis*–**26**: 2,3–*trans*–**26**) at 0 °C, it was expected that the Pd(0)–catalyzed equilibrated reaction of *N*–activated 2,3–*trans*–3–alkyl–2–vinylaziridines **27** would give the 2,3–*cis*–isomers **26** as shown in the Scheme 2.16. Indeed, the thermodynamically less stable *trans*–2–vinylaziridines **27** upon treatment with 5 mol% $Pd(PPh_3)_4$ in THF at 0 °C isomerizes to the more stable *cis*-isomers **26** via the π-allyl palladium(II) intermediates **28**, **29**, and **30** following π-σ–π mechanism.[69]



Scheme 2.16: Pd(0)–catalyzed isomerization of *trans*-vinyl aziridine to *cis*-vinyl aziridine

Taking these results into consideration, it was expected that the Pd(0)–catalyzed equilibrated reaction of the *N*-Bus 2,3-*trans*-3-ethylcarboxy-2-(*E*)-alkenyl aziridine (*trans*-**6b**) would give the corresponding 2,3-*cis*-isomer (*cis*-**6b**). Hence the *trans*-vinylaziridine carboxylate (**6b**) was subjected to a Palladium-catalyzed isomerization reaction by treatment with 5 mol % $Pd(PPh_3)_4$ in THF at 0 °C. Unfortunately, only the diene **31** was isolated in 95% yield after 18 h (Scheme 2.17).



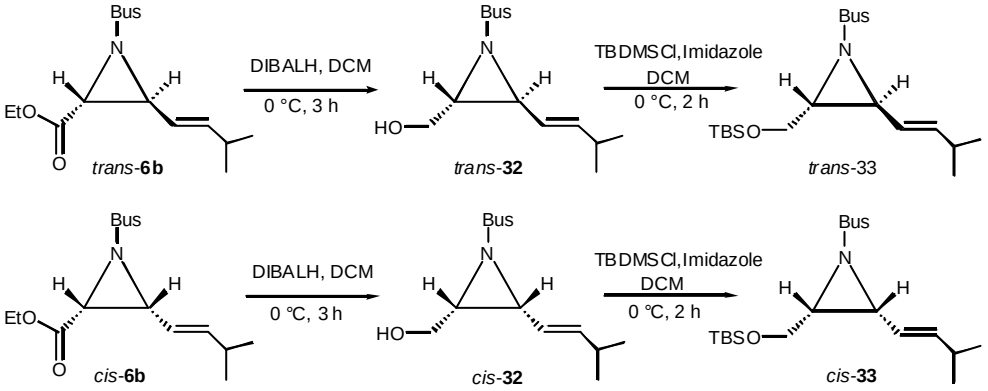
Scheme 2.17: Reaction of vinyl aziridine carboxlate *trans*–**6b** with $Pd(PPh_3)_4$

This observation is in accordance with results obtained by Matano *et al.* They found that *trans*-2-(2,2-dimethyl-1-oxopropyl)-3-(*E*)-(2-phenylethenyl)-1-tosylaziridine upon treatment with $Pd(PPh_3)_4$ in DMSO at 50 °C gives the dieneamine[71] (Figure 2.15).

Figure 2.15. Synthesis of diene aminoketone by Matano et al.[71]

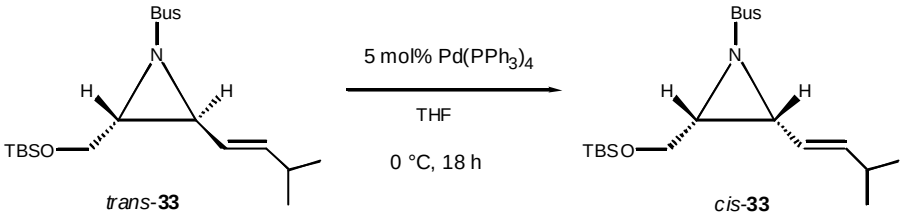
The reason for the formation of the diene is the presence of an acidic proton adjacent to the carbonyl group, which can be easily transferred to the intermediate Pd(II)-complex during the catalytic cycle, resulting in elimination rather than substitution. Hence it was decided to reduce the ester group of the *trans*-vinylaziridine carboxylate **6b** to alcohol group before subjecting it to a Pd(0)-catalyzed equilibration.

Thus, the *trans*-vinylaziridine carboxylate **6b** was treated with a freshly prepared solution of DIBAL-H[72] (1.2 equiv) in dry CH_2Cl_2 at 0 °C for 3 h, which gave the alcohol **32** in 90% yield (Scheme 2.18). Alcohol **32** was then protected as the silyl ether *trans*-**33** by treatment with TBDMSCl and imidazole in dry CH_2Cl_2 at 0 °C for 2 h (89 % yield). Similarly, the silyl protected *cis*-alkenylaziridine methanol derivative *cis*-**33** was prepared with 90 % overall yield in two steps.



Scheme 2.18: Synthesis of *cis/trans*-silyl protected alkenyl aziridine methanol derivatives

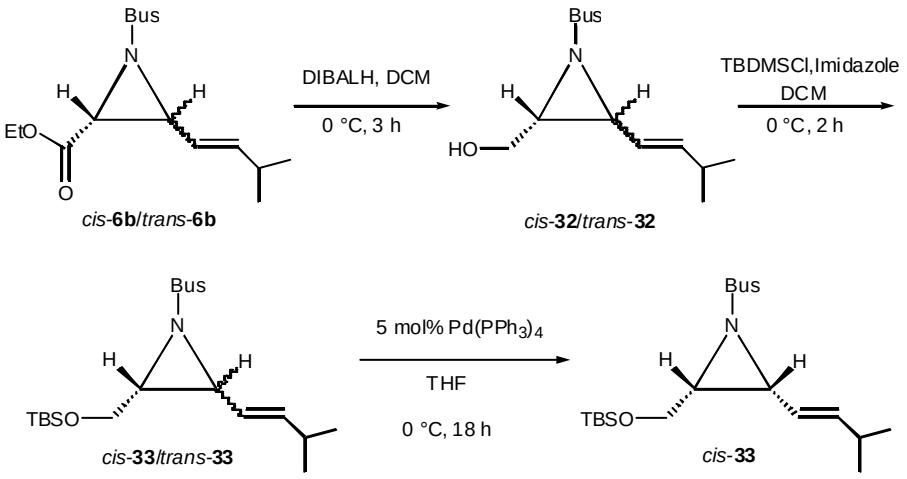
To our delight, treatment of the 2,3-*trans*-configured alkenyl aziridine *trans*-**33** with 5 mol % of $Pd(PPh_3)_4$ in THF at 0 °C gave the *cis*-configured isomer *cis*-**33** with ≥ 98 % de in 84% yield. The optical rotation value of *cis*-**33** obtained by the Pd(0) isomerization was the same as a probe of *cis*-**33** (Scheme 2.19) synthesized directly from the *cis*-alkenyl aziridine carboxylate (*cis*-**6b**).



trans-**33** *cis*-**33**

Scheme 2.19: Pd(0)−catalyzed equilibration reaction

Similarly, a mixture of *cis*-**6b**/*trans*-**6b** was converted to the silyl protected *cis*-**33**/*trans*-**33** via *cis*-**32**/*trans*-**32** and treated with 5 mol % of $Pd(PPh_3)_4$. Aziridine *cis*-**33** was isolated with ≥ 98% de in 81% overall yield, in 18 h, as shown in scheme 2.19. To summarize the Pd(0)−isomerization reaction, the *trans*-(*E*)-aziridine **33** was transformed into *cis*-(*E*)-aziridine **33** with ≥ 98 % de in good yield.



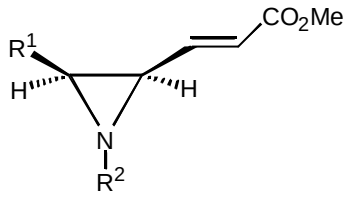
cis-**6b**/*trans*-**6b** *cis*-**32**/*trans*-**32**

cis-**33**/*trans*-**33** *cis*-**33**

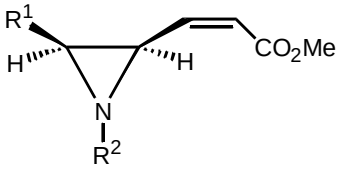
Scheme 2.20: Stereoselective synthesis of *cis*-alkenyl aziridine methanol derivatives

Surprisingly, however, the *E*-configured aziridine *cis*-(*E*)-**33** was formed and not the *Z*-configured isomer *cis*-(*Z*)-**33** which would have been expected on the basis of the reaction of a $\pi-\sigma-\pi-$isomerization mechanism.

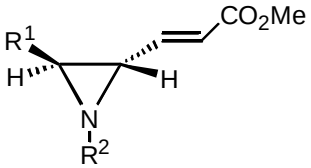
Ibuka et al. investigated the Pd(0) isomerization of substituted vinyl aziridines in order to see how the double bond configuration changes during the reaction. They treated various *N*-arylsulfonyl-alkenyl aziridines[73] with $Pd(PPh_3)_4$.



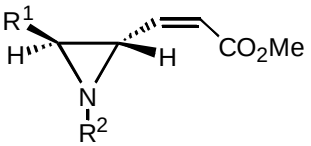
cis-E-**34**: R^1 = Me; R^2 = Ts
cis-E-**35**: R^1 = Me; R^2 = Mts
cis-E-**36**: R^1 = *i*Pr; R^2 = Mts



cis-Z-**34**: R^1 = Me; R^2 = Ts
cis-Z-**34**: R^1 = Me; R^2 = Mts
cis-Z-**34**: R^1 = *i*Pr; R^2 = Mts



trans-E-**34**: R^1 = Me; R^2 = Ts
trans-E-**35**: R^1 = Me; R^2 = Mts
trans-E-**36**: R^1 = *i*Pr; R^2 = Mts



trans-Z-**34**: R^1 = Me; R^2 = Ts
trans-Z-**34**: R^1 = Me; R^2 = Mts
trans-Z-**34**: R^1 = *i*Pr; R^2 = Mts

Figure 2.16: *N*-arylsulfonyl-alkenyl aziridines

Exposure of the alkenyl aziridine *trans-E*-**34** to a catalytic amount of $Pd(PPh_3)_4$ in dry THF at 15 °C for 15 h yielded an 85.09 : 5.12 : 9.79 : < 0.01 mixture of *cis-E*-**34**, *cis-Z*-**34**, *trans-E*-**34**, and *trans-Z*-**34** in which the new isomer *cis-E*-**34** dominated (Figure 2.17). Within the limits of experimental error, essentially identical results were obtained by treatment of the isomeric aziridines *cis-E*-**34**, *cis-Z*-**34**, and *trans-Z*-**34** under the same reaction conditions.[3] The optical activity of *cis-E*-**34** was the same before and after $Pd(PPh_3)_4$ equilibrated reaction. In the same way, when a catalytic amount of $Pd(PPh_3)_4$

was employed in the equilibration of *cis*-*Z*-**35**, *trans*-*E*-**35**, and *trans*-*Z*-**35** the desired *cis*-*E*-**35** was obtained with a selectivity as high as 9:1 [*cis*-*E*-**35**:(*cis*-*Z*-**35** + *trans*-*E*-**35** + *trans*-*Z*-**35**)]. Similarly, the $Pd(PPh_3)_4$ catalyzed reaction of *cis*-*Z*-**36**, *trans*-*E*-**36**, and *trans*-*Z*-**36** provided 94:0.5:5.5:<0.001 mixtures of four stereoisomers *cis*-*E*-**36**, *cis*-*Z*-**36**, *trans*-*E*-**36**, and *trans*-*Z*-**36.**

From these results, it is evident that Pd(0)-catalyzed reactions led to an equilibrium of all the possible stereoisomers, the ratio of which is function of their relative stabilities. Clearly the thermodynamic stabilities of the *trans*-(*Z*)-isomers *trans*-*Z*-**34**, *trans*-*Z*-**35**, and *trans*-*Z*-**36** are lower than those of the corresponding *cis*-(*E*)-isomers *cis*-*E*-**34**, *cis*-*E*-**35**, and *cis*-*E*-**36**. In addition, it is apparent that the greater steric bulk of the nitrogen protecting group (Mts) and the alkyl group (*i*Pr) on the aziridine ring tended to afford considrably higher ratios of the desired *N*-arylsulfonyl-alkenyl aziridines.

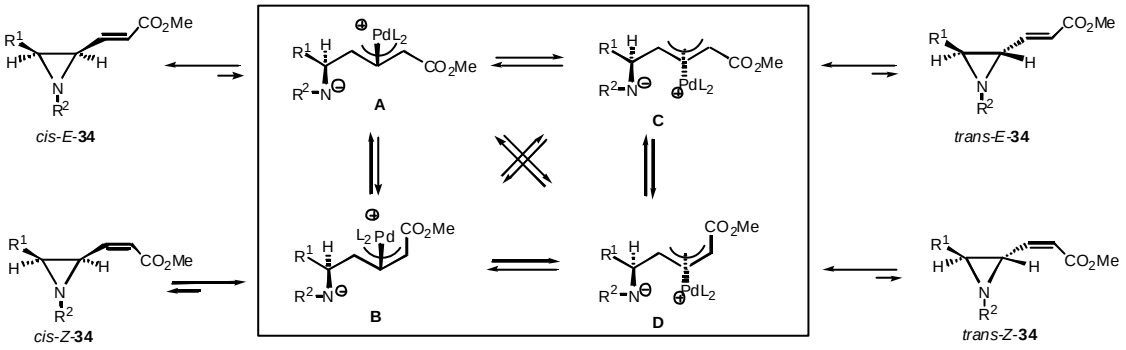


Figure 2.17 Pd(0)-catalyzed isomerization reaction

Ibuka et al. proposed that the Pd(0)-catalyzed isomerization reaction involves an equilibrium between the four π-allyl-Pd-complexes[74] **A**–**D** as shown in Figure 2.17. Strangely, however, nothing was said about the possible mechanism of the interconversions of **A**–**D**, which cannot be formed purely by a π–σ–π−mechanism.

The stereochemical outcome of the Pd-catalyzed isomerizations disclosed above can be explained as follows. The transformation of **A** to **D** and **B** to **C** can proceed via π−σ–π

interconversion.[74,75] However, the transformations of **A** to **C**, **B** to **C**, **A** to **B** and **C** to **D** canot be explained by a π–σ–π interconversion. Because the Pd–catalyzed isomerization cannot go through a standard mechanism without changing the double bond configuration. But these transformations can be explained as follows. Similar to nucleophilic addition in allylic substitutions, the electrophilic allyl system bound to Pd(II) can react with a Pd(0) complex. The Pd(0) complex adds to the free π-face of the allyl ligand and displaces the Pd(II) complex on the backside (Figure 2.18).[76a] Therefore, this process results in an inversion of configuration at all three allyl carbon atoms in contrast to apparent allyl rotation that does not change the configuration of the allyl ligand.[76]

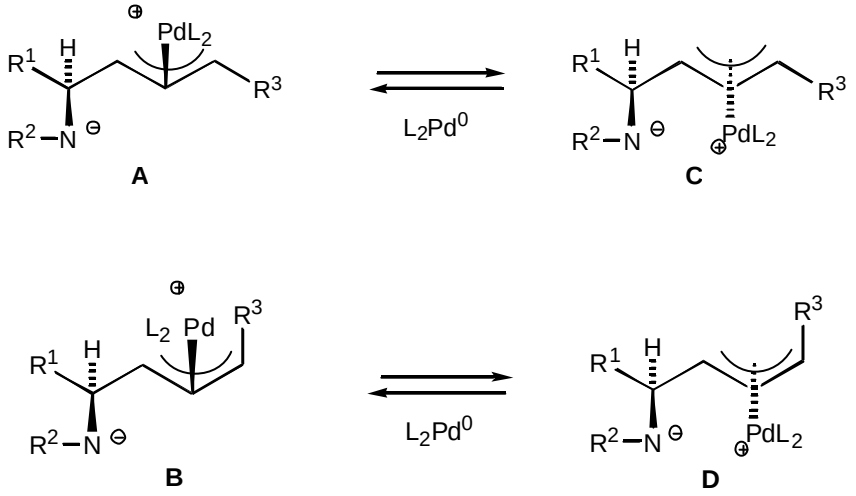


Figure 2.18: Pd(0) -catalyzed allyl exchange

Hence, it can be explained that the Pd(0)-catalyzed transformations of *trans*-*E*-alkenyl aziridine carboxylates, *trans*-*E*-**6a-e**, to the *cis*-*E*-alkenyl aziridine carboxylates, *cis*-*E*-**6a-e**, proceeds without changing the double bond configuration.

2.4 Conclusions

We have devised a method for the generation of conjugated acyclic allyl aminosulfoxonium ylides and successfully applied them in the asymmetric synthesis of chirally pure *cis*/*trans*-*N*-*tert*-butylsulfonyl substituted-3-alkenyl aziridine-2-ethyl carboxylates in good yields with good diastereoselectivities and with moderate to good enantioselectivities. The advantage of this synthesis is that it provides access to aziridines having both the *vinyl* and the *ester functionality*, for which only a few enantioselective syntheses had been described in the literature. Interestingly 1-alkenyl (dimethylamino) sulfoxonium salts show a synthetically highly useful dichotomy in their reactivity toward different bases. Sterically small bases like F^- produces proline derivatives where as bulky bases like DBU produces aziridine derivatives. Finally it was shown that palladium-catalyzed equilibrated reactions of mixtures of *cis*/*trans*-(*E*)-alkenyl aziridines afford the desired *cis*-(*E*)-alkenyl aziridines with good yields.

CHAPTER 3

Asymmetric synthesis of alkenyl aziridine carboxylates by treatment of allyl aminosulfoxonium ylides with *α*-imino ester

3 Asymmetric synthesis of alkenyl aziridine carboxylates by treatment of allyl aminosulfoxonium ylides with *a*-imino ester

3.1 Introduction

The formation of the alkenyl aziridine carboxylates *cis*-**6a-d** and *trans*-**6a-d** in the reaction of the amino–substituted aminosulfoxonium salts **5a-d** with DBU suggested another entry to the same aziridines by preparing the allyl aminosulfoxonium ylides **9a-d** from alkenyl aminosulfoxonium salts separately followed by a treatment with the *N*-Bus α-imino ester **3**.

3.1.1 Chiral conjugated allyl sulfonium ylides

Although chiral alkyl S-ylides are well established reagents,[77,29] only a few examples of chiral conjugated allyl sulfonium ylides had been described.[78] In 2003 Aggarwal et al. reported the synthesis of chiral allyl sulfur ylides and applied them to the synthesis of alkenyl oxiranes, which proceeded with low yields but with good selectivities.[78a] (Figure 3.1)

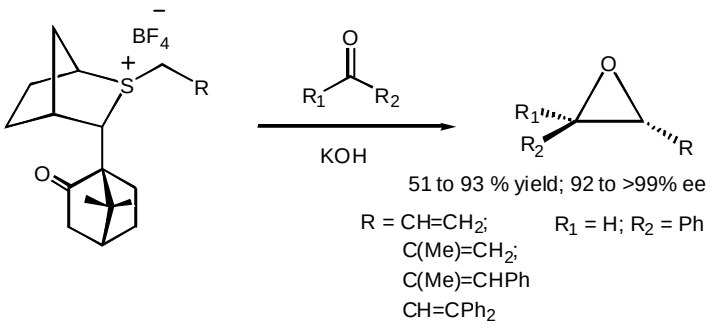


Figure 3.1: Aggarwal's chiral allyl sulfonium ylide

The first enantioselective synthesis of vinyl oxiranes from aldehydes and chiral allyl ylides was described by Metzner et al. in 2002.[78b] The chiral allyl ylides were prepared from allyl halides and chiral sulfides as shown in Figure 3.2.

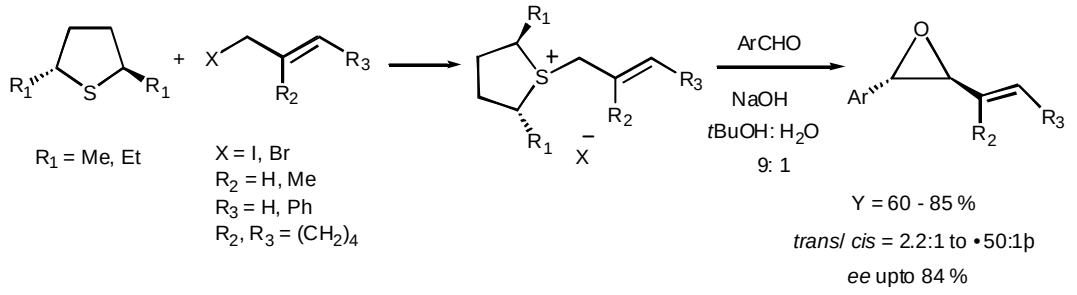


Figure 3.2: Metzner's application of chiral allyl sulfonium ylides

In 1995, Gladysz et al. carried out an enantioselective synthesis of organosulfur compounds via [2,3] rearrangements of chiral ylides derived from di(allyl)and di(propargyl) sulfide complexes[78c] (Figure 3.2).

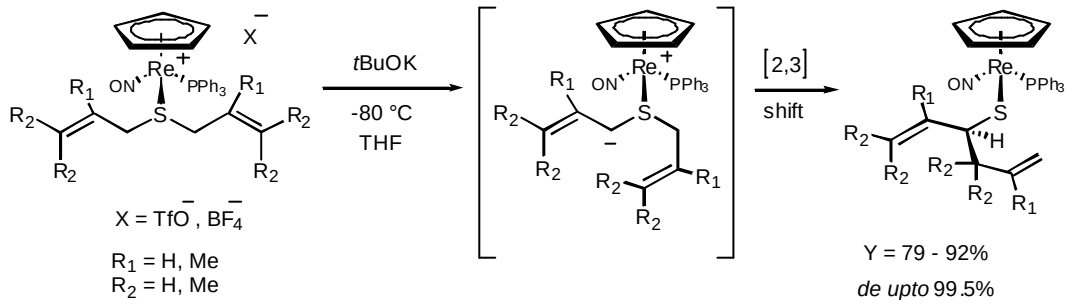


Figure 3.3: Gladysz et al. application of chiral allyl sulfonium ylide

3.1.2 Aminosulfoxonium ylides

Sulfur ylides are now well established as reagents for organic synthesis. In large part the synthetic achievements with these reagents originated from the work of Corey and coworkers.[79] Later in 1968 Johnson et al. introduced a new series of oxosulfonium salts and their ylides.[80] Johnson et al. prepared the dimethyl amino aryloxosulfonium alkylidenes and applied them as nucleophilic alkylidene transfer reagents in order to prepare epoxides and cyclopropanes[81] (Figure 3.4).

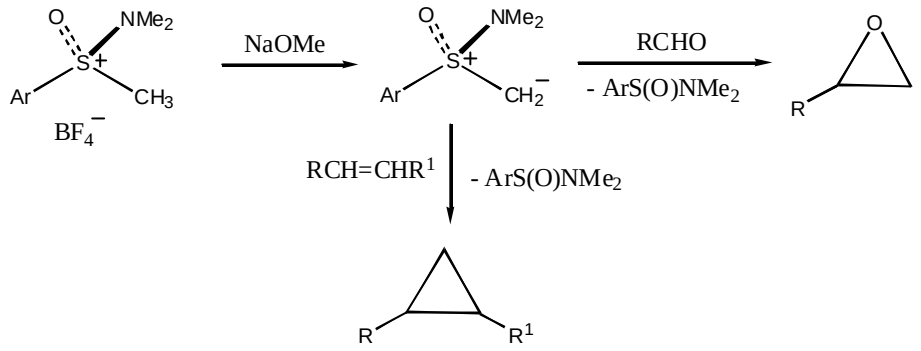
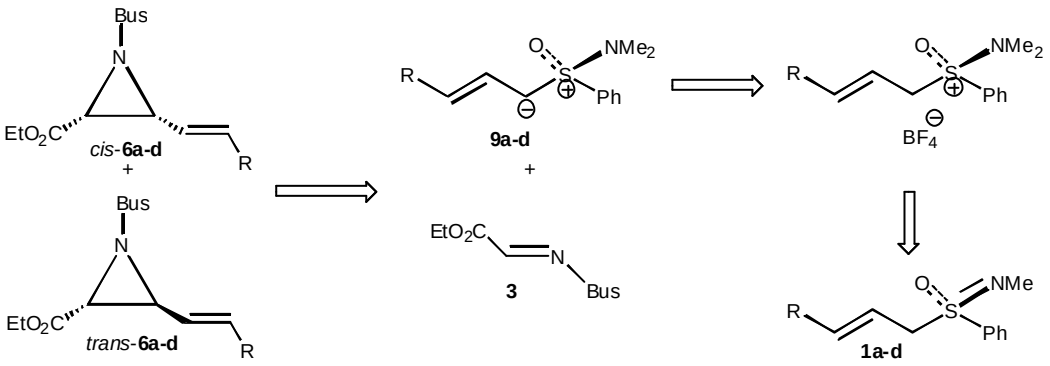


Figure 3.4. Johnson's aminosulfoxonium ylides

3.2 Results and Discussion

3.2.1 Retrosynthetic analysis

The proposed mechanism for aziridination detailed in the foregoing chapter is based on the involvement of allyl aminosulfoxonium ylides **9a-d** as reactive intermediates, which combine with the *N*-Bus *a*-iminoester **3** to furnish alkenyl aziridine carboxylates *cis*-**6a-d** and *trans*-**6a-d**. Hence it can be assumed that the allyl sulfoxonium ylides **9a-d** can perhaps be derived directly from the corresponding allyl sulfoximines **1a-d**. We therefore focused on the asymmetric synthesis of alkenyl aziridine carboxylates **6** directly from the allyl sulfoximines in a much shorter route (Scheme 3.1). The synthesis of the same alkenyl aziridine carboxylates by this shortened route would bypass the synthesis of the bis(allyl) titanium complexes **2a-d** and thus that of the *g*-amino–substituted vinylsulfoximines **4a-d**.

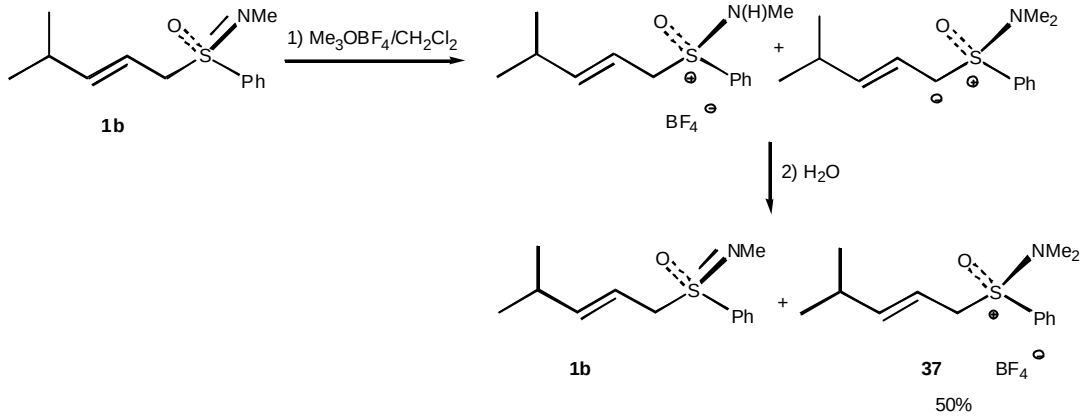


Scheme 3.1: Retrosynthetic analysis of alkenyl aziridine carboxylates

The synthesis of the allyl sulfoximines **1a-d** from (*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximine (**10**) has already been described in the previous chapter (cf. Scheme 2.5).

3.2.1.1 Synthesis of allyl (dimethylamino)sulfoxonium salts

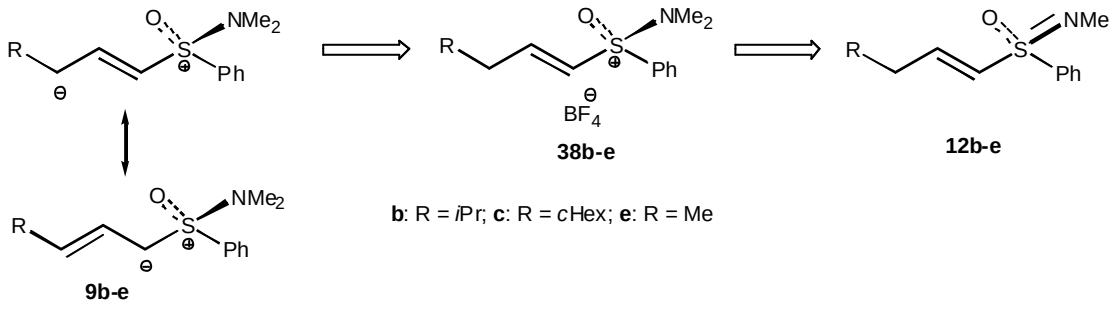
The attempted synthesis of allyl (dimethylamino)sulfoxonium salts **37** commenced with the preparation of allylic sulfoximines as already described in the previous chapter (cf. Scheme 2.5). Then, the allyl sulfoxomine **1b** was treated with 1.1 equiv of Me_3OBF_4 to first methylate the sulfoximine group. But the methylation resulted in only 50% conversion of **1b** according to ^{1}H NMR spectroscopy; a dimethylamino signal was observed at δ 3.08 ppm, with a similar integral value as the allyl sulfoximine *NMe* signal (δ 2.74 ppm). A 1:1 mixture of allyl aminosulfoxonium salt **37** and unreacted starting allyl sulfoximine **1b** was isolated upon aqeous workup after 3 h. The ratio of the products was almost the same even after treatment of **1b** with an excess of Me_3OBF_4. It was speculated that after methylation with Me_3OBF_4, the *α*-proton of the allyl sulfoxonium salt **37** becomes acidic enough to react with the basic allyl sulfoximine **1b** resulting in the formation of a *N*-protonated sulfoxonium salt (Scheme 3.2). This *N*-protonated aminosulfoxonium salt does not react with Me_3OBF_4, and complete *N*-methylation is no longer being possible. After the aqueous workup the N-protonated aminosulfoxonium salt hydrolyses to give the starting allyl sulfoximine **1b**. Thus, only 50% of the allyl sulfoximine **1b** reacts with Me_3OBF_4 and the rest reacts with the proton to form the *N*-protonated allyl sulfoxonium salt.



