Iridium-Catalyzed Asymmetric Hydrogenation: Development of New N,P Ligands and Hydrogenation of Alkenyl Boronic Esters

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For my family

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Chapter 1

Introduction

1.1 The Development of Asymmetric Synthesis

Since the work of *L. Pasteur* in 1848,[1] scientist were aware of significance of stereoisomers in relation to biological activity.[2] Nevertheless, until 1992 most of the chiral drugs launched on the market were racemates, while only few new products were developed as enantiomeric pure compounds.[3] With the improvement of separation techniques, the progress of synthetic organic chemistry, insights of different pharmacokinetic behavior of enantiomers and tightened government regulations the situation changed.[2] Nowadays most of the newly launched chiral synthetic drugs are pure enantiomers.[3] As the result of growing demand for enantiopure compounds the development of stereoselective synthesis got more attention. Basically four different approaches are used to access enantiopure synthetic molecules:[3]

- Chiral pool strategy
- Resolution of racemic mixtures
- Diasteoreoselective synthesis
- Enantioselective synthesis

One possibility is to use naturally occurring molecules, which are transformed to target compounds.[4] This so called "chiral pool" strategy seems to be very attractive at first glance, as Nature produces many different molecules with a variety of functionalities. However, there are two major limitations. The abundance of many natural products is limited, which makes their isolation difficult and expensive. Furthermore, most of the natural products appear only in one configuration, for example 20 out of the 21 proteinogenic amino acids. Very often several synthetic steps are required to invert the stereogenic center, which prolongs the reaction sequence. Nevertheless, this approach is still frequently applied in pharmaceutical industry.[3, 5]

On the other hand, the preparation of racemates and separation of the enantiomers by resolution is also still popular in pharmaceutical industry.[3, 5] In this case three different categories are distinguished.[6] One is using chiral external resolving reagents, which form diasteroemeric salts with racemic targets. In contrast to enantiomers, diastereomeres can be separated by traditional techniques, for example by fractional crystallization. Alternatively, the separation of enantiomers is also possible in the absence of an external chiral reagent, for example by "simulated moving bed chromatography" on chiral stationary phase[7] or by "preferential crystallization" using enantiopure seed crystals.[8] These methods are very laborious as usually numerous recycling cycles are required in order to obtain pure

enantiomers. Furthermore, a maximum yield of 50% is possible, unless the "undesired" enantiomer can undergo racemization and further resolution. However, it should be mentioned that modern methods are available, where fast racemization of the starting material is induced, in order to obtain yields over 50%. This process is named as dynamic kinetic resolution (DKR) or also as dynamic kinetic asymmetric transformation (DYKAT).[9]

Alternatively, chiral auxiliaries can be used in order to control stereoinduction.[10] Over the years several auxiliaries were introduced, which are based on naturally occurring molecules. Some of the privileged systems are depicted in scheme 1.1, like *Evans'* oxazolidinones,[11] *Enders'* SAMP[12] or *Myers'* pseudoeffedrine[13] auxiliaries. Such chiral auxiliaries are covalently bound to a substrate (the positions are showed by arrows) and they are able to influence the stereochemical outcome of a reaction. Moreover as the stereoisomers formed during the reaction are diasteromers, their separation is also easily achieved by traditional separation techniques. After the reaction the auxiliaries are removed from the molecules and can be recycled. Therefore, there are always at least two additional steps in the synthetic sequence required, which prolong the synthesis.[10] Nevertheless, this methodology is still frequently applied in the pharmaceutical industry, especially in the early stages of process development as relatively short development times are usually required.[5]

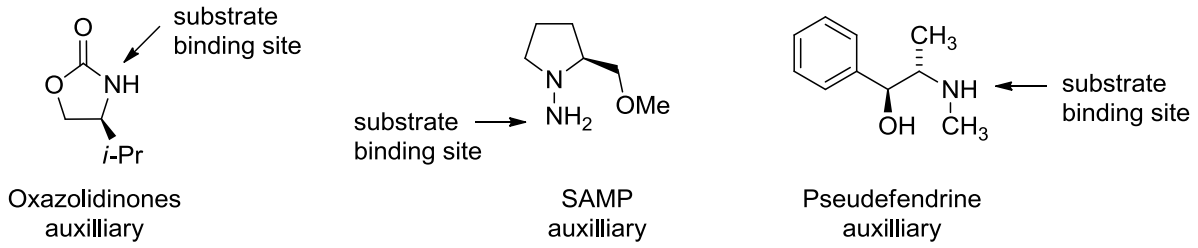


Figure 1.1: Selected chiral auxiliaries for diastereoselective synthesis.[10]

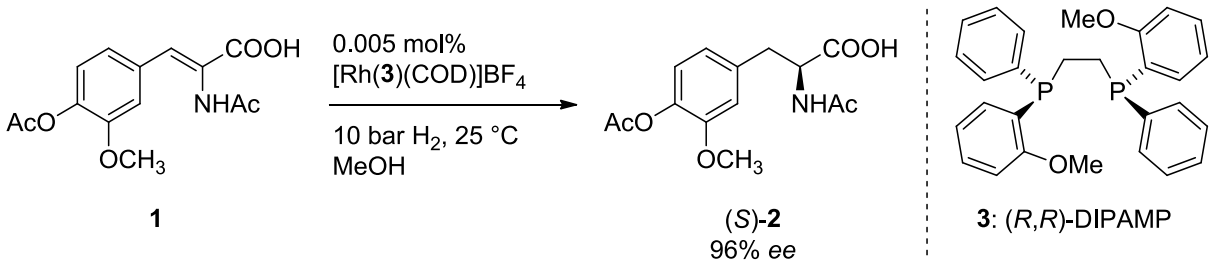
In addition, to the diastereomeric synthesis, the stoichiometric use of chiral reagents for an asymmetric transformation is also possible. However, this approach is only interesting for chiral reagents which are based on cheap and readily available starting materials (for example α–pinene, ephedrine, cinchona alkaloids or tartaric acid). In contrast to the auxiliary approach this does not prolong the reaction sequence. Nevertheless, additional work is required for separation and recycling of the chiral reagent, in order to reduce the amount of waste and disposal.[5]

Among all possible approaches to enantiomerically pure compounds, asymmetric synthesis using catalytic procedures is in the majority of the cases superior. Asymmetric synthesis allows the fast and direct generation of enantiopure compounds from simple and readily

available starting materials by using a substoichiometric amount of a chiral catalyst. Moreover, taking the limitation of raw materials and environmental issues in account, the catalytic synthesis of complex organic molecules will gain more importance in the near future. Over the past years several catalytic asymmetric transformations were investigated, which found numerous applications.[14] Metal-catalyzed asymmetric hydrogenation is one example, which allows the atom economic[15] incorporation of dihydrogen into unsaturated olefins and carbonyl compounds.[16] The importance of asymmetric hydrogenation was recognized by awarding *W. Knowles*[17] and *R. Noyori*[18] with the Nobel Prize in 2001 together with *B. Sharpless* for his work on catalytic asymmetric oxidation reactions.[19]

1.2 Asymmetric Hydrogenation Using Rh- and Ru-Complexes

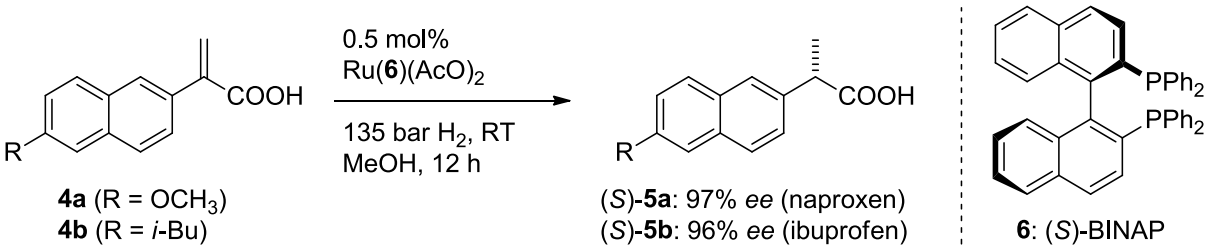
Asymmetric hydrogenation is a powerful tool to convert prochiral substrates into chiral products with high enantiomeric purity. The reaction fulfills all the requirements of modern asymmetric synthesis, such as perfect atom economy, mild conditions, low catalyst loading and high conversion.[20] Since the pioneering work of *W. Knowles* and *R. Noyori* these reactions enjoyed an unrivaled success in organic chemistry. *W. Knowles* implemented rhodium complexes in combination with P-chiral diphosphine ligands **3** for the hydrogenation of α,ß-dehydroamino acids such as **1**, which was the key step in the *Monsanto* process for large-scale production of L-Dopa, a rare natural amino acid for the treatment of Parkinson's disease.[17, 21]



1 (*S*)-**2** 96% *ee* **3**: (*R*,*R*)-DIPAMP

Scheme 1.1: Rh-catalyzed asymmetric hydrogenation as the key step in the *Monsanto* process for L-Dopa production.

On the other hand *R. Noyori* introduced BINAP ligands **6** as versatile systems for the Rh- and Ru-catalyzed reduction of functionalized C=C and C=O bonds.[18] For instance, these catalysts showed high activity in the hydrogenation of substrates **4a**[22] and **4b**,[23] providing access to the antiinflammatory agents[24] naproxen (*S*)-**5a** and ibuprofen (*S*)-**5b**.



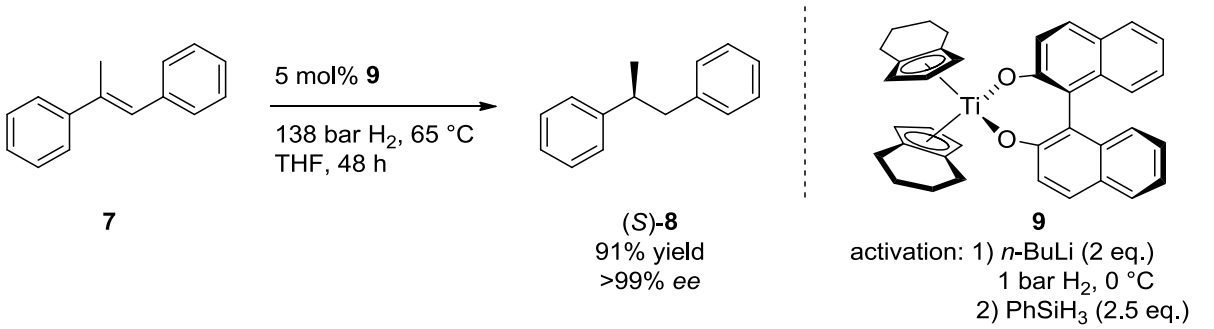
4a (R = OCH_3)
4b (R = *i*-Bu)

(*S*)-**5a**: 97% *ee* (naproxen)
(*S*)-**5b**: 96% *ee* (ibuprofen)

6: (*S*)-BINAP

Scheme 1.2: Ru-BINAP-catalyzed asymmetric hydrogenation of C=C bonds, providing access to drugs naproxen **5a** and ibuprofen **5b**.[22-23]

Despite the vast variety of chiral Rh and Ru catalyst developed so far (many of them are commercially available), the scope of substrates that can be hydrogenated with high enantioselectivity remains limited. In general, both rhodium und ruthenium complexes require substrates bearing a coordinating functional group adjacent to the C=C bond in order to achieve high levels of *ee*.[25] In 1993, *R. Broene* and *S. Buchwald* reported a chiral titanocene complex,[26] as an efficient catalyst for the hydrogenation of unfunctionalized trisubstituted olefins.[27] For example, in the hydrogenation of α-methylstilbene **7** an excellent *ee* was obtained (scheme 1.3). Furthermore, also a zircocene derived catalyst was developed for the asymmetric hydrogenation of tetrasubstituted olefins.[28] Due to the tedious preparation, moisture- and air-sensitivity and relatively high catalyst loadings such metallocenes have not found any general applicability.



7

(*S*)-**8**
91% yield
>99% *ee*

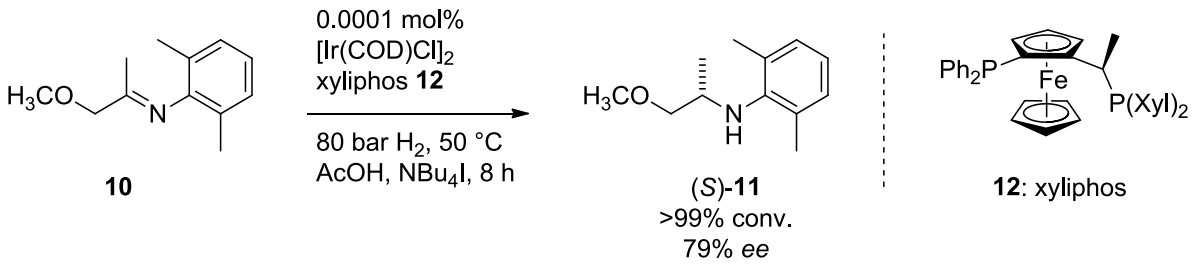
9
activation: 1) *n*-BuLi (2 eq.)
1 bar H_2, 0 °C
2) $PhSiH_3$ (2.5 eq.)

Scheme 1.3: First successful asymmetric hydrogenation of unfunctionalized olefins, like **7** using a chiral titanocene catalyst **9**.[27]

1.3 Ir-Catalyzed Asymmetric Hydrogenation

For a long period, iridium complexes were considered to be only interesting to provide isolable analogs of species thought to be important in rhodium catalysis.[29] However, the pioneer work of *R. Crabtree*, demonstrated clearly that Ir-complexes derived from mixed donor ligands are more active in the hydrogenation of tri- and tetrasubstituted olefins lacking coordinating groups.[30]

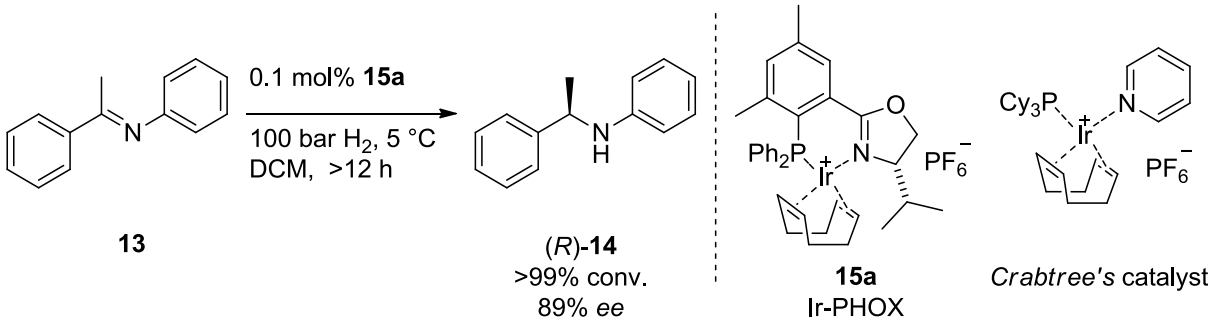
Thanks to the high activity iridium catalysts are attractive for industrial applications. One such very successful example is the Ir-catalyzed asymmetric hydrogenation of imine **10** mediated by a chiral ferrocenyl based diphosphine ligand called Xyliphos **12**, a member of the extremely successful Josiphos[31] ligand family (scheme 1.4). The chiral amine obtained **11** is used for the production of an important grass herbicide named (*S*)-metolachlor. This process is running since 1996 at *Syngenta* and delivers the target compound on a large scale (>10000 t/y).



