New mixed bidentate phosphine ligands and their application in enantioselective transformations

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New mixed bidentate phosphine ligands and their application in enantioselective transformations

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

vorgelegt von

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Tag der mündlichen Prüfung: 15.05.2013

for Geert-Jan

“Science is like sex: Sometimes something useful comes out, but that is not the reason we are doing it.”

R.P. Feynman

Der experimentelle Teil der vorliegenden Arbeit wurde in der Zeit von März 2008 bis März 2011 am Institut für Technische und Makromolekulare Chemie der Rheinisch-Westfälischen Technischen Hochschule unter Anleitung von Univ.-Prof. Dr. Walter Leitner angefertigt.

Teile dieser Arbeit wurden bereits publiziert unter:

M. Eggenstein, A. Thomas, J. Theuerkauf, G. Franciò, W. Leitner *Adv. Synth. Catal.* **2009**, *351*, 725.

Abstract

In this thesis the synthesis of new mixed bidentate phosphine ligands and their application in selected enantioselective transformations is presented.

Based on a phosphine-phosphoramidite lead structure, a modular synthetic pathway was used to synthesise different types of mixed bidentate phosphine ligands. Variation of the organic moiety at the amine or at the diol building block afforded three novel phosphine-phosphoramidites, while replacement of the diol by an aminoalcohol gave four different phosphine-phosphorodiamidites. Phosphine-phosphorodiamidites are not known in literature so far and this is the first study on their synthesis, purification, stability and application in asymmetric catalysis.

The application of these new structures as ligands in selected enantioselective transformations enabled a systematic study of the influence of variations in the lead structure on the behaviour in catalytic reactions. The novel phosphine-phosphoramidites and -phosphorodiamidites were applied in different asymmetric hydrogenation reactions (C=C, C=N, C=O) using different active metal centres (Rh, Ir and Ru, respectively). In addition, the phosphine-phosphorodiamidites were applied in Rh-catalysed asymmetric hydroformylation and Pd-catalysed hydrophosphorylation.

The results of the catalytic reactions prove a high versatility of the new structures and include one of the highest enantioselectivities for the hydrogenation of 2-substituted quinolines (using phosphine-phosphoramidites). Replacement of the diol bulding block in the phosphine-phosphoramidite lead structure by a diamine afforded the first phosphine-phosphortriamide ligand, whose application in enantioselective transformations needs to be explored in future research.

Kurzbeschreibung

Die vorliegende Doktorarbeit befasst sich mit der Synthese von gemischten bidentaten Phosphinliganden und deren Anwendung in ausgewählten asymmetrischen Transformationen.

Ausgehend von einer bekannten Phosphin-Phosphoramiditstruktur wurde deren modularer Syntheseweg zur Herstellung unterschiedlicher Typen von gemischten bidentaten Phosphinliganden verwendet. Variation des Substituenten am Amin-, bzw. am Diol-Baustein lieferte drei neue Phosphin-Phosphoramiditliganden, während ein Austausch des Diols durch einen Aminoalkohol die Synthese vier verschiedener Phosphin-Phosphordiamidite ermöglichte. Da Phosphin-Phosphordiamidite in der Literatur bisher unbekannt sind, ist dieser Teil der Arbeit die erste Studie zu deren Synthese, Aufreinigung, Stabilität und Verwendung in der asymmetrischen Katalyse.

Die Verwendung der neuen Strukturen als Liganden in ausgewählten enantioselektiven Reaktionen ermöglicht ausserdem eine systematische Studie des Einflusses von Strukturvariationen auf das Verhalten in katalytischen Reaktionen. Hierfür wurden die neu synthetisierten Phosphin-Phosphoramidite und –phosphordiamidite unter Verwendung unterschiedlicher Übergangsmetalle (Rh, Ir, Ru) als Liganden in unterschiedlichen asymmetrischen Hydrierungen (C=C, C=N, C=O) getestet. Zusätzlich wurden die Phosphine-Phosphordiamidite in der asymmetrischen Rh-katalysierten Hydroformylierung und Pd- katalysierten Hydrophosphorylierung verwendet.

Die Ergebnisse der Katalysen belegen eine hohe Vielseitigkeit der neuen Ligandstrukturen und beinhalten einen der höchsten Enantiomerenüberschüsse für die Hydrierung von 2-substituierten Chinolinen (unter Verwendung von Phosphin-Phosphordiamiditen). Ein Austausch des Diolbausteins in der Phosphin-Phosphoramiditleitstruktur gegen ein Diamin lieferte ausserdem den ersten bisher bekannten Phosphin-Phosphortriamidliganden, dessen Einsatz in der enantioselektiven Katalyse noch für zukünftige Forschungsprojekte aussteht.

Contents

1 Introduction

1.1 Chirality and asymmetric synthesis

A chiral (optically active) molecule lacks an internal plane of symmetry and has a non-superimposable mirror image (Figure 1.1.1). These stereoisomers are called enantiomers and can differ in their biological activity.

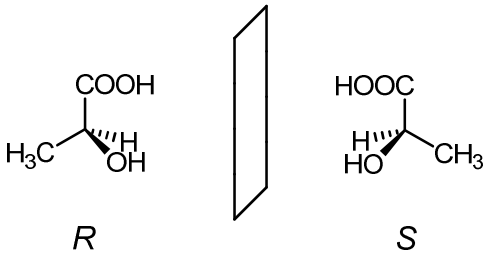
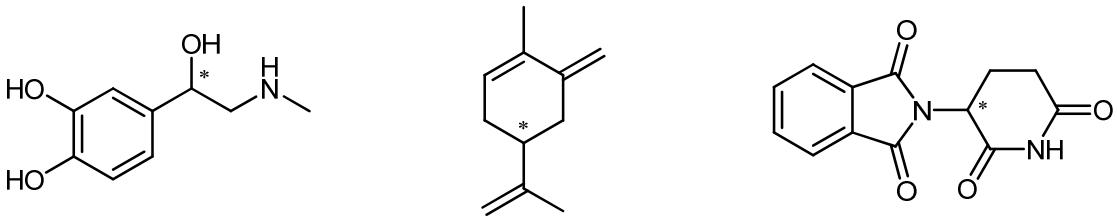


Figure 1.1.1: *Central Chirality*

For instance, *R*-adrenaline is more active affecting bodily functions than *S*-adrenaline.[1] In the case of carvone (**2**), the enantiomers have a completely diverse smell. *S*-carvone smells of caraway while *R*-carvone smells of spearmint.[2] Both enantiomers are used in food and flavour industry and therefore it is necessary to have them enantiomerically pure. Many pharmaceutical compounds are optically active molecules where one enantiomer provides the desired medical effect (eutomer) while the other one is not active or even very toxic (distomer).



1 **2** **3**

Figure 1.1.2: *Adrenaline (**1**), carvone (**2**), thalidomide (**3**)*

A well-known example is thalidomide (**3**), which was sold in racemic form as a drug against morning sickness during pregnancy by the German company Grünenthal (trade names: Contergan, Softenon). Indeed thalidomide had a sedative effect but unfortunately it also turned out to be highly teratogenic causing numerous birth defects (deformities). Further investigations showed that *S*-thalidomide was claimed to be responsible for the unwanted adverse reactions, but since the enantiomers of thalidomide quickly interconvert *in vivo,* this assumption is not completely proven.[3] Nevertheless, this incident forced the pharmaceutical industry to put more effort in exploring the diversity of enantiomers. Many countries prescribe that both enantiomers are to be tested separately to identify their (side-)effects. In general, there are three possible approaches to produce non-racemic molecules:[4,5]

1. Racemic synthesis is followed by resolution-wise crystallisation, chromatography or chemical kinetics
2. The desired product is obtained as a derivative of a readily available chiral substance from the natural “chiral pool”
3. A prochiral molecule is converted selectively via a stereocontrolled (catalytic) transformation (→asymmetric synthesis)[6]

The first route is generally not very resource efficient since the unwanted enantiomer is 50% by-product at the beginning and the mixture always needs further purification. For some separations a costly chiral auxiliary[7,8] is needed in stoichiometric amounts. But for several components, a racemisation of the unwanted enantiomer or dynamic kinetic resolution methods can push the theoretical yield up to 100 % making the process more atom-economical. Route 2 is limited to the naturally available chiral molecules as building blocks. That is why a lot of research in academia focusses on the development and improvement of asymmetric synthetic pathways. For an efficient asymmetric transformation a highly enantioselective chiral source is needed in catalytic amounts. This chiral source can be an organic molecule (organocatalysis[9]), a transition metal complex where chiral ligands are attached to the catalytically active metal atom,[10,11,12] an enzyme (biocatalysis[13,14,15]) or a chiral medium.[16,17,18,19]

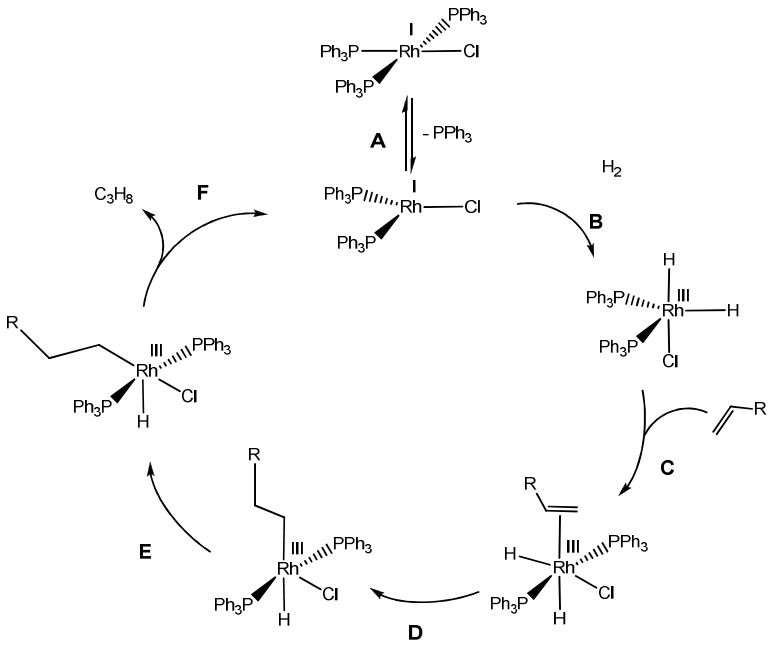
Particularly transition metal catalysts promote a large variety of asymmetric transformations like C-C bond forming reactions, hydrogenation of unsaturated bonds or oxidation reactions with high activity and enantioselectivity.[12] Despite numerous

efforts in academical research, the number of industrial applications remains limited,[20,21,22] since a lot of requirements need to be fulfilled. A “perfect” system is not only highly selective but also highly productive, stable, cost-efficient, easily available and environmentally-friendly. Nevertheless, there is a continuous growth in single-enantiomer drug sales[1] signifying a growing interest in developing pathways to enantiomerically pure compounds. Most of the asymmetric homogeneous processes in industry are hydrogenation reactions.

1.2 Development of asymmetric homogeneous hydrogenation

Asymmetric hydrogenation is one of the most important enantioselective processes used in industry.[21] It is a synthetic pathway to many enantiomerically pure compounds for pharmaceuticals, fragrance compounds or plant protection chemicals.[23] The first publication of a homogeneous (not yet asymmetic) hydrogenation was presented by Calvin in 1938 using copper acetate in a solution of quinoline.[24] Only one year later rhodium was introduced as an active metal for homogeneous hydrogenation by Iguchi.[25] A lot of systems nowadays consist of a transition metal atom coordinated by taylor-made ligands for specific reactions. Within the constantly rising number of ligands, phosphorus ligands took over a significant role in the development of asymmetric hydrogenation reactions right from the beginning.[26]

One of the most distinguished studies on the mechanism of homogeneous hydrogenation of alkenes was done during the 1960s by the groups of Halpern and Wilkinson on the Rh/PPh_3 catalytic system.[27] According to these studies, a hydrogenation catalysed by “Wilkinson’s catalyst” follows a cycle (Scheme 1.2.1) starting with the dissociation of a phosphine ligand (A). The formed 14-electron species consecutively undergoes an oxidative addition with H_2 (B) and an attachment of the alkene (C). The rate determining step is the insertion of the alkene into the metal-H bond (D). After a *trans* → *cis* rearrangement (E), a reductive elimination (F) generates the desired product regenerating the active catalytic species.



Scheme 1.2.1: *Mechanism by Wilkinson & Halpern*[27]

The “Wilkinson catalyst” was the basis for the idea of using chiral phosphine ligands to induce enantioselectivity. During the late 1960s, Mislow,[28] Knowles[29] and Horner[30] did pioneering research on monodentate tertiary phosphines featuring chirality directly at the phosphorus, but mainly achieved low enantioselectivities. In 1971, an important break-through was made by Kagan and Dang with the development of the tartaric acid-derived bidentate ligand DIOP (1).[31,32]

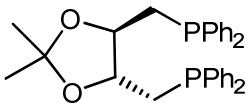


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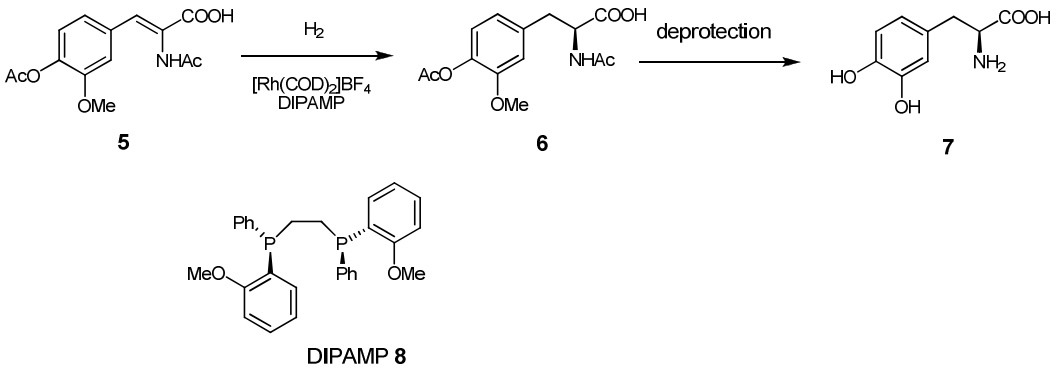
Figure.: 1.2.1: *Bidentate phosphine ligand DIOP (**4**)*

In this bisphosphine the chiral information is no longer located at the phosphorus atom itself but at carbon atoms in the backbone structure. This leads to significantly more variable structures. In the hydrogenation of acetamidocynnamic and phenylacetamidoacrylic acid enantioselectivities up to 68% were induced by **4**. Due to these results it was believed that a rigid bidentate ligand structure is necessary to induce high *ee*s. Therefore, most research was focused on the development of

bidentate phosphine ligands during the following years.[26] Very important was the establishment of an industrial process for the production of *L*-DOPA (**7**, anti Parkinson's desease) by Knowles *et al*.[33]



Scheme 1.2.2: *Synthesis of L-DOPA (**7**)*

The key step in this process is the enantioselective hydrogenation of a prochiral dehydroaminoacid **5** (Scheme 1.2.2). Using a [Rh(COD)(DIPAMP)]BF_4 complex enantioselectivities up to 95% were achieved. Another milestone in the development of chiral phosphorus-based ligands for asymmetric transformations was reported in 1980 by Noyori and Takaya: BINAP[34] (**9**, Figure 1.2.2). This ligand was applied in a lot of different catalytic reactions inducing high enantioselectivities and is therefore known to be a "priviledged ligand".[35] Since then, many ligands have been reported that feature an axially chiral backbone moiety.[36,37,38,39] Also successfully used for a broad variety of substrates are DuPHOS (**10**) and BPE (**11**) by Burk *et al.* (Figure 1.2.2).[40,41]

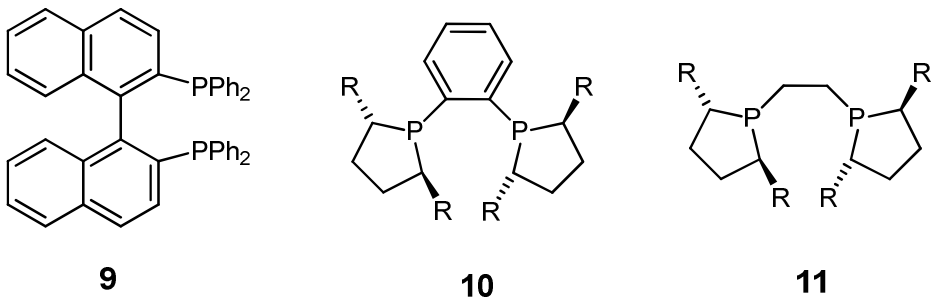
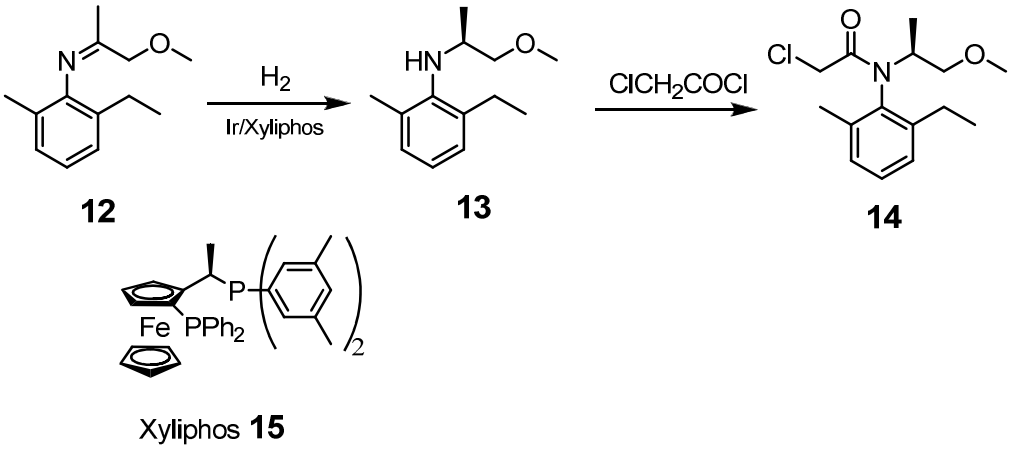


Figure 1.2.2: *Bisphosphine ligands BINAP (**9**), DuPHOS (**10**) and BPE (**11**)*

Another industrial application of great importance is the production of the herbicide (*S*)-metholachlor (**14**) developed by the company Novartis in 1999 (Scheme 1.3).[42] Xyliphos is used as a ligand for the asymmetric key step – an iridium catalysed enantioselective hydrogenation of an enamide (**12**).



Scheme 1.2.3: *Synthesis of S-metolachlor (**14**)*

A relatively low enantiomeric excess of ca 80% is achieved but due to an extremely high TOF and TON this is still acceptable for this type of application.

Since 1999 monodentate phosphorous ligands have come back into the focus of research. In hydrogenation studies of α-dehydroaminoacid esters, enantioselectivities of more than 92% could be induced by phophoramidites,[43] phosphites[44] or phosphonites[45] (Figure 1.2.3). The use of two equivalents of the monodentate species was even more effective than one equivalent of the corresponding bridged ligand. These results clearly show that a rigid bidentate chelating structure is not mandatory to achieve high enantiomeric excesses.

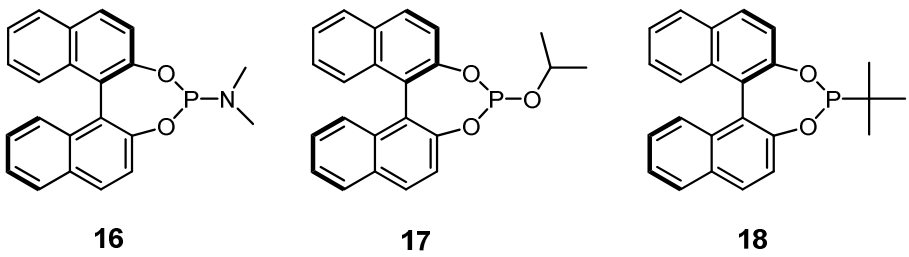


Figure 1.2.3: *Monodentate phosphorus ligands*

Apart from simple phosphorous ligands, countless investigations in mixed ligands containing additional N- or O-donor atoms have been reported. For example, P,N ligands[46] are a very important type of structures for asymmetric hydrogenation reactions. A well-known and successfully applied system is the combination of iridium and phosphino oxazolines by Pfaltz *et al*.[47] Complex **19** was used for a broad pool of substrates inducing high enantioselectivities >99%.

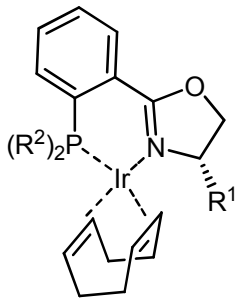


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Figure 1.2.4: *Phosphino oxazoline system (Ir)*

A combinatorial approach of de Vries *et al.* applied successful monodentate chiral phosphine ligands (like phosphoramidites) together with simple phosphines (like PPh_3) in one catalytic reaction.[48] This approach enables the induction of electronic asymmetry via two different phosphorus donor atoms while using monodentate ligands. This combination of a phosphine group with a heteroatom-substituted phosphorous moiety is well established in bidentate ligands. Over the last three decades, a lot of different mixed bidentate phosphine ligands have been reported.

1.3 Mixed bidentate phosphine ligands[36]

Although a lot of chiral ligands prepared for asymmetric catalysis are C_2-symmetrical diphosphines, mixed bidentate phosphine ligands – where a phosphine group is combined with a heteroatom-substituted phosphorous moiety – are the ligands of choice for an increasing number of applications. In many cases they are easier to prepare than bisphosphines and are available via highly modular synthetic pathways, that also opens the possibility to produce ligand libraries. Bearing two different phosphorus donor atoms, they are able to generate electronic asymmetry on

the catalytically active metal atom and often induce high enantioselectivities. A selection of the most common mixed bidentate phosphine ligands described in literature will be presented in the following part of this chapter. A structural overview is shown in figure 1.3.1.

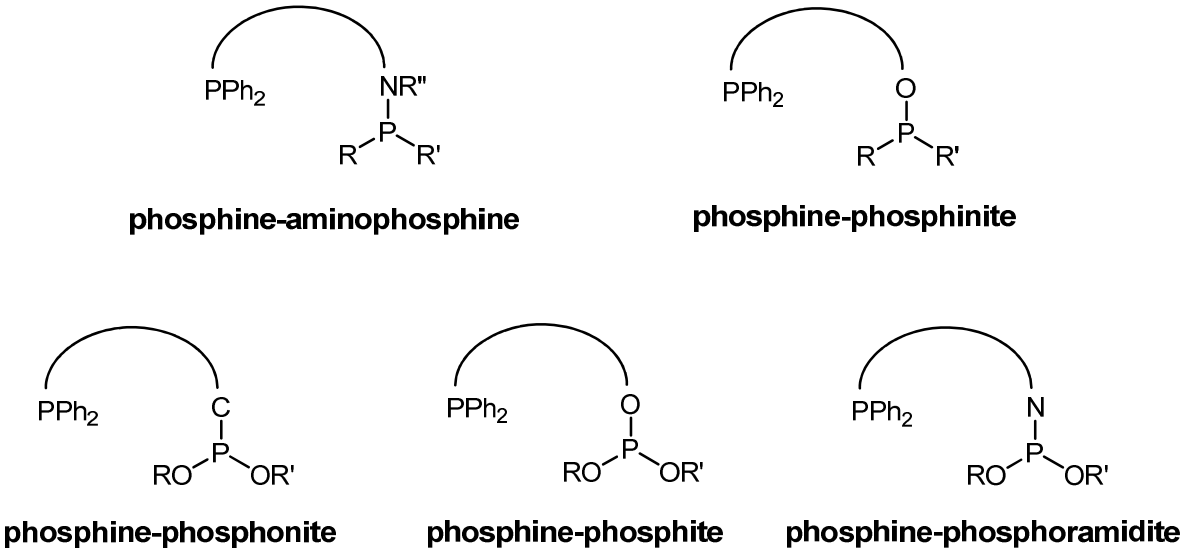
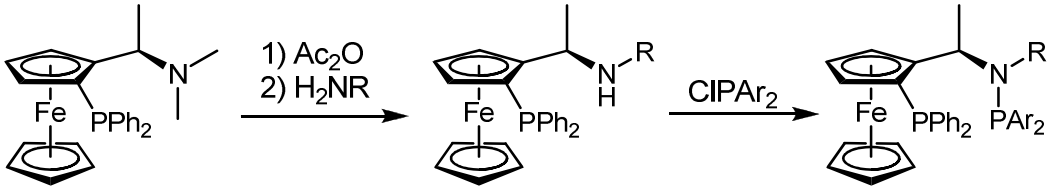


Figure 1.3.1: *General structures for typical mixed bidentate phosphorus ligands*

Phosphine-aminophosphines, which have one nitrogen and two carbon substituents at the heterophosphorous moiety, are rather underrepresented in use for asymmetric catalysis.

Figure 1.3.2: *Selected phosphine-aminophosphines*

The first phosphine-aminophosphine ligand (**20**) reported in literature is a proline-derived species complexed with palladium that was not explored in catalysis. In 2002, Boaz and co-workers presented ligands (example: **21**) containing planar and central chirality that were synthesised from enantiomerically pure *N,N*-1-dimethylaminoethyl(2diphenylphosphino)ferrocene in a two-step synthesis that is shown in scheme 1.3.1. They were successfully used in the Rh-catalysed asymmetric hydrogenation of C=C bonds.[49,50]



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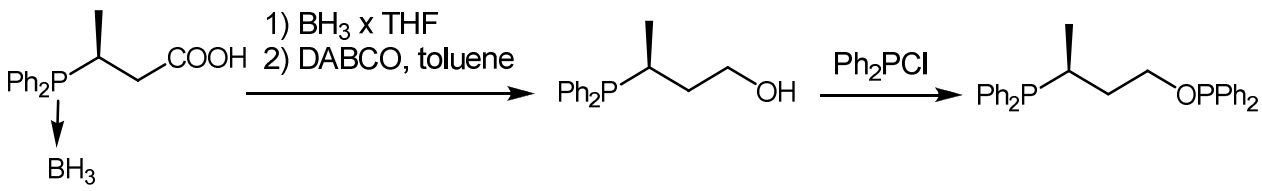
Scheme 1.3.1: *Synthesis of phosphine-aminophosphine* ***21***

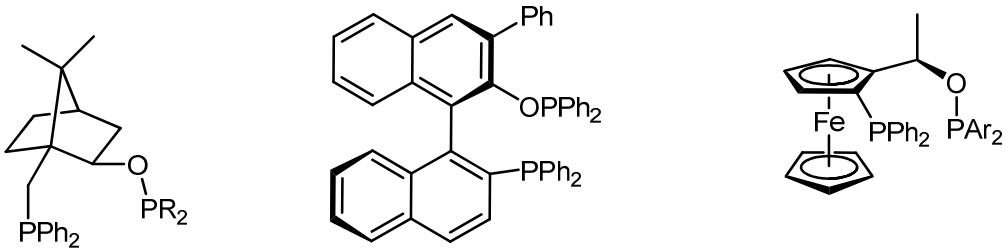
This system was remarkably air-stable but has a narrow substrate scope. Due to its air-stability Barnard *et al.* developed an immobilised version anchored on carbon in 2005.[51] Attached to ruthenium, the same type of ligands was applied in the asymmetric hydrogenation of *ß*-keto esters achieving *ee*s up to 94%.[52] With the introduction of a fluorinated moiety in this structure, Chan *et al.* created an effective and water/air stable system for the asymmetric hydrogenation of enamides and dehydro-aminoacids.[53]

Phosphine-phosphinites have a heterophosphorous moiety with one P-O and two P-C bonds. Typically, they are synthesised by the coupling of a hydroxy-phosphine intermediate with a chlorodiarylphosphine in the presence of a base as shown in scheme 1.3.2.



Scheme 1.3.2: *Synthesis of a phosphine-phosphinite*

Since several molecules from the chiral pool have hydroxy groups, they are often used as readily accessible building blocks for this type of synthesis. The first phosphine-phosphinite containing a bicyclic moiety was published by Brunner *et al.* in 1980 (**22**).[54] More recently structures based on binaphthyl (**23**)l[55] or ferrocenyl (**24**)[56] backbones have been published.

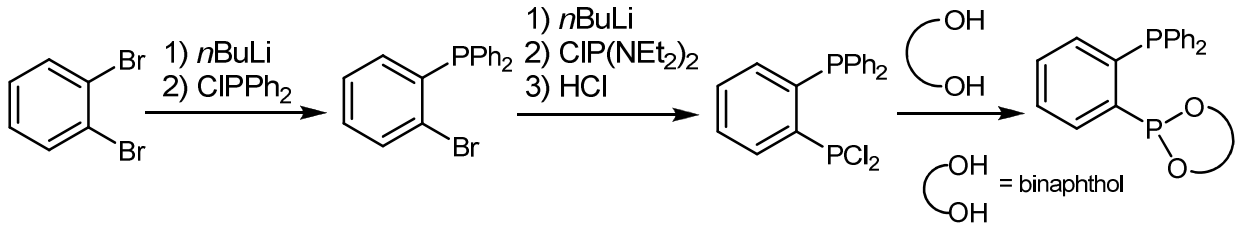


22 **23** **24**

Figure 1.3.3: *Phosphine-phosphinites - structure and examples*

There are much less successful applications of phosphine-phosphinites in catalysis compared to applications of the corresponding phosphite species that are synthesised in an analogous way. Apart from classical hydrogenation and hydroformylation reactions of selected substrates, where the best results were obtained by the binaphthyl- and ferrocene-based phosphine-phosphinites, only tests in allylic substitution reactions with low enantioselectivities were reported.

Phosphine-phosphonite ligands contain a heterophosphorous moiety with one P-C and two P-O bond. Apart from some publications on their synthesis there is only one paper that also involves their use in asymmetric catalysis. Reetz and Gosberg produced a set of structures within a three-step synthesis from *o*-dibenzyl bromide (Scheme 1.3.3).



Scheme 1.3.3: *Synthesis of phosphine-phosphonites by Reetz and Gosberg*

These ligands showed moderate enantiomeric excesses up to 88 % (induced by **25**) in the Rh-catalysed hydrogenation of dimethyl itaconate.[57]

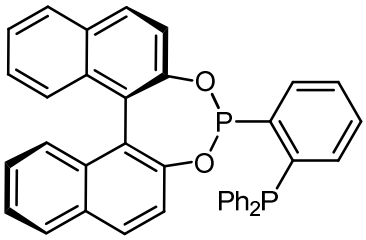


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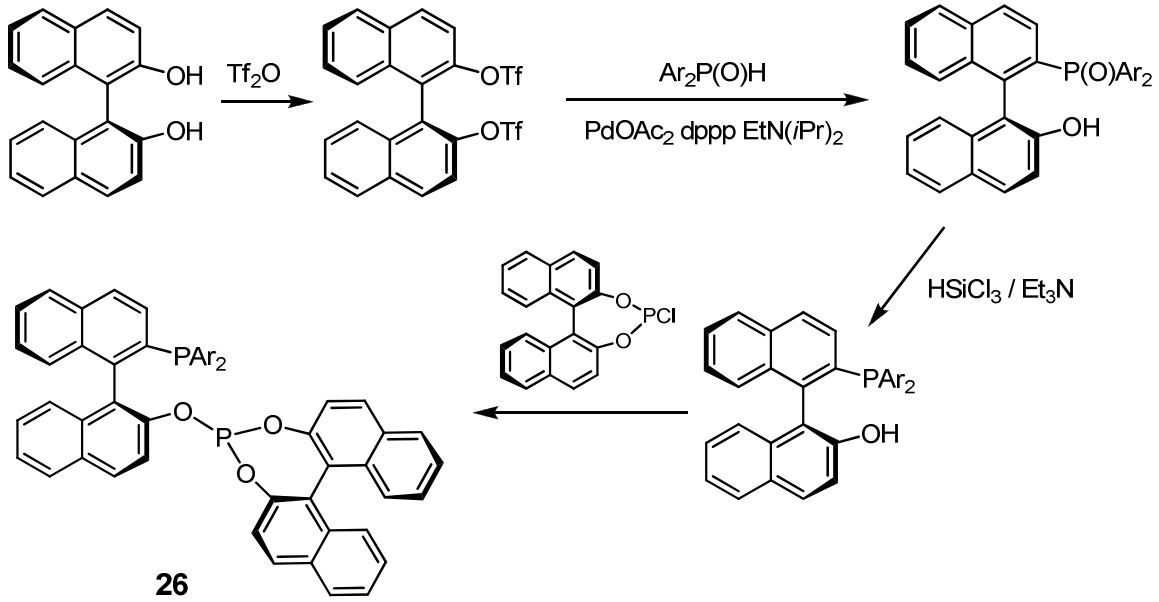
Figure 1.3.4: *Example for a phosphine-phosphonite*

Phosphine-Phosphites possess a heterophosphine moiety that contains three P-O bonds. Since Takaya[58] and Pringle[59] simultaneously reported the first examples of enantiopure phosphine-phosphites, a lot of different structures have been published in literature. Most of them follow the same synthetic route coupling a phosphine that includes a hydroxy-function with a chlorophosphite. Scheme 1.3.4 exemplarily shows the synthesis of Takaya's (*R,S*)-BINAPHOS (**26**).[58]



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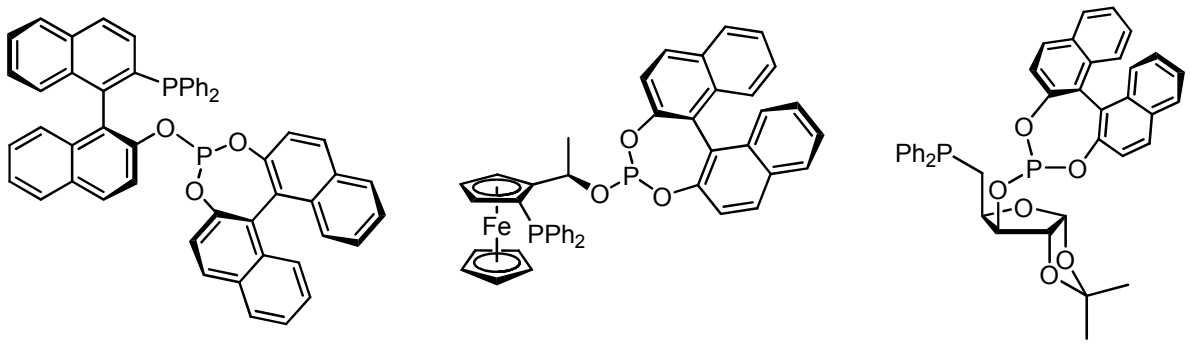
Scheme 1.3.4: *Synthesis of (R,S)-BINAPHOS (**26**)*

BINAPHOS is one of the most extensively studied ligands in enantioselective catalysis. The ligand was successfully applied in various asymmetric transformations (especially in hydroformylation)[60] and is therefore a “privileged chiral ligand”.[35] Surprisingly, its high efficiency in asymmetric hydrogenation was revealed ony fairly recently.



26 **27** **28**

Figure 1.3.5: *Selected phosphine-phosphites*

An alternative synthetic pathway to new phosphine-phosphites, reported mainly by van Leeuwen,[61] Vidal-Ferran[62] and Bakos,[63] combines enantiomerically pure epoxides and nucleophilic phosphorus-containing reagents. Chan and Yeung introduced phosphine-phosphites containing a ferrocene moiety (**27**). Although this type of bidentate mixed phosphine ligands was successfully applied for many different asymmetric transformations (conjugate addition, allylic substitution, etc.), most publications still report results in hydrogenation or hydroformylation.

Because of it’s outstanding catalytic properties, a lot of published structures in this field are related to (*R,S*)-BINAPHOS.[64] Most common variations include substitution or partial hydrogenation of one or both of the binaphthyl moieties or replacement of the linker between the phosphorus units by a similar skeleton. More recently, new phosphine-phosphites have also been synthesised in a multi-step reaction using building blocks from the chiral pool (example: **28**).[65]

Phosphine-phosphoramidites have two P-O and one P-N bond and are electronically similar to the corresponding phosphites. However, they differ a lot in their steric demand because the nitrogen atom is trisubstituted. Since the first phosphine-phosphoramidite (**29**, QUINAPHOS[66]) was reported in 2000 by Franciò, Leitner and Faraone, a lot of different structures have been published.

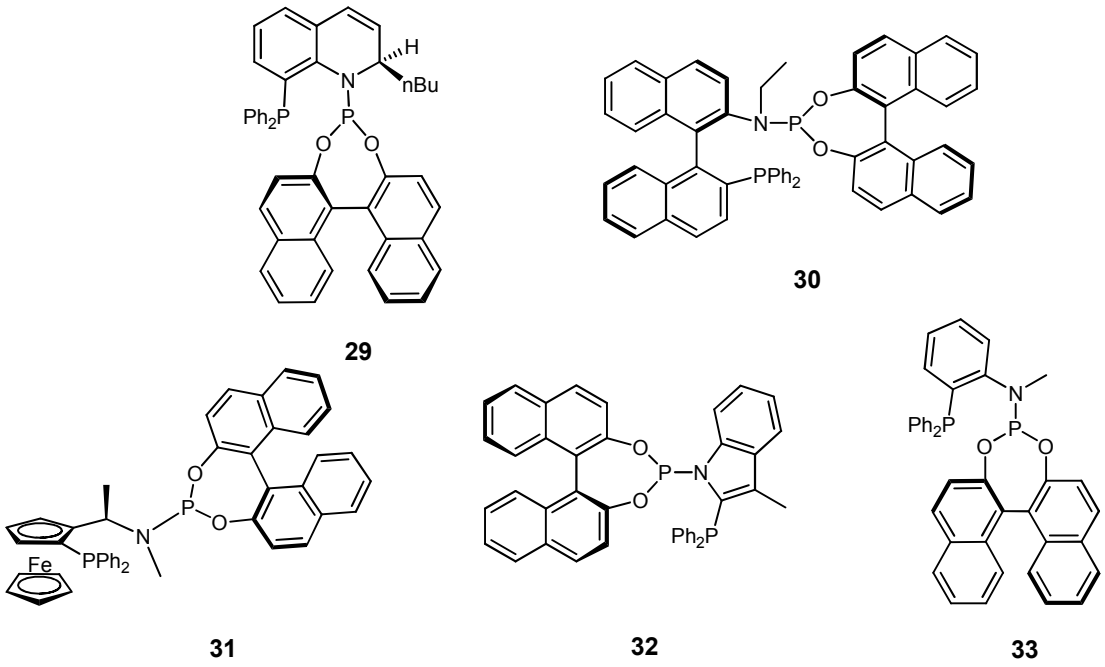
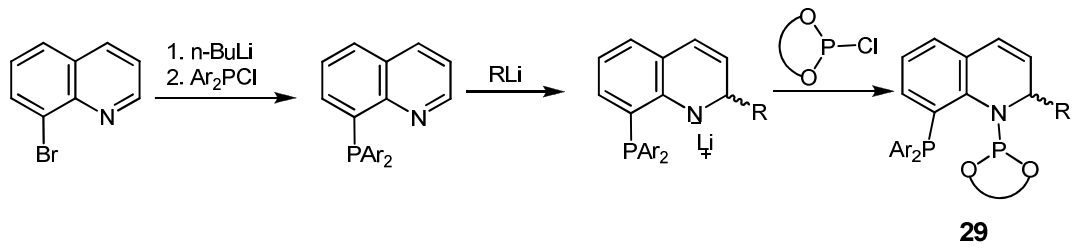


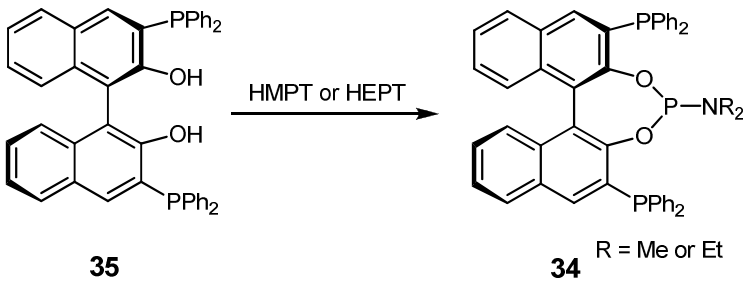
Figure 1.3.6: *Selected phosphine-phosphoramidites*

In Crévisi's review[67] they are divided into four classes based on their amine moiety: Cyclic amines, ferrocene-amine, benzyl/aryl-amines and chiral-pool diphenylphosphino-amines. Reek's classification[68] is based on the linker unit between phosphine and phosphoramidite: a rigid cyclic amine (class 1), rigid (bi)cyclic moiety (class 2) or a flexible chain containing at least one non-cyclic sp^3-hybridised carbon atom (class 3). In general there are two classical ways to synthesise a phosphine-phosphoramidite: The reaction of a prepared phosphine-amine with A) a chlorophosphite or B) with phosphorus trichloride followed by a reaction with a diol. Most phosphine-phosphoramidites are available via pathways that only differ from these common routes in small details. For example, in the synthesis of Quinaphos (**29**) the lithium organyl is not only used as a base but also as a building-block providing a substituent to the structure (Scheme 2.1.2).[66]



Scheme 1.3.5: *Synthesis of Quinaphos*

A structure that is synthesised in a different sequence is a bisphosphine-phosphoramidite (**34**) published by Zhang and coworkers in 2006 (Scheme 2.1.3).[69,70] To create this bisphosphine-phosphoramidite structure, a readily prepared bisphosphine-diol (**35**) is treated with HMPT or HETP, respectively.

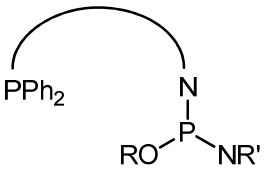


35 **34**

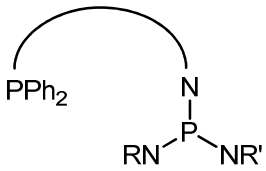
Scheme 1.3.6: *Synthesis of* ***34***

Most phosphine-phosphoramidites are used for asymmetric hydrogenation of C=C bonds and show good to excellent results for various substrates.[71] For example, Me-Anilaphos (**33**) by Börner *et al.* is able to induce up to 98 % *ee* in the hydrogenation of acetamidocinnamate.[72] Some of the ligands were also successfully applied in the hydrogenation of C=N or C=O bonds, or hydroformylation reactions. So far, **30** is known as the best ligand for the hydroformylation of styrene, being even superior to (*R,S*)–BINAPHOS.[73] One phosphine-phosphoramidite was tested in a Cu-catalysed conjugated addition of diethylzinc to enones, but gave just moderate enantiomeric excess.[74] Recently, Eggenstein presented a phosphine-phosphoramidite structure in his PhD thesis that is based on Me-Anilaphos bearing an additional stereocentre at the amine moiety and applied it successfully in various asymmetric hydrogenations.[75] The synthetic route of this ligand is very modular and therefore bears a high potential for structural variations.

Other mixed bidentate phosphorus ligand structures that logically follow along the line of heteroatom substitution are for example phosphine-phosphorodiamidites or phosphine-phosphortriamides (Figure 1.3.7).



phosphine-phosphorodiamidite



phosphine-phosphortriamide

Figure 1.3.7: *Possible types of mixed bidentate phosphorus ligands*

Syntheses or applications of these ligand structures have not been reported in literature yet, so that the potential of these ligand-classes in catalytic reactions is completely unexplored.

1.4 Research objective

Aim of this thesis is the synthesis of new mixed bidentate phosphine ligands and their application in asymmetric catalysis. Because of its modular synthetic pathway and good results in asymmetric hydrogenation phosphine-phosphoramidite **36**[75] is used as the lead structure. Modifications of this structure will be investigated to explore the variability of the established synthetic pathway and the influence on applications in catalytic reactions.