Scheme 3.2: Reaction of allylic sulfoximine **1b** with Me_3OBF_4

3.2.2 Synthesis of allyl (dimethylamino)sulfoxonium salts from vinyl sulfoximines

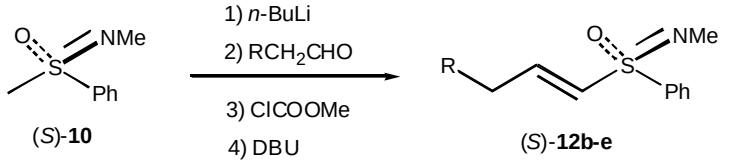
The functionalized vinyl sulfoximines **4a-d** reacted readily with Me_3OBF_4 under methylation of the *N*-atom of the sulfoximine group (cf. Scheme 2.2). It was expected that the vinyl sulfoximines **12b-e** would also react with Me_3OBF_4 to form the vinyl aminosulfoxonium salts **38b-e**. Because of the acidic allylic proton, it should be possible to deprotonate **38b-e** with a base like DBU resulting in the formation of allylic ylides **9b-e**.



Scheme 3.3: Synthesis of allyl aminosulfoxonium ylides from vinyl sulfoximines

3.2.2.1 Asymmetric synthesis of alkenyl aziridine carboxylates

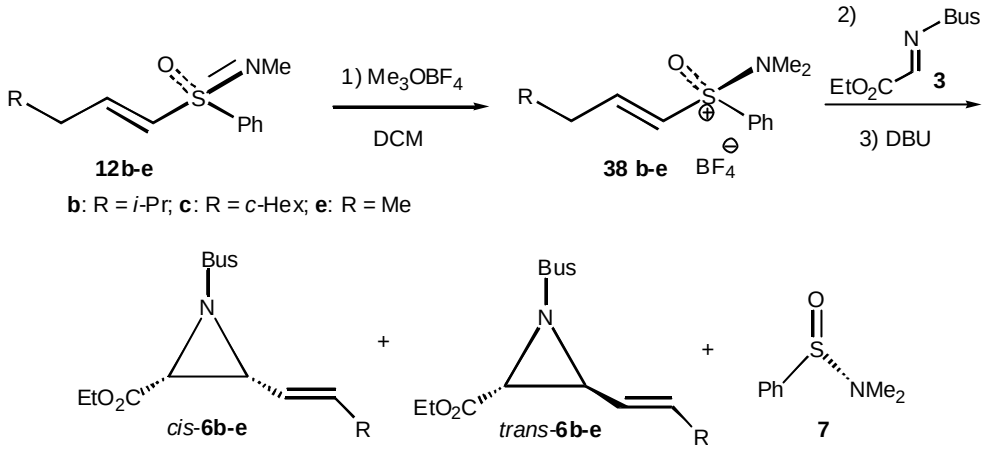
To our delight, the vinyl sulfoximines **12b**, **12c**, and **12e**[11] reacted readily with Me_3OBF_4 (1.2 equiv) at 0 °C in 2 h and afforded the corresponding vinyl aminosulfoxonium salts **38b**, **38c**, and **38e** (98% yield by NMR). The synthesis of the vinyl sulfoximines **12b**, **12c**, and **12e** from (*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximine (**10**) and the corresponding aldehydes was carried out without isolation of the corresponding intermediates. The lithiated (*S*)-sulfoximine was reacted with the respective aldehydes to produce the corresponding *b*-alkoxy sulfoximines (cf. Scheme 2.5). Salts Li-**11b**, Li-**11c**, and Li-**11e** were trapped, *in situ*, by treatment with ClCOOMe followed by the addition of DBU, which afforded the (*E*)-configured vinyl sulfoximines in 89%, 95%, and 78% yields, respectively.[7]



b: R = *i*-Pr; **c**: R = *c*-Hex; **e**: R = Me

Scheme 3.4: Synthesis of vinyl aminosulfoximines

The vinyl aminosulfoxonium salts **38b-e**, obtained from the corresponding vinyl sulfoximines **12b-e** upon treatment with Me_3OBF_4 (Scheme 3.5), were then treated with the *N*-Bus *a*-imino ester **3** (1.1 equiv) followed by the addition DBU (1.3 equiv). This gave mixtures of aziridines *cis*-**8b-e**/*trans*-**8b-e** along with sulfinamide **7** within 30 min. Column chromatography afforded mixtures of *cis*-/*trans*-aziridines **6b-e** in 70%, 68% and 65 % yields, respectively, along with the sulfinamide **7** (≥ 98% ee) in good yields (Table 3.1).



Scheme 3.5: Synthesis of alkenyl aziridine carboxylates from vinyl sulfoximines and the imino ester **3**

Table 3.1. Synthesis of alkenyl aziridine carboxylates from 1-alkenyl aminosulfoxonium salts and **3**

vinyl sulfoximine (**12**)	R	aziridines (**6b-e**) *cis*:*trans*	yield (%)	*cis* ee[a] (%)	*trans* ee[a] (%)	sulfinamide (**7**)
b	*i*Pr	64:36	70	76	49	92
c	cC_6H_{11}	70:30	68	47	45	90
e	Me	60:40[b]	65	65	-[c]	90

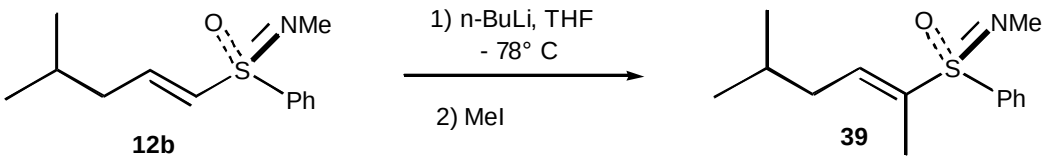
[a] Determined by HPLC, Chiralpack-IA. [b] Inseparabile mixture. [c] Could not be determined

The conversion of **12b-e** to the aziridines **6b-e**, respectively, has also been carried out with similar results without isolation of **38b-e**. By this shortened route the aziridines were obtained in good yields but with moderate diastereoselectivities and with low to moderate enantioselectivities. The diastereoselectivities and enantioselectivities of the aziridine formation from the vinyl aminosulfoxonium salts **38b** and **38c** in the presence of *N*-Bus *a*-imino ester **3** are significantly lower (Table 3.1) than those derived from the amino alkylated aminosulfoxonium salts **5b** and **5c**, where the imino ester **3** is generated in situ. Finally as illustrated in the foregoing section, a mixture of *cis*-**6b**/*trans*-**6b** was

stereoselectively transformed into cis-**33** with ≥98 % de via cis-**32**/trans-**32** and cis-**33**/trans-**33** in 80 % overall yield.

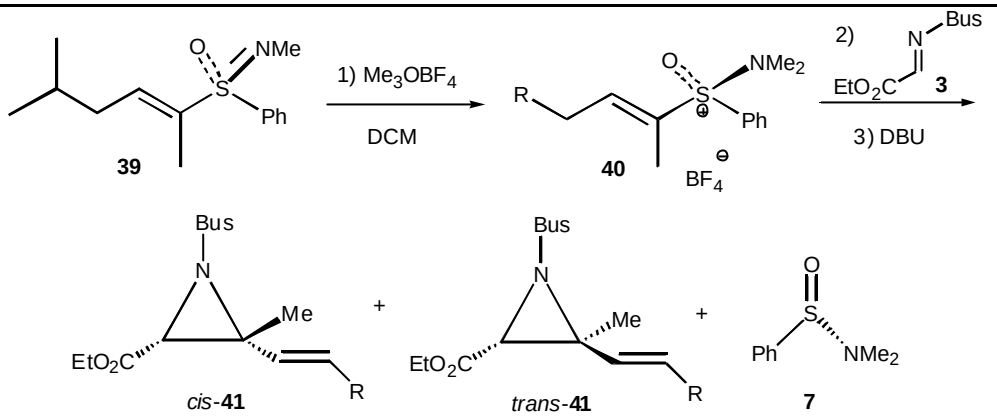
3.3 Synthesis of alkenyl aziridine carboxylates from a substituted allyl aminosulfoxonium ylide

Because of the high reactivity of the unsubstituted ylides **9a-d** towards the imino ester **3**, it was of interest to see whether an allyl ylide carrying an alkyl group at the C-atom can be generated and to study its reactivity. Thus, the Cα-methyl-substituted vinyl sulfoximine **39**[82] was prepared starting from the vinyl sulfoximine **12b**. The vinyl sulfoximine **12b** was lithiated at the α-position[83] with *n*-BuLi in THF at − 78° C and the solution was allowed to warm to 0° C over 45 min, which was then cooled to −78° C and quenched with an excess of MeI to afford the *a*-methyl substituted vinyl sulfoximine **39** in 95% yield (Scheme 3.6).



Scheme 3.6: Synthesis of a α-substituted vinyl sulfoximine

Having obtained the Cα-methylated vinyl sulfoximine **39**, it was methylated by a treatment with Me_3OBF_4 at 0° C, which gave the amino sulfoxonium salt **40** in 98% yield. Salt **40** was then treated with DBU in the presence of the N-Bus α-imino ester **3** at 0° C. This furnished the methyl-substituted allyl aminosulfoxonium ylide which readily reacted with **3** to produce aziridines *cis*-**41** and *trans*-**41** in a ratio of 60:40 in 81% yield. Besides aziridines *cis*-**41** and trans-**41**, sulfinamide **7** of ≥98% ee was isolated in 92% yield. Pure *cis*-**41** was obtained by preparative HPLC, but pure *trans*-**41** could not be obtained.

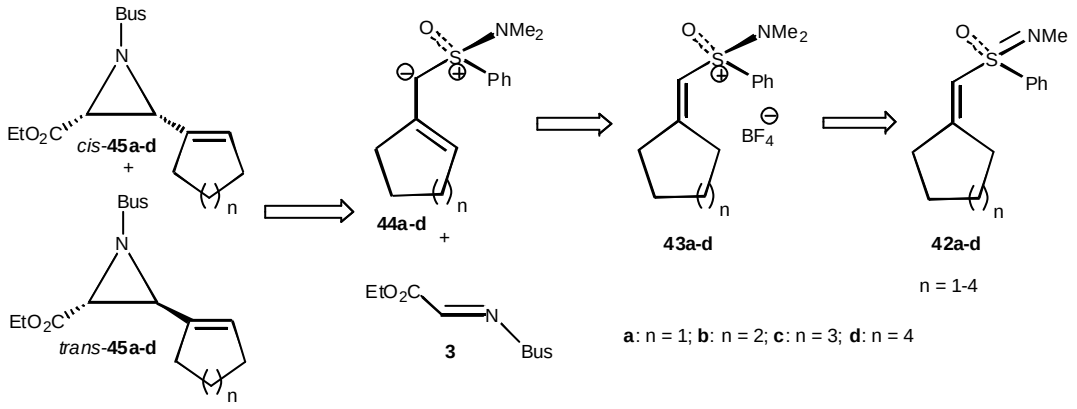


Scheme 3.7: Synthesis of alkenyl aziridine carboxylate from a substituted allyl aminosulfoxonium ylide

3.4 Synthesis of cycloalkenyl aziridine carboxylates from cyclic 1-alkenyl sulfoximines and imino ester 3

3.4.1 Retrosynthetic analysis of cycloalkenyl aziridine carboxylates

The synthesis of the alkenyl aziridine carboxylates *cis*-**6b-e** and *trans*-**6b-e** from the vinyl sulfoximines **12b-e** *via* their corresponding salts **38b-e** and the *N*–Bus *a*–imino ester **3** suggested the possibility of a similar synthesis of cyclic alkenyl aziridines *cis*-**45a-d** and *trans*-**45a-d** from cyclic 1-alkenyl sulfoximines **42a-d**[84] and **3** (Scheme 3.8).

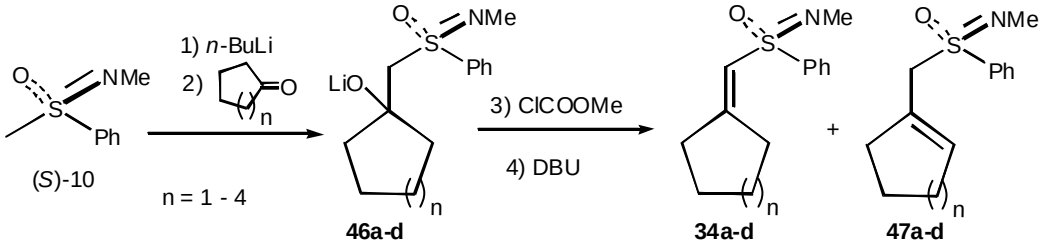


Scheme 3.8: Retrosynthetic analysis of cycloalkenyl aziridine carboxylates

The required cyclic 1-alkenyl sulfoximines **42a-d** can be derived from the (*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximine (**10**) by the addition-elimination route.[11]

3.4.2 Synthesis of cyclic 1-alkenyl sulfoximines

The cyclic 1-alkenyl sulfoximines **42a-d**[84] can be prepared on a preparative scale because of the ready availability of the cycloalkanones and the enantiomerically pure (*S*)-*N*,*S*-dimethyl-*S*-phenyl sulfoximine (**10**). Addition of the lithiomethyl derivative of **10**[11] to the corresponding cycloalkanones, which is well-exemplified mainly through the work of Johnson et al.,[2c] led to the corresponding hydroxy sulfoximines which were not isolated but treated with ClCOOMe followed by DBU at -78 °C according to the reported experimental procedure,[84] which afford the cyclic vinyl sulfoximines **42a-d** along with small amounts of the cyclic allyl sulfoximines **47a-d**. The pure cyclic vinyl sulfimines were obtained by column chromatography in 73%, 82%, 80% and 75% yield, respectively.[84]



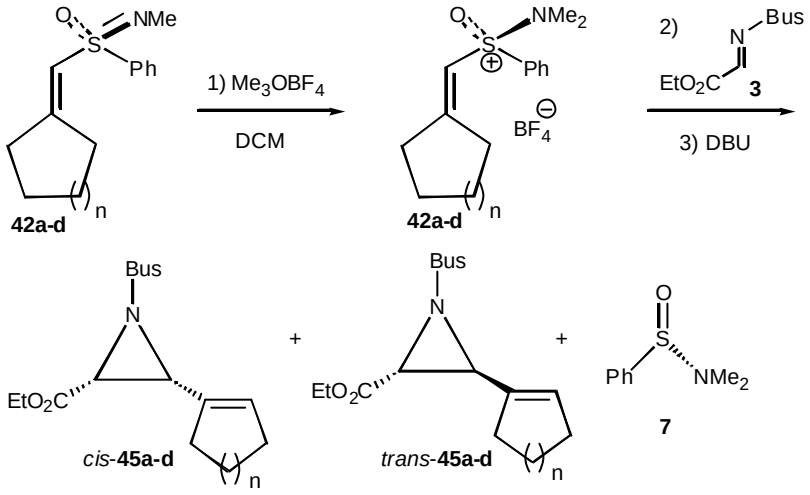
a: n = 1; **b**: n = 2; **c**: n = 3; **d**: n = 4

Scheme 3.9: Synthesis of cyclic 1-alkenyl sulfoximines

3.4.3 Synthesis of cycloalkenyl aziridine carboxylates

According to the synthetic strategy for aziridines **37a-d**, the first step is the activation of the *N*-methyl sulfoximine group of the cyclic alkenyl sulfoximines **42a-d** with Me_3OBF_4. Hence, based on our earlier observations the cyclic 1-alkenyl sulfoximines were treated

with Me_3OBF_4 in CH_2Cl_2 at 0 °C, which gave the (dimethylamino)sulfoxonium salts **43a-d** in quantitative yields (Scheme 3.10). The salts thus obtained were treated with DBU in CH_2Cl_2 to generate the corresponding cyclic aminosulfoxonium ylides **44a-d**, the key intermediates, in the presence of the *N*-Bus *a*-imino ester **3**. To our delight, the cyclic aminosulfoxonium ylides **44a-d** also combined with the imino ester **3** and afforded the cycloalkenyl aziridine carboxylates *cis*-**45a-d** and *trans*-**45a-d** with low diastereoselectivities and medium enantioselectivities in good yields (Table 3.2). Besides the aziridines the sulfinamide **7** (≥ 98 % ee) was isolated in good yield in each case.



Scheme 3.10: Synthesis of cycloalkenyl aziridine carboxylates from cyclic 1-alkenyl sulfoximines and imino ester 3

Table 3.2. Synthesis of cycloalkenyl aziridine carboxylates

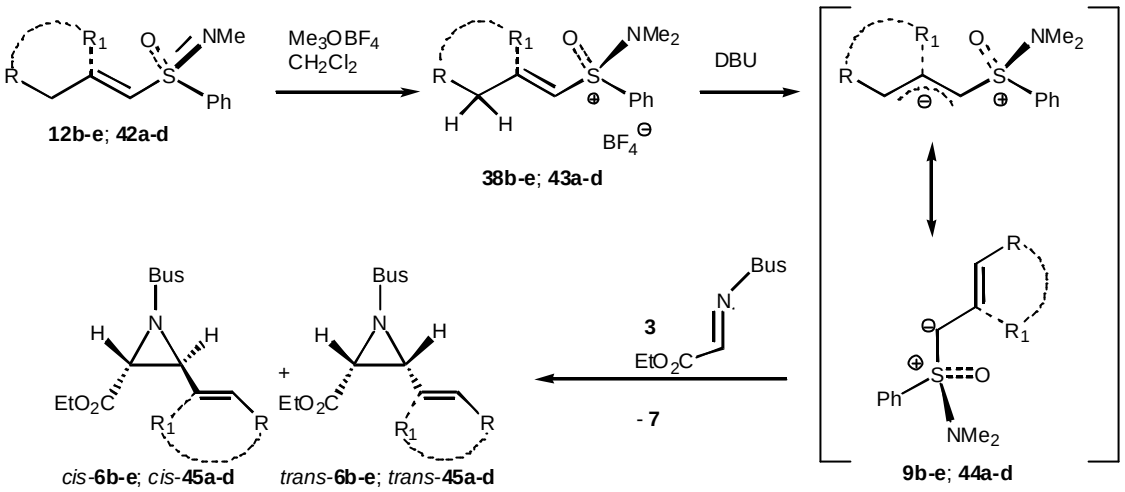
vinyl sulfoximine (**42**)	n	aziridine (**45**) *cis*:*trans*	yield (%)	*cis*		*trans*		Sulfinamide (**7**)
				ee[a] (%)	yield (%)	ee[a] (%)	yield (%)	
a	1	60:40[b]	70	79	–	90	–	80
b	2	60:40	73	76	42	56	28	81
c	3	60:40	71	78	41	57	26	76
d	4	50:50	66	70	29	25	30	70

[a] Determined by HPLC, Chiralpack-IA. [b] Inseparable mixture.

In fact, the conversion of **42a-d** to *cis*-**45a-d** and *trans*-**45a-d** could also be carried out with similar results without isolation of the salts **43a-d**. The 2,3-*cis*/*trans*-pair of chiral aziridines were obtained in a 3:2 ratio, respectively, in the case of cyclopentenyl, cyclohexenyl and cycloheptenyl aziridine derivatives, where as in the case of the cyclooctenyl aziridine derivative the *cis*/*trans* ratio was 1:1. The *cis*- and *trans*-configuration was assigned based on the ^{1}H NMR data. In the case of the 2,3-*cis*-aziridines the $J(H_2,H_3)$ values were ~ 7.66 Hz, and in the case of 2,3-*trans*-aziridines the $J(H_2,H_3)$ values were ~ 3.85 Hz. This is in accordance with the literature values[63] for *cis* and *trans* aziridine derivatives.

3.5 Mechanistic considerations of the alkenyl aziridine carboxylates formation from allyl aminosulfoxonium ylides and 3

The formation of the acyclic alkenyl aziridine carboxylates *cis*-**6b-e** and *trans*-**6b-e** from the aminosulfoxonium salts **38b-e** and the cycloalkenyl aziridine carboxylates **45a-d** from the cyclic aminosulfoxonium salts **43a-d**, respectively, through a treatment with DBU and *a*-imino ester **3** can be mechanistically described as shown in Scheme 3.11. Methylation of the acyclic and cyclic alkenyl sulfoximines **12b-e** and **42a-d** with Me_3OBF_4 gave the (dimethylamino) sulfoxonium salts **38b-e** and **43a-d**, respectively. When these salts **38b-e** and **43a-d** were treated with DBU a deprotonation took place at the *g*-position producing the highly reactive allyl ylides **9b-e** and **44a-d**, respectively, which react with the *N*-Bus *a*-imino ester **3** to afford the corresponding *cis*/*trans*-aziridine derivatives **6b-e** and **45a-d** along with sulfinamide **7**.



Scheme 3.11: Mechanism for aziridine formation from the allylic sulfoxonium ylides **9b-e** and **44a-d** by combining with **3**

It is assumed that the first step of the aziridine formation is the stereoselective addition of the allylic aminosulfoxonium ylides **9b-e** and **44a-d** to the imino ester **3** to form a betaine, while establishing a new C-C bond. The second step will be the irreversible anti attack of the *N*-atom on the carbon bearing the amino sulfoxonium group, to eliminate sulfinamide **7**. The reason for the observed stereoselective addition of the allylic aminosulfoxonium salts **38b-e** and **43a-d** on the imino ester **3** can be explained as described below.

3.5.1 Mechanistic consideration of the stereoselective aziridination

In the literature, the ylide aziridination is regarded as a two-step process.[85] Although the detailed mechanistic pathway is not clear, we propose the following mechanism for the stereoselective attack, which allows the generation of enantiomerically enriched aziridine derivatives (Figure 3.5). As shown in path A, the aminosulfoxonium ylide **9b-e**, **44a-d** attacks the *N*-Bus *a*-iminoester **3** from the *Si*-face, where the allylic chain of the ylide and the ester group of the imino ester are facing opposite sides, also the bulky *N*-Bus group is on the side of smallest substition, oxygen, of sulfoxonium sulfur as shown in the

Figure 3.4. Hence it is the most favorable direction of addition of sulfoxonium ylide **9b-e**, **44a-d** to the imino ester **3** as it is evidenced by the formation of the major (2*R*,3*R*)-*cis*-**6b-e**,**45a-d** enantiomer. On the other hand when the sulfoxonium ylide **9b-e**, **44a-d** adds to the imino ester **3** from the *Re*- face, following path B, the allylic substitution of the ylide and the ester functionality of the imine are *trans* to each other but the Bus group of the imine and the dimethylamine group of the sulfoxoniumylide approach from the same side, which is sterically not favourable. Hence, path B which produces a (2*S*,3*S*)-*ent-cis*-**6b-e**,**44a-d** aziridines is not a facile approach. Thus the major *cis*-enantiomer obtained from path A and has the (2*R*,3*R*)-configuration.

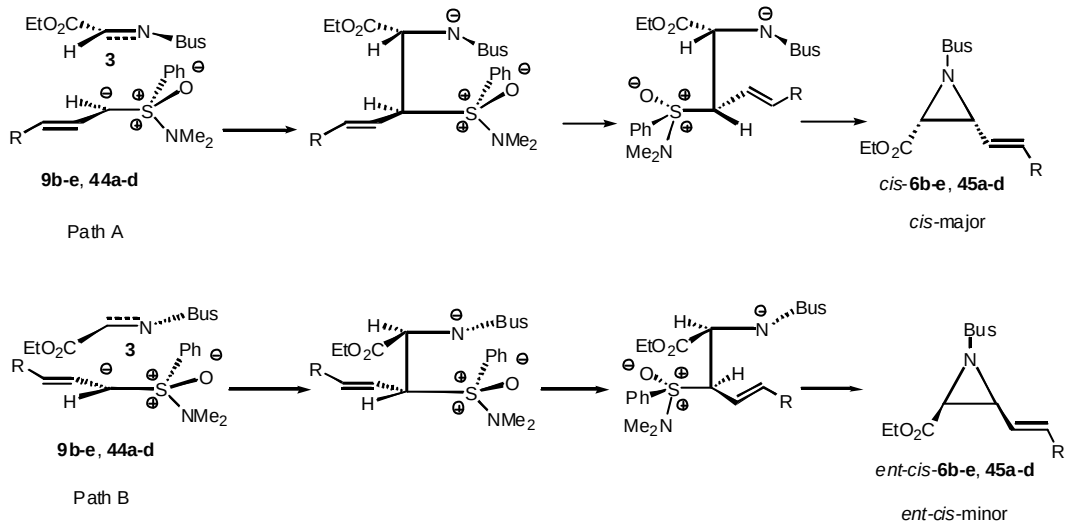


Figure 3.5: Stereoselective formation of *cis*-aziridines

Similarly, the formation of the *trans*-major and the *trans*-minor enantiomers from the allylic aminosulfoxonium ylide and the *N*-Bus *a*-imino ester **3** can be explained as follows. The sulfoxonium ylide **9b-e**, **44a-d** adds to the imino ester from the *Si*-face having both the allylic side chain of the ylide and the ester group of the imino ester on the same side to follow path C, in order to form *trans*-aziridine derivative *trans*-**6b-e**, **45a-d**. But during this addition the Bus substituent of the imine approaches towards the oxygen of the sulfoxonium group, hence the steric orientation of the *N*-Bus is favoured during this addition but the allylic functionality and the ester functionality undergo steric

interactions. When following path D, the allylic substitution of the ylide and the ester substitution of the imine experience unfavourable steric interactions and also the *N*-Bus group and the dimethyl amino substituent of the sulfoxonium group are approaching from the same side. Since this addition is the most hindered approach path D will lead to the formation of the minor enantiomer of the *trans*-aziridine derivative *ent-trans*-**6b-e**, **45a-d**.

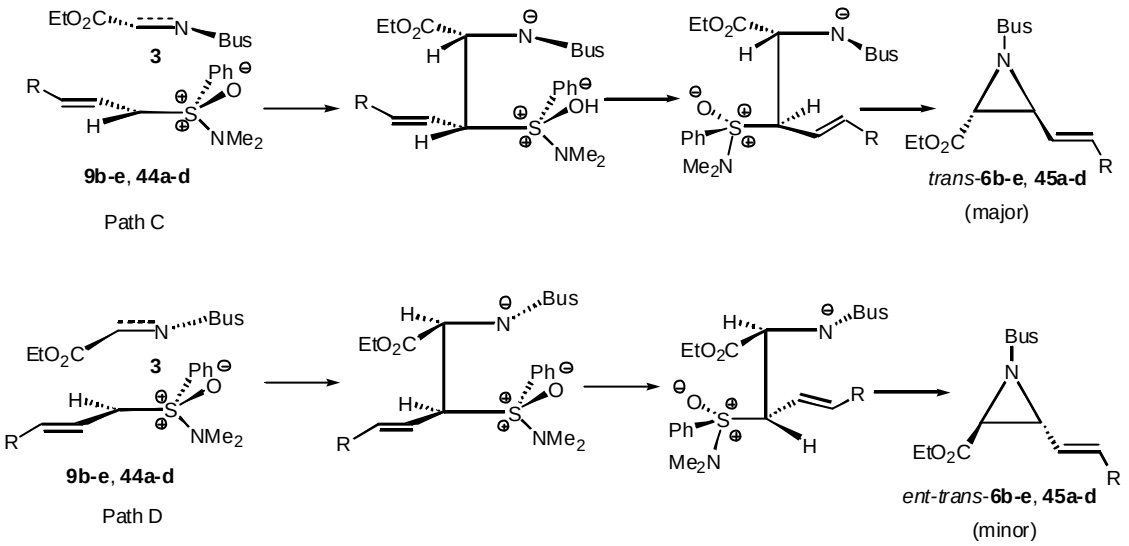


Figure 3.6: Stereoselective formation of *trans*-aziridines

3.6 Conclusions

In summary, we have achieved a highly efficient asymmetric synthesis of N-Bus protected acyclic and cyclic alkenylaziridine carboxylates by a reagent controlled asymmetric synthetic approach. There are only two reports of reagent-controlled asymmetric aziridination in the literature. We succesfully applied the cyclic allylic sulfoxonium ylides for aziridination and synthesized a variety of cyclic alkenylaziridine carboxylates. The *tert*-ylides were generated *in situ* and applied successfully for the chirally pure *tert*- substituted aziridine derivatives in a one pot reaction with good yields and diastereoselectivities.

CHAPTER 4

Michael addition of thiophenol to vinyl sulfoximines

4 Michael addition of thiophenol to vinyl sulfoximines

4.1 Introduction

4.1.1 Michael addition of vinyl sulfoximines

The Michael addition is one of the efficient methods in organic synthesis for the formation of carbon-carbon, carbon-sulphur, carbon-oxygen, carbon-nitrogen and carbon-phosphorous bonds.[86] The Michael addition of *a,b*-unsaturated sulphur derivatives has been reported in the case of sulphones,[87] sulphoxides,[7,8a,88] and sulphimides.[89] However, in the case of vinyl sulfoximines the conjugate addition reactions had not been well explored until the end of mid-1980s. A serious obstacle present at that time was the rather limited number of efficient routes to isomerically pure vinyl sulfoximines. With the number of methods for the preparation of these compounds growing, the number of their successful applications in organic synthesis steadily increased. α, β-Unsaturated sulfoximines have unique properties: the double bond is strongly activated, as in the case of the sulphonyl group, towards nucleophilic addition; moreover, the presence of a chiral sulphur atom could lead in principle to the occurence of asymmetric induction and/or kinetic resolution. Michael addition of variety of nucleophiles to α, β-unsaturated sulfoximines has been studied.