Scheme 1.4: Ir-catalyzed asymmetric hydrogenation of imine **10** as a key step for the industrial production of herbicide (*S*)-metolachlor.[32]

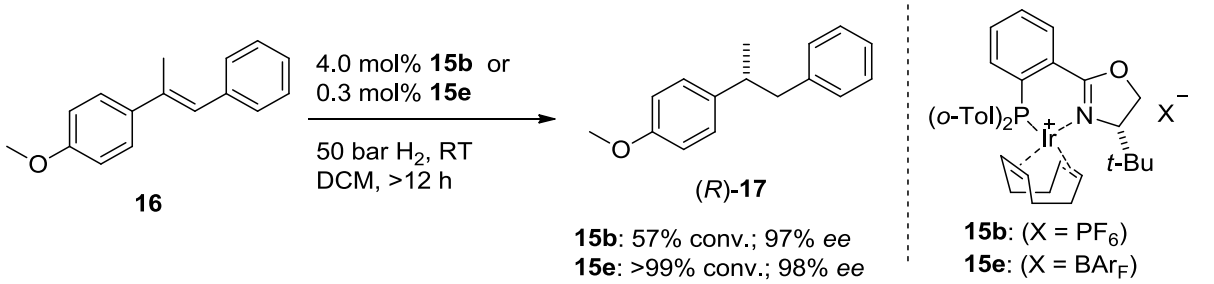
1.3.1 N,P Ligands Early Development

All previously described ligands contained two phosphorus atoms, which coordinate to the metal center. In contrast to the ligands mentioned above chiral phosphinooxazoline (PHOX) were developed in order to coordinate to the metal *via* a hard σ-donor (N) and a soft σ-donor (P).[33] These N,P ligands were initially employed in the allylic substitution, but found also use in other asymmetric reactions.[34] Because of the obvious coordination similarity to the achiral *Crabtree's* catalyst, *A. Pfaltz* and co-workers considered to use PHOX ligands in the asymmetric hydrogenation. Indeed, the results obtained in the reduction of imines were promising. Under optimized conditions the model substrate **13** could be fully reduced to afford the chiral amine (*R*)-**14** with 89% *ee* (scheme 1.5).[35]



Scheme 1.5: Asymmetric hydrogenation of imine **13** mediated by Ir-PHOX catalyst **15a**.[35]

Encouraged by these positive results, Ir-PHOX catalysts were investigated for the asymmetric hydrogenation of unfunctionalized olefins. Again the initial results using olefin **16** were very promising as enantiomeric excess up to 97% could be obtained (scheme 1.6).[36] However, catalyst deactivation during the reaction led to incomplete conversions. Therefore, relatively high catalyst loadings (>4 mol%) were required, in order to achieve reasonable yield of hydrogenation product. Attempts to increase the catalyst activity by variation of the hydrogen pressure, temperature, solvent or concentration failed. The use of additives such as halides, amines or carboxylates was also not succesfull, due to catalyst poisoning. After extensive experimental studies, a relatively simple solution to avoid catalyst deactivation was found. By changing the counterion from PF_6^- to a bulky, apolar, weakly coordinating anion like tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BAr_F),[37] full conversions could be achieved even at low catalyst loadings (0.3 mol%, scheme 1.6).[36, 38]

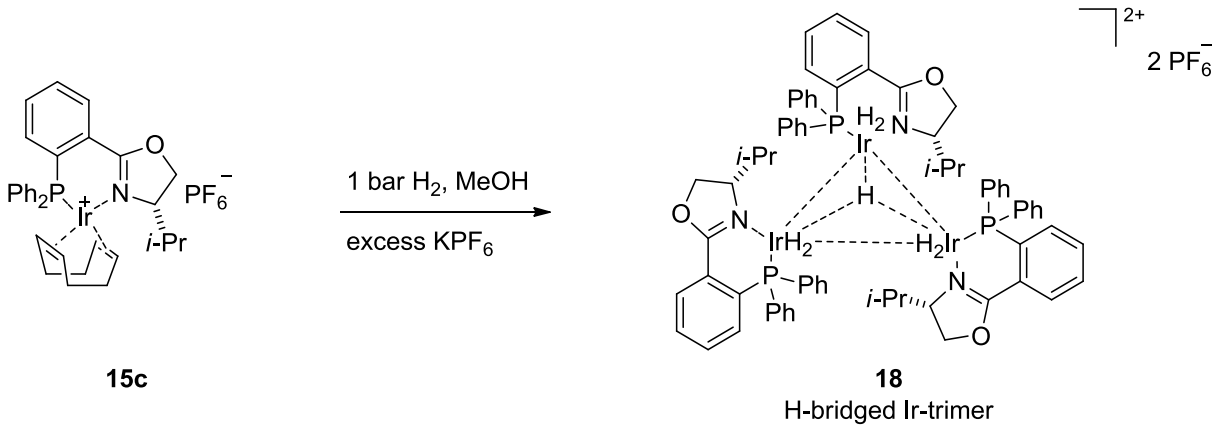


Scheme 1.6: Ir-catalyzed asymmetric hydrogenation of unfunctionalized olefin **16** using PHOX ligands.[36]

1.3.2 The Counterion Effect

As already mentioned, the initially high catalyst loading for the asymmetric hydrogenation of unfunctionalized olefins was required due to the catalyst deactivation during the hydrogenation. Such a deactivation pathway was already reported *R. Crabtree* for his achiral

catalyst.[30] An irreversibly formed trinuclear iridium species was identified as the inactive form of the catalyst. Similar species were also observed by ^{1}H-NMR analysis in the *Pfaltz* group for the deactivation of the Ir-PHOX **15** catalyst. However, the final proof was achieved when the trinuclear hydride-bridged-complex **18** was isolated and fully characterized (scheme 1.7). All attempts to use complex **18** for hydrogenation or to generate the active catalyst from this species failed.[39]

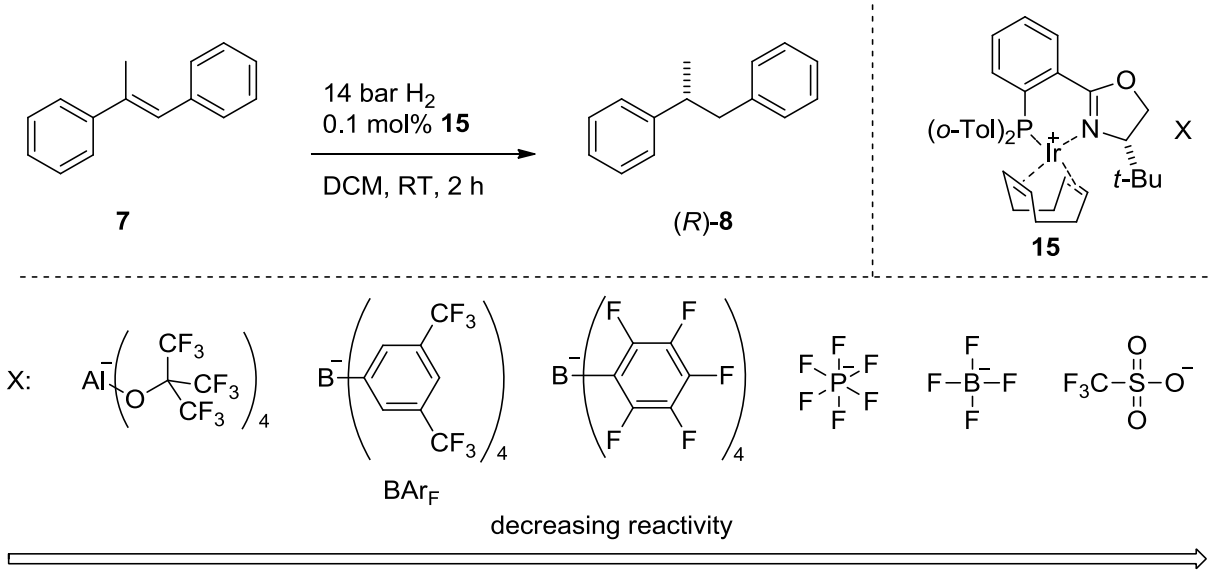


15c **18**
H-bridged Ir-trimer

Scheme 1.7: Formation of H-bridged trinuclear Ir-complex **18**.[39]

As mentioned above, the solution to the deactivation problem was the change of the counterion to BAr_F. By using this virtually non-coordination anion Ir-complexes showed higher stability under the hydrogenation conditions and were less sensitive to moisture. Moreover, the purification of the pre-catalyst by column chromatography became possible.[36]
A systematic screening of several anions in combination with kinetic studies showed that tetrakis(perfluoro-tertbutoxy)aluminate and tetrakis(pentafluorophenyl)borate were performing with essentially same efficiency as BAr_F in the hydrogenation reaction, whereas more coordinating anions like PF_6 or BF_4 gave slow reactions and incomplete conversion or even inhibit (triflate) the reaction (scheme 1.8).[40] From these kinetic studies a first order rate dependence on catalyst and hydrogen gas concentration in solution was obtained for both counterions (PF_6 and BAr_F). Also a first order dependence on olefin concentration was found for the PF_6-complex, whereas the rate dependence for the corresponding BAr_F-complex was close to zero. This implies that the olefin is involved in the turnover-limiting step for the PF_6-complex, but not for the BAr_F-complex. The explanation for this discrepancy is the different stability of the bishydride-intermediates. These bishydride-intermediates form a tighter ion-pair between the metal center and PF_6. As a consequence the substrate is competing with the counterion to access the metal center. In this respect, the deactivation observed occurs

presumably under the hydrogenation conditions. Whereas the metal center remains "naked" with BAr_F and the olefin can access the metal faster. Therefore, the hydrogenation pathway predominates over the deactivation pathway.[38, 40]



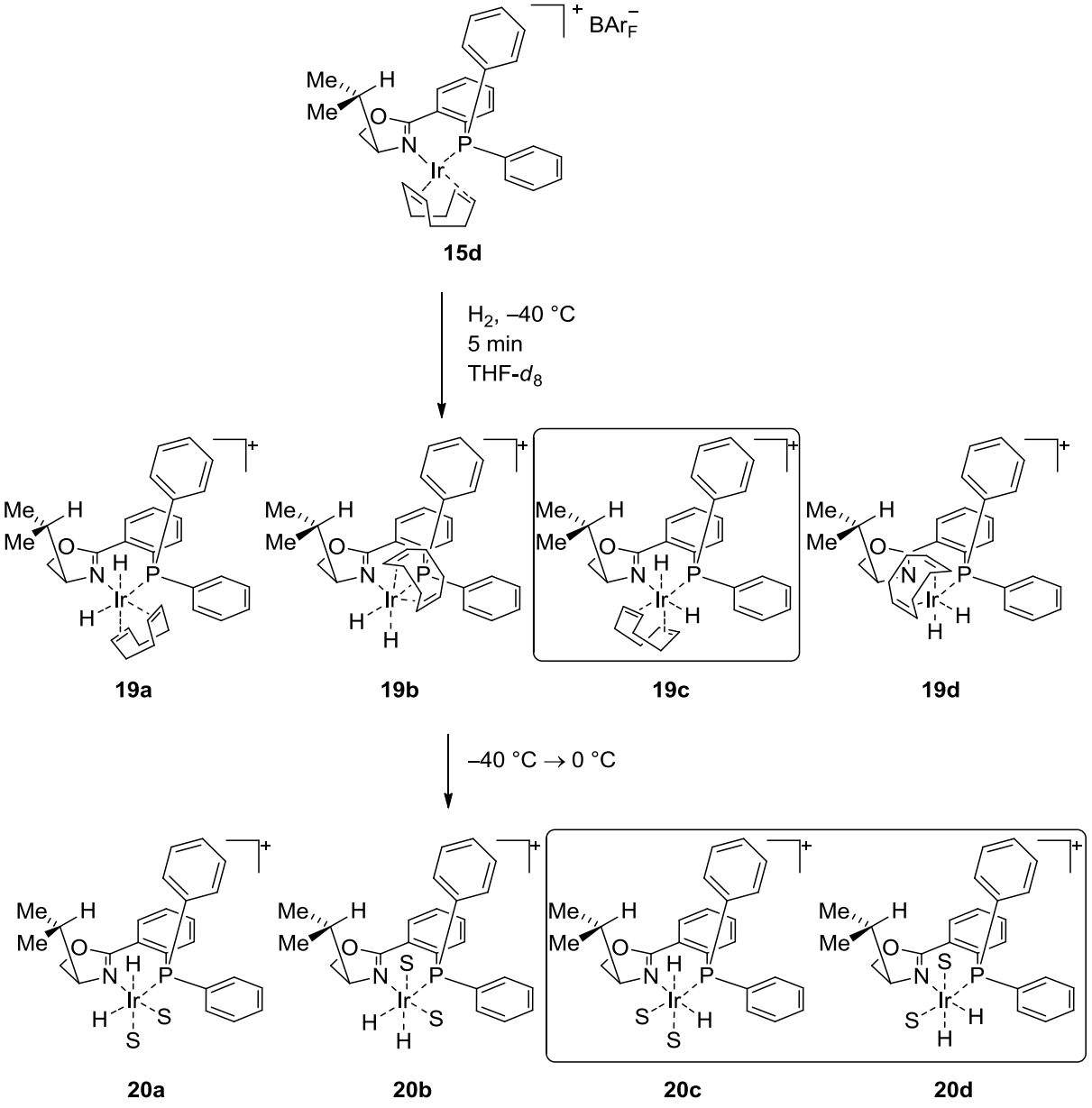
Scheme 1.8: Counterion effect in the Ir-catalyzed hydrogenation of unfunctionalized olefins.[40]

1.3.3 NMR Study on Catalyst Activation

Despite the remarkable progress over the last fifteen years in the field of iridium-catalyzed asymmetric hydrogenation, the catalytic cycle of this reaction is not yet fully understood. On the basis of *Crabtree's* work,[41] where olefin dihydride intermediates were identified and characterized by NMR, *A. Pfaltz* and co-workers performed complementary NMR studies using the PHOX derived complex **15d** (scheme 1.9).[42]

Addition of dihydrogen to a solution of complex **15d** in THF at −40 °C gave already after 5 min the COD-dihydride intermediates **19a-d**, which were characterized by NMR spectroscopy. Because of its coordinating properties, THF had to be used as solvent for this study to observe clean spectra, whereas the standard solvent for the Ir-catalyzed hydrogenation, dichlormethane gave complex reaction mixtures. Two new hydride signals appeared in the high field region of the ^{1}H-NMR spectrum (at −12.7 and −15.6 ppm), which were assigned to complex **19c**. Like in intermediate **19d**, one of the hydride is *trans* to the N donor, which is electronically favored over the *trans* orientation to the P donor found in intermediates **19a** and **19b**. These observations are in agreement with previous work obtained with *Crabtree's* catalyst.[41] The predominance of **19c** over **19d** is explained by steric strain

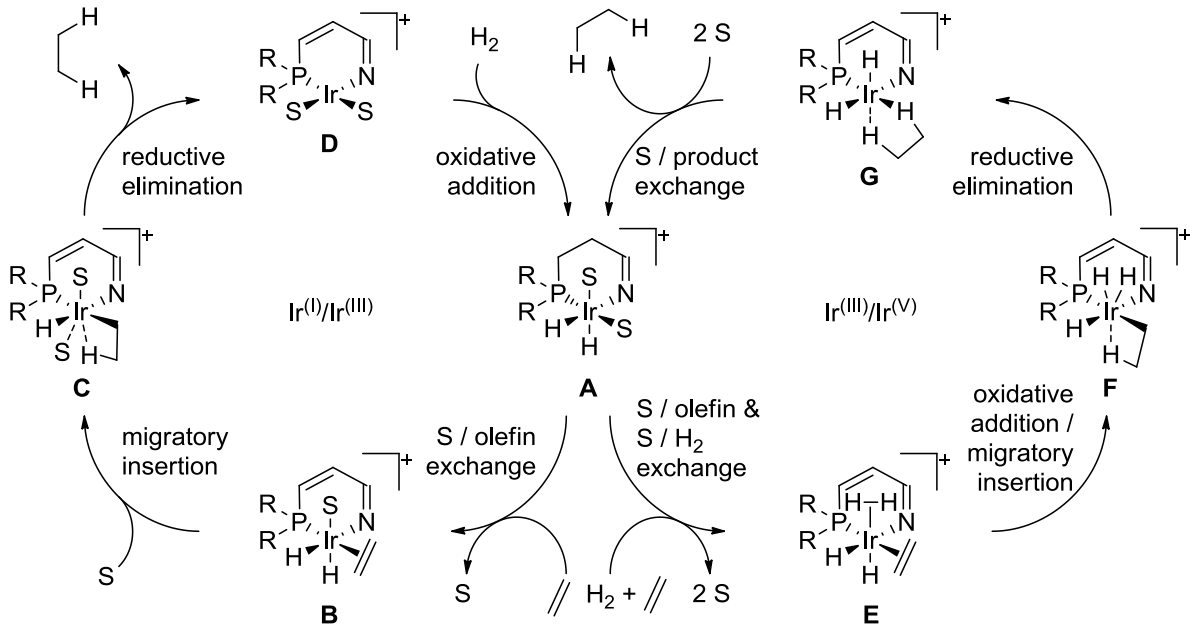
between the COD ligand and isopropyl group in the oxazoline and the pseudoaxial phenyl rings on phosphorus atom found in **19d**. After increasing the temperature to 0 °C under hydrogen atmosphere the signals assigned the COD ligand slowly disappeared. Two new hydrides were observed, which were assigned to the isomers **20c** and **20d**. Again both complexes contain the hydrides *trans* to the nitrogen atom and *cis* to phosphorus atom. These complexes are considered as the potential first active intermediates in the catalytic cycle. In a next step the complexes **20c** and **20d** should substitute one of the solvent molecule by the olefin in order to form again an olefin-metal complex. However, all attempts to gain more information about other possible intermediates being involved in the catalytic cycle by NMR spectroscopy failed so far.[38, 43]