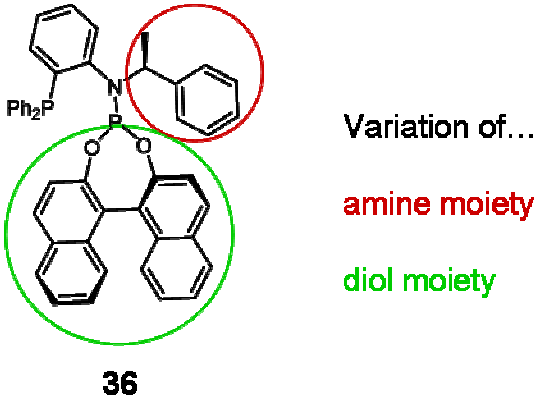
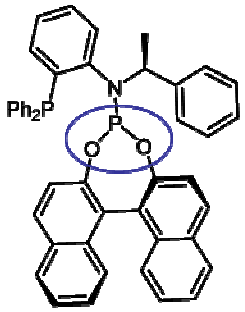


Figure 1.4.1: *Possible variations of* ***36*** *leading to new phosphine-phosphoramidites*

Figure 1.4.1 shows aspired variations of **36** that lead to new phosphine-phosphoramidites wich will be the first main topic of this thesis. To vary the phosphine-amine moiety, new phosphine-amines have to be prepared as building-blocks that can be tested in the synthetic route of **36**. Another interesting modification of the general structure that leads to a new phophine-phosphoramidite is the utilisation of other diols.

An exchange of the diol moiety at the phosphoramidite leads to different types of mixed bidentate phosphine ligands (Figure 1.4.2). Since phosphine-phosphorodiamidite and -phosphortriamide structures are unknown in literature the synthesis of those types will be the second key issue of this thesis. Therefore, the diol will be replaced by an aminoalcohol or a diamine following the same general synthetic pathway.



Variation of…

heteroatoms

(N,O N,N)

36

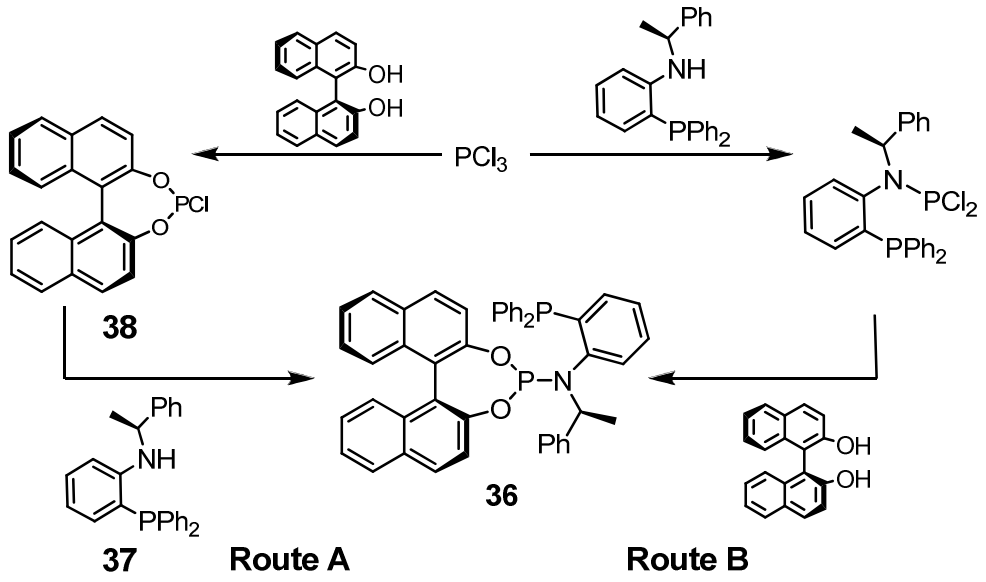
Figure 1.4.2: *Variations of* ***36*** *leading to new types of mixed bidentate phosphine ligands*

The performance of all new ligands in asymmetric homogeneous catalyses needs to be tested and compared. They will be benchmarked in hydrogenations of C=C, C=N, or C=O bonds, since **36** was successfully used for these types of transformations. The newly synthesised phosphine-phosphorodiamidites will also be tested in other asymmetric transformations like hydrophosphorylation or hydroformylation.

2 Results & Discussion

2.1 General routes for the synthesis of phosphine-phosphoramidites

The synthesis of phosphine-phosphoramidites usually consists of consecutive reactions that combine different building blocks in a modular way.[36] As already mentioned in the introduction, the last step in such a synthetic route usually is the reaction of a readily prepared phosphine-amine with **A**) a chlorophosphite or **B**) with phosphorus trichloride followed by a reaction with a diol. These possible synthetic pathways are shown in scheme 2.2.1 exemplified by routes to **36**.

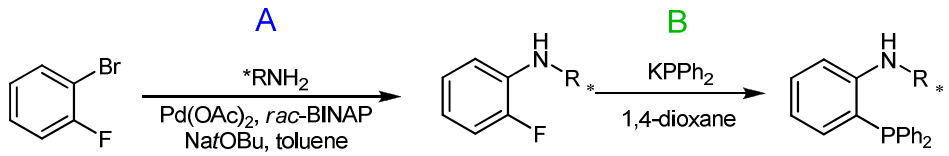


Scheme 2.1.1: *General synthetic pathways to* ***36***

The synthesis of **36** has been demonstrated to be possible via route **A**.[75] Thus, a solution of phosphine-amine **37** is treated with *n*-butyllithium in the presence of TMEDA at -78°C and a solution of chlorophosphite **38** is consecutively added to the mixture. To vary the substituent at the amine moiety, the first aim of the thesis will be the synthesis of alternative phosphine-amines.

2.2 Synthesis of phosphine-amines

The synthesis of new phosphine-amines was carried out according to the procedure used for the preparation of phosphine-amine **37**.[76,77] A chiral primary amine was coupled via a palladium-catalysed Buchwald-Hartwig amination with 1-bromo-2-fluorobenzene (Scheme 2.2.1).



Scheme 2.2.1: *General synthetic route of phosphine-amines*

This coupling reaction is selective towards the bromo substituent, so that the obtained product is a fluorinated secondary amine. After extraction with DCM the product was purified via column chromatography.

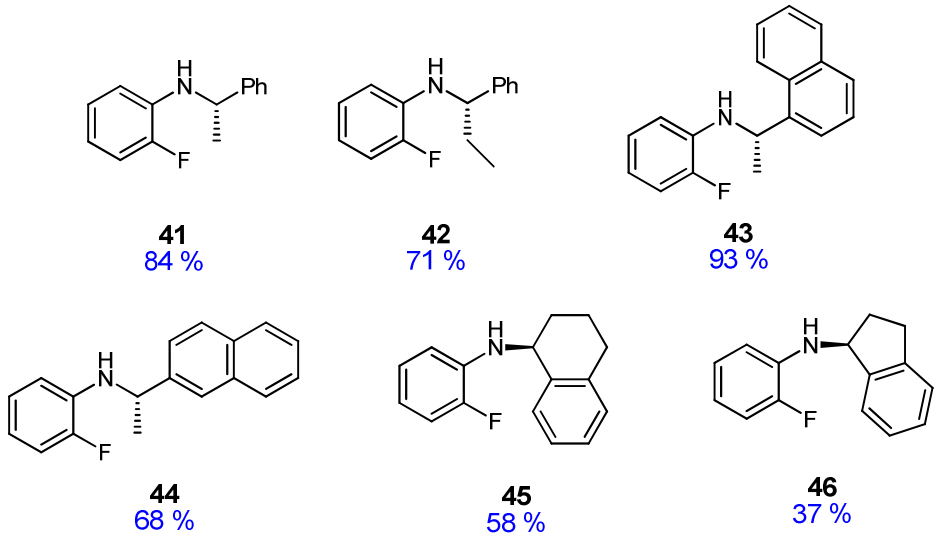
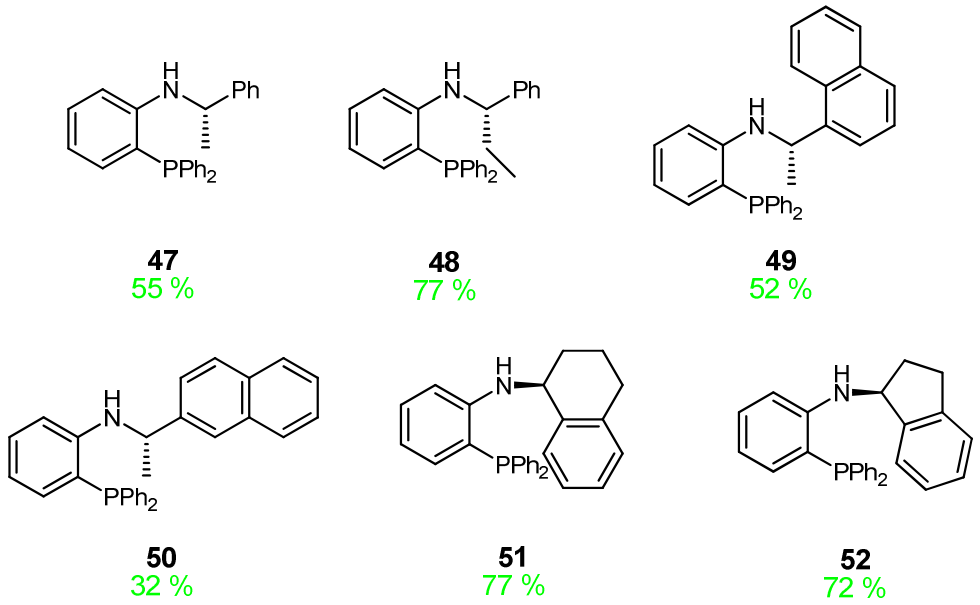


Figure 2.2.1: *Synthesised secondary amines*

To produce a small library of building blocks six chiral amines were converted into fluorinated secondary amines (Figure 2.2.1). The yields of the purified product vary from 37-93 % depending on the amine.

These secondary amines are all air-stable solids or liquids. Under inert atmosphere they could be converted into the corresponding air-sensitive phosphine-amines (Scheme 2.2.1, B) by stirring under reflux with potassium diphenylphosphite in 1,4-dioxane. The product was extracted with DCM and purified via filtration over basic alumina and precipitation. The products (Figure 2.2.2) were obtained as solids or highly viscous oils in reasonable yields (32-77%).



47 55 %

48 77 %

49 52 %

50 32 %

51 77 %

52 72 %

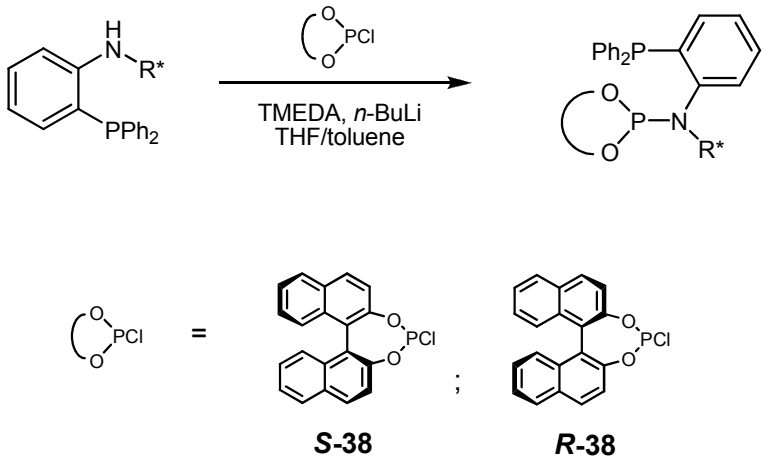
Figure 2.2.2: *Synthesised phosphine-amines*

The phosphine-amines are all water-stable but air-sensitive. Neither compounds **48**-**52** nor their corresponding fluorinated amines **42**-**46** have been reported in literature prior to this work (Scifinder, February 2011).

2.3 Synthesis of new phosphine-phosphoramidites

The first coupling experiments to obtain new phosphine-phosphoramidites were performed under the same conditions as for the synthesis of **36** (Scheme 2.3.1).[75] Under argon the phosphine-amine was stirred with *n*-butyl lithium and TMEDA in THF for 2 h at –87 °C to form the lithium amide. TMEDA was added for the disaggregation of *n*-butyl lithium to induce higher conversions. Consecutively, a THF solution of the

PCl-species **38**[71] was added to obtain the desired phosphine-phosphoramidite and LiCl as a byproduct.



Scheme 2.3.1: *Synthesis of phosphine-phosphoramidites*

After 16 h of stirring at room temperature the conversion was monitored via ^{31}P-NMR analysis. Every newly synthesised phosphine-amine was tested in the coupling with *S*-**38** and *R*-**38** in THF and additionally in toluene. The results are shown in table 2.3.1. Equivalent experiments using NEt_3 as a base instead of *n*-butyllithium/TMEDA at 0°C showed no conversion to phosphine-phosphoramidites for all phosphine-amines.

Table 2.3.1: *Results of coupling experiments*[a)]

entry	phosphine-amine	coupling (THF) *R*/*S*	coupling (toluene) *R*/*S*	purification
1	**48**	-/-	-/-	n.d.
2	**49**	-/+	+/+	+/+
3	**50**	-/-	-/-	n.d.
4	**51**	+/+	+/+	-/-
5	**52**	-/-	-/-	n.d.

a) 0.5 mmol phosphine-amine, 1.2 eq TMEDA, 1 eq *n*-BuLi, 1.1 eq enantiomerically pure 4-chlorodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine, 10 mL + 5mL solvent, -78 °C

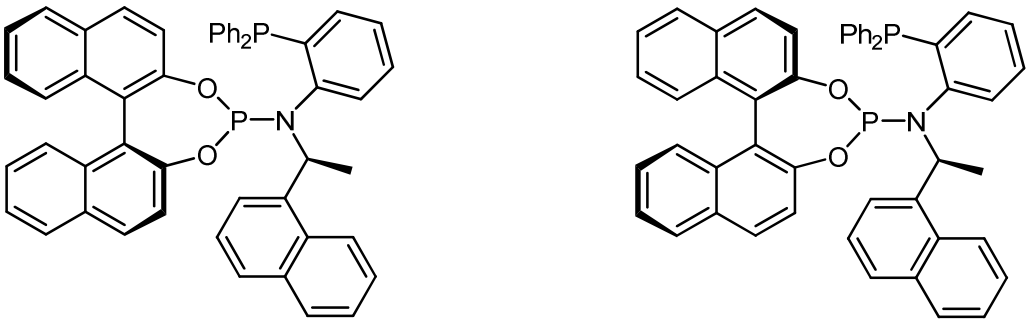
\+ = successful - = not successful

The coupling experiments of phosphine-amines **48**, **50** and **52** with both PCl-species showed no traces of phosphine-phosphoramidite. For **49**, the reaction with *S*-**38** was successful in toluene and THF while the reaction with *R*-**38** only proceeded in toluene. The coupling of **51** with *R*-**38** and *S*-**38** was successful in both solvents. The chemical shifts of the obtained phosphine-phosphoramidites were detected between -15 and -18 ppm for $P_{phosphine}$ and 135 - 140 ppm for P_{PO_2N}. The synthesis was repeated several times and usually high conversions (80-95%) were obtained. However, ^{31}P-NMR analysis always showed a signal of unconverted phosphine-amine around -18 to -20 ppm and small signals around 40 ppm due to oxidised species, such as oxidised starting material. Possible causes for impurities and differences in conversion, that can be excluded are the water content of the components (checked by Karl-Fischer titration) and a variation of the concentration of *n*-butyl lithium stock solution (checked by titration with 2,2-diphenylacetic acid).

Since the desired phosphine-phosphoramidites are sensitive towards air and moisture, purification must also be performed under inert conditions. First, the crude product was dissolved in toluene to remove LiCl (unsoluble in toluene) via filtration. The filtration was done over a small patch of degassed and dried basic alumina to remove oxidised materials at the same time. Even though oxidised materials and LiCl were successfully removed, it turned out to be important to use a small amount of basic alumina (column: Ø~ 3cm, h~3-4cm), because the P-N bond of the phosphoramidite unit in **49** and **51** tends to cleavage being flushed over this material. This decomposition was observed by ^{31}P-NMR analysis before and after filtration. Therefore the resonances' integrations of the phosphine-amine (substrate) and the phosphine-phosphoramidite (product) were compared. This decomposition excludes column chromatography where larger amounts of alumina would have been necessary. The phosphoramidite unit of **49** and **51** was even more sensitive towards silica, so that the usage of that must be excluded as well. To completely avoid cleavage of the P-N bond, LiCl can also be removed via filtration through a PTFE membrane. A disadvantage of this method is that other impurities like oxidised materials or rests of unconverted phosphine-amine are not removed at the same time.

For separation of the phosphine-phosphoramidite from remaining impurities (mainly phosphine-amine) different recrystallisation or precipitation methods with different solvent combinations were tested. The phosphine-phosphoramidites based

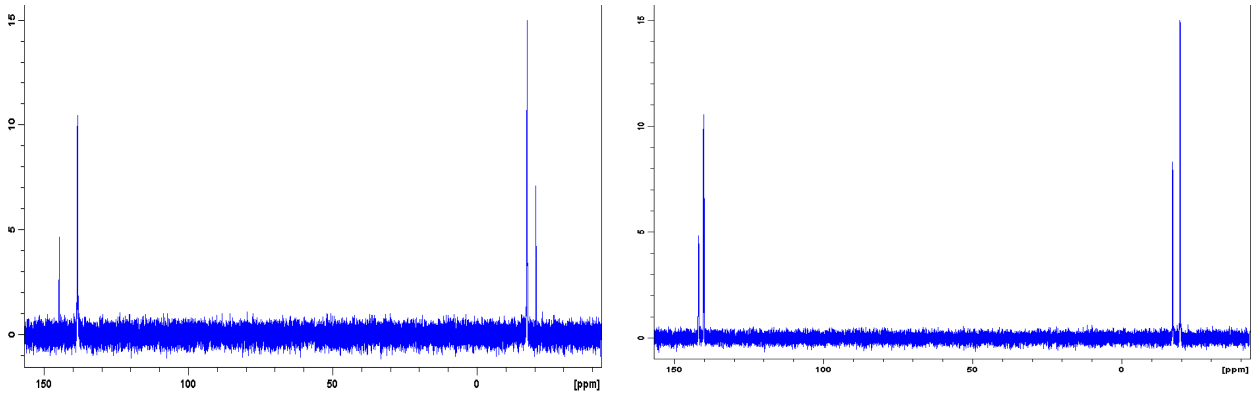
on phosphine-amine **51** could not be purified by any of the tested methods. Both phosphine-phosphoramidites based on phosphine-amine **49** could be purified via precipitation from toluene with ethanol and were obtained in analytically pure form.



L1 **L2**

Figure 2.3.1: *Analytically pure phosphine-phosphoramidites*

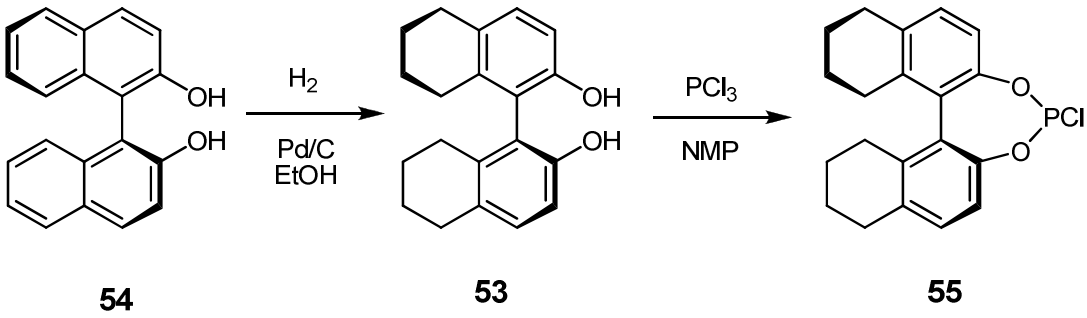
After one precipitation **L1** and **L2** were obtained with a purity of 86 % (**L1**, yield: 66 %) and 94 % (**L2**, yield: 44 %). Purer material was obtained via a second precipitation at the expense of the isolated yield (**L1**: 5 %; **L2**: 7 %).



^{31}P-NMR of **L1** ^{31}P-NMR of **L2**

Figure 2.3.2: *^{31}P-NMR spectra of **L1** and **L2***

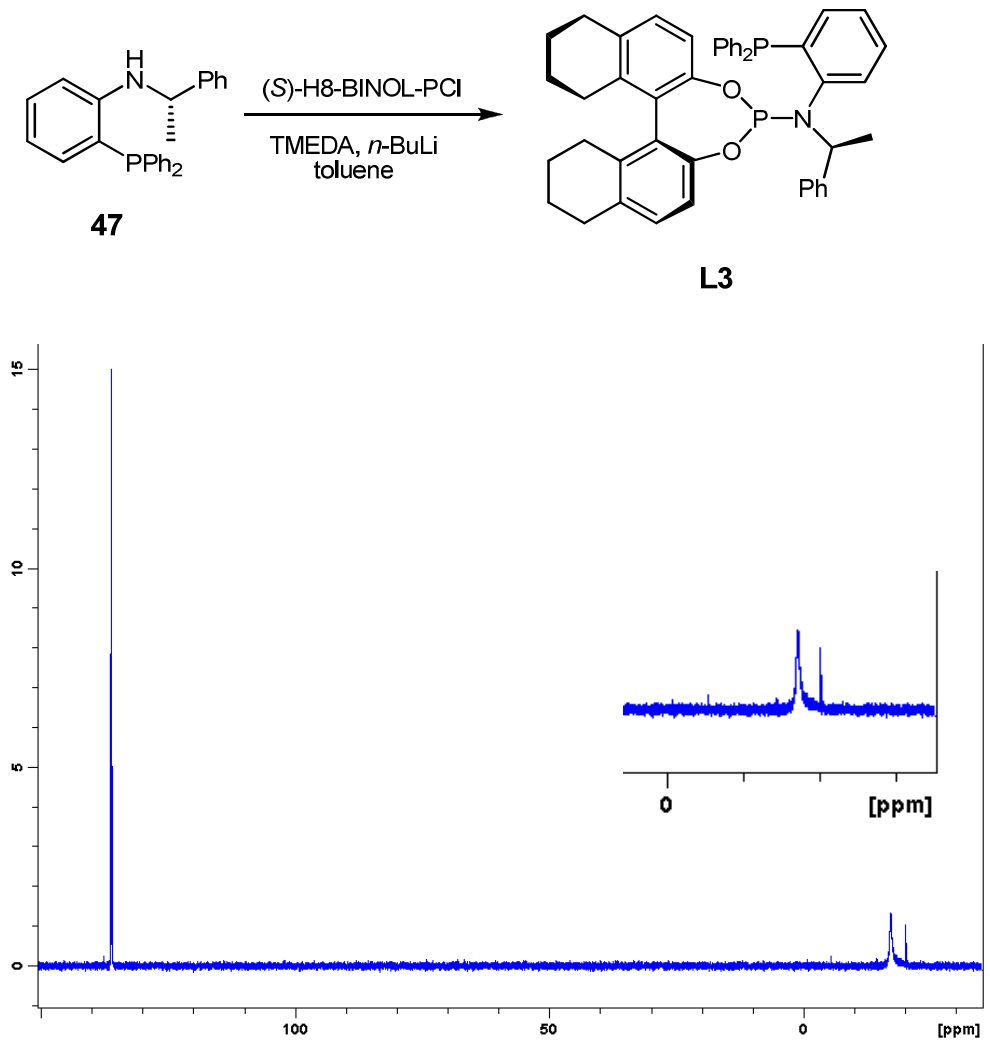
Another desired variation of **36** is a phosphine-phosphoramidite with an alternative diol building-block. Particularly interesting is the usage of a partially hydrogenated BINOL (**53**) species instead of the normal BINOL (**54**) since this exchange is known to give higher enantiomeric excesses in many cases.[78] Therefore, commercially available *S*-BINOL was hydrogenated at 100 °C and 80-90 bar of hydrogen using palladium on charcoal as catalyst (Scheme 2.3.2).[79]



54 **53** **55**

Scheme 2.3.2: *Synthesis of H8-BINOL-PCl compound (**55**)*

PCl-compound **55** could be obtained by refluxing **53** with PCl_3 in toluene. After removing the excess of PCl_3 under reduced pressure**, 55** was obtained as a white-yellowish powder that could be used directly in the next step. In a coupling experiment under the same conditions that were used to synthesise **L1** and **L2**, PCl-compound **55** reacted with the lithiated phosphine-amine **47** (Scheme 2.3.3). ^{31}P-NMR analysis showed high conversion to the desired phosphine-phosphoramidite **L3**, which could be purified via filtration and precipitation from toluene with ethanol. In contrast to the compounds with non-hydrogenated BINOL backbones, **L3** is also soluble in *n*-pentane.



Scheme 2.3.3: *Synthesis of **L3** and ^{31}P-NMR analysis*

^{31}P-NMR data of **L1**-**L3** showed that the resonances for $P_{phosphine}$ and P_{PO_2N} were observed at chemical shifts that are typical for phosphine-phosphoramidites (Table 2.3.2). The ^{31}P-NMR spectrum of phosphine-phosphoramidite **L1** shows two broad singlets, which were also observed in the the spectrum of **36**. This line broadening may be due to hindered rotation within the molecule. Molecules **L2** and **L3** already show two different rotamers (listed as major and minor) at room temperature. The rotamers of **L2** show a ratio of 1.3:1 and give broad doublet for both $P_{phosphine}$ and P_{PO_2N}. The coupling constant $^*J_{PP}$ of the major rotamer is ca. twice as high as the one for the minor rotamer. **L3** shows a broad singlet for $P_{phosphine}$ and two sharp overlaping singlets for P_{PO_2N}. The partially hydrogenated backbone of **L3** results in a

slight upfield shift (~136 ppm) for the P_{PO_2N} compared to the aromatic BINOL backbone (~140 ppm). The ratio of rotameric isomers for **L3** and **L2** are very similar (1.26:1 vs. 1.3:1).

Table 2.3.2: *^{31}P-{^{1}H}-NMR-shifts and coupling constants of synthesised phosphine-phosphoramidites*[a)]

entry	compound	$\delta P_{phosphine}$ / ppm	mult.	δP_{PO_2N} / ppm	mult.	J_{P-P} / Hz
1[b]	**36**	-17.1	b	140.1	b	-
2	**L1**	- 17.2	b	138.4	b	-
3	**L2**	maj: - 19.4	d	140.3	d	32.1
		min: - 17.1	d	141.8	d	16.4
4	**L3**	-17.1	b	maj: 136.2	s	-
				min: 135.9	s	-

a) measurements at room temperature in CD_2Cl_2

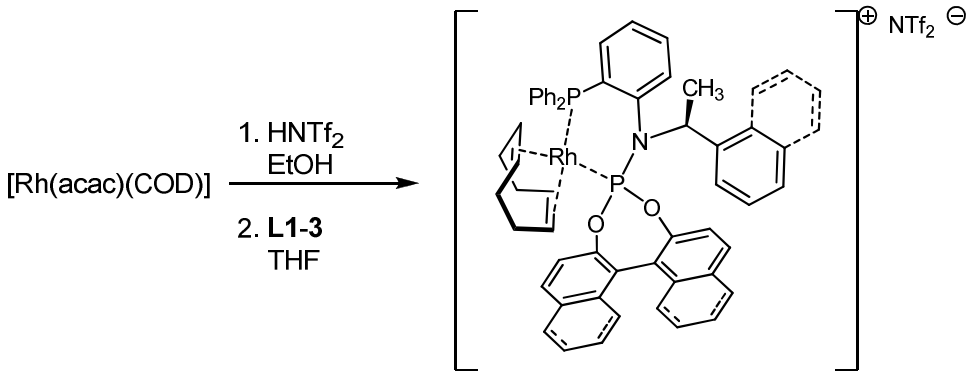
b) data of M.Eggenstein

2.4 Rh-complexes of phosphine-phosphoramidites

The synthesis of transition metal complexes can be used to support the assumption that different rotamers of one molecule are the cause for line broadening in NMR analysis. The coordination to a transition metal should “freeze” the rotation and sharp signals should be observed. Rhodium is the transition metal of choice for complexation of ligand **L1**-**L3**, since its rhodium complex can be used as a readily preformed species for catalytic reactions. Former results showed that the preformed metal complex of **36** induced slightly higher enantiomeric excesses in the asymmetric hydrogenation of C=C bonds than a complex produced *in situ*.[75]

A convenient synthesis for rhodium complexes of bidentate phosphorus ligands starts from [Rh(acac)(COD)] (Scheme 2.4.1). The rhodium precursor is stirred with $HNTf_2$ in ethanol to protonate the acetyl acetonato ligand in order to get two free coordination sites. The obtained complex is stabilised by coordinating solvent molecules. In contrast to [Rh(acac)(COD)], the $[Rh(EtOH)_2(COD)]$ species is soluble in ethanol and the formation of a clear yellow solution indicates that the reaction is

complete. Adding the phosphine-phosphoramidite the solution turns from yellow to orange while the desired complex is formed.



Scheme 2.4.1: *Synthesis of Rh-phosphine-phosphoramidite-complexes*

Upon removal of the solvent, the desired complex was obtained as an orange solid that was purified via precipitation from THF/Et_2O or DCM/pentane. Rhodium complexes with a NTf_2^- counter ion of all newly synthesised phosphine-phosphoramidites and **36** were prepared (Figure 2.4.1).

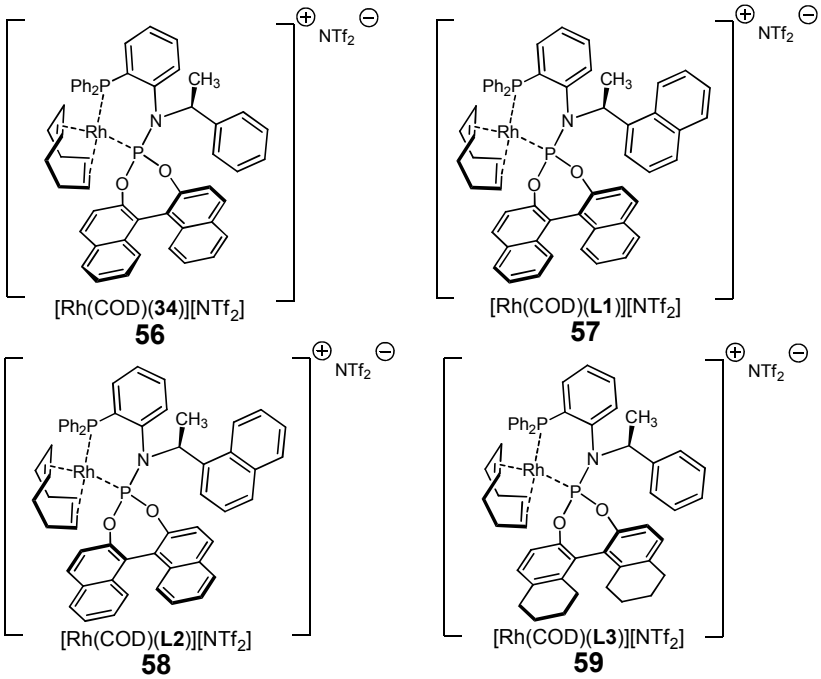


Figure 2.4.1: *Structure of Rh-complexes* ***56-59***

Ligand chelation to the transition metal is confirmed by a huge shift of both phosphorus signals in NMR analysis (Table 2.4.1). For the obtained rhodium complexes, the resonances for $P_{phosphine}$ and P_{PO_2N} were observed between 13-22 ppm and 135-150 ppm, respectively. While a free ligand molecule can assume different conformations, coordination to a metal atom blocks this interconversion even at room temperature. Due to the more fixed structure, sharp signals in NMR analysis should be obtained. For **56**-**59**, both phosphorus signals are indeed sharp doublets of doublets. The P-P coupling constants of the complexes (J_{PP} ≈ 60 Hz) are twice compared to the free ligands.

Table 2.4.1: *^{31}P-{^{1}H}-NMR shifts of [Rh(COD)(PP*)][NTf_2] complexes*[a)]

entry	compound	$\delta P_{phosphine}$ / ppm (J_{P-Rh} / Hz)	mult.	δP_{PO_2N} / ppm (J_{P-Rh} / Hz)	mult.	J_{P-P} / Hz
1	**56**	21.5 (136.4)	dd	136.4 (249.3)	dd	61.2
2	**57**	13.4 (135.1)	dd	149.6 (237.7)	dd	67.5
3	**58**	14.3 (141.1)	dd	141.1 (242.9)	dd	58.7
4	**59**	15.0 (142.0)	dd	135.4 (236.6)	dd	61.1

a) measurements at room temperature in CD_2Cl_2,

2.5 Phosphine-phosphoramidites in asymmetric hydrogenation reactions

Apart from applications in hydroformylation reactions[80] and few applications in conjugate additions on enones[81] and Pd-catalysed allylic alkylations[82], phosphine-phosphoramidite ligands were still most often very successfully applied in asymmetric hydrogenations.[83,84]

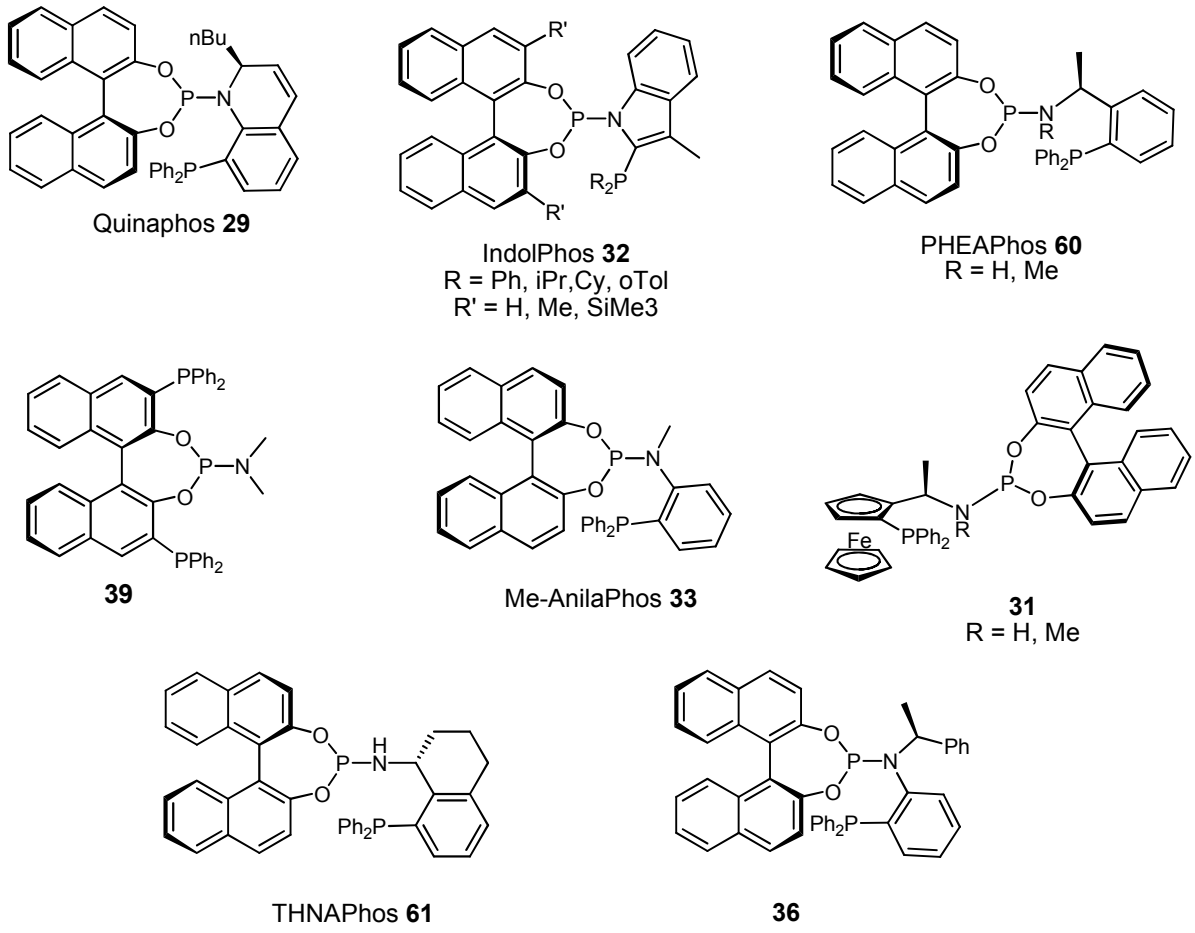


Figure 2.5.1: *Selected phosphine-phosphoramidites used for hydrogenation*

Common benchmark substrates such as dimethyl itaconate (**dmi**) and methyl-2-acetamidoacrylate (**maa**) can be hydrogenated by phosphine-phosphoramidites with *ee*s up to 96-99% (Figure and table 2.5.1).[85]

***Table 2.5.1: dmi** hydrogenation results of phosphine-phosphoramidites*[a]

entry	ligand (config. binol)	pH_2 (bar)	*ee* (%)
1	Quinaphos (*R*)	30	99 *R*
2	IndolPhos (*S*)	10	98 *S*
3[b]	**39** (*R*)	1	99 *R*
4	THNAPhos (*R*)	10	99 *R*
5	Me-AnilaPhos (*R*)	1	96 *R*
6	**36** (*S*)	10	99 *S*
7	**31** (*S*)	10	99 *S*
8	PEAPhos (*S*)	10	99 *nd*

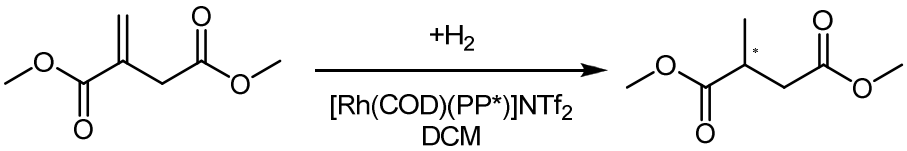
a)Rh/L ≤ 1:1.1, Rh/substrate ≤ 1:100, 25 °C, DCM, ≤ 24h
using $[Rh(nbd)_2]BF_4$ or $[Rh(COD)_2]BF_4$; b) solvent:trifluoroethanol

The first phosphine-phosphoramidite, Quinaphos, was also tested in the Ru-catalysed hydrogenation of ketones inducing *ee*s up to 94%.[66,86] IndolPhos has been tested in the hydrogenation of **dmi**, **maa**, α-dehydroamino acid esters, β-dehydroamino acid esters, 2-hydroxymethylacrylates, arylenamines, α-enamido and α-enol phosphonates and cinnamic acid derivatives also inducing high enantiomeric excesses.[87,88] Ligand **39** developed by Zhang gave *ee*s up to 99% in the hydrogenation of arylenamides, dehydroamino acid esters and itaconic acid derivatives.[69,70] TNHAPhos by the group of Zheng is also very successful in the Rh-catalysed hydrogenation of various prochiral olefins including α-enol phosphonates, dehydroamino acids, arylenamides, hydroxymethylacrylates and α-dehydroamino acid esters.[89,90] *Ee*s up to 99.9% were obtained for a broad range of stubstrates including β-dehydroamino acid esters using ligand **31** developed by the groups of Chang and Zheng.[91] Also developed by Zheng, PEAPhos was evaluated in the hydrogenation of α-dehydroamino acid esters, arylenamides and **dmi**.[92]

Since **36** has successfully been applied in the asymmetric hydrogenation of olefins, β-ketoesters and quinolines,[75] the synthesised ligands **L1**-**L3** were also tested in these types of reaction (see chapters 2.5.1-3). A comparison of the results between **36** and **L1**-**L3** can show the influence of different structural characteristics on activity and enantioselectivity of the catalyst.

2.5.1 Rh-catalysed hydrogenation of C=C bonds

As a first benchmark reaction the new phosphine-phosphoramidites **L1**-**L3** were used in the asymmetric homogeneous hydrogenation of dimethyl itaconate (Scheme 2.5.1.1). For this reaction, preformed Rh-complexes **57**-**59** were applied in a substrate/catalyst ratio of 1000:1 in a stainless steel autoclave with glass inlet at room temperature in DCM with 10 bar of hydrogen.



dmi

Scheme 2.5.1.1: *Asymmetric hydrogenation of* ***dmi***

After a reaction time of 1 h the conversion and enantiomeric excess were determined (Table 2.5.1.1). All three newly synthesised ligands showed full conversion and therefore *turn over frequencies* are estimated to exceed on ≥ 1000 h^{-1}.

Table 2.5.1.1: *Hydrogenation of* ***dmi*** *- results*[a)]

entry	ligand	*ee* (%)	TOF (h^{-1})
1[b)]	**36**	>99 *S*	≥1000
2	**L1**	>99 *S*	≥1000
3	**L2**	94 *R*	≥1000
4	**L3**	>99 *S*	≥1000

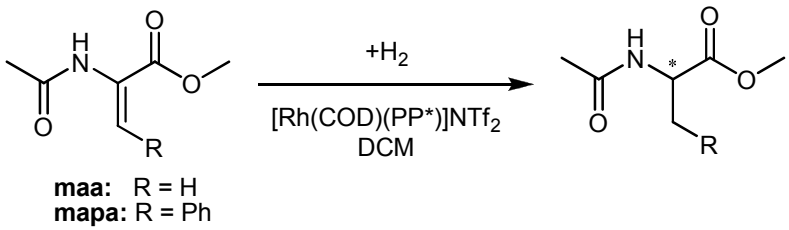
a) 1 mmol S, S/Rh = 1000:1, 2 mL DCM, 1h, pH_2 = 10 bar, RT, conversion >99%

b) data: [75]; BF_4^--counter anion

Phosphine-phosphoramidite **L1** – where the phenyl substituent is replaced by a naphthyl rest compared to **36** – induced the same high enantioselectivity as **36** (>99% *S*). Hydrogenation using **L2** (the diastereomer of **L1**) shows that the axial configuration of the BINOL backbone is mainly responsible for the configuration of the product. Changing from an S_a- to an R_a-configurated BINOL moiety, the configuration of the produced dimethyl-2-methylsuccinate also changes from *S* to *R*

with a slightly lower enantiomeric excess of 94 % *R*. Thus, the two distinct chiral elements of the structure (axial chirality at the BINOL backbone and chirality at the amine moiety) result in a matched or in a miss-matched fashion and the combination of S_a,S_c leads to higher enantioselectivities than the combination of R_a,S_c. Changing the BINOL-backbone into a partially hydrogenated H_8-BINOL-moiety does not show a significant effect. By achieving full conversion and >99% *ee* for the *S*-configurated product, the application of ligand **L3** is as successful as **36** and **L1**.

To broaden the substrate scope, ligands **L1**-**L3** were applied in the hydrogenation of methyl 2-acetamidoacrylate (**maa**) and (*E*)-methyl 2-acetamido-3-phenylacrylate (**mapa**) (Scheme 2.5.1.2).



Scheme 2.5.1.2: *Asymmetric hydrogenation of* ***maa*** *and* ***mapa***

Hydrogenation of α-dehydroamino acid esters **maa** and **mapa** was performed using the preformed Rh-complexes under the same conditions as the hydrogenation of **dmi**. Within one hour, full conversion (TOF≥1000 h^{-1}) and high enantioselectivities were achived in all cases (Table 2.5.1.2).

Table 2.5.1.2: *Hydrogenation of* ***maa*** *and* ***mapa*** *- results*[a)]

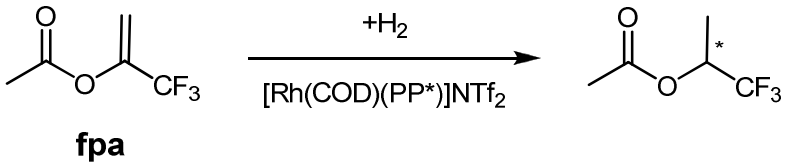
entry	ligand	substrate	*ee* (%)	TOF (h^{-1})
1[b)]	**36**	**maa**	99 *R*	≥1000
2	**L1**	**maa**	98 *R*	≥1000
3	**L2**	**maa**	96 *S*	≥1000
4	**L3**	**maa**	98 *R*	≥1000
5[b)]	**36**	**mapa**	99 *R*	≥1000
6	**L1**	**mapa**	97 *R*	≥1000
7	**L2**	**mapa**	97 *S*	≥1000
8	**L3**	**mapa**	99 R	≥1000

a) 1 mmol S, S/Rh = 1000:1, 2 mL DCM, 1h, pH_2 = 10 bar, RT, conversion: >99%

b) Data: [75]; BF_4^--counter anion

Again a chiral switch of the product's conformation depending on the conformation of the BINOL backbone and a minor match/miss-match effect of the ligand's chiral elements were observed.