One of the first successful asymmetric conjugate addition of carbon nucleophiles to a chiral vinyl sulphoximines appeared in 1986.[90] Pyne et al. synthesized the (+)-norephedrine derived 1-alkenyl sulphoximines via the corresponding diastereomeric sulfinamides (Figure 4.1). Conjugate additions of organolithium reagents and Gilman-cuprates (R_2CuLi) occured from the *Si*-face of C-2 whereas organocopper compounds (RCu) attacked the double bond from its *Re*-side. The attained diastereoselectivities were quite high (80–96% *de*) and were explained by a complexation model involving the sulfoximine heteroatoms as well as the methoxy group of the auxiliary.[91,92]

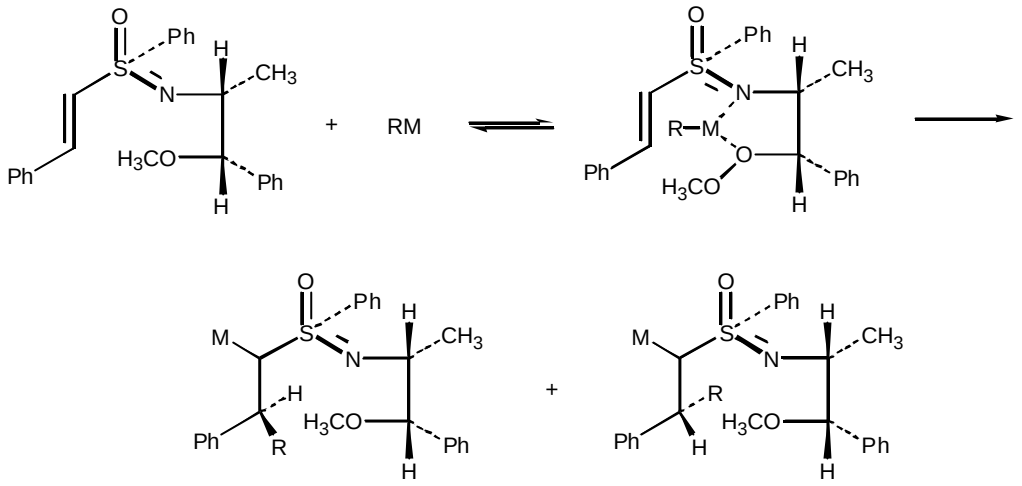


Figure 4.1. Conjugate addition of organometallic reagents to chiral vinyl sulfoximines

In 1979 Annunziata et al. published the kinetic resolution of the *N*-phthaloyl vinyl sulfoximine by using (–)-ephedrine as the nucleophile (Figure 4.2).[93] The enantiomer differentiating conjugate addition reaction enriched the unsaturated starting material to 46% *ee*.

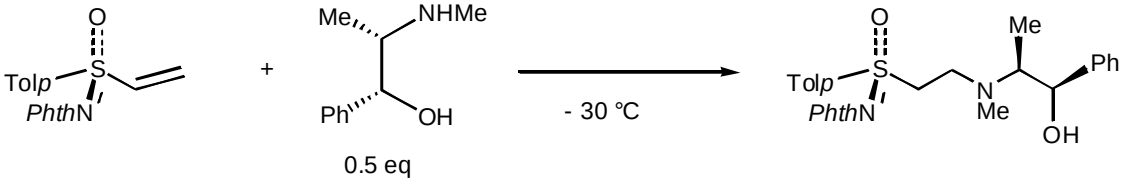


Figure 4.2. Aza–Michael addition of amines to vinyl sulfoximines

Taking this precedent as a starting point, Tye et al. investigated the generality of the conjugate addition of nitrogen nucleophiles into vinyl sulfoximides.[94]

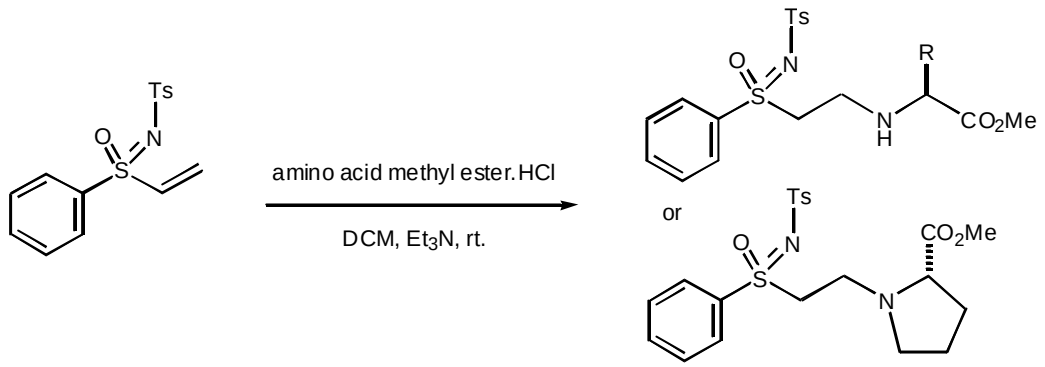


Figure 4.3. Aza–Michael addition of amino acids to vinyl sulfoximines.

In 1998 Reggelin et al. combined the diastereoselective reactions of titaned allyl sulfoximines with a diastereoselective cyclisation yielding highly substituted diastereomerically pure pyrrolidines[92] (Figure 4.4).

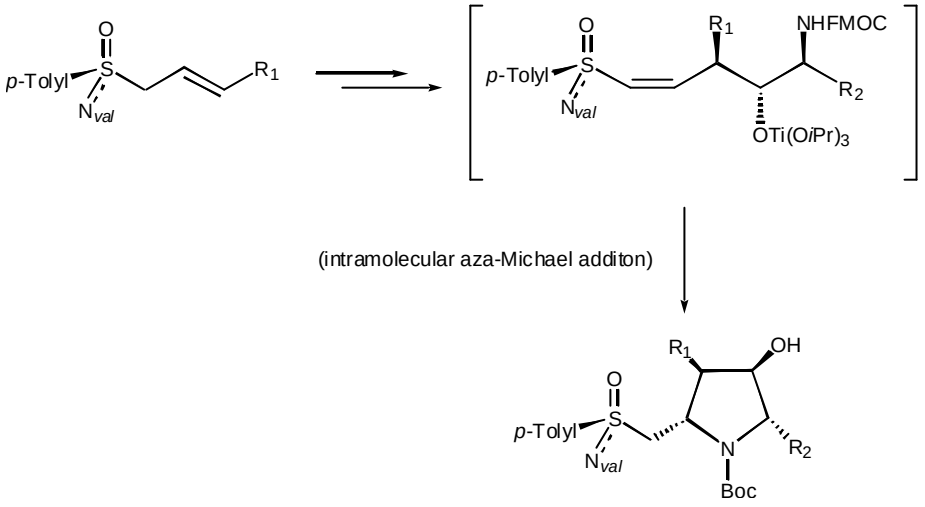


Figure 4.4. Intramolecular aza–Michael addition to vinyl sulfoximines

In 2003, Gais et al. studied the intramolecular carbamate amination of δ-hydroxy-α,β-unsaturated sulfoximines to form diastereomerically pure oxazinone derivatives (Figure 4.4).[17d]

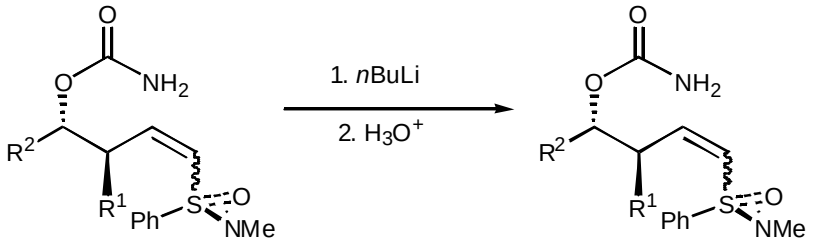
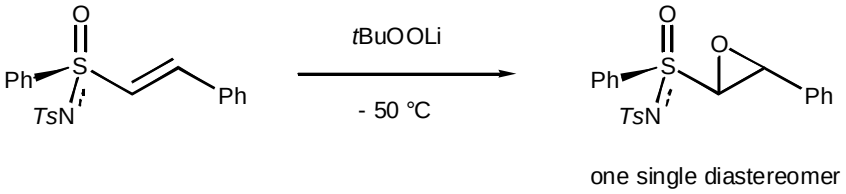


Figure 4.4. Intramolecular aza–Micahel addition to vinyl sulfoximine

In 1988 Meth-Cohn et al. described the synthesis of epoxy sulfoximines *via* conjugate addition of *t*BuOOLi to vinyl sulfoximines. In 1993 the same author together with Jackson reported the synthesis of a series of epoxy sulfoximines by a slight modification of the above mentioned nucleopilic epoxidation procedure (–50 °C instead of –20 °C (Figure 4.5).[95]



one single diastereomer

Figure 4.5. Oxo–Michael addition to vinyl sulfoximines

4.2 Present Work

4.2.1 Aim

From the above discussion it is clear that alkenyl sulfoximines can act as Michael acceptors toward various nucleophiles. However the range of neucleophiles for the conjugate addition of alkenyl sulfoximines has yet to be explored. Hence, asymmetric Michael addition of vinyl sulfoximines is still a topic of considerable interest. For a study of such reactions the important point to be considered is the electrophilic nature of the

sulfoximine group. It has been reported that the substituent present on nitrogen atom greatly effects the electrophilicity of the sulfoximine group.[2a]

Recently, C. F. Yao et al. reported the iodine-catalyzed Michael addition of mercaptanes to *a*,*b*-unsaturated ketones under solvent-free conditions[96a] (Figure 4.6). They demonstrated a simple and efficient methodology to prepare a wide variety of Michael adducts using iodine in catalytic amounts. This environmentally benign process for the generation of Michael adducts represents a suitable option to the existing procedures with different substitution.

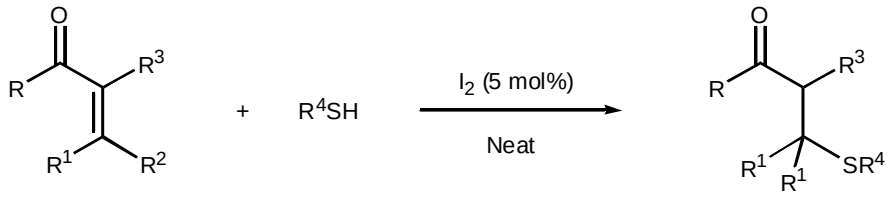


Figure 4.6. Michael addition of mercaptanes under solvent free conditions

The above-mentioned mercaptane conjugate addition under solvent free conditions encouraged us to study a similar reaction of vinyl sulfoximines.

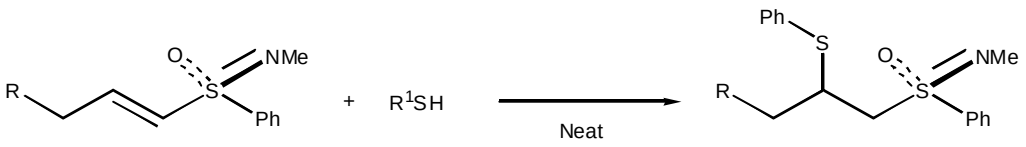


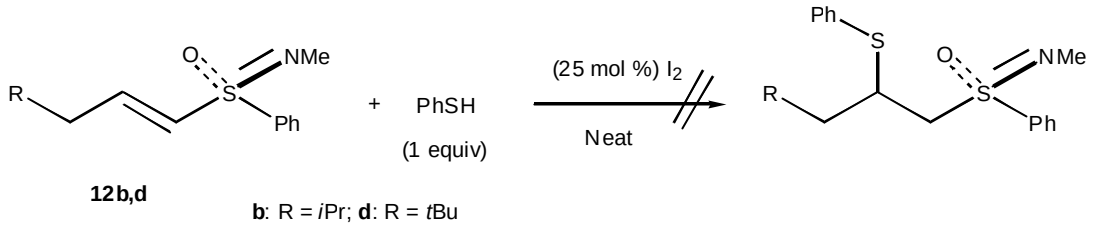
Figure 4.7. Conjugate addition of mercaptane to vinyl sulfoximine

4.2.2 Results and Discussion

4.2.2.1 Michael addition to simple vinyl sulfoximines

To study the conjugate addition of mercaptanes to vinyl sulfoximines, the simple *N*-methyl vinyl sulfoximines **12b** and **12d** were selected and treated with 1 equiv of

thiophenol together with 25 mol% iodine, at room temperature under argon atmosphere. Even after stirring the reaction mixture for 8 h no product formation was observed.

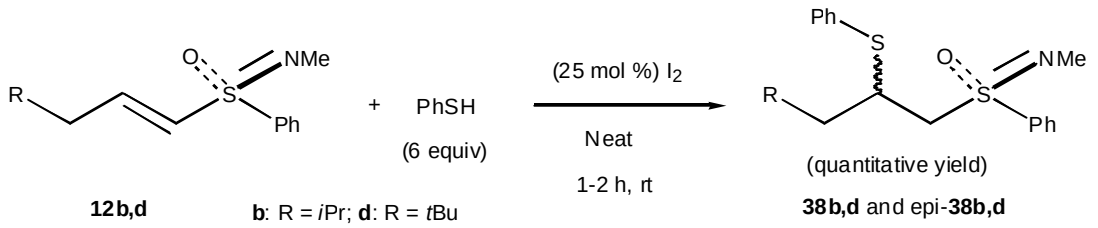


12b,d

b: R = *i*Pr; **d**: R = *t*Bu

Scheme 4.1: Thia−Michael addition of vinyl sulfoximine

However, treatment of the vinyl sulfoximines **12b,d** with excess thiophenol (6 equiv) together with iodine (25 mol%) gave sulfides **38b** and epi-**38b** as well as **38d** and epi-**38d**, respectively, in almost quantitative yields. The diastereoselectivity was found to be approximately 2 : 1 in both cases. The synthesis of the vinyl sulfoximines **12b,d** has already been described in the chapter 2, Scheme 2.5.



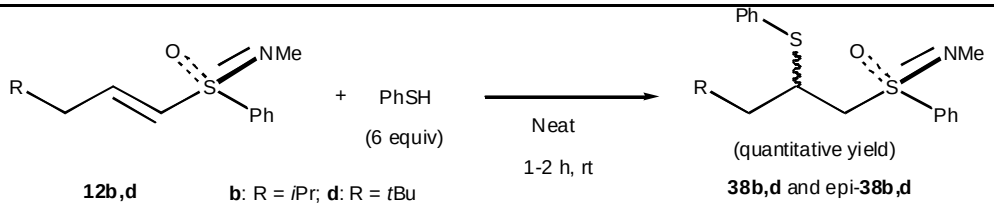
12b,d

b: R = *i*Pr; **d**: R = *t*Bu

38b,d and epi-**38b,d**

Scheme 4.2: Thia−Michael addition of vinyl sulfoximine

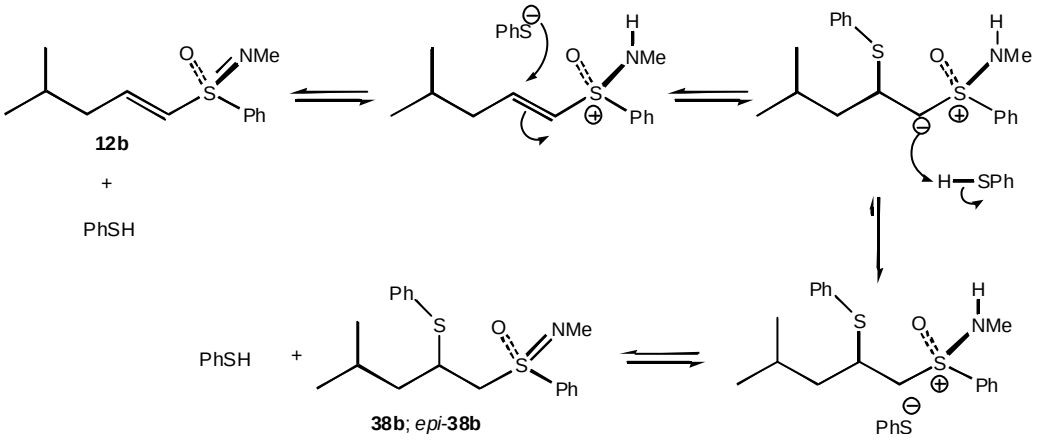
Further studies of the reaction of vinyl sulfoximine **12b,d** with thiophenol were carried out in the absence of iodine and sulfides **38b,d** and epi-**38b,d** were also obtained. Therefore iodine has no effect on the Michael addition of thiophenol to vinyl sulfoximines (Figure 4.3).



Scheme 4.3: Thia–Michael addition to vinyl sulfoximines

4.2.2.2 Mechanism of the Michael addition of thiophenol to vinyl sulfoximines

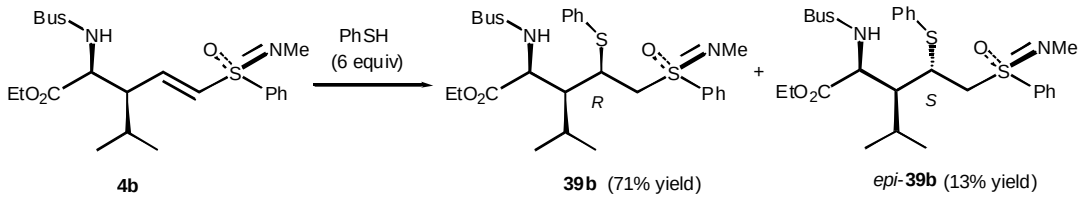
A possible mechanism for the thia-Michael addition of the alkenyl sulfoximines is shown in Scheme 4.4. Thiophenol (pKa ˜ 10.3) protonates the *N*–atom of the sulfoximine **12** to give the aminosulfoxonium salt (pKa ˜ 10). Then the thiophenolate ion attacks the double bond to form a C-S bond and generate the ylide, which is protonated by thiophenol to generate thiophenolate ion. The thiophenolate ion takes the proton from the sulfoxonium *N*–atom of the sulfide formed to give a diastereomeric mixture of sulfides (**38** and *epi*-**38**) and thiophenol. Hence the reaction cycle continues to furnish the sulfides **38** and *epi*-**38**.



Scheme 4.4: Mechanism for the addition of thiophenol to vinyl sulfoximines

4.2.2.3 Michael addition of thiophenol to functionalized vinyl sulfoximines

Having developed a facile synthesis of sulfides **38b,d** and *epi*-**38b,d** from the corresponding simple vinyl sulfoximines **12b,d**, it was of interest to see whether this method could also be applied to the highly functionalized vinyl sulfoximines such as the *d*-sulfoximine substituted *g*,*d*-unsaturated *a*-amino acid derivatives **4a-b**, the synthesis of which has already been described in the chapter 2, Scheme 2.6. Thus, the vinyl sulfoximine **4b** was treated with 6 equiv of thiophenol at room temperature under argon atmosphere. Interestingly, the reaction was completed in 3 h and furnished the sulfides **39b** and epi-**39b** in a ratio of 4:1 in 90% yield. The pure sulfides **39b** and epi-**39b** were obtained by flash chromatography in 71% and 13% yield, respectively.



Scheme 4.5: Thia–Michael addition of the functionalized vinyl sulfoximine **4b**

The sulfides **39b** and **epi-39b** are colourless crystalline compounds. Single crystals of the major diastereomer **39b** were obtained in EtOAc/n-hexane solvent system and its structure was determined the X-ray crystal analysis (Figure 4.8). The X-ray structure showed that the newly created chiral center in **39b** has *R*-configuration.

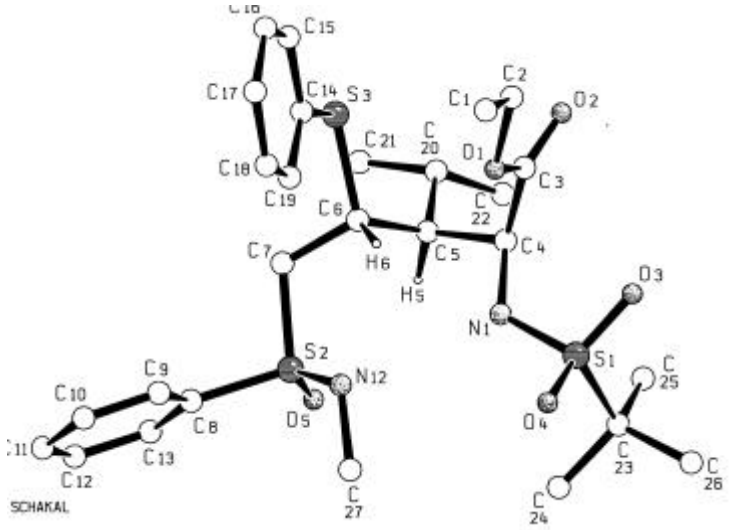
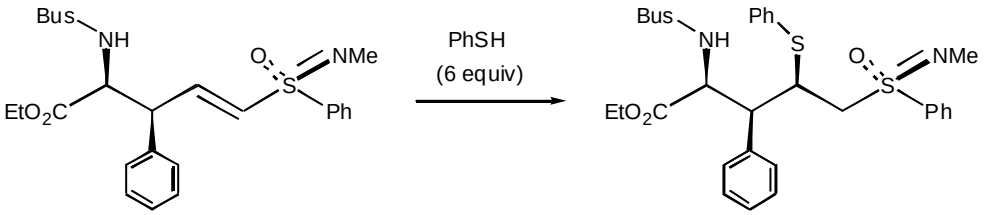


Figure 4.8. Structure of sulfide **39b** in the crystal

The vinyl sulfoximine **4a** was also treated with 6 equiv of thiophenol at room temperature under argon atmosphere. Greatifyingly, the reaction was completed in 1 h and gave sulfide **39a** as a single diastereomer with complete conversion of the starting material **4a**. But unfortunately while removing the excess thiophenol by flash column chromatography, the sulfide **39a** underwent a slow reverse Michael-addition reaction to give back the starting material **4a** and, thus, prohibiting the isolation of **39a** in pure form.



4a **39a** (88% yield)

Scheme 4.6: Thia–Michael addition of thiophenol to the functionalized vinyl sulfoximine **4a**

The preference for the '*Re-face*' attack of thiophenol to the vinyl sulfoximines **4a,b** can be rationalized as follows by considering the crystal structure of **4b**. The structure of **4b**[58] shows that the *S*-phenyl group, *N*-Bus group and the ester group together provide for a concave side of the vinyl sulfoximine **4b** whereas the isopropyl group is on the convex side (Figure 4.9).

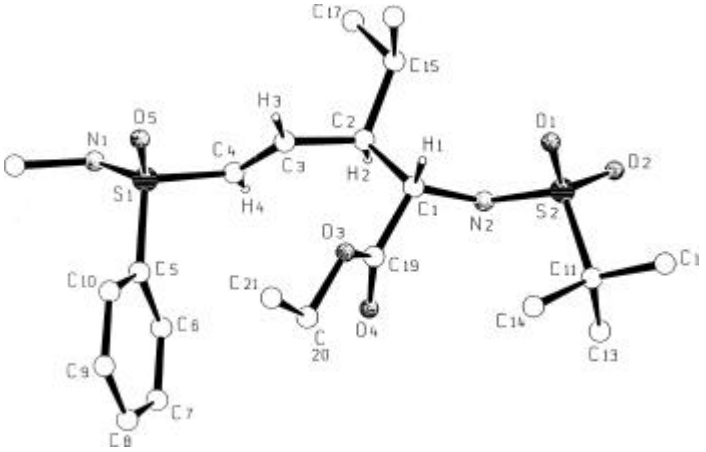
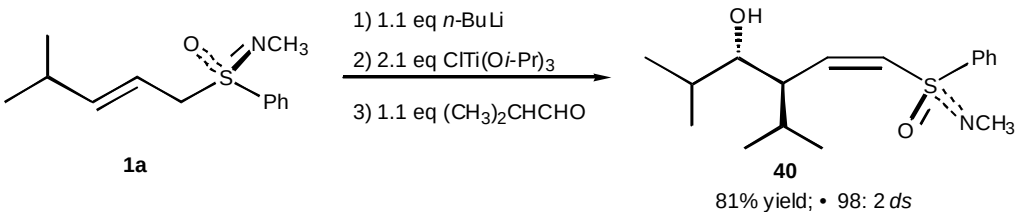


Figure 4.9. Structure of the amino−substituted vinyl sulfoximine **4b** in the crystal

The structure of **4b** shows that the bulky ester and the phenyl group of sulfoximine group block the *Si*-face of the double bond, where as the isopropyl group blocks the *Re*-face to a less extent. It is assumed that the sulfide **4b** adopts the same structure in solution. Hence for the Michael addition, the *Re*-face addition is more favoured than the *Si*-face addition. Thus, thiophenol undergoes a preferential *Re*-face addition, to give sulfide **39b** as a major diastereomer and to a small extent *Si*-face addition to yield the sulfide *epi*-**39b** as a minor diastereomer.

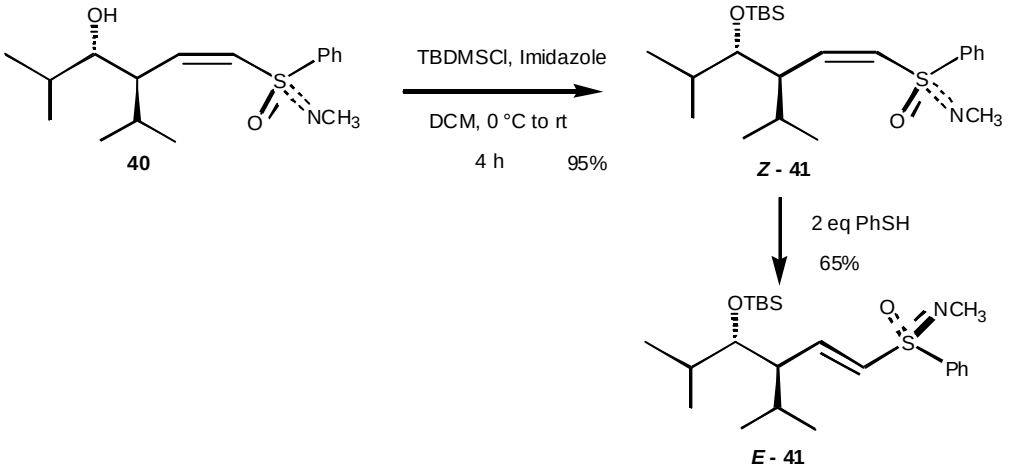
After having obtained favorable results in the Michael addition with the δ-sulfoximine–substituted γ,δ-unsaturated α-amino acid derivatives, a similar reaction with δ-sulfoximine substituted γ,δ-unsaturated homoallylic alcohols was studied. Former members of our research group disclosed a method for the regio- and stereoselective hydroxyalkylation of allylic sulfoximines **1** through successive treatment with *n*BuLi and 2.1 equiv $Cl(Ti(O\,iPr)_3$ followed by treatment with aldehydes, which leads to the formation of the *anti*-configured δ-*N*-methylsulfonimidoyl substituted homoallylic

alcohols (eg. **40**).[11,97] Thus the sulfoximine–substituted homoallylic alcohol **40**[83] was synthesized from the allyl sulfoximine **1a** with ≥96% de in 81% yield (Scheme 4.7).



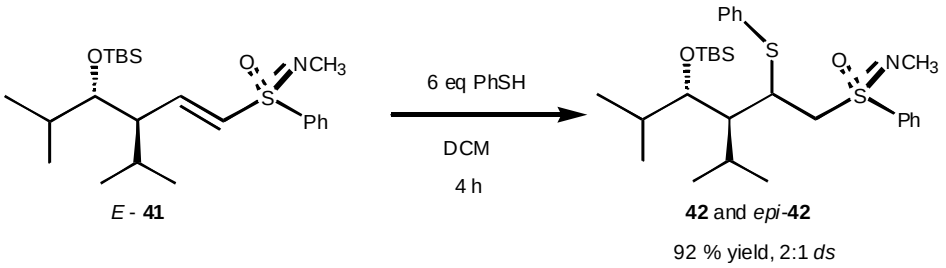
Scheme 4.7: Asymmetric synthesis of the sulfoximine–substituted (*Z*)–homoallylic alcohol **40**.

The thus obtained (*Z*)–homoallylic alcohol **40** was silylated by treatment with TBDMSCl (2 equiv) in the presence of excess of imidazole (4 equiv) in CH_2Cl_2, which furnished sulfoximine **41** in 95% yield (Figure 4.8). The silyl protected (*Z*)-configured vinyl sulfoximine **41** was treated with 2 equiv of thiophenol at room temperature under argon atmosphere. Interestingly, thiophenol caused a change in the double bond configuration of vinyl sulfoximine from Z-**41** to *E*–**41** but no Michael addition was observed. Hence, sulfoximine *E*-**41** was isolated in 65% yield along with the unreacted sulfoximine *Z*–**41** in 20% yield (Scheme 4.8).



Scheme 4.8: Reaction of the silyl–protected *Z*–configured vinyl sulfoximine with thiphenol

After having observed a tendency of thiophenol to isomerize the *Z*-configured vinyl sulfoximine *Z*-**41** to *E*-configured vinyl sulfoximine *E*-**41**, it seemed of interest to study the Michael addition of thiophenol to the *E*-configured vinyl sulfoximine *E*-**41**. Therefore *Z*-**41** was first transformed into *E*-**41** through α–lithiation followed by protonation.[82] The lithiation of the Z-alkenyl sulfoximine *Z*-**41** with *n*BuLi at −78 °C occurred selectively at the α-position and gave the corresponding Z-alkenyllithium derivative which suffered at −20 °C a complete isomerization to the *E*-configured alkenyllithium derivative, the protonation of which gave *E*-**41**. The resulting *E*-**41** was treated with 6 equiv of thiophenol at room temperature under argon atmosphere. The reaction was finished in 4 h and furnished sulfides **42** and *epi*-**42** in 92% yield in a ratio of 2:1. Preparative HPLC (EtOAc/*n*-hexane; 1:9) afforded the pure sulfide **42** in 58% yield and sulfide *epi*-**42** in 33% yield. The stereochemistry of both the diastereomers was not determined.



E - **41**

42 and *epi*-**42**

92 % yield, 2:1 *ds*

Scheme 4.9: Michael addition of thiophenol to silyl protected *E*-configured vinyl sulfoximine.

4.3 Conclusions

In summary, we have achieved an efficient thia−Michael addition of thiophenol to a variety of 1-alkenyl sulfoximines, including simple vinyl sulfoximines **12b,d**, δ-sulfoximine substituted γ,δ-unsaturated α-amino acid derivatives **4a,b**, and silyl protected δ-sulfoximine substituted γ,δ-unsaturated homoallylic alcohols **40**. The Michael addition went well in all cases to give the sulfides in very good yields. It was interesting to observe a high diastereoslectivity in the case of δ-sulfoximine−substituted γ,δ-unsaturated α-amino acid derivatives **4a,b**. These results can serve as interesting starting point for the synthesis of biologically important molecules like highly substituted proline derivatives as explained in the following chapter.