Scheme 1.9: Activation of the pre-catalyst **15d** with dihydrogen gas and formation intermediates **19** and **20** (the BAr_F counterions were omitted for clarity).[43]

1.3.4 Catalytic Cycle

Two different catalytic cycles, either *via* $Ir^{(I)}/Ir^{(III)}$ (left) or *via* $Ir^{(III)}/Ir^{(V)}$ (right) intermediates, which have been proposed are shown in scheme 1.10.[44] In analogy to the established cycle found for Rh-diphosphine complexes,[45] *P. Chen* and *R. Dietiker* postulated the $Ir^{(I)}/Ir^{(III)}$ cycle (left). They suggested this pathway on the basis of experimental data obtained from electrospray ionization tandem mass spectrometry by investigating the hydrogenation of styrene using Ir-PHOX complex **15c**.[43] As suggested by the NMR study, this pathway starts from the $Ir^{(III)}$-dihydride intermediate **A** (scheme 1.9; labeled as **20c** and **20d**). The first step consists of a ligand exchange of the coordinating solvent for an alkene, to obtain the olefin-dihydride intermediate **B**. Migratory insertion of the Ir-hydride into the C=C bond, together with coordination of a solvent molecule leads to an alkyl-hydride complex **C**, which releases the hydrogenation product upon reductive elimination leading to the $Ir^{(I)}$-complex **D**. Oxidative addition of dihydrogen regenerates the active $Ir^{(III)}$-dihydride intermediate **A**.



Scheme 1.10: Postulated catalytic cycles for the Ir-catalyzed asymmetric hydrogenation. S = solvent.[44]

However, this pathway is in contrast with DFT calculation studies performed by *P. Brandt et al.* where an $Ir^{(III)}/Ir^{(V)}$ cycle was energetically favored.[46] In this case the solvent molecules are initially replaced by olefin and additional dihydrogen to generate the intermediate **E**. A step combining oxidative addition and migratory insertion was proposed to take place, leading to the complex with a polyhydride $Ir^{(V)}$ intermediate **F**. Again reductive elimination gives the $Ir^{(III)}$ intermediate **G**, which releases the hydrogenation product and reforms the dihydride-

solvate complex **A**. However, since a very simplified model for the ligand (CH_3-N-$(CH)_3$-P-$(CH_3)_2$) and substrate (ethylene) were used for these studies, which completely neglect important steric interaction, $Ir^{(I)}/Ir^{(III)}$ cycle could not be completely ruled out.[38] However, recent studies using comprehensive quantum mechanical calculations and the active catalyst derived from Ir-PHOX **15c** support the $Ir^{(III)}/Ir^{(V)}$ cycle.[47]

1.3.5 Selected N,P Ligands and Their Substrate Scope

Soon after the first report on Ir-PHOX complexes as catalysts for asymmetric hydrogenation,[36] the investigation of new N,P ligand scaffolds started. Some selected ligands developed in the *Pfaltz* group are shown in figure 1.2. Like PHOX ligands, the majority of these systems is based on enantiopure molecules derived from the chiral pool, which are assembled to furnish a heterocyclic ring and connected to a phosphine or a phosphinite unit.[38b] Their application to the iridium-catalyzed asymmetric hydrogenation is discussed in the next sections.

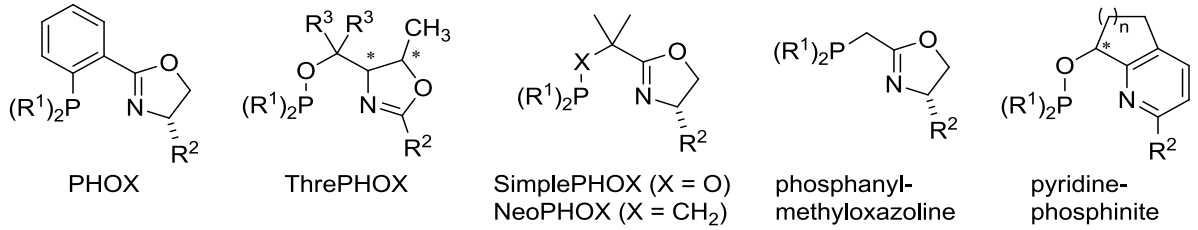
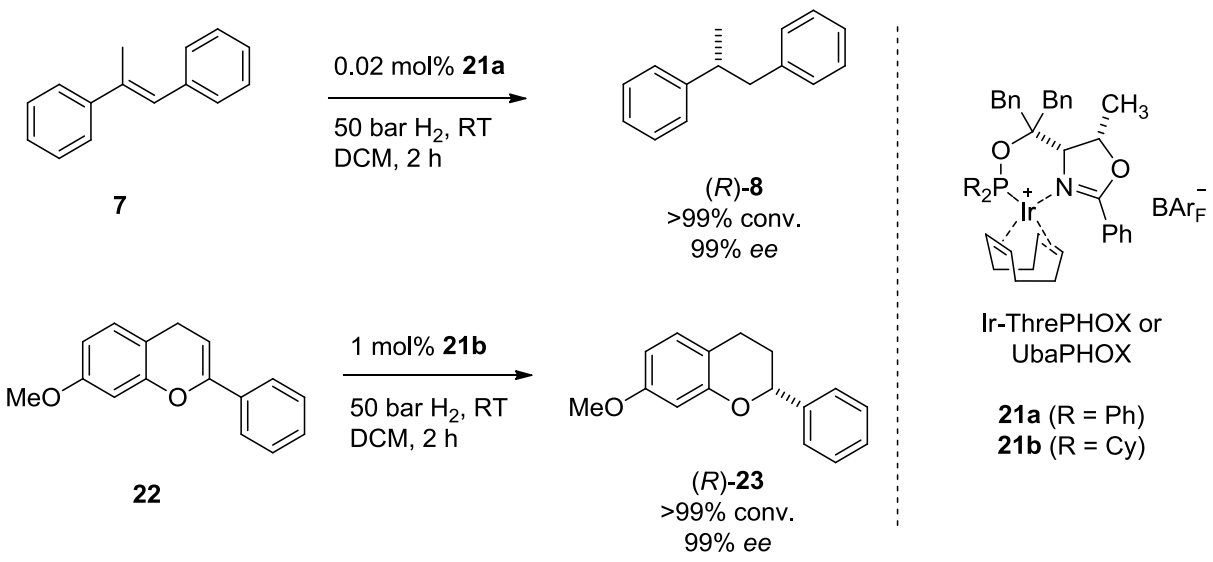


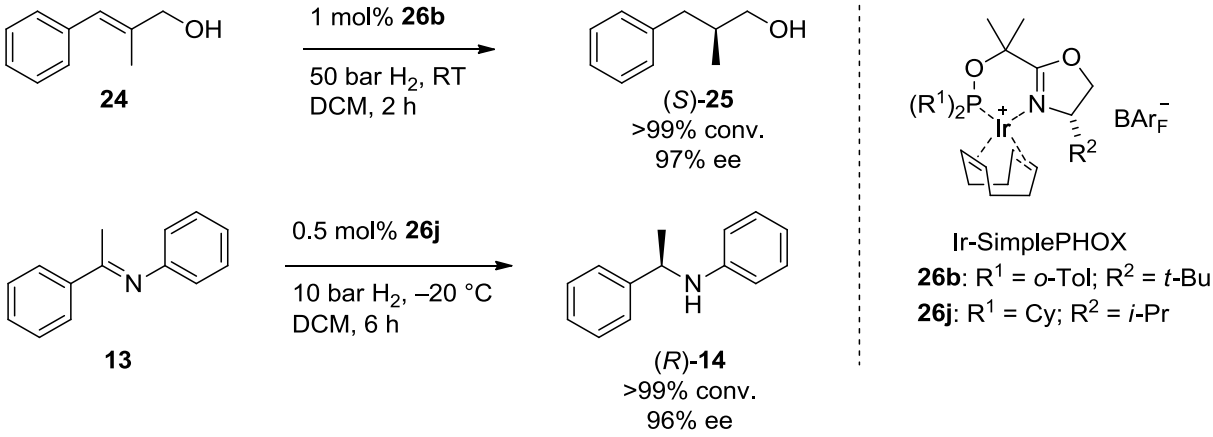
Figure 1.2: Selected N,P ligands developed in the *Pfaltz* group.[38b]

One example of very successful ligands is ThrePHOX, which is obtained from the amino acid threonine.[48] Some of its Ir-complexes are commercially available named as UbaPHOX **21**. These catalysts gave excellent enantioselectivities for several model substrates usually applied in the hydrogenation. Using catalyst **21a**, for example, α-methylstilbene **7** was hydrogenated with 99% *ee* (scheme 1.11 top).[48] Furthermore, ThrePHOX derived catalysts were used in the hydrogenation of terminal C=C bonds[49] and they showed also high activity and selectivity in the hydrogenation of 2-alkyl and 2-aryl-4*H*-chromenes providing access to chiral flavenes like **23**.[50]



Scheme 1.11: Selected applications of ThrePHOX derived Ir-catalysts **21** in asymmetric hydrogenations.[48]

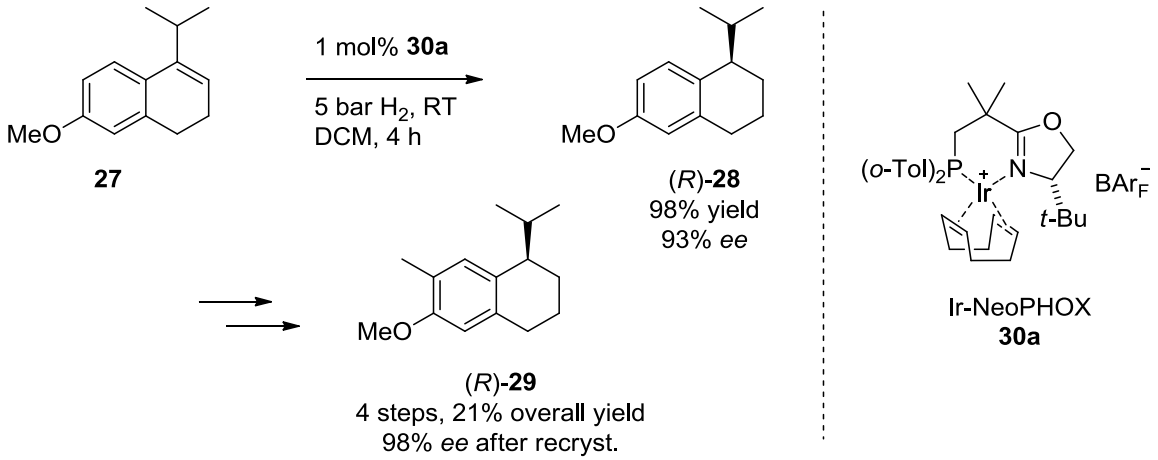
SimplePHOX ligands consist also of the oxazoline scaffold, which is accessible in one step from amino alcohols and 2-hydroxy-2-methylpropionic acid. These ligands are the first reported examples that provide high *ee*s for functionalized olefins, like allylic alchol **24** using complex **26b** (scheme 1.12).[51] Furthermore, the P-alkyl complexes **26j** of this ligand family gave the best enatioselectivities in the hydrogenation of imines.[52]



Scheme 1.12: Selected applications of Ir-SimplePHOX complexes **26** in asymmetric hydrogenation.[51]

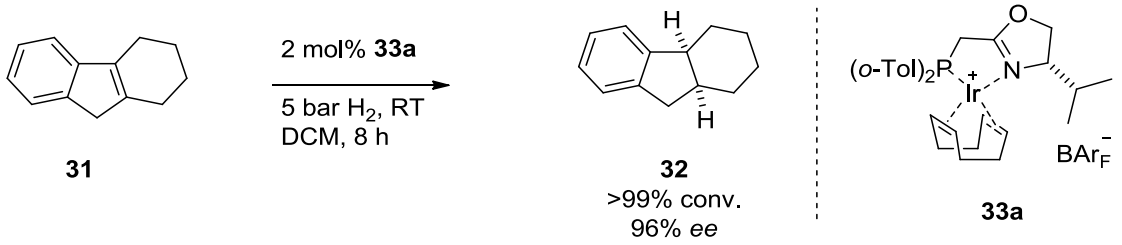
Their phosphine analogues, which were named NeoPHOX provided access to the important chiral tetraline motif. For example complex **30a** was applied to the enantioselective (98% *ee*) four steps total synthesis of the antitumor natural product (*R*)-(+)-7-demethyl-2-

methoxycalamenene **29** (scheme 1.13).[53] Furthermore, they were also used for the diastereoselective hydrogenation of polyene pyridine natural products.[54]



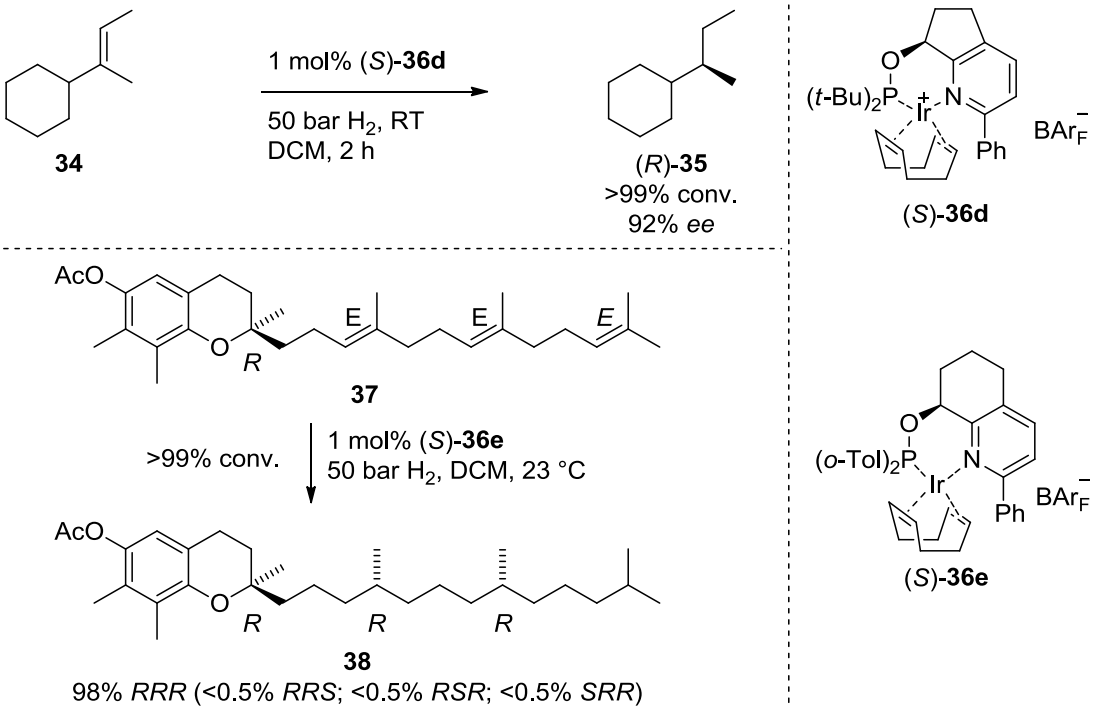
Scheme 1.13: Selected application of Ir-NeoPHOX complexes **30** in asymmetric hydrogenation.[53]

