Synthesis of Chiral Phosphino-Sulfoximines Through Phospha-Michael Addition and Their Evaluation as 1,5-$P,N$-Ligand in Asymmetric Allylic Alkylation

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften der RWTH Aachen University zur Erlangung des akademischen Grades eines Doktors der Naturwissenschaften genehmigte Dissertation

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A. Theoretical Part
1. Introduction

1.1. Chirality

Chirality is an important and interesting phenomenon in nature. Most of the chiral molecules such as amino acid derivatives or sugars are present in high enantiomeric excess. The origin of homochirality in biomolecules and thus the origin of life is still unknown, despite many theories which are debated in the scientific community.\(^1\)

Enantiomers, which are defined as mirror image from each other and not superimpose, exhibit the same physical and chemical properties, except the capability to polarize the light to the right (+) for the dextrorotatory isomer and to the left (−) for the levorotatory isomer. Louis Pasteur was the first who separated enantiomers. He succeeded in the separation of both enantiomers of tartaric acid by careful look at the shape of the crystals. He observed that each solution of the separated enantiomers deviated the light either to the right or to the left, whereas a solution of both crystals did not polarized the light. Pasteur proposed as explanation two different structures of tartaric acid and thus opened the field of stereochemistry.\(^2\)

The physical and chemical properties of enantiomers become different in the presence of other chiral molecules by formation of diastereoisomers. This is nicely exampled when a drug interacts with its receptor site. Huge differences can be observed in the drug activity of enantiomers. In the best cases, one of the enantiomer shows less activity or even no activity than the other one, as for example propanalol 1 which exhibits β-blocker activities. The (+)-R-1 isomer is 100 times less reactive than its isomer (−)-S-1 (Figure 1).\(^3\) Another pertinent example is illustrated by limonene 2. The (+)-R-2 isomer has an orange smell whereas the (−)-S-2 isomer has a lemon smell.
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The differences in drug activity between enantiomers can be much more impactful (Figure 2). While the (+)-S-ketamine 3 is an active anesthetic and analgesic, the (−)-R-ketamine 3 is responsible for undesirable side-effects like hallucinations. The famous case of Thalidomide 4 is also a tragic example of the physiological properties of enantiomers. Thalidomide 4 was prescribed to pregnant women as an antiemetic to combat morning sickness. The (+)-R-4 form was responsible for these effects, whereas the (−)-S-4 enantiomer causes fetal deformities.4 Unfortunately, even if the (−)-R-4 isomer would be used in optically pure form, it epimerizes in vivo. This drug is still used in the treatment of tuberculosis, leprosy and some cancers.

Figure 1: Harmless differences in the biological properties of enantiomers.

![Diagram of enantiomers and molecules]
Nevertheless, even in the early 1990s, about 90% of synthetic chiral drugs were still racemic, reflecting the difficulty in the practical synthesis of single-enantiomeric compound and the cost of this operation.\(^5\) In 1992, the Food and Drug Administration in USA introduced a guideline regarding “racemic switches”, in order to encourage the commercialization of clinical drugs consisting of single enantiomers.\(^6\) Therefore, the synthesis of optically pure enantiomers is a challenge.

The ultimate source of chirality in all asymmetric synthesis is nature. The chiral compounds which occur in nature provide enormous range and diversity of possible starting materials, such as amino acids, hydroxy acids, alkaloids, terpenes and carbohydrates. The synthesis of chiral pure compounds can be performed by:

- substrate control methods, i.e. starting from a chiral pure starting material.\(^7\)
- reagent control methods, which involve the use of equimolar amount of chiral reagents.\(^8\)
- using a chiral auxiliary, which is utilized in equimolar amount and additional steps for attaching and removing the auxiliary are required.\(^9\)
- resolution method, which involve the synthesis of a racemate and the use of at least 0.5 equivalent of chiral pure reagent.\(^10\)
- Kinetic resolution.\(^11\)
- chiral catalysts, which required a catalytic amount of organic or organometallic catalysts.\(^12\)
Also the synthesis of optically pure compounds can be carried out using the above methods, the use of chiral catalysts is advantageous because of the costs of the required chiral information and thus, asymmetric catalysis represents a very attractive method, not only in term of costs but also in term of atom economy.

1.2. Asymmetric Catalysis

1.2.1. Historical

In 1971, Kagan et al. introduced the C₂ symmetric diphosphine DIOP 5 prepared from enantiomerically pure tartric acid (Scheme 1). For the first time, high enantiomeric excess were obtained in Rh-catalyzed hydrogenation of dehydroamino acids at room temperature and atmospheric pressure leading to amino acids. For example phenylalanine was obtained in 95% yield with 72% ee. As cited by Knowles, “It is most appropriate that this invention using tartric acid should have come from a Frenchman in the land of Louis Pasteur, who, of course, was the one who got it all started”. Afterwards, Knowles came out with his own C₂ symmetric diphosphine DIPAMP 6, where the chirality resides at the phosphorus atoms (Scheme 1). Hydrogenation of Z-enamides using rhodium-DIPAMP complexes led to excellent enantioselectivities. In particular the synthesis of non natural amino acids like L-DOPA, used for the treatment of Parkinson disease, was prepared in an industrial scale by Mosanto using a Rh-catalyzed asymmetric hydrogenation of Z-enamide as a key step.

![Scheme 1: Rh-catalyzed hydrogenation of enamides using (R,R)-DIOP 5 and (R,R)-DIPAMP 6 leading to phenylalanine derivative and L-DOPA.](image-url)
Two breakthroughs were made in 1980, making the year a pivotal date in the development of asymmetric catalysis. Sharpless and Katsuki described a very general method for epoxidation of allylic alcohols using titanium catalysts and chiral diethyl tartrate. The asymmetric hydrogenation was boosted towards synthetic applications with the preparation of the C\textsubscript{2} symmetric diphosphine BINAP, which found spectacular applications in hydrogenation of unsaturated substrates like alkenes or ketones (Scheme 2). Ru-BINAP complex was used in hydrogenation for the synthesis of naproxene, and for the isomerization of enamines in a key step of the industrial scale synthesis of (−)-menthol (Scheme 2).

Later C\textsubscript{2} symmetric bidentate N,N semicorrins ligands were investigated by Pfaltz et al. and gave excellent results in Cu-catalyzed cyclopropanation of olefins and Co-catalyzed conjugated reduction of α,β-unsaturated carboxylic acid derivatives (Figure 3). Reported independently by different research groups in 1990-1991, the analogous C\textsubscript{2} symmetric bidentate N,N bisoxazoline (BOX) ligands were developed (Figure 3). They have been established as one of the most versatile ligand classes for asymmetric catalysis.
One advantage of $C_2$ symmetric ligands is that the number of possible isomeric metal complexes as well as the number of different substrate-catalyst arrangements and reaction pathways is reduced. Mechanistical investigations are therefore easier to perform due to the restricted reaction intermediates involved in the reaction. Although the concept of $C_2$ symmetry has been very successful, there is no fundamental reason why $C_2$ symmetric ligands should exhibit higher enantiocontrol and reactivity than $C_1$ symmetric ligands. The BOX ligands were desymmetrized independently by three research groups, i.e. Pfaltz, Helmchen and Williams, by replacing one of the oxazoline moiety by a phosphino group, leading to phosphine oxazoline ligands (PHOX) (Figure 4).²⁴

The distinctly different characteristics of a soft $P$-ligand with $\pi$-acceptor properties and a hard $N$-ligand acting primarily as a $\sigma$-donor will affect the coordinated substrates in a different way than $P,P$ or $N,N$ bidentate ligands.²⁵ The $C_1$ symmetric ligand PHOX 12 was successfully used in asymmetric catalysis including Heck reactions, Cu-catalyzed 1,4-additions, Ir-catalyzed hydrogenation of alkenes and imines, as well as Pd-catalyzed asymmetric allylic alkylation.²⁴
1.2.2. Asymmetric Allylic Alkylation

Asymmetric allylic alkylation belongs to the most intensively studied homogenous catalytic process. These reactions are highly versatile and have become part of the standard repertoire of the modern organic synthesis (Scheme 3).^{26,27}

\[
\begin{align*}
\text{Scheme 3: General representation of allylic substitution.}
\end{align*}
\]

Typical leaving groups $X^-$ are acetates, carbonates, or more reactive chlorides or sulfonates, and the use of appropriate nucleophiles leads to C–C, C–H, C–O, C–S or C–N bond formation. A variety of transition metal complexes derived from palladium, nickel, platinum, rhodium, iron, ruthenium, iridium, cupper, molybdenum and tungsten are known to catalyze allylic substitutions. But the most widely used catalysts are palladium complexes and their structure and mode of action are well understood.^{27} Since the first example of an enantioselective metal-catalyzed allylic alkylation has been reported by Trost \textit{et al.} in 1977,^{28} strong efforts were done in order to understand the chemical pathway and thus to design efficient catalysts to perform allylic alkylations with a high enantiocontrol on various types of substrates.
As depicted above (Scheme 4), the catalytic active species is a Pd (0) complex having 2 “type L” ligands in its coordination sphere. This complex can coordinate the olefin 13 and undergoes an oxidative addition leading to the cationic (η3-allyl)palladium(II) complex 14. The electrophilic Pd(II) centre activates the allyl system for nucleophilic attack at the allyl termini. Attack at the centre atom is rarely observed. The addition of the nucleophile generates Pd(0)-olefin complex 15 which can release product 16 to undergo a second oxidative addition with the substrate. Thus, if the intermediate allyl complex does not undergo any isomerization that changes its configuration, the overall process proceeds with retention of configuration, i.e. the oxidative addition as well as the nucleophilic addition take place with inversion of configuration. This is true for so called nucleophile “soft” nucleophiles (typically its conjugated acid having pKa < 25). In contrary, “hard” nucleophiles (typically its conjugated acid having pKa > 25) would not directly attack the allyl ligand but first coordinate to the metal and then be transferred to the allyl ligand intramolecularly. This will lead to a retention of configuration during the nucleophilic addition.

Scheme 4: Simplified catalytic cycle of palladium catalyzed allylic alkylation.
In order to obtain high conversion together with high enantioselectivity starting from a racemic substrate, the palladium-allyl complex must isomerize. Two different pathways are admitted. The first one is a Pd(0)-catalyzed allyl exchange. As shown below (Scheme 5), the electrophilic allyl system bound to Pd(II) can react with a Pd(0) complex.

![Scheme 5: Pd(0)-catalyzed allyl exchange.](image)

Addition of the Pd(0) complex to the free face of the allyl ligand displaces the Pd(II) complex on the backside. Therefore, this process results in an inversion of configuration at all the three allyl carbon atoms.\(^{27}\) Due to the low concentration of Pd(0) compare to these of the product and substrate, this isomerization process is rather slow. Isomerization pathways involving the palladium(II)-allyl complex depicted in Scheme 6 are much more faster. The \(\pi-\sigma-\pi\) isomerization can result in syn-anti interconversion by rotation around the \(\sigma-(C-C)\) bond in the \(\eta^1\)-intermediate. In general, the thermodynamic equilibrium is shifted in favour of the \textit{syn}-isomer and only if a substituent is sufficiently small (\(R^2 = H/D, \text{alkyl}\)) the \textit{anti}-isomer is present in notable amount. However, certain ligands which exert strong steric hindrance in the coordination plane of the \textit{syn}-isomer can shift this equilibrium to the other side.\(^{31}\)
The second isomerization process is denoted as apparent allyl rotation. The two termini \( R^1 \) and \( R^2 \) of the allyl system switch position with respect to the other two coordination sites, and at the same time, the central allyl C-atom moves from one side of coordination plane to the other. If the two ligands \( L^A \) and \( L^B \) are different or chiral as, e.g., in complexes with unsymmetrical bidentate ligands, this isomerization leads to a diastereomeric complex even if the allyl system has structurally identical termini. However, if \( L^A \) and \( L^B \) are identical as, e.g., in symmetrical \( C_2 \)-symmetrical chiral bidentate ligands, allyl rotation generates two identical structures and, therefore, has no consequences.
In contrary to the C\textsubscript{2} symmetric ligands DIOP 5, DIPAMP 6, BOX 11 or Trost 17, phosphine oxazolines ligands (PHOX) 12 break this symmetry and have two different coordinating atoms: a “hard” nitrogen atom which is σ-donor, and a “soft” phosphorus atom which is σ-donor but also π-acceptor (Figure 5).

\[ \text{Figure 5: C}_2\text{-symmetric DIOP, DIPAMP, BOX and Trost ligands versus C}_1\text{-symmetric PHOX ligand.} \]

σ-donor ligands provide electron density to the metal centre, stabilizing metals with high degree oxidation state. Π-acceptor ligands have the ability to accept electron density from the metal d orbitals into either d orbitals or π-antibonding orbitals, stabilizing metals with low degree oxidation state (back-bonding). The π-allyl-palladium complexes bearing a bidentate \( P,N \)-ligand will exhibit two electronically non-equivalent allyl termini. This electronic differentiation of the allylic termini is clearly reflected in the Pd-C bond lengths in X-ray analysis of PHOX-palladium allyl complexes.\(^{32}\) The one trans to the π-acceptor coordinating atom is less electron-rich due to the π-back bonding to the phosphorus atom (\textit{trans} influence\(^{29b}\),\(^{33}\)) and thus this bond become weaker than the one trans to the σ-donor atom N. This is reflected by a longer P-C bond trans to the phosphorus atom compared to this trans to the nitrogen atom.
In the case of PHOX ligands, NMR studies and computational calculations showed that the more stable exo and the endo isomers are in rapid equilibrium. However, the energy difference between these two complexes is not the origin of the enantioselectivity induced by these ligands because the nucleophilic attack is slow compared to the interconversion endo-exo. The product distribution depends in fact on the energy between the four transition states leading to the complexes A, B, C and D (Scheme 7).

![Scheme 7: Origin of the selectivity using PHOX ligand.](image)

The nucleophile will attack the π-allyl system in trans to the phosphorus atom, excluding the pathways leading to the complexes A and B. Helmchen and Reggelin were able to identify the complex C at low temperature and characterized it by NMR spectroscopy. The pathway leading to the complex D is disfavoured due to steric interaction between the coordinated olefin and the ligand backbone.
1.3. Sulfoximines

1.3.1. Historical

Sulfoximine chemistry\textsuperscript{36,37} started in the late 1940s by a series of papers about a toxic factor occurring in many proteins treated with “agene” (NCl\textsubscript{3}).\textsuperscript{38,39} The responsible substance was synthesized and isolated in 1949 by Bentley and Whitehead by reaction of methionine sulfoxide with HN\textsubscript{3}.\textsuperscript{39} They also observed the presence of 2 diastereoisomers and deduced that the new functional group should have a stereogenic centre. The new class of compound was called sulfoximines following the proposal of Sir Robinson\textsuperscript{40} and the toxic factor 18 named methionine sulfoximine (Figure 6).

![Figure 6: Methionine sulfoximine 18.](image)

Since 1965 the official IUPAC name is sulfoximide\textsuperscript{41} but this designation is rarely used. General structure of sulfoximine group is schematized as follows (Figure 7).

![Figure 7: General representation of sulfoximine features.](image)

The sulfoximine group is usually drawn with two double bonds between the sulphur and the 2 heteroatoms. According to ab initio calculations, a more appropriate representation of the electronic structure of the sulfoximine group is the polar structure drawn on the right (Figure 7).\textsuperscript{42} Due to its configurationally stable sulphur atom, sulfoximines found numerous
applications in asymmetric synthesis as chiral auxiliary, as chiral ligands or in peptide mimetic.

1.3.2. Synthesis of Sulfoximines

Sulfoximines can be synthesized either by imination of the corresponding sulfoxide or by oxidation of the corresponding sulfilimine 21 (Scheme 8).

![Scheme 8: Possible ways for the synthesis of sulfoximine 22 starting with thioether 19.]

Oxidation of thioether 19 with H₂O₂ in CH₃CO₂H followed by imination of the corresponding racemic sulfoxide 20 with NaN₃ and H₂SO₄ leads to racemic sulfoximine 22. The sequence order of the synthesis can be inverted and started by the imination of thioether 19 to the corresponding sulfilimine 21. Imination of the sulfoxid is also possible by using either bis(N-Tosyl) sulfurdilimide, N-sulfinyl-p-toluene sulfonamide or aryl sulfonamides in the presence of P₂O₅/NEt₃, which produces sulfilimine 21. The oxidation of sulfilimine 21 affords the corresponding sulfoximine 23, which should be deprotected to access the N-unsubstituted sulfoximine 22. The oxidation of sulfilimine 21 to sulfoximine 23 can be achieved using a large range of oxidizing agents including KMnO₄, MCPBA, NaIO₄/RuO₂ and alkaline H₂O₂, and dimethyl dioxirane. Since Brandt and Gais developed an efficient method for the resolution of racemic (±)-S-methyl-S-phenylsulfoximine 24, both enantiomers are accessible in optically pure form on a
molar scale through a separation with camphorsulfonic acid following the method of half-quantities (Scheme 9)\textsuperscript{50}.

\[
\begin{align*}
\text{HN} & \quad \text{SO} \quad \text{Ph} \quad \text{CH}_3 \\
\text{rac-24} & \quad 0.5 \text{ equiv } (+)-\text{CSA} \quad \text{acetone, RT} \quad (+)-24 / (+)-\text{CSA} \quad \text{base} \quad \text{O} \quad \text{NH} \\
& \quad \begin{array}{c}
\text{Ph} \\
\text{S} \\
\text{CH}_3
\end{array} \quad (+)-24 \\
\text{HN} & \quad \text{SO} \quad \text{Ph} \quad \text{CH}_3 \\
\text{rac-24} & \quad 0.5 \text{ equiv } (-)-\text{CSA} \quad \text{acetone, RT} \quad (-)-24 / (-)-\text{CSA} \quad \text{base} \quad \text{O} \quad \text{NH} \\
& \quad \begin{array}{c}
\text{Ph} \\
\text{S} \\
\text{CH}_3
\end{array} \quad (-)-24
\end{align*}
\]

\textbf{Scheme 9:} Resolution of (±)-S-methyl-S-phenylsulfoximine 24.

Unfortunately, the resolution can not be applied for a wide range of sulfoximines. In order to access chirally pure sulfoximines 22, asymmetric oxidation of prochiral sulfoxides 19 can be performed either by Kagan\textsuperscript{51} or Bolm\textsuperscript{52} procedures or by addition of an organometallic reagent to diastereomerically pure sulphur derivatives 25 (Scheme 10)\textsuperscript{53}.

\[
\begin{align*}
\text{R}^1\text{S} & \quad \text{R}^2 \\
19 & \quad \text{asymmetric } \text{oxydation} \\
& \quad \begin{array}{c}
\text{O} \\
\text{R}^1 \\
\text{S} \\
\text{R}^2
\end{array} \\
& \quad \begin{array}{c}
\text{R}^2 \text{M} \\
\text{R}^1\text{S} \text{XR}^3
\end{array} \quad (+) \text{ or } (-)-20 \\
& \quad \text{imination} \\
\text{R}^4\text{N} & \quad \text{O} \quad \text{R}^1\text{S} \quad \text{R}^2 \\
23 & \quad \text{deprotection} \\
& \quad \begin{array}{c}
\text{HN} \\
\text{O} \\
\text{R}^1 \\
\text{S} \\
\text{R}^2
\end{array} \quad 22
\end{align*}
\]

\textbf{Scheme 10:} Synthesis of enantiomerically enriched sulfoximines.

Imination of chiral sulfoxides 20 by the methods described above (except the procedure involving NaN$_3$-H$_2$SO$_4$ which lead to partial racemisation) proceeds under retention of configuration and affors chiral sulfoximines 22\textsuperscript{54} The imination of optically pure sulfoxides 20 can also be performed using BocN$_3$\textsuperscript{55} and the deprotection of the nitrogen atom of sulfoximines 23 can be carried out using either with CF$_3$CO$_2$H or a lewis acid (TiCl$_4$ or AlCl$_3$) together with PhOMe\textsuperscript{56} Other reagents for the imination of optically pure sulfoxides 20 are
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TsN$_3$, PhI=NTs with and catalytic amount of Cu, Fe, Mn, or Ru. Alternatively, the imination is possible by using amide or sulfonamide catalyzed by Rh, Ag, Fe. The major disadvantage of these methods is the cleavage of the N-bond substituent of sulfoximines to access N-unsubstituted sulfoximines. It is worth noting that Johnson developed an efficient and direct method for the imination of chiral sulfoxides to access enantiomerically pure “free” sulfoximines using o-mesitylene sulfonyl hydroxylamine (MSH).

1.3.3. Sulfoximines as Ligands

Due to the chelating properties of the nitrogen of sulfoximines and its proximity to the chiral sulphur atom, sulfoximines can be used as ligand in asymmetric catalysis. The first application of chiral sulfoximines as ligands in asymmetric transformations was reported in 1979 by Johnson and Stark. Acetophenone was reduced in the presence of sulfoximine and diborane to give the alcohol in 69% yield and 82% ee (Scheme 11).

\[
\begin{align*}
\text{MeN::S} & \quad \text{Ph} \quad \text{OH} \\
\text{Me} & \quad \text{Ph} \quad \text{Me} \\
\text{B}_2\text{H}_6 \\
\end{align*}
\]

Scheme 11: First asymmetric transformation using chiral sulfoximine as ligand.

Fourteen years later, Bolm et al. used chiral β-hydroxy sulfoximines in the catalytic reductions of ketones with BH$_3$-SMe$_2$ as hydride source to afford secondary alcohols with up to 95% ee (Figure 8). Afterwards, many ligands were designed for catalytic asymmetric transformations like Diels-Alder and hetero Diels-Alder reaction, hydrogenation, 1,4 additions, Mukaiyama Aldol and vinylogous aldol reaction and allylic alkylations. (Figure 8).
The C₁ symmetric N,N sulfoximine 36 was the first ligand used in Pd-catalyzed asymmetric allylic alkylation and the acetate 43 was converted to malonate 44 with ee up to 73% (Scheme 12, Table 1, entry 1).
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Scheme 12: Pd-catalyzed allylic alkylation of acetate 43 using sulfoximine ligands.

**Table 1:** Sulfoximines used as ligand in Pd-catalyzed allylic alkylation of acetate 43.

<table>
<thead>
<tr>
<th>Entry</th>
<th>ligand</th>
<th>T (°C)</th>
<th>base</th>
<th>Pd precatalyst</th>
<th>Catalyst loading (%)</th>
<th>time</th>
<th>Yield of 44 (%)</th>
<th>ee of 44</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>-5</td>
<td>BSA, KOAc</td>
<td>[Pd(allyl)Cl]₂</td>
<td>10</td>
<td>-</td>
<td>77</td>
<td>73 (S)</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>0</td>
<td>BSA, KOAc</td>
<td>[Pd(allyl)Cl]₂</td>
<td>10</td>
<td>11 d</td>
<td>75</td>
<td>93 (S)</td>
</tr>
<tr>
<td>3</td>
<td>41</td>
<td>66</td>
<td>BSA, KOAc</td>
<td>Pd₂(DBA)₃</td>
<td>2.5</td>
<td>3.5 h</td>
<td>69</td>
<td>86 (R)</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>20</td>
<td>BSA, KOAc</td>
<td>Pd₂(DBA)₃·CHCl₃</td>
<td>4</td>
<td>-</td>
<td>95</td>
<td>64 (-)</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>20</td>
<td>BSA, KOAc</td>
<td>[Pd(allyl)Cl]₂</td>
<td>10</td>
<td>1 h</td>
<td>95</td>
<td>95 (R)</td>
</tr>
<tr>
<td>6</td>
<td>31</td>
<td>20</td>
<td>BSA, NaOAc</td>
<td>[Pd(allyl)Cl]₂</td>
<td>5</td>
<td>48 h</td>
<td>72</td>
<td>93 (R)</td>
</tr>
<tr>
<td>7</td>
<td>34</td>
<td>-</td>
<td>BSA, NaOAc</td>
<td>[Pd(allyl)Cl]₂</td>
<td>-</td>
<td>-</td>
<td>88</td>
<td>66 (R)</td>
</tr>
</tbody>
</table>

*: information not available

C₂ symmetric N,N sulfoximines 35 and 41 proved to be also excellent ligand for this transformation (entry 2 and 3), as well as C₁ symmetric P,N ligands 29, 30, 31 (entry 4, 5, 6 respectively). Finally, the BINOL derived N-phosphino sulfoximines showed moderate ee of the malonate 44 in the Pd-catalyzed allylic alkylation of acetate 43 (entry 7).

1.4. Phospha-Michael Addition

1.4.1. Introduction

Except the well-known Michaelis-Arbuzov⁸² and Michaelis-Becker⁸³ reactions (reaction of trialkyl phosphite with alkyl halides and of dialkyl phosphonate alkali salts with alkyl halides, respectively), the phospha-Michael addition is probably one of the most important and powerful tool for P–C bond formation.⁸⁴ The phospha-Michael addition is a base catalyzed so called Pudovik reaction (or hydrophosphination). The Pudovik reaction is an addition of an organophosphorous compound having a labile P–H bond to an unsaturated substrate.⁸⁵ This can be performed under acidic, basic or radical conditions. Furthermore, the phospha-Michael
addition and, to a greater extend, the Pudovik reaction is an atom economy reaction since all the atoms are used for the formation of the product (Scheme 13).

Scheme 13: Hydrophosphination of substituted alkenes.

Reviewed in 1979 by Pudovik, the reaction of phosphorus acid ester with various substituted alkenes in the presence of alkali metal alkoxides afforded air stable phosphonates (Scheme 14). In fact, diarylphosphites exist in two tautomeric forms, the phosphate and the H-phosphonate.

Scheme 14: Phospha-Michael addition of monosubstituted alkene.

Not only phosphorus acid esters undergo Michael-addition, but phosphates, phosphonites, dialkyl phosphinites and their thio-analogues, alkyl phosphorothioites, phosphoramidates and monoalkyl phosphates react also with α,β-unsaturated esters. Phosphine (PH₃), primary and secondary phosphines undergo Michael addition (Scheme 15) to produce primary, secondary and/or tertiary phosphines. These transformations are often catalyzed by an alkoxide. This is a valuable alternative to SN₂ reaction to access phosphines, which are widely used as ligand for transition metal catalysis. Knochel et al. reported the reaction between secondary phosphines and activated alkenes in the presence of t-BuOK (Scheme 15). The addition proceeded in moderate to excellent yield to give phosphines, which could potentially be used as ligand.
Since phosphine ligands are widely used in asymmetric catalysis, asymmetric variants of the phospha-Michael addition have been studied. In 1990, Feringa et al. reported the stereoselective trans-addition of lithium diphenylphosphide to the chiral furanone 45 (Scheme 16). Changing the methoxy group to menthyl, the one pot sequence involving the phospha-Michael addition of lithium diphenylphosphide to furanone 45 and in situ quenching of the anion with diphenylphosphine chloride afforded diposphine 46 as a single isomer. Three further steps were required to access the (S,S)-CHIRAPHOS in 35% overall yield after purification by crystallization via the Bosnich’s procedure involving nickel salts. Helmchen et al. reported in 1995 the highly diastereoselective addition of lithium diphenylphosphide to the myrtenate derivative 47 (Scheme 16). After hydrolysis of the ester and removal of the borane, this ligand showed excellent enantioselectivities and activities in palladium catalyzed allylic alkylation of cyclic substrates.
Apart from this work, the addition of various organophosphorous reagents towards N-vinyl sulfoximines was studied by Gais et al. (Scheme 17).

Since the hydrophosphination reactions carried out in this work were base-catalyzed, the term phospha-Michael addition will be used to describe these reactions.

1.4.2. Vinyl Sulfoximines as Michael Acceptor

Due to the electron-withdrawing properties of the sulfoxime group, vinyl sulfoximines are prompt to undergo Michael additions with a variety of nucleophiles. Moreover, due to the chiral sulfur atom, the Michael additions can proceed in a diastereoselective way. One of the first successful asymmetric conjugated addition of carbon nucleophiles to a chiral vinyl sulfoximine was reported in 1986 by Pyne et al. (Scheme 18). The addition of organolithium
reagents or Gilman-cuprates (\(R_2\text{CuLi}\)) occurred from the Si-face at the \(\beta\)-position of the vinyl sulfoximine 49, whereas organocopper compounds (RCu) attacked the double bond from its Re-side. The diastereoselectivity of sulfoximine 50 was quite high (80 to 96\% de) and explained by a complexation model involving the sulfoximine heteroatoms as well as the methoxy group of the auxiliary.

Scheme 18: Michael addition of carbon nucleophile with vinyl sulfoximines.

Aza- and oxa-Michael additions\(^9,96\) were mainly investigated by Gais and Reggelin. Highly substituted enantiomerically pure pyrrolidines, tetrahydrofurans and oxabicyclic systems were synthesized\(^97\) using the highly stereoselective \(\gamma\)-hydroxy- and \(\gamma\)-amino-alkylation reactions\(^97,98\) combined with a stereoselective intramolecular oxa- and aza-Michael addition, respectively (Scheme 19).

Scheme 19: Michael addition of vinyl sulfoximines with oxygen and nitrogen nucleophiles.
Although a variety of nucleophiles were investigated, no phospha-Michael addition of vinyl sulfoximines was reported at the beginning of this project.

1.5. Aim of the Project

Despite the availability of several classes of $P,N$-ligands, there is still a quest for this new type of ligands. Among them, 1,5-$P,N$-ligands, which are prompt to form 6-membered chelate with a transition metal, proved to be very effective in various catalyzed asymmetric transformations (Figure 9). 

![Figure 9: $\beta$-phosphino-sulfoximine and PHOX ligands.](image)

The strategy chosen to access the new class of $P,N$-phosphino-sulfoximines $51$ is based on a phospha-Michael addition of the vinyl sulfoximines to introduce the phosphine functionality (Scheme 20).

![Scheme 20: Retrosynthetic analysis for the synthesis of 1,5-$P,N$-phosphino-sulfoximines.](image)
The first part of this work described the synthesis of acyclic 1,5-$P,N$-phosphino-sulfoximines which were then tested in Pd-catalyzed allylic alkylation. The results obtained with the acyclic 1,5-$P,N$-phosphino-sulfoximines led in the second part to the modification of the ligand backbone and to the design of cyclic 1,5-$P,N$-phosphino-sulfoximines which were also evaluated in Pd-catalyzed asymmetric allylic alkylation.
2. Acyclic Phosphino-Sulfoximines

2.1. Introduction

Due to the pronounced acidity of the NH-proton of free sulfoximine 24 (pKa = 24.3), its substitution by electrophiles is straightforward. Silylation, alkylation, sulfonylation and carbamoylation can easily be achieved.\textsuperscript{100} Also interesting N-vinylation and N-arylation reactions of the sulfoximine 24 were developed by Bolm \textit{et al.}\textsuperscript{101} All these transformations allow the introduction of a broad range of substituents, which have a direct effect on the basicity and the nucleophilicity of the nitrogen, and on the acidity of the protons attached to the S-methyl group. For example, the pKa value of the N-methylsulfoximine 52 is 32, whereas, the pKa of N-tosylsulfoximine 54 is 23.\textsuperscript{102}

![Scheme 21: Functionalization of sulfoximine 24 at the nitrogen atom.](image)

In the present studies, the NH-proton of sulfoximine 24 was substituted by four different groups (Scheme 21, Table 2). An efficient methylation of sulfoximine 24 under Eschweiler-Clark conditions afforded sulfoximine 52 in excellent yield (93%).\textsuperscript{103} The synthesis could be performed on 50 g scale without complication as sulfoximine 52 could be easily purified by distillation. The synthesis of N-benzylsulfoximine 53 was carried out following the protocol of Johnson\textsuperscript{104} by using KH, PhCH\textsubscript{2}Br and Bu\textsubscript{4}NBr as phase transfer catalyst.\textsuperscript{105}

\begin{table}[h]
\centering
\begin{tabular}{llll}
\hline
sulfoximines & R\textsuperscript{1} & reagents & yields (\%) \\
\hline
52 & Me & HCHO, HCO\textsubscript{2}H, H\textsubscript{2}SO\textsubscript{4} & 93 \\
53 & Bn & BnBr, KH, Bu\textsubscript{4}NBr, DME & 90 \\
54 & Ts & TsCl, pyridine & 92 \\
55 & TBDPS & t-BuPh\textsubscript{2}SiCl, imidazole, DMF & 96 \\
\hline
\end{tabular}
\caption{Yields and conditions for the functionalization of sulfoximine 24.}
\end{table}
In this case, an excellent yield of sulfoximine 53 was obtained on a 10 g scale following purification by distillation. Tosylation of sulfoximine 24 using tosyl chloride in pyridine afforded the N-tosylsulfoximine 54 in excellent yield (92%), and silylation using t-BuPh₂SiCl and imidazole in DMF afforded N-t-butyldiphenylsilylsulfoximine 55 in 96% yield. The N-substituted sulfoximines 52–55 were used as starting materials for the following transformations.

2.2. Synthesis of Acyclic Vinyl Sulfoximines

Several protocols have been developed for the synthesis of vinyl sulfoximines. In 1985, Gais et al. reported an “in situ Peterson olefination” for their synthesis. Good yields were obtained with a high E-selectivity. This method has been successfully applied in an asymmetric synthesis of isocarbacyclin. Vinyl sulfoximines are also accessible by using a one pot procedure involving a Wittig-Horner reagent and an aldehyde. This method provides N-tosylsulfoximines in good to excellent yields with high E-selectivity. Vinyl sulfoximines can also be prepared using a hydroxyalkylation/elimination sequence (addition/elimination), which involves the addition of an aldehyde or ketone to a metallated sulfoximine, conversion of the hydroxyl group to a leaving group (sulfonyl, carbonate) and a base-promoted elimination. This procedure was used here to synthesize vinyl sulfoximines 58–61 (Scheme 22).
Thus, the S-methylsulfoximines 52–55 were metallated with \( n\)-BuLi and the resulting anion was trapped with benzaldehyde to give the alkoxides 56 as a mixture of epimers. Alkoxides 56 were not isolated but treated immediately with \( \text{ClCO}_2\text{Me} \) which afforded the corresponding carbonates 57. The elimination was effected by adding DBU as a base to the reaction mixture and the corresponding \( E \)-configured vinyl sulfoximines 58–61 were obtained as single isomer in 85 to 92% yield. The vinyl sulfoximines 58–61 were then tested as Michael acceptors towards secondary phosphines.

2.3. Phospha-Michael Addition of Acyclic Vinyl Sulfoximines

2.3.1. Reactivity of Organophosphorous Compounds

Most phosphines are subject to oxidation and the simple mono-, di and trialkylphosphines have great affinity for atmospheric oxygen. For example, trimethylphosphine vapour is spontaneously inflammable in air. Arylphosphines, especially the tertiary phosphines, are somewhat more stable in this respect. The oxidation of phosphines depends on their basicity.\(^{113}\) Trialkylphosphines are more basic than dialkylphosphines and, therefore, more
reactive toward oxygen. Consequently the handling of phosphines should be performed under an oxygen-free atmosphere using degassed solvents.

The handling of such air sensitive compounds requires precautions and specific apparatus (e.g. Schlenk flasks or glove box), especially for purification processes. Useful methods to overcome this problem have been designed which protect the lone pair of the phosphorus atom. One of these methods is to carry out the synthesis with a phosphorus (V) derivative, which is already oxidized. Phosphine oxides and phosphine sulfides are commonly used. Working with such organophosphorous compounds not only has the benefit of avoiding phosphorus oxidation, it also increased the pKa values of the neighbouring protons, facilitating deprotonation and further functionalizations. However one of the major drawbacks of these protecting groups is that reduction of phosphorus (V) to phosphorus (III) is required. In the case of phosphine oxides, their reduction is carried out using either aluminium hydrides (LiAlH₄ or i-Bu₂AlH) or silanes at elevated temperature (typically 100 °C). In the case of phosphine sulfides, their reduction is typically performed with LiAlH₄, Raney nickel or silane. These methods require relatively harsh reaction conditions and side-reactions can occur at other functional groups in the molecule.