CHAPTER 5

Asymmetric synthesis of 3-substituted 4-phenylsulfenyl prolines

5 Asymmetric synthesis of 3-substituted 4-phenylsulfenyl prolines

5.1 Introduction

Having observed a diastereoselective thia–Michael addition of thiophenol to δ-sulfoximine–sulbstituted γ,δ–unsaturated α–amino acids **4a,b**, a conversion of the corresponding sulfides into a 4–thia substituted proline derivative was envisioned.

5.1.1 Sulfur–containing biologically active molecules

Sulfur-containing compounds can be found in all living organisms and, therefore, play an important role in biochemistry.[98] Biosynthetically, sulfur–containing functionalities are introduced by a variety of chemical processes, including the thia-Michael addition.[99] Coenzyme M is synthesized in methanogenic bacteria involving an initial addition of bisulfite to phosphoenolpyruvate to form the α-hydroxy acid,[100], which is subsequently, transformed into the coenzyme M over 5 steps (Figure 5.1).

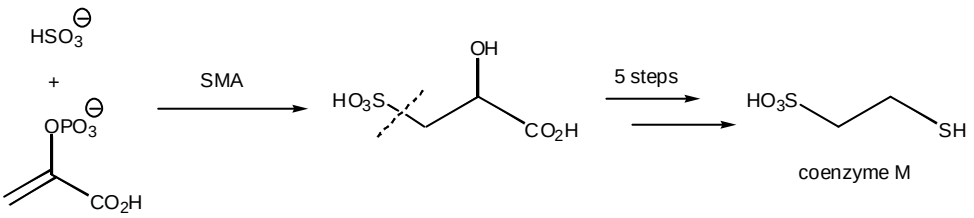


Figure 5.1. Biosynthesis of coenzyme M following SMA

Among the various important biosynthetic compounds proline derivatives have found considerable application.[101] Peptide mimetics containing modified prolines are interesting probes for receptor studies and for the development of new drugs. Highly substituted prolines are being currently considered as conformationally restricted arginine, norleucine, phenylalanine, tyrosine, aspartic acid, and glutamic acid analogues[102] for the development of small molecule drugs. Proline has been found to be an excellent catalyst of asymmetric Aldol and Mannich reactions and of the asymmetric α-amination of

carbonyl compounds.[103] There are several methods known in the literature for the synthesis of 2-, 3-, and 5-substituted prolines. But not many promising methods exist for 4–substituted prolines.[104] In particular 4–thia substituted proline derivatives have found a few important biological applications. The thiamethylene linkage for example, offered from a 4-mercapto proline, in peptides generates a maximum rigidity and provides the desired dihedral angle.[105]

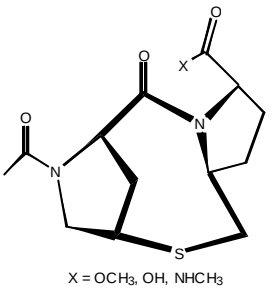


Figure 5.2. 4-Thia substituted prolines and thiamethylene linkage in peptides

Natural products containing 4-thia–substituted prolines are known. For example meropenem is an important β-lactam antibiotic drug.[106]

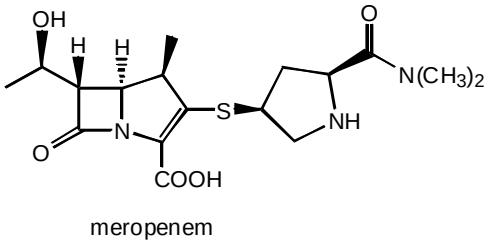


Figure 5.3. 4-Thia proline substituted natural products

A widely used method for the synthesis of 4-thia substituted prolines[107] involves a Finkelstein type reaction of the corresponding activated hydroxyproline derivative (Figure 5.4).

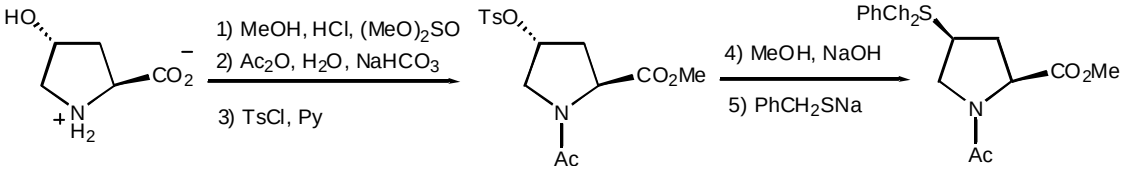


Figure 5.4. Synthesis of 4-thia prolines

The 1,3-dipolar cycloaddition of azomethine ylides with alkenes is good method for the synthesis of substituted prolines.[102]

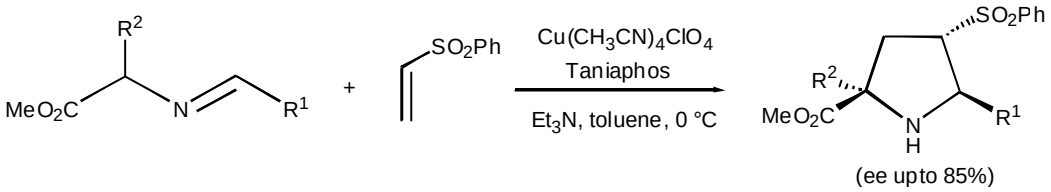
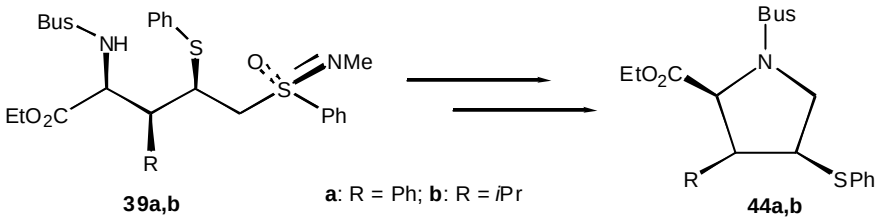


Figure 5.5. Synthesis of 4-thia prolines by 1,3-cycloaddition reaction

5.2 Present Work

5.2.1 Aim

As illustrated in the previous section, substituted prolines are valuable compounds in organic synthesis. Having developed a diastereoselective thia-Michael addition of thiophenol to the δ-sulfoximine–sulbstituted γ,δ-unsaturated α-amino acids **4a,b** (Chapter 4; Scheme 4.5, 4.6), we envisioned a synthesis of the 3-substituted 4-thia prolines **44a,b** from sulfides **39a,b** (Scheme 5.1).



Scheme 5.1: Synthesis of 3-substituted-4-thiophenyl prolines

5.2.2 Results and Discussion

5.2.2.1 Substitution of sulfoximine group by a Cl-atom

The synthesis of sulfides **4a,b** has been described in chapter 4. The successive synthesis of proline derivatives from **39a,b** would involve a substitution of sulfoximine group by a

Cl-atom followed by intramolecular cyclization. The substitution of a sulfoximine group by a Cl-atom has been accomplished in the case of vinyl sulfoximines[57] and β-amino substituted sulfoximine derivatives[10,17d] by a treatment with $ClCO_2Me$ or $ClCO_2CH(Cl)Me$. Vinyl sulfoximines upon treatment with $ClCO_2CH(Cl)Me$ give the corresponding allyl chlorides.[57] Where as the β-amino substituted sulfoximine derivatives can be transformed into β-amino chlorides upon treatment with $ClCO_2CH(Cl)Me$, which presumably undergo a neighbouring group participation of β-substituted amino group (Figure 5.6).

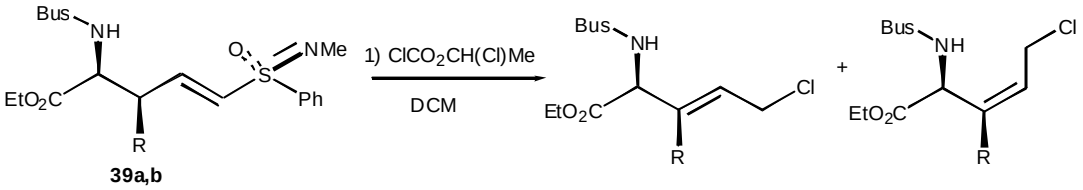
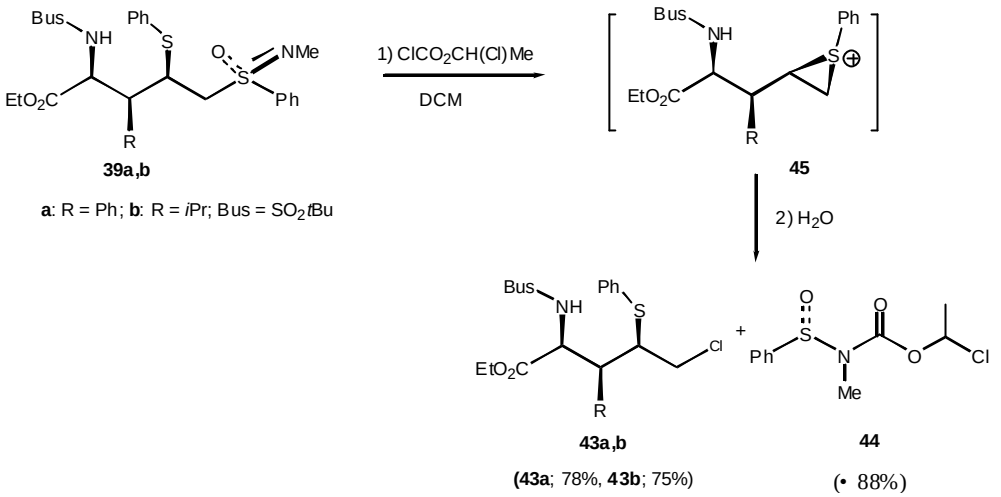


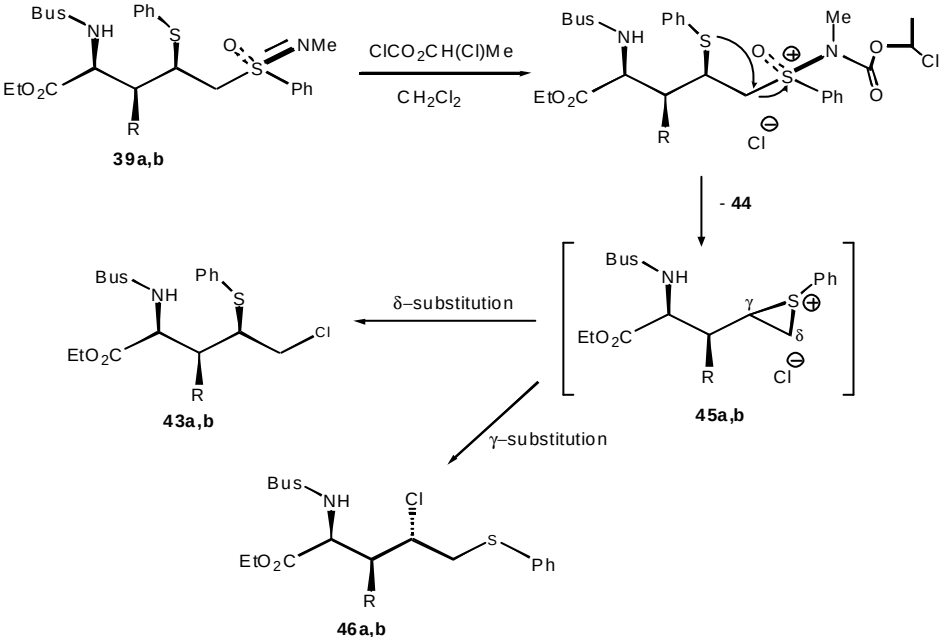
Figure 5.6: Substitution of sulfoximine by a Cl-atom

Similarly, it was envisioned that β-thio sulfoximines could also be transformed into their corresponding β-thio chlorides. It was expected that a neighbouring group participation from S-atom may take place during the chloride substitution of sulfoximine group. Indeed, sulfides **39a,b** were transformed into chlorides **43a,b** in 78% and 75% yield, respectively, upon treatment with 2 equiv of $ClCO_2CH(Cl)Me$ in CH_2Cl_2 at 0 °C for 2-3 h (Scheme 5.2). Besides chlorides **43a,b** sulfinamide **44** was isolated in 88% and 90% yield, respectively.



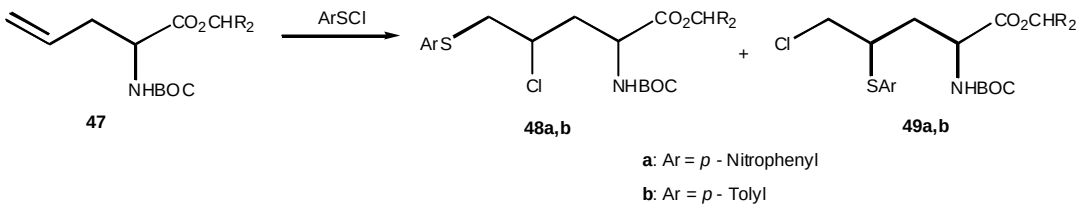
Scheme 5.2: Substitution of sulfoximine group by a Cl-atom

However, we were still apprehensive as to the structure of the chlorides. The chloride substitution of sulfoximines **39a,b** could proceed with a neighbouring group participation of S-atom with formation of episulfide **45**. Attack of Cl^- can occur both at γ-position and also at the δ-position (Scheme 5.3).



Scheme 5.3: Substitution of the sulfoximine group by a Cl-atom under neighbouring group participation.

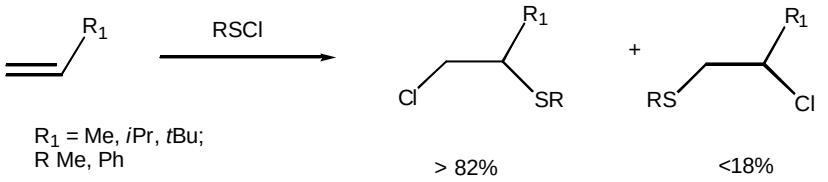
However, the structure of the chlorides was confirmed by comparing their NMR data with the literature reports.[108,109] In 1980 C. Walsh and R. A. Firestone reported the preparation of amino acids **48a,b** and **49a,b** (Scheme 5.4) for a study of mechanism-based enzyme inactivation.[108]



Scheme 5.4: Addition of arylsulfenyl chloride to terminal olefine

According to Walsh and Firestone addition of arylsulfenyl chlorides to the double bond of **47** was fast and quantitative to give the regio isomers **48a,b** and **49a,b**. The structures of **48a,b** and **49a,b** were confirmed by their NMR data. NMR of **48a** showed a δ-value of 3.3–3.7 ppm for CH_2S and 3.9–4.35 ppm for CHCl where as its regio isomer **49a** gave a multiplet together for CH_2Cl and CHS at 3.7 ppm. Similarly, the addition of *p*-tolylsulfenyl chloride to **47** was studied, it was observed that the product was principally **49b** by NMR as it showed a multiplet, corresponding to CHS and CH_2Cl together, at 3.0–3.8 ppm.

The factors influencing the nature of the episulfonium ion in sulfenyl chloride addition to terminal olefins has been studied. It was quoted that, in general, protons α or β to chlorine are considerably deshielded relative to those α or β to sulfur.[109] The NMR parameters compiled[109] show relative differences in chemical shift for the signals of such α–methylene or methane protons on the order of 0.7–1 ppm. When methane or benzenesulfenyl chloride was added to alkyl-substituted olefins, the initial adduct isomer mixture obtained was predominantly the anti-Markonikov product Scheme **5.5**. With increasing size of the substituent on the double bond (*e.g.*, going from methyl as in propylene to isopropyl and *t*-butyl as in 3-methylbutene) with 3,3-dimethylbutene higher selectivity for the anti-Markonikov-oriented product was observed according to NMR.[109]

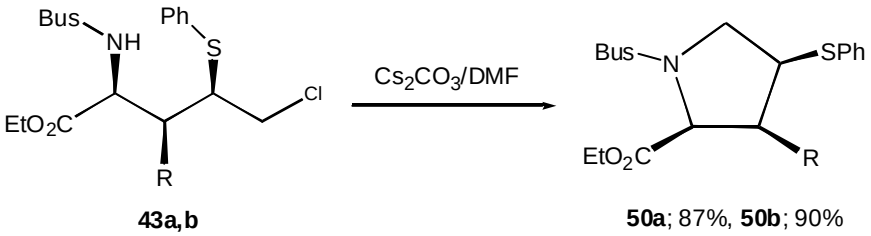


Scheme 5.5: Addition of methane- and benzene sulfenyl chloride to terminal olefine[109]

Thus, considering these results, the structure of chlorides obtained from the episulfonium ions **45a,b** was assigned. According to the NMR **39b** gave only one regio isomer after the chloride substitution and it showed a multiplet at 3.28 ppm for CHS and two doublet of doublets at 3.61 ppm and at 3.73 ppm for CH_2Cl. Whose δ–values are in the range of those reported in the literature. Hence, the structure of chloride can be assigned as **43b**. Similarly, **39a** gave only one regio isomer and whose structure can be assigned as **43a** according to the NMR.

5.2.2.2 Synthesis of 3-substituted-4-thiophenyl prolines

The chlorides **43a,b** upon treatment with Cs_2CO_3 in DMF at 40 °C underwent a cyclization to afford the proline derivatives **50a,b** in 87% and 90% yield, respectively (Scheme 5.6). The structure of the prolines was determined by NoE measurements of the deprotected proline **50b** (Figure 5.6).

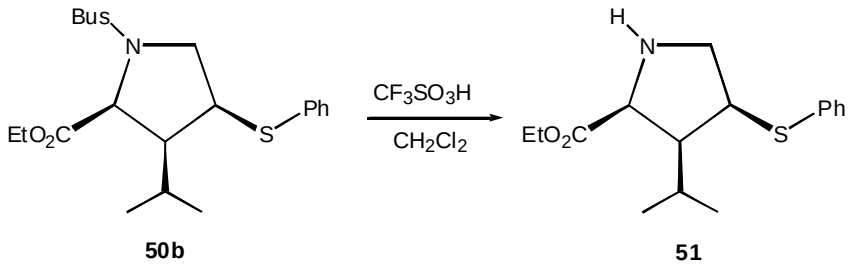


43a,b **50a**; 87%, **50b**; 90%

Scheme 5.6: Synthesis of N-Bus 3-substituted-4-thiophenyl proline derivatives

5.2.2.3 Deprotection of the Prolines

The final step of the synthesis of the 4-thiophenyl substituted proline derivative is the deprotection of the N-atom of **50**. Because of the deliberate selection of the Bus group, this transformation should be possible by applying a water-free acid.[110] Indeed, treatment of the proline derivative **50b** with CF_3SO_3H in CH_2Cl_2 (0.05-0.1M) in the presence of an excess of anisole (8-10 equiv), afforded the proline ester **51** in 84% yield (Scheme 5.4). The excess anisole was used in order to trap the *in situ* generated *tert*-butyl carbo cation. Care had to be taken in the case of the isolation of **51** from the acidic reaction mixture. Workup was carried out by the addition of water and extraction with CH_2Cl_2 following the adjustment of the pH of the mixture to a value of 7.1 by the addition of 0.1 M NaOH.



50b **51**

Scheme 5.4: Deprotection of the *N*-Bus proline **50b**

5.3 NoE measurements of proline 51

NOE measurements of **51** were carried out in order to prove its constitution. NOE's between H_4–H_6, H_4–H_7, H_4–H_{5a} and H_4–H_8 were observed. No NOE's were observed between H_4 and H_{5b}, H_4–H_3, H_2–H_3, H_4–H_3, and H_2–H_3.

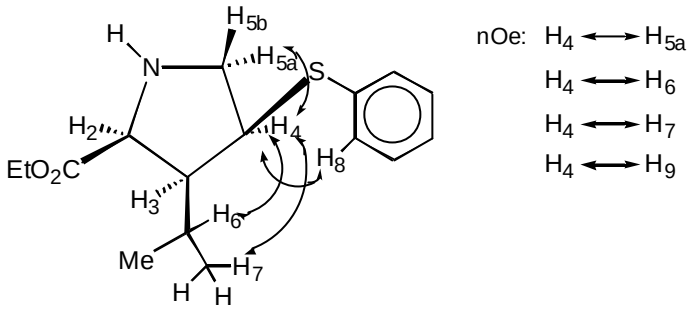


Figure 5.6. NOE measurements of proline **51**

5.3 Conclusions

In summary, we have achieved an efficient asymmetric synthesis of highly substituted prolines. 3-Alkyl(aryl)-4-thiophenyl substituted proline derivatives were synthesized *via* the δ-chloro-γ-thiophenyl β-alkyl(aryl)- substituted α-amino acid derivatives obtained from the thia-Michael addition of the δ-sulfonimidoyl substituted γ,δ-unsaturated β-substituted α-amino acid derivatives.

CHAPTER 6

Experimental Part

6 Experimental Part

6.1 General Information

All reactions with water and oxygen sensitive compounds were carried out in dry solvents under argon with syringe and schlenk techniques in oven-dried glassware. THF and toluene were distilled under nitrogen from sodium-lead/benzophenone. CH_2Cl_2 was distilled from CaH_2. Commercially available DMF (water free, 99.8%) was used. Commercial Me_3OBF_4 was washed with dry CH_2Cl_2 and dry Et_2O before use. Vinyl sulfoximines **12a-d**,[11] allyl sulfoximines **1a-d**,[11] cyclic vinyl sulfoximines **42a-d**,[84] sulfoximine-substituted homoallyl amines **4a-d**,[15] sulfoximine-substituted homoallyl alcohol **40**[83] and α-iminoester **3**[54] were prepared according to the literature. All other chemicals were obtained from commercial sources and used without further purification. Thin layer chromatography (TLC) was performed on silica gel 60 (Merck F_{254}) plates. Column chromatography and flash chromatography were performed on silica gel 60 (Merck 0.040–0.063 mm). HPLC: Varian SD-1 pump, prostar 320, Knauer RI-detector, Kromasil Si 100 (diameter: 30 mm or 40 mm, length: 250 mm). Solutions of crude reaction mixtures were filtered through Celite (Fluka 535).

6.2 Analytic

^{1}H NMR Spectroscopy:

Varian Mercury 300 (300 MHz)

Varian Inova 400 (400 MHz)

Varian Unity 500 (500 MHz)

Internal Standard: Tetramethylsilan

The following abbreviations are used to designate the multiplicity of the peaks in the ^{1}H NMR spectra:

s = Singlet

d = Doublet

t = Triplet

q = Quartet

quin = Quintet

sext = Sextet

sept = Septet

m = Multiplet

br = broad

^{13}C NMR Spectroscopy:

Varian Mercury 300 (300 MHz)

Varian Inova 400 (400 MHz)

Varian Unity 500 (500 MHz)

Internal Standard: Tetramethylsilan

Peaks in the ^{13}C NMR spectra are designated with the abbreviations, 'u' for carbons with zero or two attached protons and 'd' for carbons with one or three attached protons, as determined from APT pulse sequence.

Infrared Spectroscopy:

IR spectra were taken with a Perkin-Elmer PE 1759 FT, Perkin Elmer FTIR 1760 S, and only peaks of ? >800 cm^{-1} are listed.

w = weak (Absorption 20–40%)

m = medium (Absorption 40–70%)

s = strong (Absorption > 70%)

Mass Spectroscopy:

Varian Mat 212 S
Finnigan MAT 312
Varian MAT 95

Electron impact (EI) 70 eV; Chemical ionization (CI) 100 eV; Direct chemical ionization (DCI) 70 eV; High resolution mass spectroscopy (HRMS) 70 eV.

Only peaks of *m/z* >70 and an intensity >20%, expect decisive ones, are listed.

Elemental Analysis:

Heraeus CHN-O-RAPID
Elemental Vario EI

Optical Rotation:

Optical rotations were measured on a Perkin Elmer Model 241 polarimeter at ˜23° C

6.3 General Procedures

6.3.1 General Procedure for the Synthesis of Alkenyl Aziridine Carboxylates 6 from the Sulfoximine Substituted a -Amino Acids 4 (*GP1*):

To a solution of the vinyl sulfoximine **4** (1.0 mmol) in dry CH_2Cl_2 (5 mL) was added Me_3OBF_4 (1.2 mmol) at room temperature. Me_3OBF_4 is not soluble in CH_2Cl_2 but the vinyl sulfoxonium salt is freely soluble in CH_2Cl_2. After stirring the mixture for 2-3 h, DBU (1.2 mmol) was added. Aziridine formation was completed in <5 min. Then the mixture was quenched with distilled water and extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), and the solvent was removed in vacuo. Purification

of the residue by chromatography (EtOAc/hexane, 15:85) gave a mixture of *cis*-**6** and *trans*-**6** as a colour less liquid and sulfinamide **7**.

6.3.2 General Procedure for the Synthesis of Alkenyl Aziridine Carboxylates 6 from the Vinyl Sulfoximines 12 and a-imino ester 3 (*GP2*):

To a suspension of Me_3OBF_4 (1.2 mmol) in dry CH_2Cl_2 (5 mL) was added a solution of the vinyl sulfoximine **12** (1.0 mmol) in dry CH_2Cl_2 (10 mL) under stirring at 0 °C. After 15 min the mixture was allowed to stir for 1.5 h at room temperature. Then the iminoester **3** (1.2 mmol) and DBU (1.3 mmol) were successively added. The aziridine formation was completed in 20-30 min. Then the mixture was quenched with distilled water and extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), and the solvent was removed in vacuo. Purification of the residue by chromatography (EtOAc/hexane, 10:90) gave a mixture of *cis*-**6** and *trans*-**6** as a colour less liquid along with sulfinamide **7**.

6.3.3 General Procedure for the Synthesis of Cycloalkenyl Aziridine Carboxylates 45 from the Vinyl Sulfoximines 42 (*GP3*):

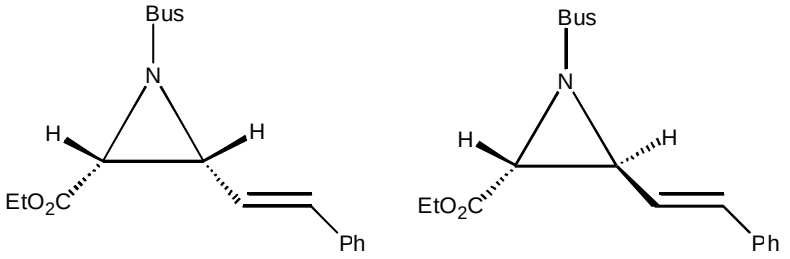
To a suspension of Me_3OBF_4 (1.2 mmol) in dry CH_2Cl_2 (5 mL) was added a solution of vinyl sulfoximine **42** (1.0 mmol) in dry CH_2Cl_2 (10 mL) under stirring at 0 °C. After 30 min Me_3OBF_4 (0.5 mmol) was added and the mixture was allowed to stir for 30 min at room temperature. Then the iminoester **3** (1.4 mmol) and DBU (1.8 mmol) were successively added. The aziridine formation was completed in 20-30 min. Then the mixture was quenched with distilled water and extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. Purification of the residue by chromatography (EtOAc/hexane, 10:90) gave a mixture of *cis*-**45** and *trans*-**45** as a colour less liquid along with sulfinamide **7**.

6.3.4 General Procedure for Thiophenol Addition to Vinyl Sulfoximines (*GP 4*):

To the vinyl sulfoximine (1 mmol) in a conical bottom flask at 0 °C was added neat thiophenol (6 mmol) under an argon atmosphere. After the mixture was allowed to warm to room temperature, it was stirred until TLC indicated the consumption of the sulfoximine (1-2 h). The mixture was directly subjected to flash column purification (EtOAc:*n*-hexane, 1:4), which gave the excess thiophenol and the sulfides.

6.4 Synthesis of aziridines

6.4.1 (2*R*,3R)- and (2*R*,3*S*)-Ethyl 3-styryl-1-(2-methylpropane-2-sulfonyl)aziridine-2-carboxylate (*cis*-6a and *trans*-6a):



Following *GP1*, the aziridines *cis*-**6a** and *trans*-**6a** were synthesized from the vinyl sulfoximine **4a** (500 mg, 1.02 mmol) by activating with Me_3OBF_4 (180 mg, 1.22 mmol) followed by the treatment with DBU (186 mg, 1.22 mmol). A mixture of *cis*-**6a** and *trans*-**6a** (320 mg, 94%) was obtained in a ratio of 93:7. Preparative HPLC afforded *cis*-**6a** (279 mg, 82%) and *trans*-**6a** (17 mg, 5%) as colorless syrupy liquids with ee-values of ≥98% (Chiralpack-AD, *n*-heptane/EtOH, 97:3, R_f = 18.0) and 30% (Chiralpack-AD, *n*-heptane/EtOH, 97:3, R_f = 15.3, ent–R_f = 17.9) respectively. The sulfinamide **7** (160 mg, 93%) was collected as a biproduct.

***cis*-6a:**

^{1}H NMR (300 MHz, C_6D_6): d = 0.78 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.32 (s, 9 H, $C(CH_3)_3$), 3.54 (dd, *J* = 15.58, *J* = 7.17 Hz, 1 H, CH=CHC*H*), 3.68 (d, *J* = 7.17 Hz, 1 H,

COC*H*), 3.79 (dq, *J* = 7.17, *J* = 2.23 Hz, 2 H, C*H*$_2$CH$_3$), 6.32 (dd, *J* = 16.2, *J* = 8.29 Hz, 1 H, CHC*H*=CH), 6.47 (d, *J* = 16.08 Hz, 1 H, CHCH=C*H*), 6.98–7.16 (m, 5 H, Ph).

^{13}C NMR (75 MHz, C_6D_6): d 13.5 (d), 23.5 (d), 41.5 (d), 45.2 (d), 59.2 (u), 61.2 (u), 120.3 (d), 126.6 (d), 128.0 (d), 128.4 (d), 135.7 (u), 137.4 (d), 165.5 (u).

IR ($CHCl_3$) ? 3276 (s), 2936 (s), 1740 (s), 1623 (w), 1451 (m), 1368 (w), 1318 (s), 1235 (w), 1128 (s), 1022 (m), 972 (m) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %) 338 (M^+ + H, 3), 274 (5), 264 (6), 246 (8), 218 (100), 172 (4), 144 (4), 115 (4).