Another interesting substrate for asymmetric hydrogenation is 3,3,3-trifluoroprop-1-en-2-yl acetate (**fpa**) (Scheme 2.5.1.3). A derivative of the hydrogenated chiral form of **fpa** is known to be an important building block for an active pharmaceutical drug used for the treatment of neurological and neuropsychiatric disorders.[93]



fpa

Scheme 2.5.1.3: *Asymmetric hydrogenation of* ***fpa***

Since the product is very volatile, dichloromethane can not be used as a solvent because it would interfere with the standard work-up procedure and GC analysis that has been used for **dmi**, **maa** and **mapa**. Therefore, these catalytic reactions with **fpa** were performed without any solvent, dissolving the preformed Rh-complex in neat substrate. For 0.5 mL of substrate a hydrogen pressure of 15 bar was used at room temperature for 1 h. ^{1}H-NMR spectra, taken directly from the reaction mixture showed full conversion for every tested catalyst.

Table 2.5.1.3: *Hydrogenation of* ***fpa*** *- results*[a)]

entry	ligand	*ee* (%)	TOF (h^{-1})
1	**L1**	98 *R*	≥1000
2	**L2**	95 *S*	≥1000
3	**L3**	>99 *R*	≥1000

a) 3.9 mmol S, S/Rh = 1000:1, 1h, pH_2 = 15 bar, RT, conversion >99%

Enantiomeric excess was measured by GC analysis directly from the gas phase above the mixture without any work-up. For the hydrogenation of **fpa** excellent enantioselectivities were achieved (Table 2.5.1.3). The dependence of the chiral

outcome of the reaction on the BINOL backbone conformation was also observed in this case. The highest enantiomeric excess (>99% *R*) was achieved with ligand **L3**. In summary, all new phosphine-phosphoramidites gave full conversion after 1 h and induced high enantiomeric excess for every tested substrate showing excellent potential for asymmetric C=C hydrogenation reactions. The diastereomers **L1** and **L2** show that the conformation of the BINOL backbone has the strongest influence on the chiral outcome of the reaction.

To gain more precise information of the initial catalyst activity, further experiments were carried out at higher substrate to catalyst ratio by monitoring the hydrogen consumption. A substrate to catalyst ratio of 5000:1 and a slightly increased hydrogen starting pressure (15 bar at t_0) were used at a constant temperature of 20 °C. The hydrogen pressure over time was monitored and plotted using labview software. Figures 2.5.1.1-3 show the obtained pressure curves for the reactions with complexes **57** (**L1**), **58** (**L2**) and **59** (**L3**), respectively.

The characteristics of the three curves are very similar and are typical for a homogeneous hydrogenation with a prelocated equilibrium (Bodenstein kinetics).[94] At the beginning of the reaction the hydrogen pressure decreases in a linear fashion and reaction order seems to be pseudo *n* = 1. The concentration of the active species can be considered as quasi-stationary since the concentration of the substrate is very high.

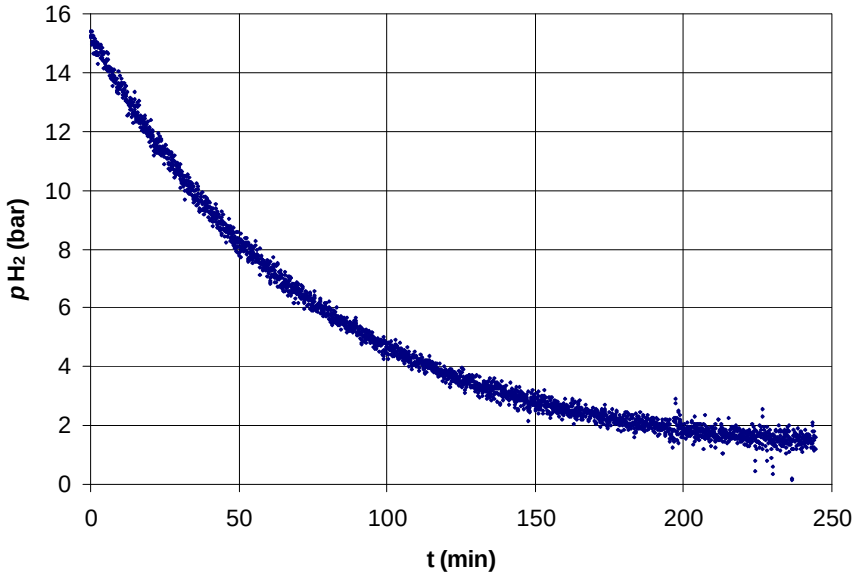


Figure 2.5.1.1 *Hydrogen consumption, hydrogenation of* ***dmi*** *using* ***57***

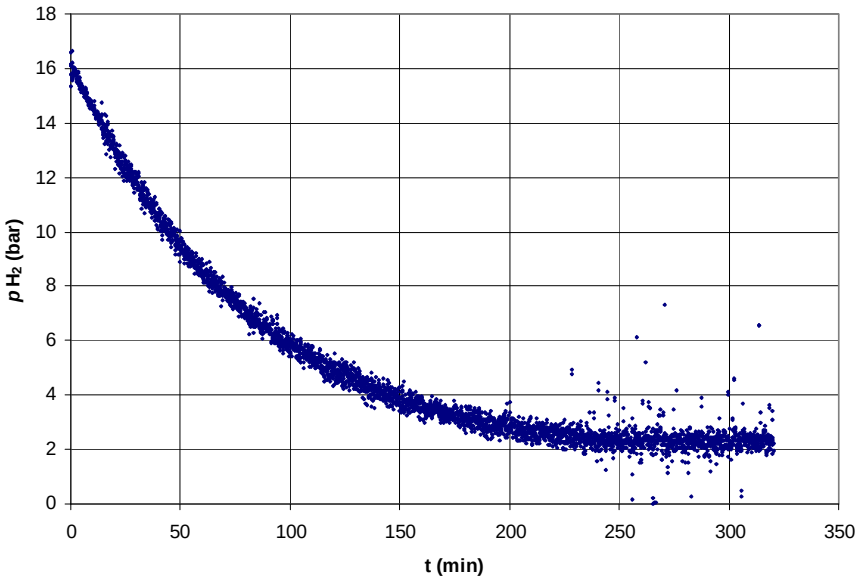


Figure 2.5.1.2 *Hydrogen consumption, hydrogenation of* ***dmi*** *using* ***58***

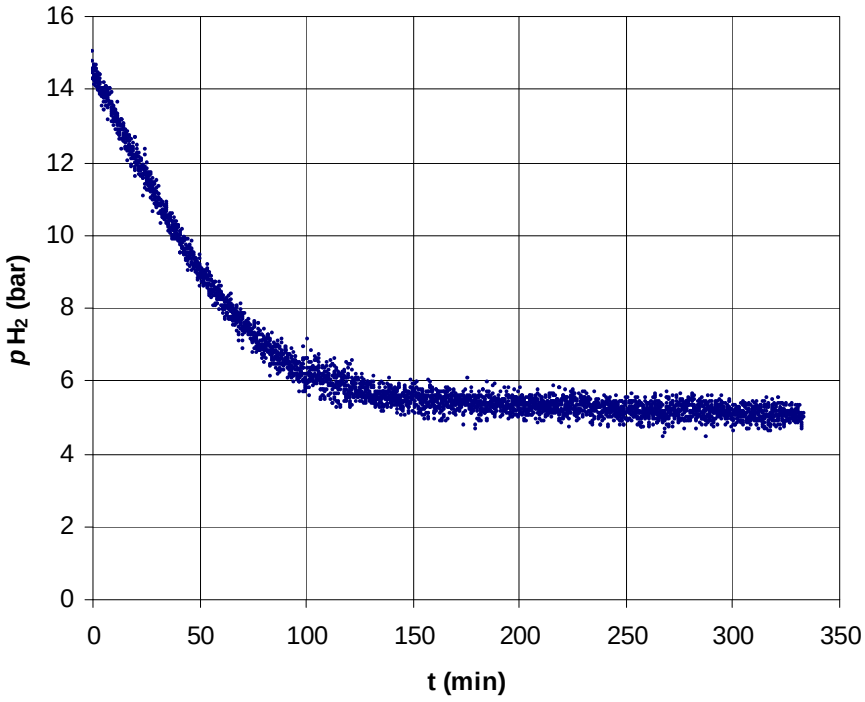


Figure 2.5.1.3 *Hydrogen consumption, hydrogenation of* ***dmi*** *using* ***59***

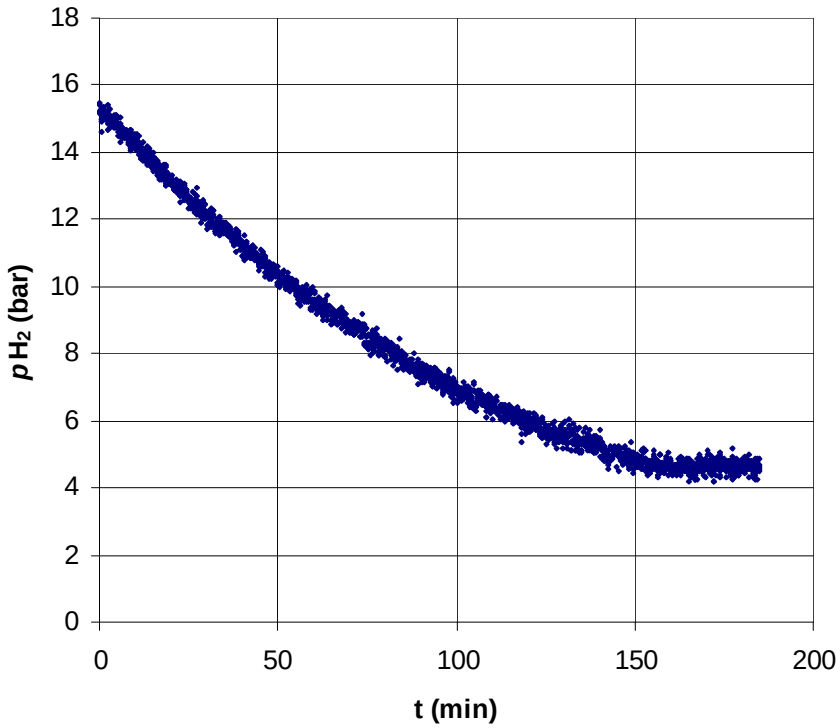


Figure 2.5.1.4 *Hydrogen consumption, hydrogenation of* ***dmi*** *using* ***56***

At higher conversion (lower substrate concentration), the hydrogen pressure decreases exponentially. The point in time where hydrogen pressure becomes stable is defined as 100% conversion (verified via GC analysis). The observation, that achieved stable hydrogen pressures vary from two to five bar should be taken into account for the estimation of accuracy of this method. Therefore, a qualitative comparison of the results can be made but further investigation is necessary to achieve quantitatively reliable results.

Table 2.5.1.4: *TOF-, $TOF_{init.}$, T50 and T100 of kinetic experiments 1-4*[a)]

entry	complex	TOF /h^{-1}	$TOF_{init.}$ /h^{-1} calculated at (min)		T50 (h)	T100 (h)
1	**57**	1250	3333	18.00	0.83	4.00
2	**58**	1250	2789	17.75	0.98	4.00
3	**59**	972	2673	19.08	0.70	5.14
4	**56**	1859	1946	18.50	1.08	2.69

a) TOF = n(substrate)/{n(catalyst)*h} at 100 % conversion

$TOF_{init.}$ = n(substrate)/{n(catalyst)*h} at a particular time within linear part of graph

T50: Time at 50 % conversion; T100: Time at 100% conversion

For the [Rh(PP)(COD)]BF_4 complex of **36** conversion was complete after 32 min (TOF: 9600 h^{-1} , $TOF_{init.}$: 14100 h^{-1}). The curves for the complexes of the new phosphine-phosphoramidites show that they are less active in the hydrogenation of **dmi**. Table 2.5.1.4 presents all data calculated from the graphs.

For the [Rh(PP)(COD)]NTf_2 complexes of the naphthyl-substituted phosphine-phosphoramidites **57** and **58**, an average turnover frequency of 1250 h^{-1} was obtained. This is about seven times less active than the complex of **36** possessing a phenyl moiety. The relative configuration of the BINOL backbone does not seem to have an influence on activity, since the TOFs of **57** and **58** are the same. Also the initial TOFs calculated from the first linear part of the curves are in the same range. The productivity of the complex of the phosphine-phosphoramidite with the partially hydrogenated backbone **L3** is almost ten times lower than for the Rh-complex of **36** even if the initial TOF is in the same range as for complexes **57** and **58**.

Beside the ligand, a difference between the newly synthesised complexes and the Rh-complex of **36** is that they have an NTf_2^- counterion instead of BF_4^-. To investigate whether the counterion has an influence on the activity, [Rh(**36**)(COD)]NTf_2 (**56**) was synthesised for comparison and tested in catalysis. A turnover frequency of 1859 h^{-1} was obtained for **56**, which is higher than that of the complexes of **L1**-**L3**, but still considerably lower than for [Rh(**36**)(COD)]BF_4^-. These data support the notion that the anion has an influence on the activity of the catalyst, which is contradictory to the assumption of Heller *et al*. Studying [Rh(BINAP)(diolefin)]anion compexes with different anions in the hydrogenation of dimethyl itaconate, they came to the conclusion that different anions have no effect on activity or enantioselectivity.[95]

A brief qualitative look at the curves comparing $TOF_{init.}$, T50 and T100 shows that a catalytic system, which was most active in the beginning, was not necessarily the fastest in achieving 100 % conversion. The catalytic system with complex **65** for example showed the lowest $TOF_{init.}$ and the highest T50, but was the fastest to reach 100 % conversion (lowest T100).

$$C + S \underset{}{\overset{K}{\rightleftharpoons}} CS \qquad CS + H_2 \xrightarrow{k_2} C + P$$

$K = k_1/k_{-1}$ C = catalyst, S = substrate, P = product

Scheme 2.5.1.4: *Equations for hydrogenation with prelocated eqilibrium*

Looking at the equations for a hydrogenation with prelocated equilibrium (Scheme 2.5.1.4), one can roughly estimate that the $TOF_{init.}$ represents the reactivity of the catalyst-substrate complex (k_2), while differences in T50 and expecially in T100 express differences in the equilibrium constant K, which consist of association constant k_1 and dissociation constant k_{-1} (→ stength of substrate-catalyst interaction).[96]

2.5.2 Ir-catalysed hydrogenation 2-substituted quinolines

In contrast to the asymmetric hydrogenation of prochiral olefins, ketones or imines, the asymmetric hydrogenation of heteroaromatic compounds is much less explored.[97] A very interesting field is the enantioselective hydrogenation of substituted quinolines, since 1,2,3,4-tetrahydroquinolines are constituents of natural alkaloids and therefore important for the synthesis of many pharmaceutical and agrochemical agents.[98] Often the extraction of single pure alkaloids from natural sources is not very successful, so that the development of efficient synthetic pathways is very beneficial.

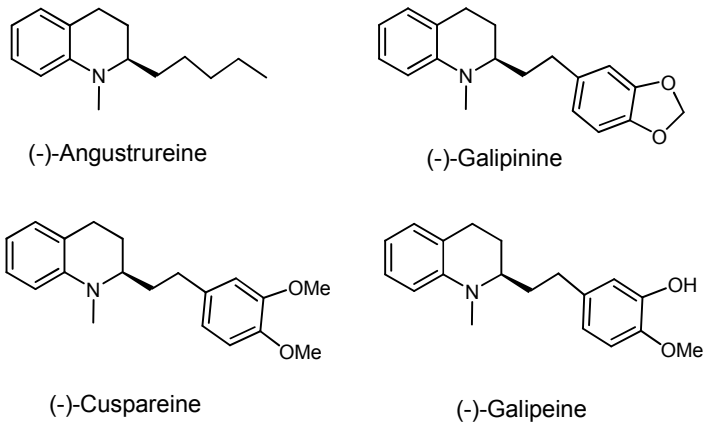
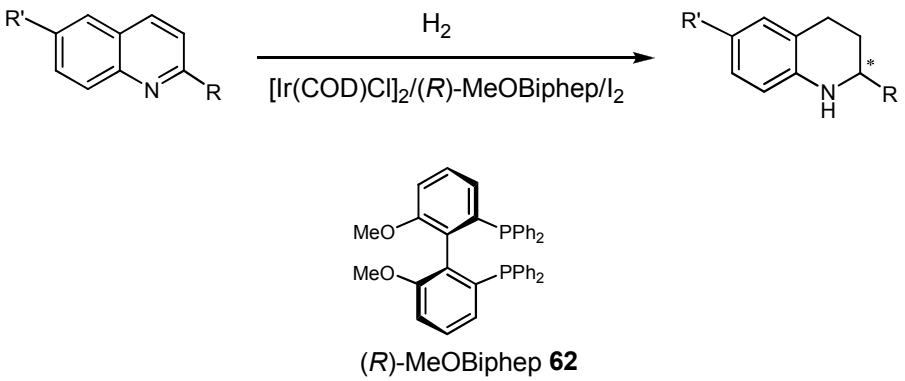


Figure 2.5.2.1: *Examples of biologically active quinoline alkaloids*

The first successful example for the asymmetric hydrogenation of 2-substituted quinolines was reported in 2003 by the group of Zhou (Scheme 2.5.2.1).[99] They used the bisphosphine (*R*)-MeO-Biphep (**62**) in combination with $[Ir(COD)Cl]_2$ as metal precursor and iodine as an additive to obtain full conversion and enantioselectivities up to 96%. Without iodine as an additive activities and

enantioselectivities are much lower. More recently, this system has been used by Zhou *et al.* as a key step in the total synthesis of the alkaloid (-)-galipeine.[100]



Scheme 2.5.2.1: *Hydrogenation of quinolines with MeOBiphep (**62**)*

Apart from MeOBiphep, other ligands have been successfully applied for the Ir-catalysed asymmetric hydrogenation of quinolines. In many cases, bisphosphines that induce good enantioselectivities are structural variations of MeOBiphep (for example: P-Phos (**65**),[101,102] tunable bisphosphines[103,104]) or BINAP (for example: (*S*)-SegPhos **63**,[105] (*S*)-SynPhos,[106] (*S*)-GenDenBINAP,[107] H8-BINAPO[108]).

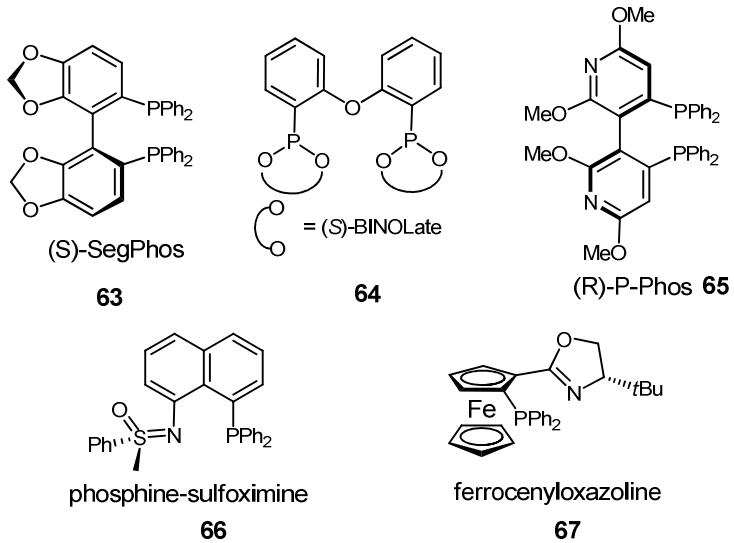
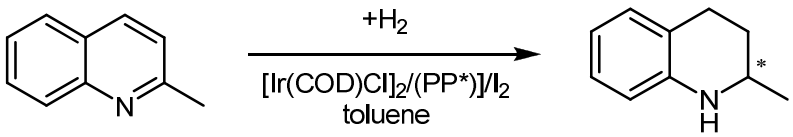


Figure 2.5.2.2: *Examples of ligands used for hydrogenation of quinolines*

Besides bisphosphines, Zhou and coworkers have also investigated P,N-ligands, such as ferrocenyloxazolines (**67**, up to 95 % *ee*).[109] A chiral phosphine-sulfoximine

(**66**, P,N) was successfully used for the Ir-catalysed hydrogenation of 2-methylquinoline by the group of Bolm (up to 92 % *ee*).[110] In 2010 Zhou *et al.* used water/silane as a hydrogen source in the hydrogenation of quinolines via an Ir-(*S*)-Segphos (**63**) system at room temperature and normal pressure obtaining enantioselectivities up to 93 %.[111] An extremely active and enantioselective phosphine-free Cp*-Ir-system was presented by the group of Xu.[112] The only successful system using another active transition metal was published by the group of Chan. They achieved some excellent enantioselectivities up to 99 % with a diamine ligand coordinated to ruthenium using an ionic liquid as a solvent.[113]

Feringa combined a monodentate chiral phosphoramidite in a 1:1 ratio with an achiral phosphine and obtained enantioselectivities up to 89 %.[114] Because of the similar mixed donor system phosphine-phosphoramidite **36** was applied in the hydrogenation of 2-substituted quinolines and induced enantiomeric excesses up to 96 %.[75] Therefore, ligands **L1**-**3** were also tested in the hydrogenation of the common benchmark substrate 2-methylquinoline (**2mq**, scheme 2.5.2.2).



2mq

Scheme 2.5.2.2: *Asymmetric hydrogenation of* ***2mq***

The conditions optimised by the group of Zhou[99] and also by Eggenstein[75] were adapted to test the ligands, so $[Ir(COD)Cl]_2$ was used as metal precursor and iodine as an additive. The reaction was performed in toluene at 40 bar of hydrogen and room temperature (Table 2.5.2.1).

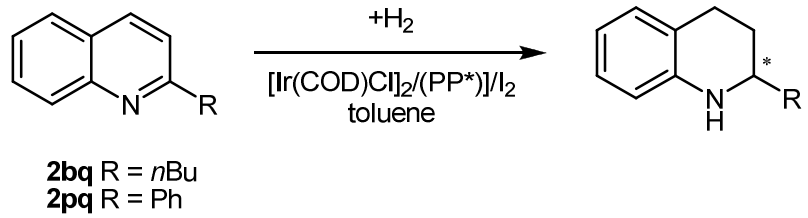
Table 2.5.2.1: *Asymmetric hydrogenation of* ***2mq*** *- results*[a)]

entry	ligand	time (h)	conversion (%)	*ee* (%)
1[b]	**36**	16	>99	96 *R*
2	**L1**	48	>99	97 *R*
3	**L2**	48	>99	81 *S*
4	**L3**	16	96	96 *R*

a) 1 mmol S, S/Ir/Lig/I_2 = 100:1:1.1:5, 2 mL toluene, pH_2 = 40 bar, RT

b) Data: [75]

Ligand **L1**, where the phenyl moiety at the amine part is changed into a naphthyl moiety, showed full conversion after an increased reaction time of 48 h but also gave a slightly increased enantiomeric excess of 97 % *R*. The corresponding diastereomer **L2** induced 81 % enantioselectivity for *S*. Again a strong dependence of the stereochemical outcome on the configuration of the BINOL moiety and a match-mismatch effect of the two stereochemical elements was observed. Ligand **L3** with the partially hydrogenated backbone gave almost full conversion in 16 h and the same enantioselectivity as **36**.



2bq R = *n*Bu
2pq R = Ph

Scheme 2.5.2.3: *Asymmetric hydrogenation of* ***2bq*** *and* ***2pq***

The reaction scope was briefly evaluated using 2-*n*butyl- (**2bq**) and 2-phenylquinoline (**2pq**) as substrates (Scheme 2.5.2.3). These derivatives have a higher sterical demand than 2-methylquinoline and their asymmetric hydrogenation is known to be more challenging. Diastereomers **L1** and **L2** induce slightly lower enantioselectivities than **36** for both substrates (Table 2.5.2.2).

Table 2.5.2.2: *Asymmetric hydrogenation of* ***2bq*** *and* ***2pq*** *- results*[a)]

entry	ligand	substrate	time (h)	conversion (%)	*ee* (%)
1[b]	**36**	**2bq**	16	>99	94 *R*
2	**L1**	**2bq**	48	>99	92 *R*
3	**L2**	**2bq**	48	>99	81 *S*
4	**L3**	**2bq**	16	84	97 *R*
5[b]	**36**	**2pq**	16	>99	90 *S*
6	**L1**	**2pq**	48	>99	89 *S*
7	**L2**	**2pq**	48	92	65 *R*
8	**L3**	**2pq**	16	78	95 *S*

a) 1 mmol S, S/Ir/Lig/I_2 = 100:1:1.1:5, 2 mL toluene, pH_2 = 40 bar, RT

b) Data: [75]

Again a switch in the stereochemical outcome of the reaction and a match-mismatch effect between stereochemical elements of the ligand can be observed. Replacement of the BINOL backbone with the partially hydrogenated analogue (**L3**) results in increased enantiomeric excesses at good conversions for both substrates. An enantiomeric excess of 95 % is the highest selectivity for the hydrogenation of 2-phenylquinoline known in literature to date (SciFinder, Feb 2011).

Table 2.5.2.4: *Asymmetric hydrogenation of* ***2mq****,* ***2bq*** *and* ***2pq*** *using KI - results*[a)]

entry	ligand	substrate	conversion (%)	*ee* (%)
1[b]	**36**	**2mq**	90	97 *R*
2[b]	**36**	**2bq**	95	95 *R*
3[b,c]	**36**	**2pq**	59	92 *S*
4	**L1**	**2mq**	24	89 *R*
5	**L1**	**2bq**	58	93 *R*
6	**L1**	**2pq**	33	87 *S*
7	**L2**	**2mq**	30	74 *S*
8	**L2**	**2bq**	39	81 *S*
9	**L2**	**2pq**	10	79 *R*

a) 1 mmol S, S/Ir/Lig/KI = 100:1:1.1:100, 2 mL toluene, 48 h, pH_2 = 40 bar, RT

b) Data: [75]

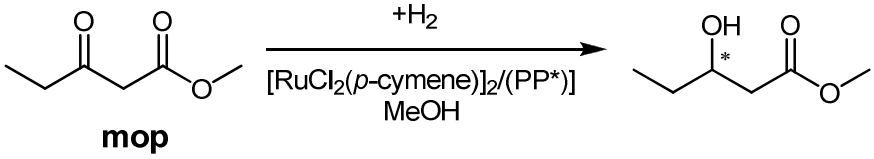
c) 72 h

Since the additive has a big influence on conversion and selectivity, potassium iodide was tested as an alternative additive. For ligand **36**, lower activity but slightly higher enantioselectivities were observed using KI instead of iodine. In contrast, **L1**, **L2** and **L3** induced lower enantioselectivities using KI, except for ligand **L2** in the hydrogenation of **2pq** (Table 2.5.2.4). The decrease in conversion is also much higher than for ligand **36**. In general, the new phosphine-phosphoramidites are excellent ligands for the Ir-catalysed hydrogenation of 2-substituted quinolines, showing high conversions and among the highest enantioselectivities for these substrates.

2.5.3 Ru-catalysed hydrogenation of β-keto esters

Chiral β-hydroxy esters are important structural building blocks in a number of pharmaceuticals (for example atorvastatin, a drug to lower cholesterol level; trade names: Sortis®, Lipitor®) and the asymmetric hydrogenation of β-keto esters is a valuable method for their synthesis.[115,116] Although nickel[117] and rhodium[118,119] have been reported as an active centre, most successful catalytic systems are based on ruthenium[120,121] and for long time the ligands of choice for this transformation were C_2-symmetric bisphosphines.

A milestone was the introduction of BINAP for this transformation by Noyori *et al*.[122,123] BINAP-Ru(II) catalysts were able to hydrogenate several different β-keto esters with full conversion and high enantioselectivities. Recently, several bidentate C_1-symmetrical phosphines, phosphinites or chiral amine and imine ligands have been developed.[116] Even monodentate phosphine ligands have been used with success.[124,125] Another concept is the combination of a chiral amine or imine ligand with a chiral or achiral diphosphine ligand to induce high enantioselectivities in the hydrogenation of simple ketones.[115]



Scheme 2.5.3.1: *Asymmetric hydrogenation of* ***mop***

Ligand **36** was able to induce 96% enantiomeric excess in the hydrogenation of benchmark substrate methyl 3-oxopentanoate (**mop**), so **L1**-**3** were also tested for this reaction (Scheme 2.5.3.1). The catalyst was preformed by stirring the ligand with $[RuCl_2(p\text{-cymene})]_2$ for 1 h in toluene at 80 °C. Toluene was removed and methanol and substrate were added to the solid catalyst. The hydrogenation was performed at 60 °C and 60 bar of hydrogen pressure (Table 2.5.3.1).

Table 2.5.3.1: *Asymmetric hydrogenation of* ***mop*** *– results*[a)]

entry	ligand	conversion (%)	*ee* (%)
1[b]	**36**	>99	96 *R*
2	**L1**	>99	94 *R*
3	**L2**	>99	81 *S*
4	**L3**	>99	86 *R*

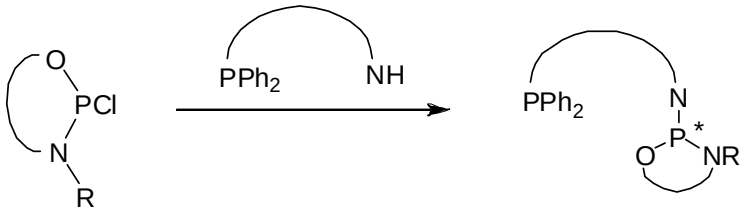
a) 1 mmol S, S/Ru/L = 100:1:1, 16 h, 60°C, pH_2=60bar, 2mL MeOH;
(Preform: 1 h, 80°C, 1 mL toluene)

b) Data: [75]

All three ligands led to full conversion after 16 h. Ligand **L1** (where the phenyl moiety at the nitrogen is replaced by a naphthyl substituent) induced nearly the same high enantiomeric excess as **36**. The ligand with the partially hydrogenated backbone **L3** resulted in a lower enantioselectivity of 86%. The lowest selectivity was obtained with ligand **L2**, which again afforded the opposite enantiomer. Even if the obtained enantioselectivities for this reaction are slightly below the benchmark of 99 % *ee*, the good results attest the versatility of the synthesised phosphine-phosphoramidites. These new ligands are able to induce high enantioselectivities in three completely different types of hydrogenation reactions using rhodium, iridium or ruthenium as an active metal centre.

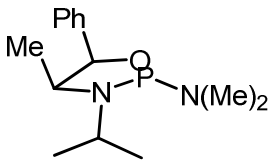
2.6 Phosphine-phosphorodiamidites

In the literature many different mixed phosphine ligands – where a phosphine group is combined with a heteroatom-substituted phosphorous moiety – have been reported. Common combinations like phosphine-phosphites or phosphine–phosphoramidites have already been described in the introduction (Chapter 1.3). To develop a new class of ligands, one can attempt to combine a different heteroatom-substituted moiety with a phosphine group. For the phosphine-phosphoramidites **L1-3** a diol unit is always used to create the phosphoramidite part. Replacing the diol with an aminoalcohol, the phosphoramidite unit would turn into a phosphorodiamidite moiety (Figure 2.6.1). This combination would be very interesting to synthesise since phosphine-phosphorodiamidites are not known in literature so far.



Scheme 2.6.1: *Creating a phospine-phosphorodiamidite*

In contrast to phosphoramidites, phosphorodiamidites are in general rather rare in literature.[126] In 1974, a phosphorodiamidite structure derived from ephedrine **68** was reported by the group of Burgada but they did not use it as a ligand in asymmetric catalysis.[127] Arzoumanian *et al.* synthesised a phosphorodiamidite based on (*S*)-prolinol **69** in 1988 and used it for the Pd-catalysed carbonylation of α-methylbenzyl bromide achieving moderate enantioselectivities.[128] More recently, these structures were used by the group of Alexakis for the asymmetric conjugate addition of organocopper reagents to enones, giving moderate to high enantioselectivities.[129,130] In 1995, Bentrude reported on the conformational equilibria of a phosphorodiamidite structure **70**.[131]



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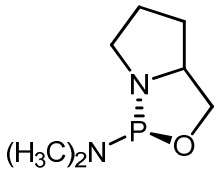

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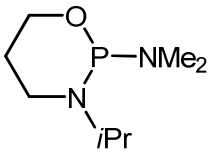

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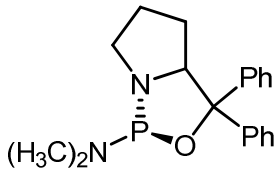


71

Figure 2.6.1: *Examples of phosphorodiamidites*

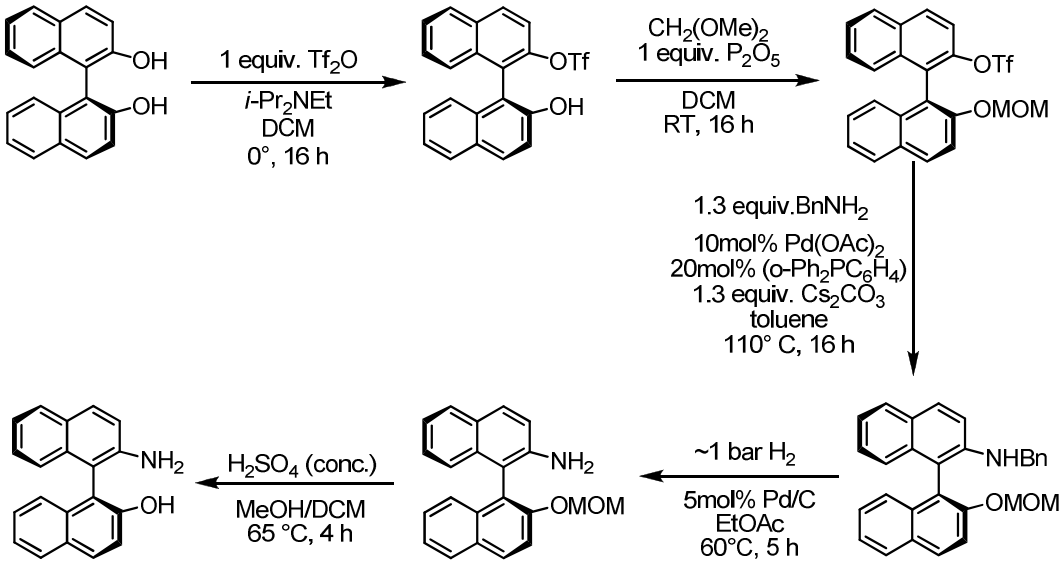
Bondarev and coworkers used an (*S*)-α,α-diphenylprolinol derived phosphorodiamidite **71** in the Rh-catalysed asymmetric hydrogenation of C=C bonds. The hydrogenation of methyl α-acetamidoacrylate gave enantioselectivities up to 91%.[132] Besides ligands where an aminoalcohol is combined with an amine there are also a few examples of ligands where a diamine moiety is combined with a diol to get an OPN,N type structure.[133,134] These structures are different because they can be C_2-symmetric whereas structures derived from an aminoalcohol and an amine can not.

Comparison of a phosphorodiamidite moiety with a phosphoramidite structure shows some distinctive differences. Changing one of the oxygen atoms to a nitrogen atom not only affects the electronical properties of the phosphorus donor atom but also changes the possible sterical properties of the molecule since nitrogen is trivalent. Another difference is that the phosphorus atom becomes a chiral centre with three different substituents and a free electron pair. This can have an influence on the outcome of asymmetric catalytic reactions.

2.7 Synthesis of new phosphine-phosphorodiamidites

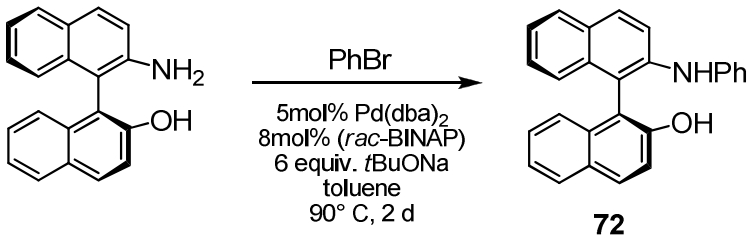
To study the change in behaviour in catalytic reactions going from a phosphoramidite moiety to a phosphorodiamidite, the rest of the ligand structure

should remain unmodified. The easiest phosphine-phosphorodiamidite most closely related to **36** will be based on enantiomerically pure 2'-amino-1,1'-binaphthyl-2-ol (NOBIN) instead of BINOL. Since enantiomerically pure NOBIN is expensive, it was synthesised via a route published by Brückner in 2009 (Scheme 2.7.1).[135]



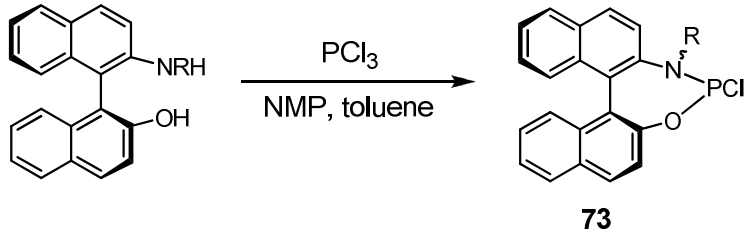
Scheme 2.7.1: *Synthesis of (S)-NOBIN*

The synthesis starts with the monotriflation of enantiomerically pure (*S*)-BINOL followed by protection of the unreacted alcohol moiety via a MOM ether. To avoid the use of the carcinogenic chloromethyl methyl ether, phosphorus pentoxide and dimethoxymethane were used instead. Subsequently, a Buchwald-Hartwig amination at the triflate moiety introduces a benzyl amine group, which can be debenzylated with hydrogen. Methanolysis of the MOM group afforded the desired product with an overall yield of 28 % (Lit.: 67 %).



Scheme 2.7.2: *Synthesis of (S)-2'-(phenylamino)-1,1'-binaphthyl-2-ol*

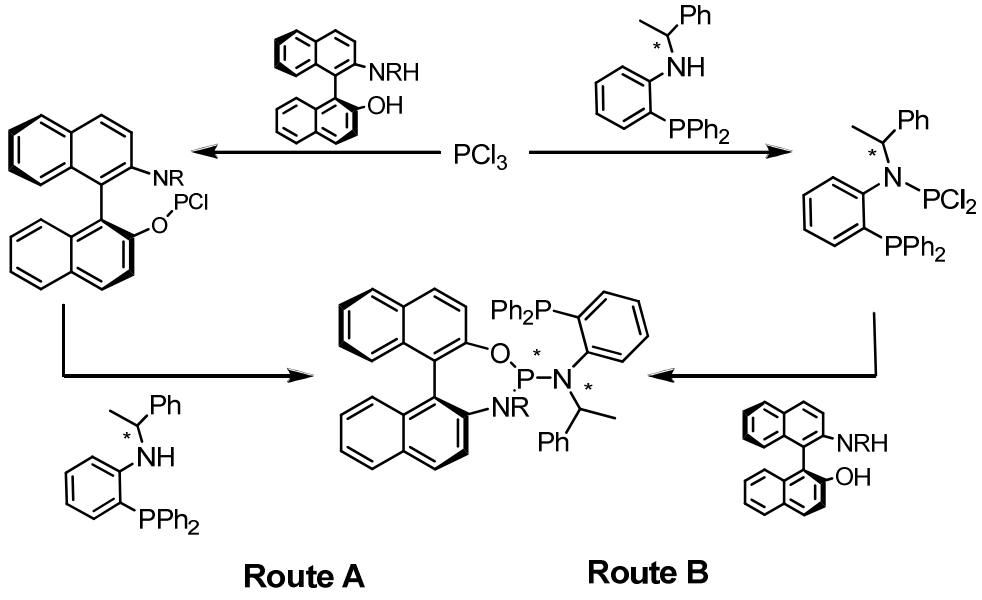
To introduce a substituent at the nitrogen atom, a part of the produced NOBIN was reacted in a Buchwald-Hartwig amination with phenyl bromide to obtain the phenyl-substituted *(S)*-2'-(phenylamino)-1,1'-binaphthyl-2-ol **72** (Scheme 2.7.2).[136] Both aminoalcohols have to be tranformed into a PCl-species that can be coupled with the readily prepared phosphine-amine **47** analogous to the phosphorochloridites of (*R*)- and (S)-BINOL. This reaction was attempted by refluxing the aminoalcohol (NOBIN or **72**) with PCl_3 in toluene adding a drop of *N*-methyl-2-pyrrolidone (NMP) (Scheme 2.7.3). Theoretically, two different stereoisomers of **73** can be produced by this reaction.



73

Scheme 2.7.3: *Synthesis of phosphorochloridites using aminoalcohols*

While **72** was converted selectivly into one enantiomer of the corresponding chlorophosphorodiamidite (^{31}P-NMR: δ = 176.16 ppm), ^{31}P-NMR analysis showed that the reaction of unsubstituted (*S*)-NOBIN with PCl_3 delivered various products.



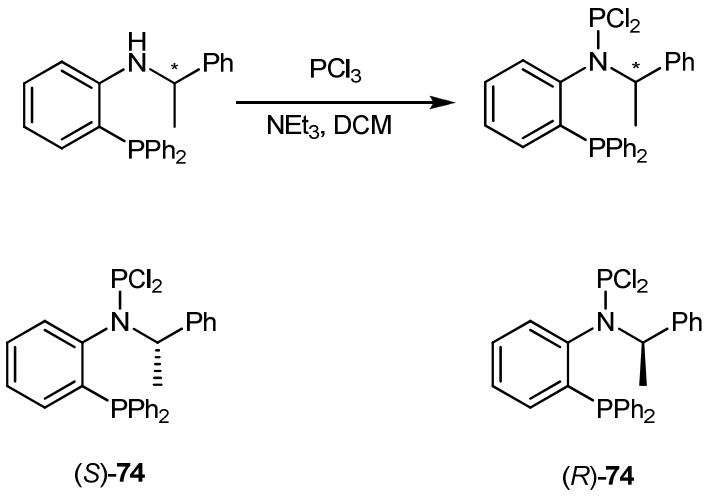
Scheme 2.7.4: *General synthetic pathways for phosphine-phosphorodiamidites*

Without a pure PCl-compound in hand, the synthetic pathway **A** (Scheme 2.7.4) is no opportunity. Another possibility is the generation of a PCl_2-compound of the phosphine-amine to obtain the desired ligand via synthetic pathway **B**. To be able to produce different diastereomers without repeating the five-step synthesis of NOBIN, the corresponding enantiomer of the phosphine-amine (*S*)-**47** has been synthesised ((*R*)-**47**) via the two-step synthesis described in chapter 2.2.

S-**47** *R*-**47**

Figure 2.7.1: *Pair of enantiomers of phosphine-amines used for ligand synthesis*

The desired PCl_2-species **74** were obtained by stirring the phosphine-amines *S*-**47** and *R*-**47** with an excess of PCl_3 in the presence of NEt_3 in dichloromethane (Scheme 2.7.5). The toluene-insoluble ammonium chloride by-product could be removed from the reaction mixture via filtration through a PTFE membrane.



(*S*)-**74** (*R*)-**74**

Scheme 2.7.5: *Synthesis of phosphine-amine PCl_2-compounds* ***74***

The first coupling experiment towards a phosphine-phosporodiamidite followed synthetic pathway **A** via lithiation of phosphine-amine **47** with *n*-buthyllithium in the presence of TMEDA in THF (Scheme 2.7.6).