Another approach to overcome oxidation is to protect the phosphine as a phosphine borane adduct. This strategy was used for the first time by Imamoto in the synthesis of chiral phosphines having a stereogenic phosphorus centre. In the same way, phosphines, phosphoramidites and phosphites form an adduct with BH₃, which is more or less labile depending upon the electronic properties of the phosphorus. These borane adducts can be handled like common organic compounds allowing, for example, purification by standard silica gel column chromatography. Moreover, the deboronation is most of the time carried out using an amine under mild conditions. This topic will be developed in detail in section 2.5.
2.3.2. Phospha-Michael Addition of Vinyl Sulfoximine 58

In order to find the optimal conditions for the phospha-Michael addition, different experimental procedures were tested by using the N-methylsulfoximine 58 as substrate (Scheme 23).

\[
\text{58} \xrightarrow{1) 1.1 \text{ equiv. KPPh}_2, \text{THF} \quad -78 \degree C, 30 \text{ min}} \xrightarrow{2) 2.2 \text{ equiv. alcohol} \quad -78 \degree C, 1 \text{ h}} \xrightarrow{3) 4 \text{ equiv. BH}_3\text{-THF,}} \quad 0 \degree C, 2h \quad \xrightarrow{4) 1N \text{ HCl until pH 5}} \text{products 62, 63, 65, and 66.}
\]

Scheme 23: Attempted phospha-Michael addition of vinyl sulfoximine 58 using KPPh₂.

KPPh₂ from a commercial 0.5 M solution in THF was first investigated as nucleophile. The reaction was carried out at −78 °C using 1.1 equiv. of KPPh₂. After 30 min, 2 equiv. of MeOH were added to quench the postulated anion 67 and give the addition products 68 and 69 (Scheme 24).
After 2 h, BH$_3$-THF was added at 0 °C to the reaction mixture and the mixture was stirred for 1 h at RT. The workup was performed using 1N HCl to hydrolyse the excess of borane. Only 18% of the desired phosphino-sulfoximine $62$ could be isolated, together with alkene $64$, bis-phosphine borane $65$ and sulfinamide $66$ (Table 3). However, the phosphine borane $S_3R-$ was formed in excellent diastereoselectivity ($de > 98\%$).

The more hindered alcohol $t$-BuOH was used to protonate anion $67$. Here, the yield of phosphine boranes $62$ and $63$ slightly increased (28%) in detriment to the $de$ (86%).

Evidence for the formation of phosphino-sulfoximine borane $62$ is the broad signal appearing in the $^{31}$P NMR spectrum at 25 ppm, which is typical for a diarylalkylphosphine boranes. Of note, the broadness of the signal is due to the $^{1}J_{P,B}$ coupling.$^{121,122}$
**Table 3:** Product distribution for the phospha-Michael addition of vinyl sulfoximine 58 using KPPh₂.

<table>
<thead>
<tr>
<th>alcohol</th>
<th>conversion of vinyl sulfoximine 58 (%)</th>
<th>isolated yields of products</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOH</td>
<td>100</td>
<td>18 (&gt;98:2)</td>
</tr>
<tr>
<td>t-BuOH</td>
<td>100</td>
<td>28 (93:7)</td>
</tr>
</tbody>
</table>

It was suspected that the alkene 64 and the bis-phosphine borane 65 were formed through the mechanism depicted above (Scheme 24). The anion 67, generated by the addition of KPPh₂ to vinyl sulfoximine 58, is protonated by methanol, which leads to the formation of KOMe and phosphines 62 and 63. The methoxide can then deprotonate phosphines 62 and 63 at the alpha position of the phosphino group and the anion 70 undergoes an E₁CB elimination to form sulfinamide 71 and alkene 72. Moreover, the achiral alkene 72 can act as a Michael acceptor and reacts further with KPPh₂ to afford the bis-phosphine borane 74 without any asymmetric induction (ee = 0%), which is in accordance with the postulated mechanism. The high de value (>98%) of the phosphine borane 62 can be explained either by a highly stereoselective addition of KPPh₂ on the vinyl sulfoximine 58 or by the higher reactivity of the other isomer 69 towards elimination.

An alternative to the use of stoichiometric amount of the nucleophilic salts is to generate the KPPh₂ in situ from diphenylphosphine with a catalytic amount of base. This can be done easily with an equimolar amount of primary or secondary phosphine and a catalytic amount of an alkoxide. At room temperature, the deprotonation of diphenylphosphine by t-BuOK is fast and the addition proceeded smoothly. All of the starting material was consumed within 1 h according to TLC analysis. BH₃-THF was added to the reaction mixture to protect the phosphine and after hydrolysis with HCl, phosphine boranes 62 and 63 were obtained in a 78% combined yield. Unfortunately, the diastereoselectivity decreased under these conditions (dr: 78:22). The major isomer 62 could be isolated from a mixture of both isomers 62 and 63 by crystallization from CH₂Cl₂/hexane.
### Table 4: Phospha-Michael addition of vinyl sulfoximine 58 using various nucleophiles.

<table>
<thead>
<tr>
<th>entry</th>
<th>Conditions</th>
<th>Time (h)</th>
<th>Conversion of vinyl sulfoximine</th>
<th>Yield of phosphine boranes</th>
<th>dr (62:63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1) HPPh₂, 10% t-BuOK, RT 2) BH₃–THF, 0 °C, 2 h</td>
<td>1</td>
<td>100</td>
<td>78</td>
<td>78:22</td>
</tr>
<tr>
<td>2</td>
<td>HPPh₂(BH₃), 10% t-BuOK, 0 °C, 50 h</td>
<td>50</td>
<td>85</td>
<td>41</td>
<td>50:50</td>
</tr>
<tr>
<td>3</td>
<td>LiPPH₂(BH₃), −50 °C, 26 h</td>
<td>26</td>
<td>50</td>
<td>28</td>
<td>69:31</td>
</tr>
</tbody>
</table>

In an attempt to achieve higher diastereomeric excesses of phosphate borane 62, the bulky diphenylphosphine borane was tested in combination with a catalytic amount of t-BuOK. The mixture of phosphate boranes 62 and 63 was isolated in 41% in a ratio of 1:1 (entry 2). A small amount of the saturated sulfoximine 75 was formed as a side product (Scheme 25).

Hydroboration of alkenes using phosphate borane adducts has been studied by Pelter et al. ¹²³ 1-Octene and cyclohexene could be hydroborated with triphenylphosphine borane adduct in 97% yield in both cases. Indeed, the phosphate borane adduct and the free phosphate are in equilibrium. Free borane is therefore present in the reaction mixture and can hydroborate the double bond. Similarly, following the equilibrium depicted below, vinyl sulfoximine 58 is hydroborated by the free borane which is in equilibrium with the phosphate borane adduct and, after acidic treatment, saturated sulfoximine 75 is isolated (Scheme 25). ¹²⁴

![Scheme 25: Hydroboration of vinyl sulfoximine 58 in the presence of HPPh₂(BH₃).](image-url)
In order to induce a better control of the selectivity during the diphenylphosphine addition to vinyl sulfoximine 58, the reaction was carried out at lower temperature. Diphenylphosphine borane was deprotonated with n-BuLi prior to reaction with vinyl sulfoximine 58. Half conversion occurred after one day, and the mixture was worked up. Only 28% of the diastereomeric mixture of 62 and 63 could be isolated with a diastereomeric ratio of 69:31 respectively. Traces of hydroborated sulfoximine 75 were also detected by $^1$H NMR.

2.3.3. Phospha-Michael Addition of $N$-Substituted Vinyl Sulfoximines

The procedure which gave the best yield of phosphine-boranes 62 and 63 was applied to the $N$-substituted vinyl sulfoximines 59–61 (Scheme 26). The results are listed in Table 5.

![Scheme 26: Synthesis of borane protected acyclic phosphino-sulfoximines 62, 63 and 76–81.](image)

**Table 5: Synthesis of borane protected acyclic phosphino-sulfoximines 62, 63 and 76–81.**

<table>
<thead>
<tr>
<th>Vinyl sulfoximine</th>
<th>$R^1$</th>
<th>Phosphino-sulfoximines ($S_S R_C : S_S S_C$)</th>
<th>Yield</th>
<th>Diastereomeric ratio ($S_S R_C : S_S S_C$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>Me</td>
<td>62 : 63</td>
<td>78</td>
<td>78:22</td>
</tr>
<tr>
<td>59</td>
<td>Bn</td>
<td>76 : 77</td>
<td>78</td>
<td>64:36</td>
</tr>
<tr>
<td>60</td>
<td>Ts</td>
<td>78 : 79</td>
<td>70</td>
<td>27:73</td>
</tr>
<tr>
<td>61</td>
<td>TBDPS</td>
<td>80 : 81</td>
<td>80</td>
<td>58:42</td>
</tr>
</tbody>
</table>

The phosphino-sulfoximines 62, 63 and 76–81 were obtained in 70 to 80% yield. For the $N$-methyl- and $N$-benzylvinyl sulfoximine 58 and 59 respectively, the major isomers have both the $S_S R_C$ configuration. But for the $N$-tosyl vinyl sulfoximine 60, the selectivity of the
addition is reversed and the major phosphino-sulfoxime borane 79 has the opposite $S_3R_C$ configuration.

Although the diastereoselectivities of the phospha-Michael addition of the vinyl sulfoximines are not high, the causes of discrimination can be postulated as followed. Both vinyl sulfoximines 58 and 59 ($R^1 = \text{Me and Bn respectively}$) have a basic nitrogen atom, which can form a 6-membered transition state during the addition via coordination of the cation to the nitrogen of the sulfoximine (Scheme 27). Two 6-membered transition states having a chair conformation can be postulated, where the phenyl group of the sulfoximine adopts either an equatorial position ($Re$-face addition) or an axial position ($Si$-face addition). The $Re$-face addition would be favoured because the equatorial position of the phenyl group of the sulfoximine moiety minimizes the 1-3 diaxial repulsions.

![Diagram of favored and disfavored transition states](image)

**Scheme 27:** Postulated 6-membered transition state during the phospha-Michael addition of the vinyl sulfoximines 58 and 59.

In contrary, for sulfoximine 60 having an electrowithdrawing tosyl group, the nitrogen is much less basic. In the case of sulfoximine 61, the bulky silyl group TBDPS prevents any coordination to the nitrogen atom. Consequently for the sulfoximines 60 and 61, the addition will not proceed via the 6-membered transition state depicted in Scheme 27. For sulfoximine
only a coordination via the oxygen atom would be possible and consequently the configuration at the C-stereogenic centre will be opposite.

During the conduct of this research project, Reggelin et al. reported an intermolecular phospha-Michael addition of unsubstituted vinyl sulfoximine 82 (Scheme 28).

The phospha-Michael addition was carried out with the unsubstituted vinyl sulfoximine 82 using HPPh$_2$(BH$_3$) and t-BuOK. Phosphine borane 83 was isolated in 80% yield. In this case, a hydroboration of the activated double bond was apparently not observed.

2.4. Determination of the Absolute Configuration of Acyclic Phosphine Boranes

The absolute configuration of phosphine borane ($R_S$)$_C$-ent-62 was determined by X-ray crystal structure analysis (Figure 10). Crystals of phosphine borane ($R_S$)$_C$-ent-62 suitable for X-ray crystal structure analysis were obtained in CH$_2$Cl$_2$/hexane solution. Phosphine borane ($R_S$)$_C$-ent-62 was synthesized from the corresponding $R$-configured vinyl sulfoximine ent-58. The absolute configuration of the stereogenic carbon atom of phosphine borane ($R_S$)$_C$-ent-62 could be assigned because of the known $R$ configuration of the sulphur atom. Phosphine borane ($R_S$)$_C$-ent-62 crystallized in two symmetric independent molecules in the asymmetric unit. The B-P bond lengths (1.923(3) and 1.922(3) Å) are in the average of P-B bond lengths. Moreover, in the solid state, the borane group is bonded to the phosphorus atom and does not interact with the basic nitrogen atom of the sulfoximine moiety.
The $^1$H and $^{13}$C NMR spectra of $(S_R S_C)$ phosphine borane 62 could be fully assigned with the help of the 2D $^1$H-$^1$H, $^1$H-$^{13}$C and $^{31}$P-$^1$H as well as $^1$H{$^{31}$P} and $^{13}$C{$^{31}$P} NMR spectroscopy (Figure 11 and Figure 12).
An inspection of the signals of the aromatic protons of the $S_3R_C$-configured phosphino-sulfoximine boranes 62, 76 and 78 revealed a similarity for the signals assigned to the protons i, j and k. Indeed, the signal of the ortho and meta protons i and j appear at the same chemical shift at 6.80 ppm and are overlapped, whereas the signals of the para protons k appear at 6.90 ppm (Figure 13). In contrast, the $S_3S_C$-configured phosphino-sulfoximine boranes 77, 63 and 79 do not exhibit the same chemical shift for the ortho and meta protons i and j and their signals are well separated (Figure 13).
Figure 13: Region of the aromatic protons in the NMR spectra of N-substituted phosphino-sulfoximine boranes. $S, R_{C}$ (top) and $S,S_{C}$ (bottom) configuration.
The absolute configuration of acyclic phosphino-sulfoximine boranes were suggested from these observations. Only in the case of the N-silyl phosphino-sulfoximine boranes 80 and 81, the chemical shifts of the protons i, j and k could not be distinguish due to the high number of aromatic protons (total 30). After several trials, a crystal of \( (S,S,R,C) \) phosphino-sulfoximine borane 80 suitable for X-ray crystal structure analysis was obtained in \( n \)-heptane/isopropanol (95:5).

![Figure 14: Structure of phosphino-sulfoximine borane \( (S,S,R,C) - 80 \) in the crystal. Selected bonding parameters: S–O 1.453(4), S–N 1.489(4), C–S 1.796(5), P–B 1.913(5), C–P 1.858(4).](image)

For N-silyl phosphino-sulfoximine boranes 80, the borane group is also bounded to the phosphorus atom and does not interact with the nitrogen atom of the sulfoximine moiety. The P-B bond length is 1.913(6), which is shorter than phosphino-sulfoximine borane \( \text{ent-62} \) (P-B bond length of phosphine borane \( \text{ent-62}: 1.923(3) \)).

### 2.5. Deboronation of Acyclic Phosphine Boranes

As enounced in section 2.3.1, borane is often used as protecting group for phosphines. Several methods have been found to convert the phosphine boranes into tricoordinated phosphines. The most common methods involve a nucleophilic amine such as diethylamine, N-methylmorpholine, TMEDA or DABCO. Brønsted acids (HBF₄ or CF₃SO₂H) can be used for electron-rich phosphines like trialkylphosphines. All these methods proceed with retention of configuration, which is really advantageous for compounds containing a chiral phosphorus atom.

The reaction of a phosphine borane with an amine leads to an equilibrium in which the position of the borane group depends on the relative basicity of the amine and the phosphine.
The more basic phosphorus atom is, the more difficult the cleaving of P-B bond is.

\[ R_3P-BH_3 + NR'_3 \rightleftharpoons PR_3 + R'_3N-BH_3 \]

**Scheme 29:** Equilibrium between phosphine borane and amine borane.

The decomplexation of phosphino-sulfoximine boranes 62, 63 and 76–81 was carried out using 1.1 equiv. DABCO in toluene (Scheme 30). The reaction proceeded smoothly at 40 °C and could be easily monitored by \(^{31}\)P NMR spectroscopy. Phosphino-sulfoximine boranes 62, 63 and 76–81 exhibit a broad singlet around 26 ppm whereas the corresponding free phosphines exhibited a sharp singlet around 1 ppm. After 2 h, complete conversion was observed for phosphino-sulfoximine boranes 62, 63 and 76–80. The equilibrium depicted in Scheme 29 is pulled towards the right side, showing that DABCO is more basic than the free phosphines. Furthermore, the \(^1\)H NMR spectrum exhibited a signal for DABCO-BH\(_3\) at 2.93 ppm. A sharp singlet was also sometimes observed at 3.14 ppm and was attributed to DABCO-(BH\(_3\))\(_2\).

**Scheme 30:** Deboronation of phosphino-sulfoximine boranes 62, 63 and 76–80.

In all cases, the reaction proceeded quantitatively without traces of side products, except for phosphino-sulfoximine borane 79 where the deboronation reaction was not completed due to the low solubility of the compound. The purification of the phosphino-sulfoximines 68, 69 and 84–88 was carried out by passing the crude mixture through a plug of silica gel. The polar DABCO-BH\(_3\) remained on the top of the column and after evaporation of the solvents, phosphines 68, 69 and 84–88 were obtained for most of them as a white solid in >95% yields.
Precautions regarding the exclusion of oxygen were required for the synthetic steps involving the presence of the phosphines and diphenylphosphine since they react with oxygen to give the corresponding phosphine oxide. Therefore, the solvents used for the manipulations of the phosphines were degassed prior to use, and the reactions were performed under argon. All the attempts to purify phosphino-sulfoximines 68, 84 and 87 by crystallization failed. The white solid, which was collected after crystallization exhibited a $^{31}$P NMR signal around 33 ppm, characteristic of diarylalkylphosphine oxides.122b

2.6. Reactivity of Phosphine Boranes and Phosphino-Sulfoximines

Although the phosphino-sulfoximine boranes were stable towards oxygen, they showed a tendency to decompose with formation of the corresponding sulfinamide and phosphino-alkene borane (see section 2.3.2). This degradation was much faster in solution than in the solid state, and the rate of this degradation depended on the substituent attached to the nitrogen of the sulfoximine. The stability of the phosphine boranes decreases in the following order:

$$\begin{align*}
\text{TBDPS} - \text{N} & \text{O} \text{PPh}_2 \text{Ph} \\
\text{Ph} & \text{H}_3 \text{B}
\end{align*}$$

$$\begin{align*}
\text{Ts} - \text{N} & \text{O} \text{PPh}_2 \text{Ph} \\
\text{Ph} & \text{H}_3 \text{B}
\end{align*}$$

$$\begin{align*}
\text{Bn} - \text{N} & \text{O} \text{PPh}_2 \text{Ph} \\
\text{Ph} & \text{H}_3 \text{B}
\end{align*}$$

$$\begin{align*}
\text{Me} - \text{N} & \text{O} \text{PPh}_2 \text{Ph} \\
\text{Ph} & \text{H}_3 \text{B}
\end{align*}$$

80 and 81

78 and 79

62 and 63

**Figure 15:** Stability scale of the phosphino-sulfoximine boranes.

As seen in the previous section, an equilibrium exists between the phosphine borane and the phosphine in the presence of an amine (Scheme 29). Therefore it seems reasonable to suppose that the borane group can migrate from the phosphorus atom to the basic nitrogen of the sulfoximine moiety in an intra- and/or intermolecular way. This would result in an equilibrium between structure I and II ($R^1 = \text{Me, Bn, Ts, } t-\text{BuPh}_2\text{Si}$) (Scheme 31). Phosphino-sulfoximine borane I can deprotonate the $N$-boronato-sulfoximine II which undergoes an elimination. The corresponding $N$-methyl sulfinamide 90 and $N$-benzyl sulfinamide 91 as well as the alkene 64 were isolated for the $N$-methyl phosphino-sulfoximines 62 and 63 and $N$-benzyl phosphino-sulfoximines 76 and 77 respectively.
The simplest way to overcome this problem is to deboronate the phosphino-sulfoximine boranes into phosphines. In fact, the phosphines are oxygen sensitive in solution, but are much more stable towards oxidation in the solid state. Their handling is therefore very easy (no use of a glove box to weigh an appropriate quantity of phosphine). The phosphines were stored under argon at 4 °C, and neither oxidation nor decomposition was observed after 6 months.

The characterisation of phosphino-sulfoximine boranes 62, 63 and 76–80 by high resolution mass spectroscopy was not possible. The high temperature required for the evaporation of the sample and the high energy transfer (electronic impact: 70 eV) during the measurement led to decomposition of the phosphino-sulfoximine boranes.
2.7. Acyclic Phosphino-Sulfoximines in Asymmetric Allylic Alkylation

2.7.1. Phosphino-Sulfoximine 62 in Asymmetric Allylic Alkylation

The phosphino-sulfoximines 68, 69 and 84–88 were tested as ligands in the allylic alkylation of the standard substrate rac-(E)-1,3-diphenyl-2-propenyl acetate rac-43 (Scheme 32). Following the procedure of Trost, the dimethyl malonate anion was generated as nucleophile using the combination of dimethyl malonate, bis-trimethylsilylacetamide (BSA) and a catalytic amount of acetate (typically 1%).

\[
\begin{align*}
\text{Ph} & \quad \text{OAc} \\
\text{Ph} & \quad \text{Ph} \\
43 & \\
+ & \quad \text{MeO}_2\text{C} - \text{CO}_2\text{Me} \\
\text{BSA, MOAc,} & \quad \text{x mol\% ligand} \\
\text{solvent, temperature} & \quad \text{y mol\% Pd}(\text{DBA})_3 \cdot \text{CHCl}_3 \\
\rightarrow & \quad \text{MeO}_2\text{C} \quad \text{CO}_2\text{Me} \\
\text{Ph} & \quad \text{Ph} \\
44 & \\
\end{align*}
\]

Scheme 32: Pd-catalyzed allylic alkylation of acetate 43 using the phosphino-sulfoximines as ligands.

Since this reaction is strongly influenced by the reaction conditions, like the solvent or the counterion, various parameters were first investigated using phosphino-sulfoximine 68 as ligand.

2.7.2. Solvent Variation

A variety of solvents can be used in allylic alkylation ranging from benzene and CH$_2$Cl$_2$ to more polar media such as THF or DMF that strongly influence the reaction rate and the ee value. Therefore, in a first set of experiments, the coordinating polar solvent THF and the less polar non coordinating CH$_2$Cl$_2$ were tested. These experiments were carried out using the crude mixture obtained in the deboronation reaction of phosphine borane 62 with DABCO (Scheme 33). The results are sum up in Table 6.
Scheme 33: Pd-catalyzed allylic alkylation of acetate 43 with ligand 68 and 89.

Table 6: Effect of the solvent and the amount of nucleophile towards the allylic alkylation reaction.

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>m (equiv. of dimethyl malonate)</th>
<th>n (equiv. of BSA)</th>
<th>time (h)</th>
<th>recovered starting material</th>
<th>yield of 44</th>
<th>ee(^{1}) of 44 (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>1.1</td>
<td>1.1</td>
<td>42</td>
<td>84</td>
<td>8</td>
<td>59</td>
</tr>
<tr>
<td>2</td>
<td>CH(_2)Cl(_2)</td>
<td>1.1</td>
<td>1.1</td>
<td>42</td>
<td>36</td>
<td>60</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>THF</td>
<td>2.5</td>
<td>2.5</td>
<td>40</td>
<td>66</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>CH(_2)Cl(_2)</td>
<td>2.5</td>
<td>2.5</td>
<td>30</td>
<td>0</td>
<td>96</td>
<td>60</td>
</tr>
</tbody>
</table>

\(^{1}\) The ee value of malonate 44 was determined by chiral HPLC: chiralcel-OD-H column, detector 254 nm, n-heptane/isopropanol: 95/5, flow: 0.75 ml/min, 40 bar, R\(_t\) ((R)-44): 15.28 min; R\(_t\) ((S)-44): 19.53 min. The absolute configuration of malonate 44 was determined by comparison of the optical rotation with the literature value.\(^{133}\)

The first catalytic reaction was carried out in THF. After 42 h reaction, the malonate 44 was isolated in poor yield (8%) but promising ee (59%, Table 6, entry 1). When the reaction was carried out in CH\(_2\)Cl\(_2\), the yield of the malonate 44 increased to 60% (entry 2). Only a minor decrease of 3% of the enantioselectivity was observed.

To perform a catalytic reaction with complete conversion of the acetate 43, the amount of base (dimethyl malonate and BSA) was raised from 1.1 equiv. to 2.5. This was beneficial in term of kinetic in THF as well as in CH\(_2\)Cl\(_2\). The yield of malonate 44 in THF increased to 22%, while the ee dropped drastically to 25% (entry 3). When performed in CH\(_2\)Cl\(_2\), a complete conversion of acetate 43 was observed and the malonate 44 was obtained in 96% yield with an ee value of 60% (entry 4).

The non-reacted acetate 43 was always recovered in a racemic form, indicating that no kinetic resolution occurred during the reaction.\(^{134}\)
These first experiments showed that the catalytic reactions proceeded faster in CH$_2$Cl$_2$ than in the more polar and coordinating solvent THF, and complete conversions were reached in CH$_2$Cl$_2$ using an excess of nucleophile. The enantioselectivities obtained at this early stage was promising.

2.7.3. Ligand to Metal Ratio, DABCO-BH$_3$ and Counterion Effects

The previous experiments were performed using phosphino-sulfoximine 68, which was synthesized by reaction of phosphine borane 62 and DABCO. After evaporation of the solvent, the crude mixture containing the phosphine 68 and the DABCO-BH$_3$ 89 were used as ligand. As DABCO-BH$_3$ 89 contains a free nitrogen atom which can coordinate to the palladium atom, its influence was investigated.

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>$x$ (equiv. of ligand in mol%)</th>
<th>$y$ (equiv. of Pd in mol%)</th>
<th>cation</th>
<th>yield of 44</th>
<th>ee of 44 (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68 + 89</td>
<td>2</td>
<td>2</td>
<td>K</td>
<td>84</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>68 + 89</td>
<td>3</td>
<td>2</td>
<td>K</td>
<td>96</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>68 + 89$^1$</td>
<td>3</td>
<td>2</td>
<td>K</td>
<td>80</td>
<td>46</td>
</tr>
<tr>
<td>4</td>
<td>68</td>
<td>3</td>
<td>2</td>
<td>K</td>
<td>89</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>68 + 89</td>
<td>4</td>
<td>2</td>
<td>K</td>
<td>99</td>
<td>33</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>6.6</td>
<td>3</td>
<td>K</td>
<td>96</td>
<td>46</td>
</tr>
<tr>
<td>7</td>
<td>68</td>
<td>2</td>
<td>3</td>
<td>K</td>
<td>12</td>
<td>61</td>
</tr>
<tr>
<td>8</td>
<td>68</td>
<td>3</td>
<td>3</td>
<td>K</td>
<td>40</td>
<td>65</td>
</tr>
<tr>
<td>9</td>
<td>68</td>
<td>3</td>
<td>3</td>
<td>NBu$_4$</td>
<td>54</td>
<td>43</td>
</tr>
<tr>
<td>10</td>
<td>68</td>
<td>3</td>
<td>3</td>
<td>Li</td>
<td>96</td>
<td>65</td>
</tr>
</tbody>
</table>

$^1$ The reaction was performed with double amount of solvent.

The role of DABCO-BH$_3$ 89 was not fully understood.$^{135}$ It gave a beneficial effect on the yield of the product 44, but contentious results in term of ee values (Table 7, entry 1-5). The variation of the ligand to metal ratio (L:M) also affected the yield as well as the ee value. When this ratio increased, the yield of the malonate 44 raised, but the ee value decreased.
(entry 6). At a ratio L:M = 1:1, product 44 was isolated in only 40% yield, but with the highest ee (65%, entry 8). At a ratio L:M = 2:3, malonate 44 was isolated in poor yield (12%) with an ee value of 65% (entry 7). A similar study has been reported by Burgess et al. The higher ligand to metal ratio was, the poorer enantioselectivities were obtained. This was explained by the fact that the bidentate phosphine-oxazoline ligand 92 is hemilabile (Scheme 34). Complex 93, formed at L:M ≤ 1:1 and in which the ligand 92 acts as a chelate, could efficiently transfer the chirality to the substrate and thus malonate 44 was obtained in high ee. But complex 94, formed at L:M > 1:1, in which two ligands 92 coordinate as mono-phosphine, led to low ee of malonate 44. As complex 94 catalyzed faster than complex 93, the overall enantioselectivities obtained were lower at L:M ratio higher than 1:1.

Scheme 34: Burgess hemilabile phosphine-oxazoline 92 acting as mono and bidentate ligand in Pd-catalyzed allylic alkylation of acetate 43.

Trost et al. examined the role of the counter ion on the enantioselectivity of the palladium catalyzed allylic alkylation of cyclic allylic carbonates using ligand 17 (Figure 16).
Their studies demonstrated that the bigger the counter ion is, greater the $ee$ value is. For this reason, several counter ions were tested in the catalytic reaction using the ligand 68. The trend which came out from these experiments was reversed to those observed by Trost. The hindered counter ion NBu$_4^+$ was generated following the Trost’s procedure, and interestingly the $ee$ value of malonate 44 decreased (43%) compared to the less hindered cation K (Table 7, entry 9). Therefore the smallest cation Li was tested in the reaction, and malonate 44 was isolated in 96% yield with an $ee$ value of 65% (entry 10). The smallest cation Li proved to be the best choice for this catalytic system and similar observations were reported by Helmchen et al. on the role of the cation.

2.7.4. Phosphino-Sulfoximines 68, 69 and 84–88 in Asymmetric Allylic Alkylation

The acyclic phosphino-sulfoximine ligands 68, 69, 84–88 depicted below (Scheme 35) were tested under the reaction conditions which gave the highest $ee$ value of malonate 44. The results are summarized in Table 8.
ACYCLIC PHOSPHINO-SULFOXIMINES

\[
\text{rac-43} \quad \text{Me-N-} \quad \text{Ph-S-O} \quad \text{PPh}_2 \quad \text{Ph} \\
S\_R_C\_68
\]

\[
\text{Me-N-} \quad \text{Ph-S-O} \quad \text{PPh}_2 \quad \text{Ph} \\
S\_S_C\_69
\]

\[
\text{Bn-N-} \quad \text{Ph-S-O} \quad \text{PPh}_2 \quad \text{Ph} \\
S\_R_C\_84
\]

\[
\text{Ts-N-} \quad \text{Ph-S-O} \quad \text{PPh}_2 \quad \text{Ph} \\
S\_S_C\_85
\]

\[
\text{TBDPS-N-} \quad \text{Ph-S-O} \quad \text{PPh}_2 \quad \text{Ph} \\
S\_S_C\_87
\]

**Scheme 35**: Pd-catalyzed allylic alkylation of acetate 43 using acyclic phosphino-sulfoximines 68, 69, 84–88 as ligands.

**Table 8**: Pd-catalyzed allylic alkylation of acetate 43 using acyclic phosphino-sulfoximines 68, 69, 84–88 as ligands.

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>absolute configuration</th>
<th>T(^{\circ})</th>
<th>solvent</th>
<th>cation</th>
<th>yield of malonate 44</th>
<th>ee of 44 (R) (^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68</td>
<td>S_R_C</td>
<td>RT</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>96</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>69</td>
<td>S_S_C</td>
<td>RT</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>40</td>
<td>−10</td>
</tr>
<tr>
<td>3</td>
<td>84</td>
<td>S_R_C</td>
<td>RT</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>98</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td>S_S_C</td>
<td>RT</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>72</td>
<td>−40</td>
</tr>
<tr>
<td>5</td>
<td>87</td>
<td>S_S_C</td>
<td>RT</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>86</td>
<td>S_R_C</td>
<td>RT</td>
<td>CH(_2)Cl(_2)</td>
<td>K</td>
<td>17</td>
<td>−5</td>
</tr>
<tr>
<td>7</td>
<td>84</td>
<td>S_R_C</td>
<td>−1</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>40</td>
<td>89</td>
</tr>
<tr>
<td>8</td>
<td>84(^1)</td>
<td>S_R_C</td>
<td>−1</td>
<td>CH(_2)Cl(_2)</td>
<td>Li</td>
<td>57</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>84</td>
<td>S_R_C</td>
<td>RT</td>
<td>CH(_3)CN</td>
<td>Li</td>
<td>28</td>
<td>69</td>
</tr>
<tr>
<td>10</td>
<td>84</td>
<td>S_R_C</td>
<td>RT</td>
<td>Toluene</td>
<td>Li</td>
<td>5</td>
<td>88</td>
</tr>
</tbody>
</table>

\(^1\) Using 6 mol% of ligand and palladium.
\(^2\) A – sign refers to the S-configured product which was obtained as major isomer.

Interestingly, using the S\_S_C phosphino-sulfoximine 69 as ligand, the malonate 44 was isolated in 40% yield and 10% ee (Table 8, entry 2). It is worth noting that product 44 have the opposite absolute S-configuration compared to the reaction catalyzed with S\_R_C phosphino-sulfoximine 68. This shows that the stereogenic C-atom but also the stereogenic S-atom plays an important role in the selectivity and activity of the catalyst. The nitrogen
substituent has also a significant effect on the selectivity of the catalyst. While the reaction in
the presence of $N$-methyl substituted phosphino-sulfoximine 68 gave malonate 44 with 65%
$ee$, the $N$-benzyl substituted phosphino-sulfoximine 84 gave product 44 in almost quantitative
yield and 82% $ee$ (entry 1 and 3). Decreasing the reaction temperature to $-1$ °C was
favourable for the enantioselectivities of malonate 44 which increased to 89%, but the
conversion was lower (50%, entry 7). Even an increase of the catalyst loading (3% to 6%) had
only a minor effect on the yield of malonate 44 which increased to 57% (entry 8). The $ee$
value of product 44 was in the same range at 90%.

The $N$-benzyl isomer $S_S_C$85 was also tested in the catalytic experiment and exhibited a
better activity than the $N$-methyl $S_S_C$-isomer 69. Product 44 was isolated in 72% yield with
an $ee$ value of 40% in favour of the $S$-isomer (entry 4). The $S$-configuration of the stereogenic
$C$-atom led in the case of $N$-methyl and $N$-benzyl substituted ligands 69 and 85 to the $S$
configured product 44, whereas the $R$-configuration led to the $R$-configured product 44.

The catalytic experiments carried out with the $N$-tosyl and $N$-silyl substituted ligand 86 and 87
revealed very low activities of these catalysts, in term of yield and enantioselectivities (entry 5
and 6). It is most probably due to the reactivity of the nitrogen atom which is, as previously
pointed out, reacting neither with electrophiles nor Lewis acids.100,138 Therefore it is
meaningful to think that these phosphino-sulfoximines are not coordinating in a bidentate
fashion to the Pd-atom, but most probably as monodentate phosphine. Consequently for
$L:M = 1:1$, there is not enough ligand to coordinate the metal centre to produce an active
catalyst and therefore the reaction rate is low.

Acetonitrile and toluene were tested as solvent in the catalytic experiment using the best
candidate 84. In the first case, the reaction rate diminished and product 44 was isolated in
28% yield with an $ee$ of 69% (entry 9). In contrary, the use of toluene as solvent increased the
$ee$ value of malonate 44 from 82 to 88%, but unacceptable yield (5%) was obtained (entry 10).
Cyclic substrate 95 was investigated in the Pd-catalyzed allylic alkylation in the presence of ligand 68 (Scheme 36). Unfortunately, no conversion was observed after 24 h reaction.

2.7.5. C-N and C-S Bond Formation

Aza nucleophiles were investigated using the crude mixture obtained in the deboronation reaction of the phosphine borane 62 with DABCO. (Boc)₂NH, phtalimide, 1,2,4-triazol and benzyl amine were chosen as nucleophile (Scheme 37).

Unfortunately, none of the catalytic reactions showed any conversion. This may be due to the coordinating properties of amines. The catalyst could be deactivated by coordination of the nucleophile to the metal centre.