Phosphanylmethyloxazoline ligands were first reported by *M. Sprinz* and *G. Helmchen* in 1993,[33a] but were not been used until recently in iridium catalysis. In contrast to previously described systems, they form a five-membered chelate ring with the metal center. Ir-complexes such as **33a** were successfully applied to the asymmetric hydrogenation of tetrasubstituted olefins. For example the tricyclic olefin **31** was hydrogenated generating two stereogenic centers in excellent selectivity (scheme 1.14).[55]



Scheme 1.14: The application of Ir-phosphanylmethyloxazoline catalyst **33** for the hydrogenation of the tetrasubstitued olefin **31**.[55]

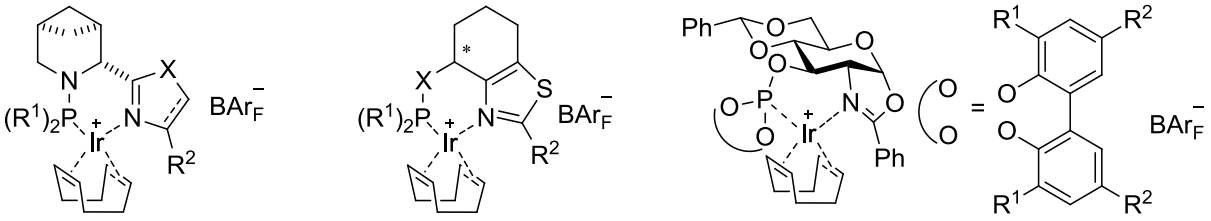
Despite the achievements made so far, asymmetric hydrogenation of purely alkyl substituted olefins remained challenging. With the development of bicyclic pyridine-phosphinite N,P ligands in the *Pfaltz* group even substrates like olefin **34** could be hydrogenated with high *ee* using complex **36d**.[56] Even more remarkable was the performance of structurally similar catalyst **36e** in the hydrogenation of the side chain of γ-toco-trienylacetate **37** (scheme 1.15). In this reaction three C=C bonds were fully reduced and two new stereogenic centers created in high enantiomeric purity.



Scheme 1.15: Selected applications of byclic pyridine-phosphinite derived Ir-catayst **36** in the asymmetric hydrogenation of purely alkyl substituted olefins **34** and **37**.[56]

Additionally, these catalysts provide also excellent *ee*s in the hydrogenation of several trisubstituted model olefins.[57] Furthermore, they were also successfully applied to the hydrogenation of heterocyclic aromatic compounds, like furans[57] and indoles.[58] Finally, their potential was also demonstrated in the synthesis of several natural products, such as Mutisianthol,[59] Macrocidin A,[60] and (+)-Torrubiellone C.[54]

Besides the ligands developed in the *Pfaltz* group, many N,P ligands were developed in other research groups for the asymmetric hydrogenation of C=C and C=N bonds. Among them most notable examples are the systems reported by *P. G. Andersson* and co-workers (figure 1.3). For example the PHOX type catalysts **39** with three additional stereogenic centers were found to be useful for the reduction of imines,[61] enamines,[62] enol phosphinates,[63] vinylboronates,[64] α,β-unsaturated esters[65] and unsaturated sulfones.[66] On the other hand, the rigid bicyclic thiozole complexes **40**[67] were quite successful in the hydrogenation of terminal diaryl olefins,[68] vinylfluorides[69] and vinylphosphonates.[70] More recently *P. G. Andersson* and co-workers introduced pyrinoside phosphite-oxazoline Ir-complexes **41** for the asymmetric hydrogenation of minimally functionalized olefins.[71] Most remarkably these catalysts provided excellent enantioselectivities for the usually challenging terminal olefins.[72]



39

X = O, S
R^1 = Ph, *o*-Tol
R^2 = *i*-Pr
→ imines & enamines
→ enol phosphonates
→ vinylboronates
→ α,β–unsaturated esters
→ unsaturated sulfones

40

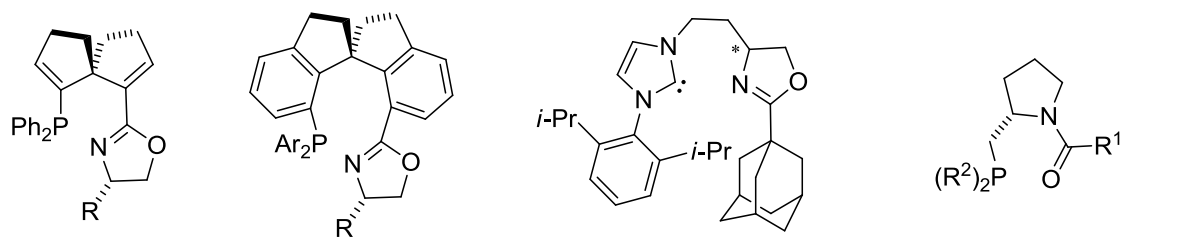
X = CH_2, NMe
R^1 = Ph, *o*-Tol
R^2 = H, Ph
→ α,α-diaryl olefins
→ vinylsilanes
→ vinylfluorides
→ vinylphosphonates

41

R^1 = *t*-Bu, $SiMe_3$
R^2 = *t*-Bu, H
→ minimaly functionilized olefins
→ terminal disubstitued olefins

Figure 1.3: Selected Ir-complexes developed in the *Anderssons*' research group and their use in asymmetric hydrogenation.

Ligands that form larger than six-membered chelate rings with iridium were also introduced. Some, successful examples are shown in figure 1.4, for example the SpinPHOX ligands **42** (seven-membered metal cycle)[73] or SIPHOX ligand **43** (nine-membered metal cycle).[74] Although N,P ligands still represent the most utilized mixed donor ligands for the iridium-catalyzed asymmetric hydrogenation, C,N ligands **44**[75] and O,P ligands **45**[76] have also been successfully employed for this reaction. Both of them form a seven membered chelate ring within iridium complexes. While C,N ligand **44** provides unique results in the asymmetric hydrogenation of dienes,[77] all of these ligands were also successfully employed in the Ir-catalyzed asymmetric hydrogenation of α,β-unsaturated carbonyl compounds. SpinPHOX **42** was reported to be useful for the reduction α,β-unsaturated Weinreb amides,[78] while SIPHOX **43** gave excellent results in the hydrogenation of α,β-unsaturated carboxylic acids.[74] On the other hand C,N ligand **44** and O,P ligands **45** were used for the hydrogenation of α,β-unsaturated carboxylic esters[76, 79] and ketones.[76]



SpinPHOX **42**
R: *t*-Bu, Bn

SIPHOX **43**
Ar: 3,5-(*t*-Bu)$_2$C$_6$H$_3$
R: *i*-Pr, Bn, Ph

C,N ligand **44**

O,P ligands **45**
R^1: Ph_3C, Ph_3CNH, Cy_2N
R^2: Ph, *o*-Tol, Cy, *t*-Bu

Figure 1.4: Selected mixed donor ligands, which form larger than six-membered chelate rings with the metal.

1.3.6 Important Parameters in the Ir-Catalyzed Asymmetric Hydrogenation

The proper choice of the reaction parameters is very important in order to achieve high enantioselectivities in the iridium-catalyzed asymmetric hydrogenation. As the exact catalytic cycle of this reaction has not been identified yet, the role of these parameters is also not fully understood. Some of the variable parameters are discussed herein:

- Ligand / Complex
- Solvent
- Pressure
- Temperature
- Substrate geometry

The outcome of the reaction strongly depends on the ligand structure. As rational tools for prediction of the enantioselectivity are not available yet, screening of different complexes is usually the first step. High-throughput screening might be helpful in order to cover a huge variety of ligands, but it also requires expensive automation equipments.[80] Therefore, traditional screening based on previous observations will still be continued.

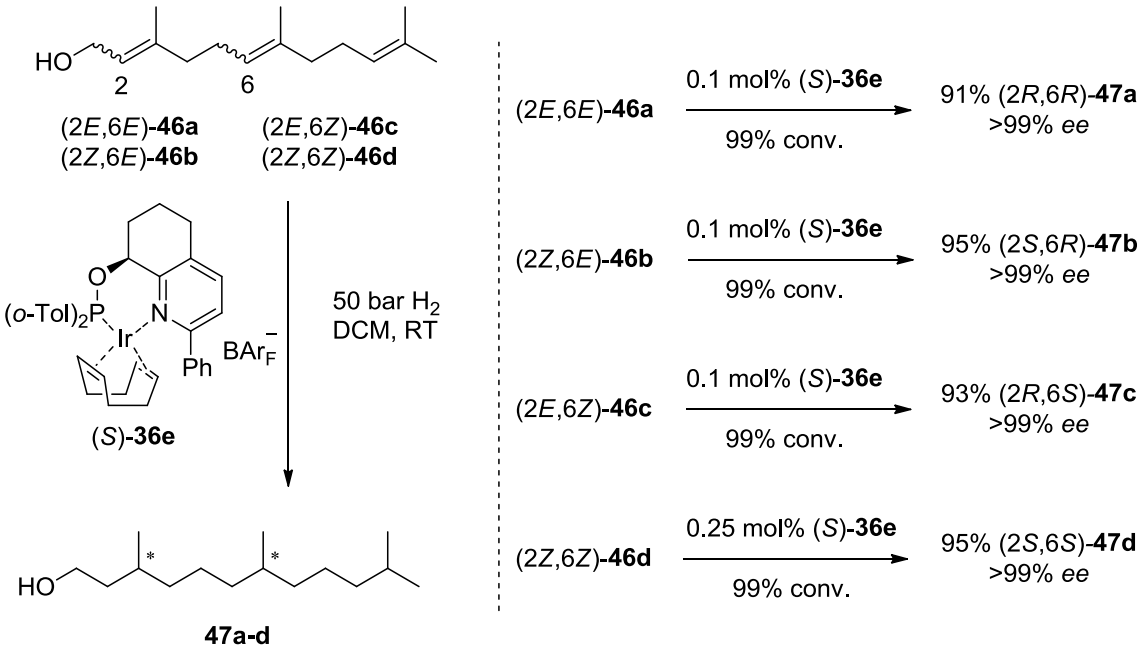
The activity and selectivity of an iridium catalyst strongly depends also on the solvent choice. Usually, the hydrogenations are carried out in weakly coordinating solvents like dichloromethane or 1,2-dichloroethane.[38, 81] Further apolar solvents, like toluene, chlorobenzene[82] or trifluorotoluene[68] have been also successfully employed. Usually the selectivity and reactivity drops down in strongly coordinating solvent, like THF, ethyl acetate or acetone,[81] however the use of propylene carbonate[83] and even methanol[74] have been reported with some success.

Kinetic experiments revealed a first order dependence for dihydrogen in solution. Therefore, most of the hydrogenation are conducted at elevated hydrogen pressure (>5 bar) in order to accelerate the reaction. In contrast to the usually small influence of the pressure on the selectivity for trisbustitued olefins, for the hydrogenation of terminal and tetrasubstitued olefins lower pressures were found to have a distinctively positive influence.

Furthermore, the temperature plays also an important role in the hydrogenation. In general, the enantioselectivity increases by lowering the temperature, whereas the activity is increased at higher temperature.

The substrate geometry plays a major role in the Ir-catalyzed asymmetric hydrogenation. By changing the configuration at the double bond, opposite stereoisomers are obtained by using

the same catalyst. The hydrogenation of double isomers of farnesol **46a-d** is clearly demonstrating this effect.[84] By proper choice of the double bond geometry all four stereosiomers of **47a-d** could be obtained in high enantiomeric purity using catalyst (*S*)-**36e**. On the other hand, the preparation and purification of the substrates is becoming extremly important. In order to achieve high *ee*s a high purity of each isomer of the olefin is required. Therefore, methods which exclusively allow the preparation of (*E*)- and (*Z*)-alkenes are receiving more interest.



Scheme 1.16: Substrate geometry effect on the Ir-catalyzed asymmetric hydrogenation of farnesol isomers **46a-d**.

1.4 Thesis Outline

Iridium-catalyzed asymmetric hydrogenation is nowadays an established method in organic chemistry in order to prepare chiral compounds. In contrast to Rh- and Ru-catalysts, Ir-complexes do not require the presence of coordinating groups adjacent to the double bond. Many N,P ligands have been successfully implemented for this reaction. However, as no ligand has a universal substrate scope, the development of new ligand scaffolds, which provide different activity and selectivity, is of great interest. The aim of this thesis is to study N,P ligands based on the rigid bicyclic pyridine scaffold. In the initial part a new synthetic pathway to such ligands is described. The next three chapters are dealing with the potential variations of the ligand scaffold in order to tune the reactivity and selectivity of their respective Ir-complexes. Furthermore, the application of N,P ligands to the hydrogenation of alkenyl boronic esters will be covered. During this study an unusual reactivity of imidazole-phosphinite derived catalyst was observed, which will be discussed in the last chapter.

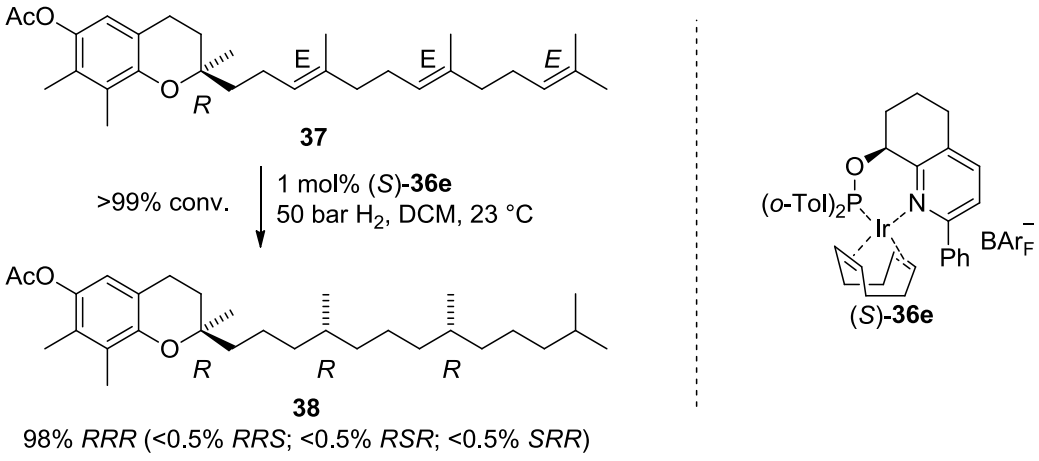
Chapter 2

Development of a New Synthetic Route to Bicyclic Pyridine-Phosphinite Ligands and Their Corresponding Ir-Complexes

2.1 Introduction

2.1.1 Bicyclic Pyridine-Phosphinite Ligands for Ir-Catalyzed Asymmetric Hydrogenation

Bicyclic pyridine-phosphinites represent the most successful N,P ligand family developed so far for Ir-catalyzed asymmetric hydrogenation.[57] Their iridium complexes show high reactivity and are able to introduce very high enantioselectivity for several classes of trisubstitued olefins, as illustrated in the hydrogenation of γ-toco-trienylacetate **37** (scheme 2.1). In this reaction three C=C bonds were fully reduced and two new stereogenic centers were created in high enantiomeric purity (98% of the major *RRR* isomer). All the previously reported iridium catalysts failed to induce such a high level of enantioselectivity.[56]