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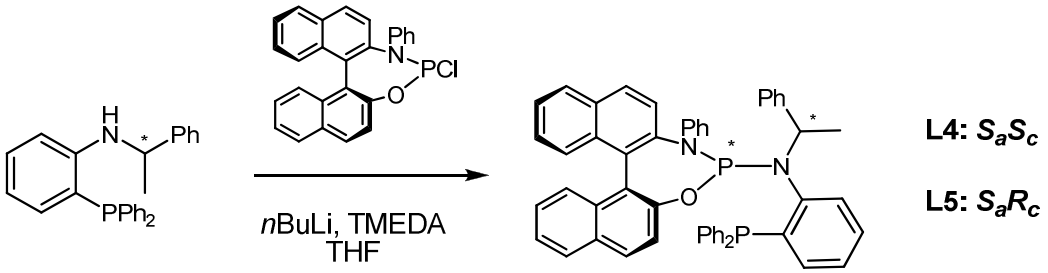
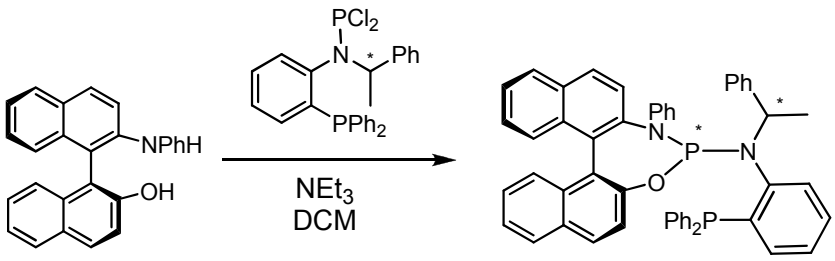


Scheme 2.7.6: *Coupling experiment pathway* ***A***

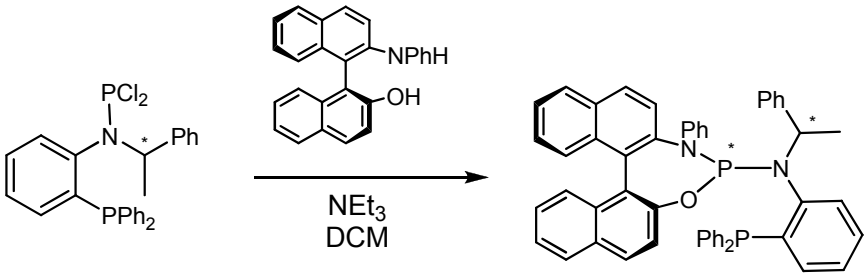
To this mixture (11bS)-4-chloro-5-phenyl-4,5-dihydrodinaphtho[2,1-d:1',2'-f][1,3,2] oxazaphosphepine (*S*-**73**) in THF was added dropwise and the reaction mixture was stirred for 16 h. Since ^{31}P-NMR analysis showed a very low conversion of 5 % to a possible phosphine-phosphorodiamidite, the experiment was repeated with a reaction time of 48 h. Another experiment was performed in toluene instead of THF. However, both longer reaction time and a different solvent did not improve the conversion. Therefore, the coupling of the ligand fragments was attempted via pathway **B**.

In the first coupling experiment following route **B**, the phenyl-substituted *S*-NOBIN was stirred with an excess of NEt_3 in DCM and one equivalent of the PCl_2-compound (*S*)-**73** in DCM was added dropwise (Pathway B-1, scheme 2.7.7). ^{31}P-NMR analysis showed one broad singlet in the phosphine region and two broad singlets at 128.8 ppm and 135.9 ppm, respectively (Figure 2.7.2, p.52, red spectrum).



Scheme 2.7.7: *Coupling experiments pathway* ***B****-1*

The signal in the phosphine region and the latter match with the obtained chemical shifts for the coupling experiment via pathway **A** (Scheme 2.7.6). To find a way to purify and identify the products, TLC on alumina and silica plates were perfomed. A mixture of THF and pentane (1:4) on a silica TLC plate showed the best separation results after removing residual NEt_3 via filtration over a small amount of silica. Filtration over a bigger amount of silica was done to test the stability of the products during a column chromatography. Finally, the two different products could be separated by column chromatography over silica using dried THF and pentane (1:4) under inert gas conditions. One of the products could be identified by NMR and mass spectroscopy as the desired phosphine-phosphorodiamidite **L4**. The other product could be either the corresponding diastereomer or another coupling product consisting of three building blocks (for example: 2x PCl_2-compound + aminoalcohol or 2x amioalcohol + PCl_2-compound) but this could not be veryfied via NMR or mass spectroscopy. To optimise the selectivity of the reaction towards the desired product, the reaction pathway was slightly changed.



Scheme 2.7.8: *Coupling experiments pathway* ***B****-2*

In a second coupling experiment the aminoalcohol was stirred with an excess of NEt_3 in dichloromethane and that solution was added dropwise to one equivalent of 1,1-dichloro-*N*-(2-(diphenylphosphino)phenyl)-*N*-(1-phenylethyl)phosphinamine (**72**) dissolved in DCM (Pathway **B**-2, Scheme 2.7.8). NMR analytics showed that this sequence of addition preferentially gave the desired species (Figure 2.7.2, p. 52, blue spectrum).

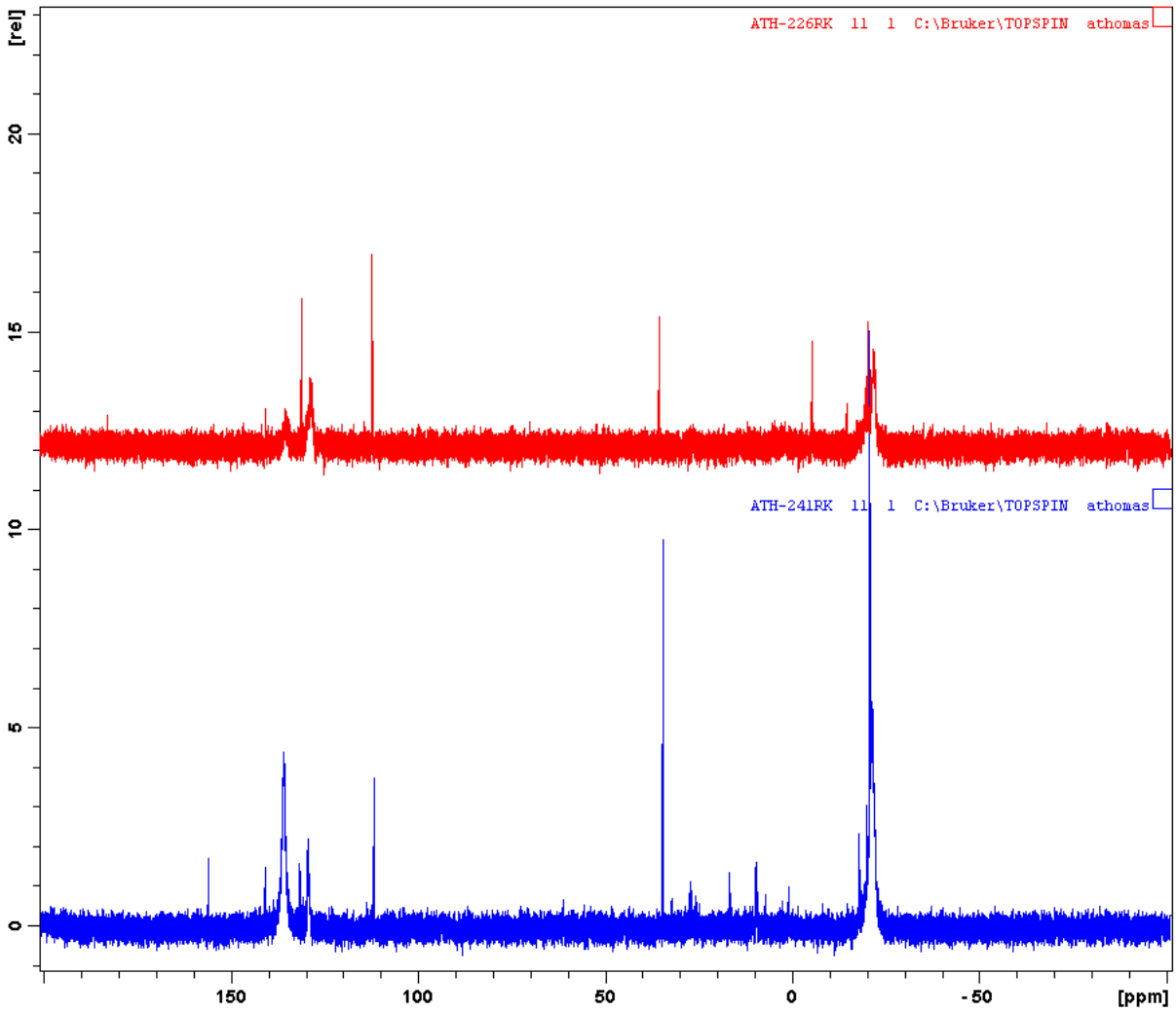
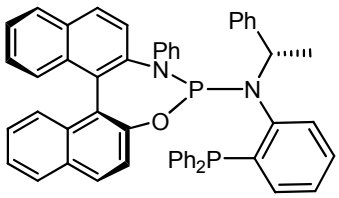
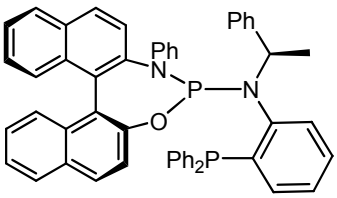


Figure 2.7.2: *$^{31}P\{^{1}H\}$-NMR spectra (crude mixture) reaction pathway **B**-1 and **B**-2*

L5 was obtained by the same reaction pathway using (*R*)-**74** instead of (*S*)-**74**. Via column chromatography the new phosphine-phosphorodiamidites **L4** and **L5** could be isolated in 31% and 25 % yield, respectively (Figure 2.7.3).



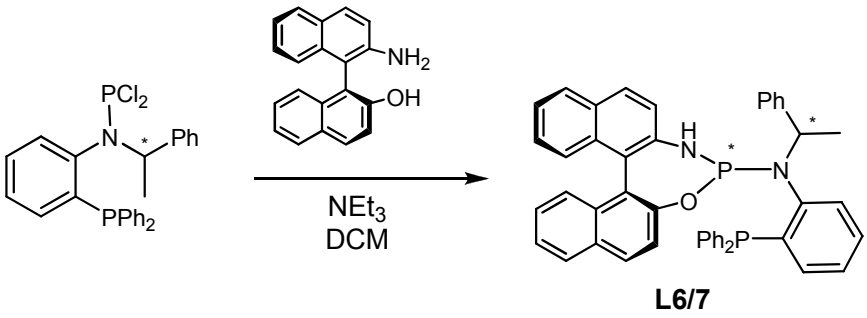
L4



L5

Figure 2.7.3: *New phosphine-phosphorodiamidites **L4** and **L5***

To obtain phosphine-phosphorodiamidites based on unsubstituted NOBIN coupling experiments were performed with (*S*)-NOBIN and (*S*)-**74** as well as (*R*)-**74** (Scheme 2.7.9). (*S*)-NOBIN was stirred with an excess of NEt_3 in DCM and was added dropwise to one equivalent of the PCl_2-compound **74** dissolved in DCM.



Scheme 2.7.9: *Coupling experiments pathway B-2, unsubstituted NOBIN*

For both combinations, the ^{31}P-NMR spectra indicated high conversion to a single phosphine-phosphorodiamidite species **L6** / **L7** showing one broad singlet for a phosphorodiamidite and a sharp doublet signal for a phosphine (Figure 2.7.4).

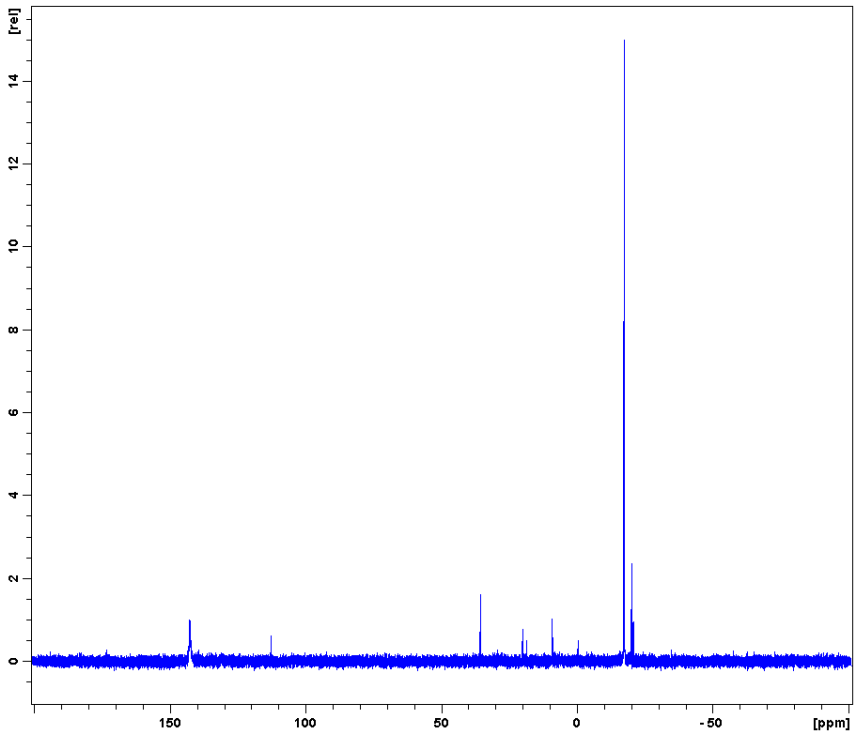
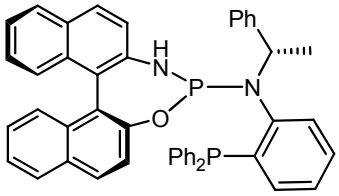
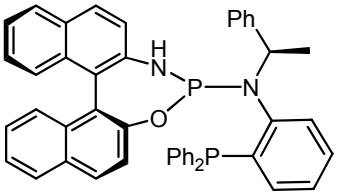


Figure 2.7.4: *$^{31}P\{^{1}H\}$-NMR spectrum of crude reaction mixture containing **L6***



L6



L7

Figure 2.7.5: *New phosphine-phosphorodiamidites **L6** and **L7***

The purification method that was developed for the phenyl-substituted phosphine-phosphorodiamidite could not be adapted since **L6**+**7** are not stable enough. Flushing a solution of crude product in toluene or THF over a pad of silica or alumina gave cleavage of the P-N bond, as indicated by an increased phosphine signal of **47**. Stability tests in which the silica or alumina patch were pretreated with NEt_3 or where NEt_3 was added to the eluent were successful in the case of alumina.

Finally, both synthesised phosphine-phosphorodiamidite species (**L6** and **L7**) could be isolated via column chromatography under argon using alumina and an eluent of THF:pentane:NEt_3 (Figure 2.7.5). An overview of the ^{31}P-NMR data of all new phosphine-phosphorodiamidites is given in Table 2.7.1.

Table 2.7.1: *$^{31}P\{^1H\}$-NMR-shifts and coupling constants of synthesised phosphine-phosphorodiamidites[a)]*

entry	compound	$\delta P_{phosphine}$ / ppm	mult.	δP_{PON_2} / *ppm*	mult.	J_{P-P} / Hz
1	**L4**	-21.1	b	135.9	b	-
2	**L5**	-22.0	b	132.2	b	-
3	**L6**	-17.8	d	142.2	b	42.4
4	**L7**	-19.4	b	138.3	b	-

a) measurements at room temperature in CD_2Cl_2

The chemical shifts for the phosphine and the phosphorodiamidite resonances are in the same range as those observed for the phoshine-phosphoramidites. The chemical shifts $\delta P_{phosphine}$ are at around -20 ppm while δP_{PON_2} are between 132 and

142 ppm. All observed signals are broad, with the exception of the phosphine signal of ligand **L6,** which is a sharp doublet with a coupling constant of 42.4 Hz.

The observation of several broad signals in the ^{31}P- and ^{1}H-NMR spectra suggests the existence of different rotational isomers. This can be proven by additional measurements at lower temperatures to freeze out the rotation. Ligands **L4** and **L6** were dissolved in CD_2Cl_2 and at first ^{1}H- and ^{31}P-NMR spectra were recorded at room temperature (blue, figure 2.7.6). The second set of spectra was recorded at 283 K (red), then the temperature was lowered in steps of 10 K to record a ^{1}H- and a ^{31}P-spectrum at each temperature. For ligand **L4**, variable temperature measurements down to 243 K were recorded. In the ^{31}P-NMR spectra series (left in figure), a simultaneous split of the phosphine and the phosphorodiamidite signal can be observed. At a temperature of 243 K (orange) two sharp signals instead of one broad singlet can be identified for each phosphorus atom, respectively. Therefore, the existence of two different rotamers can be presumed.

To identify the part in the molecule where this rotation takes place a look into the set of ^{1}H-NMR spectra is necessary. The right spectra set of figure 2.6.1.6 shows the broad singlet for the CH_3-group of the ligand, which also splits up into two signals at lower temperature. Hence, the identified rotation can be located along the N-C bond at the phenyl-ethyl rest of the amine moiety. A ratio of 17:83 between the two rotamers can be determined from ^{31}P-as well as from ^{1}H-NMR measurement.

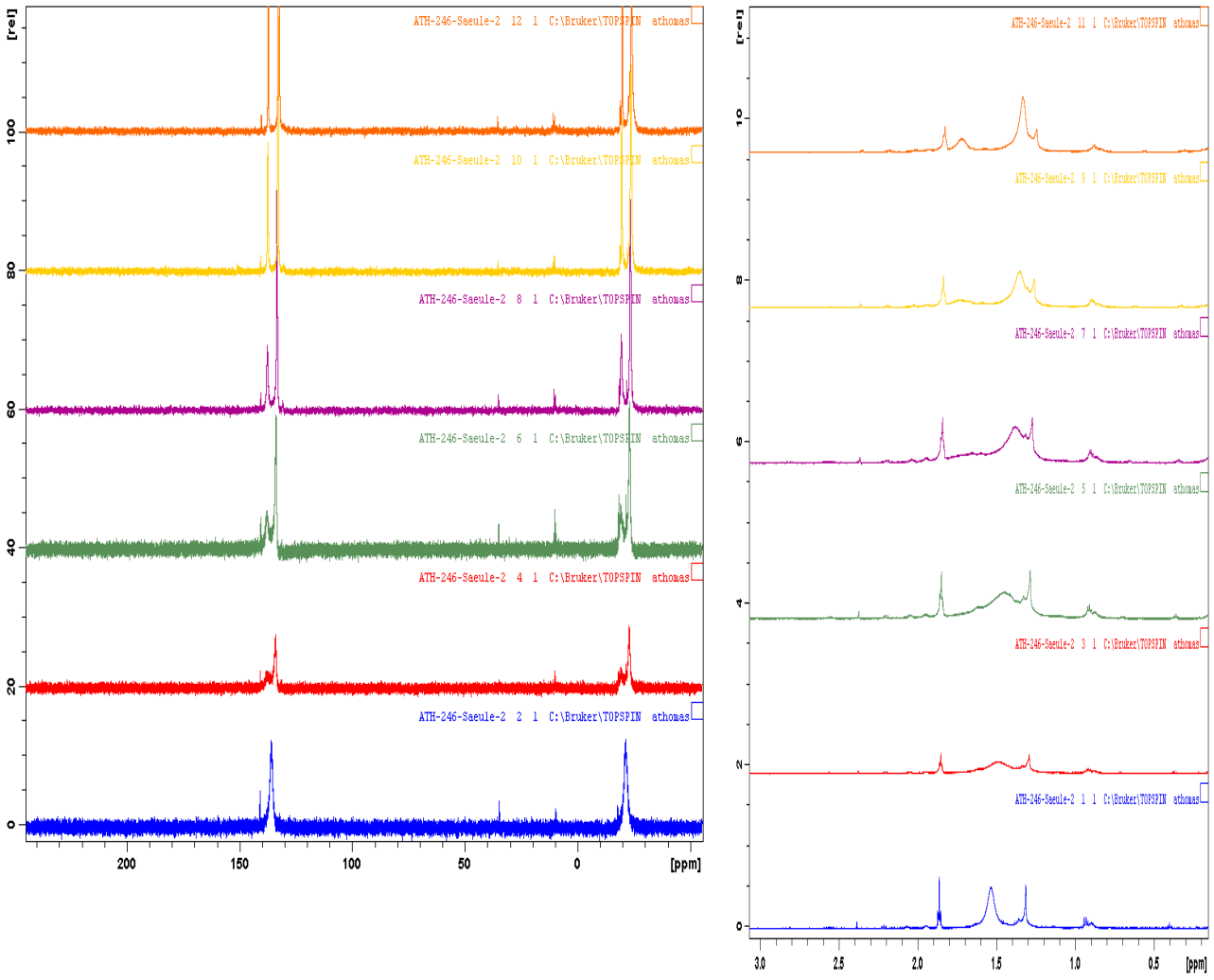


Figure 2.7.6: *Low temperature NMR measurement* ***L4****: left =* $^{31}P\{^{1}H\}$*; right =* ^{1}H *spectra*

In the ^{31}P-NMR spectrum of ligand **L6** at room temperature the signal of the phosphine group is already a sharp doublet. The set of low temperature ^{31}P-NMR spectra in the figure 2.7.7 (left) only shows the varying signal for the phosphorodiamidite. For this ligand the measurements are carried out down to 223 K (pink). At this temperature the former broad singlet is split 50:50 into two signals. The set of ^{1}H-NMR spectra (Figure 2.7.7, right) also shows a 50:50 split of the (at room temperature very broad) N*H*-signal and an initiating split of the C*H*-signal. Therefore, rotation of the same moiety as for ligand **L4** along the C-N bond in the molecule can be presumed.

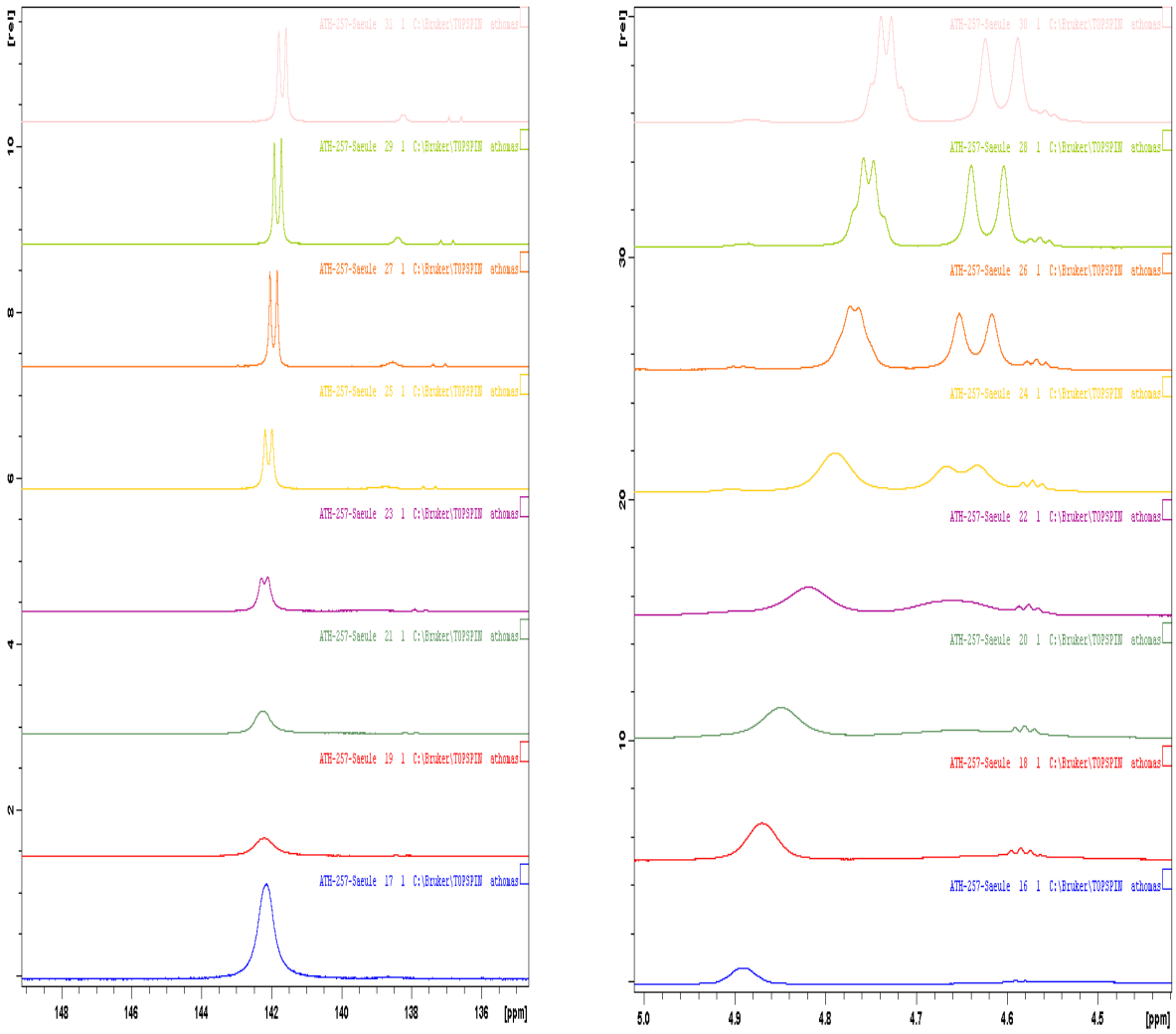
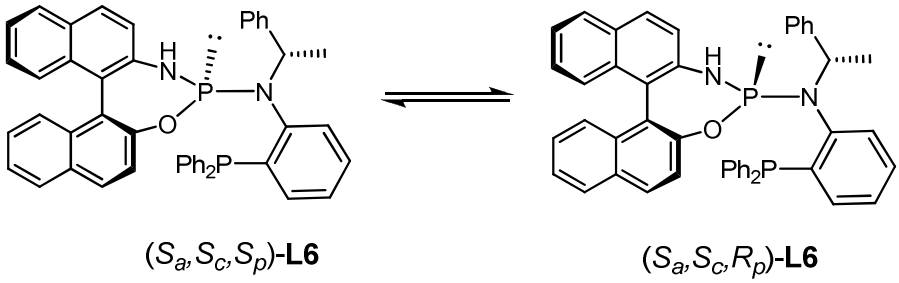


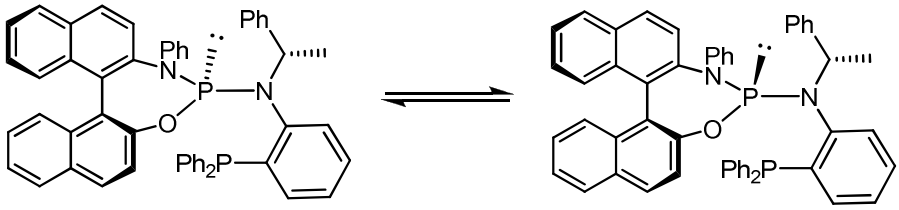
Figure 2.7.7: *Low temperature NMR measurement of* ***L6****: left =* $^{31}P\{^{1}H\}$*; right =* ^{1}H *spectra*

Another theoretically possible configurational change in the molecule that can be responsible for signal splitting in low-temperature NMR-measurements is a change in chirality at the phosphorus of the phosphorodiamidite moiety (See scheme 2.7.10). To exclude that possibility, the energies for this transition have been calculated by DFT simulations for ligands **L4** and **L6**. Activation energies (ΔG_{rel}) of 67.9 Kcal/mol for ligand **L4** and 73.4 Kcal/mol for ligand **L6** were obtained, which exclude a change of the chiral configuration at room temperature. Thus, the signal splitting observed at lower temperatures while obtaining broad signals at room temperature can definitely be attributed to the existence of rotational conformers.



(S_a,S_c,S_p)-**L6** (S_a,S_c,R_p)-**L6**

ΔG_{rel} = 73.4 Kcal/mol

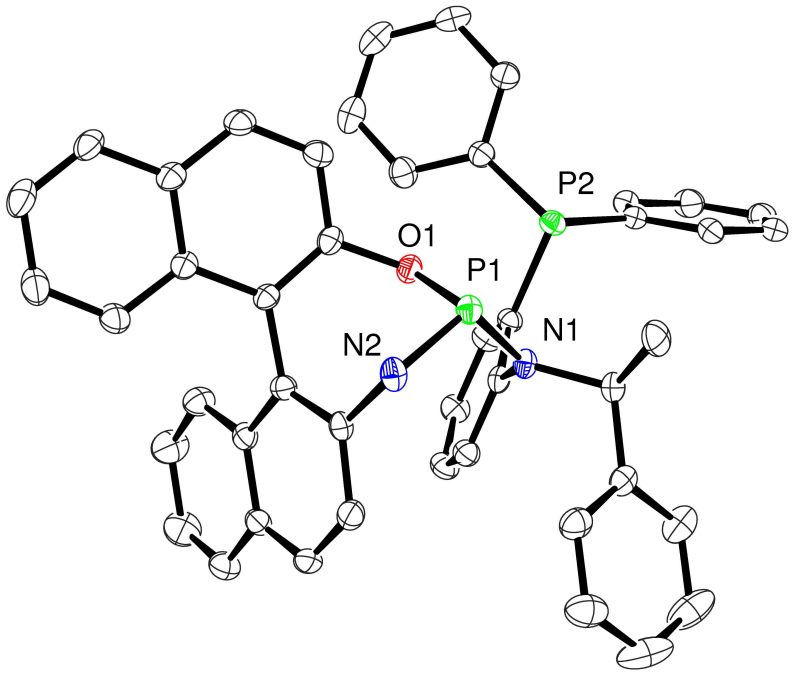


(S_a,S_c,S_p)-**L4** (S_a,S_c,R_p)-**L4**

ΔG_{rel} = 67.9 Kcal/mol

Scheme 2.7.10: *Transition of the phosphorodiamidite conformation*

To identify the absolute configuration at the phosphorus of the phosphorodiamidite moiety, crystallisation from different solvents or solvent combinations was attempted to obtain single crystals for X-ray analysis. For ligand **L6,** single crystals could be obtained by slow evaporation of a concentrated solution in acetonitrile. X-ray diffraction measurements indicate an absolute configuration of *S* at the phosphorodiamidite moiety. The obtained structure and selected data is shown in figure 2.7.8.



Bond distance (Å)	
P1-O1	1.6573(15)
P1-N1	1.6890(17)
P1-N2	1.7142(19)

Angle (˚)	
O1-P1-N1	92.95(8)
N1-P1-N2	110.18(9)
N2-P1-O1	97.27(8)

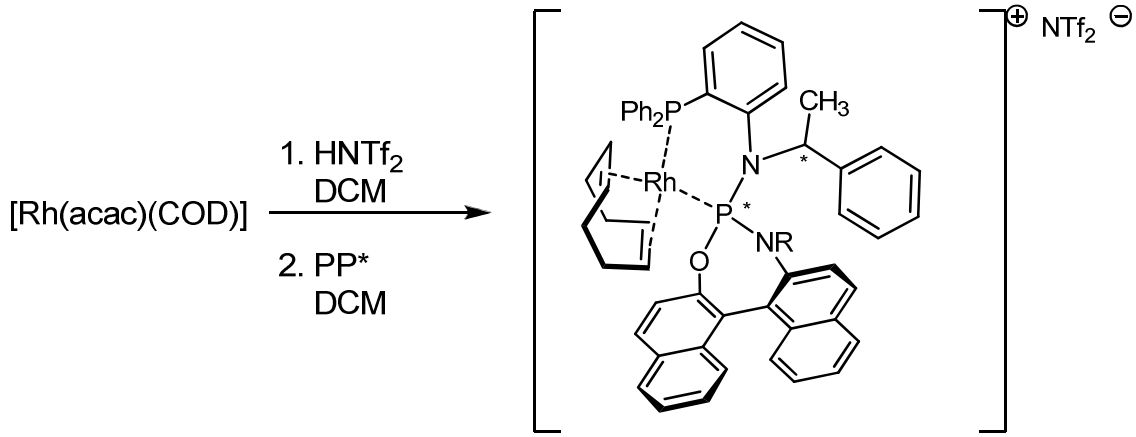
Angle sum (˚)	
N1	359.36
N2	351.43

Figure 2.7.8: *Crystal structure of ligand* ***L6***

Taking the free electron pairs into account both phosphorus-containing moieties have a tetrahedral structure. The free electron pairs face each other so that a chelating coordination to a metal atom is easily possible. This can also result in a through space coupling of the phosphorus atoms in the free ligand, which was actually observed for **L6** in the $^{31}P\{^{1}H\}$-NMR (p.54, table 2.7.1; $J_{P\text{-}P}$ = 42.4 Hz). The distance between P1 and P2 of 3.599 Å is larger than the distance between the two phosphorus donors in Quinaphos (**29**, 3.140 Å). That would lead to a larger bond angle of P1-M-P2 in a metal complex, and can have an influence on catalysis. The seven-membered OPN-containing heterocycle is asymmetric and distorted with a bond length of 1.6573(15) Å for P1-O1 and 1.7142(19) Å for P1-N2. The phenyl-ethyl amine substituent and the PPh_2-moiety are twisted relative to the binaphthyl backbone. P2 is closer to O1 than to N2 of the binaphthyl moiety. A comparison of the sum of angles at N1 and N2 suggests that N2 is significantly less planar than N1. It must be taken into account however, that the position of the proton at N2 is determined by calculation rather than full refinement by X-ray crystallography. The torsion angle of the NOBIN moiety is 61.61˚.

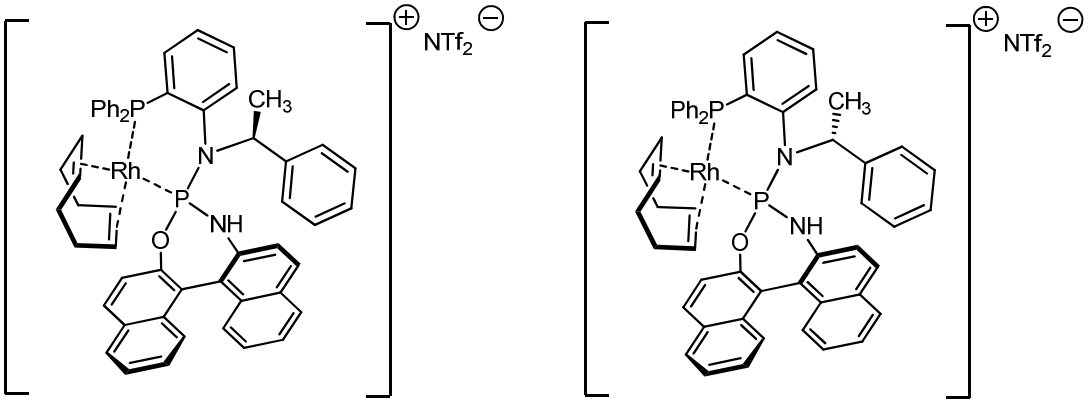
2.8 Rh-complexes of phosphine-phosphorodiamidites

To be able to get results that can be compared to the application of phosphine-phosphoramidites in asymmetric C-C double bond hydrogenation, rhodium complexes of the new phosphine-phosphorodiamidites have been synthesised (Scheme 2.8.1).



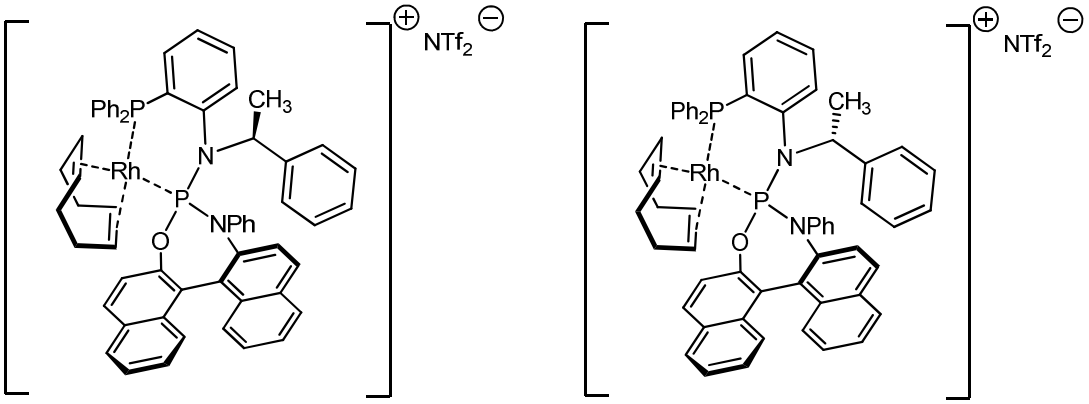
Scheme 2.8.1: *Synthesis of Rh-phosphine-phosphorodiamidite-complexes*

Unfortunately, the synthetic method that was developed for Rh-phosphine-phosphoramidite complexes could not be adapted one to one, because phosphine-phosphorodiamidites were found to decompose in ethanol. Instead, the procedure was performed in dichloromethane, stirring [Rh(acac)(COD)] and $HNTf_2$ for 30 min before adding the ligand to the mixture. Although DCM is not a coordinating solvent that could form an intermediate $[Rh(solvent)_2(COD)]NTf_2$ species like ethanol, ^{31}P-NMR analysis showed full conversion to the desired products. A rhodium complex of every new phosphine-phosphorodiamidite could be isolated (Figure 2.8.1)



[Rh(COD)(**L6**)][NTf_2]
75

[Rh(COD)(**L7**)][NTf_2]
76



[Rh(COD)(**L4**)][NTf_2]
77

[Rh(COD)(**L5**)][NTf_2]
78

Figure 2.8.1: *Synthesised Rh-complexes* ***75****-****78***

The chemical shifts of the doublets of doublets (Table 2.8.1) were in the same region as for the corresponding complexes containing phosphine-phosphoramidites. One can see a coupling of the two different phosphorus atoms wich differs depended on the N-substituent. For complexes **77** and **78** the coupling constant is around 65 Hz while for complexes **75** and **76** at around 40 Hz. The phosphorus-rhodium coupling constants are also dependend on the N-substituents. For complexes **77** and **78** it is around 140 Hz (phosphine) and 200 Hz (phosphorodiamidite) while for complexes **75** and **76** at around 150 Hz and 220 Hz.

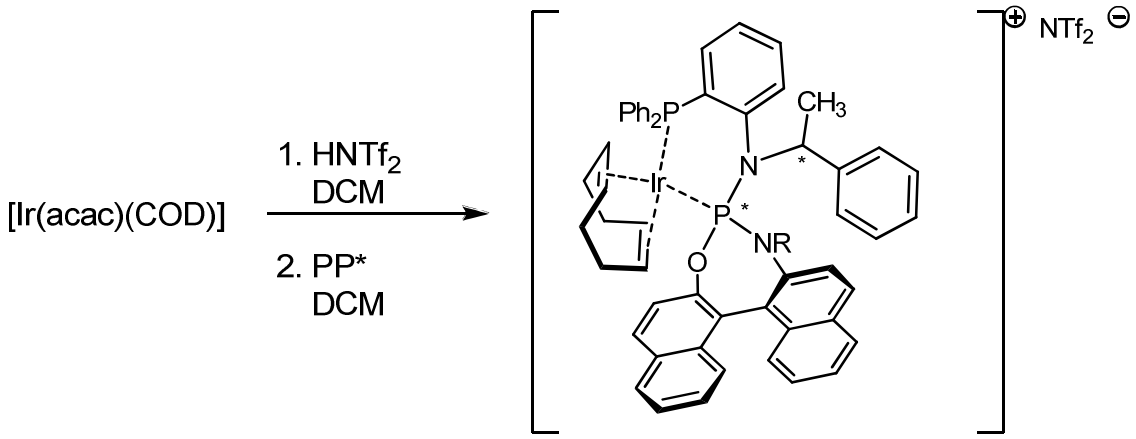
Table 2.8.1: *$^{31}P\{^{1}H\}$-NMR shifts of [Rh(COD)(PP*)][NTf_2] complexes*[a)]

entry	compound	$\delta P_{phosphine}$ / ppm	mult.	δP_{PON_2} / *ppm*	mult.	J_{P-P} / Hz	J_{P-Rh} / Hz
1	**77**	13.18	dd	138.58	dd	68.5	141.3/199.3
2	**78**	12.98	dd	138.71	dd	66.4	140.6/202.3
3	**75**	13.78	dd	138.71	dd	40.0	151.1/219.2
4	**76**	12.75	dd	140.40	dd	36.2	152.2/221.4

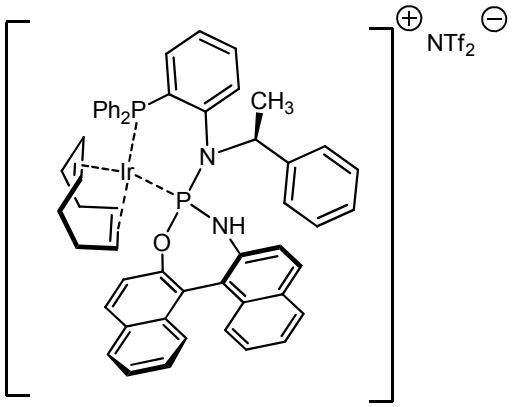
a) measurements at room temperature in CD_2Cl_2

2.9 Ir-complexes of phosphine-phosphorodiamidites

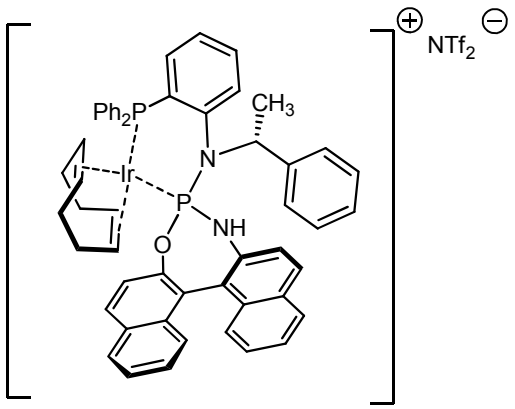
The phosphine-phosphorodiamidites were also applied in the synthesis of iridium complexes. The same method as for the rhodium complexes was used (Scheme 2.9.1). Ir(acac)(COD) was stirred with an equivalent of $HNTf_2$ in DCM for 30 min and the ligand was added dissolved in DCM. ^{31}P-NMR spectroscopy showed that the reaction of the N*Ph*-substituted ligands **L4** and **L5** gave a mixture of several different species that could not be separated. Only for the N*H*-substituted ligands **L6** and **L7** well-defined species could be isolated (Figure 2.9.1).



Scheme 2.9.1: *Synthesis of Ir-phosphine-phosphorodiamidite-complexes*



[Ir(COD)(**L6**)][NTf_2]
79



[Ir(COD)(**L7**)][NTf_2]
80

Figure 2.9.1: *Synthesised Ir-complexes **79** and **80***

The data from the ^{31}P-NMR spectra of complexes **79** and **80** are collected in table 2.8.1. Chemical shifts for the iridium complexes are very different from those obtained for the rhodium-complexes. The phosphine resonance appears at <10 ppm, which is significantly higher while the phosphorodiamidite signal comes at ~115 ppm, which is significantly lower. The phosphorus-phosphorus coupling constants amount ~44 Hz, which is comparable to the $^*J_{PP}$-values for the Rh-complexes of the phenyl-substituted ligands **L4** and **L5**.

Table 2.9.1: *^{31}P-{^{1}H}-NMR shifts of [Ir(COD)(PP*)][NTf_2] complexes[a)]*

entry	compound	$\delta P_{phosphine}$ / ppm	mult.	δP_{PON_2} / ppm	mult.	J_{P-P} / Hz
1	**79**	8.92	d	115.87	d	43.8
2	**80**	6.42	d	113.87	d	43.5

a) measurements at room temperature in CD_2Cl_2

2.10 Application of phosphine-phosphorodiamidites in asymmetric catalyses

2.10.1 Rh-catalysed hydrogenation of C=C double bonds

First of all, the rhodium-complexes of the phosphine-phosphorodiamidites were tested for the hydrogenation of asymmetric hydrogenation of prochiral olefins. The first benchmark substrate that was used is dimethyl itaconate (**dmi**, figure 2.10.11). Under the same reaction conditions as used for the phosphine-phosphoramidites, phosphine-phosphorodiamidites **L4-7** showed different trends in conversion and enantioselectivity (Table 2.10.1.1). The ligands with S_a,S_c-configuration induced conversions of more than 99 % in contrast to the ligands with R_a,S_c-configuration (max: 47 %).