A sulfinate was also investigated as nucleophile. The reaction was quenched after 24 hours and vinyl sulfone 97 was isolated in 60% yield with an ee value of 42%. Unfortunately, the absolute configuration of the product was not determined.
2.7.6. Origin of the Selectivity for the Acyclic Phosphino-Sulfoximine Ligands

As asymmetric allylic alkylation has been extensively studied in the mechanistical aspects,\textsuperscript{27} models of the $\pi$-allyl palladium complex bearing the $S_2R_C$ phosphino-sulfoximine ligand 68 or 84 can be drawn (Scheme 38). The 6-membered palladacycle could adopt a boat conformation, which places the phenyl group of the sulfoximine as well as the phenyl group at the C-stereogenic centre in pseudo equatorial position. Thus the 1-3 diaxial interactions will be minimised. A chair conformation will not be favoured because these both phenyl substituents would be in axial position. Following this conformation, the two phenyl groups attached to the phosphorus atom are non-equivalent, e.g. one adopts a pseudo-axial position and the other a pseudo-equatorial position. In the case of PHOX ligands, the two phenyl groups are non-equivalent and therefore induce a discrimination between the \textit{endo} and the \textit{exo} isomers.\textsuperscript{35} Also in this case, two $\pi$-allyl complexes could be formed: the complex 98 where the R substituents of the allyl fragment are above the P-Pd-N plane, and complex 99 where they point below it.

\begin{center}
\textbf{Scheme 38:} Origin of the selectivity using acyclic phosphino-sulfoximines 68 and 84.
\end{center}
The origin of the selectivity depends on the energy difference between the two transition states leading to the Pd(0)olefin complexes \textbf{100} and \textbf{101}. For complex \textbf{101}, steric repulsions between the olefin and the ligand would destabilize the transition state and consequently the attack of the π-allyl complex \textbf{98} would be favoured, leading to the Pd(0)olefin complex \textbf{100}.

\textbf{2.8. Conclusion}

The acyclic phosphino-sulfoximines \textbf{68}, \textbf{69}, \textbf{84–88} were synthesized in a 3 steps procedure in good overall yields starting from \textit{N}-substituted sulfoximines \textbf{52–55}. The feasibility of the phospha-Michael addition of substituted vinyl sulfoximines was demonstrated and applied to introduce the phosphine functionality. The diastereoselectivities of these additions were low to moderate, allowing the screening of both isomers of the phosphino-sulfoximine in Pd-catalyzed allylic alkylation. Both the sulfoximine moiety and the proper (\textit{R})-configuration at the stereogenic \textit{C}-atom are required to induce a high level of selectivity in the catalytic process. A matched (\textit{S}_3\textit{R}_3) and a mismatched (\textit{S}_3\textit{R}_5) effect were observed for these phosphino-sulfoximines. Moreover, the non-coordinative solvent CH$_2$Cl$_2$, as well as the lithium counterion were required to achieve excellent yield and high enantioselectivity toward the substrate (\textit{E})-1,3-diphenyl-2-propenylacetate \textbf{43} with dimethyl malonate. The use of amine as nucleophile completely inhibited the catalytic reaction and acyclic phosphino-sulfoximine \textbf{68} did not show any activity towards cyclic substrate 2-cyclohexenylacetate \textbf{95}. The investigation of the ligand to metal ratio revealed that a L:M = 1:1 was required to achieve high enantioselectivities. The fact that the acyclic phosphino-sulfoximine coordinates in a monodentate fashion at higher L:M ratio could not be excluded. This could mean that the acyclic phosphino-sulfoximines are hemilabile. The substituent at the nitrogen atom of the sulfoximine is also crucial in the chelation of the metal centre and to induce a high degree of enantiocontrol.
3. Cyclic Phosphino-Sulfoximines

The enantioselectivities obtained with the acyclic phosphino-sulfoximines in Pd-catalyzed allylic alkylation of (E)-1,3-diphenyl-2-propenylacetate 43 were high, especially in the case of phosphine 84. The optimisation of the ligand structure was required to achieve even greater ee values. As seen in the preview chapter, the hemilability of acyclic phosphino-sulfoximine ligands was suggested by the drop in enantioselectivity at high L:M ratio. Indeed, the S–CH₂ as well as the CH₂–CH sp³ bonds can easily rotate, making both coordinating sites N and P to move away from each other (Figure 17). Thus, a bidentate coordination mode will not be favoured.

![Image of cyclic phosphino-sulfoximine backbone](image)

Figure 17: Design of a more conformational stable phosphino-sulfoximine backbone.

Therefore, both sulfoximine and phosphino groups were embedded into a more conformational stable backbone to confine its flexibility. Both coordinative nitrogen and phosphorus atoms would be forced to stay close to each other, and thus chelate the metal centre.
3.1. Synthesis of Cyclic Vinyl Sulfoximines

As the phospha-Michael addition methodology proved to be successful for the acyclic vinyl sulfoximines, the same strategy was planned to introduce the phosphino functionality to synthesize cyclic phosphino-sulfoximines. To access the key intermediate cyclic vinyl sulfoximine 102, three retrosynthetic pathways were designed (Scheme 39). The first route (A) involved a halogenation-dehydrohalogenation sequence of cycloalkyl derivative 103. The route B involved the formation of carbanions in alpha position of vinyl sulfoximines, which was already reported.\textsuperscript{139,140} The intermediate 104 could be synthesized via the well established Addition-Elimination one-pot procedure. The third pathway C involved a ring closing metathesis of triene 105, which could be accessed from vinyl sulfoximine 106. The vinyl sulfoximine 106 would also be synthesized by the one-pot Addition-Elimination procedure.
Scheme 39: Retrosynthetic analysis of cyclic phosphino-sulfoximine.
3.1.1. Route A: Dehydrohalogenation

This first route involves the formation of the carbocycle moiety prior to the formation of the alkene functionality by dehydrohalogenation. Following the procedure described by Peter Bruns, sulfoximine 107 was prepared starting from sulfoximine 52 and dibromopentane (Scheme 40).

As reported, only 50% of the desired sulfoximine 107 was isolated. Indeed, sulfoximine 52 is metallated with n-BuLi and alkylated to give ω-bromo-sulfoximine 109. As soon as this alkylation occurs, ω-bromo-sulfoximine 109 is deprotonated by lithiated sulfoximine 108, and cyclizes faster than the alkylation of lithiated sulfoximine 108. Consequently only 50% yield can be obtained among with 50% of starting material 52. Optimisation of the reaction using 2.2 equiv. of base (n-BuLi or LDA) was not successful.

The next step involved the halogenation of the tertiary carbon atom of sulfoximine 107. In 1978, Johnson reported an efficient chlorination procedure of sulfoximines involving t-butyl-hypochlorite. If this procedure works well for the chlorination of the N-S-dimethylsulfoximine 52, they were not able to achieve the chlorination of the cyclohexyl derivative 107. Four years later, Johnson published the halogenation of N-tosylsulfoximines using hexahalooethanes. Under these conditions, mono-, bis- and tri-substituted α-halosulfoximines were synthesized. Following this procedure, no reaction occurred on sulfoximine 107 (Scheme 41). This is probably due to the pKa difference between the N-
methyl- and the \(N\)-tosylsulfoximines.\(^{100}\) Therefore NaH, which was used as base for the \(N\)-tosylsulfoximines, is not strong enough to deprotonate \(N\)-methylsulfoximine 107. The use of \(n\)-BuLi was required to achieve the deprotonation of sulfoximine 107 and addition of 2 equiv. of 1,2-dibromo-1,1,2,2-tetrachloroethane led to a 55:45 inseparable mixture of \(\alpha\)-chloro and \(\alpha\)-bromosulfoximines 111 and 112 respectively in 91\% yield (Scheme 41).

\[
\begin{align*}
1 &. 3 \text{ equiv. NaH} \\
2 &. 2 \text{ equiv. BrCl}_2\text{CCl}_2\text{Br} \\
\text{DMF}
\end{align*}
\]

\[
\begin{align*}
\text{Me-N=S} & \quad \text{1. 1.1 equiv. } n\text{-BuLi} \\
\text{Ph} & \quad 2. 2.0 \text{ equiv. BrCl}_2\text{CCl}_2\text{Br} \\
\text{DMF} & \text{THF, 91\%}
\end{align*}
\]

Scheme 41: \(\alpha\)-halogenation of cyclohexylsulfoximine 107.

The GC-MS spectra of the mixture of 111 and 112 confirmed the presence of a chloride and a bromide atom. This inseparable mixture was then subjected to dehydrohalogenation upon treatment with \(t\)-BuOK in THF. Sulfinamide 90 and cyclohexylsulfoximine 107 were isolated as major products. Only traces of the desired product could be detected (afterwards) in the crude \(^1\)H NMR. A mechanism for the formation of these side products is proposed below (Scheme 42).

\[
\begin{align*}
\text{pathway 1: } & \text{E}_2 \text{ mechanism} \\
\text{pathway 2: } & \text{X-philic reaction}
\end{align*}
\]

Scheme 42: Postulated mechanism for the formation of compounds 90 and 107.
As the $^1$H and $^{13}$C NMR spectra of both chloro and bromo-sulfoximines 111 and 112 exhibit similar chemical shifts, their conformation should be the same. Although their conformation in solution is not known, the sulfoximine group could adopt an axial position to explain the formation of sulfimamide 90 through an E$_2$ mechanism. If the sulfoximine moiety would be in equatorial position, the halogen would adopt an axial position, and the dehydrohalogenation would be favoured. The formation of the dehalogenated sulfoximine 107 can be rationalized by a bromo- and/or chlorophilic reaction.\textsuperscript{145}

As route B was giving more promising results, the dehydrohalogenation reactions were not further studied using different bases (nitrogen containing bases such as DBU or quinoline)\textsuperscript{141} and solvents.

### 3.1.2. Route B: Alpha Lithiation and Cyclization

The second route was planned on the basis of several results. First the Addition/Elimination route is a well established procedure which gives very good to excellent yield using functionalized aldehydes.\textsuperscript{146} The second step involving the deprotonation of a vinyl sulfoximine in α-position is known\textsuperscript{139} and was also investigated in the laboratory.\textsuperscript{140} The cyclization of such systems with the parent functional group sulfoxide was reported by Tanaka et al. under treatment of bromo and iodo sulfoxides 113 with LDA at –78 °C in THF (Scheme 43).\textsuperscript{147}

![Scheme 43: Cyclization of vinyl sulfoxides 113.](image_url)

The 5, 6 and 7 membered ring sulfoxides 114 were isolated in very good yields (81, 82 and 79\% respectively) without loss of chirality at the sulphur atom, which could occur in the case of sulfoxides.\textsuperscript{148} It was postulated that the base deprotonated the sulfoxide 113 to give the α-lithio vinyl sulfoxide which underwent cyclization to give the cyclic vinyl sulfoxide 114. Even the (Z) configured sulfoxide was subjected to the standardized reaction conditions and
also led to the same product 114, presumably via rapid Z-E isomerization of the double bond. The Z-E isomerization was also observed in the case of vinyl sulfoximines, but at higher temperature.\(^\text{140}\)

ω-Bromo-vinyl sulfoximines 115 and 116 were synthesized starting from sulfoximines 52 and 53 respectively and 5-bromo-pentanal in good yields (83 and 73\%, Scheme 44). 5-Bromo-pentanal was prepared by Swern oxidation from the commercially available 5-bromo-pentanol.\(^\text{149}\)

\[
\text{Scheme 44: Synthesis of } \omega\text{-bromo-vinyl sulfoximines 115 and 116.}
\]

ω-Bromosulfoximines 115 and 116 were purified by flash column chromatography but were still contaminated by a non identified side product which could not be removed by preparative HPLC. The ω-bromosulfoximines 115 and 116 were not stored for a long time but further subjected to cyclization due to slow decomposition of these compounds. Based on Tanaka’s work, the cyclization reaction was initiated by deprotonation at the α-position of the sulfoximine moiety using LDA as base (Scheme 45). The cyclic vinyl sulfoximines 117 and 118 were obtained in very good yields (80 and 92\% respectively).

\[
\text{Scheme 45: Synthesis of cyclic vinyl sulfoximines 117 and 118.}
\]
The use of 1.5 equiv. LDA diminished the yield of cyclic sulfoximine 118 and allyl sulfoximine 119 were formed as side products in 8% yields as a mixture of epimers (Scheme 46).

![Scheme 46: Formation of the allyl sulfoximine 119 as side product using an excess of base.](image)

Both cyclic vinyl sulfoximines 117 and 118 were then tested as Michael acceptor in the phospha-Michael addition.

### 3.2. Phospha-Michael Addition of Cyclic Vinyl Sulfoximines

Both cyclic vinyl sulfoximines 117 and 118 were tested in the phospha-Michael addition using the standardized procedure developed for the acyclic substrates (Scheme 47). As 2 stereogenic centers are generated, four possible diastereomers can be formed. In both cases, only the trans isomers $S_S R_C R_C$ and $S_S S_C S_C$ were isolated in good yields with a $dr$ of 1:1:0:0 (determined by $^1$H NMR, Table 9). The formation of the cis isomers might be prevented by steric repulsions between the sulfoximine and the phosphino borane group. The isomers $S_S R_C R_C$ and $S_S S_C S_C$ could be easily separated by flash chromatography.
**Scheme 47:** Synthesis of cyclic phosphine boranes 120–123 via Michael addition.

**Table 9:** Synthesis of cyclic phosphine boranes 120–123.

<table>
<thead>
<tr>
<th>Starting material</th>
<th>R</th>
<th>Products</th>
<th>$d_r$</th>
<th>yield (%)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$S_3R_2R_C$</td>
<td>$S_3S_2S_C$</td>
<td>$S_3R_2S_C$</td>
<td>$S_3S_2R_C$</td>
</tr>
<tr>
<td>117</td>
<td>Me</td>
<td>120:121:124:125</td>
<td>1:1:0:0</td>
<td>35</td>
<td>46</td>
</tr>
<tr>
<td>118</td>
<td>Bn</td>
<td>122:123:126:127</td>
<td>1:1:0:0</td>
<td>41</td>
<td>39</td>
</tr>
</tbody>
</table>

As discussed above (section A.2.6), the acyclic phosphine boranes tend to fragment into sulfinamide and alkene. This is also true for the cyclic phosphine boranes, especially for $N$-methyl substituted phosphine boranes 120 and 121 which rearrange very fast in solution as well as “neat”. Therefore phosphine boranes 120 and 121 were subjected to deboronation directly after purification by flash column chromatography to avoid this rearrangement.
3.3. Optimisation of the Diastereoselectivity of Phospha-Michael Addition of Cyclic Vinyl Sulfoximines

The diastereomeric ratio obtained in the phospha-Michael addition of \( N \)-methyl cyclic vinyl sulfoximine 117 and \( N \)-benzyl cyclic vinyl sulfoximine 118 was 1:1:0:0 in both cases, and only the trans-isomers (\( S_5R_5R_5 \)) and (\( S_5S_5S_5 \)) were formed. To obtain a higher overall yield of the desired phosphino-sulfoximine, a more diastereoselective phospha-Michael addition of the cyclic vinyl sulfoximine 117 and 118 was investigated.

3.3.1. Diastereoselective Phospha-Michael Addition with Substrate Control

The phospha-Michael addition of vinyl sulfoximine with diphenylphosphine is a base catalyzed reaction, but the sulfoximine has itself a basic feature. Therefore, speculations were done about a hypothetical 6-membered transition state where an intermolecular hydrogen bond between the acidic proton of diphenylphosphine and the basic nitrogen of cyclic vinyl sulfoximine 118 would direct the addition (Figure 18).

![Figure 18: Speculated 6-membered transition state during the phospha-Michael addition of cyclic vinyl sulfoximines 117 and 118 and HPPh2 without addition of base.](image)

The first reaction was performed in toluene to increase the hydrogen bonding between cyclic vinyl sulfoximine 118 and diphenylphosphine but unfortunately, no reaction was observed at RT for 12 h nor at 70 °C. Even neat, the reaction did not proceed at RT, 90 °C nor 130 °C during 1 day (Scheme 48). Some decomposition of the starting material was observed.
Cyclic Phosphino-Sulfoximines

The pKa value of a protonated N-methylsulfoximine is around 11, whereas the pKa value of diphenylphosphine is 22.9. This large difference of pKa values may be the reason why the reaction did not occur.

The role of the cation during the phospha-Michael addition was also investigated at room temperature using t-BuOLi instead of t-BuOK. Unfortunately, the reaction catalyzed by the lithium salts did not occur. This may be due to the stronger ion pair of t-BuOLi compared to t-BuOK.

The hydrophosphination was also investigated under acidic conditions to enhance the electrophilicity of the Michael acceptor. Yao reported a titanium catalyzed
hydrophosphonylation of activated alkenes.\textsuperscript{152} The reaction was catalyzed by 14 mol\% Ti(OiPr)\textsubscript{4} but no conversion was observed after 24 hours (Scheme 49).

The phospha-Michael addition of acyclic vinyl sulfoximine \textsuperscript{58} with KPPH\textsubscript{2} at $-78$ °C and subsequent treatment with MeOH as proton source was not satisfactory due to the basicity of the generated KOMe (section 2.3.2). The stronger acid camphorsulfonic acid was used to quench the reaction because its conjugated base should not interfere during the reaction. Moreover, camphorsulfonic acid is a solid and therefore easier to handle as a liquid for small scale reactions. A closer look to the pKa values of the protagonists in this reaction revealed that HPPH\textsubscript{2} (pKa = 22.9) is more acidic than the phosphinosulfoximine (pKa > 32) and thus, the anion \textsuperscript{128} could be protonated by a further equivalent of HPPH\textsubscript{2} (Scheme 50).

\begin{center}
\begin{tikzpicture}

\node [compound, rectangle, draw] (a) at (0,0) {Bn\textsubscript{2}N\textsubscript{O}Ph\textsubscript{2}};
\node [compound, rectangle, draw] (b) at (2,0) {Bn\textsubscript{2}N\textsubscript{O}PPh\textsubscript{2}};
\node [compound, rectangle, draw] (c) at (4,0) {Bn\textsubscript{2}N\textsubscript{O}PPh\textsubscript{2}};

\draw [thick, <->] (a) -- (b) node [midway, above] {$\text{THF}$};
\draw [thick, <->] (b) -- (c) node [midway, above] {$\text{MeOH}$};
\draw [thick, <->] (c) -- (a) node [midway, below] {$\text{HPPH}_2$};
\draw [thick, <->] (a) -- (b) node [midway, below] {$\text{LiPPh}_2$};
\draw [thick, <->] (b) -- (c) node [midway, below] {$\text{KPPH}_2$};
\draw [thick, <->] (c) -- (a) node [midway, above] {$\text{HPPH}_2$};
\end{tikzpicture}
\end{center}

\textbf{Scheme 50:} Phospha-Michael addition of cyclic vinyl sulfoximine \textsuperscript{118} using an excess of HPPH\textsubscript{2} as proton source.

The first set of experiments was carried out at low temperature either using LiPPh\textsubscript{2} (generated by reaction of $n$-BuLi with HPPH\textsubscript{2}) or KPPH\textsubscript{2} (from a commercial 0.5 M solution in THF). Different ratios of diphenylphosphine and metallated diphenylphosphide were tested and the results are summarized below (Table 10).
Table 10: Phospha-Michael addition of cyclic vinyl sulfoximine 118 using an excess of HPPh₂ as proton source.

<table>
<thead>
<tr>
<th>equiv. HPPh₂</th>
<th>equiv. MPPh₂</th>
<th>cation</th>
<th>Time (min)</th>
<th>Diastereomeric ratio (S₈R₈C₈:S₈S₈C₈: S₈R₈C₈:S₈S₈C₈)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>1.9</td>
<td>Li</td>
<td>60</td>
<td>1:3:0:0</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>Li</td>
<td>10</td>
<td>1:2.3:0:0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>K</td>
<td>30</td>
<td>1:2.5:0:0</td>
</tr>
</tbody>
</table>

At lower temperature, the addition of diphenylphosphide proceeded in a more selective way. Changing the amount of diphenylphosphine and diphenylphosphide as well as the cation had a minor effect of the diastereomeric ratio. In all the cases, the major isomer was the \((S₈S₈C₈)\) configured phosphine borane 123. These experiments showed that at low temperature, the sulfoximine moiety directs the addition of HPPh₂ to the \(\text{Si}\) face of cyclic vinyl sulfoximine 118.

The phospha-Michael addition of the cyclic and acyclic vinyl sulfoximines using diphenylphosphine and a catalytic amount of \(n\)-BuLi at low temperature was not investigated but with consideration, these reaction conditions could have been tested.

3.3.2. Diastereoselective Phospha-Michael Addition Using Chiral Catalysts

Chiral phosphines, which are valuable ligands for metal-catalyzed enantioselective transformations, are generally prepared either from an enantiopure starting material, by resolution, or by using a stoichiometric amount of chiral auxiliary.\(^{87}\) Although hydrophosphinations proved to be valuable for the synthesis of phosphines, methodologies for enantioselective P-H additions are limited.\(^{153}\) The use of metal catalyzed processes is not trivial due to the coordination ability of the phosphorus atom. Even though, a few metal catalyzed asymmetric hydrophosphinations were reported using lanthanide or aluminium\(^{154}\), platinum\(^{155}\) and nickel\(^{153}\) catalysts.

Togni \textit{et al.} reported an asymmetric hydrophosphination of methacrylonitrile using a chiral nickel catalyst (Scheme 51). Methacrylonitrile coordinates to the nickel centre via the nitrile nitrogen which enhance the electrophilicity of the activated double bond.
Thus, the addition of secondary phosphine is much more facilitated, and as the methacrylonitrile ligand is sterically contained within a chiral environment, the overall process induces chirality.

Chemists overcame the problem of the coordination capability of the phosphorus atom to metal centres using organocatalysts, and some processes are very efficient.\textsuperscript{156} Even though, the use of secondary amine based catalysts implies the formation of an iminium ion\textsuperscript{157} or an enamine\textsuperscript{158} and therefore the presence of an aldehyde or a ketone is required, limiting the scope of such catalysts. Chiral organocatalysts derived from alkaloids as well as phase transfert catalysts proved also to be effective catalysts in asymmetric alkylations and Michael additions of glycerine derivatives.\textsuperscript{159}

Asymmetric hydrophosphination of styrene derivative was reported by Melchiorre \textit{et al.} using cinchona alkaloid derivatives (Scheme 52).\textsuperscript{160} Using (DHQ)\textsubscript{2}PHAL 131 as catalyst, phosphine borane 130 was obtained in poor \textit{ee} (18\%) but in promising 76\% yield.
Cyclic Phosphino-Sulfoximines

Scheme 52: Asymmetric organocatalytic hydrophosphination of nitrostyrene using cinchona alkaloids derivatives.

After a short catalyst screening, the bifunctional thiourea derivative 132 proved to be the most efficient for this transformation. Phosphine borane 130 was isolated in 86% yield with an ee value of 67%. The amino group of catalyst 132 activates the phosphino group whereas the thiourea functionality activates the nitro group, which leads to a better stereocontrol.

The commercially available quaternary ammonium salt 134 was tested as phase transfer catalyst for the diastereoselective phospha-Michael addition of cyclic vinyl sulfoximines 117 and 118 with diphenylphosphine (Scheme 53). The results are listed in Table 11. The first reaction was performed in CH₂Cl₂ using 10% of chiral quaternary ammonium salt 134 and BTPP 133 as a base (Figure 19, Table 11, entry 2).

![Figure 19: Schwesinger base BTPP 133.](image)

The advantages of using the Schwesinger base 133 are multiple: it is a non ionic base and therefore soluble in many organic solvents, and the pKa is rather high (pKa = 17 in
DMSO).\textsuperscript{161} No conversion was observed after 24 h (entry 2), which may be due to the ability of the base to deprotonate diphenylphosphine, i.e. a too low pKa value.

![Chemical Structure]

Scheme 53: Diastereoselective phospha-Michael addition of cyclic vinyl sulfoximine 117 and 118 using the chiral ammonium salt 134.

Table 11: Diastereoselective phospha-Michael addition of cyclic vinyl sulfoximine 117 and 118 using the chiral ammonium salt 134.

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>concentration of substrate (mol/L)</th>
<th>phosphorous reagent (equiv.)</th>
<th>Base</th>
<th>equivalent of 134</th>
<th>solvent</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>118</td>
<td>0.125</td>
<td>HPPH2 (1.1)</td>
<td>t-BuOK</td>
<td>-</td>
<td>THF</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>118</td>
<td>0.3</td>
<td>HPPH2 (1.4)</td>
<td>133</td>
<td>0.1</td>
<td>CH2Cl2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>117</td>
<td>0.06</td>
<td>HPPH2 (1.1)</td>
<td>t-BuOK</td>
<td>0.1</td>
<td>THF</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>117</td>
<td>0.13</td>
<td>HP(O)PH2 (1.1)</td>
<td>133</td>
<td>0.1</td>
<td>CH2Cl2</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>117</td>
<td>0.19</td>
<td>HP(O)PH2 (1.1)</td>
<td>t-BuOK</td>
<td>-</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>118</td>
<td>0.03</td>
<td>HPPH2 (1.1)</td>
<td>t-BuOK</td>
<td>0.1\textsuperscript{1}</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>118</td>
<td>0.005</td>
<td>KPPH2 (1.1)</td>
<td>t-BuOK</td>
<td>1.1</td>
<td>THF</td>
<td>0</td>
</tr>
</tbody>
</table>

\textsuperscript{1} The NR\textsuperscript{4} 134 was dried over P\textsubscript{2}O\textsubscript{5} under high vacuo for 3 days.

A second experiment was carried out using t-BuOK as base in THF (entry 3). Due to the rather low solubility of quaternary ammonium salt 134 in THF, the amount of solvent was increased. Nevertheless after 24 h, the reaction was treated with BH\textsubscript{3}−THF and worked up. Around 10% conversion was observed by \textsuperscript{1}H NMR spectroscopy.

The more acidic diphenylphosphine oxide (pKa = 20.6 in DMSO)\textsuperscript{113} was chosen as nucleophile (entry 4). The pKa difference between the acid (diphenylphosphine oxide) and the base 133 is around 3.6 units. Disappointingly, the reaction did not proceed even after 24 h. As
the reactivity of the diphenylphosphine oxide towards vinyl sulfoximines was not investigated, the standard conditions for the phospha-Michael addition, i.e. the use of $t$-BuOK as base were tested (entry 5). Interestingly, the addition did not occur.

The reactivity of organophosphorus compounds in the Pudovik reaction was investigated by Koenig et al. Radical as well as anionic pathways were studied and from the experimental results the following order of reactivity was proposed:

$$(\text{EtO})_2\text{P(O)H} < \text{Ph}_2\text{P(O)H} < \text{Ph}_2\text{P(S)H} < \text{Ph}_2\text{PH}$$

pKa: $20.8, 20.7, 12.8, 22.9$

The order of the reagents in the reactivity scale corresponds to the one in the acidity scale except for diphenylphosphine which is out of line dramatically. This explains why the phospha-Michael addition did not occur with diphenylphosphine oxide.

When the phospha-Michael additions were not performed under strict oxygen-free conditions, no conversion of the vinyl sulfoximine was observed. If 10% of HPPh$_2$ is oxidized to the corresponding phosphine oxide, the catalytic amount of $t$-BuOK will deprotonate preferentially the more acidic phosphine oxide and thus, the reaction will be inhibited.

The quaternary ammonium salt 134 was dried over P$_2$O$_5$ during 3 days under high vacuo to remove the residual water which could hydrolyse the base, and the reaction was repeated but without success (entry 6). In a last experiment, the quaternary ammonium salt was used in equimolar amount with KPPh$_2$. As KBr is low soluble in THF, HPPh$_2$ and quaternary ammonium salt 134 would be forced to build an ion pair. But also in this reaction, no conversion of the cyclic vinyl sulfoximine was observed. A quinoline derivative could be isolated after column chromatography, as well as an aromatic phosphorated unidentified compound.

Interestingly, the phospha-Michael addition proceeds smoothly without quaternary ammonium salt 134 but is inhibited by its use. Several side reactions can be considered. Quinolines react in position 2 under treatment with an organolithium or Grignard reagents to form the corresponding functionalized dihydroquinolines. This type of nucleophilic addition with potassium diphenylphosphide can not be excluded but seems improbable. Upon prolonged treatment over KOH, quaternary ammonium salts 134 reacts to afford the enol
ether 135 (Scheme 54). Interestingly, in the presence of a nucleophile, a substitution occurred and led to the tertiary amine 137 and to the alkylated iminoester 138.  

![Scheme 54: Decomposition of quaternary ammonium salt](image)

3.4. Determination of the Absolute Configuration of the Cyclic Phosphine Boranes

The configuration of phosphine boranes 120–123 was determined by $^1$H, $^1$H($^{31}$P), 2D $^1$H-$^1$H, $^1$H-$^1$C, $^1$H-$^{31}$P NMR and NOE experiments and was later confirmed by a X-ray crystal structure analysis of phosphine borane 122. For cyclic phosphine boranes 120–123, no coupling as well as no correlation peaks in 2D $^1$H-$^1$H spectrum was observed between the protons $\alpha$ to sulfoximine moiety (proton H$_a$, Figure 20) and $\alpha$ to phosphino group (proton H$_b$). Protons H$_a$ and H$_b$ were unambiguously assigned by 2D $^1$H-$^1$C spectroscopy. Indeed, C$_a$ and C$_b$ are both tertiary carbons. C$_a$ appears around 60 ppm, which is typical for a sp$^3$ carbon atom in alpha position of a sulfoximine group. C$_b$ appears around 25-30 ppm, which is also typical for a sp$^3$ carbon atom in alpha position of a borane protected diphenylphosphino group. Furthermore, both carbon atoms C$_a$ and C$_b$ are coupled with the phosphorus atom and appear as doublet.
According to the Karplus equation, this would imply a dihedral angle between these two protons of nearly 90 °. Therefore, in the most favoured conformation, both sulfoximine moiety and phosphino group should adopt almost an axial position: both substituents are in trans position to each other. However, for a dihedral angle of 180 ° between the sulfoximine and the phosphino group, the dihedral angle between protons H\textsubscript{a} and H\textsubscript{b} would be around 60 °. Therefore the dihedral angle between the sulfoximine and the phosphino group should be significantly smaller, around 140 °. Moreover a NOE was observed between both protons H\textsubscript{a} and H\textsubscript{b} in the phosphine boranes 120 and 121. The NOE observed by irradiation the protons H\textsubscript{a} and H\textsubscript{b} of the phosphine boranes 120 and 121 are depicted below (Figure 21 and Figure 22).

Figure 20: General formula of cyclic phosphine boranes and nomination of the ring protons.

Figure 21: NOE observed by irradiation of proton H\textsubscript{a} (left) and H\textsubscript{b} (right) in the phosphine borane 120.
For phosphine boranes 120–123, both protons H_a and H_b exhibit a multiplicity of doublet of doublet. Each proton H_a and H_b is coupled with the phosphorus atom and with the neighbour protons H_{fax} and H_{cax} respectively. The $^3J_{Ha-Hfeq}$ and $^3J_{Hb-Hceq}$ coupling are not observed and are therefore smaller than 2 Hz. The J values are represented in Figure 23.

It is worth noting that in the four phosphine boranes 120–123, the sulfoximine moiety should adopt a conformation in which the smallest substituent, the oxygen atom, points below the cyclohexyl ring to minimise the steric interactions, whereas the N-methyl and the phenyl substituents are directed in the opposite direction. A major difference is observed in the $^1$H NMR spectra of $S,S,R,R_C$ configured phosphine boranes 120 and 122 and $S,S,S,S_C$ configured phosphine boranes 121 and 123. In the case of the $S,S,R,R_C$ configured phosphine boranes 120 and 122, the proton H_b appears at 4.57 ppm and 4.70 respectively, which is close to the average value found for the acyclic phosphine boranes (4.5 ppm). In contrary, for the $S,S,S,S_C$ configured phosphine boranes 121 and 123, the proton H_b arises at 3.53 and 3.70 ppm respectively, which is a high field displacement of 1.07 and 1.00 ppm respectively. In fact for
the phosphine boranes 121 and 123, the proton $H_b$ is in the anisotropic cone exerted by the phenyl ring of the sulfoximine moiety which induces an upfield displacement (Figure 24).

![Figure 24: Anisotropic effect of the phenyl group of the sulfoximine moiety in cyclic phosphine boranes 120–123.](image)

In the case of $S_3R_C R_C$ configured phosphine boranes 120 and 122, the $H_{\text{eq}}$ proton is affected by the anisotropic cone of the phenyl group of the sulfoximine moiety. For the phosphine borane 120, this induces a high field displacement of 0.73 ppm for the $H_{\text{eq}}$ proton and 0.09 ppm for the $H_{\text{ax}}$ proton compared to phosphine borane 121. This induces a high field displacement of 0.79 ppm of proton $H_{\text{eq}}$ of the phosphine borane 122 compared to phosphine borane 123.

Due to these chemical shifts similarities, the absolute configuration of the phosphine boranes 120 and 122 was assigned as $S_3R_C R_C$ and the absolute configuration of the phosphine boranes 121 and 123 was assigned as $S_3S_C S_C$. The absolute configuration of the phosphine borane 122 was unambiguously confirmed by an X-ray crystal structure analysis (Figure 25). Single crystals of phosphine borane 122 suitable for X-ray crystal structure were grown at $-26^\circ C$ in ether.
The crystal contains two symmetrically independent molecules in the asymmetric unit. The P-B bond length is 1.927(6), which is almost the same as in the acyclic phosphine borane ent-62 (1.923(3)) but longer than in the phosphine borane 80 (1.913(5)). The sulfoximine moiety as well as the phosphino group adopts an axial conformation. The dihedral angle between the phosphorus and the sulphur atom is 140.7 °, and the one calculated between H₄ and H₅ is nearly 82 °. This is in accordance with the spectroscopic data obtained in solution. In the crystal structure, the oxygen of the sulfoximine moiety points towards the cyclohexyl ring and thus reduces steric hindrances. The conformation adopted by the phosphine borane 122 in the crystal and in solution should be similar at least for the P-C-C-S part and the sulfoximine moiety.

3.5. Deboronation of Cyclic Phosphine Boranes

Phosphino-sulfoximine boranes 120–123 were deprotected using the same procedure as for the acyclic phosphino-sulfoximine boranes. The reaction was performed in toluene at 40 °C under complete exclusion of air and monitored by 31P NMR.
Cyclic phosphino-sulfoximines

\[
\begin{align*}
R - N &\quad S &\quad O \\
\text{Ph} &\quad \text{PPh}_2 &\quad \text{BH}_3
\end{align*}
\]

1.1 equiv. DABCO
Toluene, 40 °C, 1 h

\[
\begin{align*}
S,R,R &\quad R = \text{Me}: 120 \\
&\quad \text{Bn}: 122 \\
S,S,S &\quad R = \text{Me}: 121 \\
&\quad \text{Bn}: 123 \\
S,R,R &\quad R = \text{Me}: 139 \\
&\quad \text{Bn}: 140 \\
S,S,S &\quad R = \text{Me}: 141 \\
&\quad \text{Bn}: 142
\end{align*}
\]

Scheme 55: Deboronation of cyclic phosphino-sulfoximine boranes 120–123.

The reaction time decreased from 2 to 1 hour, which reflects the less basic character of the cyclic phosphines compared to the acyclic phosphines. This is also reflected by the longer P-B bond length of the cyclic phosphine borane (cf section 3.4).

Cyclic phosphines 139–142 were obtained in excellent yields (>93%) without side reaction.

3.6. Cyclic Phosphino-Sulfoximines in Asymmetric Allylic Alkylation

3.6.1. rac-(E)-1,3-Diphenyl-2-propenyl Acetate as Substrate

The cyclic phosphines were tested in Pd-catalyzed asymmetric allylic alkylation of the substrate rac-(E)-1,3-diphenyl-2-propenyl acetate 43.

\[
\begin{align*}
\text{Ph} &\quad \text{OAc} \\
\text{Ph} &\quad \text{Ph}
\end{align*}
\]

x mol% ligand
y mol% Pd from Pd$_2$(DBA)$_3$.CHCl$_3$
2.5 equiv. dimethyl malonate
2.5 equiv. BSA
LiOAc, CH$_2$Cl$_2$, RT

\[
\begin{align*}
\text{MeO}_2C - \text{CO}_2\text{Me} \\
\text{Ph} &\quad \text{Ph}
\end{align*}
\]

Scheme 56: Pd-catalyzed asymmetric allylic alkylation of acetate 43 using cyclic phosphines 139–142.
As listed below (Table 12), the catalytic experiment carried out with a L:M ratio of 1:1 furnished the malonate 44 in 97% yield with 86% ee (entry 1).