Optical rotation: $[a]_D$ −14.1 (*c* 1.75, $CHCl_3$).

Elemental Analysis:

$C_{17}H_{23}NO_4S$	C	H	N
calcd	60.51	6.87	4.15
found	60.19	6.57	3.90

***trans*-6a:**

^{1}H NMR (300 MHz, $CDCl_3$): d = 1.32 (t, *J* = 7.17 Hz, 3 H, CH$_2$C*H*$_3$), 1.49 (s, 9 H, C(CH$_3$)$_3$), 3.54 (d, *J* = 3.71 Hz, 1 H, COC*H*), 3.68 (dd, *J* = 9.64, *J* = 3.71 Hz, 1 H, CH=CHC*H*), 4.27 (q, *J* = 7.18 Hz, 2 H, C*H*$_2$CH$_3$), 6.27 (dd, *J* = 15.83, *J* = 9.65 Hz, 1 H, CHC*H*=CH), 6.89 (d, *J* = 15.83 Hz, 1 H, CHCH=C*H*), 7.27–7.42 (m, 5 H, Ph).

^{13}C NMR (75 MHz, $CDCl_3$): d 14.1 (d), 23.9 (d), 45.0 (d), 48.8 (d), 61.0 (u). 62.0 (u), 121.1 (d), 126.7 (d), 128.5 (d), 128.6 (d), 135.6 (u), 137.9 (d), 166.8 (u).

IR (KBr) ? 3483 (w), 2989(s), 1750 (s), 1453 (m), 1403 (m), 1308 (s), 1199 (s), 1128 (s), 1031 (s), 986 (m), 938 (s) cm^{-1}.

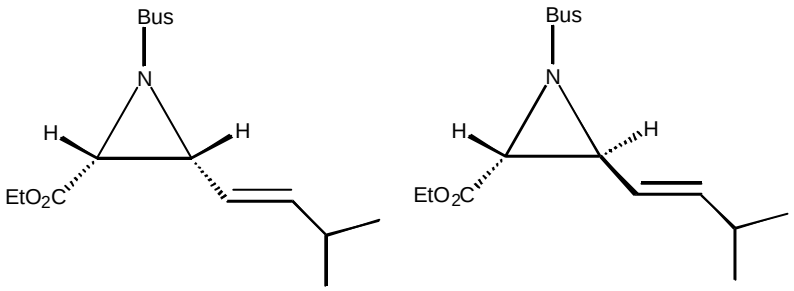
MS (CI, CH_4) *m/z* (relative intensity, %) 337 (58) (M^+), 282 (6), 217 (100), 200 (9), 188 (75), 170 (17), 144 (70), 133 (32), 115 (40), 102 (26), 69 (8), 57 (100).

Optical rotation: $[a]_D$ +6.4 (*c* 1.5, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{17}H_{23}NO_4S$	calcd	found
	337.134832	337.134781

6.4.2 (2*R*,3R)- and (2*R*,3*S*)-Ethyl 3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine-2-carboxylate (*cis*-6b and *trans*-6b):



Following *GP1*, the aziridines **6b** and **6b** were synthesized from the vinyl sulfoximine **4b** (450 mg, 0.98 mmol) by activating with Me_3OBF_4 (174 mg, 1.17 mmol) followed by the treatment with DBU (179 mg, 1.17 mmol). A mixture of *cis*-**6b** and *trans*-**6b** (270 mg, 91 %) was obtained in a ratio of 91:9 along with sulfinamide **7** (154 mg, 93 %). Preparative HPLC afforded *cis*-**6b** (227 mg, 76%) and *trans*-**6b** (16 mg, 6%) as colorless syrupy liquids with ee-values of 92% (Chiralcel OD-H, *n*-heptane/isopropanol, 98:2, R_f = 15.8, ent–R_f = 19.3) and 26% (Chiralcel OD-H, *n*-heptane/isopropanol, 98:2, R_f = 16.0, ent–R_f = 17.3) respectively.

Following *GP2*, the vinyl sulfoximine **12b** (400 mg, 1.68 mmol) was activated with Me_3OBF_4 (298 mg, 2.01 mmol) followed by successive treatment with the imino ester **3** (447 mg, 2.02 mmol) and DBU (334mg, 2.19 mmol), which afforded the aziridines *cis*-**6b** and *trans*-**6b** (356 mg, 70%) in a ratio of 64:36 and with ee values of 76% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 11.8, ent–R_f = 12.5) and 49% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 34.3, ent–R_f = 37.3), respectively, along with the biproduct **7** (262 mg, 92%). *cis*-**6b** (197 mg, 39%) and *trans*-**6b** (106 mg, 21%) were separated by preparative HPLC.

***cis*-6b:**

^{1}H NMR (400 MHz, $CDCl_3$): d = 0.98 (d, *J* = 6.59 Hz, 3 H, CH(C*H*3)(CH_3)), 1.0 (d, *J* = 6.59 Hz, 3 H, CH(CH3)(C*H*$_3$)), 1.29 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.49 (s, 9 H, C(CH_3)$_3$), 2.33 (m, 1 H, C*H*(CH_3)$_2$), 3.41 (dd, *J* = 15.65, *J* = 7.41 Hz, 1 H, COCHC*H*), 3.47 (d, *J* = 7.14 Hz, 1 H, COC*H*), 424 (q, *J* = 7.14 Hz, 2 H, C*H*$_2$CH$_3$), 5.31 (ddd, *J* = 15.66, *J* = 7.71, *J* = 1.37 Hz, 1 H, CHNC*H*=CH), 5.99 (dd, *J* = 15.66, *J* = 6.59 Hz, 1 H, CHNCH=C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.3 (d), 21.9 (d), 22.0 (d), 24.0 (d), 31.2 (d), 41.4 (d), 45.1 (d), 59.8 (u), 61.7 (u), 118.0 (d), 147.0 (d), 165.6 (u).

IR ($CHCl_3$): ? 2964 (s), 1750 (s), 1465 (m), 1377 (m), 1316 (s), 1197 (s), 1130 (s), 1036 (s), 975 (m), 937 (m), 873 (m), 835 (m) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %): 304 (M^+ + H, 2), 276 (3), 240 (5), 230 (9), 224 (4), 212 (9), 184 (100), 167 (58), 154 (3), 138 (5), 121 (4), 108 (7), 93 (4).

Optical rotation: $[a]_D$ –10.8 (*c* 2.3, $CHCl_3$).

Elemental Analysis:

$C_{14}H_{25}NO_4S$	C	H	N
calcd	55.42	8.30	4.62
found	55.19	8.26	4.72

***trans*-6b:**

^{1}H NMR (400 MHz, $CDCl_3$): d = 1.0 (d, *J* = 6.6 Hz, 3 H, CH(C*H*3)(CH_3)), 1.02 (d, *J* = 6.6 Hz, 3 H, CH(CH3)(C*H*$_3$)), 1.30 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.46 (s, 9 H, $C(CH_3)_3$), 2.38 (m, 1 H, C*H*(CH_3)$_2$), 3.41 (d, *J* = 3.84 Hz, 1 H, COC*H*), 3.48 (dd, *J* = 9.34, *J* = 3.85 Hz, 1 H, COCHC*H*), 4.24 (q, *J* = 7.14 Hz, 2 H, CH_2CH_3), 5.51 (dd, *J* = 15.38, *J* = 9.56 Hz, 1 H, CHNC*H*=CH), 6.02 (dd, *J* = 15.38, *J* = 6.86 Hz, 1 H, CHNCH=C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.2 (d), 21.8 (d), 22.0 (d), 24.0 (d), 31.2 (d), 44.9 (d), 48.8 (d), 60.9 (u), 61.9 (u), 119.2 (d), 147.2 (d), 166.9 (u).

IR ($CHCl_3$): ? 2964 (s), 1745 (s), 1514 (w), 1466 (m), 1369 (w), 1317 (s), 1232 (s), 1134 (s), 1028 (m), 970 (m), 914 (s), 852 (m), 822 (m) cm^{-1}.

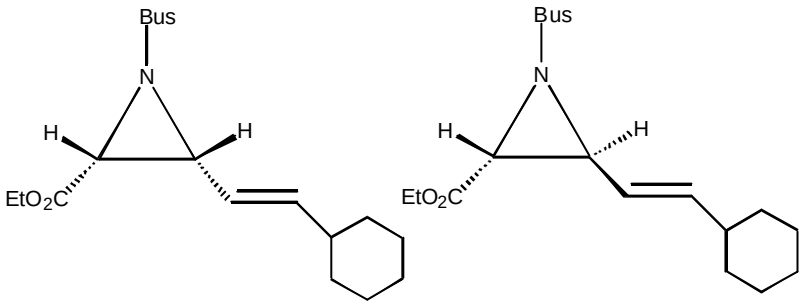
MS (CI, CH_4) *m/z* (relative intensity, %): 304 (M^+ + H, 28), 262 (4), 240 (5), 230 (11), 216 (7), 184 (100), 167 (90), 113 (32).

Optical rotation: $[a]_D$ +5.9 (*c* 3.2, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{14}H_{25}NO_4S–C_4H_9O_2S$	calcd.	found.
	182.118179	182.118104

6.4.3 (2*R*,3R)- and (2*R*,3*S*)-Ethyl 3-((*E*)-2-cyclohexylvinyl)-1-(2-methylpropane-2-sulfonyl)aziridine-2-carboxylate (*cis*-6c and *trans*-6c):



Following *GP1*, the aziridines *cis*-**6c** and *trans*-**6c** were synthesized from the vinyl sulfoximine **4c** (520 mg, 1.04 mmol) by activating with Me_3OBF_4 (185 mg, 1.25 mmol) followed by the treatment of DBU (190 mg, 1.25 mmol). A mixture of *cis*-**6c** and *trans*-**6c** (332 mg, 93 %) was obtained in a ratio of 90:10 along with the byproduct N-methyl-S-phenyl sulfinamide **7** (165 mg, 94%). Preparative HPLC afforded *cis*-**6c** (266 mg, 75%) and *trans*-**6c** (29 mg, 9 %) as colorless syrupy liquids with ee-values of 71% (Chiralpack-IA, *n*-heptane/isopropanol, 98:2, R_f = 7.6, ent–R_f = 9.6) and 48% (Chiralpack-IA, *n*-heptane/isopropanol, 98:2, R_f = 7.5, ent–R_f = 8.8) respectively.

Following *GP2*, the vinyl sulfoximine **12c** (380 mg, 1.37 mmol) was activated with Me_3OBF_4 (243 mg, 1.64 mmol) followed by successive treatment with the imino ester **3** (363 mg, 1.64 mmol) and DBU (271 mg, 1.78 mmol), which afforded the aziridines *cis*-**6c** and *trans*-**6c** (320 mg, 68%) in a ratio of 70:30 and with ee values of 47% (Chiralpack-IA, *n*-heptane/isopropanol, 98:2, R_f = 11.2, ent–R_f = 14.0) and 45%

(Chiralpack-IA, *n*-heptane/*i*sopropanol, 98:2, R_f = 14.6, ent–R_f = 15.6), respectively, along with the biproduct **7** (217 mg, 94%). *cis*-**6c** (205 mg, 43%) and *trans*-**6c** (75 mg, 16%) were by preparative HPLC.

***cis*-6c:**

^{1}H NMR (300 MHz, $CDCl_3$) : d = 1.04–1.28 (m, 5H, $CH_2CH_2CH_2$), 1.29 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.5 (s, 9 H, $C(CH_3)_3$), 1.7 (m, 5 H, $CH_2CH_2CH_2$), 2.00 (m, 1 H, CH_2CHCH_2), 3.40 (dd, *J* = 15.58, *J* = 7.42 Hz, 1 H, COCHCH), 3.46 (d, *J* = 7.66 Hz, 1 H, COCH), 4.22 (q, *J* = 7.17 Hz, 2 H, CH_2CH_3), 5.32 (ddd, *J* = 15.58 Hz, *J* = 6.68 Hz, *J* = 1.24 Hz, 1 H, CHNCH=CH), 5.95 (dd, *J* = 15.58 Hz, *J* = 6.68 Hz, 1 H, CHNCH=CH).

^{13}C NMR (75 MHz, $CDCl_3$): d 14.1 (d), 23.9 (d), 25.8 (u), 26.0 (u), 32.9 (u), 40.5 (d), 41.2 (d), 45.3 (d), 59.7 (u), 61.6 (u), 118.4 (d), 145.9 (d), 165.7 (u).

IR ($CHCl_3$): ? 2927 (s), 1749 (s), 1662 (w), 1450 (m), 1378 (m), 1315 (s), 1197 (s), 1130 (s), 1036 (s), 972 (m), 939 (m), 870 (w), 836 (m) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %): 344 (M^+ + H, 1), 316 (4), 280 (5), 270 (7), 252 (10), 224 (100), 207 (50), 178 (4), 161 (6), 148 (7), 133 (17), 121 (7), 102 (3).

Optical rotation: $[a]_D$ –7.8 (*c* 1.25, $CHCl_3$).

Elemental Analysis:

$C_{17}H_{29}NO_4S$	C	H	N
calcd	59.44	8.51	4.08
found	59.19	8.42	3.93

***trans*-6c:**

^{1}H NMR (300 MHz, $CDCl_3$): d = 1.06–1.28 (m, 5 H, $CH_2CH_2CH_2$), 1.3 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.46 (s, 9 H, $C(CH_3)_3$), 1.63-1.76 (m, 5 H, $CH_2CH_2CH_2$), 2.05 (m, 1 H, CH_2CHCH_2), 3.42 (d, *J* = 3.71 Hz, 1 H, COC*H*), 3.48 (dd, *J* = 9.40, *J* = 3.71 Hz, 1 H, COCHC*H*), 4.24 (q, *J* = 7.17 Hz, 2 H, CH_2CH_3), 5.50 (ddd, *J* = 15.58, *J* = 6.68, *J* = 1.24 Hz, 1 H, CHNC*H*=CH), 6.0 (dd, *J* = 15.58, 6.68 Hz, 1 H, CHNCH=C*H*).

^{13}C NMR (75 MHz, $CDCl_3$): d 14.1 (d), 23.9 (d), 25.8 (u), 26.0 (u), 32.3 (u), 40.5 (d), 44.9 (d), 48.8 (d), 60.8 (u), 61.9 (u), 119.6 (d), 146.1 (d), 167.0 (u).

IR ($CHCl_3$): ? 2927 (s), 1744 (s), 1450 (m), 1370 (w), 1316 (s), 1227 (s), 1194 (s), 1132 (s), 1028 (m), 968 (m), 915 (s), 847 (w), 816 (s) cm^{-1}.

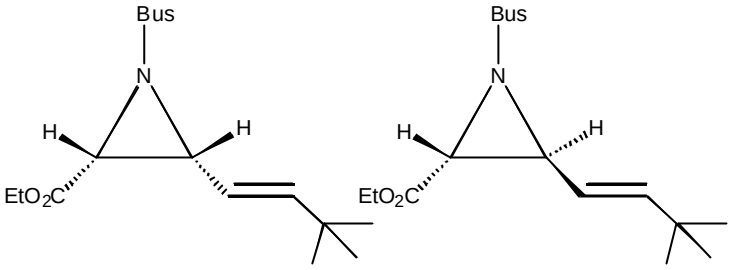
MS (CI, CH_4) *m/z* (relative intensity, %): 384 (M + $C_3H_5^+$, 1), 344 (M^+ + H, 4), 316 (3), 280 (5), 270 (7), 252 (10), 222 (100), 207 (48), 194 (3), 178 (4), 161 (5), 148 (9), 133 (17), 121 (6), 102 (3).

Optical rotation: $[a]_D$ +5.7 (*c* 1.5, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{17}H_{29}NO_4S - C_4H_9O_2S$	calcd	found
	347.137816	347.137760

6.4.4 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl 3-((*E*)-3,3-dimethylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine-2-carboxylate (*cis*-6d and *trans*-6d):



Following *GP1*, the aziridines *cis*-**6d** and *trans*-**6d** were synthesized from the vinyl sulfoximine **4d** (550 mg, 1.16 mmol) by activating with Me_3OBF_4 (207 mg, 1.39 mmol) followed by the treatment with DBU (213 mg, 1.39 mmol). The inseparable mixture of *cis*-**6d** and *trans*-**6d** (347 mg, 94 %) was obtained in a ratio of 91:9 and with ee−values of 50% (Chiralcel OD-H, *n*-heptane/isopropanol, 98:2, R_f = 13.4, ent–R_f = 18.8) and 5% (Chiralcel OD-H, *n*-heptane/isopropanol, 98:2, R_f = 19.8, ent–R_f = 24.1) respectively. The biproduct **7** (184 mg, 93 %) was collected.

***cis*-8d:**

^{1}H NMR (400 MHz, $CDCl_3$): d 1.01 (s, 9 H, CHC(C*H*$_3$)$_3$), 1.3 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.46 (s, 9 H, $SO_2C(CH_3)_3$), 3.41 (dd, *J* = 15.38, *J* = 7.69 Hz, 1 H, COCHC*H*), 3.47 (d, *J* = 714, COCH), 4.23 (q, *J* = 7.14 Hz, 2 H, C*H*$_2$CH$_3$), 5.26 (dd, *J* = 15.93, *J* = 8.24 Hz, 1 H, CHNC*H*=CH), 6.04 (dd, *J* = 15.93, *J* = 10.98 Hz, 1 H, CHNCH=C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.2 (d), 23.9 (d), 29.1 (d), 33.5 (d), 41.3 (d), 45.2 (d), 59.7 (u), 61.5 (u), 115.8 (d), 150.7 (d), 165.5 (u).

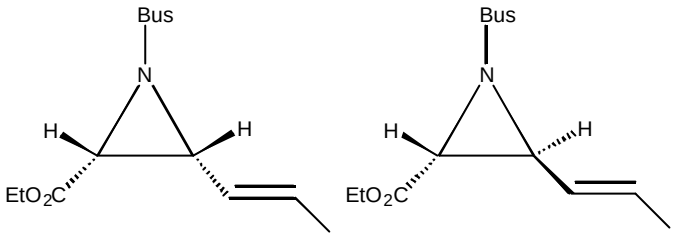
***trans*-5d:**

^{1}H NMR (400 MHz, $CDCl_3$): d 1.04 (s, 9 H, CHC(C*H*$_3$)$_3$), 1.3 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.50 (s, 9 H, $SC(CH_3)_3$), 3.41 (d, *J* = 4.12 Hz, 1 H, COCH), 3.48 (dd, *J* = 9.34Hz, *J* = 3.84 Hz, 1 H, COCHC*H*), 4.24 (q, *J* = 7.14 Hz, 2 H, C*H*$_2$CH$_3$), 5.46 (dd, *J* =

15.66, *J* = 9.34 Hz, 1 H, CHNC*H*=CH), 6.04 (dd, *J* = 15.93, *J* = 10.98 Hz, 1 H, CHNCH=C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.0 (d), 23.9 (d), 29.0 (d), 30.8 (d), 44.8 (d), 48.8 (d), 60.7 (u), 61.8 (u), 117.1 (d), 150.8 (d), 166.8 (u).

6.4.5 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl 3-((*E*)-prop-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine-2-carboxylate (*cis*-6e and *trans*-6e):



Following *GP2*, the vinyl sulfoximine **12e** (520 mg, 2.49 mmol) was activated with Me_3OBF_4 (442 mg, 2.98 mmol) followed by the successive treatment with the imino ester **3** (660 mg, 2.98 mmol) and DBU (490 mg, 3.23 mmol), which afforded aziridines *cis*-**6e** and *trans*-**6e** (445 mg, 65%), with *cis*-**6e** having an ee-value of 65% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 11.3, ent–R_f = 11.8). The ee value of the *trans* isomer could not be determined. The biproduct **7** (378 mg, 90%) was collected. Pure *cis*-**6e** (106 mg, 24%) could be separated from the mixture by preparative HPLC but the pure *trans*-**6e** could not be separated from the mixture.

***cis*-5e:**

^{1}H NMR (400 MHz, $CDCl_3$): d = 1.29 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.50 (s, 9 H, $C(CH_3)_3$), 1.82 (dd, *J* = 7.14, *J* = 1.92 Hz, 3 H, CH=CHCH_3), 3.54 (d, *J* = 7.42 Hz, 1 H, COCH), 3.69 (m, 1 H, COCHC*H*) 4.23 (dq, *J* = 7.15 Hz, *J* = 1.64 Hz, 2 H, CH_2CH$_3$), 5.32 (m, 1 H, CH_3C*H*=CH), 5.91 (m, 1 H, CH_3CH=C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): d 13.4 (d), 14.1 (d), 23.8 (d), 40.5 (d), 41.0 (d), 59.8 (u), 61.6 (u), 121.0 (u), 133.4 (u), 165.5 (u).

IR ($CHCl_3$): ? 2984 (s), 1751 (s), 1478 (m), 1382 (m), 1316 (s), 1195 (s), 1130 (s), 1060 (w), 1028 (m), 942 (s), 869 (m), 835 (m) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %): 276 (M^+ + H, 1), 248 (1), 220 (7), 202 (9), 184 (5), 156 (100), 129 (1), 110 (5), 80 (6).

Optical rotation: $[a]_D$ –23.1 (*c* 1.25, $CHCl_3$).

HRMS (EI, 70 eV):

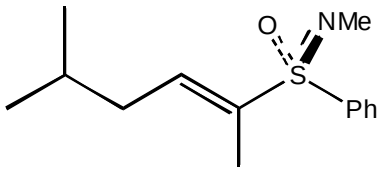
$C_{12}H_{21}NO_4S$–$C_4H_9O_2S$	calcd	found
	154.086771	154.086804

***trans*-5e**:

^{1}H NMR (400 MHz, $CDCl_3$): d = 1.31 (t, *J* = 7.15 Hz, 3 H, CH_2CH_3), 1.46 (s, 9 H, $C(CH_3)_3$), 1.84 (dd, *J* = 7.14, *J* = 1.65 Hz, 3 H, $CH=CHCH_3$), 3.40 (d, *J* = 3.84 Hz, 1 H, COCH), 3.76 (dd, *J* = 9.89, *J* = 3.84 Hz, 1 H, COCHCH), 4.26 (q, *J* = 7.14 Hz, 2 H, CH_2CH_3), 5.54 (m, 1 H, $CH_3CH=CH$), 5.98 (m, 1 H, $CH_3CH=CH$).

^{13}C NMR (100 MHz, $CDCl_3$): d = 13.3 (d), 14.0 (d), 23.9 (d), 43.4 (d), 45.0 (d), 60.9 (u), 61.9 (u), 121.6 (d), 134.0 (d), 166.3 (u).

6.4.6 (+)-(*E,S*)-*N*-Methyl-*S*-(4-methyl-1-methyl-1-pentenyl)-*S*-phenyl sulfoximine (39)



To a solution of sulfoximine **12b** (830 mg, 3.50 mmol) in THF (10 mL) was added at −78 °C BuLi (4.2 mmol, 2.7 ml of 1.6 M in hexane) and the reaction mixture was stirred at 0 °C for 1 h. Then a solution of MeI (2.2 mL, 35 mmol) in THF (3 mL) was added at −78 °C and the resulting mixture was stirred first at −78 °C for 30 min and then warmed upto room temperature over a period of 2 h. Subsequently saturated aqueous NH_4Cl (10 mL) was added and the resulting mixture was extracted with EtOAc. The combined organic phases were dried (MgSO4) and concentrated in vacuo. Purification by column chromatography (EtOAc/cyclohexane, 1:3) gave sulfoximine **39** in 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): d = 0.89 (d, *J* = 6.6 Hz, 3 H, CH(C*H*$_3$)(CH$_3$)), 0.91 (d, *J* = 6.59 Hz, 3 H, CH(CH$_3$)(C*H*$_3$)), 1.77 (m, 1 H, C*H*(CH$_3$)$_2$), 1.81 (s, 3 H, CH=CC*H*$_3$), 2.05 (m, 2 H, CH$_2$), 2.77 (s, 3 H, NCH$_3$), 6.86 (tm, *J* = 7.69 Hz, 1 H, C=CH), 7.51 (m, 3 H, Ph), 7.87 (m, 2 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): d = 12.4 (d), 22.5 (d), 28.3 (d), 29.6 (d), 37.8 (u), 128.8 (d), 128.9 (d), 132.3 (d), 136.1 (u), 138.4 (u), 140.3 (d).

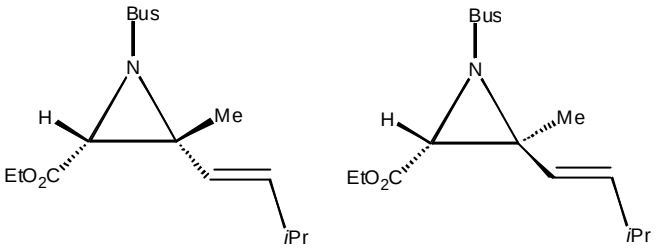
IR (neat): ? 2956 (s), 2872 (s), 1447 (s), 1381 (m), 1245 (s), 1141 (s), 1109 (s), 1076 (s), 925 (m), 859 (s) cm^{-1}.

MS (EI, 70 eV): *m/z* (%): 251 (M$^+$, 10), 208 (4), 155 (28), 139 (6), 126 (55), 107 (100), 95 (10), 78 (35), 55 (41).

HRMS (EI, 70 eV):

$C_{14}H_{21}NOS$	calcd	found
	251.134465	251.134387

6.4.7 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl-3-methyl-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine-2-carboxylate (*cis*-41 and *trans*-41):



Following *GP2*, the vinyl sulfoximine **39** (547 mg, 2.18 mmol) was methylated with Me_3OBF_4 (419 mg, 2.83 mmol) followed by the successive treatment with the imino ester **3** (626 mg, 2.83 mmol) and DBU (464 mg, 3.05 mmol), which afforded aziridines *cis*-**41** and *trans*-**41** (558 mg, 81%) in a ratio of 60:40, with *cis*-**41** having an ee-value of 28% (Chiralpack-IA, *n*-heptane/isopropanol, 98:2, R_f = 25.1, ent–R_f = 37.1). The ee value of the *trans* isomer could not be determined. The biproduct **7** (338 mg, 92%) was collected. Pure *cis*-**41** (317 mg, 43%) was isolated by preparative HPLC but the pure *trans*-**41** could not be separated from the mixture.

***cis*-41:**

^{1}H NMR (300 MHz, $CDCl_3$): d = 0.89 (d, *J* = 6.68 Hz, 3 H, CH(C*H*$_3$)(CH$_3$)), 0.90 (d, *J* = 6.68 Hz, 3 H, CH(CH$_3$)(C*H*$_3$)), 1.20 (t, *J* = 7.17 Hz, 3 H, CH$_2$C*H*$_3$), 1.44 (s, 9 H, C(CH$_3$)$_3$), 1.76 (s, 3 H, CCH$_3$), 2.21 (dsext, *J* = 1.48 Hz, *J* = 6.92 Hz, 1 H, C*H*(CH$_3$)$_2$), 3.44 (s, 1 H, COCH), 4.12 (m, 2H, C*H*$_2$CH$_3$), 5.21 (dd, *J* = 1.48 Hz, *J* = 15.83 Hz, 1 H, *i*PrCH=C*H*), 5.76 (dd, *J* = 6.93 Hz, *J* = 15.83 Hz, 1 H, *i*PrC*H*=CH).

^{13}C NMR (75 MHz, $CDCl_3$): d = 14.2 (d), 18.8 (d), 22.1 (d), 23.8 (d), 30.8 (d), 50.7 (d), 51. 9 (u), 61.2 (u), 61.4 (u), 123.6 (d), 142.7 (d), 165.9 (u).

IR ($CHCl_3$): ? 2966 (s), 1746 (s), 1464 (m), 1388 (m), 1313 (s), 1196 (s), 1130 (s), 1035 (m), 967 (m), 884 (m), 838 (m) cm^{-1}.

MS (CI, isobutane**)** *m/z* (relative intensity, %): 317 (40), 290 (7), 270 (7), 238 (10), 214 (87), 196 (77), 181 (100), 170 (6), 154 (7), 138 (8), 113 (7), 81 (8), 71 (12).

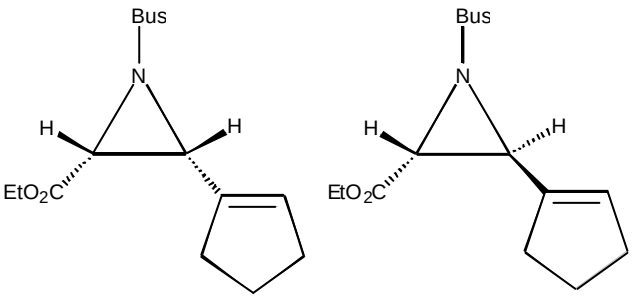
HRMS (EI, 70 eV):

$C_{15}H_{27}NO_4S–C_4H_9O_2S$	calcd	found
	196.133947	196.133754

***trans*-41:**

^{1}H NMR (300 MHz, $CDCl_3$): d = 0.97 (d, *J* = 6.87 Hz, 6 H, $CH(CH_3)_2$), 1.23 (t, *J* = 7.16 Hz, 3 H, CH_2CH_3), 1.50 (s, 9 H, $C(CH_3)_3$), 1.48 (s, 3 H, CCH_3), 2.30 (m, 1 H, $CH(CH_3)_2$), 3.52 (s, 1 H, COCH), 4.18 (q, *J* = 7.17 Hz, 2 H, CH_2CH_3), 5.57 (dd, *J* = 1.24 Hz, *J* = 15.58 Hz, *i*PrCH=C*H*), 5.83 (dd, *J* = 6.92 Hz, *J* = 15.83 Hz, 1 H, *i*PrC*H*=CH).

6.4.8 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl 3-(*E*)-cyclopentenyl-1-(2-methylpropane-2-sulfonyl) aziridine-2-carboxylate (*cis*-45a and *trans*-45a):



Treatment of **42a** (770 mg, 3.27 mmol) with Me_3OBF_4 (727 mg, 4.91 mmol) followed by successive treatment with the imino ester **3** (869 mg, 3.93 mmol) and DBU (698 mg, 4.58 mmol) according to *GP3* gave an inseparable mixture of *cis*-**45a** and *trans*-**45a** (690 mg, 70%) in a ratio of 3:2 and with ee-values of 79% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 9.9, ent–R_f = 11.0) and 90% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 12.0, ent R_f = 12.7) respectively, along with the sulfinamide **7** (443 mg, 80%) and unreacted starting vinylsulfoximine **42a** (69 mg, 9%) was recovered.