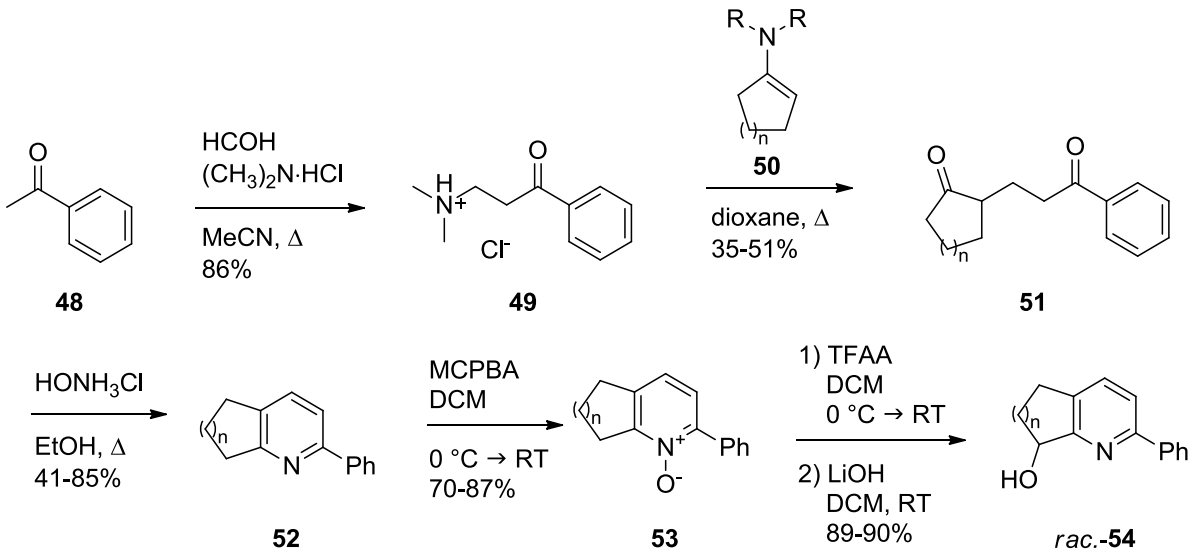


Scheme 2.1: Asymmetric hydrogenation of γ-toco-trienylacetate **37** using an Ir-complex **36e** derived from bicyclic pyridine-phosphinite ligand.[2]

2.1.2 First Generation Synthesis of Pyridyl Alcohols

The Ir-complex **36e** shown in scheme 2.1 consist of N,P ligand, which is built from a pyridine unit. The pyridine moiety is connected to a phosphinite over a fused ring that also bears a stereogenic center. The phenyl group *ortho* to the pyridine nitrogen acts as the shielding group in the Ir-catalyst. As these ligands are of great value, generally applicable and highly modular syntheses of them are required. The synthetic route initially developed for the synthesis of the ligand backbone **54** is described in scheme 2.2. Acetophenone **48** is subjected to a Mannich reaction to afford **49**, that is then reacted with enamine **50** to give the 1,5-diketone **51**.

Treatment of 1,5-diketone **51** with hydroxylamine and subsequent dehydration furnishes pyridine **52**, that can be transformed into the corresponding N-oxide **53**. The N-oxides undergo a Boekelheide rearrangement[85] followed by subsequent hydrolysis to give the desired racemic pyridiyl alcohol *rac.*-**54** in 14-20% overall yield over 7 steps.[57] This synthetic sequence is relatively long and does not allow for easy elaboration of the substituents at a late stage of the synthesis (the phenyl group is introduced in the 1st step).



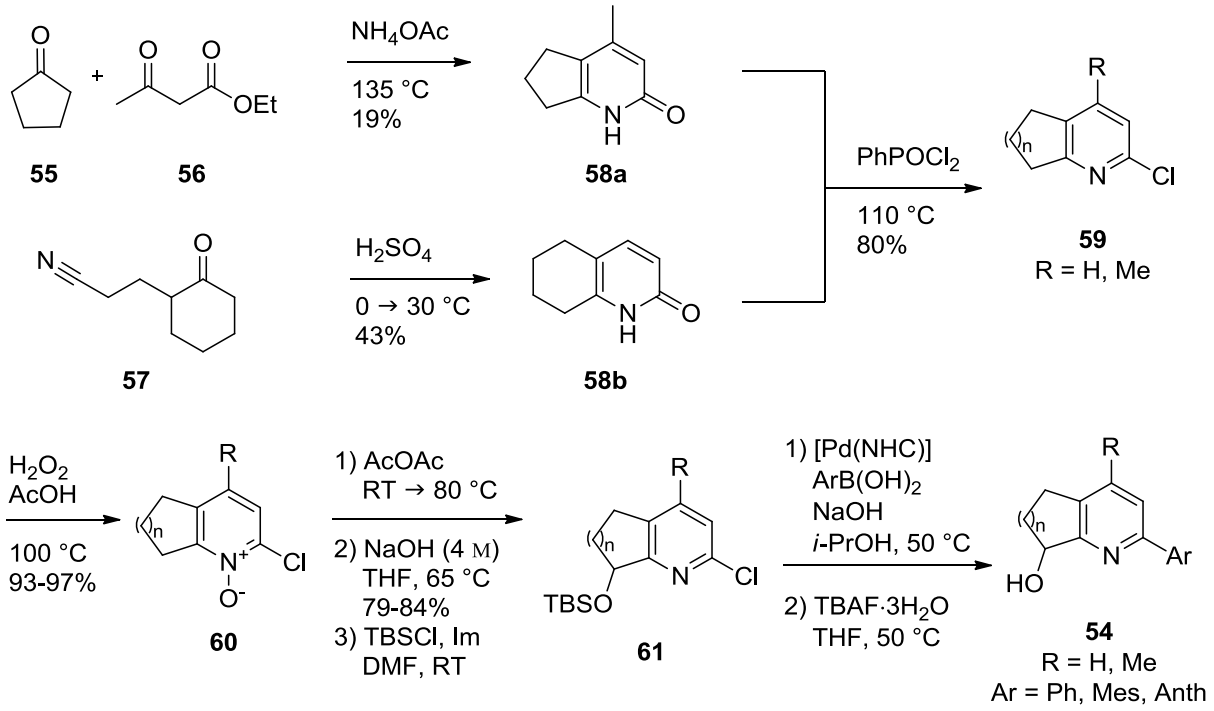
Scheme 2.2: First generation synthesis of racemic pyridyl alcohols **54**.[57]

2.1.3 Second Generation Synthesis of Pyridyl Alcohols

To overcome some of the disadvantages of the synthetic sequence described in scheme 2.2, *D. Woodmansee* optimized a previously published synthetic route[86] to obtain pyridyl alcohol (scheme 2.3).[87] The idea of the new reaction pathway is to incorporate a chlorine atom in the pyridyl scaffolds **59**, which would allow the introduction of various aryl groups by performing late stage Suzuki-Miyaura couplings on a common intermediate (i.e. **61**, scheme 2.3)

The synthesis of the key chlorinated intermediates **59** was accomplished starting with the corresponding pyridone **58**, that was obtained either *via* a condensation of ethyl acetoacetate **56**, cyclopentanone **55** and $AcONH_4$,[88] or by cyclization of **57** under acidic conditions.[89] Both procedures afforded the desired pyridones **58** in low yield. Chlorination using phenylphosphonic dichloride gave **59** in high yield.[90] After *N*-oxidation, Boekelheide rearrangement, subsequent hydrolysis and TBS protection, the chloro pyridines **61** were obtained. Late-stage Suzuki-Miyaura coupling and TBS deprotection gave the racemic pyridyl

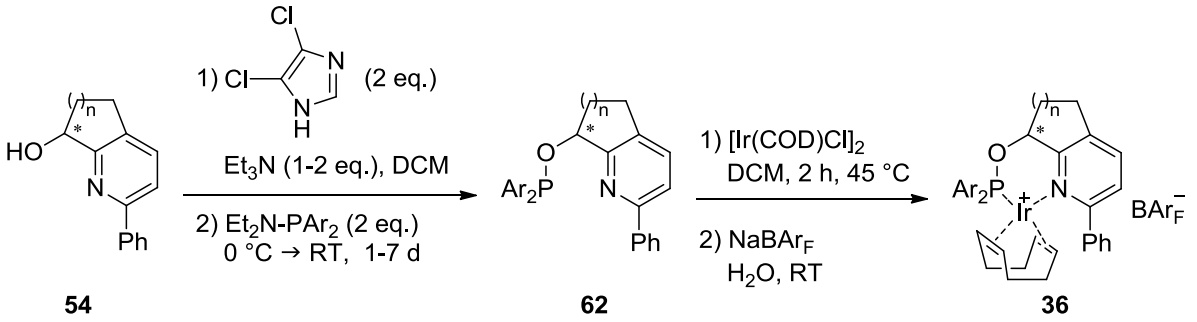
alcohols *rac.*-**54**. However, it should be mentioned that enzymatic kinetic resolution is also possible of 2-chloro-pyridine derivatives prior to the TBS protection, giving access to enantiopure pyridyl alcohols **54**.



Scheme 2.3: Second generation synthesis of racemic pyridyl alcohols **54**.[87]

2.1.4 Formation of N,P Ligands and Their Ir-complexes

The next problematic step is the preparation of *P*-Aryl phosphinite ligands **62**. In fact, the choice of the base, that is required to enhance the nucleophilicity of the pyridyl alcohol, was difficult. The use of strong bases like *n*-BuLi resulted in partial racemization of the stereogenic center, whereas weaker bases like sodium hydride gave unsatisfactory results in the formation of the P-O bond. Therefore, *S. Kaiser* employed a mild method which is commonly used in nucleotide chemistry. Using an excess of 4,5-dichlorimidazole and of pre-isolated diethylamino-phosphine the *P*-Aryl ligands **62** were formed in moderate to good yields (45-88%, scheme 2.4).[57] Unfortunately, since this procedure requires very long reaction times (up to 7 day to reach full conversion), it becomes impractical in handling such air-sensitive compounds.

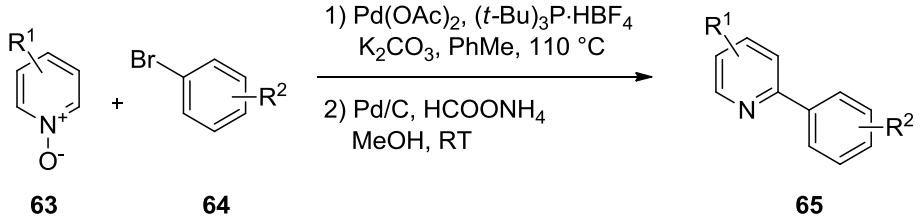


Scheme 2.4: Preparation of P-aryl N,P ligands **62** and their Ir-complexes **36**.[57]

2.1.5 Objective of This Work

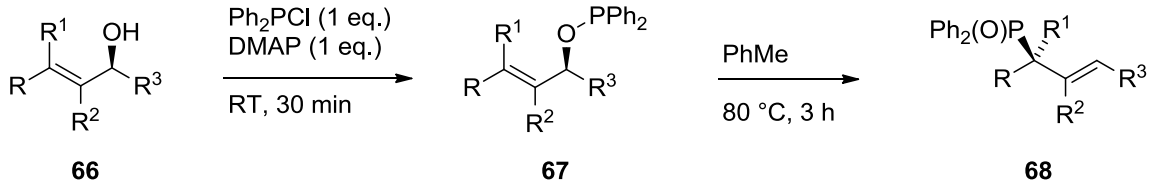
Although the two described procedures give access to valuable N,P ligands, they are still far from being ideal. Therefore, the aim of this study was to develop an easy-to-handle and fast synthetic route for the generation of pyridyl alcohols **54**, of their corresponding N,P ligands and iridium complexes.

The idea for the synthesis of the pyridyl alcohol **54** was inspired by the work of *K. Fagnou* on Pd-catalyzed regioselective direct arylation of pyridine N-oxides **63**.[91] The authors reported excellent yields (up to 90%) of arylated pyridines **65** employing a wide range of aryl bromides **64** (scheme 2.5).



Scheme 2.5: Palladium-catalyzed regioselective direct arylation of pyridine N-oxides **63**.[91]

For the formation N,P ligands the reaction conditions reported by *Knochel* and *Liron* are very attractive.[92] For their study on [3,3]-sigmatropic rearrangement reactions of acyclic allylic phosphinites **67** to allylic phosphine oxdides **68**, the authors treated allylic alcohols **66** with chlorodiphenylphosphine in the presence of DMAP in diethyl ether. The reaction is completed within 30 min at room temperature and phosphinites **67** were obtained quantitatively (scheme 2.6).



66 **67** **68**

Scheme 2.6: Formation of allylic phosphine oxdides **68** from allylic alcohols **66** *via* [3,3]-sigmatropic rearrangement reaction of arylphosphinites **67**.[92]

2.2 Development of the New Synthesis

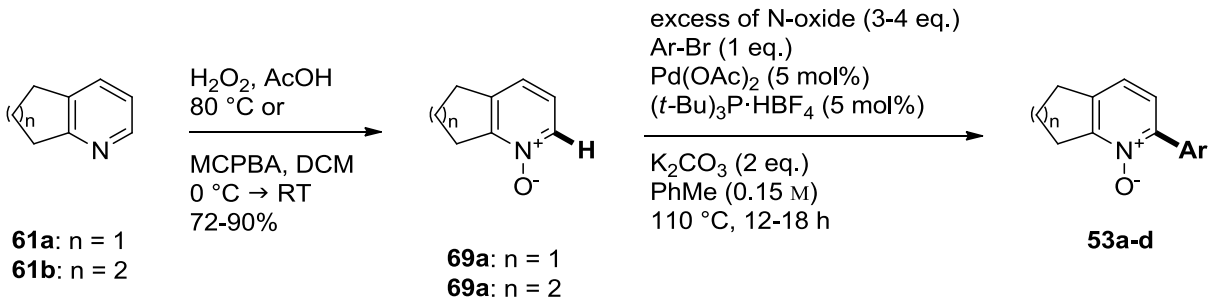
2.2.1 New Synthetic Route to Racemic Pyridyl Alcohols

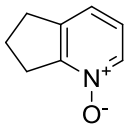
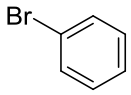
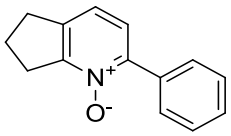
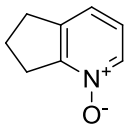
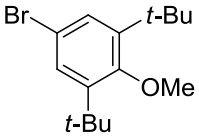
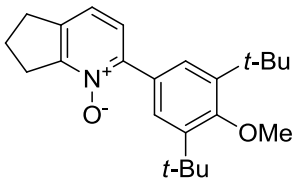
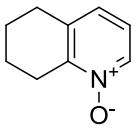
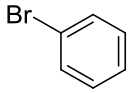
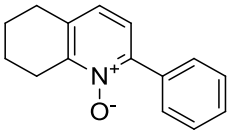
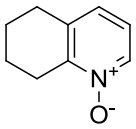
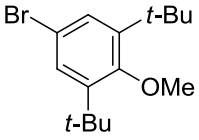
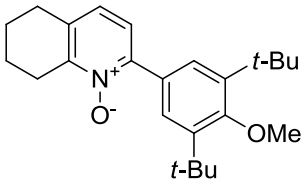
One of the disadvantages of the reaction sequence described by *S. Kaiser* lies within its low degree of modularity (scheme 2.2).[57] The important aryl residue on the pyridine ring that is required for shielding of the metal center is installed at the beginning of the sequence and in the next steps the pyridine ring is assembled. In order to overcome these issues, an attractive alternative reaction sequence would rely on a selective C−H arylation of pyridine N-oxides **69a-b**.[91]

For this purpose the commercially available heterocycles **61a** and **61b** were converted to their N-oxides **69a-b**. This oxidation can be performed either by using *in situ* generated peracetic acid[93] or by addition of MCPBA.[94] Both approaches provided the desired N-oxides **69a-b** in good yields (72-90%). In the next step the *ortho*-selective arylation was explored. Employing the same conditions reported by *K. Fagnou* and co-workers, arylation products **53a-d** were obtained in moderate yields (33-55%, Table 2.1).