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>x (equiv. of ligand in mol%)</th>
<th>y (equiv. of Pd in mol%)</th>
<th>L:M cation</th>
<th>yield of 44</th>
<th>ee of 44 (R)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>139</td>
<td>3</td>
<td>3</td>
<td>1:1 Li</td>
<td>97</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>139</td>
<td>6</td>
<td>3</td>
<td>2:1 Li</td>
<td>95</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>139</td>
<td>3</td>
<td>3</td>
<td>1:1 K</td>
<td>96</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>141</td>
<td>3</td>
<td>3</td>
<td>1:1 Li</td>
<td>95</td>
<td>−73</td>
</tr>
<tr>
<td>5</td>
<td>140</td>
<td>3</td>
<td>3</td>
<td>1:1 Li</td>
<td>98</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>142</td>
<td>3</td>
<td>3</td>
<td>1:1 Li</td>
<td>96</td>
<td>−79</td>
</tr>
</tbody>
</table>

¹ A – sign refers to the S-configured product which was obtained as major isomer.

The same results were obtained at L:M = 2:1 (entry 2). This implies that the same catalytic active complex is formed at low and high L:M ratio and thus that the cyclic phosphine \((S_S R R C) - 139\) most probably acts as a chelate ligand. In the case of the acyclic phosphino-sulfoximines, the L:M ratio influenced the yield as well as the ee value and therefore, it was postulated that the acyclic phosphino-sulfoximines act as a hemilabile ligand. These first two experiments proved that the design of the cyclic phosphino-sulfoximines was gainful in term enantioselectivity. The best results obtained with acyclic \(N\)-methylphosphino-sulfoximine 68 gave the malonate 44 in 96% yield with 65% ee. Thus, the catalyst containing the cyclic ligand \((S_S R R C) - 139\) exhibited a higher enantioselectivity than this derived from the acyclic ligand 68. The use of the K as counterion did not influence the yield neither the ee value (entry 3).

The isomer \((S_S C S C) - 141\) was also investigated in Pd-catalyzed allylic alkylation of the acetate 43 under the same conditions used for \((S_S R R C)\) configured phosphine 139. The ee values obtained with the \((S_S C S C)\) configured phosphine 141 was slightly lower than this obtained with its isomer \((S_S R R C) - 120\) (entries 4 and 1, 73 versus 86% respectively). But the major change is in the absolute configuration of the malonate 44. The use of phosphine \((S_S R R C) - 139\) as ligand led to the \(R\) configured malonate 44, whereas the use of its isomer \((S_S C S C) - 141\) led to the opposite \(S\) configured malonate 44.
For the acyclic phosphino-sulfoximines, the replacement of the N-methyl group of the sulfoximine by a benzyl group had a beneficial effect in term of yield and enantioselectivity of the product 44. This is also true for the cyclic phosphino-sulfoximines. Using the \((\text{S}_3\text{R}_C\text{R}_C)\) configured \(N\)-benzyl phosphine 140 as ligand, the malonate 44 was isolated in 95% yield with an \(ee\) value of 97% (entry 5). Moreover, the kinetic of the reaction was much faster than those observed with any catalysts derived from the cyclic or acyclic phosphino-sulfoximines. Indeed, the catalytic experiment was completed at RT within 50 min using 3 mol% of catalyst. The corresponding reaction of the acetate 43 in the presence of the diastereomeric \((\text{S}_3\text{S}_C\text{S}_C)\) configured phosphine 142 furnished the opposite \(S\)-configured malonate 44 in 96% yield with \(ee\) of 79% (entry 6).

The \((\text{S}_3\text{R}_C\text{R}_C)\) configured phosphino-sulfoximines 139 and 140 led to the \(R\)-configured malonate 44 whereas the \((\text{S}_3\text{S}_C\text{S}_C)\) configured phosphino-sulfoximines 141 and 142 led to the opposite \(S\)-configured malonate 44. In fact, the 2 \(C\)-stereogenic centres created during the phospha-Michael addition have the opposite configuration. These results show that the chiral backbone is the main criterion which influences the selectivity of the reaction whereas the sulfoximine moiety exerts only minor role. If the sulfoximine moiety would be discarded, the \((\text{S}_3\text{R}_C\text{R}_C)\)- and \((\text{S}_3\text{S}_C\text{S}_C)\)-configured phosphines would be enantiomers. Therefore the \((\text{S}_3\text{R}_C\text{R}_C)\) configured phosphines 139 and 140 have a so called matched configuration whereas the \((\text{S}_3\text{S}_C\text{S}_C)\) configured phosphines 141 and 142 have a mismatched configuration.

3.6.2. Substrate, Nucleophile and Solvent Variations

Cyclic phosphino-sulfoximines 139–142 proved to be excellent ligands in Pd-catalyzed allylic alkylation of \((E)\)-1,3-diphenyl-2-propenyl acetate 43, and especially phosphine \((\text{S}_3\text{R}_C\text{R}_C)-140\). Further catalytic reactions were carried out to explore the scope and the limitations of \((\text{S}_3\text{R}_C\text{R}_C)\) configured cyclic ligands 139 and 140 (Scheme 57).

Several methods are available to generate the dimethyl malonate anion. The one used until now was the BSA method.\(^{132}\) The dimethyl malonate anion can also be prepared by reaction of dimethyl malonate with NaH. Using phosphine 139 as ligand, the allylic alkylation of the acetate 43 provided the product 44 in 87% \(ee\) but with a dramatic decrease of the yield (Table 13, entry 1, 20%). This trend was also observed for the acyclic phosphines when the reaction was performed in THF (section 2.7.2).
Cyclic Phosphino-Sulfoximines

Scheme 57: Allylic substitution of acetate 43 using aza, sulfa and carbo-nucleophiles in the presence of \((S,S,R,R,C)\) configured cyclic phosphines 139 and 140.

Table 13: Allylic substitution of acetate 43 using aza, sulfa and carbo-nucleophiles in the presence of \((S,S,R,R,C)\) configured cyclic phosphines 139 and 140.

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>nucleophile</th>
<th>solvent</th>
<th>yield (product)</th>
<th>ee of product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>139</td>
<td>dimethyl malonate, NaH</td>
<td>THF</td>
<td>20 (44)</td>
<td>87 (R)</td>
</tr>
<tr>
<td>2</td>
<td>139</td>
<td>Benzyamine</td>
<td>CH₂Cl₂</td>
<td>11¹ (143)</td>
<td>n.d.</td>
</tr>
<tr>
<td>3</td>
<td>140</td>
<td>PhSO₂Na</td>
<td>CH₂Cl₂/H₂O (3:1)</td>
<td>45 (97)</td>
<td>6 (-)²</td>
</tr>
<tr>
<td>4</td>
<td>140</td>
<td>PhSO₂Na</td>
<td>THF</td>
<td>13 (97)</td>
<td>20 (-)²</td>
</tr>
</tbody>
</table>

¹ Conversion calculated on the crude \(^1\)H NMR spectroscopy.
² The absolute configuration was not determined.

Benzyl amine as well as benzyl sulfinate were also tested as nucleophile in allylic substitution using cyclic phosphines 139 and 140 as ligand. The reaction of the acetate 43 in the presence of the phosphine 139 and involving benzyl amine as nucleophile showed a very low conversion (entry 2). The yield of allylic amine 143 could be evaluated by \(^1\)H NMR of around 11%. The allylic amination of the acetate 43 could not be performed in reasonable yield using either the cyclic or the acyclic phosphino-sulfoximines as ligand. The more rigid backbone of cyclic phosphine 139 did not increase the reactivity of the catalyst towards allylic amination of acetate 43.

Sodium sulfinate was also investigated as nucleophile in allylic substitution of acetate 43 in the presence of the phosphine 140 as ligand. The first catalytic experiment was carried out in a biphasic solvent system composed of CH₂Cl₂/H₂O (3:1) with a catalytic amount of NB₄Br. A moderate yield (45%) of the corresponding allylic sulfone 97 was isolated in almost
racemic form (6% ee, entry 3). The use of THF as solvent led to a decrease of the yield (13%) with a slightly better ee value (20% ee, entry 4). Unfortunately, as CH₂Cl₂ was not investigated as solvent for this nucleophile, the comparison with the acyclic phosphines is not possible.

Although high yields and ee values were obtained in allylic alkylation with the phosphino-sulfoximine ligands, a drawback is the purification of the phosphino-sulfoximines which is carried out by chromatographic column under strict oxygen exclusion. This is the trickiest procedure for the synthesis of the phosphines and therefore, if this purification step can be avoided, i.e. if the activity of the catalyst is not impaired by the DABCO-BH₃ adducts 89, their use would be consequently easier. Phosphine 140 was synthesised as usual from phosphine borane 122 and without any purification, the crude mixture containing phosphine 140 was used to generate the active catalyst and reacted with acetate 43. The R-configured malonate 44 could be isolated within 1 hour in 96% yield with an ee value of 95%, which is a loss of only 2% of enantioselectivity compared to the purified phosphine 140. The same procedure was repeated with its diastereomer (S₃S₃C₅)-142 and in this case, the S-configured malonate 44 was isolated in 96% yield with an ee value of 79%, which are exactly the same results obtained with the purified phosphine 142. The DABCO-BH₃ adduct do not impair the catalyst activity or at least in a minimal proportion.

1,3-Diphenyl-2-propenyl acetate 43 is often used as substrate to test the catalytic activity of a new catalysts in asymmetric allylic alkylation. The two phenyl groups at the allyl termini are much more bulky than alkyl groups and therefore the ee values obtained with this substrate are often high compared to those obtained with 1,3-dimethyl-2-propenyl acetate 144. The phosphine 140, which exerts the highest enantioselectivity in the allyl alkylation of 1,3-diphenyl-2-propenyl acetate 43 with dimethyl malonate, was tested as ligand in the corresponding reaction with rac-1,3-dimethyl-2-propenyl acetate 144 (Scheme 58).
**Scheme 58:** Pd-catalyzed allylic alkylation of rac-(E)-1,3-dimethyl-2-propenyl acetate 144 using the cyclic phosphine 140 as ligand.

After 3.5 h, the catalytic experiment was quenched and the $R$-configured malonate 145 was isolated in 95% yield with an $ee$ value of 59%. The absolute configuration of malonate 145 was the same than this obtained with the corresponding diphenyl substituted malonate 43. The asymmetric allylic substitution of cyclic substrates having a cyclopentenyl or cyclohexenyl backbone is of great interest because these structures are commonly found in natural products. The asymmetric allylic alkylation of rac-cyclohex-2-enyl acetate 95 was studied in the presence of phosphine 140.

**Scheme 59:** Pd-catalyzed allylic alkylation of rac-cyclohex-2-enyl acetate 95 with phosphine 140.

After 24 h reaction, the $R$-configured malonate 96 was isolated in 70% yield with an $ee$ value of 36%. Also in this case, the absolute configuration of the cyclic malonate 96 was the same than this obtained with the dimethyl and diphenyl malonates 145 and 44. To date, only few ligands induce a high degree of selectivity with such cyclic systems.
3.7. Structure of the Palladium Complex

Excellent results were obtained in Pd-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate 43 using cyclic phosphino-sulfoximine 140 as ligand. A deeper understanding of the active catalyst could allow further modifications of the ligand structure. The coordination mode of cyclic phosphino-sulfoximine 140 was assumed to be bidentate but no concrete evidences were found.

3.7.1. Pd$_2$DBA$_3$.CHCl$_3$ and Ligand 140

The coordination mode of cyclic phosphino-sulfoximine 140 was examined. Two different solutions of the catalyst were prepared in CD$_2$Cl$_2$ from the cyclic phosphino-sulfoximine ligand 140 and Pd$_2$(DBA)$_3$.CHCl$_3$. Several complexes can be considered (Figure 26).

![Figure 26: Conceivable complexes formed by reaction of phosphino-sulfoximine 140 and Pd$_2$(DBA)$_3$.CHCl$_3$.](image)

The first solution of the catalyst contained a ratio L:M = 1:1 (solution A), whereas the second solution of the catalyst a ratio L:M = 2:1 (solution B). Both solutions A and B were analysed by NMR and mass spectroscopy.

Due to the broadness of the signals appearing in the $^1$H NMR spectra of both solutions, the signal assignments were difficult. In contrary, the $^{31}$P NMR spectra were easier to analyze. The spectra of the solution A exhibited a sharp signal at 36.4 ppm and another small broad signal appeared around 40 ppm. The broadness of this signal may be due to dynamic phenomena. Indeed, the DBA can adopt different conformation in complexes [Pd(140)DBA] and [Pd(140)$_2$DBA] leading to diastereomeric complexes which can be in fast equilibrium with each other. The $^{31}$P NMR spectrum of the solution B exhibited four signals. Among them, two signals corresponding to those in solution A were observed. The third signal at −13.1 ppm was assigned to the free ligand 140. The lowest field signal appeared at 41.4 ppm.
The assignment of the signals observed in $^1$H NMR and $^{31}$P NMR spectra was not trivial and therefore mass spectroscopy was used.

The solution A was evaporated and the crude mixture was dissolved in CHCl$_3$ and diluted with MeOH. A mass spectrum of this mixture A was recorded (Figure 27).

The cluster appearing at m/z = 838 was attributed to the complex 146 with formula [Pd(DBA)(140)H]$^+$, and the MS/MS fragmentation showed its parent relationship by loss of DBA with the cluster at m/z = 604, which was attributed to complex 147 (Scheme 60). The isotopic distribution showed the presence of a palladium atom and the simulated isotopic pattern is in accordance with these formulas (see experimental part, Figure 32 and Figure 31, section B.12).

The cluster appearing at m/z = 1441 was attributed to the ion of the dinuclear complex 148 with formula [Pd$_2$(DBA)(140)$_2$]$^+$ which showed a parent relationship by loss of DBA with complex 149 at m/z = 1207 with formula [Pd$_2$(140)$_2$H]$^+$. The m/z value of 1209 (Figure 27)
corresponds to one of the isotope of complex 149. The fragmentation of complex 149 led to a peak at m/z = 894, matching with the structure of ion 150.

Scheme 61: Proposed structures and fragments for the clusters at m/z = 1441 and 1209.

The isotopic distribution of these clusters is in accordance with those obtained with the simulated spectra (see experimental part, Figure 33, section B.12). Such palladium(0) dinuclear complexes were rarely described in the literature. The proposed structures and fragmentations presented in Scheme 60 and Scheme 61 are drawn for a better comprehension and may differ from the exact structure of these complexes.
The mass spectrum of mixture B was recorded under the same conditions as for mixture A.

![Figure 28: ESI-mass spectrum of the crude mixture B.](image)

The cluster at m/z = 904 was attributed to complex 151 and the loss of phosphine 152, observed by MS/MS, showed its parent relationship with complex 153 appearing at m/z = 638 (Scheme 62).

![Scheme 62: Proposed structures and fragment for the clusters appearing at m/z = 904 and 638.](image)

The MS/MS fragmentation of the cluster appearing at m/z = 1271 led to two ions with m/z = 1206 and 648 (Scheme 63). The structure of these ions remained unknown.

![Scheme 63: Fragmentation of the cluster appearing at m/z = 1271.](image)
The MS/MS fragmentation of the cluster appearing at m/z = 1257 led to an ion with m/z = 1026. Its further fragmentation led to an ion of m/z = 759 (Scheme 64). The structure of these ions remained also unknown.

Only traces of the complex \([\text{Pd}(140)_2]\) (m/z = 1100) could be detected in the mixture B which is a hint for the bidentate behaviour of ligand 140. The formation of complex 151 can be explained as follow. As two equivalents of ligand 140 are present in solution, the excess (calculated for a bidentate ligand) undergoes a rearrangement to phosphino-alkene 152 and sulfinamide (see section 2.6 for a similar mechanism with phosphine boranes). Thus, phosphino-alkene 152 acts as a ligand to form complex 151.
3.7.2. [Pd(diphenylallyl)Cl]$_2$ and Ligand 140

Although a crystal structure of a complex does not represent its behaviour in solution, this is still a valuable source of information. Therefore growing a crystal of [Pd(diphenylallyl)(140)] complex 155 was considered. The synthesis of the π-allyl complex required the preparation of the starting palladium complex [Pd(diphenylallyl)Cl]$_2$ 154, which was synthesized following Bosnich procedure (Scheme 65).$^{170}$

![Scheme 65: Synthesis of the [Pd(diphenylallyl)Cl]$_2$ complex 154.](image)

[Pd(diphenylallyl)Cl]$_2$ complex 154 was reacted with phosphino-sulfoximine 140 and an anionic metathesis was performed using AgSbF$_6$. After removal of the salts and the solvents, an orange sticky solid containing complex 155 was obtained (Scheme 66).

![Scheme 66: Synthesis of [Pd(diphenylallyl)(140)]$^+\cdot$SbF$_6$ 155.](image)

Unfortunately, all attempts to crystallize complex 155 failed. Black palladium was observed after 2 weeks. Nevertheless, the orange sticky solid containing complex 155 was analyzed by NMR spectroscopy. Among the major signals assigned to complex 155, signals of lower intensity were also observed. Selected chemical shifts of phosphino-sulfoximine 140 and allyl complex 155 are reported below (Table 14).
Table 14: Selected NMR spectroscopic data (from $^1$H, $^{13}$C($^1$H) and $^{31}$P($^1$H) spectra) of phosphino-sulfoximine 140 and $\pi$-allyl complexes 155 and 156\textsuperscript{171} recorded at room temperature in CDCl$_3$, THF-d$_8$ and CDCl$_3$ respectively.

<table>
<thead>
<tr>
<th>entry</th>
<th>atom number</th>
<th>$\delta$H (ppm)</th>
<th>$\delta$C (ppm)</th>
<th>$\delta$H (ppm)</th>
<th>$\delta$C (ppm)</th>
<th>$\delta$H (ppm)</th>
<th>$\delta$C (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>3.15</td>
<td>59.4 (d)</td>
<td>5.10</td>
<td>63.8 (d)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>4.14</td>
<td>29.4 (d)</td>
<td>3.12</td>
<td>28.0 (d)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>g</td>
<td>3.95</td>
<td>2.55</td>
<td>4.11 (d)</td>
<td>67</td>
<td>4.28 (d)</td>
<td>70.9</td>
</tr>
<tr>
<td>4</td>
<td>g'</td>
<td>4.30</td>
<td>45.9</td>
<td>4.40</td>
<td>47.8 (s)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>$\pi_1$</td>
<td>-</td>
<td>-</td>
<td>6.80 (n.d.)</td>
<td>106 (d)</td>
<td>5.84 (dd)</td>
<td>100.2 (d)</td>
</tr>
<tr>
<td>6</td>
<td>$\pi_2$</td>
<td>-</td>
<td>-</td>
<td>6.60 (m)</td>
<td>110</td>
<td>6.82 (dd)</td>
<td>111.6</td>
</tr>
<tr>
<td>7</td>
<td>$\pi_3$</td>
<td>-</td>
<td>-</td>
<td>4.11 (d)</td>
<td>67</td>
<td>4.28 (d)</td>
<td>70.9</td>
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<table>
<thead>
<tr>
<th>$\delta$P (ppm)</th>
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<tbody>
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<table>
<thead>
<tr>
<th>coupling constants (Hz)</th>
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<tbody>
<tr>
<td>9</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td>12</td>
</tr>
<tr>
<td>13</td>
</tr>
</tbody>
</table>

$^1$H, $^{13}$C and $^{31}$P NMR spectra of phosphine 140 were fully and unambiguously assigned through 2D $^1$H-$^1$H, $^1$H-$^{13}$C, $^{31}$P-$^{13}$C and DEPT and NOE experiments. Protons H$_a$ and H$_b$ were assigned by 2D $^1$H-$^{13}$C. C$_a$ and C$_b$ are both tertiary carbons. C$_a$ appears at 59.4 ppm, which is in the range of a sp$^3$ carbon atom in alpha position of a sulfoximine group. C$_b$ appears at 29.4 ppm, which is typical for a sp$^3$ carbon atom in alpha position of a diphenylphosphino group. Moreover, both carbon atoms C$_a$ and C$_b$ are coupled with the phosphorus atom and appear as doublet.

The first obvious difference between phosphino-sulfoximine 140 and complex 155 lies in the chemical shift in the $^{31}$P NMR spectrum. The chemical shift of phosphino-sulfoximine 140
appears at $\sim$13.1 ppm, whereas the chemical shift of complex 155 appears at 33.1 ppm (Table 14, entry 8). This low field displacement is typical for a coordinated phosphorus atom to a transition metal.\textsuperscript{172} This is the evidence that at least the phosphorus atom of phosphino-sulfoximine 140 coordinates to the palladium atom. The second observation is focused on the chemical shift displacement of protons H\textsubscript{a} and H\textsubscript{b}. Proton H\textsubscript{a} appears at 3.15 ppm for phosphino-sulfoximine 140 whereas for complex 155 it appears at 5.10 ppm. This is a downfield displacement of nearly 2 ppm (entry 1). Proton H\textsubscript{a} was assigned by 2D $^1$H-$^1$C. The chemical shift of carbon C\textsubscript{a} (63.8 ppm) is close to the one of phosphino-sulfoximine 140 and appears as a tertiary carbon in DEPT. Proton H\textsubscript{b} appears at 4.14 ppm for phosphino-sulfoximine 140 and 3.12 ppm for complex 155, which is a high field displacement of 1.02 ppm (entry 2). Proton H\textsubscript{b} was also assigned by 2D $^1$H-$^1$C. The chemical shift of carbon C\textsubscript{b} (28.0 ppm) is also close to the one of phosphino-sulfoximine 140 and appears as a tertiary carbon in DEPT. The diastereotopic protons H\textsubscript{g} suffered a high field displacement which might be due to anisotropic effects of the phenyl rings of the allyl moiety (entries 3 and 4). The conformation of phosphino-sulfoximine 140 is close to the one in phosphine borane 122, at least for the S-C-C-P dihedral angle. In both cases, no coupling (< 2 Hz) is observed between protons H\textsubscript{a} and H\textsubscript{b}, either by selective irradiation of proton H\textsubscript{a} or H\textsubscript{b}, or by COESY spectrum (entry 9). Protons H\textsubscript{a} and H\textsubscript{b} are in trans position with a dihedral angle of nearly 90°. Consequently the sulfoximine as well as the phosphino moieties adopt an almost axial position (section 3.4). This is not true anymore in allyl complex 155. The coupling constant between protons H\textsubscript{a} and H\textsubscript{b} is 11 Hz, which translates into a dihedral angle between 130° and 150° (entry 9). Thus, another conformation of phosphino-sulfoximine ligand in complex 155 is adopted. This conformation change, which is not observed in phosphino-sulfoximine 140, is favoured in complex 155 due to a coordination of both the nitrogen and the phosphorus atom to the palladium atom. This a crucial point because it means that the phosphino-sulfoximine 140 acts as a bidentate and not as a monodentate ligand.

Moreover the chemical shift of C\textsubscript{a} in phosphino-sulfoximine 140 is 59.4 ppm, whereas it appears at 63.8 ppm in complex 155 (entry 1). The $\sigma$-coordination of the nitrogen atom of the sulfoximine moiety induces an electro-deficiency of the neighbouring atoms. The chemical shift of C\textsubscript{b} in phosphino-sulfoximine 140 is 29.4 ppm, whereas it appears at 28.0 in complex 155 (entry 2).

Carbon C\textsubscript{\pi} appeared at 106 ppm as a doublet with a coupling constant $^2$J\textsubscript{P-C\textsubscript{\pi}} through the palladium atom of 17 Hz. This shows that the allyl ligand is still coordinated to the palladium atom, and these values are close to those reported for complex 156.\textsuperscript{171} Unfortunately, the
coupling constant \( ^3J_{P-H\pi} \) could not be determined because of the overlapping of aromatic protons peaks. Thus, proton \( H_{\pi 1} \) was detected via 2D \(^1\)H-\(^{13}\)C correlation (entry 5). Proton \( H_{\pi 2} \), assigned by 2D \(^1\)H-\(^1\)H, appeared at 6.60 ppm together with an aromatic proton peak, which prevented the determination of coupling constants (entry 6). Carbon \( C_{\pi 2} \) appeared at 110 ppm, whereas it appeared at 111.6 ppm in complex 156. Proton \( H_{\pi 3} \), also assigned by 2D \(^1\)H-\(^1\)H, appeared at 4.11 ppm as a doublet with a coupling constant of 10.4 Hz (entries 7 and 13). These values are close to those reported for complex 156, where proton \( H_{\pi 3} \) appeared at 4.28 ppm also as a doublet with a coupling constant of 11 Hz. For complex 156, proton \( H_{\pi 2} \) appeared at 6.82 ppm as doublet of doublet. Carbon \( C_{\pi 3} \) appeared at 67 ppm. The high field resonance of carbon \( C_{\pi 3} \) can be attributed to the amount of sp\(^3\) character due to the \( \pi \)-back donation of the metal. In contrast, carbon \( C_{\pi 1} \), which is trans to the \( \pi \)-acceptor phosphorus atom, appeared at 106 ppm.

To simplify the analysis of the \( \pi \)-allyl moiety, the following designations will be used (Figure 29). The \textit{exo} and \textit{endo} isomers refer to complexes in which the vectors \( C_{\pi 2}-H_{\pi 2} \) and \( C_b-H_b \) point in the same or the opposite direction, respectively.

![Figure 29: Exo and endo isomers.](image)

Thus, the eight possible stereoisomers of (\( \eta^3 \)-allyl) complex 155 are presented below (Figure 30). Substituents on the terminal allylic carbon atoms can assume a \textit{syn} or \textit{anti} orientation with respect to proton \( H_{\pi 2} \).
Figure 30: Eight possible stereoisomers of (η³-allyl) complex 155.

Such π-allyl complexes are usually in thermodynamic equilibrium. Anti,anti complexes are therefore not favoured due to steric hindrances, and only if the substituents R are sufficiently small, anti,syn or syn,anti isomers are present in notable amount. However, such complexes could be characterized with ligands exerting strong steric hindrance.\textsuperscript{31,173} Usually, the thermodynamically favoured complexes are the syn,syn isomers.

To differentiate between these eight isomers, the coupling constants between the allylic protons and NOE experiments can furnish helpful information. For example, a NOE observed between Hπ\textsubscript{1} and Hπ\textsubscript{2} will exclude the isomers with syn,syn and anti,syn configuration. Moreover, an exo or an endo configuration could be indicated by a NOE between the allyl protons and the ligand backbone.

As the $^{31}$P NMR spectrum exhibit only one strong singlet together with two other small singlets in a ratio 96:2:2, one major complex is present in solution or, several complexes are in fast equilibrium and the chemical shift in $^{31}$P NMR spectrum represents an average of their chemical shifts.

The $^3J_{Hπ\textsubscript{2},Hπ\textsubscript{3}}$ value was 10.4 Hz, which would imply that both hydrogens Hπ\textsubscript{2} and Hπ\textsubscript{3} are trans. The $^3J_{Hπ\textsubscript{2},Hπ\textsubscript{3}}$ value of a cis arrangement is typically smaller than 10 ppm.\textsuperscript{31,173} Thus, the anti,syn configuration of the π-allyl ligand can be excluded. A NOE was observed between proton Hπ\textsubscript{3} and one of the signals at 6.60 ppm. Although proton Hπ\textsubscript{2} appeared at 6.60 ppm, this NOE is most probably due to the proximity of proton Hπ\textsubscript{3} and either a proton of the diphenylphosphine moiety or the phenyl group of the π-allyl ligand. A second NOE was observed between proton Hπ\textsubscript{3} and a proton appearing in the aromatic region at 6.80 ppm.
Cyclic Phosphino-Sulfoximines

which could not be unequivocally assigned. A further NOE exists between signals at 6.4 ppm and 7.93 ppm. Further assignments could not be performed.

According to the spectroscopic data, the following four isomers can be proposed: endo,syn,syn, exo,syn,syn, endo,syn,anti and exo,syn,anti. π-Allyl complexes are usually in equilibrium and the major complex observed might not be the isomer which leads to the major product, i.e. the most reactive complex. The following scheme shows the allyl alkylation of these four complexes by dimethyl malonate anion (Scheme 67).

![Diagram of four isomers and their allyl alkylation](image)

**Scheme 67**: Conceivable structures of the π-allyl complexes 155 and their allylic alkylation.

The models of the four isomers of complex 155 are drawn assuming that the 6-membered matallacycle adopts a boat or twisted boat conformation. Thus, the endo complexes would be disfavoured due to steric repulsions between the allyl ligand and the diphenylphosphino group. The catalyst prepared from the N-methyl and N-benzyl substituted phosphino-sulfoximines 139 and 140 respectively lead both to the R-configured malonate 44 in 86 and 97\% ee, respectively. The small N-methyl substituent of ligand 139 does probably not exert enough steric hindrances with the π-allyl moiety to favour a syn,anti configuration. As both catalysts lead to the same R-configured malonate 44, the syn,anti configuration in complex 155 should also not be favoured, i.e. the N-benzyl substituent of ligand 140 does not exert enough steric hindrances with the π-allyl moiety. Moreover, models of complex 155 do not show strong
stERIC hinderances of the ligand backbone with the π-allyl moiety, which could stabilize a syn-anti isomer. This argumentation, which should be taken with care, would favour the exo,syn,syn and the endo,syn,syn isomers of complex 155.

A nucleophilic substitution trans to the phosphorus atom of the endo,syn,syn isomer of complex 155 would lead to the minor S-configured malonate 44, whereas a nucleophile substitution of the exo,syn,syn isomer would lead to the major R-configured malonate 44 (Scheme 67). Nucleophilic substitution trans to the nitrogen atom is not expected due to the weaker Pd-C bond trans to the phosphorus atom. Thus, the most probable configuration of the most reactive isomer of complex 155 would be the exo,syn,syn isomer.
4. Conclusion

This work was focused on the synthesis of chiral bidentate 1,5-\textit{P},\textit{N}-phosphino-sulfoximines and their application as ligand in Pd-catalyzed allylic alkylation. The key step of their synthesis was a phospha-Michael addition of vinyl sulfoximines. Although carbon, oxa, aza and sulpha-Michael additions were largely reported, no phospha-Michael addition of vinyl sulfoximines was described at the beginning of this project. Starting from \textit{N}-substituted sulfoximines 52–55, vinyl sulfoximines 58–61 were obtained in excellent yields. Phosphino-sulfoximine boranes 62, 63 and 76–81 were obtained via phospha-Michael addition of vinyl sulfoximines 58–61 in good yields (70-80%) with de up to 56%. The de values could be increased at lower temperature but with lower yields. The separation of the phosphate borane isomers was achieved by crystallization and/or chromatographic column. The absolute configuration of the \textit{R}_{5}S_{C} phosphino-sulfoximine \textit{ent}-62 was determined by X-ray crystal structure analysis. Similarity in the $^{1}$H NMR spectra of the phosphino-sulfoximine boranes led us to assume their absolute configuration. The short three steps synthesis of phosphino-sulfoximines 68, 69 and 84–88 was carried out with 14 to 48% overall yield (Scheme 68).

**Scheme 68**: Synthesis of acyclic phosphino-sulfoximines 68, 69 and 84–88.
Acyclic phosphino-sulfoximines 68, 69 and 84–88 were tested in Pd-catalyzed asymmetric allylic alkylation. Very good results were obtained with the $S_2R_C$ phosphino-sulfoximine 84 (Scheme 69).

The configuration of the chiral C-atom is important and this showed a match ($S_2R_C$) and mismatched configuration ($S_2S_C$). A hemilability of these ligands was proposed, leading to the design of the cyclic phosphino-sulfoximines, expected to confine the flexibility of the ligand backbone. The phospha-Michael addition strategy was chosen to access the cyclic phosphino-sulfoximines 139–142, and only the two trans isomers were isolated in a ratio 1:1 in good yield (80%). The absolute configuration of the cyclic phosphine boranes 120–123 was established by an X-ray crystal structure of the $S_3R_C$ configured cyclic phosphine borane 122 and NMR experiments. The overall 4 steps synthesis was carried out in 22 to 27% overall yield (Scheme 70).
The optimisation of the ligand structure proved to be successful. \(S_3R_C R_C\) configured \(N\)-benzyl phosphino sulfoximine 140 showed excellent results in Pd-catalyzed allylic alkylation of substrate 43 and the corresponding malonate 44 was obtained in 98% yield with 97% \(ee\) (Scheme 71). This is, to date, the best \(P,N\)-phosphino-sulfoximine ligand reported for Pd-catalyzed allylic alkylation of malonate 44 in terms of selectivity.26 As expected, the alkylation of less bulky dimethy substrate 144 and cyclic substrate 95 proceeded with less enantiocontrol.
Interestingly, when the $S_S S_C$ configured $N$-benzyl phosphino sulfoximine 142 was used as ligand, the other enantiomer of malonate 44 was obtained. This shows that the sulfoximine moiety does not have a major influence on the selectivity. For the cyclic phosphino-sulfoximines, there is also a match conformation $S_S R_C R_C$ and a mismatched conformation $S_S S_C S_C$. The attempt to synthesis the $S_S R_C R_C$ configured $N$-benzyl phosphino sulfoximine 140 in a better overall yield was not successful. At low temperature, the sulfoximine moiety induced a selectivity in favour to the other diastereomer $S_S S_C S_C$ 141.

The coordination mode of the cyclic phosphino-sulfoximine was examined. NMR investigations of ligand 140 showed that both sulfoximine and phosphino groups adopt an axial position, whereas in allyl complex 155 these groups adopt a equatorial position. This distortion of the ligand backbone proved a bidentate $P,N$ coordination mode of the ligand.

Analysis of a solution of the phosphino-sulfoximine 140 with Pd$_2$(DBA)$_3$.CHCl$_3$ by mass spectroscopy revealed the presence of an unexpected palladium(0) dimers.

**Scheme 71**: Most selective cyclic phosphino-sulfoximine 140 for Pd-catalyzed allylic alkylation.
5. Outlook

The synthesis of the $S_2R_C R_C$ phosphino-sulfoximine 140 in a better overall yield would be interesting to develop. Efforts should be done in a better diastereoselective phospha-Michael addition. The use of chiral amine to activate diphenylphosphine or bifunctional organocatalyst to activate simultaneously the diphenylphosphine and the Michael system could be envisaged (Scheme 72).

![Scheme 72: Conceivable diastereoselective phospha-Michael addition of cyclic vinyl sulfoximine 118 with HPPh$_2$ using either a chiral amine or a bifunctional chiral catalyst.]

The bit angle, especially for bis-phosphine, but also for $P,N$-ligands is a critical parameter for the activity and selectivity of catalysts. The cyclization of the $\omega$-bromosulfoximines was based on the work of Tanaka et al. on the corresponding sulfoxides. 5 and 7 membered cyclic vinyl sulfoximines should be also accessible by this method and phospha-Michael addition of the corresponding cyclic vinyl sulfoximines would lead to the 5 and 7 cyclic phosphino-sulfoximines (Scheme 73). Moreover, the replacement of the methyl group by a benzyl group at the nitrogen atom of the sulfoximine was beneficial in term of enantioselectivity and kinetic in the Pd-catalyzed allylic alkylation of rac-($E$)-1,3-diphenyl-2-propenylacetate 43. Thus, substitution at the nitrogen atom with bulkier substituents can be considered.
The synthesis of the acyclic and cyclic phosphino-sulfoximines starts with the functionalization at the nitrogen atom of the sulfoximine and thus, in order to test the influence of the nitrogen substituent in the Pd-catalyzed allylic alkylation, the synthesis of the ligand should start from the beginning. The convergent synthesis of the \( N \)-substituted phosphino-sulfoximine depicted in Scheme 74 shows a late functionalization at the nitrogen atom through the use of a labile silyl group, which can facilitate the screening of new phosphino-sulfoximines bearing various substituents at the nitrogen of the sulfoximine.
Scheme 74: Conceivable convergent synthesis for the screening of N-substituted phosphino-sulfoximines.