***cis*-45a:**

^{1}H NMR (400 MHz, $CDCl_3$): d 1.26 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.45 (s, 9 H, $C(CH_3)_3$), 1.89 (m, 2 H, $CH_2CH_2CH_2$), 2.34 (m, 4 H, $CH_2CH_2CH_2$), 3.51 (d, *J* = 7.41 Hz, 1 H, CH=CCH), 3.55 (d, *J* = 7.97 Hz, 1 H, COCH), 4.19 (m, 2 H, CH_3CH_2), 5.85 (m, 1 H, C=CH).

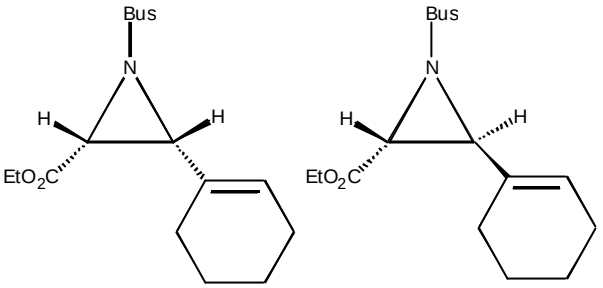
^{13}C NMR (100 MHz, $CDCl_3$): d 14.1 (d), 23.3 (u), 23.9 (d), 32.4 (u), 32.8 (u), 41.5 (d), 43.2 (d), 59.9 (u), 61.4 (u), 131.8 (d), 134.6 (u), 165.1 (u).

***trans*-45a:**

^{1}H NMR (400 MHz, $CDCl_3$): d 1.31 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.53 (s, 9 H, $C(CH_3)_3$), 1.89 (m, 2 H, $CH_2CH_2CH_2$), 2.34 (m, 4 H, $CH_2CH_2CH_2$), 3.43 (m, 1 H, COCH), 3.89 (m, 1 H, CH=CCH), 4.26 (m, 2 H, CH_3CH_2), 6.01 (m, 1 H, C=CH).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.0 (d), 23.2 (u), 23.8 (d), 31.8 (u), 32.7 (u), 43.4 (d), 46.0 (d), 60.8 (u), 62.0 (u), 134.6 (d), 136.0 (u), 166.2 (u).

6.4.9 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl 3-(*E*)-cyclohexenyl-1-(2-methylpropane-2-sulfonyl) aziridine-2-carboxylate (*cis*-45b and *trans*-45b):



Treatment of **42b** (456 mg, 1.83 mmol) with Me_3OBF_4 (460 mg, 3.11 mmol) followed by the successive treatment with the imino ester **3** (567 mg, 2.56 mmol) and DBU (500 mg, 3.29 mmol) according to *GP3* gave a mixture of *cis*-**45b** and *trans*-**45b** (419 mg, 73%) in a ratio of 3:2 and with ee-values of 76% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 43.5, ent–R_f = 46.5) and 56% (Chiralpack-IA, *n*-heptane/isopropanol, 97:3, R_f = 44.0, ent–R_f = 46.3) respectively, along with the sulfinamide **7** (250 mg, 73%) and unreacted starting vinyl sulfoximine **42b** (41 mg, 9%). Preparative HPLC afforded *cis*-**45b** (242 mg, 42%) and *trans*-**45b** (82 mg, 28%) as colorless syrupy liquids.

***cis*-45b:**

^{1}H NMR (300 MHz, $CDCl_3$): d 1.18 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.45-1.52 (m, 4 H, $CH_2CH_2CH_2$), 1.47 (s, 9 H, $C(CH_3)_3$), 1.87-1.96 (m, 4 H, $CH_2CH_2CH_2$), 3.31 (d, *J* = 7.42 Hz, 1 H, COCHCH), 3.41 (d, *J* = 7.66 Hz, 1 H, COCH), 4.11 (m, 2 H, CH_2CH_3), 5.81 (m, 1 H, C=CH).

^{13}C NMR (75 MHz, $CDCl_3$) : d 14.2 (d), 22.0 (u), 22.2 (u), 23.9 (d), 24.7 (u), 26.0 (u), 44.0 (d), 44.5 (d), 60.0 (u), 61.4 (u), 127.1 (d), 128.4 (u), 165.2 (u).

IR (neat): ? 2932 (s), 2354 (s), 1743 (s), 1461 (m), 1382 (w), 1313 (m), 1203 (s), 1129 (s), 1043 (s), 949 (s), 896 (m) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %): 316 (M^+ + H, 7), 288 (4), 252 (3), 242 (10), 196 (100), 179 (25), 150 (3), 122 (5).

Optical rotation: $[a]_D$ –21.5 (*c* 2.3 , $CHCl_3$).

HRMS (EI, 70 eV):

$C_{15}H_{25}NO_4S$–$C_3H_5O_2$	calcd	found
	242.121492	242.121477

***trans*-45b:**

^{1}H NMR (300 MHz, $CDCl_3$): d 1.24 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.37 (s, 9 H, $C(CH_3)_3$, 1.48-1.56 (m, 4 H, $CH_2CH_2CH_2$), 1.78-1.85 (m, 2 H, $CH_2CH_2CH_2$), 2.00 (m, 2 H, $CH_2CH_2CH_2$), 3.28 (d, *J* = 3.95 Hz, 1 H, COCH), 3.69 (d, *J* = 3.95 Hz, 1 H, COCHC*H*), 4.19 (m, 2 H, CH_2CH_3), 5.93 (s, 1 H, C=CH).

^{13}C NMR (75 MHz, $CDCl_3$) : d 13.9 (d), 22.0 (u), 22.1 (u), 23.9 (d), 25.3 (u), 42.6 (d), 50.9 (d), 60.8 (u), 62.1 (u), 129.9 (u), 130.7 (d), 166.7 (u).

IR ($CHCl_3$): ? 3284 (m), 2936 (s), 2361 (s), 1737 (s), 1456 (s), 1369 (s), 1213 (s), 1129 (s), 1023 (s), 934 (m), 856 (w) cm^{-1}.

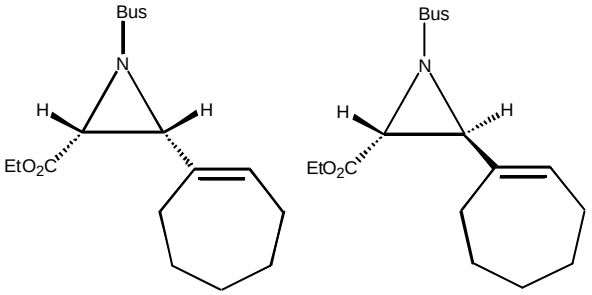
MS (CI, CH_4) *m/z* (relative intensity, %): 316 (M^+ + H, 6), 252 (3), 242 (13), 224 (4), 196 (100), 179 (36), 149 (4), 122 (7), 101 (3).

Optical rotation: $[a]_D$ –8.7 (*c* 1.3 , $CHCl_3$).

HRMS (EI, 70 eV):

$C_{15}H_{25}NO_4S–C_3H_5O_2$	calcd	found
	242.121492	242.121477

6.4.10 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl 3-(*E*)-cycloheptenyl-1-(2-methylpropane-2-sulfonyl) aziridine-2-carboxylate (*cis*-45c and *trans*-45c):



Treatment of **42c** (540mg, 2.05 mmol) with Me_3OBF_4 (516 mg, 3.49 mmol) followed by the successive treatment with the imino ester **3** (635 mg, 2.87 mmol) and DBU (561 mg, 3.69 mmol) according to *GP3* gave a mixture of *cis*-**45c** and *trans*-**45c** (479 mg, 71%) in a ratio of 3:2 and with ee-values of 78% (Chiralpack-IA, *n*-heptane/isopropanol, 98:2, R_f = 44.4, ent–R_f = 47.5) and 57% (Chiralpack-IA, *n*-heptane/isopropanol, 98:2, R_f = 43.7, ent–R_f =46.6) respectively, along with the sulfinamide **7** (260 mg, 75%) and unreacted starting vinyl sulfoximine **45c** (60 mg, 11%). Preparative HPLC afforded *cis*-**45c** (277 mg, 41%) and *trans*-**45c** (134 mg, 26%) as colorless syrupy liquids.

***cis*-45c:**

^{1}H NMR (400 MHz, $CDCl_3$) : d 1.27 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.39 (m, 2 H, $CH_2CH_2CH_2$), 1.47-1.53 (m, 2 H, $CH_2CH_2CH_2$), 1.53 (s, 9 H, $C(CH_3)_3$), 1.71 (m, 2 H, $CH_2CH_2CH_2$), 2.14 (m, 4 H, $CH_2CH_2CH_2$), 3.43 (d, *J* = 7.42 Hz, 1 H, COCHC*H*), 3.49 (d, *J* = 7.69 Hz, 1 H, COCH), 4.18 (q, *J* = 7.14 Hz, 2 H, CH_2CH_3), 6.04 (t, *J* = 6.31 Hz, 1 H, C=CH).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.1 (d), 23.9 (d), 26.3 (u), 26.6 (u), 28.17 (u), 30.1 (u), 32.0 (u), 44.0 (d), 45.9 (d), 59.9 (u), 61.4 (u), 132.2 (d), 133.9 (u), 165.0 (u).

IR ($CHCl_3$): ? 3553 (w), 2926 (s), 1743 (s), 1471 (m), 1368 (w), 1321 (s), 1200 (s), 1160 (s), 1097 (m), 1066 (w), 1028 (m), 946 (m), 919 (s), 811 (m) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %): 330 (M^+ + H, 2), 302 (3), 256 (9), 210 (100), 193 (20), 164 (2), 136 (2).
Optical rotation: $[a]_D$ −29.5 (*c* 1.4 , $CHCl_3$).

HRMS (EI, 70 eV):

$C_{16}H_{27}NO_4S–C_3H_5O_2$	calcd	found
	256.137246	256.137127

***trans*-45c:**

^{1}H NMR (400 MHz, $CDCl_3$) : d 1.32 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.44 (s, 9 H, $C(CH_3)_3$), 1.45-1.52 (m, 4 H, $CH_2CH_2CH_2$), 1.75 (m, 2 H, $CH_2CH_2CH_2$), 1.99 (m, 2 H, $CH_2CH_2CH_2$), 2.18 (m, 2 H, $CH_2CH_2CH_2$), 3.20 (d, *J* = 3.84 Hz, 1 H, COCH), 3.79 (d, *J* = 3.57 Hz, 1 H, COCHC*H*), 4.26 (m, 2 H, CH_2CH_3), 6.14 (t, *J* = 6.59 Hz, 1 H, C=CH).

^{13}C NMR (100 MHz, $CDCl_3$): d 13.9 (d), 23.9 (d), 26.3 (u), 26.4 (u), 27.1 (u), 28.5 (u), 32.0 (u), 42.8 (d), 51.3 (d), 60.7 (u), 62.0 (u), 135.2 (d), 136.0 (u), 166.3 (u).

IR ($CHCl_3$): ? 2927 (s), 1743 (s), 1471 (m), 1368 (w), 1321 (s), 1200 (s), 1160 (s), 1132 (w), 1096 (w), 1027 (m), 919 (s), 810 (m) cm^{-1}.

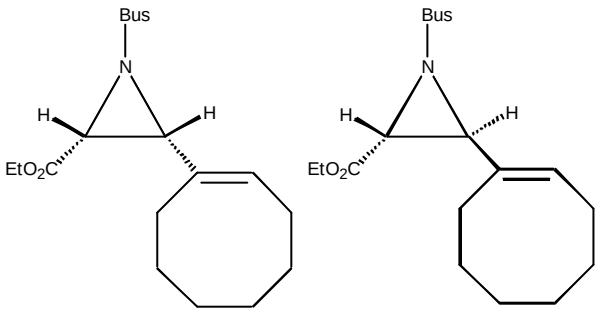
MS (CI, CH_4) *m/z* (relative intensity, %): 330 (M^+ + H, 3), 302 (2), 256 (7), 210 (100), 193 (23), 164 (2), 136 (2), 102 (2).

Optical rotation: $[a]_D$ −10.4 (*c* 1.5 , $CHCl_3$).

HRMS (EI, 70 eV):

$C_{16}H_{27}NO_4S–C_3H_5O_2$	calcd	found
	256.137246	256.137127

6.4.11 (2*R*,3*R*)- and (2*R*,3*S*)-Ethyl 3-(*E*)-cyclooctenyl-1-(2-methylpropane-2-sulfonyl) aziridine-2-carboxylate (*cis*-45d and *trans*-45d):



Treatment of **42d** (660mg, 2.38 mmol) with Me_3OBF_4 (600 mg, 4.05 mmol) followed by the successive treatment with the imino ester **3** (737 mg, 3.33 mmol) and DBU (652 mg, 4.28 mmol) according to *GP3* gave a mixture of *cis*-**45d** and *trans*-**45d** (540 mg, 66%) in a ratio of 1:1 and with ee-values of 70% (Chiralpack-IA, *n*-heptane/isopropanol, 95:5, R_f = 27.4, ent–R_f = 31.3) and 25% (Chiralpack-IA, *n*-heptane/isopropanol, 95:5, R_f = 27.2, ent–R_f = 31.0) respectively, along with the sulfinamide **7** (282 mg, 70%) and unreacted starting vinyl sulfoximine **42d** (86 mg, 13%). Preparative HPLC afforded *cis*-**45d** (236 mg, 29%) and *trans*-**45d** (245 mg, 30%) as colorless syrupy liquids.

***cis*-45d:**

^{1}H NMR (300 MHz, $CDCl_3$) : d 1.25 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.41-1.58 (m, 8 H, $CH_2CH_2CH_2$), 1.54 (s, 9 H, $C(CH_3)_3$), 2.12 (m, 2 H, $CH_2CH_2CH_2$), 2.22 (m, 2 H, $CH_2CH_2CH_2$), 3. 42 (d, *J* = 7.42 Hz, 1 H, COCHC*H*), 3.50 (d, *J* = 7.66 Hz, 1 H, COCH), 4.15 (q, *J* = 7.17 Hz, 2 H, CH_2CH_3), 5.83 (t, *J* = 8.16 Hz, 1 H, C=CH).

^{13}C NMR (100 MHz, $CDCl_3$): d 14.0 (d), 23.9 (d), 25.9 (u), 27.6 (u), 28.5 (u), 29.2 (u), 44.3 (d), 44.9 (d), 59.8 (u), 61.4 (u), 129.6 (d), 130.6 (u), 164.9 (u).

IR ($CHCl_3$): ? 2925 (s), 1747 (s), 1465 (m), 1380 (w), 1314 (s), 1202 (s), 1130 (s), 1042 (m), 951 (m), 873 (w) cm^{-1}.

MS (CI, isobutane) *m/z* (relative intensity, %): 344 (M^+ + H, 5), 280 (3), 262 (3), 224 (100), 207 (4).

Optical rotation: $[a]_D$ −30.9 (*c* 1.8 , $CHCl_3$).

HRMS (EI, 70 eV):

$C_{17}H_{29}NO_4S$–$C_4H_9O_2S$	calcd	found
	222.149604	222.149404

***trans*-45d:**

^{1}H NMR (400 MHz, $CDCl_3$) : d 1.32 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.42-1.60 (m, 8 H, $CH_2CH_2CH_2$), 1.45 (s, 9 H, $C(CH_3)_3$), 2.11-2.19 (m, 4 H, $CH_2CH_2CH_2$), 3.23 (d, *J* = 3.85 Hz, 1 H, COCH), 3.83 (d, *J* = 3.85 Hz, 1 H, COCHC*H*), 4.27 (m, 2 H, CH_2CH_3), 5.91 (t, *J* = 8.24 Hz, 1 H, C=CH).

^{13}C NMR (100 MHz, $CDCl_3$) : d 13.9 (d), 23.9 (d), 24.9 (u), 26.10 (u), 26.16 (u), 26.2 (u), 29.0 (u), 29.3 (u), 44.1 (d), 50.0 (d), 60.7 (u), 62.1 (u), 132.5 (d), 132.8 (u), 166.2 (u).

IR ($CHCl_3$): ? 2927 (s), 1741 (s), 1460 (m), 1319 (s), 1210 (s), 1130 (m), 1026 (m), 920 (m), 808 (m) cm^{-1}.

MS (CI, isobutane) *m/z* (relative intensity, %): 344 (M^+ + H, 6), 280 (2), 262 (3), 224 (100), 207 (5).

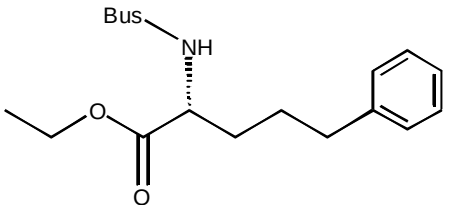
Optical rotation: $[a]_D$ −11.3 (*c* 1.4 , $CHCl_3$).

HRMS (EI, 70 eV):

$C_{17}H_{29}NO_4S$–$C_4H_9O_2S$	calcd	found
	222.149604	222.149404

6.5 Synthesis of a-amino acid

6.5.1 (*R*)-Ethyl-5-phenyl-2-(2-methylpropane-2-sulfonylamino) pentanoate (24).



After two vacuum/H_2 cycles to remove air from the reaction flask, a mixture of aziridine *cis*-**6a** (230 mg, 0.68 mmol) and 10 % Pd/C (22 mg, 10% of the weight of the substrate) in ethanol (5 mL) was stirred under a hydrogen atmosphere (balloon) at 0 °C for 3 h. The mixture was filtered through celite and the filtrate was concentrated under vacuo.

Purification by chromatography (hexane/EtOAc, 1:1) gave amino ester **24** (210 mg, 91%).

Under the same Pd/C hydrogenation conditions *trans*-**6a** also gave the amino ester **24**. The two samples of **24** showed the same NMR, MS and IR data.

^{1}H NMR (300 MHz, C_6D_6): d 0.86 (t, *J* = 7.17 Hz, 3 H, C*H*$_3$CH$_2$), 1.18 (s, 9 H, C(CH$_3$)$_3$), 1.43 (m, 1 H, COCHC*H*H, 1.61 (m, 3 H, COCHCH*HC*H$_2$), 2.42 (m, 3 H, PhC*H*$_2$), 3.84 (q, *J* = 7.18 Hz, 2 H, CH$_3$C*H*$_2$), 4.16 (m, 1 H, COC*H*), 4.43 (m, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): d 14.0 (d), 24.1 (d), 27.2 (u), 33.6 (u), 35.3 (u), 57.2 (d), 59.5 (u), 61.2 (u), 126.2 (d), 128.3 (d), 128.7 (d), 141.9 (u), 172.6 (u).

IR (neat): ? 3292 (s), 2979 (s), 1739 (s), 1602 (w), 1455 (s), 1370 (w), 1313 (s), 1199 (m), 1127 (s), 1023 (m), 917 (m), 857 (w), 811 (w) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): 268 (M$^+$, 6), 220 (46), 204 (7), 163 (25), 148 (100), 131 (37), 117 (24), 91 (25), 57 (53).

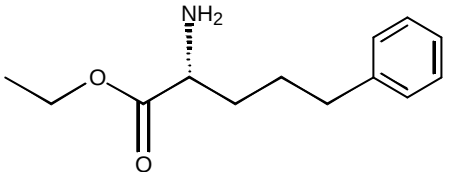
Optical rotation: [a]$_D^{23}$ +5.1 (*c* 1.2 , $CHCl_3$) (**24** obtained from *cis*-**6a**).

[a]$_D^{23}$ +4.7 (*c* 1.2 , $CHCl_3$) (**24** obtained from *trans*-**6a**).

HRMS (EI, 70 eV):

$C_{13}H_{27}NO_4S–C_3H_5O_2$	calcd	found
	220.137131	220.137127

6.5.2 (*R*)-Ethyl 2-amino-5-phenylpentanoate (23).



To a solution of the *N*-Bus amino acid **24** (130 mg, 0.38 mmol) and anisole (329 mg, 3.05 mmol) in CH_2Cl_2 (9 mL) was slowly added CF_3SO_3H (229 mg, 1.52 mmol, 0.2 N in CH_2Cl_2, 9 mL) at 0 °C. After 1 h 0.1 N aqueous NaOH was added until a pH of 8 was readed. The aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc, 1:3) to afford amino ester **23** (79 mg, 94 %) as a colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): d 1.26 (t, *J* = 7.14 Hz, 3 H, CH_3CH_2), 1.55~1.78 (m, 4 H, $PhCH_2CH_2CH_2$), 2.65 (m, 2 H, $PhCH_2$), 3.43 (m, 1 H, COCH), 4.16 (q, *J* = 7.14 Hz, 2 H, CH_3CH_2), 7.17~7.40 (m, 5 H, Ph).

^{13}C NMR (75 MHz, $CDCl_3$): d 14.2 (d), 27.4 (u), 34.5 (u), 35.5 (u), 54.3 (d), 60.7 (u), 125.8 (d), 128.31 (d), 128.38 (d), 141.9 (u), 176.1 (u).

IR (neat): ? 3382 (w), 2979 (s), 1732 (s), 1602 (w), 1495 (w), 1453 (m), 1377 (w), 1182 (s), 1027 (m), 856 (w) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): 221 (M^+, 10), 148 (100), 131 (64), 105 (10), 91 (16), 56 (9).

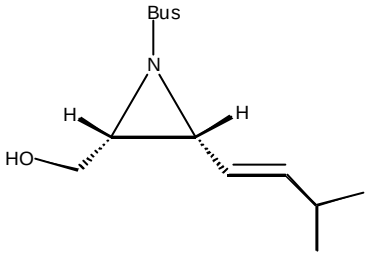
Optical rotation: $[a]_D$ –13.9° (*c* 2.0, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{13}H_{19}NO_2$	calcd	found
	221.141790	221.141579

6.6 Pd(0)-catalyzed isomerization

6.6.1 ((*2R,3R*)-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl) aziridin-2-yl) methanol (*cis*-32):



To a solution of ester **6b** (185 mg, 0.61 mmol) in CH_2Cl_2 (3 mL) at 0 °C was added DIBALH (3.3 mL, 1.83 mmol, 0.56 M solution in THF). After stirring the mixture for 3 h at 0 °C, ice pieces were slowly added and the solution was filtered and the residue was washed with hot ethyl acetate (20 mL). The filtrate was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (hexane/ EtOAc, 2:1) to afford alcohol *cis*-**32** (144 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$): d 1.01 (d, *J* = 6.87 Hz, 6 H, $CH(CH_3)_2$), 1.25 (s, 9 H, $C(CH_3)_3$), 1.83 (b, 1 H, OH), 2.35 (m, 1 H, $CH(CH_3)_2$), 3.10 (m, 1 H, CH_2CH), 3.28 (dd, *J* = 15.1, *J* = 7.4 Hz, 1 H, CH=CHC*H*), 3.73 (m, 1 H, OC*H*H), 3.81 (m, 1 H, OCH*H*), 5.25 (dd, *J* = 15.38 Hz, *J* = 7.96 Hz, 1 H, C*H*=CHCH$(CH_3)_2$), 5.92 (dd, *J* = 15.39 Hz, *J* = 6.86 Hz, 1 H, CH=C*H*CH$(CH_3)_2$).

^{13}C NMR (100 MHz, $CDCl_3$): d 21.9 (d), 22.0 (d), 24.1 (d), 31.1 (d), 42.8 (d), 46.4 (d), 59.1 (u), 59.6 (u), 118.0 (d), 146.0 (d).

IR ($CHCl_3$): ? 3519 (s), 2962 (s), 2412 (w), 1664 (w), 1465 (m), 1367 (w), 1304 (s), 1214 (w), 1125 (s), 1048 (s), 968 (s), 886 (m), 812 (m) cm^{-1}.

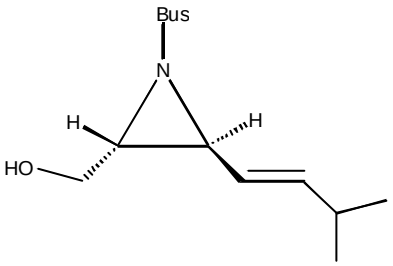
MS (CI, CH_4) *m/z* (relative intensity, %): 262 (M^+ + H, 29), 232 (18), 206 (7), 198 (9), 180 (33), 142 (49), 125 (100), 107 (10),

Optical rotation: $[a]_D$ −20.4 (*c* 1.5, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{12}H_{23}NO_3S$–$C_4H_9SO_2$	calcd	found
	140.107631	140.107539

6.6.2 ((*2R,3S*)-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl) aziridin-2-yl) methanol (*trans*-32):



Following the same procedure that had been used for the synthesis of alcohol *cis*-**32**, *trans*-**32** (93 mg, 90 %) was synthesized from ester *trans*-**6a** (120 mg, 0.40 mmol) by reduction with DIBALH (2.1 mL, 1.19 mmol, 0.56 M solution in THF) in 90% yield (93 mg).

^{1}H NMR (300 MHz, $CDCl_3$): d 1.01 (d, *J* = 6.67 Hz, 6 H, CH(C*H*$_3$)$_2$), 1.48 (s, 9 H, C(CH$_3$)$_3$), 2.33 (m, 1 H, C*H*(CH$_3$)$_2$), 2.98 (m, 2 H, *H*OCH$_2$C*H*), 3.26 (dd, *J* = 8.65 Hz, *J* = 4.45 Hz, 1 H, CH=CHC*H*), 3.85 (m, 1 H, OC*H*H), 4.12 (m, 1 H, OCH*H*), 5.16 (m, 1 H, C*H*=CHCH(CH$_3$)$_2$), 5.90 (dd, *J* = 15.58 Hz, *J* = 6.68 Hz, 1 H, CH=C*H*CH(CH$_3$)$_2$).

^{13}C NMR (75 MHz, $CDCl_3$): d 21.9 (d), 22.0 (d), 23.9 (d), 30.9 (d), 46.8 (d), 50.7 (d), 60.0 (u), 61.0 (u), 121.5 (d), 145.3 (d).

IR ($CHCl_3$): ? 3511 (s), 2961 (s), 2409 (w), 1664 (w), 1464 (m), 1366 (w), 1304 (s), 1218 (w), 1125 (s), 1046 (s), 967 (s), 886 (m), 814 (m) cm^{-1}.

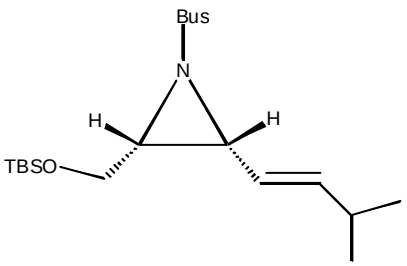
MS (EI, 70 eV) *m/z* (relative intensity, %): 262 (M^+ + H, 2), 234 (5), 206 (4), 198 (5), 188 (10), 180 (8), 170 (9), 158 (3), 142 (100), 125 (32), 107 (15), 97 (9), 81 (4), 68 (4).

Optical rotation: [a]$_D$ +6.2 (*c* 0.85, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{12}H_{23}NO_3S–C_4H_9SO_2$	calcd	found
	140.107619	140.107539

6.6.3 (*2R,3R*)-2-((tert-Butyldimethylsilyloxy)methyl-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine (*cis*-33):



To a solution of alcohol cis-**32** (85 mg, 0.33 mmol) and imidazole (88 mg, 1.30 mmol) mixture in CH_2Cl_2 (3 mL) was added TBSCl (196 mg, 1.30 mmol) and the reaction was stirred under argon for 2 h. The mixture was then quenched by addition of water (5 mL) and the mixture was extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$). The residue was purified by flash chromatography (hexane/EtOAc, 4:1) to afford *cis*-**33** (110 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$): d 0.06 (s, 1 H, $SiCH_3$), 0.07 (s, 1 H, $SiCH_3$), 0.89 (s, 9 H, $SiC(CH_3)_3$), 1.00 (d, *J* = 6.87 Hz, 6 H, $CH(CH_3)_3$), 1.48 (s, 9 H, $SC(CH_3)_3$), 2.33 (m, 1 H, $CH(CH_3)_3$), 3.02 (m, 1 H, CH_2CH), 3.27 (dd, *J* = 11.27, *J* = 5.77 Hz, 1 H, CH=CHCH), 3.66 (m, 1 H, OCHH), 3.81 (m, 1 H, OCHH), 5.22 (ddd, *J* = 15.66 Hz, *J* = 7.41 Hz, *J* = 1.38 Hz, 1 H, $CH=CHCH(CH_3)_2$), 5.89 (dd, *J* = 15.66 Hz, *J* = 6.59 Hz, 1 H, $CH=CHCH(CH_3)_2$).

^{13}C NMR (100 MHz, $CDCl_3$): d -5.38 (d), -5.31 (d), 18.2 (u), 21.93 (d), 21.99 (d), 24.1 (d), 25.7 (d), 31.0 (d), 44.2 (d), 44.4 (d), 59.1 (u), 60.3 (u), 118.4 (d), 145.0 (d).

IR ($CHCl_3$): ? 2957 (s), 2861 (s), 1662 (w), 1596 (w), 1468 (m), 1387 (w), 1364 (w), 1313 (s), 1255 (s), 1128 (s), 1101 (s), 969 (s), 944 (s), 889 (w), 836 (s) cm^{-1}.

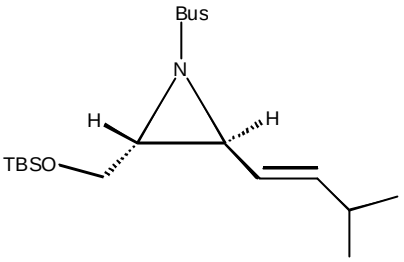
MS (CI, CH_4) *m/z* (relative intensity, %): 376 (M^+ + H, 16), 360 (9), 346 (21), 318 (15), 302 (8), 256 (100), 239 (94), 198 (48), 145 (4), 124 (11), 107 (9), 89 (7), 73 (5).

Optical rotation: $[a]_D$ –34.5 (*c* 0.65, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{18}H_{37}NO_3SSi–C_4H_9$	calcd	found
	318.156052	318.155920

6.6.4 (*2R,3S*)-2-((tert-Butyldimethylsilyloxy)methyl-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine (*trans*-33):



Following the above procedure, *trans*-**33** (77 mg, 89%) was synthesized from *trans*-**27** (60 mg, 0.23 mmol), imidazole (63 mg, 0.92 mmol) and TBSCl (139 mg, 0.92 mmol) in 89% yield (77 mg).