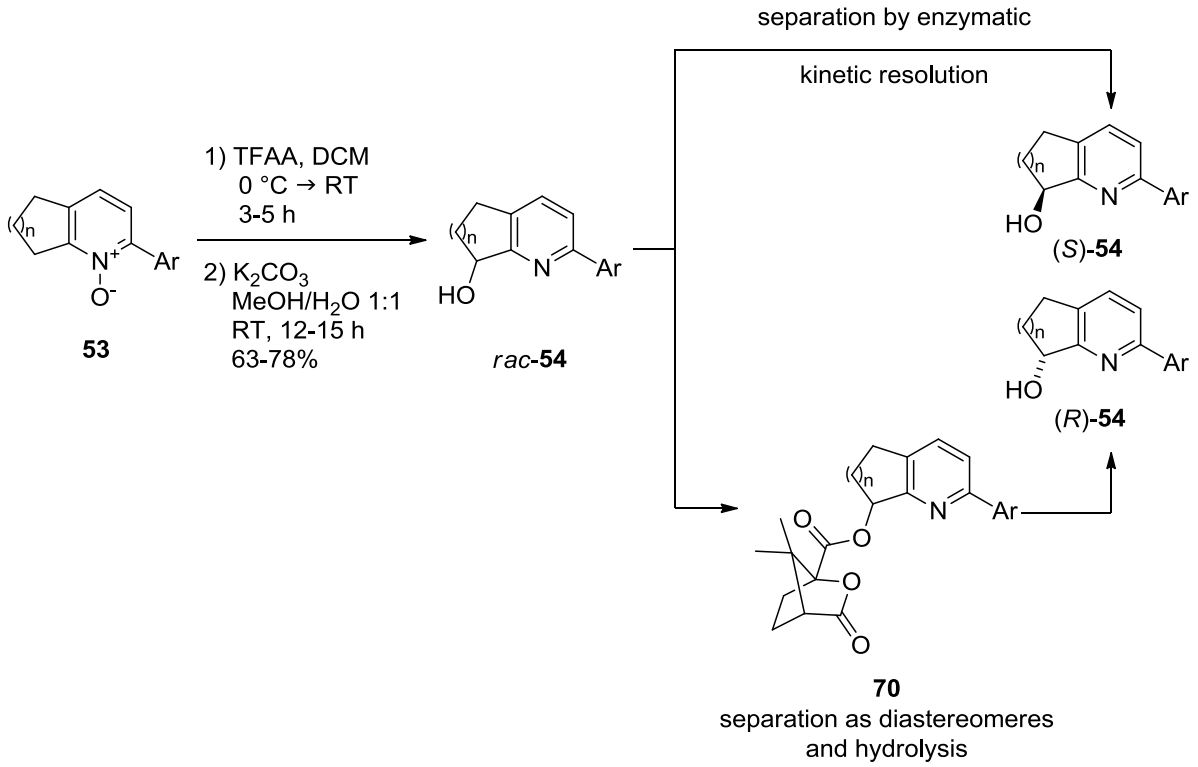
It should be mentioned that for the arylation reaction an excess of the N-oxides (3-4 eq.) is required, which is a clear drawback of the transformation. Moreover, another pitfall of this approach is that the scope of the arylhalides is limited to sterically non-hindered compounds. In fact, coupling reactions employing the bulky anthracene bromide or mesityl bromide were not successful. Nevertheless, this synthetic way is a straightforward approach to pyridyl alcohols **54**, as the products obtained are advanced intermediates in the reaction sequence described by *S. Kaiser*.[57] Continuing this sequence (Boekelheide rearrangement[85] and hydrolysis), the racemic pyridyl alcohols *rac.*-**54** were obtained in good yield (17-31% over 4 steps).

Table 2.1: Preparation and Pd-catalyzed arylation of N-oxides **69a**.



Entry	N-oxide		Ar-Br	Product		Yield [%]
1		**69a**			**53a**	55
2		**69a**			**53b**	36
3		**69b**			**53c**	33
4		**69b**			**53d**	45

Two possible ways have been developed in the *Pfaltz* group for the separation of the two enantiomers of pyridyl alcohols **54**. One possibility is the chromatography-free enzymatic kinetic resolution optimized by *M. Maywald*.[95] Alternatively, separation by flash chromatography of the camphanic acid ester **50** is possible as shown by *S. Gunzenhauser*.[96] The two separation methods provide access to both enantiomers of **54** after hydrolysis of the corresponding esters on a multi-gram scale. However, it should be mentioned that these separations were not part of this work and the enatiopure materials were kindly provided by *S. Gunzenhauser* and *M. Maywald*.

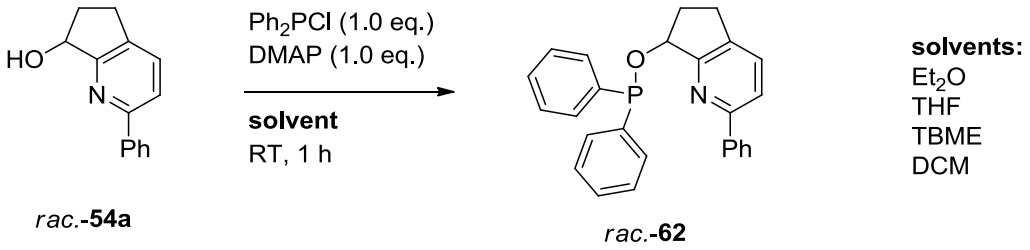


Scheme 2.7: Formation of enantiopure alcohols **54** by resolution of racemates, which were obtained from **53** after Boekelheide rearrangement and hydrolysis.[95-96]

2.2.2 Formation of N,P Ligands and Ir-Complexes

Late-stage functionalization is one of the most important goals of any modular synthesis. Ideally, valuable intermediates should be quantitatively transformed into the desired target compounds. Moreover, fast reaction times are clearly advantageous when handling air- and moisture-sensitive compounds like phosphinites. The initially developed synthesis of N,P ligands did not fulfill these requirements and therefore careful optimization of this reaction sequence was the aim of this chapter. This study was performed in collaboration with *E. Hörmann* using the methodology developed by *Knochel* and co-workers for the formation of P-O-bonds.[92]

As seen earlier (scheme 2.6), under the original conditions reported by *P. Knochel* and co-workers the phosphinite is formed within 30 minutes by using an equal amount of a (vinyl)-alcohol, chlorodiphenylphoshpine and DMAP in diethyl ether.[92] As pyridyl alcohols **54** showed poor solubility in diethyl ether, a solvent screening was performed (scheme 2.8).



Scheme 2.8: Solvent screening for the formation of phosphinite *rac.*-**62a**.

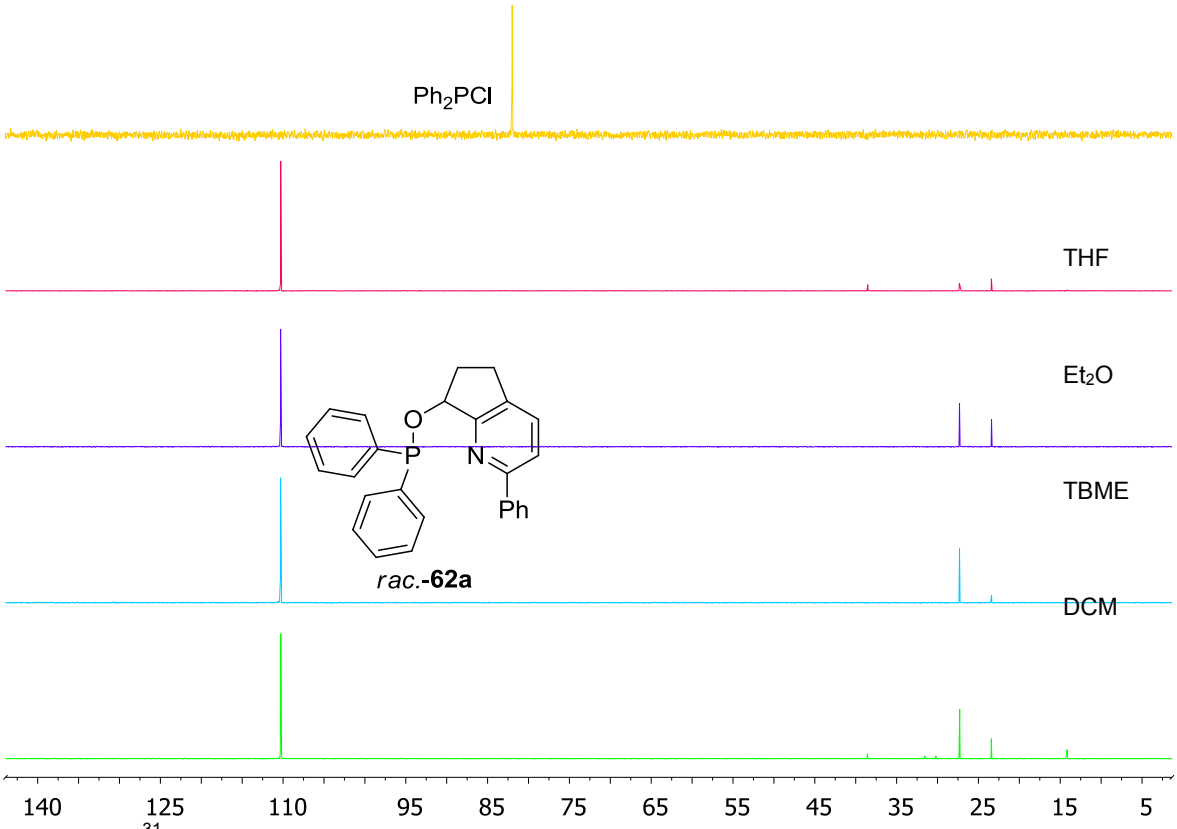


Figure 2.1: ^{31}P-NMR analysis of the reaction mixture using different solvents for the formation of *rac.*-**62a**.

The course of the reaction was followed by ^{31}P-NMR analysis and THF resulted as the best solvent for this transformation, giving the lowest amount of side-products compared to other solvents (figure 2.1; <20% total side products by integration of ^{31}P signals). However, it should be noted that the reaction also works in ethereal solvent (diethyl ether or TBME; <30% total of side products) and to a lesser extent, in DCM (<35% total of side products).

For further optimization studies THF was therefore selected as the solvent of choice and attempts to remove the precipitate from the reaction mixture (DMAP-hydrochloride) were investigated. Filtration through a disposable HPLC filter or a *Celite*® pad gave unsatisfactory results, as relatively low yield was obtained (approximately 40%) upon formation and isolation of the iridium complex **36a**. A large amount (up to 50%) of a side product, whose

structure was tentatively assigned to the neutral iridium-chloride complex, was obtained. This observation indicates that even a relatively small amount of the hydrochloride salt strongly affects the BAr_F / chloride exchange and leads to a lower yield of the desired iridium-BAr_F complex. Therefore, a filtration over a pad of basic aluminum oxide (phosphinite ligands **62** tend to decompose on silica gel) was investigated. Since the best solvent for elution was DCM, the reaction was run directly in that solvent. Moreover, the required filtration also allows the use of a small excess of chlorophosphine and DMAP (up to 1.1 eq.), as they could both be removed during the filtration.

Further complexation studies showed that these ligands do not require additional heating to form the iridium complexes. Therefore, the solution containing ligand from filtration was directly added to a premix of $[Ir(COD)Cl]_2$ (0.5 eq) and $NaBAr_F$ (1.2 eq). The ligand (see figure 2.2 for the the cyclohexyl derivative (*S*)-**62c**, blue) was completely converted to the desired iridium complex (121.8 ppm; the signal at 126.2 ppm refers to the chlorodicyclohexylphosphine) within 1-2 hours.

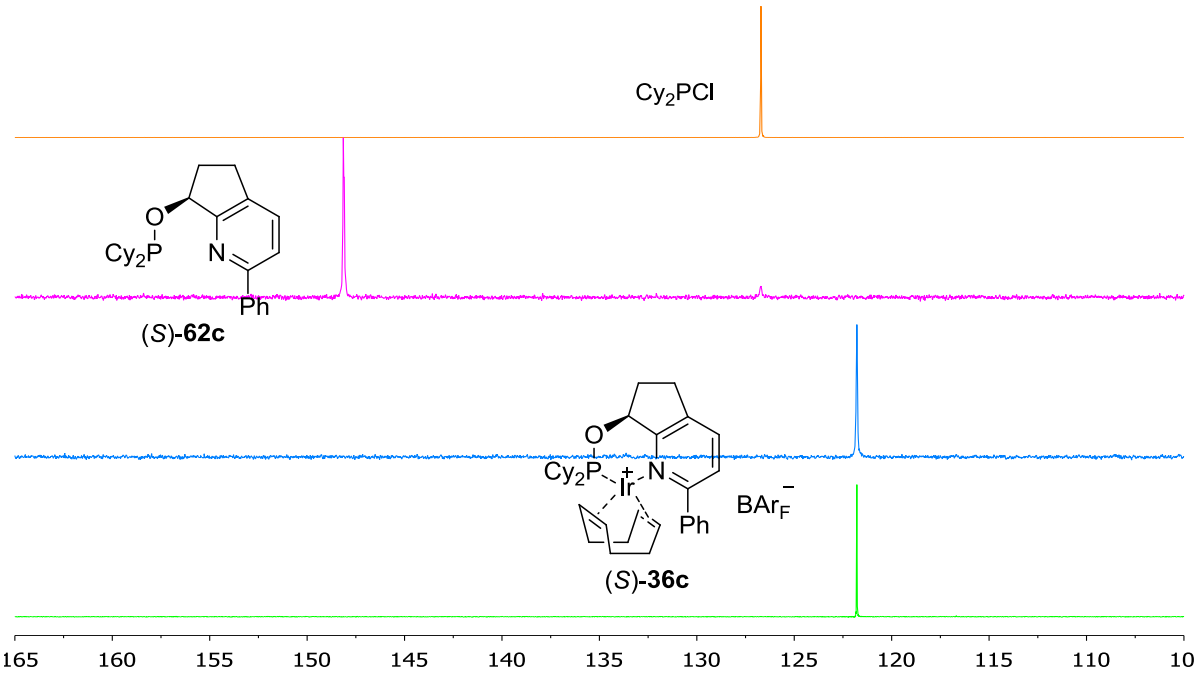


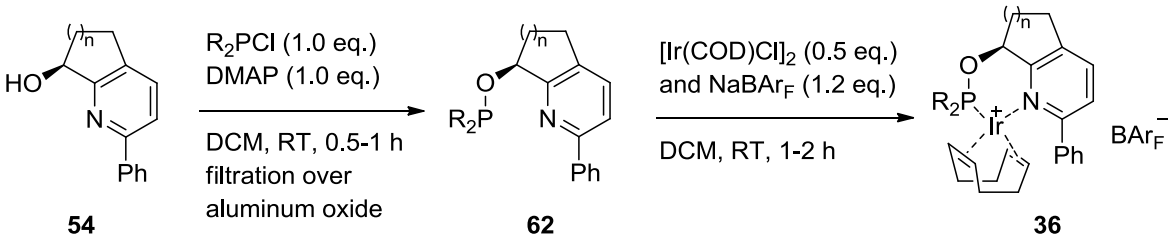
Figure 2.2: ^{31}P-NMR analysis of the formation of the ligand (*S*)-**62c** (pink) and of the corresponding Ir-complex (*S*)-**36c** (blue reaction mixture, green the isolated complex after flash chromatography).

After removal of the solvent and purification by flash chromatography the desired iridium complexes were obtained in high yields (≥60%, table 2.2). Following this procedure, the Ir-catalyst **36a** was prepared for the first time (entry 1). Initially it was reported that the ligand **62a** forms a stable but catalytically inactive $[Ir(L)_2]BAr_F$-complex.[57b] However, during this work such complex was not observed and the **36a** showed high catalytic activity.