Chiral and achiral \( P,N \) ligands are not only used in Pd-catalyzed allylic alkylation but also in Ir-catalyzed hydrogenation of alkenes and ketones, Cu-catalyzed Diels-Alder and hetero Diels-Alder reaction, Cu-catalyzed 1-4 additions, Rh-catalyzed hydroformylation. The cyclic and acyclic phosphino-sulfoximines could be tested in such catalytic reactions.

The phospha-Michael addition of vinyl sulfoximines with diphenylphosphine catalyzed by \( t\)-BuOK was investigated in this work and led to diarylalkylphosphines. The reactivity of \( HP(O\text{Ph})_2 \) towards the phospha-Michael addition of vinyl sulfoximines can be studied. If the addition is successful, diaryl alkylphosphonites could be synthesized and tested as ligand in Pd-catalyzed allylic alkylation, but also in Rh-catalyzed hydroformylation. Various aryl groups could be introduced, such as phenyl or naphtyl. A further chiral information could be introduce with a binaphtyl group. A biphenyl group could be also introduce and study the effect of the sulfoximine group on the atropoisomerism of the biphenyl group.\(^{176}\)
**Scheme 75:** Conceivable phospha-Michael addition of cyclic vinyl sulfoximines with diarylphosphonites leading to diaryl alkylphosphonites.
B. Experimental Part
1. General Remarks

All chemical operations including reactions, work-ups and purifications were carried out in a well ventilated hood, using safety glasses, lab coat and gloves.\textsuperscript{177} The reactions involving air and moisture sensitive compounds were carried out under an argon or nitrogen atmosphere using the standard Schlenck techniques. Reagents and solvents were transferred using cannulas and syringes. Air and moisture sensitive compounds were stored in Schlenk flasks with a small pressure of argon at room temperature or at 4 °C. Compounds suffering from rearrangements were kept at –60 °C.

2. Solvents and Chemicals

2.1. Solvents

Solvents used for flash chromatography, such as hexane, cyclohexane, EtOAc, Et\(_2\)O and pentane were distilled before use. In the case of sensitive reactions, the solvents were purified according to standard techniques.\textsuperscript{178}

Et\(_2\)O and THF: predried over KOH, passed through basic alumina, and distilled from sodium-benzophenone ketyl under nitrogen.

CH\(_2\)Cl\(_2\): shaken several times with concentrated sulphuric acid to remove ethanol, washed with water and NaHCO\(_3\), dried over CaCl\(_2\), refluxed several hours over CaH\(_2\) and distilled under nitrogen.

Toluene: one fifth is distilled off to remove water azeotropically, and the remaining four fifths are distilled from sodium under nitrogen.

Methanol and ethanol: refluxed over Mg-turning (activated with I\(_2\)), and distilled under argon. tert-Butanol: refluxed either over Na or LiAlH\(_4\) and then distilled under argon.

1,2-Dimethoxyethane: Aldrich, quality: extra dry, stored over molecular sieve, water < 50 ppm, used without other purification.

\(N,N'\)-Dimethylformamide: Aldrich, quality: extra dry, stored over molecular sieve, water < 50 ppm, used without any other purification.

DMSO: Aldrich, quality: 99.9\%, anhydrous.

BnOH: Aldrich, quality: 99.8\%, anhydrous.
For air sensitive compounds, oxygen-and water free solvents were used. Anhydrous solvents were degassed via three freeze-thaw cycles. The anhydrous solvents were transferred with a syringe equipped with a cannula into a Schlenck tube previously degassed and filled with argon, and closed with two Glindeumann®-sealing rings and PARAFILM®M. The Schlenck tube which remained under argon was placed in liquid nitrogen until the entire solvent freeze. Then high vacuo was applied and the Schlenck tube was carefully taken out the liquid nitrogen. When the solvent was completely melted, the procedure was repeated twice. The solvents were stored in the Schlenck tube closed with two Glindeumann®-sealing rings and further PARAFILM®M under argon without other manipulation.

2.2. Chemicals

2.2.1. Reagents

All the reagents employed were purchased from commercial suppliers (Acros, Sigma-Aldrich, Fluka, Lancaster, Merck).

$t$-BuOK and $t$-BuOLi: sublimed before use.

Diisopropylamine: refluxed over CaH$_2$ for 3 hours and then distilled under argon.

$n$-BuLi: received as a 1.6 M solution, and titrated using either diphenylacetic acid or phenantroline and dried benzyl alcohol.$^{179}$

All other chemicals were used as received without further purification.

2.2.2. Starting Materials Prepared According to the Literature

The following starting materials were prepared according the literature: Pd$_2$(DBA)$_3$.CHCl$_3$, $^{180}$ [Pd(1,3-diphenyl-π-allyl)Cl]$_2$, $^{181}$ (E)-1,3-diphenylprop-2-en-1-ol, $^{182}$ (E)-1,3-diphenylallyl acetate, $^{182}$ cyclohex-2-enol, cyclohex-2-enyl acetate, cyclohex-2-enyl methyl carbonate, (E)-pent-3-en-2-ol, (E)-pent-3-en-2-yl acetate, (S) and (R)-S-methyl-S-phenylsulfoximine$^{183}$.

2.3. Analytical Methods

2.3.1. NMR Spectroscopy

The coupling constants $^XJ_{YZ}$ are given in Hertz. $X$ refers to the number of σ-bonds between the nucleus $Y$ and $Z$. The multiplicity of the signals was denoted as follow: $s$ = singlet,
EXPERIMENTAL PART

d = doublet, t = triplet, b = broad signal, and combination of them, like bs = broad singlet, dd = doublet of a doublet. Assignments of the peaks in the $^1$H NMR spectra were made by GMQCOSY, GNOE, or GTOCSY experiments, and those in the $^{13}$C NMR spectra were made by APT, DEPT and HETCOR experiments.

$^1$H NMR: recorded on a Varian Gemini 300 (300 MHz), Varian Mercury 300 (300 MHz), Varian Inova 400 (400 MHz) or Varian Unity 500 (500 MHz). The chemical shifts are given in ppm relative to tetramethylsilane (TMS, $\delta = 0.00$ ppm) as internal reference, or to residual solvents signals (tetrahydrofuran = 1.73 and 3.58 ppm, chloroform = 7.26 ppm, methylenchlorid = 5.32 ppm). The NOE experiments were recorded on either on a Varian Inova 400 (400 MHz) or a Varian Unity 500 (500 MHz).

$^{13}$C NMR: recorded on a Varian Gemini 300 (75 MHz), varian Inova 400 (100 MHz) or Varian Unity 500 (125 MHz). The chemical shifts are given in ppm relative to tetramethylsilane (TMS, $\delta = 0.00$ ppm) as internal reference, or relative to deuterated solvent signal (tetrahydrofuran = 25.4 and 67.6 ppm, chloroform = 77.0, methylenchlorid = 53.8 ppm).

$^{31}$P NMR: recorded on a Varian Gemini 300 (75 MHz) or a varian Inova 400 (100 MHz). The chemical shifts are given in ppm relative to $\text{H}_3\text{PO}_4$ as external reference.

In the case of air and/or water sensitive compounds, dried and degassed deuterated solvent were used. The NMR tube was placed in a Schlenck tube, degassed and filled 4 times with argon. The compound was dissolved in the appropriate deuterated solvent, and transferred by using a syringe equipped with a cannula to the NMR tube by opening the Schlenck tube and keeping a flow of argon. The tube was removed from the Schlenck tube and closed rapidly with a plastic cap which was kept tight with a thin band of stretchable PARAFILM® M.

In the case of highly air and/or water sensitive compounds, the NMR measurements were effectuated in sealed NMR tubes using the following procedure. A special NMR tube having a Schenck adaptor on the top was degassed and filled with argon 4 times. The compound was dissolved in the appropriate dried and degassed deuterated solvent, and transferred to the NMR tube by using a syringe equipped with a cannula. The solution was cooled to $\sim$78 °C and vacuum was applied. The NMR tube was sealed using an acetylene torch. The sample
was allowed to warm to room temperature behind a security glass, and was kept for further 15 min aside before starting the measurement.

**2.3.2. IR Spectroscopy**

IR spectra were recorded on a *Perkin-Elmer PE 1760 FT* spectrometer as KBr pellets or in solution. Absorptions are given in cm\(^{-1}\) in a range of 4000 to 850 cm\(^{-1}\). The following abbreviations are used to describe the relative intensity of absorption: w = weak (65–85%), m = medium (26–65%), s = strong (0–25%).

**2.3.3. Mass Spectroscopy**

Mass spectra were recorded on a *Varian Mat 212 S* and *Finnigan MAT 312* for ionisation through for EI (Electronic impact, 70 eV) and CI (chemical ionization, 100 eV), ESI (electrospray ionisation) and ESI–MS/MS were recorded on a *Thermo Finnigan LCQ DECA XPlus*. The masses are given in m/z.

High resolution mass spectroscopy (HRMS) were recorded on a *Finnigan MAT 95* (EI) or on a *Micromass LCT* (LC-TOF-HRMS, column *Acquity UPLC BEH C\textsubscript{18}*) and the values are given in amu (atomic mass unit).

**2.3.4. Gas Chromatography**

Gas chromatography analysis were performed on a *Varian 3800* (Star Workstation 5.3) with FID and ECD detector, and a *Carlo Erba MEGA* (Labquest 6.4) with FID detector. The normal phase column used was CP-Sil-8, the chiral columns used were Lipodex-γ-6-Me (Macherey & Nagel) and Chiraldex βI (CP).

Temperature programme 1: 50 °C, 15 min, then 10K/min to 80 °C, 5 min, then 10K/min to 120 °C, 5 min, 100 kPa H\(_2\).

Temperature programme 2: 50 °C, 15 min, then 2K/min to 80 °C, 5 min, then 10K/min to 120 °C, 5 min, 100 kPa H\(_2\).
2.3.5. High Pressure Liquid Chromatography

- Analytical HPLC
  Analytical HPLC were performed on a Millipore Waters (UV-481), Hewlett Packard HP 1050 with DA detector. 3 types of columns have been used: Chiralcel-OD-H with precolumn, chiralpack AD and chiralpack IA.

- Preparative HPLC
  Preparative HPLC were performed with a Varian SD1 (Star Workstation 5.3) with UV and RI detector, using either a column Kromasil (Si 100, Ø 30 mm) or a Kromasil (Si 100, Ø 40 mm).

2.3.6. Elemental Analysis

Elemental analyses were performed on a Heraeus CHN-Rapid. All values are given in mass percentages.

2.3.7. Melting Point

Melting points were measured in an open glass capillary using a Büchi 510 Schmelzpunktbestimmungsapparatur SMP-20.

2.3.8. Optical Rotation

Optical rotations [$\alpha$]D were measured on a Perkin Elmer Polarimeter PE 241 and given in grad × mL/dm × g, and the concentration c in g/100 mL. The measurements were effectuated at 22 °C.

2.3.9. Thin Layer Chromatography

Thin layer chromatography (TLC) was carried out with aluminium sheets silica gel 60 F254 (Merck) with fluorescent indicator. The detection was carried out either by UV-light detection ($\lambda = 254$ nm) or using dyes.$^{184}$

Dyes used:

I2 in silica gel
p-Anisaldehyde (5.1 mL p-anisaldehyde, 2.1 mL acetic acid, 6.9 mL sulphuric acid and 185 mL ethanol)
Phosphomolybdic acid (5 g phosphomolybdic acid in 100 mL ethanol)
Potassium permanganate (1 g KMnO₄, 7 g K₂CO₃, 100 mL H₂O)
Ninhydrin (0.3 g ninhydrin, 3 mL acetic acid in 80 mL ethanol)

2.3.10. Preparative Column Chromatography

Flash column chromatography was carried out in glass columns using Merck silica gel 60, particle size 0.040-0.063 mm. The solvents used were simply distilled before use.
Air and moisture sensitive compounds:
Flash column chromatography was carried out in a glass column (20mm×1.7 mm) with an argon entry on the top and at the bottom a schlenck to collect fractions. The column was filled to a half and degassed. The solvents were dried and degassed before use.

2.3.11. Crystallisation Techniques

3 types of crystallisations have been carried out:

* The compound (or crude mixture) was dissolved in the minimum amount of solvent, and a second less polar solvent was layered on the top this solution.

* The compound (or crude mixture) was dissolved in the minimum amount of solvent and cooled down (4 °C or −26 °C).

* The compound (or crude mixture) was dissolved in a polar solvent and the solution transferred in a test tube (typically 5×1 cm) which was kept into a bottle containing a less polar volatile solvent (1 to 2 cm). The bottle was closed and kept at a lower temperature (4 °C or −26 °C).

2.3.12. X-ray Crystal Structure Analysis

X-ray crystal structure analysis have been carried out on a Bruker Proteum X8 or a Enraf-Nonius CAD4.
# 3. Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>Ar</td>
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<tr>
<td>BINAP</td>
<td>2-(diphenylphosphino)-1-(2-(diphenylphosphino)naphthalen-1-yl)naphthalene</td>
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<td>BTPP</td>
<td>t-butylimino-tri(pyrrolidino)phosphorane</td>
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4. General procedures

4.1. General Procedure for the Preparation of Acyclic Vinyl Sulfoximines (GP-1)

In an oven dried round bottom Schlenck flask, the appropriate N-substituted-S-methyl sulfoximine (1 mmol) was dissolved in anhydrous THF (2.5 mL) and cooled to –78 °C. A solution of n-BuLi (688 µL of a 1.6 M in n-hexane, 1.1 mmol) was added dropwise to the mixture, and the resulting yellow solution was stirred for 30 min. The appropriate aldehyde (1.1 mmol) was added within 5 min and the colourless solution was stirred at the same temperature for 1 h. To this mixture was added ClCO₂Me (1.1 mmol) and it was allowed to warm to room temperature. After stirring the mixture for 1 h, it was cooled to –78 °C and DBU (1.1 mmol) was added dropwise. The mixture was allowed to warm to room temperature and was stirred overnight. The heterogeneous mixture was quenched with saturated aqueous NH₄Cl and extracted with the appropriate organic solvent (4×15 mL). The combined organic phases were dried (MgSO₄) and concentrated in vacuo.

4.2. General Procedure for the Preparation of Cyclic Vinyl Sulfoximines (GP-2)

In an oven dried round bottom Schlenck flask, freshly distilled diisopropylamine (143 µL, 1.02 mmol) was dissolved in anhydrous THF (22 mL). The solution was cooled to –78 °C, and n-BuLi (638 µL of a 1.6 M in n-hexane, 1.02 mmol) was added dropwise. The mixture
was stirred for 15 min and was allowed to warm to room temperature for 5 min, and was cooled to –78 °C. A solution of the vinyl sulfoximine (1 mmol) in THF (22 mL), which was previously cooled to –78 °C, was added to the first Schlenck flask within 5 min via a double-ended cannula. The yellow mixture was stirred for 40 min and was allowed to warm to 0 °C before quenching with saturated aqueous NH₄Cl. The organic layer was separated, and the aqueous layer was extracted with EtOAc (3×30 mL). The combined organic phases were dried (MgSO₄) and concentrated in vacuo.

4.3. General Procedure for the Preparation of Phosphine Boranes (GP-3)

The synthesis was carried out under strict oxygen- and water-free conditions. In an oven dried round bottom Schlenck flask, the appropriate N-substituted vinyl sulfoximine (1 mmol) was dissolved in anhydrous and degassed THF (8 mL). Then diphenylphosphine (205 mg, 1.1 mmol) and freshly sublimed t-BuOK (11 mg, 0.1 mmol) were successively added at room temperature. The mixture was stirred at the same temperature until TLC indicated a complete conversion of the vinyl sulfoximine (1 to 2 h). The mixture was cooled to 0 °C and BH₃-THF (2.2 mL of a 1 M solution in THF, 2.2 mmol) was added dropwise. The mixture was allowed to warm to room temperature, and after 1 h it was cooled to 0 °C. 1 M H₂SO₄ (CAUTION: gas evolution) was added carefully until a pH of 5 was reached, and the mixture was extracted with CH₂Cl₂ (3×10 mL). The combined organic phases were dried (MgSO₄) and concentrated in vacuum. The ratio of diastereomeric phosphine boranes was determined by HPLC analysis or ¹H NMR spectroscopy of the crude mixture.

4.4. General Procedure for the Preparation of Phosphino-Sulfoximines (GP-4)

The solvents used in this procedure for the reaction and the purification process were dried and degassed. The synthesis was carried out in an oven dried round bottom Schlenck flask under strict oxygen- and water-free conditions. To a solution of the phosphine borane adduct (1 mmol) in anhydrous and degassed toluene (10 mL) was added DABCO (117 mg, 1.05 mmol) at room temperature. The solution was heated at 40 °C (1 h for the cyclic phosphine boranes, 2 h for the acyclic phosphine boranes), and the solvent was removed under reduced pressure to give a sticky solid. A short chromatographic column equipped with a Schlenck adaptor on the top and a 100 mL round bottom Schlenck flask at the bottom was
filled with silica gel. The chromatographic column was kept under high vacuum for 5 min and filled with argon. This was repeated 4 times. The silica gel was wetted with solvent (Et$_2$O/CH$_2$Cl$_2$, 97:3) by applying a low argon pressure on the top of the column and low vacuum at the Schlenck flask so that the silica gel remained wet. Then the crude mixture was dissolved in the minimum amount of CH$_2$Cl$_2$, and the solution was loaded on the top of the chromatographic column using a syringe. The chromatographic column was eluted with approximately 25 mL of solvent (Et$_2$O/CH$_2$Cl$_2$, 97:3) using a syringe and collected in the Schlenck flask. The Schlenck flask was disconnected from the column and the solvent was removed under high vacuo to yield the free phosphine.

4.5. General Procedure for the Catalytic Allylic Alkylation Reactions (GP-5)

This procedure was run in an oven dried round bottom Schlenck flask under oxygen- and water-free conditions. Pd$_2$DBA$_3$·CHCl$_3$ (7.4 mg, 7 µmol) and phosphine (14 µmol) were dissolved in CH$_2$Cl$_2$ (2 mL). The mixture was heated at reflux for 1 h, allowed to reach room temperature and transferred to a Schlenck flask containing the appropriate allylic acetate (480 µmol). The volume of solvent was adjusted to 3 mL through addition of CH$_2$Cl$_2$, and the mixture was treated subsequently with dimethyl malonate (138 µL, 1.19 mmol), N,O-bis(trimethylsilyl)acetamide (320 µL, 1.19 mmol) and lithium acetate (1 mg). After TLC indicated the complete conversion of the allylic acetate, the mixture was quenched with water (3 mL) and extracted with EtOAc (3×3 mL). The combined organic phases were dried (MgSO$_4$) and concentrated in vacuo.
5. Synthesis of N-Substituted S-Methyl-sulfoximines

5.1. (+)-(S)-(N-Methyl-S-methyl-sulfonimidoyl)benzene (52)

![Chemical Structure of 52](image)

C₈H₁₁NOS

MW = 169.24 g.mol⁻¹

Sulfoximine 24 (44.7 g, 290 mmol) and paraformaldehyde (19.2 g, 640 mmol) were dissolved in 98% HCO₂H (850 mL) and the mixture was heated at reflux for 3 d. Then HCO₂H was distilled off, the residue dissolved in water (400 mL) and Na₂CO₃ was added carefully until a pH of 9 was reached. The aqueous phases was extracted with EtOAc (6×150 mL) and the combined organic layers were dried (MgSO₄) and concentrated in vacuo. High vacuum distillation (0.9 mBar, 88 °C) furnished sulfoximine 52 (45.7 g, 93%) as a colourless oil.

¹H NMR (300 MHz, CDCl₃): δ = 2.59 (s, 3H, NCH₃), 3.02 (s, 3H, SCH₃), 7.47–7.60 (m, 3H, o-Ph and p-Ph), 7.84 (m, 2H, m-Ph).

¹³C NMR (75 MHz, CDCl₃): δ = 29.5 (CH₃, NCH₃), 45.0 (CH₃, SCH₃), 128.8 (CH), 129.5 (CH) (S-o-Ph and S-m-Ph), 133.0 (CH, S-p-Ph), 138.7 (C, S-i-Ph).

Analytical data are in agreements with those reported in the literature.¹⁸⁵
5.2. (+)-(S)-(N-tert-Butyldiphenylsilyl-S-methyl-sulfonimidoyl)benzene (55)

To a solution of sulfoximine 24 (5.46 g, 35.8 mmol) in anhydrous DMF (50 mL) was added imidazol (5 g, 73 mmol) and the mixture was cooled to 0 °C. A solution of t-butyldiphenyl-chlorosilane (12 g, 44 mmol) in DMF (25 mL) was added to the mixture, which was stirred for 1 h at 0 °C and then 6 h at room temperature. The mixture was poured into ice cold water (120 mL) and extracted with cyclohexane (5×100 mL). The combined organic phases were dried (MgSO₄) and concentrated in vacuo. Column chromatography (cyclohexane/EtOAc, 5:1) afforded sulfoximine 55 (14.55 g, 98%) as a colourless oil.

\[ \text{C}_{23}\text{H}_{27}\text{NOSSi} \]
MW = 393.62 g.mol⁻¹

\[^{1}H\text{ NMR}\ (400\text{ MHz},\ \text{CDCl}_3):\ \delta = 1.10\ (s,\ 9\text{H, C(CH}_3)_3),\ 2.86\ (s,\ 3\text{H, SCH}_3),\ 7.27–7.46\ (m,\ 8\text{H, S-m-Ph Si-m-Ph and Si-p-Ph}),\ 7.51\ (m,\ 1\text{H, S-p-Ph}),\ 7.71\ (m,\ 2\text{H, Si-o-Ph}),\ 7.77\ (m,\ 2\text{H, Si-o'-Ph}),\ 7.94\ (m,\ 2\text{H, S-o-Ph}).\]

\[^{13}C\text{ NMR}\ (100\text{ MHz, CDCl}_3):\ \delta = 19.3\ (C,\ Si-C),\ 27.1\ (CH_3,\ C(CH}_3)_3),\ 48.9\ (CH_3,\ S-CH}_3),\ 126.8\ (CH,\ S-o-Ph),\ 127.19\ (CH,\ Si-m-Ph),\ 127.23\ (CH,\ Si-m-Ph'),\ 128.66\ (CH,\ S-m-Ph),\ 128.79\ (CH,\ Si-p-Ph),\ 128.84\ (CH,\ Si-p-Ph'),\ 132.0\ (CH,\ S-p-Ph),\ 135.35\ (CH,\ Si-o-Ph),\ 135.41\ (CH,\ Si-o-Ph'),\ 136.0\ (C,\ Si-C),\ 136.1\ (C,\ Si-C'),\ 144.2\ (C,\ S-C).\]

Analytical data are in agreements with those reported in the literature.\[^{186}\]
5.3. (+)-(S)-(N-Tosyl-S-methyl-sulfonimidoyl)benzene (54)

To a solution of sulfoximine 24 (12.07 g, 77.76 mmol) in pyridine (52 mL) was added tosylchloride (15.00 g, 77.76 mmol) at room temperature whereby the solution turned brown. A precipitate appeared and the mixture was stirred overnight at the same temperature. The salts were filtered off and the mixture was poured into H₂O (200 mL). The mixture was extracted with CH₂Cl₂ (3x120 mL) and the combined organic phases were washed twice with 10% HCl (2x30 mL) and finally with water (50 mL). The organic phase was dried (MgSO₄) and concentrated in vacuo. Cristallisation of the residue from EtOH afforded sulfoximine 54 (22.00 g, 92%) as a white solid.

**¹H NMR** (300 MHz, CDCl₃): δ = 2.40 (s, 3H, PhCH₃), 3.43 (s, 3H, SCH₃), 7.27 (d, ³J_H−H = 8.0 Hz, 2H, SO₂-m-Ph), 7.61 (m, 2H, S-m-Ph), 7.71 (m, 1H, S-p-Ph), 7.86 (bd, ³J_H−H = 8.5 Hz, 2H, SO₂-o-Ph), 8.01 (bd, ³J_H−H = 8.0 Hz, 2H, S-o-Ph).

**¹³C NMR** (75 MHz, CDCl₃): δ = 21.5 (CH₃, PhCH₃), 46.6 (CH₃, S-CH₃), 126.5 (CH, SO₂-o-Ph), 127.3 (CH, S-o-Ph), 129.1 (CH, SO₂-m-Ph), 129.5 (CH, S-m-Ph), 134.2 (CH, S-p-Ph), 138.2 (C), 140.4 (C), 142.7 (C) (S-i-Ph, SO₂-i-Ph and SO₂-p-Ph).

Analytical data are in agreements with those reported in the literature.¹⁸⁷
5.4. (+)-(S)-(N-Benzyl-S-methyl-sulfonimidoyl)benzene (53)

\[
\begin{align*}
\text{In an oven dried round bottom Schlenck flask, sulfoximine 24 (7.76 g, 50 mmol) was} \\
\text{dissolved in anhydrous DME (50 mL). This solution was added dropwise at 0 °C using a} \\
\text{double-ended cannula to a suspension of potassium hydride (2.2 g, 55 mmol from a 35%} \\
\text{suspension in mineral oil which was weighed after washing the suspension twice with hexane} \\
\text{and dried in vacuo) in DME (50 mL). The mixture was stirred for 30 min at room temperature,} \\
\text{and then solid } n\text{-Bu}_{4}\text{NBr (0.80 g, 2.5 mmol) and benzylbromid (8.88 mL, 75 mmol) were} \\
\text{successively added. After 1 h, TLC showed the complete conversion of the starting material} \\
\text{24. Then the reaction mixture was cooled to 0 °C and ice cold 2 M sulphuric acid (CAUTION:} \\
\text{gas evolution) was carefully added until a pH of 1 was reached. Et}_{2}\text{O (120 mL) was added,} \\
\text{and the organic phase was discarded. The aqueous phase was neutralized by careful addition} \\
\text{of solid } \text{Na}_{2}\text{CO}_{3} \text{ and extracted with EtOAc (5×75 mL). The combined organic phases were} \\
\text{dried (MgSO}_{4} \text{) and concentrated in vacuo. Purification by Kugelrohr distillation (2.3 mbar,} \\
\text{160 °C) afforded sulfoximine 53 (11.26 g, 90%) as a colourless oil.}
\end{align*}
\]

\[\text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 3.14 \text{ (s, 3H, SCH}_2\text{)}, 3.98 \text{ (d, } ^2J_{H-H} = 14.3 \text{ Hz, 1H, NCH}_2\text{)}, \\
4.20 \text{ (d, } ^2J_{H-H} = 14.3 \text{ Hz, 1H, NCH}_2\text{)}, 7.19 \text{ (tt, } ^3J_{H-H} = 7.2 \text{ Hz, } ^4J_{H-H} = 1.4 \text{ Hz, 1H, CH}_2-p\text{-Ph),} \\
7.28 \text{ (m, 2H, CH}_2-m\text{-Ph), 7.35 \text{ (m, 2H, CH}_2-o\text{-Ph), 7.52–7.64 \text{ (m, 3H, S-o-Ph and S-p-Ph),}} \\
7.94 \text{ (m, 2H, S-m-Ph).}
\]

\[\text{C NMR (100.6 MHz, CDCl}_3\text{): } \delta = 45.2 \text{ (CH}_3\text{, S-CCH}_3\text{)}, 47.3 \text{ (CH}_2\text{, N-CH}_2\text{), 126.4 \text{ (CH,} \\
\text{NCH}_2-p\text{-Ph), 127.4 \text{ (CH, NCH}_2-o\text{-Ph), 128.1 \text{ (CH, NCH}_2-m\text{-Ph), 128.5 \text{ (CH, S-o-Ph), 129.3} \\
\text{ (CH, S-m-Ph), 132.7 \text{ (CH, S-p-Ph), 139.2 \text{ (C), 141.0 \text{ (C) (S-i-Ph and NCH}_2-i\text{-Ph).}} \\
R_f \text{ (cyclohexane/EtOAc, 2:1): 0.20.}\\
\]
Analytical data are in agreements with those reported in the literature.\textsuperscript{188}

**6. Synthesis of Acyclic Vinyl Sulfoximines**

6.1. (+)-(E)-(2-(\((S)-N\)-Benzyl-S-phenylsulfonimidoyl)vinyl)benzene (59)

Following GP-1, the vinyl sulfoximine \textbf{59} was prepared starting from sulfoximine \textbf{53} (2.30 g, 9.38 mmol), \(n\)-BuLi (16.45 mL, 10.32 mmol), benzaldehyde (1.10 g, 10.32 mmol), ClCO\(_2\)Me (980 mg, 10.32 mmol) and DBU (1.57 g, 10.32 mmol) in THF (30 mL). Purification by column chromatography (cyclohexane/EtOAc, 85:15) afforded the vinyl sulfoximine \textbf{59} (3.84 g, 91\%) as a pale yellow solid. Crystallisation by layering hexane on the top of a saturated solution of the crude mixture in CH\(_2\)Cl\(_2\) afforded the vinyl sulfoximine \textbf{59} as fine white needles.

\textbf{\(^1\)H NMR} (300 MHz, CDCl\(_3\)): \(\delta = 4.22\) (d, \(^2J_{HH} = 14.6\) Hz, 1H, NCH\(_2\)), 4.35 (d, \(^2J_{HH} = 14.6\) Hz, 1H, NCH\(_2\)), 6.88 (d, \(^3J_{HH} = 15.3\) Hz, 1H, SCH), 7.22 (m, 1H, Ph), 7.34 (m, 5H, Ph), 7.44 (m, 4H, Ph), 7.56 (4H, m, Ph and S-CH=CH), 8.01 (m, 2H, Ph).

\textbf{\(^{13}\)C NMR} (75 MHz, CDCl\(_3\)): \(\delta = 47.2\) (CH\(_2\)), 126.5 (CH), 127.6 (CH), 127.8 (CH), 128.3 (CH), 128.4 (CH), 128.7 (CH), 129.0 (CH), 129.3 (CH), 130.8 (CH), 132.7 (CH), 132.8 (C), 140.1 (C), 141.5 (C), 142.6 (CH).

\textbf{MS} (Cl, methane): \(m/z\) (%) = 334 [M\(^+\)+1] (100), 332 (5), 257 (4), 256 (7), 232 (5), 230 (4), 229 (13), 209 (5), 208 (12), 124 (3), 107 (3), 106 (8), 105 (6), 91 (10).
**Experimental Part**

**IR (KBr):** \( \nu = 3058 \text{ (m)}, 3027 \text{ (m)}, 2922 \text{ (w)}, 2882 \text{ (s)}, 2836 \text{ (m)}, 1750 \text{ (w)}, 1612 \text{ (m)}, 1574 \text{ (w)}, 1491 \text{ (m)}, 1445 \text{ (m)}, 1349 \text{ (w)}, 1240 \text{ (s)}, 1122 \text{ (s)}, 1074 \text{ (s)}, 1025 \text{ (w)}, 974 \text{ (s)}, 921 \text{ (w)}, 886 \text{ (m)}, 861 \text{ (m)}, 810 \text{ (m)} \text{ cm}^{-1} \).

**HRMS (EI, 70 eV):**

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**Elemental analysis:**

\( \text{MW} = 333.45 \text{ g.mol}^{-1} \)

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**Melting point:** 101 °C.

**Optical rotation:** \([\alpha]_D^{+24.0} (c 1.00, \text{ CH}_2\text{Cl}_2)\).

**R\(_f\) (cyclohexane/EtOAc, 85:15):** 0.23.

6.2. (–)-(E)-(2-((S)-N-tert-Butyldiphenylsilyl-S-phenylsulfonimidoyl)vinyl) benzene (61)

\[
\begin{align*}
\text{H}_3\text{C} & \text{Si} \quad \text{N} \quad \text{O} \\
\text{H}_3\text{C} & \text{CH}_3 \\
\text{H}_3\text{C} & \\
\end{align*}
\]

Following GP-1, the vinyl sulfoximine 61 was prepared starting from sulfoximine 55 (6.00 g, 15.24 mmol), \( n\)-BuLi (10.5 mL, 16.77 mmol), benzaldehyde (1.78 g, 16.77 mmol), CICO\(_2\)Me (1.59 g, 16.77 mmol) and DBU (2.55 g, 16.77 mmol) in THF (45 mL). Purification by column chromatography (cyclohexane/EtOAc, 12:1) afforded the vinyl sulfoximine 61 (6.23 g, 85%) as a colourless oil which solidified upon standing at 4 °C.
**EXPERIMENTAL PART**

**¹H NMR** (300 MHz, CDCl₃): δ = 1.13 (s, 9H, C(CH₃)₃), 6.63 (d, J_H-H = 15.2 Hz, 1H, SCH), 7.19 (m, 2H, Ph), 7.28 (m, 9H, Ph), 7.42 (m, 4H, Ph and S-CH=C), 7.75 (4H, m, Ph), 7.93 (m, 2H, Ph).

**¹³C NMR** (75 MHz, CDCl₃): δ = 19.5 (C), 27.2 (CH₃), 127.32 (CH), 127.34 (CH), 127.36 (CH), 128.2 (CH), 128.7 (CH), 128.8 (CH), 128.91 (CH), 128.93 (CH), 130.2 (CH), 131.8 (CH), 132.0 (CH), 132.9 (C), 135.61 (CH), 135.64 (CH), 136.3 (C), 136.4 (C), 138.8 (CH), 144.3 (C).


**IR** (KBr): ν = 3048 (m), 2952 (m), 2928 (m), 2887 (m), 2853 (m), 1616 (m), 1578 (w), 1472 (w), 1445 (m), 1425 (m), 1390 (w), 1283 (s), 1185 (w), 1140 (s), 1103 (s), 1025 (m), 999 (w), 965 (m), 870 (m), 820 (s) cm⁻¹.

**HRMS** (EI, 70 eV):

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**Elemental analysis:**

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**Melting point:** 69 °C.

**Optical rotation:** [α]_D = –62.26 (c 1.30, CH₂Cl₂).

**R₇** (cyclohexane/EtOAc, 15:1): 0.17.
6.3. (++)-(E)-(2-((S)-N-Methyl-S-phenylsulfonimidoyl)vinyl)benzene (58)

Following GP-1, the vinyl sulfoximine 58 was prepared starting from sulfoximine 52 (4.05 g, 23.93 mmol), n-BuLi (16.45 mL, 26.29 mmol), benzaldehyde (2.79 g, 26.29 mmol), ClCO₂Me (2.49 g, 26.29 mmol) and DBU (4.00 g, 26.29 mmol) in THF (60 mL). Purification by column chromatography (cyclohexane/EtOAc, 3:2) afforded the vinyl sulfoximine 58 (5.42 g, 88%) as a colourless oil, which crystallized at −26°C.

**¹H NMR** (300 MHz, CDCl₃): δ = 2.81 (s, 3H, NCH₃), 6.88 (d, J_H-H = 15.3 Hz, 1H, SCH), 7.37 (m, 3H, CH-m-Ph and CH-p-Ph), 7.47 (m, 2H, CH-o-Ph), 7.50–7.62 (m, 4H, S-o-Ph and S-p-Ph and S-CH=CH), 7.96 (m, 2H, S-m-Ph).

**¹³C NMR** (75 MHz, CDCl₃): δ = 29.5 (CH₃, N-CH₃), 127.4 (CH, S-CH), 128.4 (CH), 128.7 (CH), 129.0 (CH), 129.4 (CH) (CH-o-Ph, CH-m-Ph, S-o-Ph and S-m-Ph), 130.8 (CH), 132.7 (CH) (CH-p-Ph and S-p-Ph), 132.8 (C, CH-i-Ph), 139.4 (C, S-i-Ph), 142.6 (CH, S-CH=CH).