Table 2.10.1.1: *Hydrogenation of* ***dmi*** *- results*[a)]

entry	ligand	conversion (%)	*ee (%)*
1	**L6**	>99	79.0 *S*
2	**L4**	>99	14.4 *R*
3	**L7**	47.1	97.9 *S*
4	**L5**	7.7	41.3 *R*

a) 1 mmol S, S/Rh = 1000:1, 2 mL DCM, 1h, pH_2 = 10 bar, RT

Furthermore, a switch in the stereochemical outcome of the reaction depending on the substituent at the diamidite nitrogen atom was observed. The hydrogen-substituted ligands led preferentially to the *S*-enantiomer, while the phenyl-substituted ligands favoured the *R*-enantiomer. Since the absolute configuration of the phosphorodiamidite moiety in the phenyl substituted ligands could not be identified yet, it is not clear if the conformational switch in catalysis only depends on the different substituent or on a possible difference in configuraton. Generally, the achieved enantioselectivities are lower than the *ee*s induced by the phosphine-phosphoramidites. Ligand **L7** showed the highest enantioselectivity of the tested phosphine-phosphorodiamidites (98% *S*) and was therefore the only phosphine-phosphorodiamidite that gave *ee*s in the same range as the phosphine-phosphoramidites.

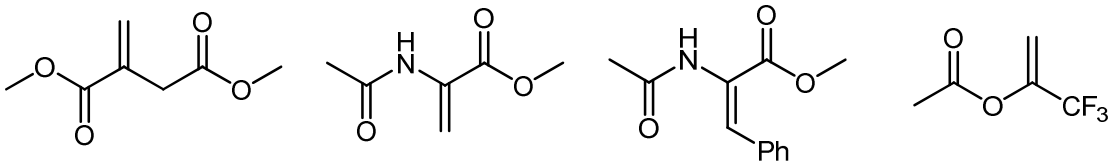


Figure 2.10.1.1: *Substrates for C=C hydrogenations*

To broaden the substrate scope other benchmark compounds (Figure 2.10.1.1) were also tested under the same conditions. The results are again very different from the hydrogenation results using phosphine-phosphoramidites (Table 2.10.1.1). The switch of the product configuration that depends on the substituent at the diamidite nitrogen atom of the ligand can be observed more or less distinctive for all substrates. On average, ligand **L7** induced the highest enantiomeric excesses for the hydrogenation of **maa**, **mapa** and **fpa**, but the observed selectivities for these substrates were lower than those induced by phosphine-phosphoramidites **L1-3**. For the hydrogenation of methyl amidoacrylate (**maa**) all phosphine-phosphorodiamidites show conversions below 56 %, respectively.

Table 2.10.1.1: *Hydrogenation of* ***maa***, ***mapa*** *and* ***fpa*** *- results*[a)]

entry	ligand	substrate	conversion (%)	*ee (%)*
1	**L6**	**maa**	32	48 *R*
2	**L4**	**maa**	1	10 *S*
3	**L7**	**maa**	56	75 *R*
4	**L5**	**maa**	2	2 *R*
5	**L6**	**mapa**	> 99	83 *R*
6	**L4**	**mapa**	14	68 *S*
7	**L7**	**mapa**	> 99	89 *R*
8	**L5**	**mapa**	2	n.d.
9	**L6**	**fpa**	3	30 *R*
10	**L4**	**fpa**	1	52 *S*
11	**L7**	**fpa**	5	82 *R*
12	**L5**	**fpa**	6	67 *S*

a) 1 mmol S, S/Rh = 1000:1, 2 mL DCM, 1h, pH_2 = 10 bar, RT

Enantioselectivities between 2% and 75% have been observed. (*E*)-methyl 2-acetamido-3-phenylacrylate (**mapa**) can be hydrogenated with enantioselectivities up

to 89%. Here the difference in conversion between the results for hydrogen- and phenyl-substituted ligands is even more distinctive. The hydrogen-substituted phosphine-phosphorodiamidites give full conversion, while the highest conversion observed for the phenyl-substituted phosphine-phosphorodiamidites is 14%. The hydrogenation of the fluorinated substrate **fpa** showed moderate to good enantioselectivities up to 82%, but low conversions < 6%.

Although the new phosphine-phosphorodiamidites **L4-7** seem to be less effective and selective for this type of reaction and substrate scope as the corresponding phosphine-phosphoramidites, they definetly show a general potential. Structural optimisations that lead to different phosphine-phosphorodiamidites and their application can be promising for future research.

2.10.2 Ir-catalysed hydrogenation of C=N double bonds

A) 2-methyl quinoline

The first model substrate for testing **L4**-**7** in iridium-catalysed asymmetric hydrogenation was 2-methylquinoline (**2mq**), which has also been used before in combination with the phosphine-phosphoramidites (Scheme 2.5.2.2). All reactions were run at room temperature for 16 h and at a hydrogen pressure of 40 bar (Table 2.10.2.1).

Table 2.10.2.1: *Hydrogenation of (**2mq**)*

entry	ligand	conversion (%)	*ee (%)*
1	**L6**	>99	78 *R*
2	**L4**	>99	84 *R*
3	**L7**	>99	77 *R*
4	**L5**	94	78 *R*

a) 1 mmol **2mq**, **2mq**/Ir/Lig/I_2 = 100:1:1.1:5, 2 mL toluene, 16 h, pH_2 = 40 bar, RT

Ligands **L4-7** were found to be very active for the hydrogenation of 2-methylquinoline. Ligand **L5** showed a conversion of 94 %; all other ligands gave full conversion. The obtained enantioselectivities were all in the range between 78% and 84%, which is lower than the enantioselectivities induced by the phosphine-

phosphoramidites (up to 97 %). Interestingly, a different substituent at the nitrogen atom of the phosphorodiamidite moiety or a difference in configuration at the amine part appears to have no influence on the configuration of the product in this reaction system. All phosphine-phosphorodiamidites used for the hydrogenation of 2-methylquinoline induced an *R*-configurated product. For the phosphine-phosphoramidites, the dependence of the chiral outcome of the reaction on a structural feature of the ligand (axial chiality of the binaphthyl moiety) could be observed in the rhodium-catalysed hydrogenation of olefines as well as in the iridium-catalysed hydrogenation of 2-substituted quinolines. Since the enantioselectivities were lower than for the tested phosphine-phosphoramidites, no other more demanding 2-substituted quinolines were tested in combination with phosphine-phosphorodiamidites.

B) (E)-N-(1-phenylethylidene)aniline

Another class of imines that has been subjected to intense investigations in literature is acyclic *N*-arylimines. Different transition metals such as rhodium, ruthenium and iridium have been used in combination with a variety of ligands to obtain chiral arylamines via enantioselective hydrogenation of their corresponding prochiral imines.[137] This is particularly interesting since chiral arylamines are very often biologically active compounds or building blocks for biologically active agents. A notable example is the industrially applied synthesis of *S*-metholachlor that is used as a herbicide.[42] The key step in the synthesis is the iridium-catalysed enantioselective hydrogenation of an *N*-aryl ketimine using a bisphosphine ligand, which was alredy presented in the introduction (Scheme 1.2.3).

Most of the systems leading to high enantioselectivities are a combination of iridium as the active metal and a bidentate ligand such as a bisphosphine or various P/N-ligands.[137] A typical benchmark substrate for the evaluation of a catalytic system in this type of reactions is (E)-*N*-(1-phenylethylidene)aniline (**pea**). One of the earliest systems that gave high enantioselectivities (up to 98%) for this substrate was published in 2001 by Zhang and co-workers using an Ir-f-binaphane catalyst (**81**).[138]

In 2005, Bolm and coworkers hydrogenated a family of ten different aryl methyl N-*p*-MeO-phenylimines via an Ir-diphenylphosphanylsulfoximine catalyst (**82**) with enantioselectivities up to 98%.[139] A bisphosphine-containing system of Imamoto

(**83**), published in 2006, even achieved 99% enantioselectivity in the hydrogenation of (E)-*N*-(1-phenylethylidene)aniline.[140] High selectivities for the hydrogenation of **pea** and a set of derivatives were also achieved by Ir-SIPHOX systems reported by Zhou (**84**),[141] by iridium-based ligands in combination with BINOL-based phosphoric acid counter ions (**85**)[142] and by the ferrocenyl P,N ligands of Knochel (**86**).[143]

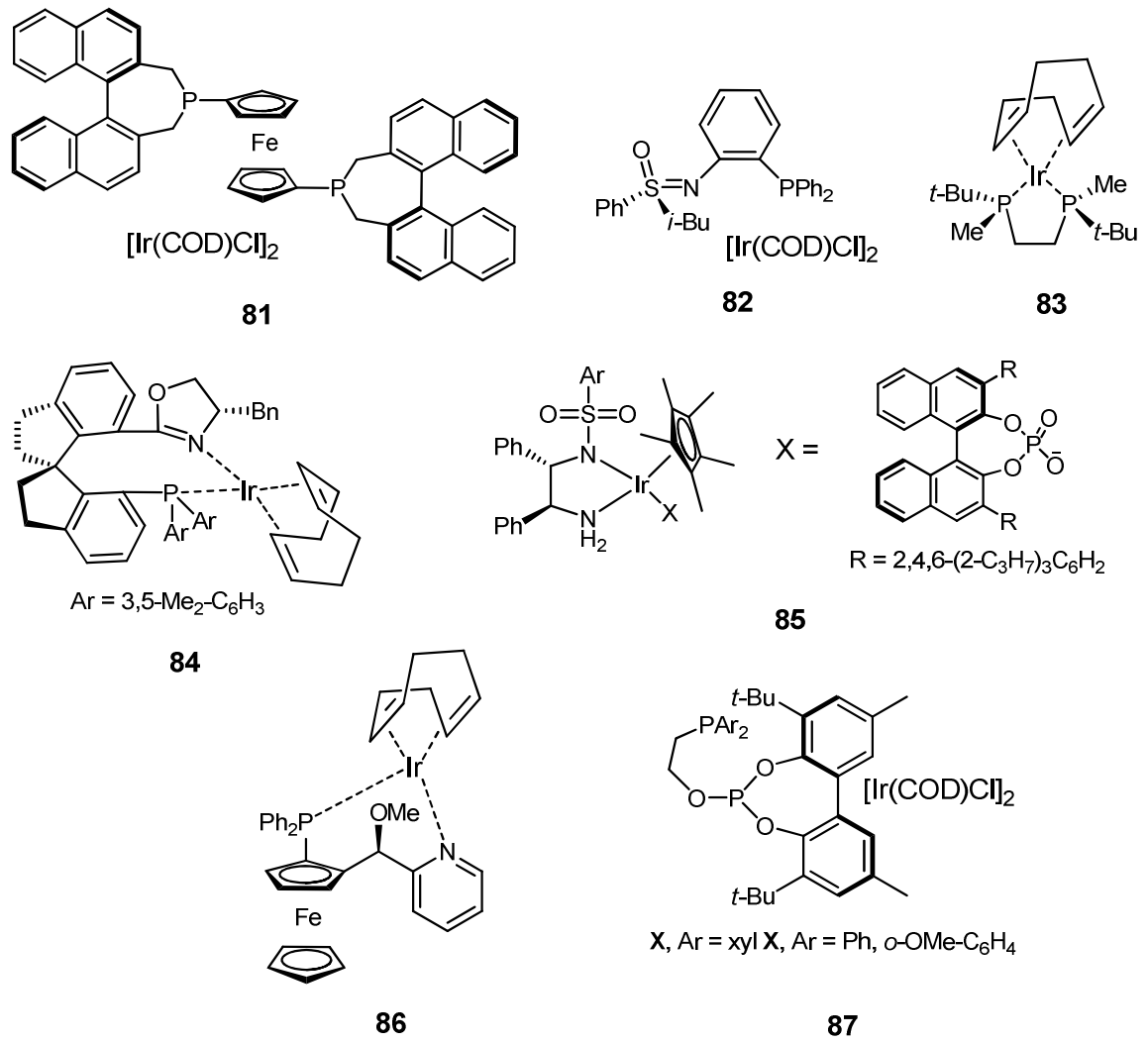
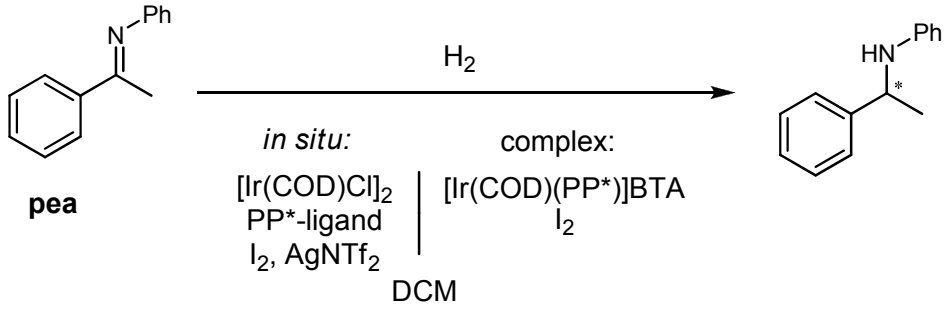


Figure 2.10.2.1: *Selected ligands for hydrogenation of acyclic N-arylimine*

Mixed bidentate phosphine ligands (phosphine-phosphites) have been used by Pizzano in 2005 (**87**) achieving good enantioselectivities up to 84% in the hydrogenation of **pea**.[144] Encouraged by these results, phosphine-phosphorodiamidites **L4-7** and their iridium-complexes **79** and **80** were applied in the hydrogenation of (E)-*N*-(1-phenylethylidene)aniline (**pea**, scheme 2.10.2.1).



Scheme 2.10.2.1: *Hydrogenation of (E)-N-(1-phenylethylidene)aniline (**pea**)*

The iridium-complexes derived from the N*H*-substituted ligands were used in catalysis in a substrate to catalyst ratio of 1000:1. Full conversion was achieved by stirring the mixture in DCM at 40°C at a hydrogen pressure of 30 bar for 20 h (Table 2.10.2.2). Addition of iodine as an additive was found to lead to higher enantioselectivities.

Table 2.10.2.2: *Hydrogenation of (E)-N-(1-phenylethylidene)aniline (**pea**) – complexes*[a)]

entry	complex	I_2	*ee (%)*
1	**79** (**L6**)	-	12 *R*
2	**79** (**L6**)	0.01mmol	70 *R*
3	**80** (**L7**)	-	*rac*
4	**80** (**L7**)	0.01mmol	78 *R*

a) S:1mmol, S/Cat./I_2 = 1000/1/10, 40°C, 20h, 2mL DCM, $p$$H_2$ = 30bar, C: [Ir(cod)L]NTf_2, cv: > 99%

The highest *ee* of 78% was induced by a combination of **80** with iodine as an additive. To also be able to compare the catalytic results of the N*Ph*-substituted ligands, an *in situ* method was developed. To optimise the conditions and to check the comparability to the method that was used before, the new procedure was evaluated with N*H*-substituted ligand **L6** first (Table 2.10.2.3).

Table 2.10.2.3: *Hydrogenation of (E)-N-(1-phenylethylidene)aniline – in situ*[a)]

entry	ligand	iodine (mmol)	$AgNTf_2$ (mmol)	conversion (%)	*ee* (%)
1	**L6**	-	-	0	nd
2	**L6**	0.01	-	>99	65 *R*
3	**L6**	-	0.001	32	38 *R*
4	**L6**	0.01	0.001	>99	68 *R*
5	**L4**	0.01	0.001	>99	24 *S*
6	**L5**	0.01	0.001	>99	21 *S*

a) S:1mmol, S/Cat./I_2 = 1000/1/10, 40°C, 20h, 2mL DCM,
pH_2 = 30bar, Cat.:$[Ir(COD)Cl]_2$ + 2eq L + 1eq $AgNTf_2$

In a first experiment, two equivalents of ligand **L6** were stirred with $[Ir(cod)Cl]_2$ and this mixture was used as a catalyst under the same conditions as for the reactions in table 2.10.2.2. In a second experiment, $AgNTf_2$ was added; the third one was treated with iodine and the fourth one contained $AgNTf_2$ and iodine. The fourth experiment gave the best results - with iodine the conversion is much higher than without and the presence of $AgNTf_2$ increases enantiomeric excess up to 68% *R*. This result is comparable to the enantiomeric excess of 70% *R* that was achieved via the preformed iridium-complex of the same ligand. The N*Ph*-substituted ligands **L4-5** have been tested with $AgNTf_2$ and iodine as well. Enantiomeric excesses up to 24% for the *S*-enantiomer and the same *N*-substitutent-dependent switch in configuration of the product were observed.

In general, the obtained results with *ee*s up to 78% are lower than the actual benchmark for this substrate, but comparable to the results obtained with Pizzano's phosphine-phosphites.

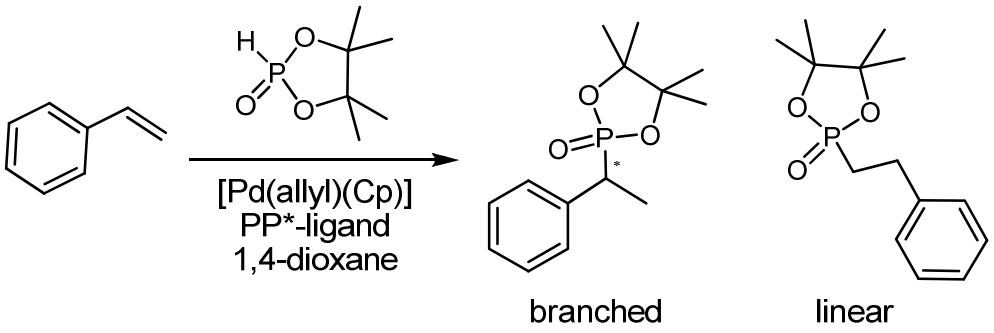
2.10.3 Asymmetric hydrophosphorylation

Organophosphonate compounds such as arylalkylphosphonic esters are particularly interesting because of their biological activity.[145] There are several possibilities to synthesise structures of this type, for example the classic Arbuzov reaction of $P(OR)_3$ with R'X.[146] A very elegant method is the direct addition of a hydrogenphosphonate to an olefin.[146] The first example of a so-called hydrophosphorylation was published in 2000 by the group of Tanaka.[147] They showed that palladium as active metal centre could induce selectivity towards the branched product in the hydrophosphorylation of various unfunctionalised olefines. In

2005, Franciò, Leitner and Beletskaya published a screening of different ligands to find suitable systems for the hydrophosphorylation of vinylarenes that favour the Markovnikov product (regioselectivity) and induce significant levels of enantiomeric excess.[148]

The most successful ligand reported was phosphine-phosphite (*R,S*)-BINAPHOS, which gave a linear:branched ratio of 7:93 and an enantiomeric excess of 56%. More recently, an improvement in enantioselectivity to 74% using a new derivative of BINAPHOS was reported.[149] The group of Han achieved enantioselectivities up to 88.5% in the hydrophosphorylation of norbonenes using JosiPhos-type ligands with NEt_3 as an additive.[150] A system that showed excellent cis:trans ratios in the hydrophosphorylation of cyclopropenes was published by Rubin and coworkers.[151]

Since mixed bidentate phosphine ligands appear to give good results for this type of reaction, **36** and **L4**-**7** were tested in the hydrophosphorylation of styrene (Scheme 2.10.3.1). The first reaction was performed under conditions that were established by Shulyupin.[148] A pinacol-derived phosphonate[152], [Pd(Cp)(allyl)][153], and 1.1 equivalents of **36** were stirred at 100 °C for 45 min in 1,4-dioxane. After addition of styrene, the mixture was stirred at 100 °C. After a reaction time of 35 h however, no conversion was observed.



Scheme 2.10.3.1: *Hydrophosphorylation of styrene*

Much better results were obtained with an alternative method, in which all components were stirred in a one-pot reaction for 8 h at 100 °C in the microwave (Table 2.10.3.1). A conversion of 64%, a linear:branched ratio of 11:89, and a moderate enantiomeric excess of 23% were observed for **36**.

Table 2.10.3.1: *Hydrophosphorylation of styrene – results*[a)]

entry	ligand	conversion (%)	linear:branched	*ee (%)*
1	**36**	64	11 : 89	23
2	**L6**	19	9 : 91	8
3	**L4**	2	n.d.	-
4	**L7**	2	n.d.	-
5	**L5**	13	23 : 77	9

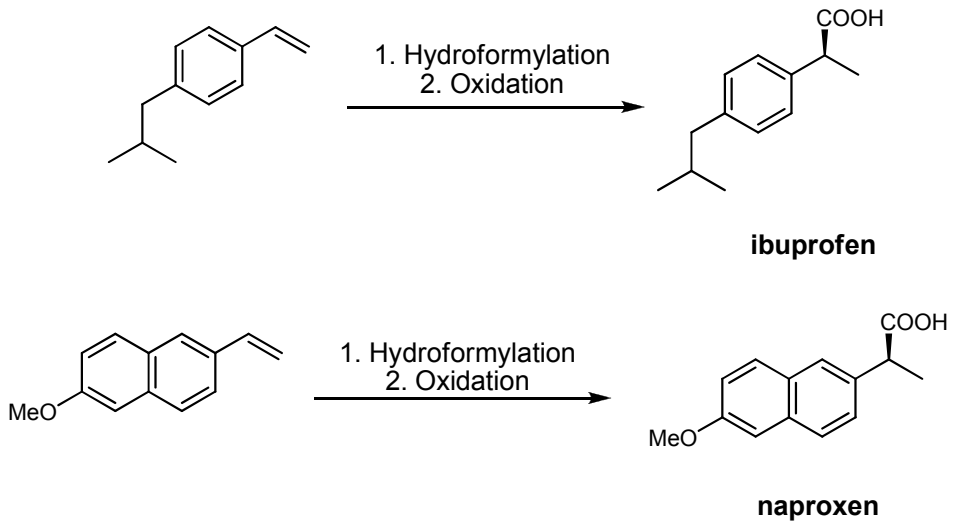
a) 0.7 mmol S (styrene), S/C/L/phosponate = 40:1:1.1:20, 1 mL 1,4-dioxane, microwave: 8 h, 100°C

To test the potential of the phosphine-phosphorodiamidites, they were also applied in the hydrophosphorylation of styrene under the one-pot conditions via microwave. Conversions were found to be too low to detect regio- and enantioselectivities for the reactions with ligands **L4** and **L7**. The best result was observed for ligand **L6**, which gave a good linear to branched ratio of 9:91, but also gave a poor enantioselectivity of 8%. From these results it can be concluded that this type of ligand is unsuitable for enantioselective hydrophosphorylation.

2.9.4 Asymmetric hydroformylation

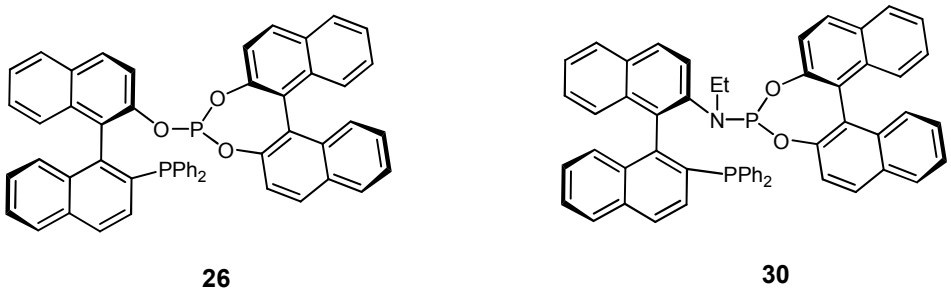
Hydroformylation reactions are one of the most important industrial applications of homogeneous catalysis. This type of reaction was discovered by Roelen in 1938, describing the reaction of an olefin with syngas (CO/H_2) to an aldehyde.[154,155] Aldehydes can be reacted to alcohols or carbonic acids which are used as softeners in plastics or as detergents. In industry, hydroformylation reactions are generally catalysed by cobalt or rhodium combined with phosphine ligands.

The hydroformylation of asymmetric olefins leads to a mixture of linear and branched products. When the substituents at the double bond of the olefin are different, the branched product is chiral. To control regio- and stereoselectivity in asymmetric hydroformylation, a combination of rhodium and bidentate chiral phosphites or chiral ligands with mixed donors is applied in most cases.[156,157] This method can be used for the enantioselective synthesis of biologically active compounds, such as ibubrofen or naproxen (Scheme 2.10.4.1).



Scheme 2.10.4.1: *Hydroformylation as possible synthetic strategy for ibuprofen and naproxen*

Ibuprofen and naproxen can be synthesised via the asymmetric hydroformylation of vinyl aromates, followed by an oxidation reaction to obtain the free arylpropionic acids. Due to its availability, styrene is often used as a benchmark substrate for the evaluation of new catalytic systems in this type of reactions. A well established ligand for the hydroformylation of styrene is Takaya's BINAPHOS (**26**), which induces a linear to branched ratio of 12:88 and 94% enantioselectivity.[60]

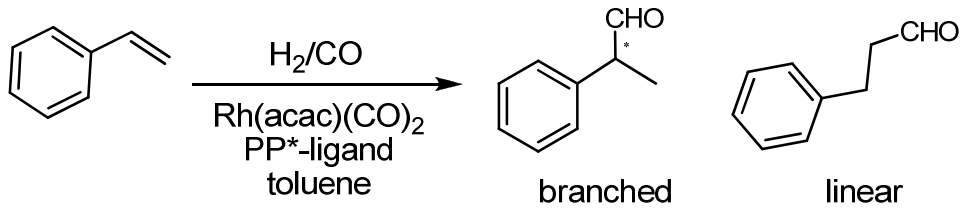


26 **30**

Figure 2.10.4.1: *Selected ligands for asymmetric hydroformylation of styrene*

These results are only topped by an analogous phosphine-phosphoramidite (**30**) published in 2006 by Zhang.[73] With **30**, a linear to branched ratio of 11:89 and an enantioselectivity of 98% have been achieved in the hydroformylation of styrene.

Phosphine-phosphorodiamidites **L4-7** were also tested in the rhodium catalysed hydroformylation of styrene (Scheme 2.10.4.2).



Scheme 2.10.4.2: *Hydroformylation of styrene*

Precursor $Rh(acac)(CO)_2$ was stirred with four equivalents of the ligand for 30 min, after which the substrate was added and the mixture was stirred for 16 h at 60 °C at a syngas pressure of 40 bar. Except for the run with ligand **L6** all reactions achieved full conversion (Table 2.10.4.1).

Table 2.10.4.1: *Hydroformylation of styrene - results*

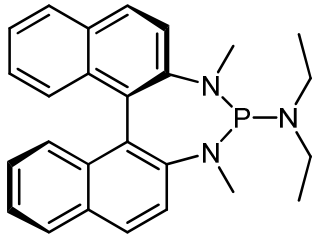
entry	ligand	conversion (%)	linear:branched	*ee (%)*
1	**L6**	56	8 : 92	8
2	**L4**	> 99	16 : 84	17
3	**L7**	> 99	7 : 93	2
4	**L5**	> 99	3 : 97	57

a) 2 mmol S, S/Rh/L = 1000:1:4, 2 mL toluene, 16 h, 60°C, *p*CO/H_2 = 40bar

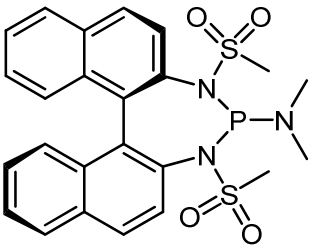
All ligands induced good to excellent selectivities towards the branched product of up to 97%. The N*Ph*-substituted ligands showed higher enantioselectivities than the N*H*-substituted ligands. The best results for this set of ligands was provided by ligand **L5**, giving a linear to branched ratio of 3:97 and an enantioselectivity of 57%. Compared to benchmark ligand **30**, the selectivity towards the branched aldehyde are higher but the enantioselectivities are much lower.

2.11 Phosphine-phosphortriamides

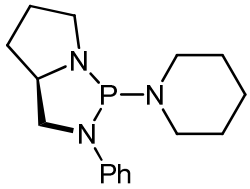
A phosphortriamide is a diaza-analogue of a phosphoramidite and therefore also a possible building block for a mixed bidentate phosphine ligand. There are phosphortriamide structures in the literature that have been used as monodentate ligands in asymmetric catalysis, but the amount of structures and applications is significantly lower compared to phosphoramidites. A first example of an application of phosphortriamides in enantioselective catalysis was given by Reetz in 2003 using **88** in the hydroformylation of styrene and in the hydrogenation of dimethyl itaconate.[158]



88



89



90

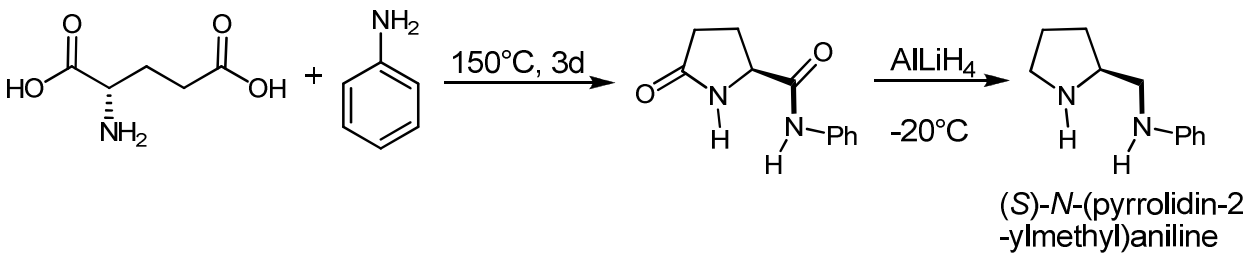
Figure 2.11.1: *Selected phosphortriamides for enantioselective catalysis*

In the hydroformylation of styrene, this ligand showed good activity but low enantioselectivity; in rhodium-catalysed hydrogenation no conversion was observed. One year later, Gennari and coworkers established a pool of 23 phosphortriamides combining amines with different sulfonylic groups.[159] Out of that pool only ligand **89** gave moderate enantiomeric excess of 75% in the copper-catalysed Michael addition of diethyl zinc to cyclohexane. All other ligands induced enantioselectivities below 20%.

Phosphortriamides based on (*S*)-phenyl-pyrollidin-2-yl-methylamine (**90**) have been synthesised by Tsarev *et al.* and were used in the allylic substitution 1,3-diphenylallyl acetate and gave enantioselectivities up to 62%.[160] In the doctoral studies of Barta[161] and Eggenstein[75] a set of phosphortriamides was synthesised and tested in the copper-catalysed Michael-addition of diethyl zinc to cyclohexenone (*ee*s up to 60%), the nickel-catalysed hydrovinylation of styrene (*ee*s up to 63%), the

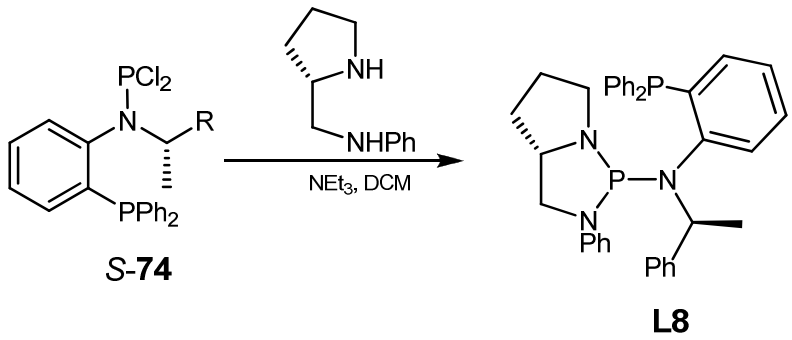
rhodium-catalysed hydroformylation of styrene (up to 28% *ee*), and the rhodium-catalysed hydrogenation of dimethyl itaconate (no conversion).

While the number of published phosphortriamides applied in asymmetric catalysis is rather limited, phosphine-phosphortriamides are completely unknown in literature. Therefore, a simple building block known for the synthesis of a monodentate phosphortriamide should be tested in the synthetic pathway for mixed bidentate phosphine ligands applied for **L1**-**7**. A diamine that is easy to synthesise and has already been used by Barta for the synthesis of a phosphortriamide is (*S*)-*N*-(pyrrolidin-2-ylmethyl)aniline. It is obtained from *L*-glutamic acid and aniline via a two-step synthesis (Scheme 2.11.1).[162]



Scheme 2.11.1: *Synthesis of (S)-N-(pyrrolidin-2-ylmethyl)aniline*

(*S*)-*N*-(pyrrolidin-2-ylmethyl)aniline was purified and degassed via distillation under reduced pressure and was applied in a coupling reaction with compound (*S*)-**74** in DCM using NEt_3 as a base (Scheme 2.11.2).



Scheme 2.11.2: *Synthesis of phosphine-phosphortriamide* ***L8***

^{31}P-NMR spectroscopy showed two doublets with a coupling constant of 52.8 Hz, indicating complete conversion to a single phosphine-phosphortriamide species **L8** (Figure 2.11.2). The chemical shift of -20.55 ppm for the phosphine signal is comparable to the phosphine resonances of the phosphine-phosphoramidites and -phosphorodiamidites. The signal of the phosphorus atom of the phosphortriamide moiety was observed at 107.7 ppm and therefore lies in the same region as the signals of the (S_P)-cofigurated monodentate phosphortriamides obtained from the same diamine by Barta.[161]

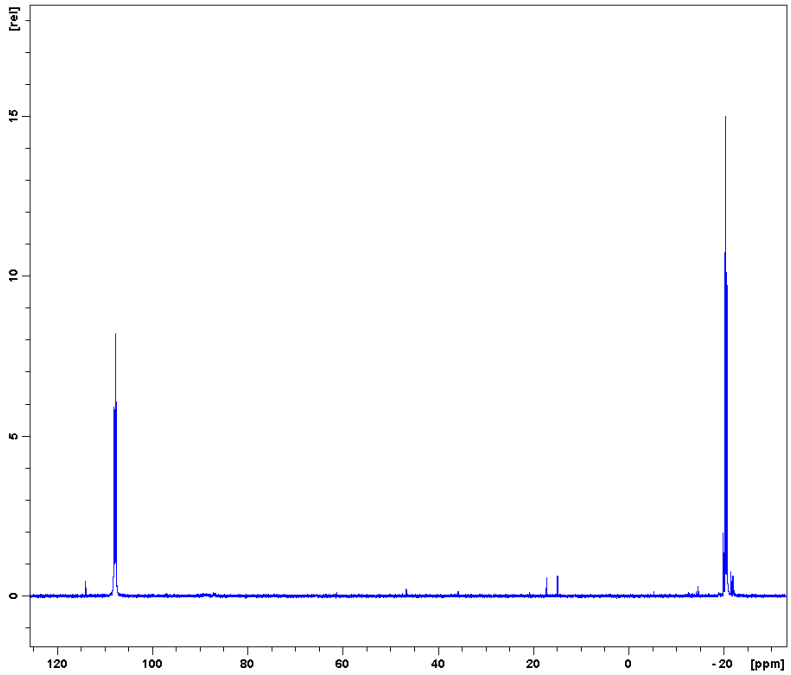


Figure 2.11.2: *^{31}P-NMR of phosphine-phosphortriamide **L8***

The compound could be purified by dissolving it in toluene and removing salts via filtration over a PTFE-membrane. A filtration over alumina or silica gave cleavage of the newly created P-N bond. Phosphine-phosphortriamide **L8** was found to be highly sensitive. A ^{31}P-NMR spectrum recorded after three weeks of storage in the glovebox just showed the signal of phosphine-amine **47**. The application of **L8** and related structures in asymmetric catalysis still needs to be evaluated in future work, but the presented results already prove the accessibility of a new class of ligands.

3 Summary & Outlook

Within this thesis eight new mixed bidentate phosphine ligands have been developed, taking **36** as a lead structure. Initially, new phosphine-phosphoramidites were synthesized by variation of the amine moiety of **36**. Instead of a phenyl-substituted phosphine-amine, a naphthyl-substituted equivalent was combined with an *S*-configurated (**L1**) and an *R*-configurated binol backbone (**L2**). **L1** and **L2** were synthesised via the same pathway as **36**, where a readily prepared phosphine-amine is coupled with a chlorophosphite. By the same route, an additional variation (**L3**) has been synthesised by replacement of the simple binol moiety with the partially hydrogenated tetrahydrobinol. NMR investigations showed the existence of different rotamers for **L1-3**.

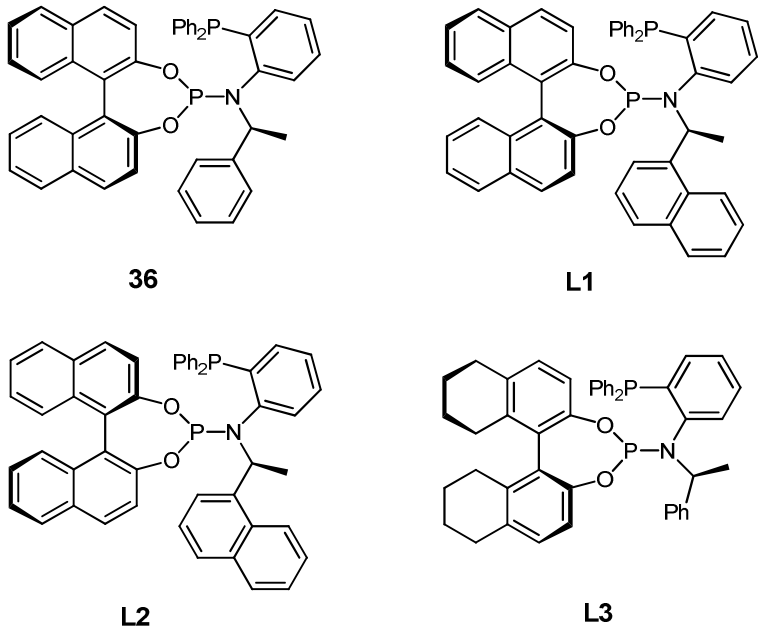


Figure 3.1: *Phosphine-phosphoramidites **36** and **L1-3***

In the asymmetric hydrogenation of C=C-, C=N- and C=O-bonds, **L1**-**3** showed high activity and enantioselectivity. Readily prepared Rh-complexes of these ligands induced up to >99 % enantiomeric excess at full conversion in the hydrogenation of unsaturated acid esters such as dimethyl itaconate with turnover frequencies of up to 1250 h^{-1}. A catalytic system of **L1-3**, an iridium salt and iodine as an additive achieved one of the highest enantiomeric excesses for the hydrogenation of 2-

substituted quinolines with up to >99 %. In combination with a ruthenium salt, **L1-3** gave high activity and acceptable enantioselectivities in the hydrogenation of a β-keto ester such as methyl 3-oxopentanoate. Interestingly, the stereochemical outcome of all hydrogenations performed with **L1-3** was mainly influenced by the configuration of the diol moiety. These results substantiate the high potential and versatility of ligands **L1-3**, so that an interesting topic for further investigations could be the application in other types of asymmetric catalysis.

The second main type of new mixed bidentate phosphine ligands presented in this thesis are phosphine-phosphorodiamidites. These ligands could not be synthesised by the same route employed before, but were prepared by the combination of *S*-NOBIN or phenyl-substituted *S*-NOBIN with a dichlorophosphite derivative of *S*- and *R*-phosphine-amine **47**. This synthetic pathway led to four different phosphine-phosphorodiamidites (**L4-7**) which have an additional chiral centre located at the phosphorus. For **L6**, the absolute configuration (S_c) at the phosphorus could be determined by single crystal X-ray analysis.

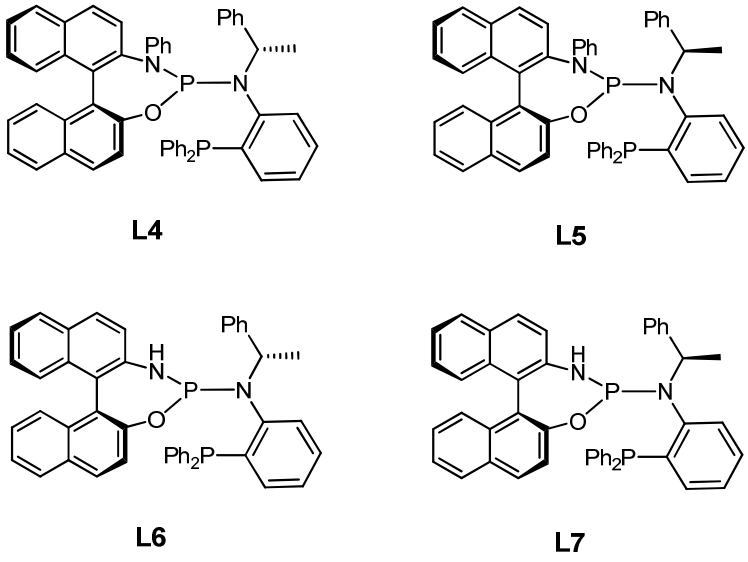


Figure 3.2: *Phosphine-Phosphorodiamidites* ***L4-7***

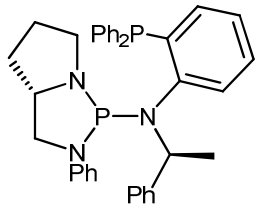
While monodentate phosphorodiamidites are rare, bidentate phosphine-phosphorodiamidites have not been reported in literature before. The similarity of chemical shifts in ^{31}P-NMR studies indicates that their electronic properties are comparable to the phosphine-phosphoramidites **L1-3**. Furthermore, variable-temperature NMR experiments also showed the existence of different rotamers that

are responsible for the existence of broad signals in proton as well as in phosphorus NMR spectra at room temperature.

Because of these similarities to **L1-3**, these ligands were also tested in asymmetric hydrogenation reactions. Readily prepared rhodium complexes of **L4-7** were applied in the hydrogenation of different unsaturated acid esters such as dimethyl itaconate. Conversion and enantioselectivities were significantly lower (up to 89 %) for these systems compared to **L1-3**. A switch of the product configuration that depends on the substituent (H- or Ph-) at the diamidite nitrogen atom of the ligand could be observed for all substrates. The iridium-catalysed hydrogenation of 2-methylquinoline resulted in high activities and moderate but notably constant enantioselectivities of ca. 80 % *R*. **L4-7** were also tested in the iridium-catalysed hydrogenation of acyclic imines such as *(E)-N*-(1-phenylethylidene)aniline. These ligands turned out to be very active for this type of reaction and here too, a switch of the product configuration that depends on the substituent (H- or Ph-) at the diamidite nitrogen atom of the ligand could be observed here. The enantiomeric excess also depends on the use of iodine as an additive.

Since **L4-7** showed very different behaviour in hydrogenation reactions compared to **L1-3** they were also tested in other asymmetric reactions such as hydrophosphorylation and hydroformylation of styrene. Hydrophosphorylation reactions catalysed by a Pd salt and **L4-7** showed good selectivities towards the branched product, but gave low conversion and enantioselectivities. The rhodium-catalysed hydroformylation of styrene led to high conversions, high selectivities to the branched product, but low enantioselectivities compared to established benchmark ligands.

Following the concept of heteroatom substitution to generate new mixed bidentate phosphine ligands the last approach of the present thesis was the synthesis of a phosphine-phosphortriamide. Bidentate phosphine-phosphortriamides are not known in literature yet, while the application of monodentate phosphortriamides has been studied for several asymmetric reactions. Within the present thesis a readily available diamine (see scheme 2.10.2) was successfully combined with the dichlorophosphite-derivative of (*S*)-phosphine-amine **47**. ^{31}P-NMR investigations showed that the obtained structure **L8** is much less stable than **L1-7**.