Furthermore, catalyst **36a** showed promising results in the hydrogenation of furan derivatives.[82]

To demonstrate that this reaction setup is also amenable to the sterically demanding *ortho*-tolyl substituents on the phosphorus atom, complexes **36b** (on 0.5 mmol scale, entry 2) and **36e** (entry 4) were prepared in good yields.

Table 2.2: New synthetic access to the phosphinite-pyridine derived complexes **36**.



Entry	n	R	Scale [µmol]	Ligand	^{31}P-Ligand [ppm]	Complex	^{31}P-Complex [ppm]	Yield [%]
1	1	Ph	139	**62a**	108.5	(*S*)-**36a**	99.5	67
2	1	*o*-Tol	500	**62b**	101.3	(*S*)-**36b**	113.6	60
3	1	Cy	453	**62c**	147.6	(*S*)-**36c**	121.8	66
4	2	*o*-Tol	110	**62e**	99.8	(*S*)-**36e**	99.3	66

2.3 Crystal Structure Analysis

Complexes (*S*)-**36a**, (*S*)-**36b**, and (*S*)-**36e** were crystallized by overlaying a saturated ethereal solution of the iridium compound with *n*-pentane. They were obtained as red ((*S*)-**36a**, (*S*)-**36a**) and orange ((*S*)-**36e**) plates, which were subjected to crystal structure analysis. *Mercury* sticks representations are shown in figures 2.3-2.5. Selected structural parameters are given in tables 2.2-2.5, whereas the full crystallization parameters can be found in the appendix (chapter 9.1). Crystal structures of **36c**, **36g** and **36f** obtained by *S. Kaiser*[57a] showed very similar structure to those obtained during this study.

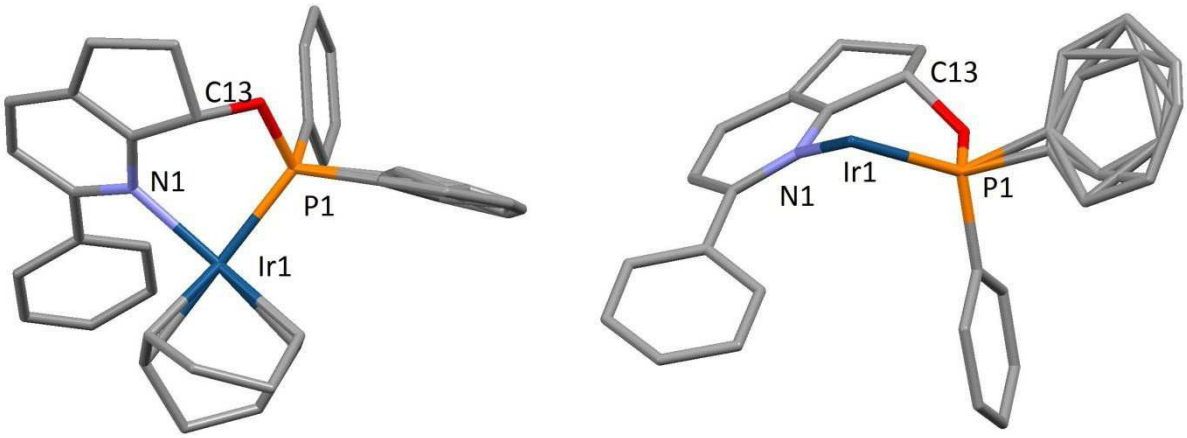


Figure 2.3: Crystal structure of (*S*)-**36a** with COD ligand (left) and without COD ligand (right); BAr_F counter-ion was omitted for clarity.

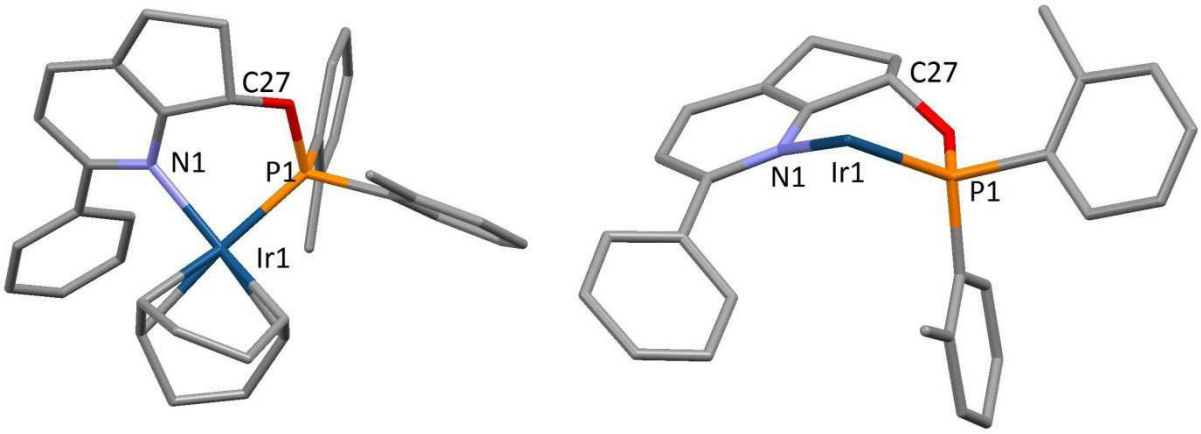
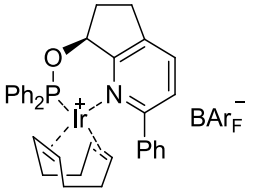
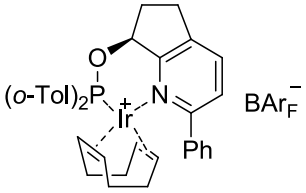
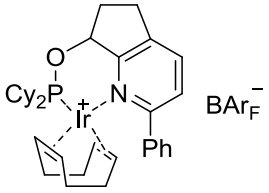


Figure 2.4: Crystal structure of (*S*)-**36b** with COD ligand (left) and without COD ligand (right). The 2nd molecule inside the unit cell and BAr_F counter-ion were omitted for clarity.

In all complexes the Ir atom displays a square planar geometry. The unit cell of (*S*)-**36a** contains one molecule (figure 2.3). One of the phenyl groups on the phosphorus atom can occupy two different orientations. In the unit cell of (*S*)-**36b** two molecules were found (figure 2.4 only one molecule is shown). The differences between bond lengths and angles of the two structures within the same unit cell are significant (see table 2.3). Comparison of these structures with the P-alkyl complex **36c** revealed a shorter Ir-P bond, while the Ir-N distance remains unchanged. These small differences are reflected in smaller bite angles (table 2.3).

Table 2.3: Selected bond lengths and bite angles of Ir-complexes having a 5-atoms-membered carbocyclic ring.

	 (*S*)-**36a**	 (*S*)-**36b**	 **36c**[57a]
Ir-P [Å]:	2.2529(9)	2.2569(9) / 2.3071(8)	2.2794(10) / 2.2808(11)
Ir-N [Å]:	2.121(2)	2.146(2) / 2.094(2)	2.1241(4) / 2.132(3)
P-O [Å]:	1.619(2)	1.626(2) / 1.641(2)	1.635(3) / 1.627(4)
Ir-C13 or Ir-C27 [Å]:	3.221	3.253 / 3.254	
∠ P-Ir-N [°]:	86.27(7)	87.21(6) / 84.62(5)	88.26(10) / 88.14(10)

Similar trends were observed for the complexes bearing a tetrahydroquinoline unit. Complex (*S*)-**36e** has again a shorter Ir-P distance and a smaller bite angle, when compared to the P-alkyl complexes **36g** and **36f** (table 2.4).

$Ir^{(I)}$-complexes embedded in a six membered chelate ring adopt a characteristic boat conformation, and this is also valid for all the complexes described in this study. For complexes having a 5-membered carbocyclic ring (*S*)-**36a** and (*S*)-**36b** this boat conformation is less distinctive compared to the more flexible systems with a 6-atoms-membered carbocyclic ring (*S*)-**36e**. A parameter that is directly reflecting that conformation is the distance between the metal center and the stereogenic carbon atom. While this distance was found to be 3.22-3.25 Å long for catalysts (*S*)-**36a** and (*S*)-**36b**, the same distance is 3.11-3.16 Å long in tetrahydroquinoline-based complexes.

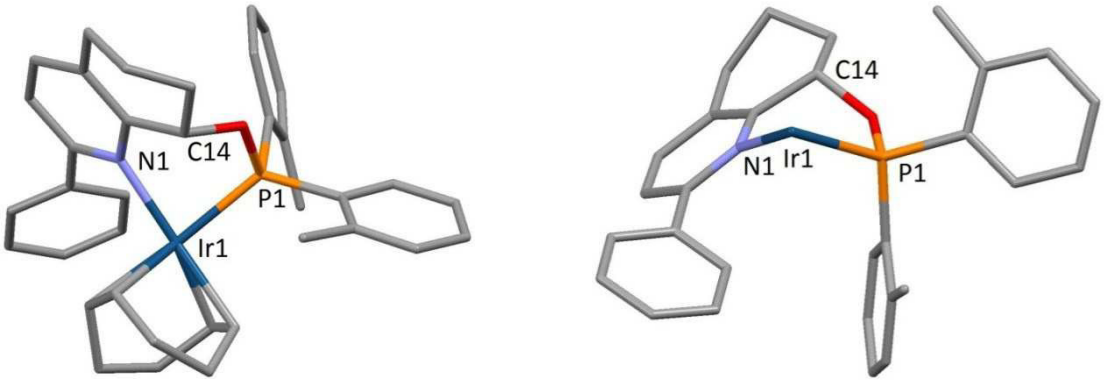
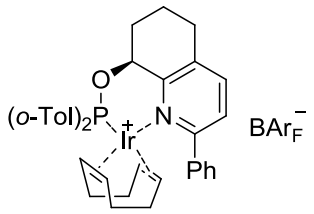
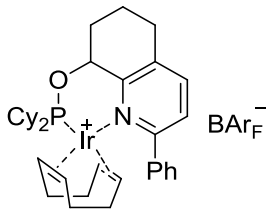
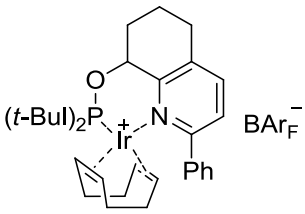


Figure 2.5: Crystal structure of (S)-**36e** with COD ligand (left) and without COD ligand (right). The BAr_F counter ion was omitted for clarity.

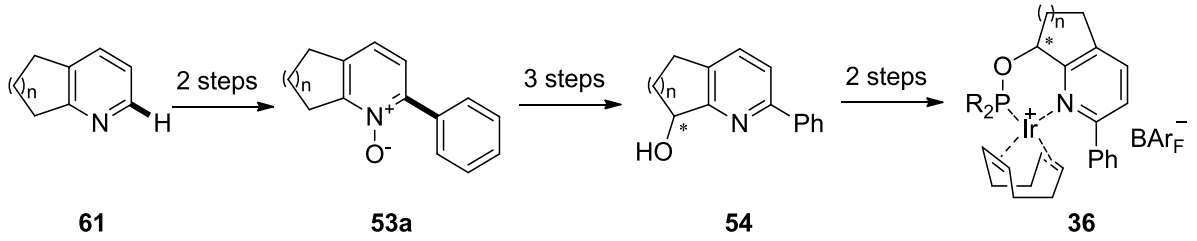
Table 2.4: Bond lengths and bite angles of Ir-complexes with a tetrahydroquinoline scaffold.

	 (*S*)-**36e**	 **36g**[57a]	 **36f**[57a]
Ir-P [Å]:	2.2794(4)	2.2881(7)	2.3522(9) / 2.3403(9)
Ir-N [Å]:	2.118(1)	2.132(2)	2.117(3) / 2.107(4)
P-O [Å]:	1.631(1)	1.625(2)	1.631(3) / 1.625(3)
Ir-C14 [Å]:	3.162	3.150	3.107 / 3.106
∠ P-Ir-N [°]:	84.11(4)	87.49(6)	87.23(8) / 86.7(1)

The crystal structures are clearly showing the structural characteristics of each precatalyst in the solid state. However, once activated, the metal is found in different oxidation state ($Ir^{(III)}$ or $Ir^{(V)}$) and the COD ligand is replaced by a substrate, hydride, dihydrogen or a solvent molecule. Therefore, it is difficult to draw direct conclusions regarding the structures of the actual catalysts.

2.4 Summary

In summary a concise synthetic route toward pyridyl alcohols **54** was implemented. The key step for the installment of the desired functionality was a regioselective C−H functionalization of simple and readily available starting materials. Following this procedure pyridyl alcohols **54** (n = 1, 2) were obtained in high yield (up to 31% prior to the resolution; scheme 2.9).



Scheme 2.9: Regioselective C−H functionalization strategy for the fast preparation of pyridyl alcohols and formation of pyridine-phosphinite based N,P ligands and their Ir-complexes.

Furthermore the synthetic protocol herein developed for the preparation of phosphinite ligands and their Ir-complexes is operationally simple and represents an efficient way to obtain valuable Ir-catalysts in high yields (≥60%) and reduced reaction times.

Chapter 3

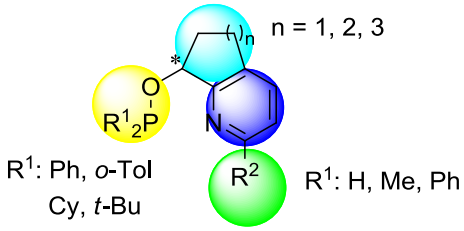
New N,P Ligands with a Quaternary Stereogenic Center and Their Ir-Complexes

3.1 Introduction

3.1.1 Model of Stereoinduction

The excellent performance of iridium complexes bearing bicyclic-pyridine-phosphinite ligands **62** in the asymmetric hydrogenation of a broad range of substrates prompted a detailed investigation into the structural characteristics of the ligand scaffold.[57] This scaffold contains four important structural parts:

- a phosphinite as the P donor
- a pyridine as the N donor
- a fused bicycle connecting the two parts and bearing the stereogenic center
- a variable group in *ortho*-position of the pyridine ring



62

Systematic variation of the residues on the "soft" P-ligand showed huge influence on the enantioselectivity in the Ir-catalyzed asymmetric hydrogenation. Most remarkably *ortho*-tolyl and *tert*-butyl residues were found to perform more efficiently compared to phenyl and cyclohexyl groups. Most likely, those residues have an electronic influence on the phosphorus atom and may direct the orientation of the other parts of the ligands and the substrate by steric effects.

In order to mimic the structure of *Crabtree's* catalyst ($[Cy_3P)Ir(pyridine)(COD)]PF_6$)[30] the pyridine part was used as the "hard" N donor. However, the electronic properties of this unit have not been investigated systematically in this particular system. The fused bicycle bears the stereogenic information of the ligand core and combines the two parts of the ligand structure. Systematic variations of the ring size revealed in general higher activity and selectivity for the smallest ring (n = 1). Finally the role of the substituents on the pyridine ring was investigated. The incorporation of an aryl group in *ortho* position of pyridine led to significant better enantioselectivity compared to unsubstituted systems.[57]

In order to rationalize the enantioselectivity of a catalyst, a simple quadrant selectivity model was implemented for the rhodium-catalyzed asymmetric hydrogenation.[17, 21] This model shows the spatial arrangement around the metal along the plane formed by the coordinating atoms and the metal center itself. Based on this model *Andersson* and co-workers[67] suggested an iridium-adapted version for the hydrogenation of trisubstituted olefins. The view

along the plane formed by phosphorus-iridium-nitrogen atoms can be divided into four quadrants. Ideally, two of these quadrants remain open, whereas one of them is blocked by a bulky ligand substituent. The last quadrant should be semi-hindered.