**Melting point:** below 20 °C.

**Rᶠ** (cyclohexane/EtOAc, 3:2): 0.23.

Analytical data are in agreements with those reported in the literature.¹⁸⁹
6.4. (–)-(E)-2-((S)-N-Tosyl-S-phenylsulphonimidoyl)vinyl)benzene (60)

Following GP-1, the vinyl sulfoximine 60 was prepared starting from sulfoximine 54 (6.80 g, 22.0 mmol), n-BuLi (15.3 mL, 24.2 mmol), benaldehyde (2.57 g, 24.2 mmol), ClCO₂Me (2.28 g, 24.2 mmol) and DBU (3.69 g, 24.2 mmol) in THF (60 mL). Purification by column chromatography (cyclohexane/EtOAc/DCM, 13:6:1) afforded the vinyl sulfoximine 60 (5.42 g, 88%) as a white solid.

**¹H NMR** (300 MHz, CDCl₃): δ = 2.36 (s, 3H, Ph-CH₃), 6.90 (d, J_H-H = 15.1 Hz, S-CH), 7.23 (m, 2H, Ph), 7.34–7.47 (m, 4H, Ph), 7.52–7.67 (m, 5H, Ph and S-CH=CH), 7.86 (m, 2H), 8.01 (m, 2H, Ph).

**¹³C NMR** (75.4 MHz, CDCl₃): δ = 21.5 (CH₃), 125.5 (CH), 126.8 (CH), 127.7 (CH), 128.9 (CH), 129.1 (CH), 129.3 (CH), 129.6 (CH), 131.7 (CH), 131.8 (C), 134.0 (CH), 138.7 (C), 140.8 (C), 142.8 (C), 143.9 (CH).

**R_f** (cyclohexane/EtOAc/CH₂Cl₂, 65:30:5): 0.25.

Analytical data are in agreements with those reported in the literature.¹⁹⁰
7. Synthesis of ω-Bromo Vinyl Sulfoximines

The vinyl sulfoximines 115 and 116 were contaminated with unidentified side products even after several purifications including preparative HPLC. Moreover, the vinyl sulfoximines 115 and 116 were not stored but used in the next step to avoid degradation.

7.1. (S,E)-(N-Methyl-6-bromohex-1-enyl-sulfonimidoyl)benzene (115)

Following GP-1, the vinyl sulfoximine 115 was prepared starting from sulfoximine 52 (540 mg, 3.19 mmol), n-BuLi (2.19 mL, 3.50 mmol), 5-bromopentanal (580 mg, 3.51 mmol), ClCO₂Me (332 mg, 3.51 mmol) and DBU (486 mg, 3.51 mmol) in THF (8 mL). Purification by column chromatography (cyclohexane/EtOAc, 3:2) afforded the vinyl sulfoximine 115 (2.65 g, 83%) as a pale yellow oil.

**1H NMR** (300 MHz, CDCl₃): δ = 1.63 (m, 2H, CHCH₂CH₂), 1.85 (m, 2H, BrCH₂CH₂), 2.27 (m, 2H, CHCH₂), 2.73 (s, 3H, NCH₃), 3.38 (t, 3J_H-H = 6.8 Hz, 2H, BrCH₂), 6.34 (dt, 3J_H-H = 15.1 Hz, 3J_H-H = 1.7 Hz, 1H, SCH), 6.85 (dt, 3J_H-H = 15.1 Hz, 3J_H-H = 6.8 Hz, 1H, SCHCH), 7.56 (m, 3H, S-o-Ph and S-p-Ph), 7.87 (m, 2H, S-m-Ph).

**13C NMR** (75 MHz, CDCl₃): δ = 26.2 (CH₂, CHCH₂CH₂), 29.4 (CH₃, NCH₃), 30.5 (CH₂, CHCH₂), 32.0 (CH₂, BrCH₂CH₂), 33.0 (CH₂, BrCH₂), 128.7 (CH, S-m-Ph), 129.3 (CH, S-o-Ph), 130.8 (CH, SCH), 132.6 (CH, S-p-Ph), 139.3 (C, S-i-Ph), 145.7 (CH, SCH=CH).

R_f (cyclohexane/EtOAc, 1:1): 0.32.
7.2. (S,E)-(N-Benzyl-6-bromohex-1-enyl-sulfonimidoyl)benzene (116)

Following GP-1, the vinyl sulfoximine 116 was prepared starting from sulfoximine 53 (4.32 g, 17.6 mmol), n-BuLi (12.1 mL, 19.3 mmol), 5-bromopentanal (3.19 g, 19.3 mmol), ClCO₂Me (1.83 g, 19.3 mmol) and DBU (2.89 mL, 19.7 mmol) in THF (65 mL). Purification by column chromatography (cyclohexane/EtOAc, 3:1) afforded the vinyl sulfoximine 116 (5.0 g, 77%) as a slightly pale yellow oil.

\[ \text{MW} = 392.35 \text{ g.mol}^{-1} \]

**1H NMR** (400 MHz, CDCl₃): \( \delta = 1.49 \) (m, 2H, CHCH₂CH₂), 1.82 (m, 2H, BrCH₂CH₂), 2.23 (m, 2H, CHCH₂), 3.35 (t, \( ^3J_{H-H} = 6.6 \text{ Hz} \), 2H, BrCH₂), 4.12 (d, \( ^3J_{H-H} = 14.6 \text{ Hz} \), 1H, NCH₂), 4.26 (d, \( ^3J_{H-H} = 14.6 \text{ Hz} \), 1H, NCH₂), 6.37 (dt, \( ^3J_{H-H} = 15.1 \text{ Hz} \), \( ^3J_{H-H} = 6.6 \text{ Hz} \), 1H, SCH), 6.88 (dt, \( ^3J_{H-H} = 15.1 \text{ Hz} \), \( ^3J_{H-H} = 6.6 \text{ Hz} \), 1H, SCHCH), 7.20 (m, 1H, NCH₂-p-Ph), 7.29 (m, 2H, NCH₂-m-Ph), 7.38 (m, 2H, NCH₂-o-Ph), 7.54 (m, 3H, S-o-Ph and S-p-Ph), 7.91 (m, 2H, S-m-Ph).

**13C NMR** (100 MHz, CDCl₃): \( \delta = 25.7 \) (CH₂, CHCH₂CH₂), 30.4 (CH₂, CHCH₂), 31.8 (CH₂, BrCH₂CH₂), 33.0 (CH₂, BrCH₂), 47.0 (CH₂, NCH₂), 126.3 (CH, NCH₂-p-Ph), 127.3 (CH, NCH₂-m-Ph), 128.0 (CH, NCH₂-o-Ph), 128.4 (CH, S-m-Ph), 129.5 (CH, S-o-Ph or S-p-Ph), 130.8 (CH, S-CH), 132.4 (CH, S-o-Ph or S-p-Ph), 139.6 (C, S-i-Ph), 141.2 (C, NCH₂-i-Ph), 145.6 (CH, S-CH=CH).

**MS** (Cl, methan) \( m/z \) (%): 394 [M⁺+1] (88), 392 [M⁺+1] (100), 390 (10), 350 (16), 349 (11), 348 (46), 312 (13), 268 (11), 266 (13), 125 (13), 91 (20).

**Rₜ** (cyclohexane/EtOAc, 4:1): 0.18.
8. Synthesis of Cyclic Vinyl Sulfoximines

8.1. (+)-(S)-(N-Methyl-(S-cyclohex-1-ene)sulphonimidoyl)benzene (117)

Following GP-2, the cyclic vinyl sulfoximine 117 was prepared starting from the ω-
obromosulfoximine 115 (4.21 g, 13.31 mmol) in THF (50 mL), diisopropylamine (1.91 mL, 13.73 mmol) in THF (420 mL) and n-BuLi (8.58 mL, 13.73 mmol). Purification by column
chromatography (cyclohexane/EtOAc, 3:2): afforded the vinyl sulfoximine 117 (2.50 g, 80%) as a white solid.

\[ \text{1H NMR} \ (400 \text{ MHz, CDCl}_3): \delta = 1.47–1.70 \ (m, 4H, CH}_2 \text{ ring), 2.06} \ (m, 1H, CH}_2 \text{ ring), 2.22–} \]
\[2.38 \ (m, 3H, CH}_2 \text{ ring), 2.76} \ (s, 3H, NCH}_3 \text{), 7.02} \ (m, 1H, SCCH), 7.50 \ (m, 3H, Ph), 7.86 \ (m, 2H, Ph). \]

\[ \text{13C NMR} \ (100 \text{ MHz, CDCl}_3): \delta = 20.9 \ (CH}_2 \text{), 22.1} \ (CH}_2 \text{), 23.6} \ (CH}_2 \text{), 25.7} \ (CH}_2 \text{), 29.4} \ (CH}_3 \text{), 128.80} \ (CH), 128.82 \ (CH), 132.1 \ (CH), 138.0 \ (C), 138.2 \ (CH), 138.5 \ (C). \]

\[ \text{MS (Cl, methane): m/z} \ (%): 236 \ [M}^+1 \] (18), 235 \ [M}^+ \] (93), 234 (10), 187 (4), 186 (4), 158 (6), 139 (11), 129 (11), 126 (11), 125 (25), 111 (9), 110 (100), 109 (16), 97 (13), 91 (8), 82 (6), 81 (58), 80 (6), 79 (45), 78 (19), 77 (33), 69 (15), 68 (18). \]

\[ \text{IR (KBr): ν = 3060} \ (w), 2935(s), 2867 \ (m), 2801 \ (m), 1444 \ (s), 1341 \ (w), 1244 \ (s), 1148 \ (s), 1110 \ (m), 1081 \ (m), 1048} \ (w), 1022 \ (w), 937 \ (m), 864} (m) \ cm}^{-1}. \]

\[ \text{HRMS (El, 70 eV):} \quad \text{C}_{13}\text{H}_{17}\text{NOS} \quad \text{Calculated} \quad \text{Found} \]
\[ \quad 235.1031 \quad 235.1031 \]

Melting point: 49 °C.

Optical rotation: \[ [\alpha]_D +31.15 \ (c 0.26, \text{Et}_2\text{O}). \]
EXPERIMENTAL PART

$R_f$ (cyclohexane/EtOAc, 1:1): 0.40.

8.2. (−)-(S)-(N-Benzyl-(S-cyclohex-1-ene)sulfonimidoyl)benzene (118)

Following GP-2, the cyclic vinyl sulfoximine 118 was prepared starting from the $\omega$-bromosulfoximine 116 (3.73 g, 9.51 mmol) in THF (90 mL), diisopropylamine (1.37 mL, 9.70 mmol) in THF (240 mL) and n-BuLi (6.06 mL, 9.70 mmol). Purification by column chromatography (cyclohexane/EtOAc, 85:15) afforded the cyclic vinyl sulfoximine 118 (2.74 g, 92%) as a white solid.

$^1H$ NMR (300 MHz, CDCl$_3$): $\delta = 1.45–170$ (m, 4H, CH$_2$ ring), 2.08 (m, 1H, CH$_2$ ring), 2.20–2.41 (m, 3H, CH$_2$ ring), 4.18 (d, $^3J_{H, H} = 14.9$ Hz, 1H, NCH$_2$), 4.27 (d, $^4J_{H, H} = 14.9$ Hz, 1H, NCH$_2$), 7.09 (m, 1H, SCCH), 7.21 (m, 1H, NCH$_2$Ph), 7.30 (m, 2H, NCH$_2$Ph), 7.41–7.60 (m, 5H, SPh and NCH$_2$Ph), 7.91 (m, 2H, SPh).

$^{13}C$ NMR (75 MHz, CDCl$_3$): $\delta = 20.9$ (CH$_2$), 22.2 (CH$_2$), 23.7 (CH$_2$), 25.8 (CH$_2$), 46.9 (CH$_2$), 126.3 (CH), 127.4 (CH), 128.1 (CH), 128.99 (CH), 129.00 (CH), 132.4 (CH), 138.63 (C), 138.74 (CH), 138.86 (C), 141.8 (C).

MS (CI, isobutane): $m/z$ (%) = 312 [M$^{+}+1$] (100), 246 (3).

IR (KBr): $\nu = 3379$ (w), 3062 (m), 3021 (w), 2934 (s), 2859 (m), 1641 (w), 1491 (w), 1445 (m), 1352 (w), 1257 (s), 1135 (s), 1078 (m), 1024 (w), 909 (m) cm$^{-1}$.

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Melting point: 61–62 °C.

Optical rotation: \([\alpha]_D -0.80 \ (c \ 1.0, \ CHCl_3)\).

\[ R_f \ (\text{cyclohexane/EtOAc, 4:1}): 0.47. \]

9. Synthesis of Phosphine Boranes

9.1. (–)-Diphenyl((1R)-1-phenyl-2-((S)-N-methyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (62) and (+)-Diphenyl((1S)-1-phenyl-2-((S)-N-methyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (63)

Following GP-3, the phosphine boranes 62 and 63 were prepared starting from the vinyl sulfoximine 58, (400 mg, 1.55 mmol), diphenylphosphine (335 mg, 1.70 mmol) and \( t \)-BuOK (17 mg, 170 µmol) in THF (12 mL). After the complete conversion of the sulfoximine 58, BH₃•THF (3.41 mL, 3.41 mmol) was added and the mixture was worked up after stirring for 1 h. The \( dr \) of 62:63 was 78:22 (Chiral OD-H column, detector 254 nm, \( n \)-heptane/isopropanol: 98/2, flow: 0.75 mL/min, 36 bar, \( R_f \) (62): 22.4 min; \( R_f \) (63): 27.1 min. Purification by column chromatography (cyclohexane/EtOAc, 4:1) afforded the phosphine borane 63 (122 mg, 17%) as a white foam and the phosphine borane 62 (430 mg, 61%) as a white crystalline solid. The major isomer 62 could be recrystallised by layering hexane on the top of a saturated solution of a mixture of both isomers in CH₂Cl₂, which gave the phosphine borane 62 as colourless single crystals suitable for X-ray analysis.

Phosphine borane 62: \(^1\text{H NMR}\) (300 MHz, CDCl₃): \( \delta = 0.4–1.4 \) (bs, 3H, BH₃), 2.51 (s, 3H, NCH₃), 3.63 (ddd, \( ^2J_{H-H} = 15.1 \) Hz, \( ^3J_{P-H} = 10.2 \) Hz, \( ^3J_{H-H} = 1.6 \) Hz, 1H, SCH₂), 4.06 (ddd, \( ^2J_{H-H} = 15.1 \) Hz, \( ^3J_{H-H} = 11.8 \) Hz, \( ^3J_{P-H} = 1.9 \) Hz, 1H, SCH₂), 4.46 (ddd, \( ^2J_{P-H} = 15.1 \) Hz, \( ^3J_{H-H} = \)
11.8 Hz, $^3J_{H,H} = 1.6$ Hz, 1H, SCH$_2$CH), 6.79 (m, 4H), 6.89 (m, 1H), 7.13–7.23 (m, 6H), 7.29 (m, 2H), 7.37 (m, 2H), 7.59 (m, 3H), 8.01 (m, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$): δ = 29.3 (CH$_3$, NCH$_3$), 38.0 (d, $^1J_{P,C}$ = 28.8 Hz, CH, SCH$_2$CH), 56.7 (d, $^2J_{P,C}$ = 7.9 Hz, CH$_2$, SCH$_2$), 125.9 (d, $^1J_{P,C}$ = 51.6 Hz, C, i-Ph), 127.0 (d, $^1J_{P,C}$ = 54.9 Hz, C, i-Ph), 127.3 (d, $^1J_{P,C}$ = 2.4 Hz, CH), 127.6 (d, $^1J_{P,C}$ = 1.9 Hz, CH), 128.2 (d, $^1J_{P,C}$ = 10.1 Hz, CH), 128.9 (CH), 129.1 (CH), 129.4 (d, $^1J_{P,C}$ = 9.7 Hz, CH), 130.0 (d, $^1J_{P,C}$ = 4.2 Hz, CH), 131.2 (d, $^1J_{P,C}$ = 1.7 Hz, CH), 131.8 (C), 132.1 (d, $^1J_{P,C}$ = 1.8 Hz, CH), 132.4 (CH), 132.5 (d, $^1J_{P,C}$ = 8.8 Hz, CH), 133.2 (d, $^1J_{P,C}$ = 8.6 Hz, CH), 136.8 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): δ = 25.48 (bs).

MS (CI, methane): m/z (%) = 456 [M$^+$+1] (1), 453 (1), 303 (4), 301 (7), 300 (23), 299 (100), 298 (24), 289 (11), 288 (7), 211 (2), 196 (6), 184 (14), 157 (5), 156 (54), 125 (28), 107 (4).

IR (KBr): ν = 3908 (w), 3654 (w), 3465 (m), 3055 (m), 2974 (w), 2932 (m), 2871 (m), 2802 (m), 2383 (s), 2348 (s), 2274(w), 1583 (w), 1491 (m), 1438 (m), 1403 (w), 1267 (m), 1236 (s), 1142 (s), 1104 (s), 1064 (s), 997 (w), 916 (m), 855 (s), 823 (m) cm$^{-1}$.

Elemental analysis:

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Melting point: 117 °C.

Optical rotation: $[\alpha]_D$ –116.54 (c 1.19, CH$_2$Cl$_2$).

$R_f$ (cyclohexane/EtOAc, 9:2): 0.10.
Phosphine borane 63: $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 0.3–1.4 (bs, 3H, BH$_3$), 2.61 (s, 3H, NCH$_3$), 3.54 (dd, $^3$J$_{H-H}$ = 14.9 Hz, $^3$J$_{P-H}$ = 10.3 Hz, $^3$J$_{H-H}$ = 1.5 Hz, 1H, SCH$_2$), 3.98 (ddd, $^3$J$_{H-H}$ = 14.9 Hz, $^3$J$_{H-H}$ = 11.8 Hz, $^3$J$_{P-H}$ = 1.9 Hz, 1H, SCH$_2$), 4.39 (ddd, $^3$J$_{P-H}$ = 16.3 Hz, $^3$J$_{H-H}$ = 11.8 Hz, $^3$J$_{H-H}$ = 1.3 Hz, 1H, SCH$_2$CH), 6.88 (m, 2H), 6.92 (m, 2H), 7.04 (m, 1H), 7.14–7.34 (m, 7H), 7.37–7.60 (m, 6H), 7.87 (m, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 29.4 (CH$_3$, NCH$_3$), 38.9 (d, $^3$J$_{P-C}$ = 28.7 Hz, CH, SCH$_2$CH), 56.7 (d, $^2$J$_{P-C}$ = 8.0 Hz, CH$_2$, SCH$_2$), 125.9 (d, $^3$J$_{P-C}$ = 51.6 Hz, C, i-Ph), 127.1 (d, $^3$J$_{P-C}$ = 56.0 Hz, C, i-Ph), 127.5 (d, $^3$J$_{P-C}$ = 2.9 Hz, CH), 127.7 (d, $^3$J$_{P-C}$ = 2.4 Hz, CH), 128.2 (d, $^3$J$_{P-C}$ = 10.1 Hz, CH), 128.9 (CH), 129.1 (CH), 129.7 (d, $^3$J$_{P-C}$ = 9.2 Hz, CH), 130.0 (d, $^3$J$_{P-C}$ = 4.3 Hz, CH), 131.2 (d, $^3$J$_{P-C}$ = 2.4 Hz, CH), 131.9 (d, $^3$J$_{P-C}$ = 2.4 Hz, CH), 132.4 (C), 132.5 (CH), 131.6 (d, $^3$J$_{P-C}$ = 8.8 Hz, CH), 133.2 (d, $^3$J$_{P-C}$ = 8.5 Hz, CH), 138.0 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ = 26.11 (bs).

MS (ESI-MS, MeOH): $m/z$ (%) = 458 [M$^+$+1] (100), 443 (28), 333 (12), 319 (24), 305 (32), 299 (44), 289 (38), 156 (28).

IR (KBr): $\nu$ = 3460 (w), 2922 (m), 2805 (w), 2375 (s), 1971 (w), 1900 (w), 1814 (w), 1673 (w), 1585 (m), 1483 (m), 1438 (s), 1245 (s), 1128 (s), 1063 (s), 915 (m), 855 (w) cm$^{-1}$.

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Melting point: 53–55 °C.
Optical rotation: \([\alpha]_D^{+} +142.94\) (c 1.80, CH\(_2\)Cl\(_2\)).

RF (cyclohexane/EtOAc, 9:2): 0.11.

9.2. (−)-Diphenyl((1R)-1-phenyl-2-((S)-N-benzyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (76) and (+)-Diphenyl((1S)-1-phenyl-2-((S)-N-benzyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (77)

Following GP-3, the phosphine boranes 76 and 77 were prepared starting from the vinyl sulfoximine 59 (700 mg, 2.10 mmol), diphenylphosphine (453 mg, 2.31 mmol) and t-BuOK (22 mg, 0.21 mmol) in THF (18 mL). After the complete conversion of the sulfoximine 59, BH\(_3\)-THF (4.62 mL, 4.62 mmol) was added and the reaction mixture was worked up after stirring for 1 h. The dr of 76:77 was 64:36 (chiralpack-IA column, detector 230 nm, n-heptane/isopropanol: 85/15, flow: 0.75 mL/min, 32 bar, R\(_f\)(77): 14.90 min; R\(_f\)(76): 21.28 min). Purification by column chromatography (cyclohexane/EtOAc, 85:15) afforded the phosphine borane 76 (592 mg, 53%) as a white crystalline solid and the phosphine borane 77 (277 mg, 25%) as a white foam. The major isomer 76 could be recrystallised by layering hexane on the top of a saturated solution of both isomers in CH\(_2\)Cl\(_2\), which gave the phosphine borane 76 as fine white needles.

Phosphine borane 76: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.4–1.5\) (bs, 3H, BH\(_3\)), 3.70 (ddd, \(^2J_{HH} = 14.8\) Hz, \(^3J_{HH} = 10.1\) Hz , \(^3J_{HP} = 1.4\) Hz, 1H, SCH\(_2\)), 3.98 (d, \(^2J_{HH} = 14.6\) Hz, 1H, NCH\(_2\)Ph), 4.04 (d, \(^2J_{HH} = 14.6\) Hz, 1H, NCH\(_2\)Ph), 4.08 (dd, \(^2J_{HH} = 14.8\) Hz, \(^3J_{HH} = 11.8\) Hz, \(^3J_{HP} = 1.8\) Hz, 1H, SCH\(_2\)), 4.54 (ddd, \(^2J_{HH} = 16.7\) Hz, \(^3J_{HH} = 11.8\) Hz, \(^3J_{HP} = 1.4\) Hz, 1H, SCH\(_2\)CH), 6.83 (m, 4H), 6.93 (m, 1H), 7.13–7.35 (m, 13H), 7.44 (m, 2H), 7.53–7.63 (m, 3H), 8.01 (m, 2H).
**Experimental Part**

$^{13}$C **NMR** (100 MHz, CDCl$_3$): $\delta = 37.9$ (d, $^1J_{P-C} = 29.8$ Hz, CH, SCH$_2$CH), 46.9 (CH$_2$, NCH$_3$Ph), 56.3 (d, $^2J_{P-C} = 8.4$ Hz, CH$_2$, SCH$_2$), 125.8 (d, $^1J_{P-C} = 51.9$ Hz, C, i-Ph), 126.3 (CH), 127.0 (d, $^1J_{P-C} = 54.2$ Hz, C, i-Ph), 127.10 (CH), 127.13 (CH), 127.4 (d, $J_{P-C} = 2.3$ Hz, CH), 128.0 (CH), 128.3 (d, $J_{P-C} = 9.9$ Hz, CH), 128.7 (CH), 128.8 (CH), 129.1 (d, $J_{P-C} = 9.9$ Hz, CH), 129.7 (d, $J_{P-C} = 4.6$ Hz, CH), 130.9 (d, $J_{P-C} = 2.3$ Hz, CH), 131.82 (C), 131.85 (CH), 132.2 (CH), 132.3 (d, $J_{P-C} = 9.1$ Hz, CH), 133.0 (d, $J_{P-C} = 9.1$ Hz, CH), 137.5 (C), 141.0 (C).

$^{31}$P **NMR** (162 MHz, CDCl$_3$): $\delta = 25.75$ (bs).

**MS** (CI, isobutane): $m/z$ (%): 534 [M$^+ + 1$] (1), 533 (1), 531 (3), 530 (7), 300 (23), 299 (100), 298 (25), 289 (4), 288 (3), 234 (3), 233 (9), 232 (56).

**IR** (KBr): $\nu = 3866$ (w), 3466 (w), 3047 (m), 2927 (m), 2879 (w), 2842 (m), 2363 (s), 2341 (s), 1555 (w), 1492 (w), 1439 (m), 1387 (w), 1251 (s), 1201 (m), 1136 (s), 1072 (s), 920 (m), 862 (w), 819 (w) cm$^{-1}$.

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**Melting point:** 140 °C.

**Optical rotation:** $[\alpha]_D -140.29$ (c 1.03, CHCl$_3$).

**R$_f$** (cyclohexane/EtOAc, 85:15): 0.18.
**Phosphine borane 77:**

1H NMR (400 MHz, CDCl₃): \( \delta = 0.35–1.40 \) (bs, 3H, BH₃), 3.60 (ddd, \( 2J_{H-H} = 14.8 \) Hz, \( 3J_{H-H} = 10.6 \) Hz, \( 3J_{P-H} = 1.4 \) Hz, 1H, SCH₂Ph), 4.00 (d, \( 2J_{H-H} = 14.9 \) Hz, 1H, NCH₂Ph), 4.06 (ddd, \( 2J_{H-H} = 14.8 \) Hz, \( 3J_{P-H} = 11.6 \) Hz, \( 3J_{H-H} = 1.7 \) Hz, 1H, SCH₂Ph), 4.16 (d, \( 2J_{H-H} = 14.9 \) Hz, 1H, NCH₂Ph), 4.57 (ddd, \( 2J_{P-H} = 16.5 \) Hz, \( 3J_{H-H} = 10.6 \) Hz, \( 3J_{H-H} = 1.7 \) Hz, 1H, SCH₂CH), 6.88 (m, 2H), 6.95 (m, 2H), 7.05 (m, 1H), 7.12–7.32 (m, 12H), 7.40 (m, 1H), 7.48 (m, 4H), 7.56 (m, 1H), 7.92 (m, 2H).

13C NMR (100 MHz, CDCl₃): \( \delta = 38.7 \) (d, \( 1J_{P-C} = 28.9 \) Hz, CH, SCH₂CH), 46.4 (CH₂, NCH₂Ph), 57.1 (d, \( 2J_{P-C} = 8.2 \) Hz, CH₂, SCH₂), 125.6 (d, \( 1J_{P-C} = 51.7 \) Hz, C, i-Ph), 126.2 (CH), 126.9 (d, \( 1J_{P-C} = 54.6 \) Hz, C, i-Ph), 127.0 (CH), 127.2 (d, \( 1J_{P-C} = 2.9 \) Hz, CH), 127.6 (d, \( 1J_{P-C} = 2.4 \) Hz, CH), 127.9 (CH), 128.0 (d, \( 1J_{P-C} = 10.1 \) Hz, CH), 128.72 (CH), 128.76 (CH), 129.0 (d, \( 1J_{P-C} = 9.6 \) Hz, CH), 129.8 (d, \( 1J_{P-C} = 4.3 \) Hz, CH), 131.0 (d, \( 1J_{P-C} = 2.3 \) Hz, CH), 131.8 (d, \( 1J_{P-C} = 2.3 \) Hz, CH), 132.2 (C), 132.39 (d, \( 1J_{P-C} = 8.9 \) Hz, CH), 132.44 (CH), 133.0 (d, \( 1J_{P-C} = 8.5 \) Hz, CH), 138.3 (C), 141.1 (C).

31P NMR (162 MHz, CDCl₃): \( \delta = 26.38 \) (bs).

**MS** (Cl, isobutane): \( m/z \) (%): 534 [M⁺+1] (20), 533 (10), 532 (19), 531 (5), 300 (20), 299 (100), 298 (24), 289 (12), 288 (11), 279 (4), 257 (7), 234 (3), 233 (10), 232 (69), 218 (8), 214 (8), 187 (11), 118 (5), 111 (5), 106 (15), 105 (10), 104 (6), 71 (7), 69 (5).

**IR** (KBr): \( \nu = 3052 \) (m), 2919 (m), 2847 (m), 2365 (s), 2344 (s), 1815 (w), 1582 (w), 1484 (m), 1439 (s), 1247 (s), 1117 (s), 1061 (s), 920 (m), 820 (w) cm⁻¹.

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Melting point: 94 °C.

Optical rotation: \([\alpha]_D +103.6\) (c 0.50, CHCl₃).

\(R_f\) (cyclohexane/EtOAc, 85:15): 0.19.

9.3. (–)-Diphenyl((1S)-1-phenyl-2-((S)-N-tosyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (79) and (+)-Diphenyl((1R)-1-phenyl-2-((S)-N-tosyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (78)

Following GP-3, the phosphine boranes 79 and 78 were prepared starting from the vinyl sulfoximine 60 (2.0 g, 5.03 mmol), diphenylphosphine (1.03 g, 5.5 mmol) and \(t\)-BuOK (56 mg, 500 µmol) in THF (60 mL). After the complete conversion of the sulfoximine 60, BH₃•THF (11 mL, 11 mmol) was added and the reaction mixture was worked up after stirring for 1 h. The \(dr\) was 73:27 (79:78) (Kromasil Si 100 column, detector 254 nm, cyclohexane/EtOAc/CH₂Cl₂: 11/2/0.5, flow: 1 mL/min, 30 bar, \(R_t(78)\): 8.49 min; \(R_t(79)\): 11.07 min). The crude mixture was dissolved in CH₂Cl₂ and silica gel was added before the evaporation so that the crude mixture was adsorbed on silica gel. This was loaded on the top of a column containing silica gel. The purification by column chromatography (cyclohexane/EtOAc/CH₂Cl₂, 11:2:1) afforded in the first collected fractions the phosphine borane 78 which was contaminated with the phosphine borane 79. After evaporation of the solvents, the residue was dissolved in the minimum amount of CH₂Cl₂ and hexane was layered on the top of the saturated solution. The phosphine borane 78 crystallized at –26 °C as colourless needles (540 mg, 18%). The major isomer was eluted with CHCl₃ to yield the phosphine borane 79 which was contaminated with the phosphine borane 78. After evaporation of the solvents, the residue was dissolved in the minimum amount of CH₂Cl₂ and hexane was layered on the top of the saturated solution. The phosphine borane 79 crystallized in CH₂Cl₂ at 4 °C as a wool-type solid (1.53 g, 51%).
Phosphine borane 79: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.4–1.4\) (bs, 3H, B\(\text{H}_3\)), 2.37 (s, 3H, \(\text{H}_3\)-C-Ph-SO\(_2\)), 4.14 (ddd, \(^2J_{H-H} = 14.8\) Hz, \(^3J_{H-H} = 11.4\) Hz, \(^3J_{P-H} = 2.4\) Hz, 1H, SCH\(_2\)), 4.24 (ddd, \(^2J_{H-H} = 14.8\) Hz, \(^3J_{P-H} = 8.6\) Hz, \(^3J_{H-H} = 2.3\) Hz, 1H, SCH\(_2\)), 4.45 (ddd, \(^2J_{P-H} = 16.1\) Hz, \(^3J_{H-H} = 11.4\) Hz, \(^3J_{H-H} = 2.3\) Hz, 1H, SCH\(_2\)CH), 6.73 (m, 2H), 6.80 (t, \(J = 7.7\) Hz, 2H), 6.93 (m, 1H), 7.13–7.24 (m, 8H), 7.28–7.44 (m, 4H), 7.64 (m, 5H), 8.01 (m, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 21.5\) (CH\(_3\), \(\text{H}_3\)-C-Ph-SO\(_2\)), 37.8 (d, \(^1J_{P-C} = 28.3\) Hz, CH, SCH\(_2\)CH), 57.8 (d, \(^2J_{P-C} = 9.2\) Hz, CH\(_2\), SCH\(_2\)), 125.0 (d, \(^1J_{P-C} = 51.8\) Hz, C, i-Ph), 126.2 (d, \(^1J_{P-C} = 55.0\) Hz, C, i-Ph), 126.3 (CH), 127.54 (CH), 127.57 (CH), 127.59 (CH), 128.1 (d, \(J = 10.1\) Hz, CH), 128.8 (CH), 128.9 (CH), 129.3 (d, \(J = 9.8\) Hz, CH), 129.5 (d, \(J = 4.2\) Hz, CH), 130.6 (C), 131.2 (d, \(J = 2.4\) Hz, CH), 132.2 (d, \(J = 2.3\) Hz, CH), 132.3 (d, \(J = 9.0\) Hz, CH), 133.0 (d, \(J = 8.6\) Hz, CH), 133.4 (CH), 136.6 (C), 140.3 (C), 142.5 (C).

\(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta = 26.27\) (bs).


IR (KBr): \(\nu = 3924\) (m), 3653 (w), 3463 (m), 3056 (m), 2922 (w), 2410 (m), 1597 (w), 1493 (w), 1436 (m), 1398 (m), 1316 (s), 1239 (s), 1182 (w), 1154 (s), 1104 (s), 1067 (s), 1018 (w), 996 (w), 911 (m), 813 (m) cm\(^{-1}\).
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Melting point: 196 °C.

Optical rotation: [α]D –86.74 (c 0.97, CH2Cl2).

\( R_f \) (hexane/EtOAc, 3:1): 0.17.

Phosphine borane 78: ¹H NMR (300 MHz, CDCl₃): \( \delta = 0.4–1.4 \) (bs, 3H, BH₃), 2.37 (s, 3H, \( H_2C\)-Ph-SO₂), 3.90 (ddd, \( J_{H-H} = 14.7 \) Hz, \( J_{P-H} = 8.2 \) Hz, \( J_{H-H} = 2.1 \) Hz, 1H, SCH₂), 4.33 (ddd, \( J_{H-H} = 14.7 \) Hz, \( J_{H-H} = 12.2 \) Hz, \( J_{P-H} = 3.0 \) Hz, 1H, SCH₂), 4.58 (ddd, \( J_{P-H} = 16.1 \) Hz, \( J_{H-H} = 12.2 \) Hz, \( J_{H-H} = 2.1 \) Hz, 1H, SCH₂CH), 6.84 (m, 4H), 6.98 (m, 1H), 7.13–7.27 (m, 8H), 7.30 (m, 1H), 7.44 (m, 1H), 7.47–7.64 (m, 5H), 7.76 (m, 2H), 8.05 (m, 2H).

\(^{13}\)C NMR (75 MHz, CDCl₃): \( \delta = 25.5 \) (CH₃, H₃C-Ph-SO₂), 39.1 (d, \( J_{P-C} = 28.0 \) Hz, CH, SCH₂CH), 59.1 (d, \( J_{P-C} = 9.8 \) Hz, CH₂, SCH₂), 124.8 (d, \( J_{P-C} = 51.7 \) Hz, C, i-Ph), 126.0 (d, \( J_{P-C} = 50.5 \) Hz, C, i-Ph), 126.3 (CH), 127.5 (d, \( J_{P-C} = 2.6 \) Hz, CH), 127.6 (d, \( J_{P-C} = 1.9 \) Hz, CH), 127.8 (CH), 128.1 (d, \( J_{P-C} = 10.2 \) Hz, CH), 128.9 (CH), 129.0 (CH), 129.1 (d, \( J_{P-C} = 9.8 \) Hz, CH), 129.8 (d, \( J_{P-C} = 4.1 \) Hz, CH), 130.3 (C), 131.2 (d, \( J_{P-C} = 2.0 \) Hz, CH), 132.1 (d, \( J_{P-C} = 2.0 \) Hz, CH), 132.4 (d, \( J_{P-C} = 8.9 \) Hz, CH), 133.3 (d, \( J_{P-C} = 8.7 \) Hz, CH), 133.6 (CH), 137.2 (C), 140.5 (C), 142.6 (C).