L8

Figure 3.3: *Phosphine-Phosphortriamide* ***L8***

Due to its high sensitivity, **L8** has not been tested yet in catalytic reactions. Further investigations could also be the synthesis of a phosphine-phosphortriamide based on a diamine with a binaphthyl backbone analogous to BINOL and an application of the resulting phosphine-phosphortriamides in asymmetric catalysis.

In general, mixed bidentate ligands are very interesting due to their wide variety of structual modifications as well as their potential for applications in different asymmetric transformations. Out of the ligands tested within this work, phosphine-phosphoramidites show the most promising results. Nevertheless, a large variety of chiral amino alcohols still opens an attractive field exploring various phosphine-phosphorodiamidite structures.

4 Experimental

4.1 General methods, solvents and reagents

4.1.1 Inert gas conditions

Reactions involving substances that are sensitive towards air or moisture were performed using standard Schlenk techniques or a glove box. Argon 4.6 (Supplier: *Westfalen*) was dried and purified via a special set-up by *MBraun* (MB 100_{HP}) and used as inert gas.

4.1.2 Autoclave techniques

For all reactions under high pressure stainless steel autoclaves made by the institute's work shop were used. They consist of a cylinder closed by a conic screw coupled with a digital or analogue pressure gauge. All catalytic hydrogenation reactions were performed in autoclaves that have a total volume of 10 mL using a glass inlet and a magnetic stirrer. The synthesis of (*S*)-4a,5,5',6,6',7,7',8,8a,8'-decahydro-1,1'-binaphthyl-2,2'-diol (literature procedure) was performed in an autoclave of 165 mL total volume.

4.1.3 Solvents

Toluene, dichloromethane and pentane were pre-distilled, then dried and degased in a set-up of IT Innovative Technology via two stainless steal columns under inert gas atmosphere packed with alumina.

Chloroform-d_1	dried over molecular sieve (4 Å), degassed under reduced pressure at 40 K, stored under argon
Dichlormethane-d_2	dried over molecular sieve (4 Å), degassed under reduced pressure at 40 K, stored under argon
Acetone-d_6	dried over molecular sieve (4 Å), degassed under reduced pressure at 40 K, stored under argon

1,4-dioxane	Aldrich 99.8%, water content < 50 ppm, dried over molecular sieve (4 Å), degassed with argon (2h)
Ethanol	pre-dried over KOH, evaporated under reduced pressure, dried over molecular sieve (3 Å), degassed with argon (2h)
Methanol	pre-dried over KOH, evaporated under reduced pressure, dried over molecular sieve (3 Å), degassed with argon (2h)
THF	pre-dried over $CaCl_2$, evaporated under reduced pressure, dried over molecular sieve (4 Å), degassed with argon (2h)

4.1.4 Commercially available reagents

(±)-BINAP	ABCR	98%
R-(+)-1,1'-Bi-2-naphtol	RCA	>99.0%
S-(+)-1,1'-Bi-2-naphtol	RCA	>99.0%
1-Brom-2-fluorbenzene	Alfa Aesar	99.0%
n-Buthyllithium (1.6M in hexane)	Alfa Aesar	
Dimethylitaconate	ABCR	99%
$KPPh_2$ (0.5M in THF)	Aldrich	
Methyl-2-acetamidoacrylate	ABCR	99%
2-Methylquinoline	Alfa Aesar	97%
Methyl-3-oxo-pentanoate	Acros	>99%
Sodium-tert-Butanolate	Aldrich	97%
N-Methyl-Pyrrolidone	Aldrich	99.5%
Palladium-(II)-acetate	Aldrich	98%
Pd/C (10% wt, dry)	Aldrich	
(*S*)-1-Phenylethylamine	ABCR	>99%

Samples of following substances were kindly provided by BASF:

(*S*)-1-(naphthalene-2-yl)ethylamine	>99%
(*S*)-1-(naphthalene-1-yl)ethylamine	98%
(*S*)-1-phenylpropane-1-amine	>99%
(*S*)-1,2,3,4-tetrahydronaphthalene-1-amine	>99%
(*S*)-2,3-dihydro-1H-indene-1-amine	>99%

All other chemicals were present in the laboratory or synthesised via known literature procedures.

4.1.5 Reagents synthesised via literature procedures

Substance	Reference
(11b*S*)-4-chlorodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine	T. Pullmann, PhD thesis, RWTH Aachen University, **2008**.
(11b*R*)-4-chlorodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine	T. Pullmann, PhD thesis, RWTH Aachen University, **2008**.
(*S*)-4a,5,5',6,6',7,7',8,8a,8'-decahydro-1,1'-binaphthyl-2,2'-diol	A. Korostylev, V.I. Tararov, C. Fischer, A. Monsees, A. Börner *J. Org. Chem.* **2004**, *69*, 3220.
(*S*)-2-fluoro-*N*-(1-phenylethyl)aniline	M. Eggenstein, A. Thomas, J. Theuerkauf, G. Franciò, W. Leitner *et al. Adv. Synth. Catal.* **2009**,*351*, 725.
(*S*)-2-(diphenylphosphino)-*N*-(1-phenylethyl)aniline	M. Eggenstein, A. Thomas, J. Theuerkauf, G. Franciò, W. Leitner *et al. Adv. Synth. Catal.* **2009**,*351*, 725.
(11b*S*)-*N*-(2-(diphenylphosphino)phenyl)-*N*-((*S*)-1-phenylethyl)dinaphtho[2,1-d:1',2'f][1,3,2]dioxaphosphepine-4-amine	M. Eggenstein, A. Thomas, J. Theuerkauf, G. Franciò, W. Leitner *et al. Adv. Synth. Catal.* **2009**,*351*, 725.
(S)-2'-hydroxy-1,1'-binaphthyl-2-yl trifluoromethanesulfonate	T. Ooi, K. Ohmatsu, K. Maruoka *J. Am. Chem. Soc.* **2007**, *129*, 2410.
(S)-2'-(methoxymethoxy)-1,1'-binaphthyl-2-yl trifluoromethanesulfonate	D. Sälinger, R. Brückner *Synlett* **2009**, *1*, 109.
(S)-N-benzyl-2'-(methoxymethoxy)-1,1'-binaphthyl-2-amine	T. Ooi, K. Ohmatsu, K. Maruoka *J. Am. Chem. Soc.* **2007**, *129*, 2410.
(S)-2'-(methoxymethoxy)-1,1'-binaphthyl-2-amine	D. Sälinger, R. Brückner *Synlett* **2009**, *1*, 109.

Substance	Reference
(S)-2'-amino-1,1'-binaphthyl-2-ol	D. Sälinger, R. Brückner *Synlett* **2009**, *1*, 109.
(S)-2'-(phenylamino)-1,1'-binaphthyl-2-ol	Š. Vyskočil, S. Jaracz, M. Smrčina, M. Štícha, V. Hanuš, M. Polášek, P. Kočovský *J. Org. Chem.* **1998**, *63*, 7727.
$[RuCl_2(p\text{-cymene})]_2$	G.T. Giuffredi, S. Purser, M. Sawicki, A.L. Thompson, V. Gouverneur *Tetrahedron:Asymmetry* **2009**, *20*, 910.
[CpPd(allyl)]	T. Yoshida, S. Otsuka *Inorg. Synth*. **1985**, *28*, 113.
pinacol H-phosphonate	A. Zwierzak *Can. J. Chem.* **1967**, *45*, 2501.
(*S*)-5-oxopyrrolidine 2-carboxanilide	K. Barta, PhD thesis, RWTH Aachen University, **2008**.
(*S*)-2-anilinomethyl-pyrrolidine	J.M. Brunel, T. Constantieux, G. Buono *J. Org. Chem.* **1999**, *64*, 8940.

4.1.6 DFT calculations

The DFT calculations* were carried out by using the Gaussian 09 program {1}. Truhlar's M06-L functional {2} was employed together with Ahlrich's triple zeta valence basis set with polarization function termed def2-TZVP {3}. Additionally the automatic density fitting option implemented in Gaussian 09 was applied {4}. The nature of stationary points located was verified by frequency calculations proving the presence of local minima (i=0) or transition states (i=1). Gibbs free energies ΔG were calculated for standard conditions.

{1} Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A.

Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

{2} Zhao, Yan; Truhlar, Donald G. Journal of Chemical Physics (2006), 125(19), 194101/1-194101/18

{3} Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297.

{4} a) Dunlap, B. I. *J. Chem. Phys.* **1983**, *78*, 3140-3142. b) Dunlap, B. *J. Mol. Struct. THEOCHEM* **2000**, *529*, 37.

* *performed by A. Uhe*

4.1.7 Analytics

Nuclear magnetic resonance (NMR)

NMR spectra were recorded at room temperature (unless indicated otherwise) on DPX-300, AV-400 and AV-600 spectrometer by Bruker. Operating frequencies:

DPX-300: ^{1}H: 300 MHz, ^{31}P: 121.5 MHz, ^{13}C: 75.5 MHz, ^{19}F: 282 MHz

AV-400: ^{1}H: 400 MHz, ^{31}P: 162 MHz, ^{13}C: 100.6 MHz, ^{19}F: 376 MHz

AV-600: ^{1}H: 600 MHz, ^{31}P: 243 MHz, ^{13}C: 151 MHz

The substance was dissolved in a deuterated solvent and the chemical shifts δ for ^{1}H and ^{13}C spectra are given in ppm using the residual solvent signals as internal standard. For ^{31}P spectra 85% phosphoric acid, for ^{19}F spectra a borotrifluoride-diethylether-complex were used as external standard. Coupling constants are given in Hertz. Multiplicity of the signals was assigned assuming spectra of first order and described by following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, m = multiplet and b = broad. For ligand characterisation several other

one dimensional (^{13}C-APT, dept45) and two dimensional NMR techniques (^{1}H-^{1}H COSY, HMBC, HSQC) were used.

Thin layer chromatography (TLC)

For thin layer chromatography POLYGRAM SIL G/UV$_{254}$ plates with a silica layer of 0.2 mm and POLYGRAM ALOX G/UV$_{254}$ with alumina layer of 0.2 mm from *Macherey-Nagel* were used. Visualisation was done by UV light.

Column Chromatography and filtration

For the purification via flash column chromatograpy basic alumina (pH >9) from Fluka or silica (KIESELGEL 60) by *Merck* with a particle size distribution of 0.040 – 0.063 mm was used. For filtration celite from Aldrich, filtration paper from *Macherey-Nagel* (under argon in combination with PTFE tubing) or PTFE syringe filter pads (0.45 µm) from Roth were used.

Gas chromatography (GC)

For identification of enantiomeric excess (or conversion) of asymmetric catalyses a SiChromat 1-4 or a SiChromat 2-8 by Siemens was used for gas chromatography under listed conditions. Integration of the observed signals was done by a HP 5890 integrator.

A) dimethyl 2-methylsuccinate

Ivadex 1, 25m, 80°C, isothermal, detector temperature 250°C (FID), 0.8 bar H_2, retention times t_r: (*R*) 15.2 min, (*S*) 15.5 min.

B) methyl 2-acetamidopropanoate

Ivadex 7, 25m, 10 min 90°C isothermal – 5°/min to 160°C – 10 min 160°C isothermal, detector temperature: 250°C (FID), 0.8 bar H_2,
retention times t_r: (*S*) 10.0 min, (*R*) 12.2 min.

C) methyl 2-acetamido-3-phenylpropanoate

Lipodex E, 25m, 100-180 °C 2°/min – 10 min 180° C isothermal, detector temperature: 250°C (FID), 0.57 bar H_2, retention times t_r: (*S*) 34.7 min, (*R*) 35.2 min.

D) 2-methyl-1,2,3,4-tetrahydroquinoline

Chirasil-Dex-CB, 25m, 80-120°C, 2°C/min, detector temperature: 250°C (FID), 1.0 bar H_2, retention times t_r: (*S*) 15.3 min, (*R*) 16.6 min.

E) methyl 3-hydroxypentanoate

Lipodex E, 25 m, 10 min 80°C isothermal – 10°/min to 150°C – 15 min 150° C isothermal, detector temperature: 250°C (FID), 0.8 bar H_2, retention times t_r: (*S*) 12.2 min, (*R*) 12.5 min.

F) 1,1,1-trifluoropropan-2-yl acetate

Chirasil-Dex-CB, 5 min 50°C isothermal - 25°C/min to 160 °C, detector temperature: 250°C (FID), 1 bar N_2, retention times t_r: (*S*) 3.04 min, (*R*) 3.45 min.

G) 3-phenylpropanal (linear) / 2-phenylpropanal (branched)

Ivadex, 25 m, 2 min 70°C isothermal – 2°C/min to 120°C – 15°C/min to 180°C, detector temperature: 250°C (FID), 1 bar H_2, retention times t_r: (branched, *S*) 12.44 min, (branched, *R*) 11.99 min, (linear) 13.97 min.

High performance liquid chromatography (HPLC)

For identification of enantiomeric excess (or conversion) of asymmetric catalyses a Jasco HPLC device with a Jasco UV diode array detector was used for HPLC measurements under following conditions.

A) 2-butyl-1,2,3,4-tetrahydroquinoline

Chiralcel OD-H, heptane/*i*PrOH 98/2, 0.5 mL/min, 20°C, UV detector 250 nm, retention times t_r: (*R*) 12.3 min, (*S*) 14.2 min.

B) 2-phenyl-1,2,3,4-tetrahydroquinoline

Chiralcel OD-H, heptane/*i*PrOH 90/10, 0.5 mL/min, 20°C, UV detector 250 nm, retention times t_r: (*S*) 19.1 min, (*R*) 23.9 min.

C) *N*-(1-phenylethyl)aniline

Chiralcel OD-H, heptane/*i*PrOH 97/3, 0.5 mL/min, 5 °C, UV detector 220 nm, retention times t_r: (*R*) 20.2 min, (*S*) 24.7 min.

D) 4,4,5,5-Tetramethyl-2-(1-phenylethyl)1,3,2-dioaphospholane 2-oxide

Chiralpak AD-H, heptane/ethanol 95/5, 0.5 mL/min, 20 °C, UV detector 209 nm, retention times t_r: 29.72 min, 42.63 min.

Mass spectroscopy (MS)

Mass spectra were recorded on a Finnigan MAT 95 (70 eV) at the IAC RWTH Aachen. Signals with an intensity >10 and the observed value of the high resolution measurement were listed for characterisation. SIMS measurements of ionic compounds were performed using an NBS matrix and a Cs^+ gun.

X-Ray analysis

For single crystal x-ray diffraction measurements* crystals were mounted on glass fibers. Geometry and intensity data were collected with a Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an Incoatec microsource (Mo-Kα radiation, λ = 0.71073 Å, multilayer optics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT+ {1} and corrected for absorption with SADABS {2}. The structure was solved by direct methods and refined on F2 with SHELXL-97 {3}.

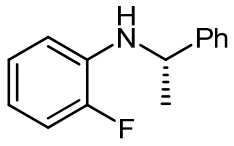
{1} Bruker AXS, SAINT+, Program for Reduction of Data collected on Bruker CCD Area Detector Diffractometer V. 6.02. Bruker AXS Inc., Madison, Wisconsin, USA,1999.

{2} Bruker AXS, SADABS, Program for Empirical Absorption Correction of Area Detector Data V 2004/1, Bruker AXS Inc., Madison, Wisconsin, USA, 2004.
{3} G. M. Sheldrick *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.
* performed in the group of Prof. U. Englert, IAC RWTH Aachen

4.2 Syntheses and general procedures

4.2.1 Syntheses

4.2.1.1 (*R*)-2-fluoro-*N*-(1-phenylethyl)aniline (**41**)



This synthesis was performed under argon. *rac*-BINAP (280.0 mg, 0.45 mmol) and palladium acetate (67.3 mg, 0.30 mmol) were dissolved in toluene (15 mL). 1-Bromo-2-fluorobenzene (60 mmol, 6.56 mL) and (*R*)-α-Methyl-benzylamine (60 mmol, 6.92 mL) were added to the yellow solution. Adding sodium *tert*-butanolate (70 mmol, 6.74 g) the solution turned purple. The mixture was refluxed for 48 h and conversion was controlled by TLC. After cooling down to room temperature the mixture was quenched with destilled water (20 mL) and extracted with dichloromethane (3x20 mL). The organic phase was dried over $NaSO_4$ and filtered. The solvent was removed under reduced pressure and the oily brownish residue was purified by column chromatography (SiO_2, pentane:ethylacetate 10:1, R_f = 0.64). The product was obtained as a colourless oil that slowly solidified to a waxy solid.

Yield: 10.7 g, (50 mmol, 83 %).

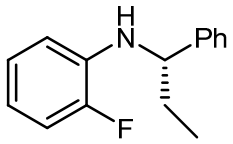
^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.51 (d, *J* = 6.6 Hz, 3H, CH_3), 4.26 (m, 1H, NH), 6.40 (m, 1H, CH), 6.52 (m, 1H, Ar), 6.78 (m, 1H, Ar), 6.92 (m, 1H, Ar), 7.20 (m, 1H, Ar), 7.31 (m, 5H, Ar) ppm.

^{13}C{^{1}H}-NMR ($CDCl_3$, 75 MHz): δ = 25.1 (CH_3), 53.3 (CH), 113.2 (d, *J* = 3.0 Hz, Ar, CH), 114.2 (d, *J* = 18.8 Hz, Ar, CH), 116.5 (d, *J* = 7.0 Hz, Ar, CH), 124.4 (d,

J = 3.4 Hz, Ar, CH), 125.8 (Ar, CH), 127.0 (Ar, CH), 128.7 (Ar, CH), 135.7 (d, *J* = 11.4 Hz, Ar, C_q), 144.8 (Ar, C_q), 151.4 (d, *J* = 237.4 Hz, Ar, C_q) ppm.

^{19}F-NMR ($CDCl_3$, 280 MHz): δ = -136.5 (s) ppm.

4.2.1.2 (*S*)-2-fluoro-*N*-(1-phenylpropyl)aniline (**42**)



This synthesis was performed under argon. *rac*-BINAP (186.7 mg, 0.30 mmol) and palladium acetate (44.8 mg, 0.20 mmol) were dissolved in toluene (15 mL). 1-Bromo-2-fluorobenzene (20 mmol, 2.2 mL) and (*S*)-1–phenylpropane-1-amine (20 mmol, 2.54 mL) were added to the yellow solution. Adding sodium *tert*-butanolate (30 mmol, 2.883 g) the solution turned purple. The mixture was refluxed for 168 h and conversion was controlled by TLC. After cooling down to room temperature the reaction was quenched with destilled water (20 mL) and extracted with dichloromethane (3x20 mL). The organic phase was dried over $NaSO_4$ and filtered. The solvent was removed under reduced pressure and the oily brownish residue was purified by column chromatography (SiO_2, pentane:ethylacetate 20:1, R_f = 0.54). The product was obtained as an orange oil.

Yield: 3.2577 g (14.2 mmol, 71 %)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.1 Hz, 3H, CH_3), 1.86 (m, 2H, CH_2), 4.23 (m, 1H, CH), 4.32 (b, 1H, NH), 6.42 (m, 1H, Ar), 6.54 (m, 1H, Ar), 6.80 (m, 1H, Ar), 6.94 (m, 1H, Ar), 7.31 (m, 5H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 11.0 (CH_3), 31.8 (CH_2), 59.7 (CH), 113.2 (d, *J* = 3.0 Hz, Ar), 114.2 (Ar), 114.4 (Ar), 116.4 (d, *J* = 6.7 Hz, Ar), 124.5 (d, *J* = 3.4 Hz, Ar), 126.5 (Ar), 127.1 (Ar), 128.6 (Ar), 136.1 (d, *J* = 12.8 Hz, Ar), 143.6 (Ar), 150.0 (Ar) 153.1 (Ar) ppm.

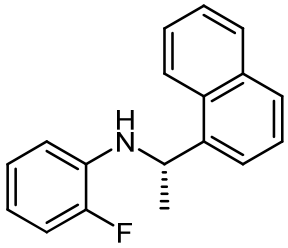
^{19}F-NMR (280 MHz, $CDCl_3$): δ = -136.43 ppm.

[α]$_D^{20}$ = -19.0 (c = 0.67, DCM)

MS (EI): m/z (rel. intensity) = 229 (M^+, 11 %), 201 (12 %), 200 (100 %), 134 (12 %), 111 (10 %), 105 (59 %), 91 (18 %), 77 (27 %).

HR-MS (ESI): $C_{15}H_{16}FN$ (M^+) calculated: 229.126
found: 229.126

4.2.1.3 (*S*)-2-fluoro-*N*-(1-(naphthalene-1-yl)ethyl)aniline (**43**)



This synthesis was performed under argon. *rac*-BINAP (62.2 mg, 0.10 mmol) and palladium acetate (16.8 mg, 0.075 mmol) were dissolved in toluene (15 mL). 1-Bromo-2-fluorobenzene (30 mmol, 3.3 mL) and (*S*)-1-(naphthalene-1-yl)ethanamine (30 mmol, 5.16 g) were added to the yellow solution. Adding sodium *tert*-butanolate (45.0 mmol, 4.33 g) the solution turned purple. The mixture was refluxed for 96 h and conversion was controlled by TLC. After cooling down to room temperature the reaction was quenched with destilled water (20 mL) and extracted with dichloromethane (3x20 mL). The organic phase was dried over $NaSO_4$ and filtered. The solvent was removed under reduced pressure and the oily brownish residue was purified by column chromatography (SiO_2, pentane:ethylacetate 20:1, R_f = 0.54). The product was obtained as a yellow oil that slowly solidified to a waxy solid.

Yield: 7.46 g (28 mmol, 93 %)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.70 (d, *J* = 6.5 Hz, 3H, CH_3), 4.42 (b, 1H, NH), 5.29 (m, 1H, CH), 6.29 (m, 1H, Ar), 6.54 (m, 1H, Ar), 6.74 (m, 1H, Ar), 6.98 (m, 1H, Ar), 7.41 (m, 1H, Ar), 7.57 (m, 3H, Ar), 7.76 (m, 1H, Ar), 7.91 (m, 1H, Ar), 8.16 (m, 1H, Ar) ppm.

$^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 75 MHz): δ = 23.8 (CH_3), 49.5 (CH), 113.2 (d, *J* = 3.4 Hz, Ar, CH), 114.2 (d, *J* = 18.9 Hz, Ar, CH), 116.5 (d, *J* = 6.8 Hz, Ar, CH), 122.5 (d, *J* = 17.5 Hz, Ar, CH), 124.5 (Ar, CH), 124.6 (Ar, CH), 125.6 (Ar, CH), 125.9 (Ar, CH),126.2 (Ar, CH), 127.6 (Ar, CH), 129.2 (Ar, CH), 130.7 (Ar, C_q), 134.2 (Ar, C_q), 135.6 (d, *J* = 11.5 Hz, Ar, C_q), 139.5 (Ar, C_q), 151.5 (d, *J* = 237.5 Hz, Ar, C_q) ppm.

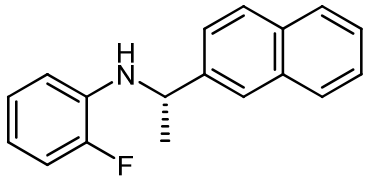
^{19}F-NMR ($CDCl_3$, 280 MHz): δ = -136.6 (s) ppm.

$[\alpha]_D^{20}$ = +166.6 (c = 0.53, DCM)

MS (EI): m/z (rel. intensity) = 265 (M^+, 27 %), 250 (9 %), 155 (100 %), 128 (8 %), 122 (6 %), 115 (5 %), 95 (3 %), 75 (2 %).

HR-MS (ESI): $C_{18}H_{16}FN$ (M^+) calculated: 265.126
found: 265.126

4.2.1.4 (*S*)-2-fluoro-*N*-(1-(naphthalene-2-yl)ethyl)aniline (**44**)



This synthesis was performed under argon. *rac*-BINAP (186.7 mg, 0.30 mmol) and palladium acetate (44.8 mg, 0.20 mmol) were dissolved in toluene (15 mL). 1-Bromo-2-fluorobenzene (20 mmol, 2.2 mL) and (*S*)-1-(naphthalene-2-yl)ethanamine (20 mmol, 3.425 g) were added to the yellow solution. Adding sodium *tert*-butanolate (30 mmol, 2.883 g) the solution turned purple. The mixture was refluxed for 72 h and conversion was controlled by TLC. After cooling down to room temperature the reaction was quenched with destilled water (100 mL) and extracted with dichloromethane (3x50 mL). The organic phase was dried over $NaSO_4$ and filtered. The solvent was removed under reduced pressure and the oily brownish residue was purified by column chromatography (SiO_2, pentane:ethylacetate 20:1, R_f = 0.54). The product was obtained as a yellow solid.

Yield: 3.5787 g (13.5 mmol, 68 %)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.52 (d, *J* = 6.6 Hz, 3H, CH_3), 4.29 (b, 1H, NH), 4.55 (quin, *J* = 6.6 Hz, 1H, CH), 6.40 (m, 2H, Ar), 6.67 (m, 1H, Ar), 6.88 (m, 1H, Ar), 7.36 (m, 3H, Ar), 7.67 (m, 4H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 25.2 (CH_3), 53.7 (CH), 113.5 (Ar), 114.3 (Ar), 114.5 (Ar), 116.7 (Ar), 124.3 (Ar), 124.6 (Ar), 125.7 (Ar), 126.3 (Ar), 127.9 (Ar), 128.7 (Ar), 133.0 (Ar), 133.7 (Ar), 135.9 (Ar), 142.5 (Ar), 150.0 (Ar), 153.2 (Ar) ppm.

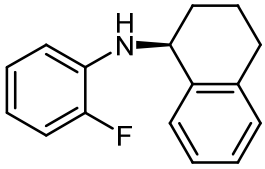
^{19}F-NMR (280 MHz, $CDCl_3$): δ = -136.47 ppm.

$[\alpha]_D^{20}$ = -12.2 (c = 0.53, DCM)

MS (EI): m/z (rel. intensity) = 265 (M^+, 5 %), 205 (19 %), 190 (16 %), 170 (40 %), 156 (11 %), 155 (100 %).

HR-MS (ESI): $C_{18}H_{16}FN$ (M^+) calculated: 265.126
found: 265.126

4.2.1.5 (*S*)-*N*-(2-fluorophenyl)-1,2,3,4-tetrahydronaphthalene-1-amine (**45**)



This synthesis was performed under argon. *rac*-BINAP (373.4 mg, 0.60 mmol) and palladium acetate (89.6 mg, 0.40 mmol) were dissolved in toluene (30 mL). 1-Bromo-2-fluorobenzene (40 mmol, 4.36 mL) and (*S*)-1,2,3,4-tetrahydronaphtalene-1-amine (40 mmol, 5.83 mL) were added to the yellow solution. Adding sodium *tert*-butanolate (60 mmol, 5.766 g) the solution turned purple. The mixture was refluxed for 120 h and conversion was controlled by TLC. After cooling down to room temperature the reaction was quenched with destilled water (100 mL) and extracted with dichloromethane (3x50 mL). The organic phase was dried over $NaSO_4$ and filtered.

The solvent was removed under reduced pressure and the oily brownish residue was purified by column chromatography (SiO_2, pentane:ethylacetate 20:1, R_f = 0.54). The product was obtained as an orange oil.

Yield: 5.583 g (23.1 mmol, 58 %)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.83 (m, 4H, CH_2), 2.75 (m, 2H, CH_2), 4.10 (b, 1H, NH), 4.57 (m, 1H, CH), 6.54 (m, 1H, Ar), 6.77 (m, 1H, Ar), 6.92 (m, 2H, Ar) 7.10 (m, 3H, Ar), 7.32 (m, 1H, Ar), ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 19.5 (CH_2), 28.9 (CH_2), 29.4 (CH_2), 51.0 (CH), 112.2 (d, *J* = 3.2 Hz, 3.2, Ar), 114.5 (Ar), 114.8 (Ar), 116.3 (d, *J* = 7.2 Hz, Ar), 124.6 (d, *J* = 3.2 Hz, Ar), 126.2 (Ar), 127.3 (Ar), 129.2 (d, *J* = 4.5 Hz, Ar), 136.0 (d, *J* = 12.1 Hz, Ar), 137.7 (d, *J* = 2.7 Hz, Ar), 146.2 (Ar) 150.0 (Ar) ppm.

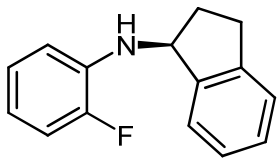
^{19}F-NMR (280 MHz, $CDCl_3$): δ = -136.15 ppm.

$[\alpha]_D^{20}$ = -6.6 (c = 0.72, DCM)

MS (EI): m/z (rel. intensity) = 241 (M, 17 %), 231 (71 %), 230 (100 %), 129 (63 %), 128 (34 %), 127 (14 %), 115 (37 %), 111 (79 %), 91 (15 %), 83 (11 %).

HR-MS (ESI): $C_{16}H_{16}FN$ (M)	calculated:	241.126
	found:	241.126

4.2.1.6 (*S*)-*N*-(2-fluorophenyl)-2,3-dihydro-1H-indene-1-amine (**46**)



This synthesis was performed under argon. *rac*-BINAP (211.0 mg, 0.34 mmol) and palladium acetate (50.6 mg, 0.22 mmol) were dissolved in toluene (30 mL). 1-Bromo-2-fluorobenzene (40 mmol, 4.36 mL) and (*S*)-1,2,3,4-tetrahydronaphtalene-1-amine (40 mmol, 5.13 mL) were added to the yellow solution. Adding sodium *tert*-butanolate

(60 mmol, 5.766 g) the solution turned purple. The mixture was refluxed for 168 h and conversion was controlled by TLC. After cooling down to room temperature the reaction was quenched with destilled water (100 mL) and extracted with dichloromethane (3x50 mL). The organic phase was dried over $NaSO_4$ and filtered. The solvent was removed under reduced pressure and the oily brownish residue was purified by column chromatography (SiO_2, pentane:ethylacetate 20:1, R_f = 0.54). The product was obtained as an orange oil.

Yield: 3.3654 g (14.8 mmol, 37 %)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.98 (m, 1H, CH_2), 2.65 (m, 1H, CH_2), 2.89-3.14 (m, 2H, CH_2), 4.24 (b, 1H, NH), 5.07 (m, 1H, CH), 6.69 (m, 1H, Ar), 6.90-7.44 (m, 11H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 30.3 (CH_2), 33.8 (CH_2), 58.5 (CH), 112.9 (Ar), 114.5 (Ar), 114.8 (Ar), 116.9 (Ar), 124.3 (Ar), 124.6 (d, *J* = 3.9 Hz, Ar), 124.9 (Ar), 125.2 (Ar), 126.7 (Ar), 128.1 (Ar), 143.6 (Ar), 144.0 (Ar) ppm.

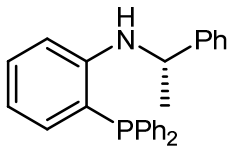
^{19}F-NMR (280 MHz, $CDCl_3$): δ = -136.14 ppm.

$[\alpha]_D^{20}$ = +41.6 (c = 0.68, DCM)

MS (EI): m/z (rel. intensity) = 227 (M, 27 %), 187 (14 %), 186 (100 %), 185 (35 %), 183 (18 %), 170 (10 %), 165 (24 %), 117 (81 %), 116 (89 %), 115 (86 %), 111 (93 %), 91 (18 %), 89 (12 %), 84 (10 %), 83 (15 %).

HR-MS (ESI): $C_{15}H_{14}FN$ (M)	calculated:	227.110
	found:	227.110

4.2.1.7 (*R*)-2-(diphenylphosphino)-*N*-(1-phenylethyl)aniline (**47**)



Synthesis and work-up were performed under argon. Potassium diphenylphosphide (60 mmol, 120 mL, 0.5M in THF) was transferred into a three-necked round bottom flask. THF was removed under reduced pressure and a solution of **41** (60 mmol, 12.9 g) in 1,4-dioxane (60 mL) was added. The reaction mixture was refluxed for 168 h and conversion was controlled via ^{31}P-NMR spectroscopy. The solvent was removed under reduced pressure and degassed water (50 mL) was added to the residue. The product was extracted with dichloromethane (3 x 40 mL). The collected organic phase was dried with degassed and dried sodium sulfate. After filtration and remove of the solvent the crude product was obtained as yellow oil. It was dissolved in toluene (10 mL) and ethanol (30 mL) was added. At -18°C the product is obtained via phase separation from the lower of two phases in sufficient purity (≥95 % → ^{31}P-NMR) for further syntheses. The product was obtained as yellow oil that slowly solidified at room temperature.

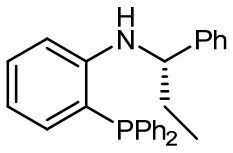
Yield: 12.6 g (32.8 mmol, 55 %)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.26 (d, *J* = 6.4 Hz, 3H, CH_3), 4.38 (quin, *J* = 6.4 Hz, 1H, CH), 4.91 (b, 1H, NH), 6.29 (dd, *J* = 5.1 Hz, *J* = 8.4 Hz, 1H, Ar), 6.48 (t, *J* = 7.5 Hz, 1H, Ar), 6.75 (td, *J* = 7.5 Hz, 1.8 Hz, 1H, Ar), 6.95-7.20 (m, 8H, Ar), 7.29 (m, 7H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 25.3 (CH_3), 53.6 (CH), 111.4 (d, *J* = 2.0 Hz, Ar, CH), 117.1 (d, *J* = 2.0 Hz, Ar, CH), 118.6 (d, *J* = 2.0 Hz, Ar, C_q), 125.8 (Ar, CH),126.7 (Ar, CH), 128.52 (Ar, CH), 128.58 (Ar, CH), 128.68 (Ar, CH), 128.82 (Ar, CH), 128.85 (Ar, CH), 130.5 (Ar, CH), 133.6 (d, *J* = 4.2 Hz, Ar, CH), 133.8 (d, *J* = 4.2 Hz, Ar, CH), 134.6 (d, *J* = 6.9 Hz, Ar, CH), 135.4 (d, *J* = 7.9 Hz, Ar, C_q), 135.5 (d, *J* = 7.9 Hz, Ar, C_q), 145.2 (Ar, C_q), 149.7 (d, *J* = 16.1 Hz, Ar, C_q) ppm.

^{31}P{^{1}H}-NMR ($CDCl_3$, 125 MHz): -19.9 (s) ppm.

4.2.1.8 (S)-2-(diphenylphosphino)-*N*-(1-phenylpropyl)aniline (**48**)



Synthesis and work-up were performed under argon. Potassium diphenylphosphide (10 mmol, 20 mL, 0.5M in THF) was transferred into a three-necked round bottom flask. THF was removed under reduced pressure and a solution of **42** (10 mmol, 2.2929 g) in 1,4-dioxane (40 mL) was added. The reaction mixture was refluxed for 72 h and conversion was controlled via ^{31}P-NMR spectroscopy. The solvent was removed under reduced pressure and degassed water (30 mL) was added to the residue. The product was extracted with dichloromethane (3 x 25 mL). The collected organic phase was dried with degassed and dried sodium sulfate. After filtration and remove of the solvent the crude product was obtained as yellow oil. It was dissolved in toluene (10 mL), filtered over neutral alumina and eluted with additional toluene (30 mL). The solvent was removed under reduced pressure and the residue was taken up in pentane (15 mL). At -18°C the product was obtained as a colourless highly viscous oil.

Yield: 3.06 g (7.73 mmol, 77 %)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 0.62 (t, *J* = 7.4 Hz, 3H, CH_3), 1.50 (qint, *J* = 7.3 Hz, 2H, CH_2), 4.09 (m, 1H, CH), 4.93 (b, 1H, NH), 6.25 (m, 1H, Ar), 6.39 (m, 1H, Ar), 6.71 (m, 1H, Ar), 7.08 (m, 16H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 10.7 (CH_3), 31.8 (CH_2), 59.5 (CH), 111.4 (d, *J* = 2.3 Hz, Ar), 117.2 (d, *J* = 3.3 Hz, Ar), 118.7 (Ar), 118.8 (Ar), 126.4 (Ar), 126.8 (Ar), 128.4 (Ar), 128.5 (Ar), 128.6 (d, *J* = 2.8 Hz, Ar), 128.7 (d, *J* = 2.8 Hz, Ar), 128.9 (Ar), 130.6 (Ar), 133.7 (d, *J* = 3.4 Hz, Ar), 133.9 (d, *J* = 3.4 Hz, Ar), 134.1 (Ar), 134.5 (Ar), 134.6 (Ar), 135.4 (Ar), 135.5 (Ar), 135.6 (Ar), 135.7 (Ar), 143.8 (Ar), 149.7 (Ar), 149.9 (Ar) ppm.

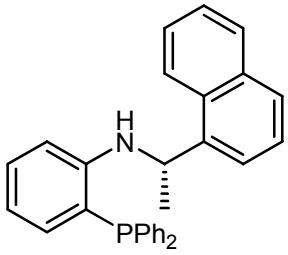
^{31}P{^{1}H}-NMR ($CDCl_3$, 125 MHz): δ = -19.41 (s) ppm.

$[\alpha]_D^{20}$ = +246.7 (c = 0.55, DCM)

MS (EI): m/z (rel. intensity) = 395 (M^+, 49 %), 367 (27 %), 366 (100 %), 305 (10 %), 304 (44 %), 288 (10 %), 277 (28 %), 276 (18 %), 262 (50 %), 261 (13 %), 202 (58 %), 201 (100 %), 200 (27 %), 186 (34 %), 183 (42 %), 182 (18 %), 124 (24 %), (70 %), 108 (42 %), 107 (20), 105 (21), 91 (28 %), 78 (21 %), 77 (40 %), 72 (47 %), 71 (44 %).

HR-MS (ESI): $C_{27}H_{26}NP$ (M^+) calculated: 395.179
found: 395.180

4.2.1.9 (*S*)-2-(diphenylphosphino)-*N*-(1-(naphthalene-1-yl)ethyl)aniline (**49**)



Synthesis and work-up were performed under argon. Potassium diphenylphosphide (30 mmol, 60 mL, 0.5M in THF) was transferred into a three-necked round bottom flask. THF was removed under reduced pressure and a solution of **43** (30 mmol, 6.3622 g) in 1,4-dioxane (30 mL) was added. The reaction mixture was refluxed for 168 h and conversion was controlled via ^{31}P-NMR spectroscopy. The solvent was removed under reduced pressure and degassed water (30 mL) was added to the residue. The product was extracted with dichloromethane (3 x 25 mL). The collected organic phase was dried with degassed and dried sodium sulfate. After filtration over Celite® and remove of the solvent the crude product was obtained as yellow oil. It was dissolved in dichloromethane (10 mL) and pentane (18 mL) was added. At -18°C the product is obtained as colourless crystals.

Yield: 6.3 g (14.6 mmol, 52 %)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.44 (d, *J* = 6.6 Hz, 3 H), 5.09 (b, 1H, NH), 5.21 (m, 1H, CH), 6.19 (m, 1H, Ar), 6.51 (m, 1H, Ar), 6.82 (m, 1H, Ar), 6.93 (m, 1H, Ar), 7.23 7.61 (m, 14H, Ar), 7.65 (m, 1H, Ar), 7.84 (m, 1H, Ar), 8.07 (m, 1H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 23.9 (CH_3), 49.7 (CH), 111.5 (Ar), 117.2 (Ar), 118.6 (d, *J* = 7.6 Hz, Ar), 122.4 (d, *J* = 8.5 Hz, Ar), 125.4 (Ar), 126.0 (d, *J* = 8.5 Hz, Ar), 127.4 (Ar), 128.3 (Ar), 128.7 (d, *J* = 7.6 Hz, Ar), 128.9 (d, *J* = 5.7 Hz, Ar), 129.2 (Ar), 130.7 (d, *J* = 5.7 Hz, Ar), 133.7 (Ar), 133.9 (Ar), 134.1 (Ar), 134.7 (d, *J* = 7.6 Hz, Ar), 135.4 (Ar), 135.5 (Ar), 135.6 (Ar), 140.0 (Ar), 149.5 (Ar), 149.7 (Ar) ppm.

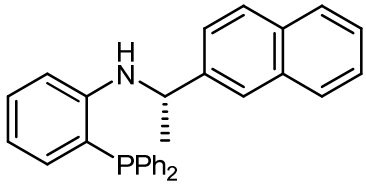
^{31}P{^{1}H}-NMR ($CDCl_3$, 125 MHz): δ = -18.8 (s) ppm.

$[\alpha]_D^{20}$ = +143.1 (c = 0.62, DCM)

MS (EI): m/z (rel. intensity) = 431 (M^+, 100 %), 416 (44 %), 338 (10 %), 304 (12 %), 303 (45 %), 288 (32 %), 276 (17 %), 261 (12 %), 198 (30 %), 183 (18 %), 155 (27 %), 153 (11 %), 77 (4 %).

HR-MS (ESI): $C_{30}H_{27}NP$ (M^+ + H) calculated: 432.187
found: 432.187

4.2.1.10 (*S*)-2-(diphenylphosphino)-*N*-(1-(naphthalene-2-yl)ethyl)aniline (**50**)



Synthesis and work-up were performed under argon. Potassium diphenylphosphide (23.98 mmol, 47.96 mL, 0.5M in THF) was transferred into a three-necked round bottom flask. THF was removed under reduced pressure and a solution of **44** (23.98 mmol, 7.5 g) in 1,4-dioxane (40 mL) was added. The reaction mixture was refluxed for 72 h and conversion was controlled via ^{31}P-NMR spectroscopy. The solvent was removed under reduced pressure and degassed water (30 mL) was

added to the residue. The product was extracted with dichloromethane (3 x 25 mL). The collected organic phase was dried with degassed and dried sodium sulfate. After filtration and remove of the solvent the crude product was obtained as yellow oil. It was dissolved in toluene (10 mL), filtered over neutral alumina and eluted with additional toluene (30 mL). After removing the solvent under reduced pressure the residue was taken up in dichloromethane (5 mL) and pentane (10 mL) was added. At -18°C the product is obtained as colourless crystals.

Yield: 2.01 g (7.56 mmol, 32 %)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.33 (d, *J* = 7.2 Hz, 3H, CH_3), 4.45 (m, 1H, CH), 4.99 (b, 1H, NH), 6.29 (m, 1H, Ar), 6.39 (m, 1H, Ar), 6.73 (m, 1H, Ar), 6.86 (m, 1H, Ar), 7.09 (m, 2H, Ar), 7.23 (m, 11H, Ar), 7.55 (m, 4H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 25.1 (CH_3), 53.8 (CH), 111.7 (d, *J* =2.3 Hz, Ar), 117.3 (d, *J* = 3.7 Hz, Ar), 118.7 (Ar), 118.8 (Ar), 124.2 (Ar), 124.5 (Ar), 125.6 (Ar), 126.0 (Ar), 127.8 (Ar), 127.9 (Ar), 128.5 (Ar), 128.7 (d, ^{3}J = 3.0 Hz, Ar), 128.8 (d, *J* = 2.3 Hz, Ar), 128.9 (Ar), 129.0 (Ar), 130.7 (Ar), 133.6 (Ar), 133.7 (Ar), 133.8 (Ar), 133.9 (Ar), 134.0 (Ar), 134.7 (d, *J* = 6.4 Hz, Ar), 135.5 (Ar), 135.6 (Ar), 135.7 (Ar), 142.8 (Ar), 149.7 (Ar), 149.9 (Ar) ppm.

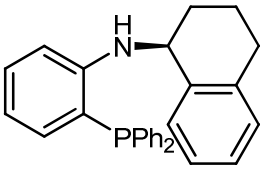
^{31}P{^{1}H}-NMR ($CDCl_3$, 125 MHz): δ = -19.92 (s) ppm.