^{1}H NMR (300 MHz, $CDCl_3$): d 0.07 (s, 2 × 3 H, 2 × $SiCH_3$), 0.89 (s, 9 H, $SiC(CH_3)_3$), 0.99 (d, *J* = 6.59 Hz, 3 H, $CH(CH_3)(CH_3)$), 1.01 (d, *J* = 6.59 Hz, 3 H, $CH(CH_3)(CH_3)$), 1.46 (s, 9 H, $SC(CH_3)_3$), 2.35 (m, 1 H, $CH(CH_3)_3$), 2.98 (m, 1 H, CH_2CH), 3.13 (m, 1 H, CH=CHC*H*), 3.85 (m, 2 H, CH_2), 5.50 (m, 1 H, CH=CHCH$(CH_3)_2$), 5.90 (dd, *J* = 15.34 Hz, *J* = 6.68 Hz, 1 H, CH=C*H*CH$(CH_3)_2$).

^{13}C NMR (75 MHz, $CDCl_3$): d -5.36 (d), -5.35 (d), 18.2 (u), 21.9 (d), 22.0 (d), 24.1 (d), 25.8 (d), 31.1 (d), 47.8 (d), 48.7 (d), 60.1 (u), 62.0 (u), 121.1 (d), 145.3 (d).

IR ($CHCl_3$): ? 2960 (s), 2860 (s), 1664 (w), 1633 (w), 1467 (m), 1383 (w), 1311 (s), 1255 (m), 1127 (s), 1101 (s), 950 (s), 890 (w), 837 (s) cm^{-1}.

MS (CI, CH_4) *m/z* (relative intensity, %): 376 (M^+ + H, 12), 360 (8), 346 (17), 318 (12), 312 (11), 296 (6), 284 (3), 256 (100), 239 (83), 198 (42), 174 (3), 145 (4), 124 (10), 107 (8), 89 (6), 73 (4).

Optical rotation: $[a]_D$ +14.8 (*c* 0.75, $CHCl_3$).

HRMS (EI, 70 eV):

$C_{18}H_{37}NO_3SSi-C_4H_9$	calcd	found
	318.155897	318.155920

6.6.5 ((*2R,3R*) and (*2R,3S*)-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl) aziridin-2-yl) methanol (*cis*-32 + *trans*-32):

Following the same procedure that had been used to synthesize *cis*-**32**, a diasreomeric mixture of *cis*-**32** and *trans*-**32** (190 mg, 92 %) was synthesized from the mixture of *cis*-**6b** and *trans*-**6b** (240 mg, 0.79 mmol) by reducing with DIBALH (4.2 mL, 2.38 mmol, 0.56 M solution in THF) in a combined yield of 92% (190 mg).

6.6.6 (*2R,3R*) and (*2R,3S*)-2-((*tert*-Butyldimethylsilyloxy)methyl-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine (*cis*-33 + *trans*-33):

Following the same procedure that used to synthesize *cis*-**33**, a mixture of *cis*-**33**and *trans*-**33** was synthesized from the mixture of *cis*-**32** and *trans*-**32**(190 mg, 0.73 mmol), imidazole (198 mg, 2.91 mmol) and TBSCl (439 mg, 2.91 mmol) in a combined yield of 94% (258 mg).

6.6.7 Pd(0)-catalyzed isomerization reaction of (*2R,3S*)-2-((*tert*-butyldimethyl silyloxy)methyl-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine (*trans*-33).

To a stirred solution of the *trans*-vinyl aziridine *trans*-**33** (64 mg, 0.17 mmol) in dry THF (3 mL) at 0 °C under argon was added by syringe a solution of $Pd(PPh_3)_4$ (12 mg, 0.01 mmol, 6 mol %) in dry THF (2 mL) and the mixture was stirred at 0 °C for 18 h. Concentration under reduced pressure at 0 °C followed by flash chromatography

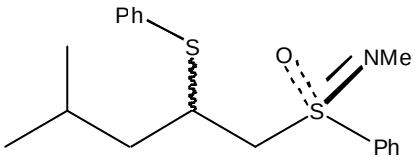
(hexane:EtOAc, 4:1) gave *cis*-**33** (54mg, 84%). According to the NMR *cis*-**33** was the only product after the Pd(0)–catalyzed isomerization.

6.6.8 Pd(0)-catalyzed isomerization of 1:2 mixture of (*2R,3S*)-2-((*tert*-butyldimethylsilyloxy)methyl-3-((*E*)-3-methylbut-1-enyl)-1-(2-methylpropane-2-sulfonyl)aziridine (*trans*-33) and its (*2R,3R*)-isomer (*cis*-33).

To a stirred solution of 1:2 mixture of the *trans*-**33** and *cis*-**33** (258 mg, 0.69 mmol) in dry THF (5 mL) at 0 °C was added by syringe a solution of $Pd(Ph_3)_4$ (24 mg, 0.02mmol, 3 mol%) in dry THF (5 mL) and the mixture was stirred at 0 °C for 18 h. Concentration under reduced pressure at 0 °C followed by flash chromatography (hexane:EtOAc, 4:1) gave *cis*-**33** (242 mg, 94 %). According to the NMR *cis*-**33** was the only product after the Pd(0)–catalyzed isomerization.

6.7 Thiophenol addition to vinyl sulfoximines

6.7.1 (4-Methyl-1-(*N*-methyl-*S*-phenylsulfonimidoyl)pentan-2-yl) phenyl sulfane (38b and *epi*-38b)



38b, *epi*-**38b**

Following *GP 1*, the vinyl sulfoximine **12b** (184 mg, 0.78 mmol) was treated with neat thiophenol (0.48 ml, 4.66 mmol). After the mixture was stirred at room temperature for 1.5 h, TLC showed the consumption of the sulfoximine **12b**. The excess thiophenol and the sulfides **38b** and *epi*-**38b** were separated by flash column chromatography (EtOAc/*n*-hexane, 1:5) in a ratio of 2:1. Sulfide **38b** (EtOAc/*n*-hexane, 1:5, R_f = 0.46) (167 mg, 61%) and sulfide *epi*-**38b** (EtOAc/*n*-hexane, 1:5, R_f = 0.27) (88 mg, 33%) were isolated

as colourless oils. The absolute configuration of sulfides **38b** and *epi*–**38b** was not determined.

sulfide 38b:

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.68 Hz, 3 H, CHC*H*$_3$), 0.92 (d, *J* = 6.43 Hz, 3 H, CHC*H*$_3$), 1.35 (m, 1 H, CH_3CHCHH), 1.73 (m, 1 H, CH_3CHCHH), 1.95 (m, 1 H, CH_3CH), 2.65 (s, 3 H, NCH_3), 3.21 (dd, *J* = 9.65, *J* = 14.34 Hz, 1 H, SOC*H*H), 3.49 (dd, *J* = 2.96, *J* = 14.34 Hz, 1 H, SOCH*H*), 3.67 (m, 1 H, SCH), 7.25 (m, 5 H, SPh), 7.55 (m, 3 H, SOPh), 7.57 (m, 2 H, SOPh).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 21.1 (d), 23.4 (d), 25.5 (d), 29.4 (d), 40.9 (d), 42.3 (u), 61.7 (u), 127.3 (d'), 129.1 (d), 129.3 (d), 129.4 (d), 131.9 (d), 132.9 (d), 133.3 (u), 138.3 (u).

IR ($CHCl_3$): ? 3062 (s), 2955 (s), 2872 (w), 1581 (m), 1472 (s), 1445 (s), 1396 (w), 1248 (s), 1144 (s), 1103 (s), 1080 (s), 1024 (w), 1000 (w), 896 (m), 871 (m) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): 347 [M^+] (2), 238 (5), 193 (100), 150 (50), 123 (45), 83 (85), 55 (37).

Optical rotation: $[\alpha]_D$ = +58.3 (c 0.84, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{19}H_{25}NOS_2$	calcd	found
	347.137816	347.137760

sulfide *epi*-38b:

^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.92 (d, *J* = 5.77 Hz, 3 H, CHC*H*$_3$), 0.94 (d, *J* = 6.32 Hz, 3 H, CHC*H*$_3$), 1.46 (m, 1 H, CH_3CHC*H*H), 1.98 (m, 1 H, CH_3C*H*), 2.04 (m, 1 H, CH_3CHCH*H*), 2.60 (s, 3 H, NCH_3), 3.34 (m, 3 H, SC*H*, SOC*HH*), 7.05 (m, 2 H, SPh), 7.15 (m, 3 H, SPh), 7.48 (m, 2 H, SOPh), 7.59 (m, 1 H, SOPh), 7.68 (m, 2 H, SOPh).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 21.0 (d), 23.4 (d), 25.5 (d), 29.4 (d), 41.0 (d), 42.7 (u), 60.7 (u), 127.2 (d), 128.9 (d), 129.1 (d), 129.2 (d), 132.2 (d), 132.6 (d), 132.8 (u), 137.1 (u).

IR ($CHCl_3$): ? 3061 (s), 3025 (m), 1582 (w), 1475 (m), 1444 (m), 1249 (s), 1146 (m), 1094 (w), 998 (w), 862 (m) cm^{-1}.

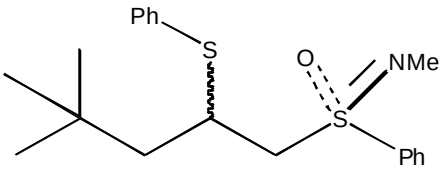
MS (EI, 70 eV) *m/z* (relative intensity, %): 347 [M^+] (1), 238 (15), 193 (82), 150 (46), 123 (48), 83 (100), 55 (47).

Optical rotation: $[\alpha]_D = -4.4$ (c 0.36, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{19}H_{25}NOS_2$	calcd	found
	347.137681	347.137760

6.7.2 (4,4-Dimethyl-1-(*N*-methyl-*S*-phenylsulfonimidoyl)pentan-2-yl)(phenyl)sulfane (38d and *epi*-38d)



38d, *epi*-**38d**

Following *GP 4*, the vinyl sulfoximine **12d** (220 mg, 0.88 mmol) was treated with neat thiophenol (0.54 mL, 5.26 mmol). After the mixture was stirred at room temperature for 2 h, TLC showed the consumption of the sulfoximine **12d**. The excess thiophenol and the sulfides **38d** and *epi*-**38d** were separated by flash column chromatography (EtOAc:*n*-hexane, 1:5). Sulfide **38d** (EtOAc/*n*-hexane, 1:5, R_f = 0.47) (190 mg, 60%) and sulfide ***epi*-38d** (EtOAc/*n*-hexane, 1:5, R_f = 0.29) (104 mg, 33 %) were isolated as colourless oils. The absolute configurations of the sulfides **38d** and *epi*–**38d** were not determined.

sulfide 38d:

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.99 (s, 9 H, $C(CH_3)_3$), 1.40 (dd, *J* = 9.61, *J* = 14.83 Hz, 1 H, $(CH_3)_3CCHH$), 2.04 (dd, *J* = 2.19, *J* = 14.84 Hz, 1 H, $(CH_3)_3CCHH$), 2.64 (s, 3 H, NCH_3), 3.23 (dd, *J* = 9.89, *J* = 14.29 Hz, 1 H, SOC*H*H), 3.39 (dd, *J* = 2.48, *J* = 14.29 Hz, 1 H, SOCH*H*), 3.79 (tt, *J* = 2.47, *J* = 9.61 Hz, 1 H, SCH), 7.22 (m, 5 H, SPh), 7.50 (m, 2 H, SOPh), 7.57 (m, 1 H, SOPh), 7.75 (m, 2 H, SOPh).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 29.4 (d), 30.4 (d), 31.2 (u), 38.5 (d), 46.4 (u), 62.1 (u), 126.8 (d), 129.1 (d), 129.2 (d), 129.4 (d), 130.6 (d), 132.7 (d), 134.4 (u), 138.6 (u).

IR ($CHCl_3$): ? 2949 (w), 1712 (w), 1598 (w), 1215 (m), 1042 (w), 991 (w), 850 (w) cm^{-1}.

Optical rotation: $[\alpha]_D$ = +76.4 (c 1.01, CH_2Cl_2)

MS (EI, 70 eV) *m/z* (relative intensity, %): 361 [M^+] (1), 252 (5), 207 (100), 149 (46), 123 (49), 97 (58), 77 (15), 57 (34).

HRMS (EI, 70 eV):

$C_{20}H_{27}NOS_2$	calcd	found
	361.153514	361.153410

sulfide *epi*-38d:

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.02 (s, 9 H, $C(CH_3)_3$), 1.48 (m, 1 H, $(CH_3)_3CCHH$), 2.30 (m, 1 H, $(CH_3)_3CCHH$), 2.57 (s, 3 H, NCH_3), 3.37 (m, 3 H, SC*H*,SOC*HH*), 7.02 (m, 2 H, SPh), 7.08–7.13 (m, 3 H, SPh), 7.43 (m, 2 H, SOPh), 7.57-7.62 (m, 3 H, SOPh).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 29.5 (d), 30.4 (d), 31.2 (u), 38.9 (d), 47.0 (u), 61.2 (u), 127.1 (d), 129.0 (d), 129.2 (d), 129.4 (d), 131.5 (d), 132.7 (d), 133.9 (u), 137.2 (u).

IR ($CHCl_3$): ? 2955 (s), 1582 (m), 1475 (s), 1444 (s), 1365 (m), 1247 (s), 1141 (s), 1081 (s), 869 (m) cm^{-1}.

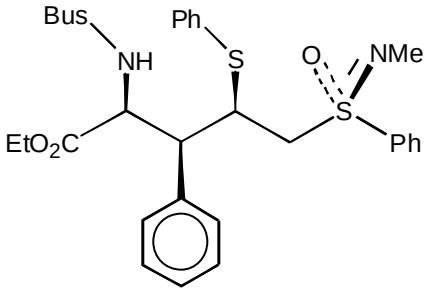
Optical rotation: $[\alpha]_D = -10.8$ (c 0.45, CH_2Cl_2)

MS (EI, 70 eV) *m/z* (relative intensity, %): 361 [M^+] (1), 252 (22), 207 (100), 150 (47), 123 (57), 97 (77), 77 (13), 57 (35).

HRMS (EI, 70 eV):

$C_{20}H_{27}NOS_2$	calcd	found
	361.153347	361.153416

6.7.3 (2*S*,3*S*,4*R*)-Ethyl 2-(1,1-dimethylethylsulfonamido)-3-phenyl-5-(*S*)-(*N*-methyl-*S*-phenyl sulfonimidoyl)- 4-(phenylthio)pentanoate (39a)



39a

To a solution of the vinyl sulfoximine **4a** (904 mg, 1.84 mmol) in dry CH_2Cl_2 (1 ml) in a conical bottom flask cooled at 0 °C was added neat thiophenol (1.13 ml, 11.0 mmol). After the mixture was warmed to room temperature, it was stirred for 2 h. Then the mixture was diluted with water (5 ml) and extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. The excess thiophenol was seperated from the sulfide **39a** by flash column chromatography (EtOAc/*n*-Hexane, 1:3). Isolation of the pure sulfide **39a** was not possible even by preparative HPLC. The sulfide slowly decomposed for the formation of the starting material **4a**. Column chromatography gave a mixture (973 mg, 88%) of sulfide **39a** and sulfoximine **4a** in a ratio of ≥97:3, respectively, according to ^{1}H NMR.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.47 (s, 9 H, $C(CH_3)_3$), 2.62 (s, 3 H, NCH_3), 3.12 (m, 2 H, $SOCH_2$), 3.34 (dd, *J* = 2.75, *J* = 11.54 Hz, 1

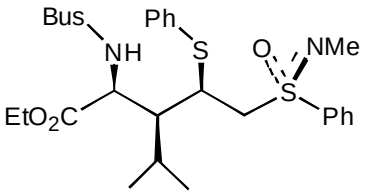
H, NCHC*H*)), 4.19 (m, 4 H, N*H*/PhSC*H*/OCH_2), 5.54 (dd, *J* = 2.75, *J* = 10.71 Hz, 1 H, NCH), 7.02 (m, 2 H, Ph), 7.31 (m, 8 H, Ph), 7.59 (m, 3 H, Ph), 7.84 (m, 2 H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.1 (d), 24.5 (d), 29.4 (d), 42.5 (d), 51.6 (d), 56.2 (u), 57.6 (d), 60.6 (u), 62.0 (u), 128.6 (d,), 129.1 (d), 129.2 (d), 129.4 (d), 129.9 (d), 133.0 (d), 134.7 (u), 136.9 (u), 137.0 (d), 138.4 (u), 171. 8 (u).

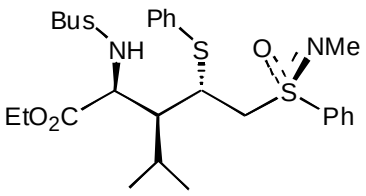
IR ($CHCl_3$): ? 3340 (m), 2982 (s), 2936 (m), 1739 (s), 1583 (w), 1448 (s), 1325 (s), 1243 (s), 1125 (s), 1022 (m), 906 (m), 859 (m) cm^{-1}.

MS (CI, isobutame) *m/z* (relative intensity, %): 603 [M^+ + 1] (3), 493 (67), 338 (8), 272 (100), 222 (63), 156 (22), 117 (29), 102 (38).

6.7.4 (2*S*,3*S*,4*R*)-Ethyl 2-(1,1-dimethylethylsulfonamido)-3-isopropyl-5-(*S*)-(*N*-methyl-*S*-phenylsulfonimidoyl)-4-(phenylthio)pentanoate (39b and *epi*-39b)



39b



epi-**39b**

To a solution of the vinyl sulfoximine **4b** (830 mg, 1.81 mmol) in dry CH_2Cl_2 (1 ml) in a conical bottom flask at 0 °C was added neat thiophenol (0.75 ml, 7.25 mmol). After the mixture was warmed to room temperature, it was stirred for 3 h. Then the mixture was diluted with water (5 ml) and extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. The excess thiophenol and the sulfides **39b** and *epi*-**39b** were separated by flash column chromatography (EtOAc/*n*-Hexane, 1:4). The sulfide **39b** (730 mg, 71%) (R_f = 0.28; EtOAc/*n*-Hexane, 1:4) and

sulfide *epi*-**39b** (133 mg, 13%) (R_f = 0.16; EtOAc:*n*-Hexane, 1:4) were isolated as colour less solids.

Sulfide 39b:

^{1}H NMR (400 MHz, $CDCl_3$): d 1.17 (d, *J* = 6.32 Hz, 3 H, $CH(CH_3)_2$), 1.23 (d, *J* = 6.59 Hz, 3 H, $CH(CH_3)_2$), 1.27 (t, *J* = 7.14, 3 H, CH_2CH_3), 1.46 (s, 9 H, $C(CH_3)_3$), 2.19 (m, 1 H, $CH(CH_3)_2$), 2.49 (dd, *J* = 10.71 Hz, *J* = 1.65 Hz, 1 H, $CHCH(CH_3)_2$), 2.62 (s, 3 H, NCH_3), 3.29 (dd, *J* = 14.28 Hz, *J* = 2.48 Hz, 1 H, PhSCHCHH), 3.60 (dd, *J* = 14.28 Hz, *J* = 10.99 Hz, 1 H, PhSCHCHH), 4.21 (m, 2 H, CH_2CH_3), 4.34 (dd, *J* = 10.99 Hz, *J* = 2.2 Hz, 1 H, PhSCH), 4.41 (dd, *J* = 7.69 Hz, *J* = 1.92 Hz, COCH), 7.24 (m, 4 H, Ph, NH), 7.42 (m, 4 H, Ph), 7.52 (m, 3 H, Ph).

^{13}C NMR (100 MHz, $CDCl_3$): d 13.9 (d), 22.5 (d), 23.5 (d), 24.2 (d), 28.4 (d), 29.3 (d), 42.5 (d), 51.4 (d), 57.1 (d), 60.0 (u), 61.4 (u), 61.5 (u), 127.5 (d), 128.8 (d), 129.1 (d), 129.4 (d), 132.1 (d), 132.6 (u), 132.9 (d), 137.2 (u), 171.4 (u).

IR ($CHCl_3$): ? 3133 (s), 2974 (s), 2877 (s), 1724 (s), 1583 (m), 1481 (s), 1446 (s), 1403 (m), 1369 (m), 1312 (s), 1239 (s), 1211 (s), 1128 (s), 1029 (m), 944 (m), 869 (s) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): 569 [M^+ + 1] (1), 459 (40), 413 (17), 340 (8), 292 (93), 236 (88), 184 (22), 155 (27), 125 (76), 110 (100), 77 (18), 57 (95).

Optical rotation: $[\alpha]_D$ = +62.3 (c 0.13, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{27}H_{40}N_2O_5S_3$–C_6H_5S	calcd	found
	459.198705	459.198742

Sulfide *epi*-39b:

^{1}H NMR (400 MHz, $CDCl_3$): d 1.17 (d, *J* = 6.59 Hz, 3 H, $CH(CH_3)_2$), 1.23 (d, *J* = 6.59 Hz, 3 H, $CH(CH_3)_2$), 1.34 (t, *J* = 7.14, 3 H, CH_2CH_3), 1.45 (s, 9 H, $C(CH_3)_3$), 2.28 (m, 1 H, $CH(CH_3)_2$), 2.62 (s, 3 H, NCH_3), 3.05 (dd, *J* = 14.83 Hz, *J* = 2.19 Hz, 1 H, PhSCHCHH), 4.28 (m, 3 H, OCH_2, PhSCH), 4.55 (dd, *J* = 5.7 Hz, *J* = 1.38 Hz, COCH), 4.61 (dd, *J* = 14.83 Hz, *J* = 11.26 Hz, 1 H, PhSCHCHH), 7.19-7.28 (m, 4 H, Ph), 7.50-7.60 (m, 4 H, Ph), 7.75 (m, 2 H, Ph), 8.61 (m, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): d 13.8 (d), 21.2 (d), 22.0 (d), 24.2 (d), 29.2 (d), 29.3 (d), 41.9 (d), 52.3 (d), 56.4 (d), 57.2 (u), 59.8 (u), 61.8 (u), 126.8 (d), 128.6 (d), 129.2 (d), 129.5 (d), 129.6 (d), 133.1 (d), 133.9 (u), 137.6 (u), 172. 3 (u).

IR ($CHCl_3$): ? 3130 (s), 2974 (s), 2882 (s), 1725 (s), 1582 (m), 1479 (s), 1401 (m), 1313 (s), 1238 (s), 1128 (s), 1031 (s), 943 (m), 866 (s) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): 569 [M^+ + 1] (5), 459 (45), 413 (16), 339 (9), 292 (100), 236 (66), 183 (22), 155 (22), 124 (51), 110 (61), 57 (67).

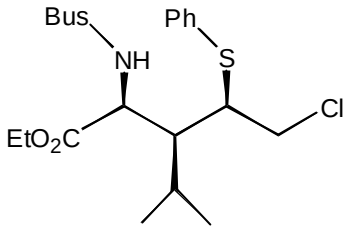
Optical rotation: $[\alpha]_D = -7.4$ (c 0.22, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{27}H_{40}N_2O_5S_3$–C_6H_5S	calcd	found
	459.198794	459.198742

6.8 Substitution of sulfoximine by a Cl-atom

6.8.1 (2*S*,3*S*,4*R*)-Ethyl 5-chloro-2-(1,1-dimethylethylsulfonamido)-3-isopropyl-4-(phenylthio)pentanoate (43b)



$ClCO_2C(Cl)HMe$ (294 mg, 2.06 mmol) was added at 0 °C to a solution of sulfide **39b** (584 mg, 1.03 mmol) in CH_2Cl_2 (8 mL). After the mixture was stirred at room temperature for 2 h, it was quenched with saturated aqueous NaCl and extracted with CH_2Cl_2. The combined organic layers were concentrated in vacuo. Purification by flash chromatography (EtOAc/*n*-Hexane, 1:9) gave chloride **43b** (344 mg, 75%) and sulfinamide **44** (255 mg, 88%) as colourless oils.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.08 (d, *J* = 4.95 Hz, 3 H, $CHC\mathit{H}_3$), 1.10 (d, *J* = 4.94 Hz, 3 H, $CHC\mathit{H}_3$), 1.22 (t, *J* = 7.14 Hz, 3 H, $CH_2C\mathit{H}_3$), 1.33 (s, 9 H, $C(CH_3)_3$), 2.12 (m, 1 H, $C\mathit{H}(CH_3)_2$), 2.24 (m, 1 H, NCHC*H*), 3.28 (ddd, *J* = 1.65, *J* = 4.95, *J* = 10.44 Hz, 1 H, SCH), 3.61 (dd, *J* = 4.94, *J* = 11.26 Hz, 1 H, ClC*H*H), 3.73 (dd, *J* = 10.71, *J* = 10.99 Hz, 1 H, ClCH*H*), 4.13 (q, *J* = 7.14 Hz, 2 H, OCH_2), 4.47 (dd, *J* = 3.30, *J* = 9.34 Hz, 1 H, NCH), 4.88 (d, *J* = 9.07 Hz, 1 H, NH), 7.24 (m, 3 H, Ph) , 7.42 (m, 2 H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.1 (d), 22.5 (d), 23.1 (d), 24.3 (d), 27.9 (d), 46.7 (u), 50.2 (d), 51.0 (d), 56.4 (d), 60.4 (u), 62.3 (u), 128.1 (d), 129.3 (d), 132.9 (d), 133.1 (u), 171.8 (u).

IR ($CHCl_3$): ? 3268 (m), 2980 (s), 1737 (s), 1582 (w), 1476 (m), 1372 (m), 1316 (m), 1244 (s), 1197 (w), 1129 (s), 1045 (m), 938 (w), 884 (m) cm^{-1}.

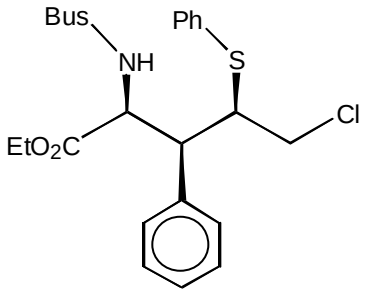
MS (EI, 70 eV) *m/z* (relative intensity, %): 449 [M^+] (8), 413 (4), 328 (12), 292 (100), 218 (21), 191 (23), 170 (19), 134 (11), 101 (39), 57 (48).

Optical rotation: $[\alpha]_D$ = +43.5 (c 1.02, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{20}H_{32}ClNO_4S_2$	calcd	found
	449.146203	449.146132

6.8.2 (2*S*,3*S*,4*R*)-Ethyl 5-chloro-2-(1,1-dimethylethylsulfonamido)-3-phenyl-4-(phenylthio)pentanoate (43a)



$ClCO_2C(Cl)HMe$ (281 mg, 1.97 mmol) was added at 0 °C to a solution of sulfide **39a** (592 mg, 0.98 mmol) in CH_2Cl_2 (6 mL). After the mixture was stirred at room temperature for 2 h, it was quenched with saturated NaCl solution and extracted with dichloromethane. The combined organic layers were concentrated in vacuo. Preparative HPLC (EtOAc:*n*-Hexane, 1:9) gave the chloride **43a** (370 mg, 78%) and sulfinamide **44** (216 mg, 90%) as colourless oils.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.34 (s, 9 H, $C(CH_3)_3$), 3.20 (dd, *J* = 4.67, *J* = 12.09 Hz, 1 H, ClC*H*H), 3.36 (bdd, *J* = 2.47, *J* = 11.54 Hz, 2 H, ClCH*H* /NCHC*H*), 3.90 (ddd, *J* = 2.74, *J* = 4.39, *J* = 11.54 Hz, 1 H, SCH), 4.15 (m, 2 H, OCH_2), 4.32 (d, *J* = 10.16 Hz, 1 H, NH), 5.32 (dd, *J* = 2.2, *J* = 10.17 Hz, 1 H, NCH), 7.07 (m, 2 H, Ph), 7.28 (m, 6 H, Ph), 7.68 (m, 2 H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.4 (d), 24.5 (d), 45.5 (u), 50.5 (d), 51.1 (d), 58.3 (d), 60.8 (u), 62.3 (u), 128.4 (d), 128.6 (d), 128.9 (d), 129.2 (d), 129.4 (d), 131.4 (u), 134.2 (u), 135.1 (d), 171.2 (u).

IR ($CHCl_3$): ? 3573 (m), 3379 (s), 2983 (s), 1739 (s), 1670 (w), 1583 (m), 1439 (s), 1372 (s), 1209 (s), 1127 (s), 1023 (s), 916 (s), 857 (w).

MS (EI, 70 eV) *m/z* (relative intensity, %): 483 [M^+] (29), 362 (32), 326 (48), 261 (61), 252 (57), 222 (15), 192 (34), 170 (47), 146 (39), 134 (27), 117 (43), 108 (47), 102 (93), 91 (33), 74 (10), 57 (100).

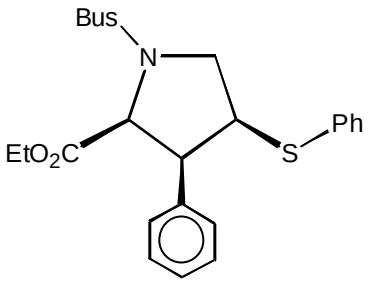
Optical rotation: $[\alpha]_D = -13.3$ (c 0.66, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{23}H_{30}ClNO_4S_2$	calcd	found
	483.130493	483.130482

6.9 Synthesis of prolines

6.9.1 (2*S*,3*S*,4*S*)-Ethyl *N*-*tert*-butylsulfonyl-3-phenyl-4-(phenylthio) pyrrolidine-2-carboxylate (50a)



Cs_2CO_3 (74 mg, 0.22 mmol) was added at room temperature to a solution of chloride **43a** (100 mg, 0.21 mmol) in DMF (5 mL). After the mixture was stirred at room temperature for 6 h, it was quenched with water and extracted with ether. The combined organic layers were concentrated under vacuo. Purification by flash chromatography (EtOAc:*n*-Hexane, 2:8) gave proline **50a** (81 mg, 87%) as a colourless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, *J* = 7.17 Hz, 3 H, CH_2CH_3), 1.52 (s, 9 H, $C(CH_3)_3$), 3.58 (dd, *J* = 7.13, *J* = 7.13 Hz, 1 H, NC*H*H), 3.74 (q, *J* = 7.17 Hz, 2 H, OCH_2), 3.99 (m, 1 H, SCH), 4.10 (dd, *J* = 7.66, *J* = 7.92 Hz, 1 H, PhC*H*), 4.22 (dd, *J* = 7.66, *J* = 11.12 Hz, 1 H, NCH*H*), 5.17 (d, *J* = 7.91 Hz, 1 H, COCH), 7.28 (m, 10 H, C-Ph/SPh).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 13.5 (d), 24.6 (d), 50.0 (d), 51.2 (d), 56.1 (u), 60.8 (u), 61.6 (u), 64.8 (d), 126.8 (d), 127.8 (d), 128.9 (d), 129.5 (d), 130.3 (d), 134.4 (u), 135.3 (u), 168.8 (u).