\(^{31}\)P NMR (162 MHz, CDCl₃): \( \delta = 26.17 \) (bs).
**Experimental Part**


**IR** (KBr): $\nu$ = 3676 (w), 3652 (w), 3593 (w), 3447 (m), 3060 (m), 2924 (m), 2392 (s), 1597 (w), 1493 (m), 1440 (m), 1399 (w), 1315 (s), 1226 (m), 1152 (s), 1091 (s), 1063 (s), 1021 (w), 997 (w), 911 (m), 816 (m) cm$^{-1}$.

**Melting point:** 122 °C.

**Optical rotation:** $[\alpha]_D +162.35$ (c 0.85, CH$_2$Cl$_2$).

$R_f$ (hexane/EtOAc, 3:1): 0.16.

9.4. (+)-Diphenyl(1-phenyl-2-((S)-N-tert-butyl(diphenyl)silyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (81) and (–)-Diphenyl(1-phenyl-2-((S)-N-tert-butyl(diphenyl)silyl-S-phenylsulfonimidoyl)ethyl)phosphine borane (80)

Following GP-3, the phosphine boranes 80 and 81 were prepared starting from the vinyl sulfoximine 61 (2.0 g, 4.16 mmol), diphenylphosphine (851 mg, 4.57 mmol) and $t$-BuOK (46 mg, 410 μmol) in THF (70 mL). After the complete conversion of the sulfoximine 61, BH$_3$•THF (9.2 mL, 9.2 mmol) was added and the mixture was worked up after stirring for 1 h. The $dr$ of 80:81 was 58:42 (chiralpack–IA column, detector 254 nm, n-heptane/isopropanol: 95/5, flow: 0.6 mL/min, 31 bar, $R_f$ (80): 12.31 min; $R_f$ (81): 19.53 min). Purification by column chromatography (cyclohexane/EtOAc, 93:7) afforded a mixture of both diastereoisomers 80 and 81 (2.27 g, 80%) as a sticky oil. The mixture was dissolved in hot n-heptane/isopropanol (95:5). After a few days at RT, colourless crystals were formed, which were collected and analysed by HPLC. The $dr$ of 80:81 was 98.5:1.5. The crystals were
once again dissolved in hot \( n \)-heptane/isopropanol (95:5), and after a few days the crystals were collected and analysed. The phosphine borane 80 (1.14 g, 40%, \( de > 99\% \)) was obtained as colourless single crystals suitable for X-ray crystal structure analysis. The first mother liqueur (enriched in minor isomer 81) was concentrated, and the residue was dissolved in hot \( n \)-heptane/isopropanol (95:5). After 2 recrystallisations at 4 °C, the minor isomer 81 could be isolated (920 mg, 32%, \( de > 99\% \)) as colourless single crystal suitable for X-ray crystal structure analysis.

\[
\text{Phosphine borane 81: } ^1H \text{ NMR (400 MHz, CDCl}_3): \delta = 0.4–1.2 \text{ (bs, 3H, BH}_3), \text{ 0.99 (s, 9H, C(CH}_3)_3), 3.38 (ddd, } ^2J_{H,H} = 14.6 \text{ Hz, } ^3J_{P,H} = 10.3 \text{ Hz, } ^3J_{H,H} = 1.2 \text{ Hz, 1H, SCH}_2), 4.03 (ddd, } ^2J_{H,H} = 14.6 \text{ Hz, } ^3J_{H,H} = 11.8 \text{ Hz, } ^3J_{P,H} = 1.7 \text{ Hz, 1H, SCH}_2), 4.43 (dd, } ^2J_{P,H} = 16.5 \text{ Hz, } ^3J_{H,H} = 11.8 \text{ Hz, } ^3J_{H,H} = 1.2 \text{ Hz, 1H, SCH}_2CH), 6.61 \text{ (m, 2H), 6.76 (t, } J = 7.7 \text{ Hz, 2H), 6.90 (m, 1H), 6.99 (t, } J = 7.8 \text{ Hz, 2H), 7.11 (m, 4H), 7.17–7.36 \text{ (m, 11H), 7.39 (m, 1H), 7.48 (m, 1H), 7.63 (m, 2H), 7.76 (4H).}
\]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3): \delta = 19.4 \text{ (C, SiC(CH}_3)_3), 27.1 \text{ (CH}_3, \text{ SiC(CH}_3)_3), 39.2 \text{ (d, } ^1J_{P,C} = 28.7 \text{ Hz, CH, SCH}_2CH), 59.9 \text{ (d, } ^2J_{P,C} = 6.8 \text{ Hz, CH}_2, \text{ SCH}_2), 125.8 \text{ (d, } ^1J_{P,C} = 51.3 \text{ Hz, C, i-Ph), 126.98 \text{ (d, } ^1J_{P,C} = 54.6 \text{ Hz, C, i-Ph), 127.00 \text{ (d, } J_{P,C} = 3.0 \text{ Hz, CH), 127.1 \text{ (CH), 127.26 \text{ (CH), 127.28 \text{ (CH), 127.35 \text{ (CH), 127.90 \text{ (CH), 127.93 \text{ (d, } J_{P,C} = 9.9 \text{ Hz, CH), 128.77 \text{ (CH), 128.82 \text{ (CH), 129.0 \text{ (d, } J_{P,C} = 9.6 \text{ Hz, CH), 129.6 \text{ (d, } J_{P,C} = 4.3 \text{ Hz, CH), 130.9 \text{ (d, } J_{P,C} = 2.4 \text{ Hz, CH), 131.3 \text{ (C), 131.50 \text{ (CH), 131.55 \text{ (d, } J_{P,C} = 2.2 \text{ Hz, CH), 132.3 \text{ (d, } J_{P,C} = 8.8 \text{ Hz, CH), 132.8 \text{ (d, } J_{P,C} = 8.4 \text{ Hz, CH), 135.40 \text{ (CH), 135.44 \text{ (CH), 135.82 \text{ (C), 135.83 \text{ (C), 142.7 (C).}}}
\]

\[ ^{31}P \text{ NMR (162 MHz, CDCl}_3): \delta = 25.42 \text{ (bs).}
\]
**EXPERIMENTAL PART**

**MS** (CI, isobutane): \(m/z\) (%) = 683 \([\text{M}^+ + 2]\) (5), 682 \([\text{M}^+ + 1]\) (15), 681 \([\text{M}^+]\) (14), 680 \([\text{M}^− 1]\) (23), 679 (6), 420 (6), 381 (5), 380 (18), 301 (4), 300 (22), 299 (100), 298 (25), 289 (12), 288 (4), 286 (8), 199 (7), 187 (9), 126 (6).

**IR** (KBr): \(\nu = 3058\) (m), 2929 (m), 2889 (m), 2853 (m), 2385 (m), 2343 (m), 1585 (w), 1483 (m), 1435 (m), 1320 (m), 1262 (m), 1149 (m), 1103 (m), 1060 (m), 999 (m), 906 (w), 819 (m) cm\(^{-1}\).

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**Melting point:** 135 °C.

**Optical rotation:** \([\alpha]_D +115.2\) (c 0.50, CHCl\(_3\)).

**R\(_f\)** (cyclohexane/EtOAc, 15:1): 0.08.

Phosphine borane 80: **\(^1\)H NMR** (400 MHz, CDCl\(_3\)): \(\delta = 0.4−1.2\) (bs, 3H, BH\(_3\)), 0.98 (s, 9H, C(CH\(_3\))\(_3\)), 3.38 (ddd, \(^2J_{H-H} = 14.7\) Hz, \(^3J_{H-H} = 10.9\) Hz, \(^2J_{P-H} = 1.3\) Hz, 1H, SCH\(_2\)), 3.92 (ddd, \(^2J_{H-H} = 14.7\) Hz, \(^3J_{P-H} = 11.7\) Hz, \(^3J_{H-H} = 1.5\) Hz, 1H, SCH\(_2\)), 4.49 (bddd, \(^2J_{P-H} = 16.7\) Hz, \(^3J_{H-H} = 10.9\) Hz, 1H, SCH\(_2\)), 6.72 (m, 2H), 6.84 (t, \(J = 7.8\) Hz, 2H), 6.94 (m, 1H), 7.04 (m, 2H), 7.09–7.23 (m, 7H), 7.27 (m, 4H), 7.34 (m, 1H), 7.43 (m, 4H), 7.53 (m, 3H), 7.62 (m, 2H), 7.89 (m, 2H).
\[ ^{13}C \text{ NMR} \text{ (100.6 MHz, CDCl}_3\text{): } \delta = 19.3 \text{ (C, SiC(CH}_3)_3\text{), 27.1 (CH}_3\text{, SiC(CH}_3)_3\text{), 38.1 (d, } ^1J_{P-C} = 28.8 \text{ Hz, CH, SCH}_2\text{CH}, 60.1 \text{ (d, } ^2J_{P-C} = 6.5 \text{ Hz, CH}_2\text{, SCH}_2\text{), 126.0 \text{ (d, } ^1J_{P-C} = 51.6 \text{ Hz, C, i-Ph), 126.99 (CH), 127.01 (CH), 127.15 (CH), 127.18 (CH), 127.21 \text{ (d, } ^1J_{P-C} = 54.4 \text{ Hz, C, i-Ph), 127.3 (d, } J_{P-C} = 2.5 \text{ Hz, CH), 128.0 (d, } J_{P-C} = 10.1 \text{ Hz, CH), 128.1 (CH), 128.66 (CH), 128.74 (CH), 129.0 (d, } J_{P-C} = 9.7 \text{ Hz, CH), 129.6 (d, } J_{P-C} = 4.4 \text{ Hz, CH), 130.9 (d, } J_{P-C} = 2.4 \text{ Hz, CH), 131.54 (CH), 131.56 (d, } J_{P-C} = 4.0 \text{ Hz, CH), 131.9 (C), 132.3 (d, } J_{P-C} = 8.8 \text{ Hz, CH), 132.9 (d, } J_{P-C} = 8.4 \text{ Hz, CH), 135.26 (CH), 135.31 (CH), 135.7 (C), 135.8 (C), 143.0 (C). \]

\[ ^{31}P \text{ NMR} \text{ (162 MHz, CDCl}_3\text{): } \delta = 26.05 \text{ (bs).} \]

**MS** (CI, isobutane): \( m/z \) (%) = 683 [M\(^+\)+2] (5), 682 [M\(^+\)+1] (15), 681 [M\(^+\)] (14), 680 (23), 420 (6), 381 (5), 380 (18), 301 (4), 300 (21), 299 (100), 298 (25).

**IR** (KBr): \( \nu = 3059 \text{ (m), 2929 (m), 2889 (m), 2853 (m), 2385 (m), 2343 (m), 1969 (w), 1585 \text{ (w), 1483 (m), 1435 (m), 1320 (m), 1262 (m), 1149 (m), 1103 (m), 1060 (m), 999 (m), 906 \text{ (w), 819 (m), 771 (m), 732 (s), 695 (s), 598 (m), 526 (m), 491 (m) cm}^{-1}. \)

**Melting point:** 124 °C.

**Optical rotation:** \([\alpha]_D -86.6 \text{ (c 0.50, CHCl}_3\text{).} \]

**R\(_f\)** (cyclohexane/EtOAc, 15:1): 0.09.

9.5. (+)-Diphenyl(((1R,2R)-2-((S)-N-methyl-S-phenylsulfonimidoyl)cyclohexyl)phosphine borane (120) and (–)-Diphenyl(((1S,2S)-2-((S)-N-methyl-S-phenylsulfonimidoyl)cyclohexyl)phosphine borane (121)

Following GP-3, the phosphine boranes 120 and 121 were prepared starting from the vinyl sulfoximine 117 (375 mg, 1.59 mmol), diphenylphosphine (330 mg, 1.77 mmol) and \( t\)-BuOK (18 mg, 590 \( \mu \)mol) in THF (12 mL). After the complete conversion of the sulfoximine 117, BH\(_3\)•THF (3.45 mL, 3.45 mmol) was added and the mixture was worked up after stirring for 1 h. The \( dr\) of 120:121 was 1:1 (determined by \(^1\)H NMR). Purification by column chromatography (cyclohexane/EtOAc, 85:15) afforded the phosphine borane 120 (240 mg,
35%) as a white crystalline solid and the phosphine borane 121 (315 mg, 46%) as a white foam.

Phosphine borane 120: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.60$–$1.40$ (bs, 3H, BH$_3$), 1.50 (m, 2H), 1.63 (m, 1H), 1.77 (bd, $J = 15.0$ Hz, 1H), 1.90–2.24 (m, 4H), 2.67 (s, 3H, NCH$_3$), 3.17 (bdd, $^3J_{P-H} = 13.8$ Hz, $^2J_{H-H} = 5.8$ Hz, 1H, SCH), 4.57 (bdd, $^2J_{P-H} = 19.6$ Hz, $^3J_{H-H} = 6.2$ Hz, 1H, SCHCH$_2$P), 7.49 (m, 11H), 7.86 (m, 2H), 8.14 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 18.5$ (CH$_2$), 20.8 (CH$_2$), 21.8 (CH$_2$), 22.0 (d, $J = 1.7$ Hz, CH$_2$), 26.0 (d, $^1J_{P-C} = 30.7$ Hz, CH, SCHCH$_2$P), 29.6 (CH$_3$, NCH$_3$), 58.5 (d, $^2J_{P-C} = 7.7$ Hz, CH, SCH), 128.4 (d, $^1J_{P-C} = 56.7$ Hz, C, i-Ph), 128.5 (d, $J_{P-C} = 9.8$ Hz, CH), 128.70 (d, $J_{P-C} = 10.0$ Hz, C, i-Ph), 128.72 (d, $^1J_{P-C} = 54.0$ Hz, C, i-Ph), 129.2 (CH), 129.7 (CH), 131.13 (CH), 131.17 (CH), 132.5 (CH), 132.6 (d, $J_{P-C} = 8.9$ Hz, CH), 133.0 (d, $J_{P-C} = 8.6$ Hz, CH), 136.8 (C, Si-Ph).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 21.98$ (bs).

MS (ESI–MS, MeOH): $m/z$ (%) = 458 [M$^+$+23] (98), 434 [M$^+$-1] (100).

IR (Capillary, dissolved in CHCl$_3$): $\nu = 3881$ (w), 3836 (w), 3674 (w), 3632 (w), 3450 (w), 3058 (w), 3012 (w), 2935 (m), 2871 (m), 2804 (w), 2391 (s), 1560 (w), 1441 (m), 1247 (s), 1137 (s), 1105(s), 1068 (s), 1002 (m), 868 (m), 832 (w) cm$^{-1}$.

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<th>C$<em>{25}$H$</em>{33}$BNOPS</th>
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<td></td>
<td>N</td>
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<td>2.94</td>
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Melting point: 72 °C.
**Optical rotation:** $[\alpha]_D^{+}70.8$ (c 0.12, CHCl$_3$).

$R_f$ (cyclohexane/EtOAc, 4:1): 0.38.

Phosphine borane 121: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.60$–1.70 (bs, 3H, BH$_3$), 1.58 (m, 3H), 1.96 (m, 2H), 2.25 (m, 1H), 2.34–2.53 (m, 2H), 2.62 (s, 3H, NCH$_3$), 3.11 (bsd, $^3$J$_{P-H}$ = 13.7 Hz, $^3$J$_{H-H}$ = 5.4 Hz, 1H, SCH), 3.53 (bsd, $^2$J$_{P-H}$ = 19.1 Hz, $^3$J$_{H-H}$ = 6.6 Hz, 1H, SCHCHP), 7.26 (m, 2H), 7.36–7.60 (m, 11H), 7.74 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 20.0$ (CH$_2$), 21.2 (CH$_2$), 21.8 (CH$_2$), 22.1 (CH$_2$), 27.7 (d, $^1$J$_{P-C}$ = 29.6 Hz, CH, SCHCHP), 29.7 (CH$_3$, NCH$_3$), 58.9 (d, $^2$J$_{P-C}$ = 7.4 Hz, CH, SCH), 127.8 (d, $^1$J$_{P-C}$ = 54.3 Hz, C, i-Ph), 127.9 (d, $^1$J$_{P-C}$ = 53.0 Hz, C, i-Ph), 128.8 (d, $^2$J$_{P-C}$ = 9.6 Hz, CH), 128.9 (d, $^1$J$_{P-C}$ = 9.8 Hz, CH), 129.5 (CH), 129.9 (CH), 131.1 (d, $^1$J$_{P-C}$ = 1.8 Hz, CH), 131.5 (d, $^2$J$_{P-C}$ = 1.8 Hz, CH), 132.5 (d, $^1$J$_{P-C}$ = 8.1 Hz, CH), 132.63 (CH), 132.63 (d, $^2$J$_{P-C}$ = 7.8 Hz, CH), 136.8 (C, Si-Ph).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 21.53$ (bs).

MS (ESI–MS, MeOH): $m/z$ (%) = 460 (100), 458 [M$^+$+23] (90), 434 [M$^+$–1] (80).

IR (Capillary, dissolved in CHCl$_3$): $\nu = 3940$ (w), 3882 (w), 3834 (w), 3783 (w), 3662 (w), 3534 (w), 3444 (m), 3160 (w), 3058 (w), 2935 (w), 2806 (w), 2393 (s), 2280 (w), 1590 (w), 1440 (s), 1301 (w), 1234 (s), 1138 (s), 1105 (s), 1070 (s), 862 (m) cm$^{-1}$.
Elemental analysis:  
\[
\begin{array}{ccc}
\text{C}_{25}\text{H}_{31}\text{BNOPS} & \text{Calculated} & \text{Found} \\
\text{C} & 68.97 & 69.12 \\
\text{H} & 7.18 & 7.26 \\
\text{N} & 3.22 & 3.03 \\
\end{array}
\]

**Melting point:** 48 °C.

**Optical rotation:** \([\alpha]_D\) –15.9 (c 1.90, CHCl₃).

\(R_f\) (cyclohexane/EtOAc, 4:1): 0.28.

9.6. (+)-Diphenyl(\((1R,2R)-2-(\text{S})-\text{N-benzyl-S-phenylsulfonimidoyl})\text{cyclohexyl})
phosphine borane (122) and (–)-Diphenyl(\((1S,2S)-2-(\text{S})-\text{N-benzyl-S-phenylsulfonimidoyl})\text{cyclohexyl})
phosphine borane (123)

Following GP-3, the phosphine boranes 122 and 123 were prepared starting from vinyl sulfoximine 118 (1.14 g, 3.66 mmol), diphenylphosphine (718 mg, 3.86 mmol) and \(t\)-BuOK (40 mg, 356 \(\mu\)mol) in THF (40 mL). After the complete conversion of the sulfoximine 118, BH₃•THF (8 mL, 8 mmol) was added and the reaction mixture was worked up after stirring for 1 h. The \(dr\) of 122:123 was 1:1 (determined by \(^1\text{H NMR}\)). Purification by column chromatography (cyclohexane/EtOAc, 9:1) afforded the phosphine borane 122 (768 mg, 41%) as a white crystalline solid, and the phosphine borane 123 (730 mg, 39%) as a white foam. The isomer 122 could be recrystallised from Et₂O at –26 °C, which gave colourless single crystals suitable for X-ray crystal structure analysis.

\[
\begin{align*}
\text{C}_{31}\text{H}_{35}\text{BNOPS} \\
\text{MW} = 511.47 \text{ g.mol}^{-1}
\end{align*}
\]
Phosphine borane 122: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.6\)–1.45 (bs, 3H, BH\(_3\)) 1.45–1.68 (m, 3H), 1.74 (m, 1H), 1.92–2.32 (m, 4H), 3.26 (dd, \(^3\)J\(_{\text{P-H}}\) = 13.5 Hz, \(^3\)J\(_{\text{H-H}}\) = 5.5 Hz, 1H, SCH), 3.91 (d, \(^2\)J\(_{\text{H-H}}\) = 14.3 Hz, 1H), 4.30 (d, \(^2\)J\(_{\text{H-H}}\) = 14.3 Hz, 1H), 4.70 (dd, \(^2\)J\(_{\text{P-H}}\) = 19.5 Hz, \(^3\)J\(_{\text{H-H}}\) = 6.3 Hz, 1H, SCHCHP), 7.27 (m, 3H), 7.34–7.50 (m, 10H), 7.55 (m, 3H), 7.83 (m, 2H), 8.06 (m, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 19.5\) (CH\(_2\)), 20.9 (CH\(_2\)), 21.9 (CH\(_2\)), 22.1 (d, \(^2\)J\(_{\text{P-C}}\) = 1.7 Hz, CH\(_2\), PCHCH\(_2\)), 26.3 (d, \(^1\)J\(_{\text{P-C}}\) = 30.5 Hz, CH, SCHCHP), 47.1 (CH\(_2\), NCH\(_2\)Ph), 58.7 (d, \(^2\)J\(_{\text{P-C}}\) = 7.7 Hz, CH, SCH), 126.3 (CH), 127.4 (CH), 128.0 (CH), 128.3 (d, \(^1\)J\(_{\text{P-C}}\) = 51.9 Hz, C, i-Ph), 128.5 (d, \(J_{\text{P-C}}\) = 9.7 Hz, CH), 128.60 (d, \(^1\)J\(_{\text{P-C}}\) = 54.2 Hz, C, i-Ph), 128.66 (d, \(J_{\text{P-C}}\) = 9.9 Hz, CH), 129.1 (CH), 129.5 (CH), 131.0 (d, \(J_{\text{P-C}}\) = 2.0 Hz, CH), 131.1 (d, \(J_{\text{P-C}}\) = 2.1 Hz, CH), 132.46 (d, \(J_{\text{P-C}}\) = 9.0 Hz, CH), 132.53 (CH), 132.9 (d, \(J_{\text{P-C}}\) = 8.7 Hz, CH), 137.2 (C, Si-Ph), 141.7 (C, NCH\(_2\)i-Ph).

\(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta = 21.61\) (bs).

MS (Cl, methane): \(m/z\) (%) = 510 [M\(^+\)–1] (2), 280 (18), 279 (100), 278 (25), 267 (5), 234 (5), 232 (86), 106 (6).

IR (KBr): \(\nu = 3794\) (w), 3685 (w), 3434 (m), 3051 (m), 2931 (m), 2855 (m), 2344 (w), 1611 (m), 1438 (s), 1258 (s), 1203 (m), 1123 (m), 1061 (m), 1001 (w), 880 (m), 832 (m) cm\(^{-1}\).

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<td>(\mathrm{N})</td>
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<td>2.62</td>
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</table>

Melting point: 124 °C.

Optical rotation: \([\alpha]_D +50.4\) (c 0.80, CH\(_2\)Cl\(_2\)).

\(R_f\) (cyclohexane/EtOAc, 92:8): 0.23.
Phosphine borane 123: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.6-1.51\) (bs, 3H, BH\(_3\)), 1.51-1.71 (m, 3H), 1.94 (m, 1H), 2.09 (m, 1H), 2.27 (m, 1H), 2.37-2.58 (m, 2H), 3.15 (dd, \(^2\)J\(_{P,H}\) = 13.7 Hz, \(^3\)J\(_{H,H}\) = 5.2 Hz, 1H, SCH), 3.70 (dd, \(^2\)J\(_{P,H}\) = 19.0 Hz, \(^3\)J\(_{H,H}\) = 6.3 Hz, 1H, SCH\(_{CHP}\)), 3.96 (d, \(^2\)J\(_{H,H}\) = 14.8 Hz, 1H, NCH\(_2\)), 4.24 (d, \(^2\)J\(_{H,H}\) = 14.8 Hz, 1H, NCH\(_2\)), 7.19 (m, 1H), 7.28 (m, 4H), 7.33-7.50 (m, 8H), 7.53-7.64 (m, 5H), 7.77 (m, 2H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 19.9\) (CH\(_2\)), 21.1 (CH\(_2\)), 21.9 (d, \(^2\)J\(_{P,C}\) = 2.3 Hz, CH\(_2\), PCH\(_2\)), 22.2 (CH\(_2\)), 27.5 (d, \(^1\)J\(_{P,C}\) = 29.8 Hz, CH, SCH\(_{CHP}\)), 47.0 (CH\(_2\)), 59.3 (d, \(^2\)J\(_{P,C}\) = 7.4 Hz, CH, SCH), 126.1 (CH), 127.0 (CH), 127.65 (d, \(^1\)J\(_{P,C}\) = 52.6 Hz, C, i-Ph), 127.74 (d, \(^1\)J\(_{P,C}\) = 54.6 Hz, C, i-Ph), 127.9 (CH), 128.6 (d, \(J_{P,C} = 9.9\) Hz, CH), 128.7 (d, \(J_{P,C} = 9.9\) Hz, CH), 129.2 (CH), 129.5 (CH), 130.9 (d, \(J_{P,C} = 3.1\) Hz, CH), 131.2 (d, \(J_{P,C} = 2.3\) Hz, CH), 132.41 (d, \(J_{P,C} = 8.4\) Hz, CH), 132.42 (d, \(J_{P,C} = 8.4\) Hz, CH), 132.5 (CH), 137.2 (C, Si-Ph), 141.4 (C, NCH\(_2\)-Ph).

\(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta = 21.70\) (bs).

**MS** (CI, isobutane): \(m/z\) (%): 511 [M\(^+\)] (7), 510 [M\(^+\)-1] (18), 509 (4), 463 (9), 280 (18), 279 (92), 278 (22), 267 (14), 266 (9), 134 (4), 234 (6), 233 (15), 232 (100), 187 (3), 106 (13).

**IR** (KBr): \(\nu = 3944\) (m), 3930 (m), 3899 (m), 3696 (s), 3677 (s), 3612 (m), 3073 (m), 2903 (m), 2871 (m), 2382 (s), 1619 (m), 1491 (w), 1438 (s), 1201 (m), 1126 (s), 1062 (s) cm\(^{-1}\).

**HRMS** (ESI–TOF):

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Melting point: 59–61 °C.

Optical rotation: \([\alpha]_D –14.5\ (c 1.03, \text{CHCl}_3)\).

\(R_f\) (cyclohexane/EtOAc, 92:8): 0.15.

10. Synthesis of Phosphino-sulfoximines

10.1. (–)-Diphenyl((1\(R\))-1-phenyl-2-((\(S\))-N-methyl-S-phenylsulfonimidoyl)ethyl)phosphine (68)

![Phosphino-sulfoximines](image)

68

\(C_{27}H_{26}NOPS\)

MW = 443.54 g.mol\(^{-1}\)

Following GP-4, phosphine 68 was prepared from the phophine borane 62 (100 mg, 218 µmol) and DABCO (26 mg, 228 µmol) in toluene (3 mL). Purification by column chromatography afforded phosphine 68 (93 mg, 96%) as a white solid.

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \(\delta = 2.40\) (s, 3H, N\(\text{CH}_3\)), 3.52 (ddd, \(^2\)\(J_{H-H}\) = 14.8 Hz, \(^3\)\(J_{P-H}\) = 7.5 Hz, \(^3\)\(J_{H-H}\) = 1.9 Hz, 1H, S\(\text{CH}_2\)), 3.77 (ddd, \(^2\)\(J_{H-H}\) = 14.8 Hz, \(^3\)\(J_{H-H}\) = 11.9 Hz, \(^3\)\(J_{P-H}\) = 2.0 Hz, 1H, S\(\text{CH}_2\)), 4.04 (ddd, \(^3\)\(J_{H-H}\) = 11.9 Hz, \(^2\)\(J_{P-H}\) = 3.3 Hz, \(^3\)\(J_{H-H}\) = 1.9 Hz, 1H, S\(\text{CH}_2\)\(\text{CH}\)), 6.66 (m, 2H), 6.76 (m, 3H), 6.91 (m, 2H), 7.00 (m, 2H), 7.08 (m, 3H), 7.22 (m, 1H), 7.35 (m, 5H), 7.55 (2H).

\(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)): \(\delta = 28.2\) (CH\(_3\), N\(\text{CH}_3\)), 38.4 (d, \(^1\)\(J_{P-C}\) = 17.7 Hz, CH, S\(\text{CH}_2\)\(\text{CH}\)), 57.0 (d, \(^2\)\(J_{P-C}\) = 24.1 Hz, S\(\text{CH}_2\)), 125.1 (d, \(J = 2.5\) Hz, CH), 126.6 (d, \(J = 1.0\) Hz, CH), 126.7 (d, \(J = 6.7\) Hz, CH), 127.45 (CH), 127.48 (CH), 127.7 (d, \(J = 5.8\) Hz, CH), 127.8 (d, \(J = 4.9\) Hz, CH), 127.9 (CH), 128.7 (CH), 130.8 (CH), 131.8 (d, \(^2\)\(J_{P-C}\) = 18.2 Hz, CH, Po-Ph), 132.98 (d, \(^2\)\(J_{P-C}\) = 21.0 Hz, CH, Po-Ph), 132.99 (d, \(^1\)\(J_{P-C}\) = 11.2 Hz, C, i-Ph), 134.0 (d, \(^1\)\(J_{P-C}\) = 15.6 Hz, C, i-Ph), 135.8 (d, \(^2\)\(J_{P-C}\) = 8.1 Hz, C, PCH\(_2\)-Ph), 136.1 (C).
\[ ^{31}\text{P NMR} \ (162 \text{ MHz, CDCl}_3): \delta = 1.47 \ (s). \]

Melting point: 146 °C.

Optical rotation: \([\alpha]_D \ -58.0 \ (c \ 0.10, \text{CH}_2\text{Cl}_2).\]

10.2. (+)-Diphenyl((1$S$)-1-phenyl-2-((S)-N-methyl-S-phenylsulfonimidoyl)ethyl) phosphine (69)

Following GP-4, phosphine 69 was prepared from the phosphine borane 63 (100 mg, 218 µmol) and DABCO (26 mg, 228 µmol) in toluene (3 mL). Purification by column chromatography afforded phosphine 69 (93 mg, 94%) as a white solid.

\[ ^{1}\text{H NMR} \ (400 \text{ MHz, CDCl}_3): \delta = 2.58 \ (s, \text{3H, NC}_3\text{H}_3), \ 3.48 \ (\text{ddd}, ^2J_{\text{H-H}} = 14.5 \text{ Hz}, ^3J_{\text{P-H}} = 7.6 \text{ Hz}, ^3J_{\text{H-H}} = 1.4 \text{ Hz}, \text{1H, SCH}_2), \ 3.78 \ (\text{ddd}, ^2J_{\text{H-H}} = 14.5 \text{ Hz}, ^3J_{\text{H-H}} = 12.0 \text{ Hz}, ^3J_{\text{P-H}} = 2.3 \text{ Hz}, \text{1H, SCH}_2), \ 3.90 \ (\text{ddd}, ^3J_{\text{H-H}} = 12.0 \text{ Hz}, ^2J_{\text{P-H}} = 2.9 \text{ Hz}, ^3J_{\text{H-H}} = 1.4 \text{ Hz}, \text{1H, SCH}_2\text{CH}), \ 6.91 \ (\text{m}, \text{4H}), \ 7.05 \ (\text{m}, \text{5H}), \ 7.15 \ (\text{m}, \text{1H}), \ 7.29–7.44 \ (\text{m}, \text{7H}), \ 7.46–7.55 \ (\text{m}, \text{3H}). \]

\[ ^{13}\text{C NMR} \ (100 \text{ MHz, CDCl}_3): \delta = 29.4 \ (\text{CH}_3, \text{NCH}_3), \ 39.9 \ (\text{d}, ^{1}J_{\text{P-C}} = 18.6 \text{ Hz}, \text{CH}, \text{SCH}_2\text{CH}), \ 58.3 \ (\text{d}, ^{2}J_{\text{P-C}} = 23.5 \text{ Hz}, \text{CH}_2, \text{SCH}_2), \ 126.4 \ (\text{d}, J = 2.5 \text{ Hz}, \text{CH}), \ 127.7 \ (\text{d}, J = 6.5 \text{ Hz}, \text{CH}), \ 127.9 \ (\text{d}, J = 1.2 \text{ Hz}, \text{CH}), \ 128.4 \ (\text{CH}), \ 128.6 \ (\text{d}, J = 7.6 \text{ Hz}, \text{CH}), \ 128.8 \ (\text{CH}), \ 128.9 \ (\text{CH}), \ 129.2 \ (\text{CH}), \ 129.6 \ (\text{CH}), \ 132.2 \ (\text{CH}), \ 132.7 \ (\text{d}, ^{2}J = 17.9 \text{ Hz}, \text{CH, Po-Ph}), \ 133.94 \ (\text{d}, ^{1}J_{\text{P-C}} = 17.1 \text{ Hz}, \text{C, i-Ph}), \ 134.03 \ (\text{d}, ^{2}J_{\text{P-C}} = 21.1 \text{ Hz}, \text{CH, Po-Ph}), \ 135.0 \ (\text{d}, ^{1}J_{\text{P-C}} = 16.4 \text{ Hz}, \text{C, i-Ph}), \ 137.3 \ (\text{d}, ^{2}J_{\text{P-C}} = 7.8 \text{ Hz}, \text{C, PCH}_2\text{Ph}), \ 137.8 \ (\text{C}). \]
EXPERIMENTAL PART

$^{31}P$ NMR (162 MHz, CDCl$_3$): $\delta = 2.30$ (s).

**Melting point:** 111–113 °C.

**Optical rotation:** $[\alpha]_D +120.71$ (c 0.14, CH$_2$Cl$_2$).

10.3. (–)-Diphenyl((1$R$)-1-phenyl-2-((S)-N-benzyl-S-phenylsulfonimidoyl)ethyl) phosphine (84)

![Phosphine Structure](image)

C$_{33}$H$_{30}$NOPS

MW = 519.64 g.mol$^{-1}$

Following GP-4, phosphine 84 was prepared from the phophine borane 76 (178 mg, 333 µmol) and DABCO (41 mg, 365 µmol) in toluene (5 mL). Purification by column chromatography afforded phosphine 84 (169 mg, 98%) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.67$ (ddd, $^2J_{H-H} = 14.7$ Hz, $^3J_{P-H} = 7.6$ Hz, $^3J_{H-H} = 1.6$ Hz, 1H, SCH$_2$), 3.87 (d, $^2J_{H-H} = 14.7$ Hz, 1H, NCH$_2$Ph), 3.90 (ddd, $^2J_{H-H} = 14.7$ Hz, $^3J_{H-H} = 12.0$ Hz, $^3J_{P-H} = 2.0$ Hz, 1H, SCH$_2$), 4.01 (d, $^2J_{H-H} = 14.7$ Hz, 1H, NCH$_2$Ph), 3.67 (ddd, $^3J_{H-H} = 12.0$ Hz, $^3J_{P-H} = 4.6$ Hz, $^3J_{H-H} = 1.6$ Hz, 1H, SCH$_2$CH), 6.76 (m, 2H), 6.87 (m, 3H), 6.96 (m, 2H), 7.06 (m, 2H), 7.11–7.26 (m, 8H), 7.32 (m, 1H), 7.43 (m, 3H), 7.48 (m, 2H), 7.63 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 39.4$ (d, $^1J_{P-C} = 17.9$ Hz, CH, SCH$_2$CH), 46.2 (CH$_2$, NCH$_3$Ph), 58.4 (d, $^2J_{P-C} = 24.0$ Hz, CH$_2$, SCH$_2$), 126.10 (CH), 126.12 (CH), 127.2 (CH), 127.69 (CH), 127.71 (d, $J = 6.9$ Hz, CH), 127.9 (CH), 128.4 (CH), 128.5 (CH), 128.7 (d, $J = 7.6$ Hz, CH), 128.8 (d, $J = 6.6$ Hz, CH), 128.9 (CH), 129.7 (CH), 132.0 (CH), 132.8 (d, $^2J_{P-C} = 18.1$ Hz, CH, Po-Ph), 133.99 (d, $^1J_{P-C} = 17.7$ Hz, C, i-Ph), 134.01 (d, $^2J_{P-C} = 20.9$ Hz, CH, Po-...
EXPERIMENTAL PART

Ph), 135.1 (d, $^1J_{P-C} = 16.0$ Hz, C, $i$-Ph), 137.0 (d, $^2J_{P-C} = 7.9$ Hz, C, PCH$i$-Ph), 137.8 (C), 141.2 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 1.67$ (s).