$[\alpha]_D^{20}$ = +29.5 (c = 0.41, DCM)

MS (EI): m/z (rel. intensity) = 431 (M^+, 100 %), 430 (16 %), 417 (16 %), 416 (49 %), 387 (11 %), 338 (10 %), 279 (19 %), 276 (13 %), 275 (12 %), 202 (61 %), 201 (100 %), 198 (14 %), 186 (33 %), 183 (41 %), 170 (10 %), 167 (29 %), 156 (12 %), 155 (70 %), 154 (18 %), 153 (14), 152 (14), 149 (70 %), 127 (16 %), 124 (25 %), 108 (42 %), 107 (20 %), 86 (29 %), 84 (45 %), 78 (20 %), 77 (31 %), 71 (13 %), 70 (12%).

HR-MS (ESI): $C_{30}H_{26}NP$ (M^+) calculated: 431.179
found: 431.179

4.2.1.11 (*S*)-*N*-(2-(diphenylphosphino)phenyl)-1,2,3,4-tetrahydronaphthalene-1 amine (**51**)



Synthesis and work-up were performed under argon. Potassium diphenylphosphide (22.30 mmol, 44.6 mL, 0.5M in THF) was transferred into a three-necked round bottom flask. THF was removed under reduced pressure and a solution of **45** (22.30 mmol, 5.383 g) in 1,4-dioxane (20 mL) was added. The reaction mixture was refluxed for 168 h and conversion was controlled via ^{31}P-NMR spectroscopy. The solvent was removed under reduced pressure and degassed water (200 mL) was added to the residue. The product was extracted with dichloromethane (3 x 30 mL). The collected organic phase was dried with degassed and dried sodium sulfate. After filtration and remove of the solvent the crude product was obtained as yellow oil. It was dissolved in toluene (10 mL), filtered over neutral alumina and eluted with additional toluene (30 mL). After removing the solvent under reduced pressure the residue was taken up in toluene (5 mL) and pentane (10 mL) was added. At -18°C the product is obtained as slightly yellowish highly viscous oil.

Yield: 6.98 g (17.13 mmol, 77 %)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.50-1.86 (m, 4H, CH_2), 2.57 (m, 2H, CH_2), 4.48 (b, 1H, NH), 4.72 (m, 1H, CH), 6.52 (m, 1H, Ar), 6.66-7.26 (m, 17H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 19.7 (CH_2), 29.0 (CH_2), 29.4 (CH_2), 51.6 (CH), 110.4 (Ar), 117.0 (d, *J* = 3.8 Hz, Ar), 119.1 (d, *J* = 8.4 Hz, Ar), 126.1 (Ar), 127.0 (Ar), 128.5 (Ar), 128.6 (Ar), 128.70 (Ar), 128.77 (Ar), 128.80 (Ar), 128.84 (Ar), 128.9 (Ar), 130.8 (Ar), 133.6 (Ar), 133.8 (d, *J* = 7.5 Hz, Ar), 133.9 (Ar), 135.1 (d, *J* = 5.8 Hz, Ar), 135.4 (Ar), 135.5 (Ar), 135.6 (Ar), 137.6 (Ar), 137.8 (Ar), 150.0 (Ar), 150.2 (Ar) ppm.

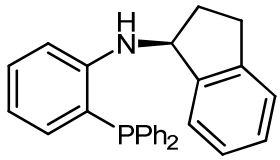
^{31}P{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = -19.72 ppm.

$[\alpha]_D^{20}$ = +34.8 (c = 0.63, DCM)

MS (EI): m/z (rel. intensity) = 407 (M, 12 %), 278 (16 %), 277 (33 %), 276 (14 %), 254 (14 %), 253 (13 %), 252 (12 %), 233 (19 %), 216 (12 %), 215 (27 %), 202 (43 %), 201 (100 %), 198 (16 %), 186 (23 %), 185 (11 %), 183 (51 %), 152 (12 %), 149 (13 %), 131 (42 %), 130 (22 %), 129 (13 %), 128 (11 %), 124 (19 %), 111 (15 %), 108 (35 %), 107 (21 %), 92 (10 %), 91 (29 %), 86 (29 %), 84 (45 %), 78 (20 %), 77 (38 %).

HR-MS (ESI): $C_{28}H_{26}NP$ (M) calculated: 407.179
found: 407.179

4.2.1.12 (*S*)-*N*-(2-(diphenylphosphino)phenyl)-2,3-dihydro-1H-indene-1-amine (**52**)



Synthesis and work-up were performed under argon. Potassium diphenylphosphide (14.72 mmol, 29.4 mL, 0.5M in THF) was transferred into a three-necked round bottom flask. THF was removed under reduced pressure and a solution of **46** (14.72 mmol, 3.3454 g) in 1,4-dioxane (15 mL) was added. The reaction mixture was refluxed for 120 h and conversion was controlled via ^{31}P-NMR spectroscopy. The solvent was removed under reduced pressure and degassed water (150 mL) was added to the residue. The product was extracted with dichloromethane (3 x 30 mL). The collected organic phase was dried with degassed and dried sodium sulfate. After filtration and remove of the solvent the crude product was obtained as yellow oil. It was dissolved in toluene (10 mL), filtered over neutral alumina and eluted with additional toluene (30 mL). After removing the solvent under reduced pressure the residue was taken up in toluene (5 mL) and pentane (10 mL) was added. At -18°C the product is obtained as slightly yellowish highly viscous oil.

Yield: 4.1679 g (10.59 mmol, 72 %)

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.69 (m, 1H, CH_2), 2.49 (m, 1H, CH_2), 2.76 (m, 2H, CH_2), 4.83 (m, 2H, NH/CH), 6.57 (m, 1H, Ar), 6.72-7.33 (m, 17H, Ar) ppm.

^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ = 30.3 (CH_2), 34.4 (CH_2), 58.9 (CH), 110.9 (d, *J* = 2.2 Hz, Ar), 117.2 (d, *J* = 3.0 Hz, Ar), 119.1 (d, *J* = 8.5 Hz, Ar), 124.1 (Ar), 124.8 (Ar), 125.4 (Ar), 126.7 (Ar), 127.8 (Ar), 128.3 (Ar), 128.5 (Ar), 128.6 (d, *J* = 1.5 Hz, Ar), 128.7 (d, *J* = 2.0 Hz, Ar), 128.8 (Ar), 128.9 (Ar), 129.2 (Ar), 130.8 (Ar), 133.7 (d, *J* = 3.4 Hz, Ar), 133.9 (d, *J* = 3.4 Hz, Ar), 134.9 (d, *J* = 5.5 Hz, Ar), 135.5 (d, *J* = 7.9 Hz, Ar), 143.4 (Ar), 144.3 (Ar), 150.5 (Ar), 150.7 (Ar) ppm.

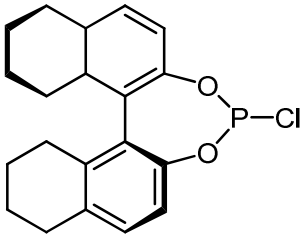
^{31}P{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = -20.04 ppm.

$[\alpha]_D^{20}$ = +60.8 (c = 0.84, DCM)

MS (EI): m/z (rel. intensity) = 393 (M, 2 %), 352 (17 %), 351 (35 %), 337 (18 %), 227 (17 %), 202 (45 %), 201 (91 %), 187 (12 %), 186 (100 %), 185 (30 %), 183 (39 %), 168 (12 %), 165 (23 %), 124 (17 %), 117 (64 %), 116 (14 %), 115 (21 %), 111 (26 %), 108 (43 %), 107 (17 %), 92 (27 %), 91 (46 %), 86 (10 %), 84 (16 %), 78 (15 %), 77 (23 %).

HR-MS (ESI): $C_{27}H_{24}NP$ (M) calculated: 393.164
found: 393.164

4.2.1.13 (*S*)-4-chloro-7a,8,9,10,11,11a,12,13,14,15-decahydrodinaphtho [2,1-d:1',2'-f][1,3,2]dioxaphosphepine (**55**)



Synthesis and work-up were performed under argon. **53** (17.46 mmol, 5 g) was dissolved in 20 mL PCl_3 and a drop of *N*-methyl pyrollidone was added. The mixture

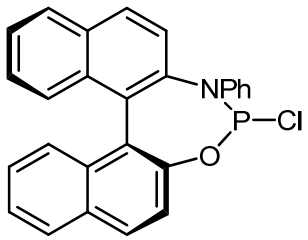
was refluxed for 1h. Excess of PCl_3 was removed under reduced pressure using an additional cooling trap (N_2) and a washing bottle filled with $KOH_{(s)}$. The yellowish residue was taken up in toluene and reduced to dryness (3 x 30 mL) to remove residues of PCl_3 via azeotropic distillation. After drying the product 16 h at 80 °C under reduced pressure it was obtained as a colourless solid.

Yield: quantitative.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.72 (m, 8H, CH_2), 2.22 (m, 2H, CH_2), 2.59 (m, 2H, CH_2), 2.76 (m, 4H, CH_2), 6.87 (d, *J* = 8.5 Hz, Ar), 6.96 (d, *J* = 8.5 Hz, Ar), 7.05 (d, *J* = 8.5 Hz, Ar) ppm.

^{31}P{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 169.08 ppm.

4.2.1.14 (11bS)-4-chloro-5-phenyl-4,5-dihydrodinaphtho[2,1-d:1',2'-f][1,3,2] Oxazaphosphepine (**73**)



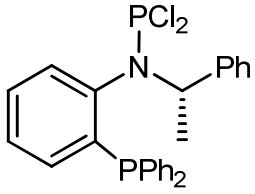
Synthesis and work-up were performed under argon. (S_a)-2'-(phenylamino)-1,1'-binaphthyl-2-ol (1.812 mmol, 0.655 g) and PCl_3 (27.18 mmol, 2.42 mL) were dissolved in toluene (10 mL) and a drop of *N*-methyl pyrollidone was added. The mixture was stirred at 85 °C for 2h then cooled down to room temperature. Excess of PCl_3 was removed under reduced pressure using an additional cooling trap (N_2) and a washing bottle filled with $KOH_{(s)}$. The yellowish residue was taken up in toluene (10 mL) and reduced to dryness to remove residues of PCl_3 via azeotropic distillation. After drying the product 16 h at 50 °C under reduced pressure it was obtained as a colourless solid.

Yield: quantitative.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.86 (d, *J* = 7.7 Hz, 2H, Ar), 6.99 (t, *J* = 7.5 Hz, 1H, Ar), 7.12 (t, *J* = 7.5 Hz, 2H, Ar), 7.26 (m, 4H, Ar), 7.43 (m, 4H, Ar), 7.87 (m, 4H, Ar) ppm.

^{31}P{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 176.16 ppm.

4.2.1.15 (*S*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl) Phosphinamine (*S*-**74**)



To a solution of (*S*)-2-(diphenylphosphino)-N-(1-phenylethyl)aniline (3.0510 g, 8.00 mmol) in CH_2Cl_2 (30 mL) NEt_3 (5.54 mL, 40 mmol) was added at 0 °C and stirred for 1 h. Then PCl_3 (10.50 mg, 120 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred over night. The solvent and excessive PCl_3 were removed under reduced pressure. The residue was taken up in toluene and filtered through a PTFE membrane. Removing the solvent under reduced pressure gave the desired product as a yellow solid.

Yield: quantitative

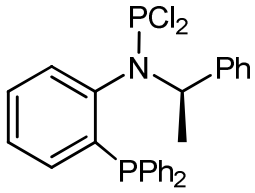
^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.91 (dd, *J* = 6.80 Hz, 3H, CH_3), 5.18 (m, 1H, CH), 6.99 (m, 1H, Ar), 7.18 (m, 8H, Ar), 7.61 (m, 4H, Ar), 7.76 (m, 2H, Ar), 8.01 (m, 2H, Ar), 8.20(m, 2H, Ar) ppm.

^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 27.3 (d, *J* = 296.2 Hz), 90.2 (d, *J* = 296.2 Hz) ppm.

^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 22.45 (CH_3), 58.08 (CH), 117.51 (Ar), 123.44 (Ar), 125.28 (Ar), 126.09 (Ar), 127.95 (Ar), 128.22 (Ar), 128.97 (Ar), 129.03 (Ar),

129.17 (Ar), 129.31 (Ar), 129.60 (Ar), 129.73 (Ar), 133.80 (Ar),134.58 (Ar), 134.68 (Ar),135.59 (Ar), 135.71 (Ar),135.88 (Ar), 135.98 (Ar), 140.99 (Ar) ppm.

4.2.1.16 (*R*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl) Phosphinamine (*R*-**74**)



To a solution of (*R*)-2-(diphenylphosphino)-N-(1-phenylethyl)aniline (3.0510 g, 8.00 mmol) in CH_2Cl_2 (30 mL) NEt_3 (5.54 mL, 40 mmol) was added at 0 °C and stirred for 1 h. Then PCl_3 (10.50 mg, 120 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred over night. The solvent and excessive PCl_3 were removed under reduced pressure. The residue was taken up in toluene and filtered through a PTFE membrane. Removing the solvent under reduced pressure gave the desired product as a yellow solid

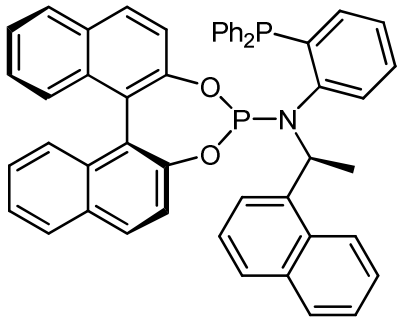
Yield: quantitative.

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.92 (dd, *J* = 6.86 Hz, 3H, CH_3), 5.18 (m, 1H, CH), 6.99 (m, 1H, Ar), 7.18 (m, 8H, Ar), 7.61 (m, 4H, Ar), 7.77 (m, 2H, Ar), 8.02 (m, 2H, Ar), 8.20(m, 2H, Ar) ppm.

^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 27.4 (d, *J* = 297.0 Hz), 90.2 (d, *J* = 297.0 Hz) ppm.

^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 22.43 (CH_3), 58.09 (CH), 117.52 (Ar), 123.64 (Ar), 125.28 (Ar), 126.09 (Ar), 127.98 (Ar), 128.20 (Ar), 128.96 (Ar), 129.01 (Ar), 129.25 (Ar),129.38 (Ar), 129.67 (Ar), 129.80 (Ar), 133.77 (Ar), 134.70 (Ar), 134.80 (Ar), 135.54 (Ar), 135.64 (Ar), 135.84 (Ar), 135.93 (Ar), 140.88 (Ar) ppm.

4.2.1.17 (11b*S*)-*N*-(2-(diphenylphosphino)phenyl)-*N*-((*S*)-1-(naphthalene-1-yl)ethyl) dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin-4-amine (**L1**)



Synthesis and work-up were performed under argon. To a solution of **49** (0.5 mmol, 214.8 mg) and TMEDA (0.6 mmol, 0.09 mL) in toluene (10 mL), *n*-Buthyllithium (0.55 mmol, 0.34 mL, 1.6M in hexane) was added dropwise at -78°C (dry ice/acetone bath). After stirring the reaction mixture for 1h at -78°C and for 1h at 0°C a solution of (11b*S*)-4-chlorodinaphtho[2,1-d:1',2'f][1,3,2]dioxaphosphepine (0.55 mmol, 192.9 mg) in toluene (5 mL) was slowly added at -78°C. The reaction was allowed to warm up to room temperature and stirred for 16h. The reaction mixture was filtered over a PTFE membrane. Toluene was removed under reduced pressure and the product was precipitated with ethanol from toluene. After the first precipitation the colourless solid had a sufficient purity (88% → ^{31}P-NMR) for catalyses. Purity after second precipitation: 100%.

Yield: 1st precipitation: 236.0 mg (0.32 mmol, 66 %)

2nd precipitation: 19.0 mg (0.02 mmol, 5 %)

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 2.04 (br, 3H, CH_3), 5.48 (br, 1H, CH), 6.38 (br, 2H, Ar), 6.69 (br, 1H, Ar), 6.92 (br, 1H, Ar), 6.69–7.81 (m, 28H, Ar) 8.26 (m, 1H, Ar) ppm.

^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 23.5 (d, *J* = 26.9 Hz, CH_3), 60.2 (CH), 122.4 (Ar, CH), 123.2 (Ar, CH), 125.3 (Ar, CH), 125.9 (Ar, CH), 126.3 (Ar, CH), 126.5 (Ar, CH), 126.8 (Ar, CH), 127.2 (Ar, CH), 127.4 (Ar, CH), 128.3 (Ar, CH), 128.4 (Ar, CH), 128.6 (Ar, CH), 128.8 (Ar, CH), 129.0 (Ar, CH), 129.2 (Ar, CH), 129.3 (Ar, CH), 129.9 (Ar, CH), 130.7 (Ar, CH), 130.9 (Ar, C_q), 131.1 (Ar, CH), 131.9 (Ar, C_q), 133.1 (d, *J* = 12.6 Hz, Ar, C_q), 133.6 (d, *J* = 19.6 Hz, Ar, CH), 134.3 (Ar, C_q), 134.5 (d, *J* = 19.6 Hz,

Ar, CH), 136.7 (Ar, CH), 138.6 (Ar, C_q), 138.8 (d, *J* = 12.6 Hz, Ar, C_q), 139.3 (Ar, C_q), 140.5 (Ar, C_q) 150.0 (Ar, C_q), 150.3 (Ar, C_q) ppm.

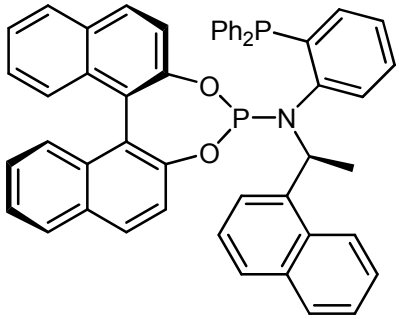
$^{31}P\{^1H\}$-NMR (250 MHz, CD_2Cl_2): δ = -17.2 (br), 138.4 (br) ppm.

$[\alpha]_D^{20}$ = +166.3 (c = 0.51, DCM)

MS (EI): m/z (rel. intensity) = 745 (M+, 1 %), 448 (11 %), 447 (34 %), 433 (26 %), 432 (100 %), 431 (50 %), 430 (12 %), 416 (23 %), 287 (19 %), 286 (100 %), 268 (13 %), 257 (13 %), 239 (16 %), 155 (12 %).

HR-MS (ESI): $C_{50}H_{37}NO_2P_2$ (M^+) calculated: 745.229
found: 745.230

4.2.1.18 (11b*R*)-*N*-(2-(diphenylphosphino)phenyl)-*N*-((*S*)-1-(naphthalene-1-yl)ethyl) dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-4-amine (**L2**)



Synthesis and work-up were performed under argon. To a solution of **49** (0.5 mmol, 214.8 mg) and TMEDA (0.6 mmol, 0.09 mL) in toluene (10 mL), *n*-Buthyllithium (0.55 mmol, 0.34 mL, 1.6M in hexane) was added dropwise at -78°C (dry ice/acetone bath). After stirring the reaction mixture for 1h at -78°C and for 1h at 0°C a solution of (11b*S*)-4-chlorodinaphtho[2,1-d:1',2'f][1,3,2]dioxaphosphepine (0.55 mmol, 192.9 mg) in toluene (5 mL) was slowly added at -78°C. The reaction was allowed to warm up to room temperature and stirred for 16h. The reaction mixture was filtered over a PTFE membrane. Toluene was removed under reduced pressure and the product was precipitated with ethanol from toluene. After the first

precipitation the colourless solid had a sufficient purity (88% → ^{31}P-NMR) for catalyses. Purity after second precipitation: 100%.

Yield: 1st precipitation: 157.3 mg (0.21 mmol, 44 %).

2nd precipitation: 16.7 mg (0.03 mmol, 7 %).

Via ^{1}H and ^{31}P NMR spectroscopy two different rotamers (major:minor = 1.3:1) were identified.

maj:^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.77 (br, 3H, CH_3), 5.62 (br, 1H, CH), 6.92 (br, 2H, Ar), 7.05–8.08 (m, 31H, Ar) ppm.
min:^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.70 (br, 3H, CH_3), 5.96 (br, 1H, CH), 6.24 (br, 1H, Ar), 6.74 (br, 1H, Ar), 6.98 (br, 2H, Ar), 7.05–7.94 (m, 28H, Ar), 8.21 (br, 1H, Ar) ppm.

^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 22.9 (CH_3, minor), 23.9 (CH_3, major) 53.3 (CH, minor), 56.7 (CH, major), 121.6 (Ar, C_q), 122.3 (Ar, CH), 122.5 (Ar, CH), 122.8 (Ar, CH), 123.1 (Ar, CH), 123.7 (Ar, CH), 124.2 (Ar, C_q), 124.8 (Ar, CH), 125.0 (Ar, CH), 125.2 (Ar, CH), 125.3 (Ar, CH), 125.4 (Ar, CH), 125.6 (Ar, CH), 126.0 (Ar, CH), 126.3 (Ar, CH), 126.4 (Ar, CH), 126.7 (Ar, CH), 127.2 (Ar, CH), 127.4 (Ar, CH), 127.7 (Ar, CH), 127.9 (Ar, CH), 128.5 (Ar, CH), 128.7 (Ar, CH), 128.9 (Ar, CH) 129.1 (Ar, CH), 129.8 (Ar, CH), 129.9 (Ar, CH), 130.4 (Ar, CH), 130.8 (Ar, C_q), 131.0 (Ar, CH), 131.2 (Ar, C_q), 131.5 (Ar, C_q), 131.8 (Ar, C_q), 132.1 (Ar, C_q), 133.1 (Ar, C_q), 133.4 (Ar, CH), 133.9 (d, *J* = 20 Hz, Ar, CH), 134.2 (d, *J* = 20 Hz, Ar, CH), 134.6 (d, *J* = 20 Hz, Ar, CH), 135.2 (Ar, CH), 137.1 (Ar, CH), 138.3 (Ar, C_q), 139.1 (Ar, C_q), 139.6 (Ar, C_q), 140.1 (Ar, C_q), 149.6 (Ar, C_q), 150.3 (Ar, C_q), 151.2 (Ar, C_q) ppm.

maj: ^{31}P{^{1}H}-NMR (250 MHz, CD_2Cl_2): δ = -19.4 (d, *J* = 32.1 Hz), 140.3 (d, *J* = 32.1 Hz) ppm.

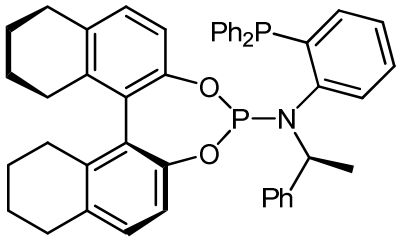
min: ^{31}P{^{1}H}-NMR (250 MHz, CD_2Cl_2): δ = -17.1 (d, *J* = 16.4 Hz), 141.8 (d, *J* = 16.4 Hz) ppm.

[α]$_D^{20}$ = -83.3 (c = 0.47, DCM)

MS (EI): m/z (rel. intensity) = 745 (M+, 3 %), 448 (33 %), 447 (100 %), 433 (12 %), 431 (81 %), 430 (27 %), 417 (11 %), 416 (33 %), 287 (18 %), 286 (100 %), 268 (21 %), 257 (12 %), 239 (12 %), 155 (10 %).

HR-MS (ESI): $C_{50}H_{37}NO_2P_2$ (M^+) calculated: 745.229
found: 745.229

4.2.1.19 (11b*S*)-*N*-(2-(diphenylphosphino)phenyl)-*N*-((*S*)-1-phenylethyl) 8,9,10,11,12,13,14,15-octahydrodinaphtho[2,1-d:1',2'-f][1,3,2] dioxaphosphepine-4-amine (**L3**)



Synthesis and work-up were performed under argon. To a solution of (*S*)-2-(diphenylphosphino)-*N*-(1-phenylethyl)aniline (1.24 mmol, 472.3 mg) and TMEDA (1.49 mmol, 0.24 mL) in toluene (5 mL), *n*-Buthyllithium (1.36 mmol, 0.85 mL, 1.6M in hexane) was added dropwise at -78°C (dry ice/acetone bath). After stirring the reaction mixture for 1h at -78°C and for 1h at 0°C a solution of **55** (1.49 mmol, 534.6 mg) in toluene (5 mL) was slowly added at -78°C. The reaction was allowed to warm up to room temperature and stirred for 16h. The reaction mixture was filtered over a short pad of basic alumina and the product was eluted with toluene (40 mL). Toluene was removed under reduced pressure and the product was precipitated with ethanol from toluene. The product is obtained as a colourless solid.

Yield: 322.2 mg (0.46 mmol, 37 %).

Via ^{31}P NMR spectroscopy two different rotamers (major:minor = 1.26:1) were identified.

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.22– 1.76 (m, 11H, CH_3/CH_2), 2.03 (m, 2H, CH_2), 2.43 (m, 2H, CH_2), 2.68 (m, 4H, CH_2), 4.46 (br, 1H, CH), 6.09 (br, 1H, Ar), 6.47 (br, 1H, Ar), 6.72 (br, 1H, Ar), 6.79–7.23 (m, 16H, Ar) ppm.

^{13}C{^{1}H}-NMR (100 MHz, CD_2Cl_2): δ = 23.0 (CH_3), 27.8 (CH_2), 28.1 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 60.2 (CH), 118.9 (Ar), 119.6 (Ar), 126.7 (Ar), 127.5 (Ar), 128.1 (Ar), 128.4 (Ar), 128.48 (Ar), 128.51 (Ar), 128.57 (Ar), 128.6 (Ar), 128.8 (Ar), 128.9 (Ar), 129.0 (Ar), 129.2 (Ar), 129.4 (Ar), 129.5 (Ar), 133.4 (Ar), 133.9 (Ar), 138.1 (Ar), 138.6 (Ar), 138.7 (Ar), 139.5 (Ar), 139.6 (Ar), 149.0 (Ar) ppm.

maj:^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = -17.1 (b), 136.2 (s) ppm.

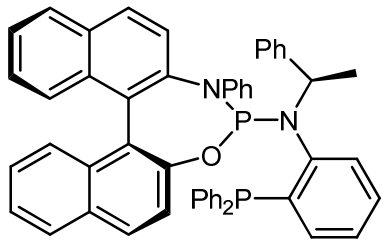
min: ^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = -17.1 (b), 135.9 (s) ppm.

[α]$_D^{20}$ = +30.3 (c = 0.48, DCM)

MS (EI): m/z (rel. intensity) = 703.1 (M, 1 %), 382 (12 %), 381 (15 %), 380 (11 %), 337 (27 %), 183 (22 %), 92 (65 %), 91 (100 %).

HR-MS (ESI): $C_{44}H_{39}NO_2P_2$ (M^+) calculated: 703.276
found: 703.275

4.2.1.20 (11b*S*)-N-(2-(diphenylphosphino)phenyl)-5-phenyl-N-((*R*)-1-phenylethyl) dinaphtho[2,1-d:1',2'-f][1,3,2]oxazaphosphepin-4(5H)-amine (**L5**)



To a solution of (*S*)-2'-(phenylamino)-1,1'-binaphthyl-2-ol (214.6 mg, 0.59 mmol) in CH_2Cl_2 (10 mL) NEt_3 (1.23 mL, 8.85 mmol) was added at 0 °C and stirred for 30 min.

This solution was added dropwise to a solution of (*R*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl)phosphinamine (284.6 mg, 0.59 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred over night. The solvent was removed under reduced pressure. The residue was taken up in toluene and filtered through a PTFE membrane. After removing the solvent under reduced pressure the crude product was purified by column chromatography under argon atmosphere over silica (eluent: THF/pentane: 1/5, R_f = 0.60). The product was obtained as colourless solid.

Yield: 113.7 mg (0.15 mmol, 25 %).

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.91 (b, 3H, CH_3), 4.52 (b, 1H, CH), 6.44 (b, 1H, Ar-H), 6.59 (b, 1H, Ar-H), 6.84 (m, 2H, Ar-H), 6.96 (t, *J* = 7.53 Hz, 1H, Ar-H), 7.08-7.15 (m, 12H, Ar-H), 7.19-7.30 (m, 10H, Ar-H), 7.34 (bs, 3H, Ar-H), 7.39 (m, 2H, Ar-H), 7.56 (bd, *J* = 8.33 Hz, 1H, Ar-H), 7.73 (d, *J* = 8.01 Hz, 1H, Ar-H), 7.90 (d, *J* = 8.33 Hz, 1H, Ar-H), 7.96 (d, *J* = 8.65 Hz, 1H, Ar-H) ppm.

^{31}P{^{1}H}-NMR (250 MHz, CD_2Cl_2): δ = -22.0, 132.2 ppm.

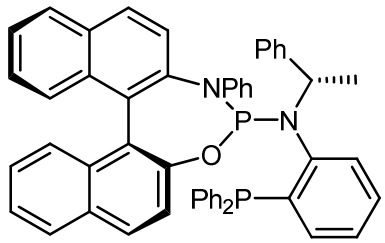
^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 21.9 (CH_3), 63.0 (CH), 121.27 (d, *J* = 4.44 Hz, Ar), 121.36 (d, *J* = 4.44 Hz, Ar, CH), 121.97 (Ar, CH), 122.31 (Ar, CH), 124.93 (Ar, CH), 125.57 (Ar, CH), 125.96 (Ar, CH), 126.40 (Ar, C_q), 126.44 (Ar, C_q), 126.49 (Ar, CH), 126.54 (Ar, CH), 126.78 (Ar, CH), 127.32 (Ar, CH), 127.60 (Ar, CH), 127.65 (Ar, CH), 128.12 (2C, Ar, CH), 128.19 (Ar, CH), 128.22 (2C, Ar, CH), 128.65 (2C, Ar, CH), 128,72 (2C, Ar, CH), 128.76 (Ar, CH), 128.78 (Ar, CH), 128.82 (2C, Ar, CH), 128.92 (2C, Ar, CH), 129.08 (Ar, CH), 129.28 (Ar, CH), 130.44 (Ar, CH), 131.66 (Ar, C_q), 131.82 (Ar, C_q), 132.62 (Ar, C_q), 133.35 (Ar, C_q), 133.84 (Ar, CH), 133.97 (Ar, CH), 134.11 (Ar, CH), 134.25 (Ar, CH), 136.73 (Ar, CH), 139.32 (Ar, C_q), 139.43 (Ar, C_q), 141.40 (Ar, C_q), 141.43 (Ar, C_q), 143.09 (Ar, C_q), 148.17 (Ar, C_q), 148.34 (Ar, C_q), 150.06 (Ar, C_q) ppm.

$[\alpha]_D^{20}$ = +316.2 (c = 0.61, DCM)

MS (ESI): m/z (%) = 771 ($[M+H]^+$, <1), 681 (10), 621 (27), 406 (18), 357 (11), 356 (100), 343 (13), 276 (54).

HRMS (ESI) = $[M+H]^+$ 771.26898 calcd. for $C_{52}H_{41}N_2OP_2$: 771.268

4.2.1.21 (11b*S*)-N-(2-(diphenylphosphino)phenyl)-5-phenyl-N-((*S*)-1-phenylethyl) dinaphtho[2,1-d:1',2'-f][1,3,2]oxazaphosphepin-4(5H)-amine (**L4**)



To a solution of (*S*)-2'-(phenylamino)-1,1'-binaphthyl-2-ol (214.6 mg, 0.59 mmol) in CH_2Cl_2 (10 mL) NEt_3 (1.23 mL, 8.85 mmol) was added at 0 °C and stirred for 30 min. This solution was added dropwise to a solution of (*S*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl)phosphinamine (284.6 mg, 0.59 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred over night. The solvent was removed under reduced pressure. The residue was taken up in toluene and filtered through a PTFE membrane. After removing the solvent under reduced pressure the crude product was purified by column chromatography under argon atmosphere over silica (eluent: THF/pentane: 1/5, R_f = 0.60). The product was obtained as colourless solid.

Yield: 141.0 mg (0.18 mmol, 31 %).

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.49 (b, 3H, CH_3), 4.83 (quin, *J* = 7.59 Hz, 1H, CH), 6.74 (b, 1H, Ar-H), 6.80 (m, 4H, Ar-H), 6.89 (m, 1H, Ar-H), 6.99 (m, 2H, Ar-H), 7.04 (m, 1H, Ar-H), 7.11 (m, 4H, Ar-H), 7.19-7.31 (m, 11 H, Ar-H), 7.31-7.40 (m, 4H, Ar-H), 7.42-7.58 (m, 5H, Ar-H), 7.81 (d, *J* = 8.14 Hz, 1H, Ar-H), 7.87 (m, 2H, Ar-H) ppm.

^{31}P{^{1}H}-NMR (250 MHz, CD_2Cl_2): δ = -21.1, 135.9 ppm.

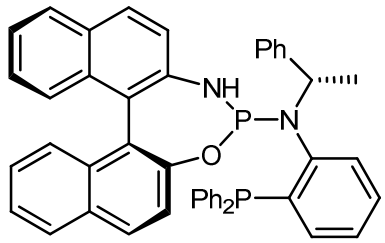
$^{13}C\{^{1}H\}$-NMR (150 MHz, CD_2Cl_2): δ = 20.6 (CH_3), 61.1 (CH), 121.10 (Ar, CH), 121.20 (Ar, CH), 121.91 (Ar, CH), 122.35 (Ar, CH), 124.91 (Ar, CH), 125.71 (Ar, CH), 126.10 (Ar, CH), 126.35 (Ar, C_q), 126.46 (Ar, CH), 126.55 (Ar, CH), 126.95 (Ar, CH), 127.84 (Ar, CH), 127.92 (Ar, CH), 128.18 (Ar, CH), 128.32 (Ar, CH), 128.44 (2C, Ar, CH), 128.60 (Ar, CH), 128.69 (2C, Ar, CH), 128.73 (3C, Ar, CH), 128.81 (Ar, CH), 128.92 (3C, Ar, CH), 129.56 (Ar, CH), 130.45 (Ar, CH), 131.64 (Ar, C_q), 132.07 (Ar, C_q), 132.88 (Ar, C_q), 133.29 (Ar, C_q), 133.68 (Ar, CH), 133.97 (Ar, CH), 134.10 (Ar, CH), 137.19 (Ar, CH), 138.89 (Ar, C_q), 138.99 (Ar, C_q), 139.63 (Ar, C_q), 139.73 (Ar, C_q), 148.00 (Ar, C_q), 148.20 (Ar, C_q), 148.57 (Ar, C_q), 148.74 (Ar, C_q), 150.08 (Ar, C_q) ppm.

$[\alpha]_D^{20}$ = +324.3 (c = 0.56, DCM)

MS (EI): m/z (%) = 770 (M^+, <1), 92 (17), 91 (25), 72 (100), 71 (96).

HRMS (ESI) = 770.26097 calcd. for $C_{52}H_{40}N_2OP_2$: 770.261

4.2.1.22 (11b*S*)-N-(2-(diphenylphosphino)phenyl)-N-((*S*)-1-phenylethyl) dinaphtho[2,1-d:1',2'-f][1,3,2]oxazaphosphepin-4(5H)-amine (**L6**)



To a solution of (S)-2'-amino-1,1'-binaphthyl-2-ol (218.8 mg, 0.77 mmol) in CH_2Cl_2 (10 mL) NEt_3 (1.60 mL, 11.5 mmol) was added at 0 °C and stirred for 30 min. This solution was added dropwise to a solution of (*S*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl)phosphinamine (371.4 mg, 0.77 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred over night. The solvent was removed under reduced pressure. The residue was taken up in toluene and filtered through a PTFE membrane. After removing the solvent under reduced pressure the crude product was purified by

column chromatography under argon atmosphere over basic alumina (eluent: THF/pentane/NEt_3: 1/4/0.025, R_f = 0.63). The product was obtained as colourless solid. Single crystals suitable for X-ray defraction were obtained via recrystallisation from acetonitrile.

Yield: 123.0 mg (0.18 mmol, 23 %).

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.62 (d, *J* = 7.07 Hz, 3H, CH_3), 4.48 (b, 1H, NH), 4.85 (b, 1H, CH), 6.89-7.08 (m, 3H, Ar-H), 7.17 (m, 5H, Ar-H), 7.26 (m, 5H, Ar-H), 7.32 (m, 8H, Ar-H), 7.42 (m, 5H, Ar-H), 7.52 (d, 1H, *J* = 8.6 Hz, Ar-H), 7.95 (m, 4H, Ar-H) ppm.

^{31}P{^{1}H}-NMR (250 MHz, CD_2Cl_2): δ = -17.8 (d, *J* = 42.4 Hz), 142.2 ppm.

^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 23.07 (CH_3), 58.93 (CH), 122.52 (Ar, CH), 122.97 (Ar, C_q), 124.38 (Ar, CH), 124.84 (Ar, CH), 125.23 (Ar, CH), 126.09 (d, *J* = 2.8 Hz, Ar, C_q), 126.17 (Ar, CH), 126.23 (Ar, CH), 127.12 (Ar, CH), 127.26 (Ar, CH), 127.46 (Ar, CH), 127.63 (Ar, CH), 128.12 (Ar, CH, 2C), 128.49 (Ar, CH), 128.69 (Ar, CH), 128.74 (Ar, CH, 2C), 128.97 (Ar, CH), 128.99 (Ar, CH), 129.02 (Ar, CH, 2C), 129.17 (Ar, CH), 129.44 (Ar, CH, 2C), 129.97 (Ar, CH), 130.28 (Ar, CH), 130.69 (Ar, C_q), 131.54 (Ar, C_q), 132.72 (Ar, CH), 133.12 (Ar, C_q), 133.68 (Ar, C_q), 134.11 (m, Ar, CH, 4C), 136.14 (Ar, CH), 138.39 (d, *J* = 11.6 Hz, Ar, C_q), 138.83 (d, *J* = 14.1 Hz, Ar, C_q), 139.24 (Ar, C_q), 139.92 (d, *J* = 6.5 Hz, Ar, C_q), 142.09 (Ar, C_q), 148.00 (m, Ar, C_q), 150.88 (Ar, C_q) ppm.

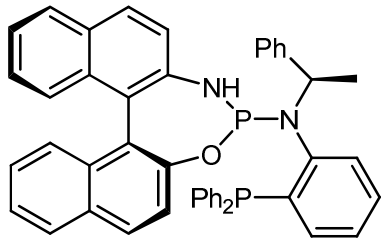
$[\alpha]_D^{20}$ = -69.4 (c = 0.49, DCM)

MS (EI): m/z (%) = 694 (M, <1), 382 (28), 381 (100), 380 (20), 367 (16), 366 (60), 337 (11), 304 (11), 303 (15), 302 (11), 288 (33), 277 (20), 276 (31), 261 (38), 199 (10), 198 (60), 194 (37), 183 (78), 181 (44), 180 (14), 167 (22), 152 (16), 107 (15), 105 (79), 104 (14), 103 (17), 79 (22), 77 (31).

HRMS (ESI) = $[M+H]^+$ 695.23724 calcd. for $C_{46}H_{37}N_2OP_2$: 695.237

Absolute configuration on phosphorus: (*S*) (X-ray data: Appendix 6.2, p.143)

4.2.1.23 (11b*S*)-N-(2-(diphenylphosphino)phenyl)-N-((*R*)-1-phenylethyl) dinaphtho[2,1-d:1',2'-f][1,3,2]oxazaphosphepin-4(5H)-amine (**L7**)



To a solution of (*S*)-2'-amino-1,1'-binaphthyl-2-ol (218.8 mg, 0.77 mmol) in CH_2Cl_2 (10 mL) NEt_3 (1.60 mL, 11.5 mmol) was added at 0 °C and stirred for 30 min. This solution was added dropwise to a solution of (*R*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl)phosphinamine (371.4 mg, 0.77 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred over night. The solvent was removed under reduced pressure. The residue was taken up in toluene and filtered through a PTFE membrane. After removing the solvent under reduced pressure the crude product was purified by column chromatography under argon atmosphere over basic alumina (eluent: THF/pentane/NEt_3: 1/4/0.025, R_f = 0.59). The product was obtained as colourless solid.

Yield: 111.2 mg (0.16 mmol, 21 %).

^{1}H-NMR (600 MHz, CD_2Cl_2): δ = 1.33 (b, 3H, CH_3), 4.62 (b, 1H, CH), 6.22 (b, 1H, NH), 7.02-7.47 (m, 27H, Ar-H), 7.72 (b, 2H, Ar-H), 7.82 (d, ^3J = 8.3 Hz, 1H, Ar-H), 7.87 (d, ^3J = 8.3 Hz, 1H, Ar-H) ppm.

^{31}P{^{1}H}-NMR (250 MHz, CD_2Cl_2): δ = -19.4, 138.3 ppm.

^{13}C{^{1}H}-NMR (150 MHz, CD_2Cl_2): δ = 24.90 (CH_3), 58.39 (CH), 122.51 (Ar, C_q), 122.62 (Ar, CH, 2C), 124.25 (Ar, CH), 124.40 (Ar, CH), 124.86 (Ar, CH), 126.19 (Ar, CH, 2C), 126.23 (Ar, C_q, 2C), 127.00 (Ar, CH), 127.26 (Ar, CH), 127.28 (Ar, CH, 2C), 127.43 (Ar, CH), 128.23 (Ar, CH, 2C), 128.75 (Ar, CH), 128.89 (Ar, CH, 2C), 128.93 (Ar, CH, 3C), 129.09 (Ar, CH, 2C), 129.14 (Ar, CH, 2C), 130.25 (Ar, CH, 2C), 130.49 (Ar, C_q), 131.58 (Ar, C_q), 132.81 (Ar, CH), 133.15 (Ar, C_q, 2C), 133.73 (Ar, CH, 2C),

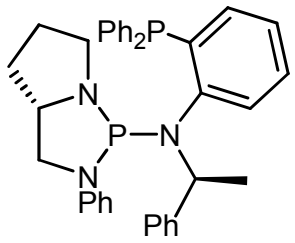
133.86 (Ar, CH, 2C), 138.27 (d, *J* = 7.9 Hz, Ar, C_q, 3C), 140.13 (d,^3J = 7.9 Hz, Ar, C_q), 143.38 (Ar, C_q), 150.57(Ar, C_q) ppm.

[α]$_D^{20}$ = 65.1 (c = 0.56, DCM)

MS (EI): m/z (%) = 694 (M, <1), 382 (28), 381 (100), 380 (20), 367 (16), 366 (60), 337 (11), 304 (11), 303 (15), 302 (11), 288 (33), 277 (20), 276 (31), 261 (38), 199 (10), 198 (60), 194 (37), 183 (78), 181 (44), 180 (14), 167 (22), 152 (16), 107 (15), 105 (79), 104 (14), 103 (17), 79 (22), 77 (31).

HRMS (ESI) = $[M+H]^+$ 695.23724 calcd. for $C_{46}H_{37}N_2OP_2$: 695.237

4.2.1.24 (3a*S*)-*N*-(2-(diphenylphosphino)phenyl)-2-phenyl-N-((*S*)-1-phenylethyl) hexahydro-1H-pyrrolo[1,2-c][1,3,2]diazaphosphol-1-amine (**L8**)



To a solution of (*S*)-N-(pyrrolidin-2-ylmethyl)aniline (103.1 mg, 0.58 mmol) in CH_2Cl_2 (4 mL) NEt_3 (1.04 mL, 7.4 mmol) was added at 0 °C and stirred for 30 min. This solution was added dropwise to a solution of (*S*)-1,1-dichloro-N-(2-(diphenylphosphino)phenyl)-N-(1-phenylethyl)phosphinamine (281.9 mg, 0.58 mmol) in CH_2Cl_2 (6 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred over night. The solvent was removed under reduced pressure. The residue was suspended in toluene (10 mL), NEt_3 (1 mL) was added and the solution was filtered through a short pad of basic alumina (ca. 1 cm, pretreated with toluene (5 mL) and of NEt_3 (0.5 mL)). The pad was washed with toluene (10 mL). After removing the solvent under reduced pressure the product was obtained as colourless solid.