IR ($CHCl_3$): ? 3022 (w), 1755 (w), 1391 (w), 1215 (m), 1125 (w), 1026 (w) cm^{-1}.

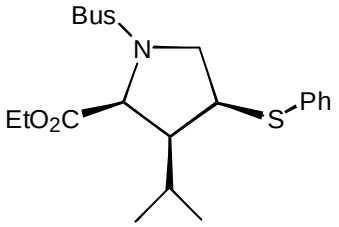
MS (EI, 70 eV) *m/z* (relative intensity, %): 447 [M^+] (100), 374 (12), 326 (26), 310 (6), 254 (90), 218 (27), 144 (47), 117 (48), 86 (9), 57 (38).

Optical rotation: $[\alpha]_D = -32.3$ (c 0.72, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{23}H_{29}NO_4S_2$	calcd	found
	447.153731	447.153804

6.9.2 (2*S*,3*S*,4*S*)-Ethyl *N*-*tert*-butylsulfonyl-3-isopropyl-4-(phenylthio) pyrrolidine-2-carboxylate (50b)



Cs_2CO_3 (160 mg, 0.49 mmol) was added at room temperature to a solution of chloride **43b** (200 mg, 0.44 mmol) in DMF (5 mL). After the mixture was stirred at 40 °C for 3 h, it was quenched with water and extracted with ether. The combined organic layers were concentrated under vacuo. Purification by flash chromatography (EtOAc/*n*-Hexane, 2:8) gave proline **50b** (166 mg, 90%) as a colourless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 6.86 Hz, 3 H, CHC*H*$_3$), 1.14 (d, *J* = 6.87 Hz, 3 H, CHC*H*$_3$), 1.29 (t, *J* = 7.14 Hz, 3 H, CH_2CH_3), 1.33 (s, 9 H, $C(CH_3)_3$), 1.83 (sept, *J* = 7.14 Hz, 1 H, C*H*$(CH_3)_2$), 2.18 (m, 1 H, *i*PrC*H*), 3.66 (m, 1 H, NC*H*H), 3.79 (m, 1 H, SCH), 4.20 (m, 3 H, OCH_2/ NCH*H*), 4.46 (bd, *J* = 7.42 Hz, 1 H, COCH), 7.24-7.38 (m, 5 H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.2 (d), 21.1 (d), 21.4 (d), 24.4 (d), 28.1 (d), 46.8 (d), 54.6 (d), 57.9 (u), 61.3 (u), 61.7 (u), 65.1 (d), 127.2 (d), 129.1 (d), 131.3 (d), 134.5 (u), 171.8 (u).

IR ($CHCl_3$): ? 2973 (s), 1738 (s), 1583 (w), 1476 (s), 1393 (m), 1374 (m), 1323 (s), 188 (s), 1132 (s), 1086 (m), 1018 (s), 838 (w) cm^{-1}.

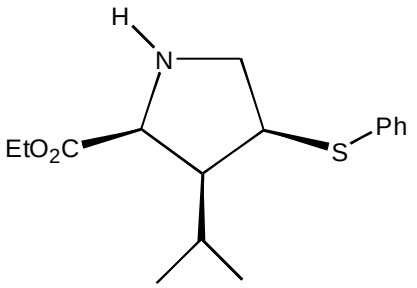
MS (EI, 70 eV) *m/z* (relative intensity, %): 413 [M^+] (38), 340 (21), 292 (63), 220 (100), 183 (11), 139 (7), 110 (23), 68 (11), 57 (27).

Optical rotation: $[\alpha]_D$ = +87.2 (c 0.56, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{20}H_{31}NO_4S_2$	calcd	found
	413.169213	413.169454

6.9.3 (2*S*,3*S*,4*S*)-Ethyl 3-isopropyl-4-(phenylthio)pyrrolidine-2-carboxylate (51)



The *N*-Bus proline **50b** (80 mg, 0.19 mmol) and anisole (168 mg, 1.55 mmol) were added to a solution of CF_3SO_3H (116 mg, 0.77 mmol) in CH_2Cl_2 (30 mL) at 0 °C. After the mixture was stirred at 0 °C for 3 h, it was neutralized with 0.1 N NaOH to a pH of 8. Then, the mixture was extracted with CH_2Cl_2, and the combined organic layers were concentrated under vacuo. Purification by flash chromatography (EtOAc*n*-Hexane, 3:7) afforded proline **51** (49 mg, 86%) as a colourless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.6 Hz, 3 H, $CHCH_3$), 1.02 (d, *J* = 6.87 Hz, 3 H, $CHCH_3$), 1.29 (t, *J* = 7.15 Hz, 3 H, CH_2CH_3), 1.86 (bm, 2 H, $CH(CH_3)_2$/NH), 2.09 (m, 1 H, *i*PrC*H*), 3.02 (m, 1 H, N*H*H), 3.61 (m, 1 H, SCH), 3.70 (m, 1 H, NH*H*), 4.02 (bd, *J* = 7.69 Hz, 1 H, COCH), 4.19 (q, *J* = 7.14 Hz, 2 H, OCH_2), 7.22-7.38 (m, 5 H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.3 (d), 20.7 (d), 22.4 (d), 28.6 (d), 47.7 (d), 55.1 (u), 55.5 (d), 60.8 (u), 63.8 (d), 126.6 (d), 128.9 (d), 130.6 (d), 136.1 (u), 173.1 (u).

IR ($CHCl_3$): ? 3394 (w), 2961 (s), 1730 (s), 1583 (m), 1472 (s), 1374 (m), 1340 (w), 1185 (s), 1093 (w), 1029 (m), 856 (w) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): [M^+ + 1] 294 (91), 264 (50), 220 (100), 184 (9), 140 (11), 110 (31), 68 (38).

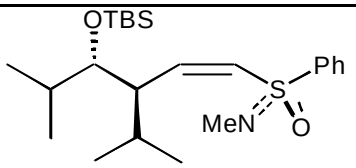
Optical rotation: $[\alpha]_D$ = +53.4 (c 0.55, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{16}H_{23}NO_2S_2$	calcd	found
	293.144923	293.144952

6.10 Thiophenol Michael addition to sulfoximine substituted homoallylic alcohols

6.10.1 *tert*-Butyl((3*S*,4*R*,*Z*)-4-isopropyl-2-methyl-6-(*N*-methyl-*S*-phenyl sulfonimidoyl) hex-5-en-3-yloxy)dimethylsilane (*Z*-41)



A solution of the alcohol **40** (806 mg, 2.61 mmol) in DCM (10 mL) was treated with imidazole (709 mg, 10.4 mmol) at 0 °C. After the mixture was stirred at 0 °C for 30 min, $ClSiMe_2$*t*-Bu (1.179 g, 7.8 mmol) was added at 0 °C. The mixture was stirred at room temperature for 4 h. It was then washed with water and extracted with CH_2Cl_2. The combined organic layers were concentrated under vacuo. Purification by flash chromatography (EtOAc/*n*-hexane, 2:8) gave the silyl ether *Z*-**41** (1.048 g, 95%) as a colourless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = –0.1 (s, 3 H, $SiCH_3$), 0.2 (s, 3 H, $SiCH_3$), 0.39 (d, *J* = 6.87 Hz, 3 H, $CHCH_3$), 0.82 (d, *J* = 6.59 Hz, 3 H, $CHCH_3$), 0.84 (s, 9 H, $C(CH_3)_3$), 1.51 (m, 1 H, $CH(CH_3)_2$), 1.79 (m, 1 H, $OCHCH(CH_3)_2$), 2.63 (s, 3 H, NCH_3), 3.32 (ddd, *J* = 9.07, *J* = 8.79, *J* = 1.1 Hz, 1 H, OCHCH), 3.57 (dd, *J* = 1.09, *J* = 6.32 Hz, 1 H, OCH), 6.30 (d, *J* = 11.54 Hz, 1 H, SCH), 6.37 (dd, *J* = 11.27, *J* = 11.26 Hz, 1 H, SCHCH), 7.49 (m, 3 H, Ph), 7.83 (m, 2H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = –3.9 (d), –3.4 (d), 18.7 (u), 18.9 (d), 19.4 (d), 20.6 (d), 21.3 (d), 26.3 (d), 29.1 (d), 29.4 (d), 33.8 (d), 45.2 (d), 77.7 (d), 128.9 (d), 129.1 (d), 129.8 (d), 132.3 (d), 140.5 (u), 148.5 (d).

IR ($CHCl_3$): ? 3385 (w), 2955 (s), 1731 (w), 1467 (m), 1381 (w), 1251 (s), 1149 (m), 1072 (s), 840 (s) cm^{-1}.

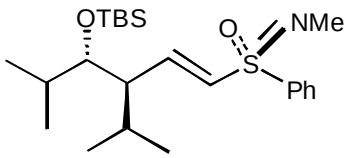
MS (CI, Methane) *m/z* (relative intensity, %): [M^+ + 1] 424 (100), 380 (54), 366 (40), 269 (5), 237 (20), 187 (7), 155 (4), 73 (8).

Optical rotation: $[\alpha]_D$ = –146.34 (c 1.04, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{23}H_{41}NO_2SSi$	calcd	found
	423.262766	423.262731

6.10.2 *tert*-Butyl((3*S*,4*R*,*E*)-4-isopropyl-2-methyl-6-(*N*-methyl-*S*-phenylsulfonimidoyl)hex-5-en-3-yloxy)dimethylsilane (*E*-41)



To a solution of the silyl ether *Z*-**41** (844 mg, 1.99 mmol) in THF (15 mL) was added at – 78° C *n*-BuLi (1.36 mL, 1.6 M in hexanes, 2.19 mmol) and the mixture was slowly allowed to warm to 0 °C and stirred for 1 h. It was then cooled to – 78° C and quenched with saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate. The combined organic layers were concentrated under vacuo. Purification by flash chromatography (EtOAc/*n*-Hexane, 2:8) gave the silyl ether *E*-**41** (830 mg, 98% yield) as a colourless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = –0.1 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$), 0.59 (d, *J* = 6.87 Hz, 3 H, $CH(CH_3)$), 0.72 (d, *J* = 6.87 Hz, 3 H, $CH(CH_3)$), 0.80 (d, *J* = 6.86 Hz, 3 H, $CHCH_3$), 0.83 (s, 9 H, $C(CH_3)_3$), 0.92 (d, *J* = 6.6 Hz, 3 H, $CHCH_3$), 1.50 (m, 1 H, $CH(CH_3)_2$), 1.75 (m, 1 H, $CH(CH_3)_2$), 1.93 (ddd, *J* = 1.93, *J* = 8.52, *J* = 8.79 Hz, 1 H, OCHCH), 2.75 (s, 3 H, NCH_3), 3.59 (dd, *J* = 2.2, *J* = 5.77 Hz, 1 H, OCH), 6.22 (d, *J* =

15.38 Hz, 1 H, SCH), 6.79 (dd, *J* = 10.71, *J* = 15.38 Hz, 1 H, SCHC*H*), 7.50 (m, 3 H, Ph), 7.85 (m, 2 H, Ph).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = –3.9 (d), –3.8 (d), 18.2 (d), 18.3 (u), 18.9 (d), 21.1 (d), 21.4 (d), 26.0 (d), 28.5 (d), 29.5 (d), 33.6 (d), 51.9 (d), 77.4 (d), 128.6 (d), 129.1 (d), 131.2 (d), 132.2 (d), 139.7 (u), 148.6 (d).

IR ($CHCl_3$): ? 2957 (s), 1627 (w), 1466 (s), 1383 (m), 1249 (s), 1148 (s), 1079 (s), 996 (w), 928 (w), 838 (s) cm^{-1}.

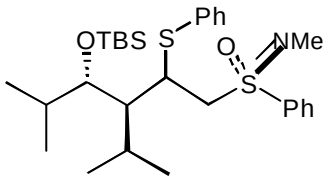
MS (EI, 70 eV) *m/z* (relative intensity, %): [M^+] 423 (5), 380 (32), 366 (100), 294 (10), 237 (63), 212 (46), 187 (27), 166 (7), 155 (7), 134 (11), 124 (13), 115 (11), 73 (62).

Optical rotation: $[\alpha]_D$ = +64.6 (c 0.33, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{23}H_{41}NO_2SSi$	calcd	found
	423.262676	423.262731

6.10.3 *tert*-Butyl((3*S*,4*R*)-4-isopropyl-2-methyl-6-(*N*-methyl-*S*-phenylsulfonimidoyl)-5-(phenylthio)hexan-3-yloxy)dimethylsilane (42 and *epi*-42)



To a solution of the vinyl sulfoximine ***E*-41** (250 mg, 0.59 mmol) in dry CH_2Cl_2 (1 mL), in a conical bottom flask, was added at 0 °C neat thiophenol (0.37 ml, 3.55 mmol). After

the mixture was warmed to room temperature, it was stirred for 4 h. The mixture was diluted with water (5 ml) and extracted with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$) and the solvent was removed in vacuo. The excess thiophenol and the sulfides (92% yield) were separated by flash column chromatography (EtOAc:*n*-Hexane, 1:9). Pure sulfide **42** (183 mg, 58%) (R_f = 0.21; EtOAc:*n*-Hexane, 1:9) and sulfide *epi*-**42** (104 mg, 33%) (R_f = 0.14; EtOAc:*n*-Hexane, 1:9) as a colour less oils.

Sulfide 42:

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.16 (s, 3 H, SiCH_3), 0.30 (s, 3 H, SiCH_3), 1.04 (s, 9 H, C(CH_3)$_3$), 1.11 (d, *J* = 6.41 Hz, 3 H, CHCH_3), 1.12 (d, *J* = 6.41 Hz, 3 H, CHCH_3), 1.16 (d, *J* = 6.72 Hz, 3 H, CHCH_3), 1.21 (d, *J* = 6.72 Hz, 3 H, CHCH_3), 2.19 (m, 1 H, CH(CH$_3$)$_2$), 2.38 (m, 1 H, CH(CH$_3$)$_2$), 2.69 (m, 1 H, SCHC*Hi*Pr), 2.75 (s, 3 H, NCH_3), 3.49 (m, 2 H, SOCH_2), 3.91 (m, 1 H, OCH), 4.96 (m, 1 H, SCH), 6.94 (m, 4 H, Ph), 7.08 (m, 2 H, Ph), 7.54 (m, 2 H, Ph), 7.73 (m, 2 H, Ph).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = –3.8 (d), –2.5 (d), 18.5 (d), 18.9 (u), 21.1 (d), 21.8 (d), 24.7 (d), 26.9 (d), 28.0 (d), 29.2 (d), 32.6 (d), 41.2 (d), 48.4 (d), 60.7 (u), 78.2 (d), 125.6 (d), 128.2 (d), 129.3 (d), 129.4 (d), 132.3 (d), 136.7 (u), 140.6 (u).

IR ($CHCl_3$): ? 2954 (s), 1581 (m), 1470 (s), 1446 (s), 1385 (w), 1247 (s), 1144 (s), 1080 (s), 1022 (w), 871 (m) cm^{-1}.

MS (EI, 70 eV) *m/z* (relative intensity, %): [M^+] 533 (2), 490 (4), 476 (5), 424 (3), 379 (5), 321 (70), 249 (48), 212 (20), 187 (100), 73 (45).

Optical rotation: $[\alpha]_D$ = +43.3 (c 0.64, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{29}H_{47}NO_2S_2Si$-C_4H_9 = $C_{25}H_{38}NO_2S_2Si$	calcd	found
	476.211455	476.211329

Sulfide *epi*-42:

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.55 (d, *J* = 6.86 Hz, 3 H, $CHCH_3$), 0.68 (d, *J* = 6.86 Hz, 3 H, $CHCH_3$), 0.86 (s, 9 H, $C(CH_3)_3$), 0.87 (d, *J* = 6.59 Hz, 3 H, $CHCH_3$), 0.91 (d, *J* = 6.59 Hz, 3 H, $CHCH_3$), 1.70 (m, 1 H, $CH(CH_3)_2$), 1.91 (m, 1 H, $SCHCH$), 1.96 (m, 1 H, $CH(CH_3)_2$), 2.48 (s, 3 H, NCH_3), 3.34 (dd, *J* = 14.84, *J* = 7.69 Hz, 1 H, $SOCHH$), 3.59 (m, 1 H, OCH), 3.83 (m, $PhSCH$), 4.19 (dd, *J* = 14.84, *J* = 5.22 Hz, 1 H, $SOCHH$), 7.08 (m, 3 H, Ph), 7.17 (m, 2 H, Ph), 7.34 (m, 2 H, Ph), 7.42 (m, 1 H, Ph), 7.66 (m, 2 H, Ph).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = –4.1 (d), –2.5 (d), 18.3 (d), 18.9 (u), 19.5 (d), 21.9 (d), 22.7 (d), 26.8 (d), 27.5 (d), 29.5 (d), 34.0 8d), 44.4 (d), 49.2 (d), 59.8 (u), 127.1 (d), 128.8 (d), 128.9 (d), 129.3 (d), 132.2 (d), 132.3 (d), 135.4 (u), 138.6 (u).

IR ($CHCl_3$): ? 2955 (s), 1739 (w), 1582 (w), 1469 (s), 1384 (m), 1249 (s), 1148 (s), 1059 (s), 905 (w), 840 (s) cm^{-1}.

MS (CI, isobutame) *m/z* (relative intensity, %): $[M^+ + 1]$ 534 (100), 476 (4), 379 (67), 321 (12), 247 (87), 187 (37), 156 (7).

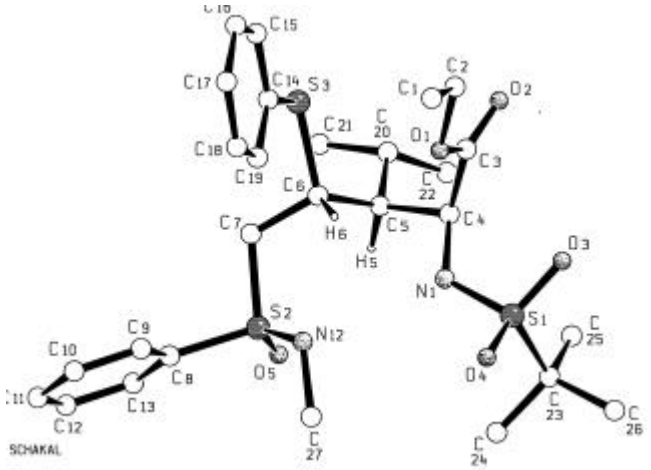
Optical rotation: $[\alpha]_D = -26.6$ (c 0.55, CH_2Cl_2)

HRMS (EI, 70 eV):

$C_{29}H_{47}NO_2S_2Si$-C_4H_9 = $C_{25}H_{38}NO_2S_2Si$	calcd	found
	476.211455	476.211329

7 Crystal Structure Analysis

7.1 Crstal structure of (2S,3S,4R)-Ethyl 2-(1,1-dimethylethylsulfonamido)-3-isopropyl-5-(N-methyl-S-phenylsulfonimidoyl)-4-(phenylthio)pentanoate (39b)



Experimental Details

Crystal data:

Chemical formula	:	$C_{27}H_{39}N_2O_5S_3$
formula weight	:	567.82
Crystal system	:	orthorhombic
Space group (No.)	:	$P2_12_12_1$ (19)
Z	:	4
a (Å)	:	10.857(2)
b (Å)	:	15.020(2)
c (Å)	:	18.797(2)
a (°)	:	90.0
ß (°)	:	90.0

? (°)	:	90.0
cell volume	:	3065.3(8)Å^3
Density calc.	:	1.230g/cm^3
Radiation	:	CuKα (1.54179Å)
Range for lattice parameters	:	12.87° <*T* <18.83°
Absorption coefficient	:	2.509mm^{-1}
Temperature	:	298K
Crystal source	:	recrystallized from
Crystal colour	:	colourless
Crystal shape	:	irregular
Crystal size	:	ca. 0.3x0.3.x0.3mm
Data Collection		
Diffractometer type	:	Enraf-Nonius CAD4
collection method	:	ω/2ϑ scans
Absorption correction	:	none
No. of reflections measured	:	6225
No. of independent reflections:		5493
No. of observed reflections	:	4978
T_{max} (°)	:	67.76
$h_{min} \rightarrow h_{max}$	:	- 13 → 12
$k_{min} \rightarrow k_{max}$	:	- 18 → 18
$l_{min} \rightarrow l_{max}$	:	- 22 → 22
Criterion for observed	:	$I > 2\sigma(I)$
R_{int}	:	0.020(34)
Standard reflections	:	-3 -3 2, -3 -2 4, -2 -3 2
Variation	:	1402(44) 883(29) 4509(118)

Refinement:

On	:	*F*
Treatment of hydrogens	:	Calculated in idealized positions. Us

		fixed at 1.5×U of the corresponding heavy atom. No refinement of hydrogen parameters
R	:	0.048
R_w	:	0.062
Weighting scheme	:	$w=1/s^2(F)$
No. of parameters refined	:	334
No. of reflections in refmnt.	:	4964
Residual electron density	:	-0.38/0.40e/Å^3
r*[1]	:	not refined
XABS[2]	:	-0.00001(310)
Goodness of fit	:	2.346
Solution	:	XTAL3.7[3]
Remarks	:	

Definitions:

$U_{eq} = 1/3 S_i S_j U_{ij} a_i^* a_j^* a_i a_j$

The anisotropic displacement factor in the structure factor expression is:

$t = \exp[-2p^2(S_i S_j U_{ij} h_i h_j a_i^* a_j^*)]$

Atomic Positional and Isotropic Displacement Parameters

Atom	x/a	y/b	z/c	U_{eq}/Å^2
S1	0.56132(9)	0.35197(6)	0.45288(5)	* 0.0466(5)
S2	0.4559(1)	0.68146(6)	0.41512(5)	* 0.0522(5)
S3	0.6633(1)	0.60420(7)	0.22420(5)	* 0.0519(5)
O1	0.7431(2)	0.4236(2)	0.3120(1)	* 0.054(2)
O2	0.6297(3)	0.3496(2)	0.2316(1)	* 0.072(2)
O3	0.6130(3)	0.2816(2)	0.4109(2)	* 0.067(2)
O4	0.6247(3)	0.3845(2)	0.5140(1)	* 0.062(2)
O5	0.3256(3)	0.6634(2)	0.4111(2)	* 0.074(2)
N1	0.5423(3)	0.4358(2)	0.4010(1)	* 0.046(2)
N2	0.5407(4)	0.6217(2)	0.4575(2)	* 0.056(2)
C1	0.9637(5)	0.4197(4)	0.3132(4)	* 0.104(5)
C2	0.8524(5)	0.3944(4)	0.2725(3)	* 0.089(4)
C3	0.6375(4)	0.3948(2)	0.2845(2)	* 0.048(2)

C4	0.5250(4)	0.4262(2)	0.3241(2)	* 0.044(2)
C5	0.4727(4)	0.5162(2)	0.2948(2)	* 0.048(2)
C6	0.5699(3)	0.5902(2)	0.3040(2)	* 0.044(2)
C7	0.5222(4)	0.6807(3)	0.3279(2)	* 0.055(2)
C8	0.4703(4)	0.7960(2)	0.4417(2)	* 0.056(2)
C9	0.5848(4)	0.8264(3)	0.4623(3)	* 0.067(3)
C10	0.5965(6)	0.9130(3)	0.4840(3)	* 0.085(4)
C11	0.4943(8)	0.9662(3)	0.4822(3)	* 0.106(5)
C12	0.3812(7)	0.9360(4)	0.4625(3)	* 0.094(4)
C13	0.3689(5)	0.8489(3)	0.4411(3)	* 0.078(3)
C14	0.8095(4)	0.6355(2)	0.2580(2)	* 0.048(2)
C15	0.9026(4)	0.6414(3)	0.2083(2)	* 0.060(2)
C16	1.0205(4)	0.6612(4)	0.2292(2)	* 0.074(3)
C17	1.0489(5)	0.6760(3)	0.2993(3)	* 0.074(3)
C18	0.9582(5)	0.6719(3)	0.3479(2)	* 0.069(3)
C19	0.8366(4)	0.6523(3)	0.3287(2)	* 0.057(2)
C20	0.4138(4)	0.5052(3)	0.2203(2)	* 0.061(3)
C21	0.3668(5)	0.5937(4)	0.1923(3)	* 0.092(4)
C22	0.3123(5)	0.4365(4)	0.2204(3)	* 0.094(4)
C23	0.4101(4)	0.3155(3)	0.4828(2)	* 0.054(2)
C24	0.3531(5)	0.3899(4)	0.5245(3)	* 0.082(3)
C25	0.3318(5)	0.2880(4)	0.4186(3)	* 0.080(3)
C26	0.4309(6)	0.2347(3)	0.5316(3)	* 0.089(4)
C27	0.5195(5)	0.6175(3)	0.5354(2)	* 0.073(3)
H5	0.4029(-)	0.5337(-)	0.3225(-)	* 0.059(-)
H4	0.4665(-)	0.3798(-)	0.3150(-)	* 0.055(-)
H6	0.6196(-)	0.5686(-)	0.3424(-)	* 0.057(-)
H25a	0.3183(-)	0.3389(-)	0.3885(-)	* 0.120(-)
H25b	0.2525(-)	0.2677(-)	0.4342(-)	* 0.120(-)
H25c	0.3706(-)	0.2429(-)	0.3927(-)	* 0.120(-)
H19	0.7729(-)	0.6498(-)	0.3636(-)	* 0.074(-)
H20	0.4752(-)	0.4869(-)	0.1878(-)	* 0.076(-)
H7a	0.4607(-)	0.6995(-)	0.2939(-)	* 0.070(-)
H7b	0.5885(-)	0.7230(-)	0.3253(-)	* 0.070(-)
H12	0.3067(-)	0.9735(-)	0.4637(-)	* 0.116(-)
H9	0.6555(-)	0.7866(-)	0.4596(-)	* 0.088(-)
H2a	0.8563(-)	0.4233(-)	0.2274(-)	* 0.113(-)
H2b	0.8513(-)	0.3316(-)	0.2651(-)	* 0.113(-)
H13	0.2886(-)	0.8246(-)	0.4248(-)	* 0.098(-)
H15	0.8826(-)	0.6331(-)	0.1591(-)	* 0.076(-)
H17	1.1345(-)	0.6889(-)	0.3128(-)	* 0.097(-)
H26a	0.4787(-)	0.2496(-)	0.5712(-)	* 0.133(-)
H26b	0.4702(-)	0.1872(-)	0.5062(-)	* 0.133(-)
H26c	0.3521(-)	0.2120(-)	0.5477(-)	* 0.133(-)
H18	0.9733(-)	0.6843(-)	0.3963(-)	* 0.084(-)
H24a	0.4032(-)	0.4069(-)	0.5639(-)	* 0.125(-)
H24b	0.2732(-)	0.3739(-)	0.5421(-)	* 0.125(-)
H24c	0.3421(-)	0.4429(-)	0.4957(-)	* 0.125(-)
H10	0.6728(-)	0.9367(-)	0.5001(-)	* 0.110(-)
H16	1.0852(-)	0.6639(-)	0.1931(-)	* 0.091(-)
H11	0.4934(-)	1.0295(-)	0.4959(-)	* 0.140(-)
H21a	0.3311(-)	0.5864(-)	0.1470(-)	* 0.137(-)
H21b	0.4321(-)	0.6357(-)	0.1898(-)	* 0.137(-)
H21c	0.3047(-)	0.6168(-)	0.2237(-)	* 0.137(-)
H1a	1.0357(-)	0.4015(-)	0.2907(-)	* 0.154(-)
H1b	0.9589(-)	0.3903(-)	0.3591(-)	* 0.154(-)
H1c	0.9639(-)	0.4819(-)	0.3215(-)	* 0.154(-)

H22a	0.2756(-)	0.4280(-)	0.1765(-)	* 0.145(-)
H22b	0.2492(-)	0.4512(-)	0.2547(-)	* 0.145(-)
H22c	0.3454(-)	0.3786(-)	0.2361(-)	* 0.145(-)
H27a	0.4758(-)	0.6709(-)	0.5507(-)	* 0.110(-)
H27b	0.5925(-)	0.6126(-)	0.5601(-)	* 0.110(-)
H27c	0.4659(-)	0.5680(-)	0.5464(-)	* 0.110(-)

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Name	Vijaya Bhaskara Reddy Iska
Date of Birth	12.08.1980
Place of Birth	Nellore
Nationality	Indian
Marital Status	Married

Education

07/1997 – 05/2000	Bachelor of Science; First Class with Distinction Sri Venkateswara University, Tirupathi, India
08/2000 – 05/2001	Master of Science in Industrial Oriented Organic Chemistry National Institute of Technology Warangal (NITW), India
08/2001 – 06/2003	Master of Science in Chemistry Indian Institute of Technology Madras (IITM), India
10/2003 – 08/2007	Ph.D, Institut für Organische Chemie der Fakultät für Mathematik, Informatik und Naturwissenschaften der Rheinisch-Westfälischen Technischen Hochschule Aachen in the research group of Prof. Dr. H.-J. Gais Title: "Enantioselective Synthesis of Alkenyl Aziridine Carboxylates and 4-Phenylsulfenyl Prolines"
10/2007 -	Post Doctoral Fellow in the research group of Prof. Dr. U. Kazmaier Universität des Saarlandes, Saarbrücken
19. 05. 2008	Ph. D Examination