Melting point: 157–158 °C.

Optical rotation: $[\alpha]_D -92.25$ (c 0.40, CH$_2$Cl$_2$).

10.4. (+)-Diphenyl((1$S$)-1-phenyl-2-((S)-N-benzyl-S-phenylsulfonimidoyl)ethyl) phosphine (85)

Following GP-4, phosphine 85 was prepared from the phophine borane 77 (100 mg, 188 $\mu$mol) and DABCO (23 mg, 205 $\mu$mol) in toluene (3 mL). Purification by column chromatography afforded phosphine 85 (92 mg, 94%) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.47$ (ddd, $^2J_{H-H} = 14.6$ Hz, $^3J_{P-H} = 7.8$ Hz, $^3J_{H-H} = 1.4$ Hz, 1H, SCH$_2$), 3.78 (ddd, $^2J_{H-H} = 14.6$ Hz, $^3J_{H-H} = 12.0$ Hz, $^3J_{P-H} = 1.9$ Hz, 1H, SCH$_2$), 3.87 (d, $^2J_{H-H} = 14.8$ Hz, 1H, NCH$_2$Ph), 4.01 (bd, $^3J_{H-H} = 12.0$ Hz, 1H, SCH$_2$CH), 4.07 (d, $^2J_{H-H} = 14.8$ Hz, 1H, NCH$_2$Ph), 6.80–6.90 (m, 4H), 6.92–7.02 (m, 5H), 7.05–7.15 (m, 2H), 7.19 (m, 4H), 7.25 (m, 4H), 7.32 (m, 1H), 7.39 (m, 3H), 7.50 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 38.8$ (d, $^1J_{P-C} = 18.6$ Hz, CH, SCH$_2$CH), 45.5 (CH$_2$, NCH$_2$Ph), 57.7 (d, $^2J_{P-C} = 23.0$ Hz, CH, SCH$_2$), 125.1 (CH), 125.3 (d, $J = 2.6$ Hz, CH), 126.0 (CH), 126.7 (d, $J = 6.5$ Hz, CH), 126.84 (CH), 126.85 (CH), 127.4 (CH), 127.6 (d, $J = 7.4$ Hz, CH), 127.7 (CH), 127.8 (d, $J = 6.4$ Hz, CH), 128.0 (CH), 128.6 (CH), 131.2 (CH), 131.7 (d,
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$^{2}J_{P,C} = 17.9$ Hz, CH, Po-Ph), 132.94 (d, $^{1}J_{P,C} = 17.3$ Hz, C, i-Ph), 133.02 (d, $^{2}J_{P,C} = 21.0$ Hz, CH, Po-Ph), 134.0 (d, $^{1}J_{C,P} = 16.4$ Hz, C, i-Ph), 136.3 (d, $J = 7.9$ Hz, C, PCH-i-Ph), 137.6 (C), 140.3 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 2.42$ (s).

Melting point: 129 °C.

Optical rotation: $[\alpha]_{D} +117.27$ (c 0.11, CH$_2$Cl$_2$).

10.5. (+)-Diphenyl((1$R$)-1-phenyl-2-((S)-N-tosyl-S-phenylsulfonimidoyl)ethyl) phosphine (86)

Following GP-4, phosphine 86 was prepared from the phophine borane 78 (46 mg, 77 µmol) and DABCO (11 mg, 98 mmol) in toluene (5 mL). Purification by column chromatography afforded phosphine 86 (42 mg, 94%) as a white solid.

$^{1}$H NMR (400 MHz, CDCl$_3$): $\delta = 2.35$ (s, 3H, SO$_2$-$p$CH$_2$Ph), 3.77 (ddd, $^{2}J_{H,H} = 14.4$ Hz, $^{3}J_{P,H} = 6.1$ Hz, $^{3}J_{H,H} = 2.0$ Hz, 1H, SCH$_2$), 4.02 (dt, $^{3}J_{H,H} = 12.3$ Hz, $^{2}J_{P,H} = 2.2$ Hz, 1H, SCH$_2$CH), 4.17 (ddd, $^{2}J_{H,H} = 14.4$ Hz, $^{3}J_{H,H} = 12.3$ Hz, $^{3}J_{P,H} = 2.7$ Hz, 1H, SCH$_2$), 6.82 (m, 2H), 6.90 (m, 2H), 6.97 (m, 3H), 7.06 (m, 2H), 7.17 (m, 3H), 7.31–7.48 (m, 5H), 7.53 (m, 3H), 7.60 (m, 2H), 7.74 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 21.4$ (CH$_3$, SO$_2$-$p$CH$_3$Ph), 40.0 (d, $^{1}J_{P,C} = 20.2$ Hz, CH, SCH$_2$CH), 60.7 (d, $^{2}J_{P,C} = 25.9$ Hz, CH$_2$, SCH$_2$), 126.4 (CH), 126.7 (d, $J_{P,C} = 2.4$ Hz, CH),
127.8 (d, $J = 6.6$ Hz, CH), 127.99 (CH), 128.03 (CH), 128.66 (CH), 128.76 (CH), 128.77 (CH), 128.84 (CH), 128.9 (CH), 130.0 (CH), 132.7 (d, $^2J_{P-C} = 18.2$ Hz, CH, Po-Ph), 133.1 (d, $^1J_{P-C} = 16.8$ Hz, C, i-Ph), 133.6 (CH), 134.20 (d, $^2J_{P-C} = 21.7$ Hz, CH, Po-Ph), 134.23 (d, $^1J_{P-C} = 15.7$ Hz, C, i-Ph), 135.6 (d, $^2J_{P-C} = 7.8$ Hz, C, PCH$i$-Ph), 137.1 (C), 140.6 (C), 142.3 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 3.39$ (s).

Melting point: 145 °C.

Optical rotation: $[\alpha]_D +56$ (c 0.1, CH$_2$Cl$_2$).

10.6. (−)-Diphenyl((R)-1-phenyl-2-((S)-N-tert-butyl(diphenyl)silyl-$S$-phenylsulfonylimidoyl)ethyl)phosphine (87)

Following GP-4, phospine 87 was prepared starting from the phospine borane 80 (80 mg, 117 μmol) and DABCO (15 mg, 134 μmol) in toluene (2.5 mL). Purification by column chromatography afforded phospine 87 (72 mg, 92%) as a sticky syrup.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.99$ (s, 9H, C(CH$_3$)$_3$), 3.38 (ddd, $^2J_{H-H} = 14.4$ Hz, $^3J_{P-H} = 8.4$ Hz, $^3J_{H-H} = 1.1$ Hz, 1H, SCH$_2$), 3.67 (m, 1H, SCH$_2$), 3.17 (m, 1H, SCH$_2$CH), 6.66 (m, 2H), 6.88 (m, 5H), 7.04 (m, 4H), 7.11–7.29 (m, 7H), 7.30–7.45 (m, 6H), 7.50–7.62 (m, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 19.3$ (C, C(CH$_3$)$_3$), 27.1 (CH$_3$, C(CH$_3$)$_3$), 39.6 (d, $^1J_{P-C} = 18.1$ Hz, CH, SCH$_2$CH), 62.3 (d, $^2J_{P-C} = 21.1$ Hz, CH$_2$, SCH$_2$), 126.0 (d, $J_{P-C} = 2.5$ Hz, CH), 126.9 (CH), 127.0 (CH), 127.2 (CH), 127.6 (CH), 127.7 (d, $J_{P-C} = 6.6$ Hz, CH), 128.0 (CH), 128.4 (CH), 128.5 (CH), 128.59 (CH), 128.65 (d, $J_{P-C} = 2.9$ Hz, CH), 129.4 (CH), 131.3 (CH), 132.7 (d, $^2J_{P-C} = 18.2$ Hz, CH, Po-Ph), 133.1 (d, $^1J_{P-C} = 16.8$ Hz, C, i-Ph), 133.6 (CH), 134.20 (d, $^2J_{P-C} = 21.7$ Hz, CH, Po-Ph), 134.23 (d, $^1J_{P-C} = 15.7$ Hz, C, i-Ph), 135.6 (d, $^2J_{P-C} = 7.8$ Hz, C, PCH$i$-Ph), 137.1 (C), 140.6 (C), 142.3 (C).
132.8 (d, $^2 J_{P-C} = 18.1$ Hz, CH, Po-Ph), 133.9 (d, $^2 J_{P-C} = 20.5$ Hz, CH, Po-Ph), 134.1 (d, $^1 J_{P-C} = 9.2$ Hz, C, i-Ph), 135.2 (d, $^1 J_{P-C} = 16.0$ Hz, C, i-Ph), 135.34 (CH), 135.37 (CH), 135.5 (C), 136.0 (C), 136.1 (C), 136.2 (d, $^2 J_{P-C} = 8.1$ Hz, C, PCHi-Ph), 143.4 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 2.26$ (s).

Optical rotation: $[\alpha]_D$ –61.3 (c 0.16, CH$_2$Cl$_2$).

10.7. (+)-Diphenyl((S)-1-phenyl-2-((S)-N-tert-butyl(diphenyl)silyl-S-phenylsulfonimidoyl)ethyl)phosphine (88)

Following GP-4, phosphine 88 was prepared starting from the phophine borane 81 (118 mg, 173 µmol) and DABCO (21 mg, 187 µmol) in toluene (3 mL). Purification by column chromatography afforded phosphine 88 (107 mg, 93%) as a white foam.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.04$ (s, 9H, C(CH$_3$)$_3$), 3.39 (ddd, $^2 J_{H-H} = 14.4$ Hz, $^1 J_{P-H} = 7.6$ Hz, $^3 J_{H-H} = 1.3$ Hz, 1H, SCH$_2$), 3.76 (ddd, $^2 J_{H-H} = 14.4$ Hz, $^3 J_{H-H} = 12.1$ Hz, $^3 J_{P-H} = 2.1$ Hz, 1H, SCH$_2$), 4.09 (m, 1H, SCH$_2$C), 6.60 (m, 2H), 6.81 (m, 2H), 6.89 (m, 3H), 7.04 (m, 4H), 7.15 (m, 1H), 7.18–7.46 (m, 14H), 7.64 (m, 2H), 7.74 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 19.4$ (C, C(CH$_3$)$_3$), 27.2 (CH$_3$, C(CH$_3$)$_3$), 40.6 (d, $^1 J_{P-C} = 18.3$ Hz, CH, SCH$_2$CH), 62.0 (d, $^1 J_{P-C} = 21.5$ Hz, CH$_2$, SCH$_2$), 126.0 (d, $^1 J_{P-C} = 2.5$ Hz, CH), 127.0 (CH), 127.2 (CH), 127.5 (CH), 127.6 (CH), 127.7 (d, $^1 J_{P-C} = 6.7$ Hz, CH), 127.8 (CH), 128.4 (CH), 128.5 (CH), 128.60 (CH), 128.62 (CH), 128.67 (d, $^1 J_{P-C} = 2.2$ Hz, CH), 129.4 (CH), 131.3 (CH), 132.9 (d, $^2 J_{P-C} = 18.3$ Hz, CH, Po-Ph), 133.9 (d, $^2 J_{P-C} = 20.8$ Hz, CH, Po-
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Ph), 134.2 (d, $^1J_{P,C} = 17.2$ Hz, C, i-Ph), 135.2 (d, $^1J_{P,C} = 16.1$ Hz, C, i-Ph), 135.43 (CH), 135.46 (CH), 136.0 (C), 136.1 (C), 136.6 (d, $^2J_{P,C} = 7.9$ Hz, C, PCHi-Ph), 142.9 (C).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = 2.43$ (s).

Melting point: 76 °C.

Optical rotation: $[\alpha]_D +109$ (c 0.1, CH$_2$Cl$_2$).

10.8. (+)-Diphenyl((1$R,2R$)-2-((S)-N-methyl-S-phenylsulfonimidoyl)cyclohexyl) phosphine (139)

Following GP-4, phosphine 139 was prepared starting from the phophine borane 120 (112 mg, 258 µmol) and DABCO (32 mg, 285 µmol) in toluene (3 mL). Purification by column chromatography afforded phosphine 139 (105 mg, 97%) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.37$ (bd, $J = 14.3$ Hz, 1H), 1.56 (bd, $J = 10.3$ Hz, 2H), 1.81–2.36 (m, 5H), 2.68 (s, 3H, NCH$_3$), 3.04 (bt, $J = 6.5$ Hz, 1H, SCH), 3.94 (bs, 1H, SCHCH$_3$), 7.31 (m, 6H), 7.49 (m, 5H), 6.65 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 21.0$ (CH$_2$), 21.2 (d, $J_{P,C} = 8.2$ Hz, CH$_2$), 21.8 (d, $J_{P,C} = 5.1$ Hz, CH$_2$), 22.7 (d, $J_{P,C} = 11.2$ Hz, CH$_2$), 29.7 (CH$_3$, NCH$_3$), 30.4 (d, $^1J_{P,C} = 14.0$ Hz, CH, SCHCH$_3$), 60.4 (d, $^2J_{P,C} = 17.6$ Hz, CH, SCH), 128.2 (d, $J_{P,C} = 7.7$ Hz, CH), 128.4 (d, $J_{P,C} = 7.5$ Hz, CH), 128.8 (CH), 128.96 (CH), 128.97 (CH), 129.6 (CH), 132.1 (CH), 133.5 (d, $J_{P,C} = 15.1$ Hz, CH), 133.7 (d, $J_{P,C} = 15.2$ Hz, CH), 136.2 (d, $^1J_{P,C} = 44.6$ Hz, C, i-Ph), 136.3 (d, $^1J_{P,C} = 46.4$ Hz, C, i-Ph), 137.5 (C, Si-Ph).
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$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = -12.79$ (s).

Melting point: 122 °C.

Optical rotation: $[\alpha]_D +207$ (c 0.10, CH$_2$Cl$_2$)

10.9. (−)-Diphenyl((1$S$,2$S$)-2-((S)-N-methyl-S-phenylsulfonimidoyl)cyclohexyl) phosphine (141)

![Phosphine 141](image)

C$_{25}$H$_{28}$NOPS

MW = 421.53 g.mol$^{-1}$

Following GP-4, phosphine 141 was prepared starting from the phophine borane 121 (71 mg, 163 µmol) and DABCO (20 mg, 178 µmol) in toluene (2.5 mL). Purification by column chromatography afforded phosphine 141 (63 mg, 91%) as a sticky syrup.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.40$ (m, 1H), 1.64 (m, 2H), 1.91 (m, 1H), 1.99–2.22 (m, 2H), 2.55 (m, 1H), 2.60 (s, 3H, NCH$_3$), 2.70 (bd, $J = 14.2$ Hz, 1H), 2.91 (bt, $J = 6.1$ Hz, 1H, SCH), 2.99 (bs, 1H, SCHCHP), 7.01 (m, 2H), 7.09 (m, 2H), 7.23 (m, 1H), 7.29 (m, 3H), 7.36 (m, 2H), 7.43 (m, 2H), 7.58 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 21.3$ (d, $J_{P,C} = 7.8$ Hz, CH$_2$), 21.61 (d, $J_{P,C} = 3.4$ Hz, CH$_2$), 21.63 (CH$_2$), 22.2 (d, $J_{P,C} = 12.0$ Hz, CH$_2$), 29.7 (CH$_3$, NCH$_3$), 31.3 (d, $^2J_{P,C} = 15.6$ Hz, CH, SCHCHP), 60.0 (d, $^3J_{P,C} = 16.9$ Hz, CH, SCH), 128.3 (d, $J_{P,C} = 7.6$ Hz, CH), 128.4 (d, $J_{P,C} = 7.9$ Hz, CH), 128.9 (CH), 129.0 (CH), 129.1 (CH), 129.8 (CH), 132.1 (CH), 133.2 (d, $J_{P,C} = 17.0$ Hz, CH), 133.4 (d, $J_{P,C} = 17.6$ Hz, CH), 135.4 (d, $^3J_{P,C} = 15.1$ Hz, C, i-Ph), 135.5 (d, $^1J_{P,C} = 14.8$ Hz, C, i-Ph), 136.9 (C, Si-Ph).
\(^{31}\text{P NMR}\) (162 MHz, CDCl\(_3\)): \(\delta = -13.67\) (s).

**Optical rotation:** \([\alpha]_D = -11.42\) (c 0.22, CH\(_2\)Cl\(_2\))

10.10. (+)-Diphenyl(1\(R,2R\))-2-((S)-N-benzyl-S-phenylsulfonimidoyl)cyclohexyl) phosphine (140)

Following GP-4, phosphine 140 was prepared starting from the phophine borane 122 (200 mg, 391 \(\mu\)mol) and DABCO (48 mg, 428 \(\mu\)mol) in toluene (6 mL). Purification by column chromatography afforded phosphine 140 (63 mg, 97\%) as a white solid.

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \(\delta = 1.38\) (m, 1H), 1.58 (m, 2H), 1.80 (bd, \(J = 14.9\) Hz, 1H), 1.93 (m, 1H), 2.06 (m, 1H), 2.18 (m, 1H), 2.38 (m, 1H), 3.15 (m, 1H, SCH), 3.97 (d, \(^2J_{H-H} = 15.0\) Hz, 1H, NCH\(_2\)Ph), 4.14 (bs, 1H, SCHCHP), 4.32 (d, \(^2J_{H-H} = 15.0\) Hz, 1H, NCH\(_2\)Ph), 7.23–7.38 (m, 9H), 7.43 (m, 4H), 7.51 (m, 3H), 7.64 (m, 2H), 7.72 (m, 2H).

\(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)): \(\delta = 19.8\) (CH\(_2\)), 20.1 (d, \(J_{P-C} = 8.0\) Hz, CH\(_2\)), 20.8 (d, \(J_{P-C} = 5.0\) Hz, CH\(_2\)), 21.7 (d, \(J_{P-C} = 11.0\) Hz, CH\(_2\)), 29.4 (d, \(^1J_{P-C} = 13.8\) Hz, CH, SCHCHP), 46.0 (CH\(_2\), NCH\(_2\)Ph), 59.4 (d, \(^2J_{P-C} = 18.0\) Hz, CH, SCH), 125.0 (CH), 126.0 (CH), 126.8 (CH), 127.3 (d, \(J_{P-C} = 7.7\) Hz, CH), 127.4 (d, \(J_{P-C} = 7.4\) Hz, CH), 127.92 (CH), 127.97 (CH), 128.04 (CH), 128.7 (CH), 131.1 (CH), 132.2 (d, \(J_{P-C} = 10.6\) Hz, CH), 132.4 (d, \(J_{P-C} = 11.2\) Hz, CH), 135.1 (d, \(^1J_{P-C} = 30.7\) Hz, C, \(i\)-Ph), 135.3 (d, \(^1J_{P-C} = 32.1\) Hz, C, \(i\)-Ph), 136.6 (C, \(Si\)-Ph), 141.0 (C, NCH\(_2\)\(i\)-Ph).
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\[ ^{31}P \text{NMR} \text{ (162 MHz, CDCl}_3\text{): } \delta = -13.09 \text{ (s).} \]

\textbf{MS} (EI): \( m/z \) (%) = 451 (5), 357 (11), 283 (7), 268 (31), 267 (66), 266 (100), 265 (28), 232 (13), 215 (8), 183 (14), 106 (20), 91 (13).

\textbf{MS} (CI, isobutane): \( m/z \) (%) = 498 [M+1] (4), 391 (6), 268 (20), 267 (100), 266 (7).

\textbf{MS} (ESI–MS, dissolved in CH\(_2\)Cl\(_2\) and diluted with MeOH): \( m/z \) (%) = 536 [M+39] and/or [M(O)+23] (100), 520 [M+23] (72), 375 (12), 297 (13), 283 (10), 185 (6).

\textbf{MS} (ESI–MS, dissolved in CH\(_2\)Cl\(_2\) and diluted with MeOH, 1 hour later): \( m/z \) (%) = 536 [M+39] and/or [M(O)+23] (100), 520 [M+23] (29), 375 (19), 297 (25), 283 (55), 267 (14), 185 (3).

<table>
<thead>
<tr>
<th>HRMS (ESI–TOF):</th>
<th>\textbf{C}<em>{31}\textbf{H}</em>{33}\textbf{NOPS}</th>
<th>\textbf{Calculated}</th>
<th>\textbf{Found}</th>
</tr>
</thead>
<tbody>
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<td>CH(_3)CN–H(_2)O + 0.1%HCO(_2)H</td>
<td>[M+1]</td>
<td>498.2015</td>
<td>498.2009</td>
</tr>
</tbody>
</table>

\textbf{Melting point:} 129 °C.

\textbf{Optical rotation:} \([\alpha]_D^{\circ} +78.0 \text{ (c 0.10, CH}_2\text{Cl}_2)\).

10.11. (–)-Diphenyl((1S,2S)-2-((S)-N-benzyl-S-phenylsulfonylimidoyl)cyclohexyl) phosphine (142)

\[
\begin{align*}
\text{142} \\
\text{C}_{31}\text{H}_{32}\text{NOPS} \\
\text{MW} = 497.63 \text{ g.mol}^{-1}
\end{align*}
\]
Following GP-4, phosphine 142 was prepared starting from the phosphine borane 123 (78 mg, 153 µmol) and DABCO (18 mg, 160 µmol) in toluene (2.5). Purification by column chromatography afforded phosphine 142 (71 mg, 93%) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.40$ (m, 1H), 1.57–1.73 (m, 2H), 1.93 (m, 1H), 2.15 (m, 2H), 2.58 (m, 1H), 2.76 (m, 1H), 2.98 (m, 1H, SCH), 3.13 (bs, 1H, SCHCHP), 3.91 (d, $^2J_{H-H} = 14.8$ Hz, 1H, NCH$_2$Ph), 4.23 (d, $^2J_{H-H} = 14.8$ Hz, 1H, NCH$_2$Ph), 7.09 (m, 4H), 7.17 (m, 1H), 7.20–7.49 (m, 12H), 7.56–7.65 (m, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 20.3$ (d, $J_{P-C} = 7.6$ Hz, CH$_2$), 20.5 (CH$_2$), 20.8 (d, $J_{P-C} = 4.8$ Hz, CH$_2$), 21.3 (d, $J_{P-C} = 11.8$ Hz, CH$_2$), 30.1 (d, $^1J_{P-C} = 15.5$ Hz, CH, SCHCHP), 46.0 (CH$_2$, NCH$_2$Ph), 59.4 (d, $^2J_{P-C} = 17.1$ Hz, CH, SCH), 125.0 (CH), 126.1 (CH), 126.8 (CH), 127.3 (d, $J_{P-C} = 7.7$ Hz, CH), 127.4 (d, $J_{P-C} = 7.8$ Hz, CH), 127.45 (d, $J_{P-C} = 7.5$ Hz, CH), 127.93 (CH), 127.98 (CH), 128.05 (CH), 128.7 (CH), 131.2 (CH), 132.2 (d, $J_{P-C} = 10.6$ Hz, CH), 132.4 (d, $J_{P-C} = 11.5$ Hz, CH), 134.4 (d, $^1J_{P-C} = 33.1$ Hz, C, i-Ph), 134.6 (d, $^1J_{P-C} = 33.1$ Hz, C, i-Ph), 136.8 (C, Si-Ph), 140.7 (C, NCH$_2$-Ph).

$^{31}$P NMR (162 MHz, CDCl$_3$): $\delta = -13.48$ (s).

Melting point: 89 °C.

Optical rotation: $[\alpha]_D -34.0$ (c 0.10, CH$_2$Cl$_2$).

11. Allylic Substitution

11.1. (+)-(R)-(E)-Dimethyl 2-(1,3-diphenylallyl)malonate (44)
Following GP-5, the malonate 44 was prepared starting from the racemic acetate 43 (120 mg, 480 µmol), phophine 140 (7.1 mg, 14 µmol), Pd$_2$DBA$_3$.CHCl$_3$ (7.4 mg, 7 µmol), dimethyl malonate (138 µL, 1.19 mmol), N,O-bis(trimethylsilyl)acetamide (320 µL, 1.19 mmol) and lithium acetate (1mg) in CH$_2$Cl$_2$ (3 mL). After stirring the mixture for 50 min (complete conversion by TLC), it was quenched and worked up as described in GP-5. Purification by column chromatography (cyclohexane/ethylacetate, 9:1) gave malonate 44 (151 mg, 98%) with 97% ee as colourless viscous oil, which solidified upon standing. The ee value was determined by HPLC (chiralcel-OD-H column, detector 254 nm, n-heptane/isopropanol: 95/5, flow: 0.75 ml/min, 40 bar, $R_t$ (44): 15.28 min; $R_t$ (ent-44): 19.53 min).

11.2. (+)-(R)-(E)-dimethyl 2-(pent-3-en-2-yl)malonate (145)

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Me} \\
\text{Me} & \quad \quad \quad \quad \text{Me}
\end{align*}
\]

MW = 200.23 g mol$^{-1}$

Following GP-5, malonate 145 was prepared starting from the racemic acetate 144 (61 mg, 480 µmol), phophine 140 (7.1 mg, 14 µmol), Pd$_2$DBA$_3$.CHCl$_3$ (7.4 mg, 7 µmol), dimethyl malonate (138 µL, 1.19 mmol), N,O-bis(trimethylsilyl)acetamide (320 µL, 1.19 mmol) and lithium acetate (1mg) in CH$_2$Cl$_2$ (3 mL). After the mixture for 3.5 h (complete conversion by TLC), it was quenched and worked up as described in GP-5. Purification by column chromatography (pentane/Et$_2$O, 8:1) gave malonate 145 (90 mg, 95%) with 59% ee as colourless viscous oil. The ee value was determined by GC (β-cyclodextrine CP column, temperature programme 1, $R_t$ (ent-145): 32.82 min; $R_t$ (145): 32.92 min).
11.3. (−)-(R)-Dimethyl 2-(cyclohex-2-enyl)malonate (96)

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Me} \\
\text{C} & \\
\end{align*}
\]

MW = 212.23 g mol\(^{-1}\)

Following GP-5, malonate 96 was prepared starting from the racemic acetate 95 (61 mg, 480 µmol), phophine 140 (7.1 mg, 14 µmol), \(\text{Pd}_2\text{DBA}_3\cdot\text{CHCl}_3\) (7.4 mg, 7 µmol), dimethyl malonate (138 µL, 1.19 mmol), N,O-bis(trimethylsilyl)acetamide (320 µL, 1.19 mmol) and lithium acetate (1mg) in \(\text{CH}_2\text{Cl}_2\) (3 mL). After the mixture for 24 h (complete conversion by TLC), it was quenched and worked up as described in GP-5. Purification by column chromatography (pentane/Et\(_2\)O, 10:1) gave malonate 96 (71 mg, 70%) with 36% ee as colourless viscous oil. The ee value was determined by GC (β-cyclodextrine CP column, temperature programme 2, \(R_t\) (ent-96): 25.30 min; \(R_t\) (96): 25.48 min).\(^{191}\)
12. Isotopic distribution and simulated isotopic patterns

Figure 31: Isotopic distribution (top) and simulated isotopic pattern (bottom) of complex 146.
Figure 32: Isotopic distribution (top) and simulated isotopic pattern (bottom) of complex 147.
Figure 33: Isotopic distribution (top) and simulated isotopic pattern (bottom) of complex 149.
13. X-ray Crystal Structure Reports


**Experimental Details**

Crystal data:

- Chemical formula: \((\text{C}_{27}\text{H}_{29}\text{BNOPS})_2\) (two symm. indep. molecules in the asymm. unit)
- Formula weight: 914.77
- Crystal system: monoclinic
- Space group (No.): \(P2_1\) (4)
- \(Z\): 4
- \(a\) (Å): 12.1863(3)
- \(b\) (Å): 16.9072(4)
- \(c\) (Å): 12.3813(6)
- \(\alpha\) (°): 90.0
- \(\beta\) (°): 100.811(1)
- \(\gamma\) (°): 90.0
- Cell volume: 2505.7(1) Å³
- Density calc.: 1.212 g/cm³
- Radiation: CuK\(\alpha\) (1.54179 Å)
- Range for lattice parameters: \(<\Theta<\)
Absorption coefficient : 1.886mm⁻¹
Temperature : 100K
Crystal source : recrystallized from CH₂Cl₂/hexane
Crystal colour : colourless
Crystal shape : irregular
Crystal size : ca. 0.6 x 0.6 x 0.6mm

**Data Collection**

Diffractometer type : Bruker Proteum X8 mit FR591 Drehanode, Pt135 CCD-Detektor

Collection method :
Absorption correction : SADABS
No. of reflections measured : 73137
No. of independent reflections: 8935
No. of observed reflections : 7841

\[ \theta_{\text{max}} (\varepsilon) : 68.04 \]

\[ h_{\text{min}} 6 h_{\text{max}} : -14 6 14 \]

\[ k_{\text{min}} 6 k_{\text{max}} : -20 6 20 \]

\[ l_{\text{min}} 6 l_{\text{max}} : -14 6 14 \]

Criterion for observed : \( I > 2\sigma (I) \)
\( R_{\text{int}} \) : 0.02(2)
Standard reflections :
Variation :

Refinement:
On : \( F \)
Treatment of hydrogens : Calculated in idealized positions. Us fixed at 1.5×U of the corresponding heavy atom prior to final refinement. No refinement of hydrogen parameters.

\( R \) : 0.042
\( R_w \) : 0.050
Weighting scheme : \( w=1/\sigma^2(F) \)
No. of parameters refined : 577
No. of reflections in refmnt. : 7841
Residual electron density : -1.06/0.34e/Å³
r*[1] : not refined
XABS[2] : 0.016(18)
Goodness of fit : 3.291
Solution : XTAL3.7[3]
Remarks : 192

Definitions:
\[ U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j a_j \]

The anisotropic displacement factor in the structure factor expression is:
\[ t = \exp[-2\pi^2(\sum_i \sum_j U_{ij} h_i h_j a_i^* a_j^* )] \]

**Experimental Details**

Crystal data:

Chemical formula : \((\text{C}_{42}\text{H}_{45}\text{BNOPSSi})_2\)

formula weight : 1363.53

Crystal system : triclinic

Space group (No.) : P1 (1)

\(Z\) : 1

\(a\) (Å) : 9.8937(8)

\(b\) (Å) : 10.0435(8)

\(c\) (Å) : 19.1219(15)

\(\alpha\) (°) : 86.839(1)

\(\beta\) (°) : 83.024(1)

\(\gamma\) (°) : 84.547(1)

Cell volume : 1875.7(3)Å³

Density calc. : 1.207g/cm³

Radiation : MoK\(\alpha\) (0.71073Å)

Range for lattice parameters : \(E<\Theta<E\)

Absorption coefficient : 0.194mm\(^{-1}\)

Temperature : 298K

Crystal source : recrystallized from

Crystal colour : colourless

Crystal shape : irregular

Crystal size : ca. 0.2x0.2.x0.2mm

**Data Collection**

Diffractometer type : Bruker SMART APEX

collection method : \(\varphi\) and \(\omega\) scans

Absorption correction : SADABS (1.0 : 0.9184)

No. of reflections measured : 79548

No. of independent reflections: 15492

No. of observed reflections : 15170

\(\Theta\)\(_\text{max}\) (E) : 26.47

\(h\)\(_{\text{min}}\) 6 \(h\)\(_{\text{max}}\) : - 12  6  12
EXPERIMENTAL PART

\[ k_{\text{min}} \leq k_{\text{max}} : -12 \leq 6 \leq 12 \]

\[ l_{\text{min}} \leq l_{\text{max}} : -23 \leq 6 \leq 23 \]

Criterion for observed reflections: \[ I > 2\sigma(I) \]

\[ R_{\text{int}} : 0.022(30) \]

Standard reflections:

Variation:

Refinement:

On: \[ F \]

Treatment of hydrogens: Calculated and not refined. Us fixed at 1.5 times U of the relevant heavy atom before final refinement.

\[ R : 0.036 \]

\[ R_w : 0.038 \]

Weighting scheme: \[ w=1/\sigma^2(F) \]

No. of parameters refined: 865

No. of reflections in refmmt.: 15170

Residual electron density: \[ -0.31/0.42e/Å^3 \]

r*[1]: not refined

XABS[2]^a): \[ -0.012(53)^a) \]

Goodness of fit: 1.867

Solution: XTAL3.7[3]

Remarks: \[^a)\text{From separate calculation}\]

Definitions:

\[ U_{eq} = 1/3 \sum_i \sum_j U_{ij} a_i^* a_j a_j \]

The anisotropic displacement factor in the structure factor expression is:

\[ t = \exp[-2\pi^2 (\sum_i \sum_j U_{ij} h_i h_j a_i^* a_j^*)] \]

**Experimental Details**

Crystal data:

Chemical formula : (C_{31}H_{35}BNOPS)_{2} two symmetrically independent molecules in the asymmetric unit

formula weight : 2\times511.48

Crystal system : monoclinic

Space group (No.) : \textit{P}2_{1} (4)

Z : 2

\(a\) (Å) : 11.516(4)

\(b\) (Å) : 13.952(1)

\(c\) (Å) : 18.732(4)

\(\alpha\) (°) : 90.0

\(\beta\) (°) : 107.01(1)

\(\gamma\) (°) : 90.0

cell volume : 2878.0(12)Å\(^{3}\)

Density calc. : 1.180g/cm\(^{3}\)

Radiation : CuK\(_{\alpha}\) (1.54179Å)

Range for lattice parameters : 14.23E < \(\Theta\) < 36.24E

Absorption coefficient : 1.693 mm\(^{-1}\)
Temperature : 298K
Crystal source : recrystallized from Et₂O
Crystal colour : colourless
Crystal shape : irregular
Crystal size : ca. 0.3x0.3.x0.3mm

**Data Collection**

Diffractometer type : Enraf-Nonius CAD4
collection method : \( \omega/2\theta \) scans
Absorption correction : none
No. of reflections measured : 11201
No. of independent reflections: 10387
No. of observed reflections : 9709
\( \theta_{\text{max}} \) (E) : 67.76
\( h_{\text{min}} \) \( h_{\text{max}} \) : -13 6 13
\( k_{\text{min}} \) \( k_{\text{max}} \) : -16 6 16
\( l_{\text{min}} \) \( l_{\text{max}} \) : -22 6 22
Criterion for observed : \( I > 2\sigma(I) \)
\( R_{\text{int}} \) : 0.023(36)
Standard reflections : 2 3 -6, -2 -3 6, 2 2 -5
Variation : 6071(159) 6180(171) 14031(387)

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

\( R \) : 0.060
\( R_w \) : 0.077
Weighting scheme : \( w=1/\sigma^2(F) \)
No. of parameters refined : 648
No. of reflections in refmnt. : 9702
Residual electron density : -0.53/0.34e/Å³
r*[1] : not refined
XABS[2] : 0.0190(245)
Goodness of fit : 2.818
Solution : XTAL3.7[3]
Remarks : 192

Definitions:

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a^*_i a_j a^*_j$$

The anisotropic displacement factor in the structure factor expression is:

$$t = \exp[-2\pi^2 \sum_i \sum_j U_{ij} h_i h_j a^*_i a_j a^*_j]$$
C. APPENDIX
References


References


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100 M. Reggelin, C. Zur Synthesis 2000, 1, 1–64.


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126 Crystallographic data have been deposited with the Cambridge Crystallographic Center as supplementary publication nos. CCDC 662848. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).


Crystallographic data have been deposited with the Cambridge Cristallographic Center as supplementary publication nos. CCDC 662849. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).


Curriculum Vitae

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1999 – 2002    Bachelor of Science in Physics and Chemistry, Université Rennes 1 (F)
2002 – 2004    Master of Science in Chemistry, Université Rennes 1 (F)
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1999           Baccalauréat Scientifique
2001           Diplôme d’Etudes Universitaires Générales Science de la Matière
2002           Licence de Chimie
2003           Maîtrise de Chimie
2004           Master Degree, Diplome d’Etudes Approfondies Chimie Moléculaire
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