Yield: 58.6 mg (0.10 mmol, 18 %).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 1.34 (m, 1H, CH_2), 1.54 (d, *J* = 7.06 Hz, 3H, CH_3), 1.67 (m, 2H, CH_2), 1.80 (m, 1H, CH_2), 3.04 (m, 1H, CH_2), 3.29 (m, 1H, CH_2), 3.44 (m, 1H, CH_2), 3.58 (m, 1H, CH_2), 3.70 (m, 1H, CH), 4.95 (quin, *J* = 6.27 Hz, 1H, CH), 6.78 (t, *J* = 7.45 Hz, 1H, Ar-H), 6.87 (m, 2H, Ar-H), 6.91 (b, 2H, Ar-H), 6.99-7.41 (m, 19H, Ar-H) ppm.

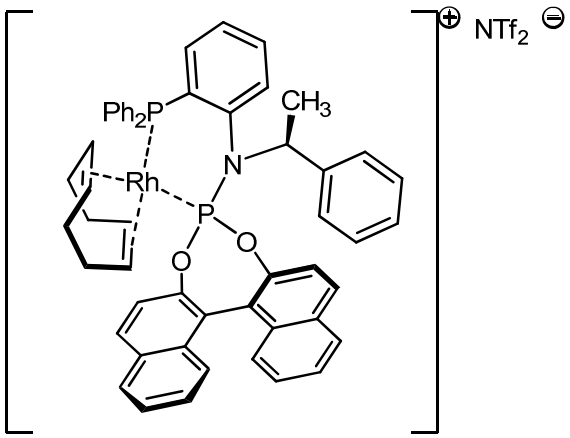
^{31}P{^{1}H}-NMR (250 MHz, $CDCl_3$): δ = -20.55 (d, J_{P-P} = 52.8 Hz), 107.7 (d, J_{P-P} = 52.8 Hz) ppm.

^{13}C{^{1}H}-NMR (150 MHz, $CDCl_3$): δ = 21.17 (d, *J* = 7.06 Hz, CH_3), 26.09 (d, *J* = 4.36 Hz, CH_2), 33.22 (CH_2), 50.69 (dd, *J* = 4.36 Hz / 39.25 Hz, CH_2), 53.37 (d, *J* = 7.99 Hz, CH_2), 58.44 (CH), 62.79 (d, *J* = 7.99 Hz, CH), 115.53 (Ar, CH), 115.62 (Ar, CH), 117.69 (Ar, CH), 125.15 (Ar, CH), 125.48 (Ar, CH), 125.72 (Ar, CH), 126.73 (Ar, CH), 127.52 (Ar, CH), 127.61 (Ar, CH), 127.77 (Ar, CH), 127.92 (Ar, CH), 127.96 (Ar, CH), 128.06 (Ar, CH), 128.10 (Ar, CH), 128.25 (Ar, CH), 128.43 (Ar, CH), 128.82 (Ar, CH), 129.04 (Ar, CH), 129.25 (Ar, CH), 132.91 (Ar, CH), 133.04 (Ar, CH), 133.08 (Ar, CH), 133.20 (Ar, CH), 137.17 (Ar, C_q), 137.27 (Ar, CH), 139.88 (Ar, C_q, 2C), 142.42 (Ar, C_q), 146.49 (Ar, C_q),150.18 (Ar, C_q) ppm.

MS (EI): m/z (%) = 585 ([M], 23), 508 (25), 480 (10), 381 (23), 380 (43), 206 (16), 205 (100), 183 (10), 136 (23).

HRMS (ESI) = [M] 585.24636 calcd. for $C_{37}H_{37}N_3P_2$: 585.246

4.2.1.25 [Rh(COD)(**36**)][NTf_2] (**56**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.077 mmol, 24.3 mg) and Bis(trifluoromethyl)sulfonamide (0.077 mmol, 21.9 mg) were dissolved in ethanol (5 mL). The mixture was stirred until a clear solution was formed (ca. 10min). A solution of **36** (0.07 mmol, 53.6 mg) in THF (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 30 min. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 83.2 mg (0.07 mmol, 91 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.19 (br, 3H, CH_3), 1.85–2.50 (m, 8H, COD), 4.50 (m, 1H, COD), 4.69 (m, 1H, COD), 5.48 (m, 1H, CH), 5.54 (m, 1H, COD), 5.66 (m, 1H, COD), 7.03–8.11 (m, 31H, Ar) ppm.

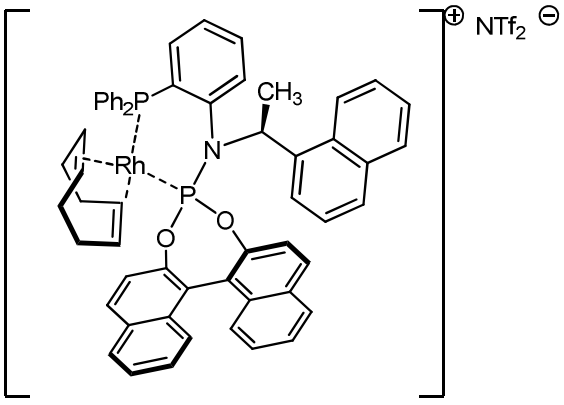
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 21.5 (dd, $J_{P\text{-}P}$ = 61.2 Hz, $J_{Rh\text{-}P}$ = 136.4 Hz), 136.4 (dd, $J_{P\text{-}P}$ = 61.2 Hz, $J_{Rh\text{-}P}$ = 249.3 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.46 ppm.

MS(Cation) (SIMS): m/z = 906.3
for: $C_{54}H_{47}NO_2P_2Rh$ [Rh(COD)(**36**)]$^{+}$ (calc.:906.2)

MS(Anion) (SIMS): m/z = 279.8
for: $C_2F_6NO_4S_2$ [NTf_2]$^{-}$ (calc.:279.9)

4.2.1.26 [Rh(COD)(**L1**)][NTf_2] (**57**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.1 mmol, 31.2 mg) and Bis(trifluoromethyl)sulfonamide (0.1 mmol, 28.6 mg) were dissolved in ethanol (5 mL). The mixture was stirred until a clear solution was formed (ca. 10min). A solution of **L1** (0.1 mmol, 74.6 mg) in THF (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 30 min. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 108.8 mg (0.09 mmol, 88 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.07 (br, 3H, CH_3), 1.70–2.40 (m, 8H, COD), 3.83 (m, 1H, COD), 4.34 (m, 1H, COD), 4.57 (m, 1H, CH), 5.49 (m, 1H, COD), 5.57 (m, 1H, COD), 6.99–8.02 (m, 35H, Ar) ppm.

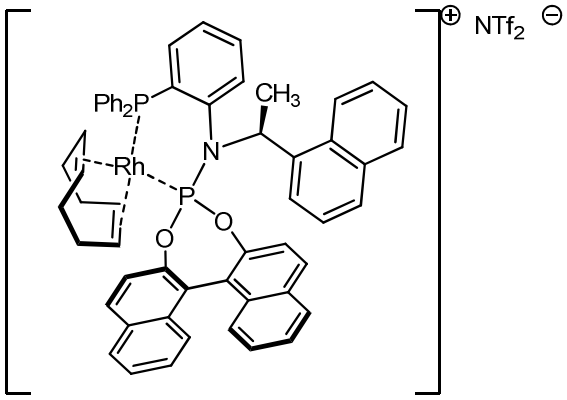
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 13.4 (dd, $J_{P\text{-}P}$ = 67.5 Hz, $J_{Rh\text{-}P}$ = 135.1 Hz), 149.6 (dd, $J_{P\text{-}P}$ = 67.5 Hz, $J_{Rh\text{-}P}$ = 237.7 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.46 ppm.

MS(Cation) (SIMS): m/z = 956.6
for: $C_{58}H_{49}NO_2P_2Rh$ [Rh(COD)(**L1**)]$^{+}$ (calc.:956.9)

MS(Anion) (SIMS): m/z = 279.6
for: $C_2F_6NO_4S_2$ [NTf_2]$^{-}$ (calc.:279.9)

4.2.1.27 [Rh(COD)(**L2**)][NTf_2] (**58**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.1 mmol, 31.2 mg) and Bis(trifluoromethyl)sulfonamide (0.1 mmol, 28.6 mg) were dissolved in ethanol (5 mL). The mixture was stirred until a clear solution was formed (ca. 10min). A solution of **L2** (0.1 mmol, 74.6 mg) in THF (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 30 min. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 101.4 mg (0.08 mmol, 82%).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.17 (d, *J* = 7.2 Hz, 3H, CH_3), 1.99–2.47 (m, 8H, COD), 4.64 (m, 1H, COD), 4.95 (m, 1H, COD), 5.73 (m, 1H, CH), 5.98 (m, 1H, COD), 6.17 (m, 1H, COD), 6.68–8.18 (m, 35H, Ar) ppm.

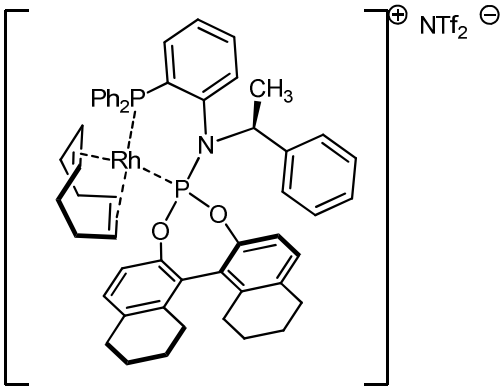
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 14.3 (dd, $J_{P\text{-}P}$ = 58.7 Hz, $J_{Rh\text{-}P}$ = 141.1 Hz), 141.1 (dd, $J_{P\text{-}P}$ = 58.7 Hz, $J_{Rh\text{-}P}$ = 242.9 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.27 ppm.

MS(Cation) (SIMS): m/z = 956.6
for: $C_{58}H_{49}NO_2P_2Rh$ [Rh(COD)(**L2**)]$^{+}$ (calc.:956.9)

MS(Anion) (SIMS): m/z = 279.7
for: $C_2F_6NO_4S_2$ [NTf_2]$^{-}$ (calc.:279.9)

4.2.1.28 [Rh(COD)(**L3**)][NTf_2] (**59**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.1 mmol, 31.2 mg) and Bis(trifluoromethyl)sulfonamide (0.1 mmol, 28.6 mg) were dissolved in ethanol (5 mL). The mixture was stirred until a clear solution was formed (ca. 10min). A solution of **L3** (0.1 mmol, 74.6 mg) in THF (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 30 min. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 118.7 mg (0.10 mmol, 96%).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.17 (d, *J* = 7.2 Hz, 3H, CH_3), 1.39–2.85 (m, 8H, COD), 4.56 (m, 1H, COD), 4.98 (m, 1H, CH), 5.04 (m, 1H, COD), 5.67 (m, 1H, COD), 5.96 (m, 1H, COD), 6.57–7.54 (m, 23H, Ar) ppm.

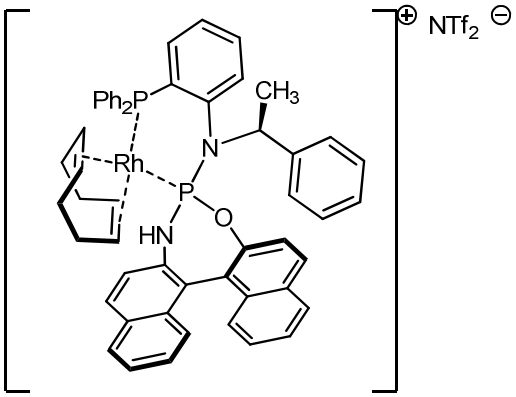
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 15.0 (dd, $J_{P\text{-}P}$ = 61.1 Hz, $J_{Rh\text{-}P}$ = 142.0 Hz), 135.4 (dd, $J_{P\text{-}P}$ = 61.1 Hz, $J_{Rh\text{-}P}$ = 236.6 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.46 ppm.

MS(Cation) (SIMS): m/z = 914.3
for: $C_{54}H_{55}NO_2P_2Rh$ [Rh(COD)(**L3**)]$^+$ (calc.:914.3)

MS(Anion) (SIMS): m/z = 279.9
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.1.29 [Rh(COD)(**L6**)][NTf_2] (**75**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.047 mmol, 14.7 mg) and Bis(trifluoromethyl)sulfonamide (0.047 mmol, 13.4 mg) were stirred in DCM (5 mL) for 1 h. A solution of **L6** (0.049 mmol, 33.8 mg) in DCM (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 16 h. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 47.4 mg (0.04 mmol, 88 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.56 (d, *J* = 7.48 Hz, 3H, CH_3), 2.20–2.55 (m, 8H, COD), 4.62 (d, *J* = 33.21 Hz, 1H, NH), (d, 4.83 (b, 1H, COD), 4.93 (b, 1H, COD), 5.30 (m, 1H, CH), 5.73 (b, overl., 2H, Ar/COD), 5.87 (m, 1H, COD), 6.19–8.03 (m, 30H, Ar) ppm.

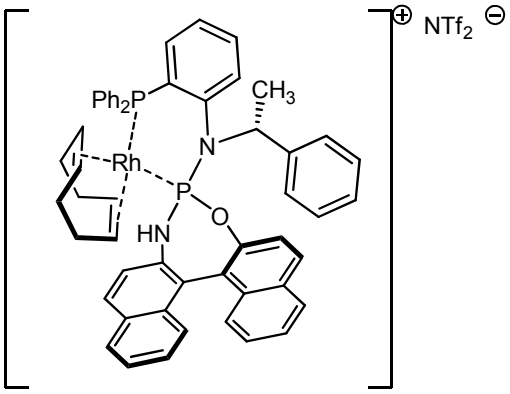
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 13.18 (dd, $J_{P\text{-}P}$ = 68.5 Hz, $J_{Rh\text{-}P}$ = 141.3 Hz), 138.58 (dd, $J_{P\text{-}P}$ = 68.5 Hz, $J_{Rh\text{-}P}$ = 199.3 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.27 ppm.

MS(Cation) (SIMS): m/z = 905.3
for: $C_{54}H_{48}N_2OP_2Rh$ [Rh(COD)(**L6**)]$^+$ (calc.:905.2)

MS(Anion) (SIMS): m/z = 279.8
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.1.30 [Rh(COD)(**L7**)][NTf_2] (**76**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.044 mmol, 13.8 mg) and Bis(trifluoromethyl)sulfonamide (0.044 mmol, 12.6 mg) were stirred in DCM (5 mL) for 1 h. A solution of **L7** (0.046 mmol, 31.8 mg) in DCM (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 16 h. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 35.6 mg (0.03 mmol, 79 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.39 (d, *J* = 6.73 Hz, 3H, CH_3), 2.21–2.71 (m, 8H, COD), 4.77 (d, *J* = 32.65 Hz, 1H, NH), 4.85 (b, 1H, COD), 4.92 (b, 1H, COD), 5.27 (m, 1H, CH), 5.76 (b, overl., 2H, Ar/COD), 5.87 (m, 1H, COD), 6.64–8.08 (m, 30H, Ar) ppm.

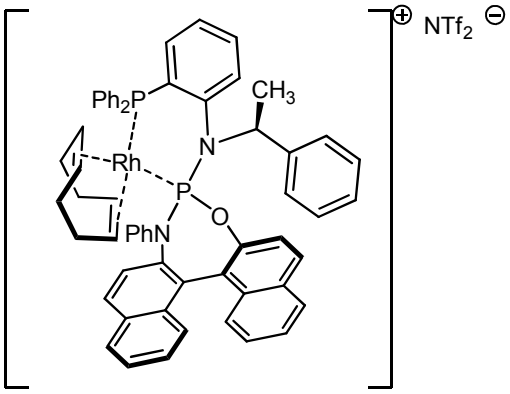
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 12.98 (dd, $J_{P\text{-}P}$ = 66.4 Hz, $J_{Rh\text{-}P}$ = 140.6 Hz), 138.71 (dd, $_{P\text{-}P}J$ = 66.4 Hz, $J_{Rh\text{-}P}$ = 202.3 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.27 ppm.

MS(Cation) (SIMS): m/z = 905.4
for: $C_{54}H_{48}N_2OP_2Rh$ [Rh(COD)(**L7**)]$^+$ (calc.:905.2)

MS(Anion) (SIMS): m/z = 279.9
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.1.31 [Rh(COD)(**L4**)][NTf_2] (**77**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.047 mmol, 14.7 mg) and Bis(trifluoromethyl)sulfonamide (0.047 mmol, 13.4 mg) were stirred in DCM (5 mL) for 1 h. A solution of **L4** (0.049 mmol, 37.8 mg) in DCM (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 16 h. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 25.2 mg (0.02 mmol, 52 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.26 (d, *J* = 6.45 Hz, 3H, CH_3), 1.75–2.62 (m, 8H, COD), 3.67 (m, 1H, CH), 4.10 (b, 1H, COD), 4.69 (b, 1H, COD), 5.57 (b, 1H, COD), 6.09 (m, 1H, Ar) 6.27 (b, 1H, COD), 6.43–8.32 (m, 34H, Ar) ppm.
ppm.

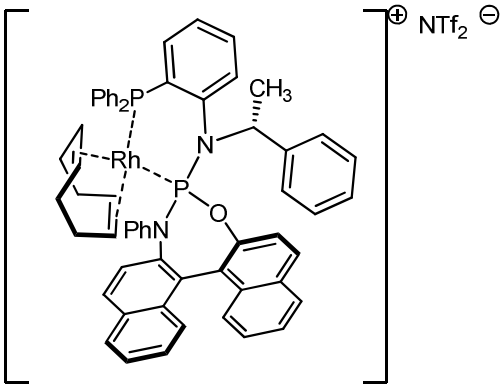
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 13.78 (dd, $J_{P\text{-}P}$ = 40.0 Hz, $J_{Rh\text{-}P}$ = 151.1 Hz), 138.71 (dd, $J_{P\text{-}P}$ = 40.0 Hz, $J_{Rh\text{-}P}$ = 219.2 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.25 ppm.

MS(Cation) (SIMS): m/z = 981.2
for: $C_{54}H_{48}N_2OP_2Rh$ [Rh(COD)(**L4**)]$^+$ (calc.: 981.3)

MS(Anion) (SIMS): m/z = 279.9
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.1.32 [Rh(COD)(**L5**)][NTf_2] (**78**)



Synthesis and work-up were performed under argon. [Rh(COD)(acac)] (0.046 mmol, 12.3 mg) and Bis(trifluoromethyl)sulfonamide (0.046 mmol, 11.2 mg) were stirred in DCM (5 mL) for 1 h. A solution of **L5** (0.048 mmol, 33.3 mg) in DCM (2 mL) was added dropwise, the yellow solution turned orange and the mixture was stirred for 16 h. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as an orange solid.

Yield: 37.9 mg (0.03 mmol, 55 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.13 (d, *J* = 7.02 Hz, 3H, CH_3), 2.14–2.77 (m, 8H, COD), 3.38 (b, 1H, COD), 3.55 (m, 1H, CH), 4.14 (bs, 1H, COD), 4.50 (b, 1H, COD), 4.64 (m, 1H, COD), 6.12–8.07 (m, 35H, Ar) ppm.
ppm.

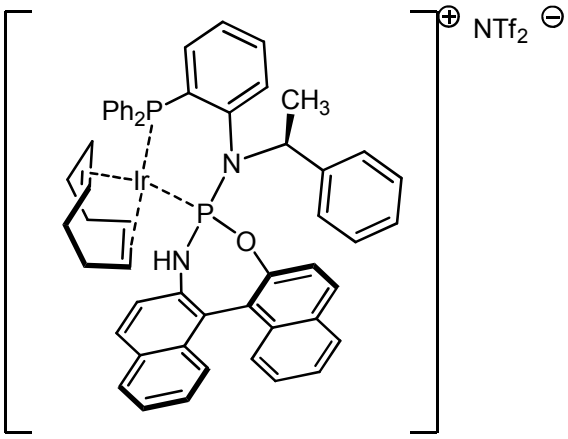
^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 12.75 (dd, $J_{P\text{-}P}$ = 36.2 Hz, $J_{Rh\text{-}P}$ = 152.2 Hz), 140.40 (dd, $J_{P\text{-}P}$ = 36.2 Hz, $J_{Rh\text{-}P}$ = 221.4 Hz) ppm.

^{19}F-NMR (280 MHz, CD_2Cl_2): δ = -79.27 ppm.

MS(Cation) (SIMS): m/z = 981.2
for: $C_{54}H_{48}N_2OP_2Rh$ [Rh(COD)(**L5**)]$^+$ (calc.: 981.3)

MS(Anion) (SIMS): m/z = 279.9
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.1.33 [Ir(COD)(**L6**)][NTf_2] (**79**)



Synthesis and work-up were performed under argon. [Ir(COD)(acac)] (0.0236 mmol, 9.4 mg) and Bis(trifluoromethyl)sulfonamide (0.0236 mmol, 6.6 mg) were stirred in DCM (5 mL) for 1 h. A solution of **L6** (0.0236 mmol, 16.4 mg) in DCM (2 mL) was added dropwise, the yellow solution turned red and the mixture was stirred for 16 h. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as a brownish solid.

Yield: 25.5 mg (0.020 mmol, 85 %).

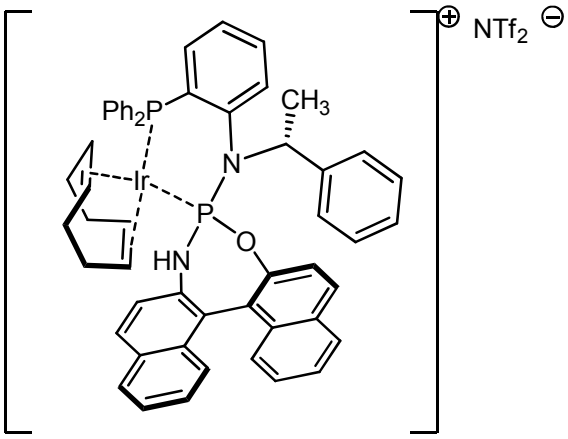
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.61 (bs, 3H, CH_3), 2.12–2.40 (m, 8H, COD), 4.52 (b, 1H, COD), 4.82 (b, 1H, COD), 5.27 (b overl., 2H, CH/COD), 5.51 (b, 1H, COD), 5.81 (d, *J* = 8.44 Hz, 1H, NH), 6.21 (m, 1H, Ar), 6.36 (m, 2H, Ar), 6.66 (m, 2H, Ar), 6.78-7.56 (m, 21H, Ar), 7.82- 7.99 (m, 5H, Ar) ppm.

^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 8.92 (d, $J_{P\text{-}P}$ = 43.8 Hz), 115.87 (d, $J_{P\text{-}P}$ = 43.8 Hz) ppm.

MS(Cation) (SIMS): m/z = 995.2
for: $C_{54}H_{48}IrN_2OP_2$ [Ir(COD)(**L6**)]$^+$ (calc.: 995.1)

MS(Anion) (SIMS): m/z = 279.9
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.1.34 [Ir(COD)(**L7**)][NTf_2] (**80**)



Synthesis and work-up were performed under argon. [Ir(COD)(acac)] (0.0236 mmol, 9.4 mg) and Bis(trifluoromethyl)sulfonamide (0.0236 mmol, 6.6 mg) were stirred in DCM (5 mL) for 1 h. A solution of **L7** (0.0236 mmol, 16.4 mg) in DCM (2 mL) was added dropwise, the yellow solution turned red and the mixture was stirred for 16 h. After removing the solvent under reduced pressure the residue was precipitated with pentane from dichloromethane. The product was obtained as a brownish solid.

Yield: 24.2 mg (0.019 mmol, 79 %).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.34 (d, *J* = 6.51 Hz, 3H, CH_3), 2.06–2.41 (m, 8H, COD), 4.55 (b, 1H, COD), 4.78 (b, 1H, COD), 5.19 (b, 1H, COD), 5.25 (m, 1H, CH), 5.46 (b, 1H, COD), 6.61 (m, 1H, Ar), 6.78–7.55 (m, 25H, Ar), 7.79-7.99 (m, 5H, Ar) ppm.

^{31}P{^{1}H}-NMR (125 MHz, CD_2Cl_2): δ = 6.42 (d, $J_{P\text{-}P}$ = 43.5 Hz), 113.87 (d, $J_{P\text{-}P}$ = 43.5 Hz) ppm.

MS(Cation) (SIMS): m/z = 995.2
for: $C_{54}H_{48}IrN_2OP_2$ [Ir(COD)(**L7**)]$^+$ (calc.: 995.1)

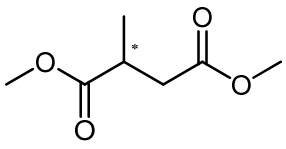
MS(Anion) (SIMS): m/z = 279.9
for: $C_2F_6NO_4S_2$ [NTf_2]$^-$ (calc.:279.9)

4.2.2 General procedures for catalytic reactions

4.2.2.1 Rh-catalysed asymmetric hydrogenation of olefines

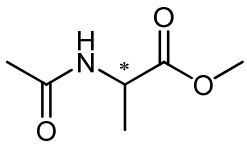
The preparation of the reaction was carried out under inert gas. In a 10 mL stainless steel autoclave with glass inlet and magnetic stirrer 1 mmol of the substrate was placed and degassed under reduced pressure. 2 mL of a stock solution of the [Rh(COD)(PP*)][NTf_2] complex (0.5µM, dried and degassed dichloromethane) were added. The mixture was stirred for 15 min, than pressurised with 10 bar of hydrogen. After 1 h of stirring at room temperature the reaction was stopped by a careful release of the hydrogen pressure. The solution was filtered over silica (eluent: DCM) and analysed via GC (conditions → chapter 4.1.7) and ^{1}H-NMR.
In case of substrate **D** the described procedure is not suitable. The retention times of the observed enantiomers are overlapping with the retention time of DCM and the products are too volatile to be separated from the solvent. The procedure was performed placing the solid Rh-complex (3.89 mmol) in the autoclave adding neat substrate (3.89 mmol, 0.5 mL) without any additional solvent. This mixture was stirred for 15 min and pressurised with 15 bar of hydrogen. After 1 h of stirring at room temperature the reaction was stopped by a careful release of the hydrogen pressure. Conversion was analysed via NMR and enantiomeric excess was determined via GC analysis of the gas phase over the reaction mixture.

A) Dimethyl 2-methylsuccinate



CAS-Nr.: (*R*) [22644-27-5], (*S*) [63163-08-6], (*rac*) [41771-07-7]
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H, CO_2CH_3), 3.67 (s, 3H, CO_2CH_3), 2.99-2.84 (m, 1H), 2.74 (dd, *J* =8.1 Hz, *J* =16.5 Hz, 1H), 2.39 (dd, *J* = 6.0 Hz, *J* = 16.5Hz, 1H), 1.21 (d, *J* = 7.1 Hz, 3H, CH_3) ppm.

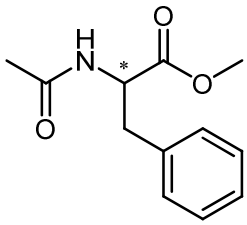
B) Methyl 2-acetamidopropanoate



CAS-Nr.: (*R*) [19914-36-4], (*S*) [3619-02-1], (*rac*) [26629-33-4]

^{1}H-NMR (300 MHz, DMSO-d6): δ = 1.37 (d, *J* = 7.3 Hz, 3H), 1.98 (s, 3H), 3.72 (s, 3H), 4.56 (q, *J* = 7.3 Hz, 1H), 6.26 (br. s, 1H, NH) ppm.

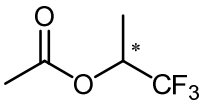
C) Methyl 2-acetamido-3-phenylpropanoate



CAS-Nr.: (*S*) [3618-96-0]

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3H), 3.07 (m, 1H), 3.16 (m, 1H), 3.73 (s, 3H, CH_3), 4.95 (m, 1H), 6.44 (d, *J* = 7.7 Hz, 1H, NH), 7.09-7.20 (m, 2H, Ar), 7.22-7.37 (m, 3H, Ar) ppm.

D) 1,1,1-trifluoropropan-2-yl acetate

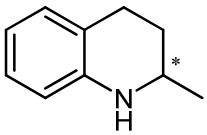


^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.32 (d, 3H, *J* = 6.6 Hz, CH*CH_3*); 2.06 (s, 3H, C*H_3*COO); 5.23 (h, 1H, *J* = 6.6 Hz, CH) ppm.

4.2.2.2 Ir-catalysed asymmetric hydrogenation of 2-sbstituted quinolines

The preparation of the reaction was carried out under inert gas. A solution of the ligand (0.011 mmol) in toluene (1.5 mL) was added dropwise to a solution of $[Ir(COD)Cl]_2$ (3.4 mg, 0.005 mmol, 0.01 mmol Ir) in toluene (1.5 mL). After 30 min of stirring iodine (12.6 mg, 0.05 mmol) was added and the mixture was stirred again for 10 min. In case of a liquid substrate (1 mmol) it was added directly to the mixture before the mixture was placed in a 10 mL autoclave with glass inlet and magnetic stirrer. A solid substrate was provided and degassed in the autoclave before. The autoclave was pressurised with 40 bar of hydrogen and stirred at room temperature for the stated time. The reaction was stopped by a careful release of the hydrogen pressure and a sample for NMR (ca 0.3 mL) analysis was taken. The rest of the mixture was diluted with DCM, and extracted with $NaHCO_{3(aq)}$, then extracted from the $NaHCO_{3(aq)}$-phase with DCM. The collected organic phases were dried over sodium sulphate and filtrated. The solvent was removed under reduced pressure and the residue was analysed via GC or HPLC.

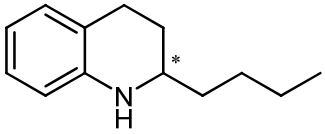
A) 2-methyl-1,2,3,4-tetrahydroquinoline



CAS-Nr.: (*R*)-(+) [63430-95-5], (*S*)-(–) [200125-70-8], (*rac*) [50830-46-1]

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.13 (δ, *J* = 6.4 Hz, 3H, CH_3), 1.51 (m, 1H), 1.85 (m, 1H), 2.71 (m, 2H), 3.32 (m, 1H), 3.61 (b, 1H, NH), 6.39 (m, 1H, Ar), 6.52 (m, 1H, Ar), 6.88 (m, 2H, Ar) ppm.

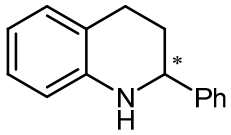
B) 2-butyl-1,2,3,4-tetrahydroquinoline



CAS-Nr.: (*R*)-(+) [608525-21-9], (*S*)-(–) [769121-83-7], (*rac*) [123612-55-5]

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 6.8 Hz, 3H, CH_3), 1.27-1.73 (m, 7H), 1.99 (m, 1H), 2.80 (m, 2H), 3.27 (m, 1H), 3.79 (br, 1H, NH), 6.50 (m, 1H, Ar), 6.62 (m, 1H, Ar), 6.98 (m, 2H, Ar) ppm.

C) 2-phenyl-1,2,3,4-tetrahydroquinoline



CAS-Nr.: (*R*)-(-) [769121-85-9], (*S*)-(+), (*rac*) [50830-46-1]

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.02 (m, 1H, CH_2), 2.15 (m, 1H, CH_2), 2.76 (m, 1H, CH_2), 2.96 (m, 1H, CH_2), 4.06 (br. s, 1H, NH), 4.48 (dd, *J* = 3.3 Hz, 9.2 Hz, 1H, CH), 6.57 (m, 1H, Ar), 6.68 (m, 1H, Ar), 7.03 (m, 2H, Ar), 7.15-7.47 (m, 5H, Ar) ppm.

4.2.2.3 Ir-catalysed asymmetric hydrogenation of (*E*)-*N*-(1-phenylethylidene)aniline

The preparation of the reaction was carried out under inert gas.

-in situ catalyst:

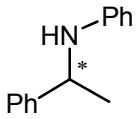
In a schlenk flask $[Ir(COD)Cl]_2$ (0.0005 mmol, 0.33 mg) and the ligand (0.001 mmol) were stirred in DCM (2 mL) for 30 min. $AgNTf_2$ (0.001 mmol, 0.25 mg) and I_2 (0.01 mmol, 1.3 mg) were added and the mixture was stirred for 15 min. The solution was placed in a 10 mL autoclave with glass inlet, magnetic stirrer and (E)-*N*-(1-phenylethylidene)aniline (1 mmol, 192 mg) and pressurised with 30 bar of hydrogen. After stirring for 20 h at 40 °C the reaction was stopped by a careful release of the hydrogen pressure. The solution was filtered over silica (eluent: DCM). Conversion and enantiomeric excess were determined via NMR and GC analysis.

-with preformed complex:

In a schlenk flask $[Ir(COD)(PP^*)][NTf_2]$ (0.001 mmol) and I_2 (0.01 mmol, 1.3 mg) were stirred in DCM (2 mL) for 15 min. The solution was placed in a 10 mL autoclave with glass inlet, magnetic stirrer and (E)-*N*-(1-phenylethylidene)aniline (1 mmol, 192 mg) and pressurised with 30 bar of hydrogen. After stirring for 20 h at 40 °C the reaction

was stopped by a careful release of the hydrogen pressure. The solution was filtered over silica (eluent: DCM). Conversion and enantiomeric excess were determined via NMR and GC analysis.

A) *N*-(1-phenylethyl)aniline



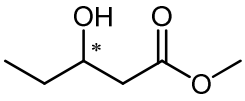
CAS-Nr.: (*rac*) [76716-27-3]

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.44 (d, *J* = 6.5 Hz, 3H, CH_3), 3.95 (b, 1H, NH), 4.41 (q, *J* = 13.34 Hz, 1H, CH), 6.43 (d, *J* = 7.5 Hz, 2H, Ar,CH), 6.56 (t, *J* = 7.5 Hz, 1H, Ar,CH), 7.01 (t, *J* = 7.5 Hz, 2H, Ar,CH), 7.12-7.32 (m, 5H, Ar,CH) ppm.

4.2.2.4 Ru-catalysed asymmetric hydrogenation of keto ester

The preparation of the reaction was carried out under inert gas. $[RuCl_2(p\text{-cymene})]_2$ (0.005 mmol, 2.9 mg) and the ligand (0.01 mmol) were stirred in a schlenk flask in toluene (1 mL) at 80 °C for 1 h. The solvent was removed under reduced pressure und the residue was taken up in methanol (2 mL). The substrate (1 mmol) was placed and degassed in a 10 mL autoclave with glass inlet and magnetic stirrer. Then, the catalyst solution was placed in the reactor, the mixture was stirred for 15 min and pressurised with 60 bar of hydrogen. After a reaction time of 16 h at 60 °C the mixture was cooled down to room temperature and the hydrogen pressure was carefully released. The solvent was removed under reduced pressure and the residue was taken up in DCM. This solution was filtered over silica and analysed via NMR and GC.

A) Methyl 3-hydroxypentanoate



CAS-Nr.: (*R*)-(-) [60793-22-8], (*S*)-(+) [42558-50-9]

^{1}H-NMR (300 MHz, Aceton-d_6): δ = 0.93 (t, 3H, CH_3), 1.47 (m, 2H, CH_2), 2.39 (m, 2H, CH_2), 3.62 (s, 3H OCH_3), 3.77 (br, 1H, OH), 3.89 (br, CH) ppm.

4.2.2.5 Pd-catalysed hydrophosphorylation of styrene

The reaction was carried out under inert gas. A dioxane solution (1 mL) of [CpPd(allyl)] (17.5 µmol, 3.7 mg), the ligand (19.25 µmol), pinacol H-phosphonate (0.35 mmol, 57.45 mg), and styrene (0.7 mmol, 0.08 mL) was placed in a closed microwave vessel with magnetic stirrer. The mixture was stirred and heated up in the microvawe to 100 °C for 8 h. The solvent was removed under reduced pressure and the residue was analysed via GC and ^{31}P-NMR.

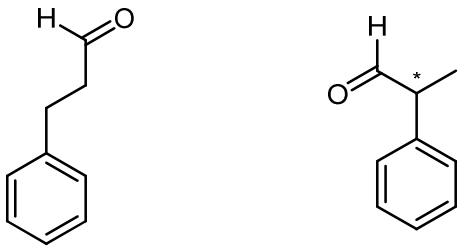
A) 4,4,5,5-Tetramethyl-2-(2-phenylethyl)1,3,2-dioaphospholane 2-oxide (linear)
4,4,5,5-Tetramethyl-2-(1-phenylethyl)1,3,2-dioaphospholane 2-oxide (branched)

^{31}P-NMR (125 MHz, $CDCl_3$): δ = 40.88 (b, linear product), 41.55 (b, branched product)

4.2.2.6 Rh-catalysed hydroformylation of styrene

The preparation of the reaction was carried out under inert gas. In a schlenk tube the ligand (8 µmol) was mixed with a stock solution of [Rh(acac)$(CO)_2$] (2 µmol in 2 mL toluene) and styrene (2 mmol, 0.22 mL). After stirring for 30 min the mixture was transferred into a 10 mL autoclave with glass inlet and magnetic stirrer. It was pressurised with 40 bar CO/H_2 and stirred for 16 h at 60 °C. At room temperature the pressure was carefully released and the solution was filtered over silica (eluent: 6 mL toluene). This mixture was analysed by NMR and GC.

A) 3-phenylpropanal (linear), 2-phenylpropanal (branched)



linear:

^{1}H-NMR (400 MHz, toluene): δ = 2.80 (t, 4H, CH_2), 7.10 (m, 5H, Ar, CH), 9.50 (s, 1H, CHO) ppm.

branched:

^{1}H-NMR (400 MHz, toluene): δ = 1.39 (b, 3H, CH_3), 3.28 (q, 1H, CH), 7.10 (m, 5H, Ar, CH), 9.55 (s, 1H, CHO) ppm.

4.2.2.7 Kinetic measurements: Rh-catalysed asymmetric hydrogenation of dimethyl 2-methylsuccinate

51 (5.0 mmol, 791.0 mg) was degassed in a 10 mL steel autoclave with glass inlet and magnetic stirrer under reduced pressure. A stock solution of a [Rh(COD)(PP*)][NTf_2] complex (2 mL, 0.5µM in DCM) was added and stirred for 30 min while the temperature was maintained via a cryostate at 20 °C. This temperature was kept constant during the whole procedure. The mixture was pressurised with 15 bar of hydrogen and the hydrogen consumption was observed via Labview. Data acquisition was stopped when a constant pressure was reached. The raction mixture was treated and analysed in the same way described before (4.2.2.1). The obtained data was used to calculate the average turnover frequency (TOF) and the initial turnover frequency ($TOF_{init.}$) using Excel.

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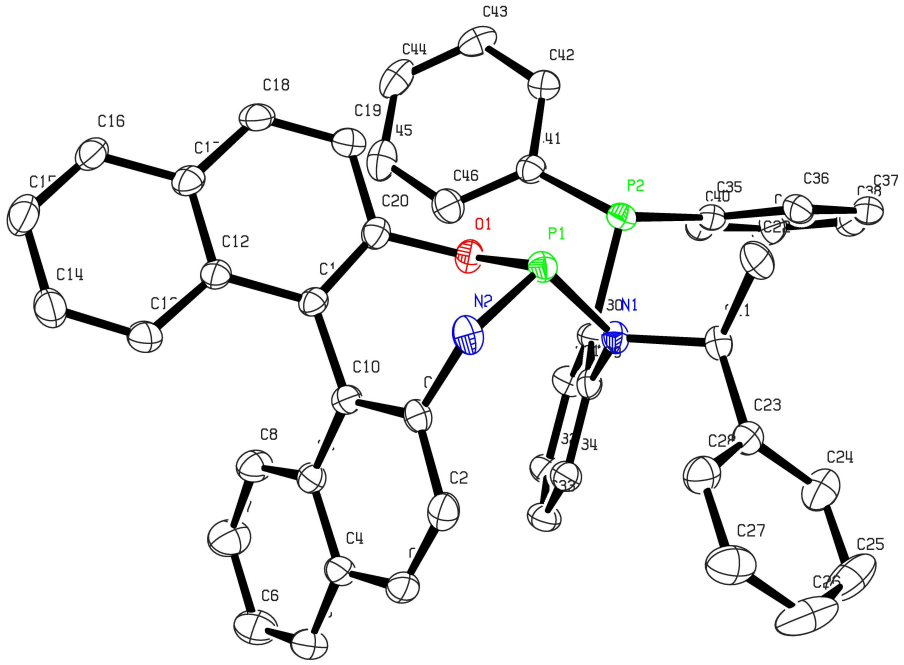
6 Appendices

6.1 Abbreviations

$[\alpha]_D^{20}$	optical rotation
Å	Ångström
acac	acetylacetonate
b	broad
BINAP	2,2’-Bis(diphenylphosphino)-1,1’-binaphthyl
BINOL	1,1’-Bi-2-naphthol
BuLi	Buthyl-lithium
C	catalyst
cod	1,4-cyclooctadiene
DCM	dichloromethane
DFT	density functional theory
DMAP	4-dimethylaminopyridine
DMSO	dimethylsulfoxide
δ	chemical shift
ee	enantiomeric excess
Et	ethyl
eq	equivalent
FID	flame ionisation detector
GC	gas chromatography
h	hour(s)
HPLC	high performance liquid chromatography
HR-MS	high resolution mass spectroscopy
Hz	Hertz
IR	infrared
J	coupling constant
L	ligand
M	Molar
m	multiplet
Me	methyl
min	minute(s)

MS	mass spectroscopy
NMP	*N*-methyl pyrollidone
NMR	nuclear magnetic resonance
NOBIN	2'-amino-1,1'-binaphthyl-2-ol
Ph	phenyl
ppm	parts per million
q	quartet
rf	retention factor
RT	room temperature
s	singlet
S	substrate
t	time
t	triplet
T	temperature
Tf	trifluormethanesulfonyl
THF	tetrahydrofurane
TLC	thin layer chromatography
TMEDA	*N,N,N,N*-tetramethylethylene diamine
TOF	turnover frequency (during reaction time)
TOF_{init}	initial turnover frequency
TON	turnover number
z	charge
*	symbol for a stereogenic centre

6.2 Crystal structure data for ligand L6



Empirical formula	$C_{46}H_{35}N_2OP_2$
M_r (g mol^{-1})	693.73
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a (Å)	9.0686(7)
b (Å)	17.5384(13)
c (Å)	22.3664(17)
α (°)	90
β (°)	90
γ (°)	90
V (Å^3)	3557.3(5)
Z	4
D_{calc} (g cm^{-3})	1.297
T (K)	143(2)
μ(Mo Kα) (mm^{-1})	0.71073
F(000)	1456
θ Range (°)	1.48 – 30.52
Number of reflections collected	53496
Number of reflections observed [$I > 2\sigma(I)$]	7928
Number of independent reflections (R_{int})	10232
Data/restraints/parameters	10232 / 0 / 463
Goodness-of-fit on F^2	0.701
R_1, wR_2 [$I > 2\sigma(I)$]	0.0472
R_1, wR_2 (all data)	0.1294
Largest difference peak and hole (e Å^{-3})	0.364 and -0.280
Flack parameter	-0.01(7)

6.3 Curriculum Vitae

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1988-1992	Elementary school: Gemeinschaftsgrundschule Ahe
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6.4 Acknowledgements

First of all, I thank Prof. Dr. Walter Leitner for his support and for giving me the opportunity to work in his group. Furthermore, I would like to thank Prof. Dr. Carsten Bolm for being my second examiner and Prof. Dr. Marcel Liauw and Prof. Dr. Wolfgang Stahl for being part of the promotion committee. I thank my subgoup-leader Dr. Giancarlo Franciò for continuous discussions and support with respect to the experimental work.

All members of the team and especially my lab colleagues Wenjing Li, Jens Langanke and Mike Schmitkamp, I want to thank for the nice and supportive atmosphere. My research student Fabian Langensiepen and my trainees Kevin Göbbels and Marcel Gerhards I would like to thank for their valuable contributions to the experimental part, as well as Andreas Uhe for performing the DFT calculations. Ines Bachmann-Remy (NMR), Hannelore Eschmann and Julia Wurlitzer (GC), Brigitte Pütz ((HR)MS) and the group of Prof. Dr. Uli Englert (X-ray), I thank for the performance of numerous analyses – without their effort this thesis would not exist.

Last but not least, I would like to thank my family for their support over the last years and especially my husband Geert-Jan for reading and correcting my thesis and for his love.