Based on these ideas, the quadrant model for the active bicylclic-pyridine-phosphinite derived catalyst (after dihydrogen addition and reduction of COD) is drawn in figure 3.1. Consistent with *Andersson's* model, the N,P ligand is expected to completely block one of the quadrants by means of the aryl residues in the *ortho*-position to the pyridine nitrogen. The semi-hindered quadrant would be occupied by a residue on the phosphorus atom. Now a trisubstitued olefin (for example (*E*)-α-methylstilbene) has two possibilities to approach and coordinate to the metal center in order to minimize the steric interactions with the ligand. The olefin will orientate with the bulky residues (phenyl groups) towards the open quadrants. The smallest part of the olefin (H atom on the C=C bond) will point towards the hindered quadrant, while the methyl group will occupy the semi-hindered quadrant. Coordination from the *Si*-face would give (*S*)-configured product, while the (*R*)-enantiomer would be obtained by attack from the *Re*-face. Experimental observations revealed that the catalyst derived from the (*R*)-configured-N,P ligand gives predominantly the hydrogenation product with (*R*)-configuration (up to 99% *ee*), therefore the graphic on the right side of figure 3.1 seems to be more realistic than the one on the left side. This orientation of the substrate is also consistent with DFT calculation reported by *P. G. Andersson et al.*[38c, 46]

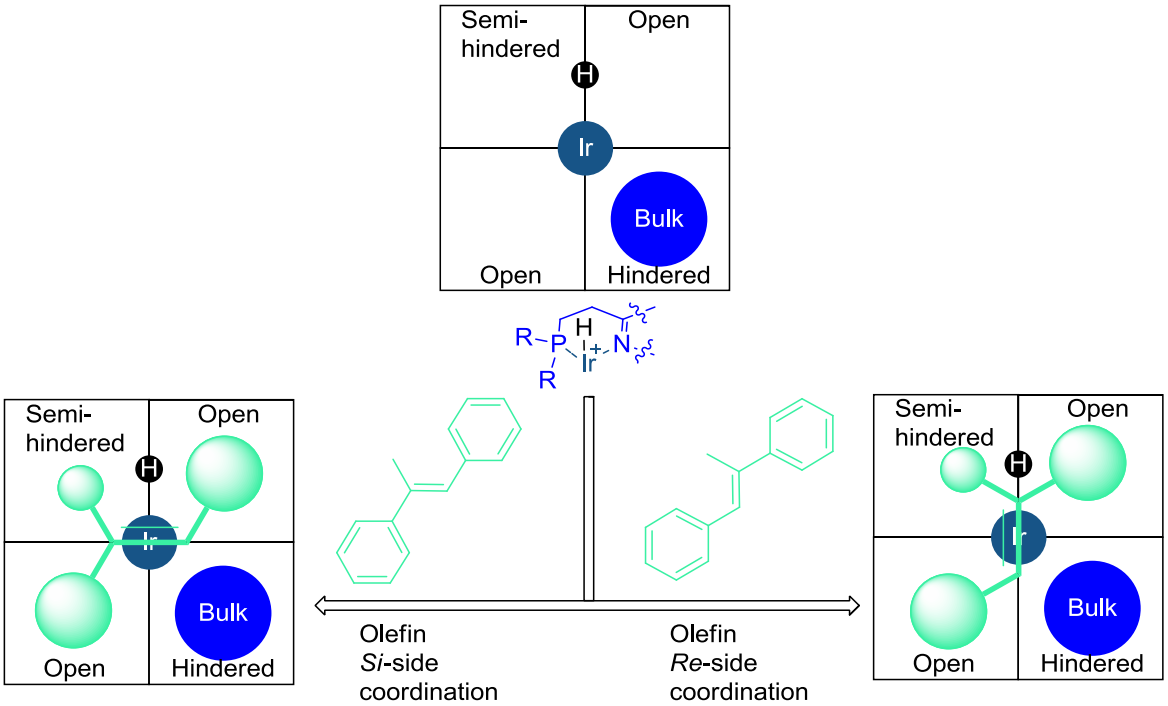


Figure 3.1: Quadrant model rationalizing the enantioselectivity in the Ir-catalyzed asymmetric hydrogenation.[67]

Figure 3.2 shows the same model in an attempted 3D-view (Ir atom dark blue, N,P ligand blue and (*E*)-α-methylstilbene green). This picture reveals that the phenyl group next to the pyridine ring is oriented out of the pyridine plane and acts as a shielding group. Indeed, this orientation is observed in the crystal structures of the precatalysts.

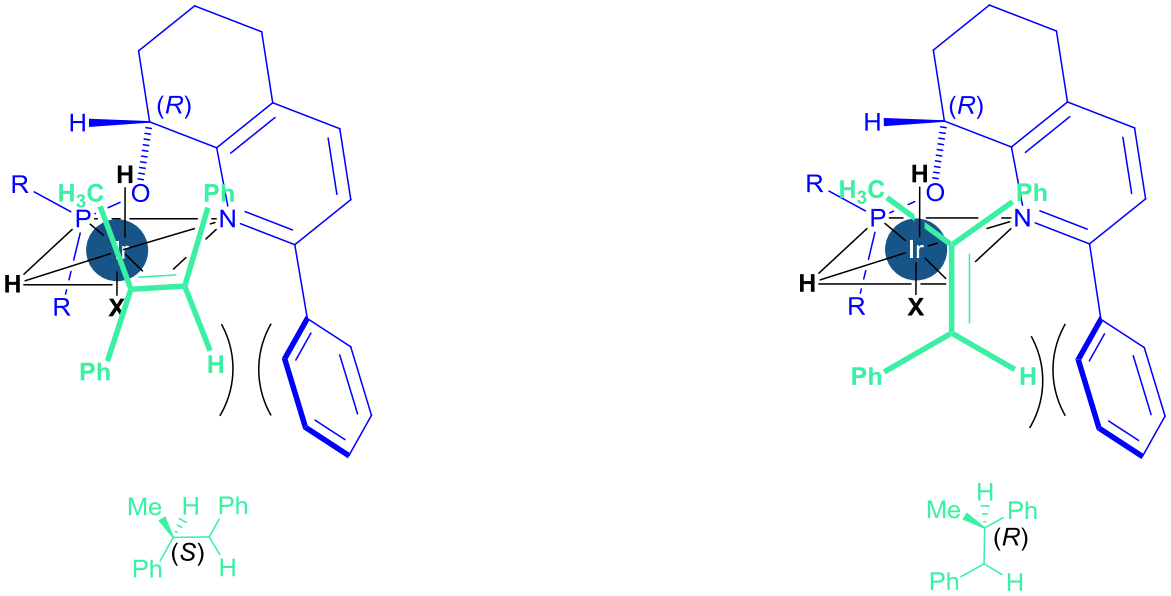
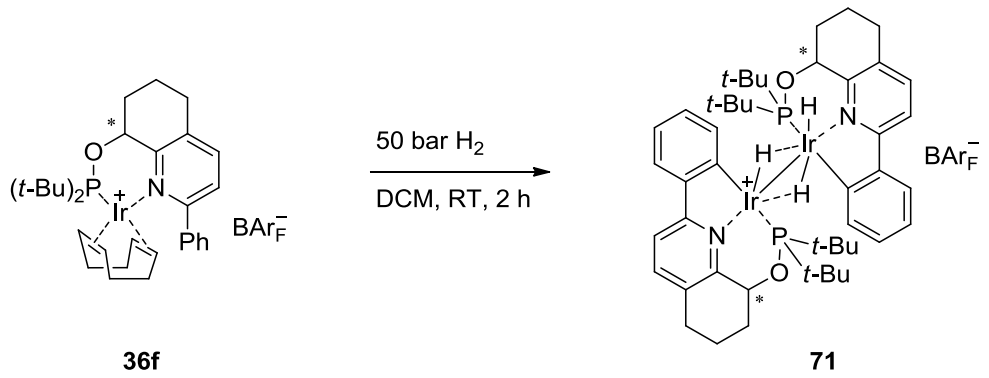


Figure 3.2: Possible substrate coordination of (*E*)-α-methylstilbene apon generation of the active catalyst.

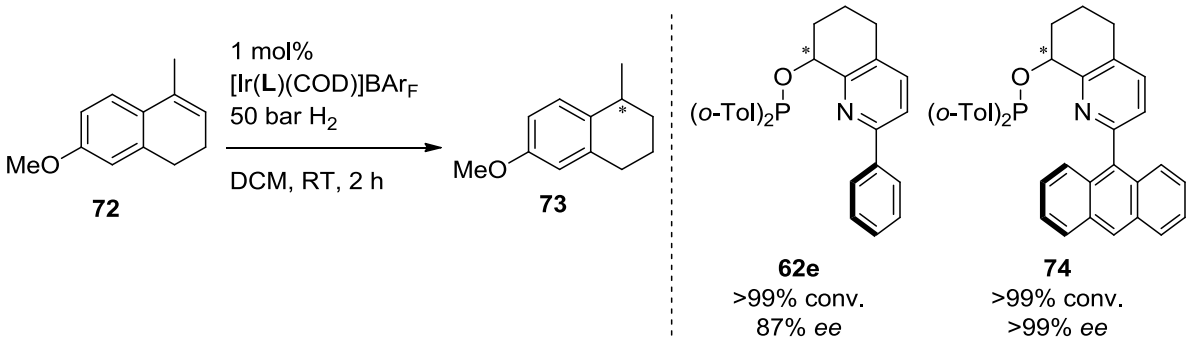
3.1.2 Cyclometallation and Formation of Inactive $Ir^{(III)}$-Complexes

Although the phenyl substituent on the pyridine ring in ligand **62** is important to achieve highly enantioselective hydrogenations, the activity of certain catalysts is relatively low. This observation could be explained with an undesired deactivation of the active catalyst. Such deactivation would arise from cyclometallation at the 2-phenyl position to form an $Ir^{(III)}$-complex bearing a tridentate C,N,P ligand. These oxidative addition reactions are known for late stage d^8-metals like iridium or rhodium and have been systematically studied for C−H activation reactions.[97] Indeed, studies of the reaction mechanism of the hydrogenation of dienes using pyridine-phosphinite Ir-complex **36f** showed the formation of a very stable dimeric $Ir^{(III)}$-complex **71** (scheme 3.1).[98]



Scheme 3.1: Deactivation of pyridine-phosphinite derived Ir-catalyst **36f** by formation of a stable $Ir^{(III)}$-complex **71**.

To avoid this undesired cyclometallatoin the installation of blocking-groups on the aromatic residue (anthracene or mesitylene; scheme 3.2) was carried out by *D. Woodmansee*.[87] Furthermore, the selectivity of these new generation pyridine-phosphinite derived complexes improved for selected substrates. The most remarkable improvement in enantioselectivity was obtained in the hydrogenation of the cyclic olefin **72**. The catalyst derived from ligands **62e** having a phenyl group gave **73** with a good *ee* of 87%, whereas the new generation catalyst derived from ligand **74** afforded enantiomerically pure tetralin **73** (>99% *ee*, scheme 3.2).



Scheme 3.2: Optimization of the pyridine-phosphinite ligand structure in order to avoid catalyst deactivation and improve the selectivity in the Ir-catalyzed asymmetric hydrogenation.

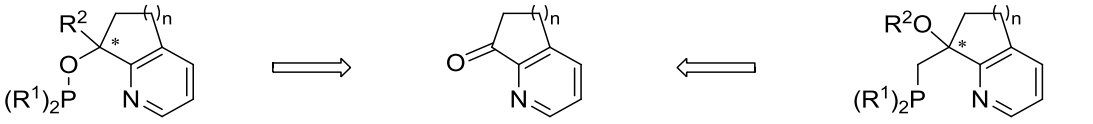
3.1.3 Objective of This Work

It should be noted that, if on one hand the presence of a mesityl or an anthracenyl group in the *ortho*-position of the pyridine ring is useful to avoid catalyst deactivation *via* cyclometallation, on the other hand the presence of these highly hindered groups mighty reduce the accessibility of the substrates to the metal center. To overcome this potential problem, a different approach for the synthesis of new bicyclic pyridine-based N,P ligands was sought. After close scrutiny of the model presented in figure 3.2, it was assumed that a

substituent at the stereogenic center of the ligand might have an appreciable influence on the substrate orientation. Therefore, the synthesis of a family of bicyclic pyridine-based N,P ligands bearing a tertiary alcohol was planned. In this case it was assumed that the installation of a residue on the sterogenic center and the removal of the substituent in the *ortho*-position of the pyridine ring (figure 3.3 left) would result in a different mode of approach of the substrate to the catalyst, according to the quadrant model depicted in figure 3.3 (right). The idea of using bicyclic pyridine-based N,P ligands with a quaternary stereogenic center was further supported by the success in the Ir-catalyzed asymmetric hydrogenation of other systems bearing a tertiary alcohol (e.g. ThrePHOX and SimplePHOX, see chapter 1).

Figure 3.3: New N,P ligands having a quaternary stereogenic center and predicted coordination of (*E*)-α-methylstilbene using the quadrant model.

As the precursors for such new phosphinite ligands **75** the pyridyl ketones **76a-b** were selected. Furthermore phosphine **77** systems should be easely accessible starting from the same precursor as well (scheme 3.3).



75
R^1: Ph, *o*-Tol, Cy
R^2: Me, *i*-Pr, Ph

76a (n = 1)
76c (n = 2)

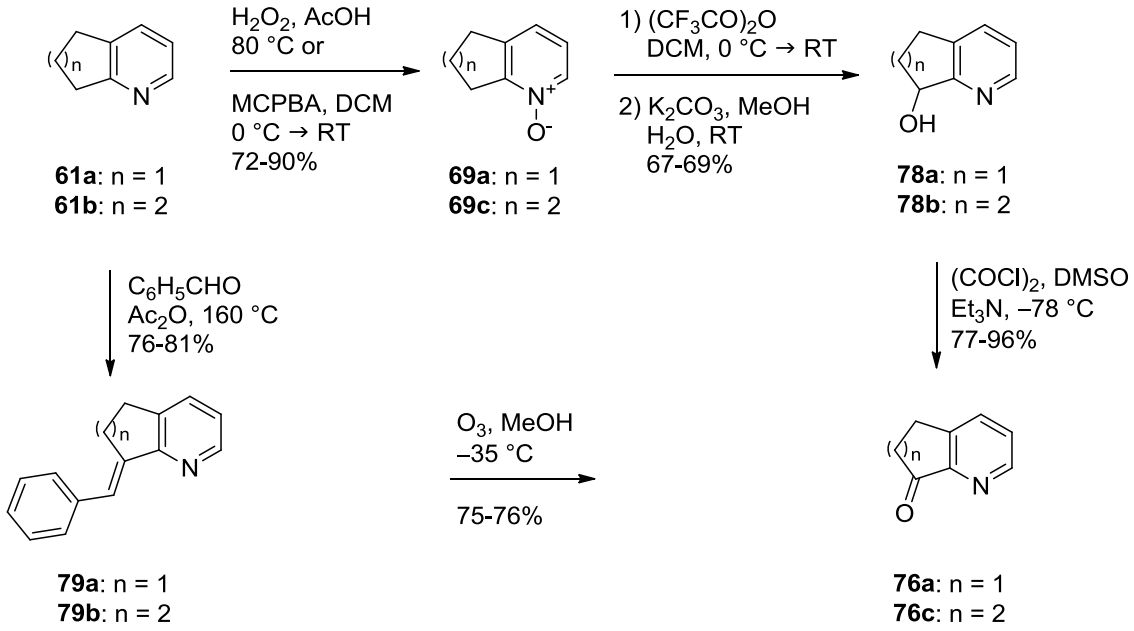
77
R^1: Ph, *o*-Tol, Cy
R^2: H, TMS, TBS, TIPS

Scheme 3.3: Retrosynthetic analysis to N,P ligand **75** and **77** *via* the key intermediate pyridyl ketones **76a** and **76c**.

3.2 Synthesis

3.2.1 Ligand Core

Two practical and fast methods were found which gave the pyridyl ketones **76a** and **76c** from commercially available starting materials. One possibility is to use the same strategy described by *S. Kaiser* for the preparation pyridine-phosphnite ligands (chapter 2, scheme 2.2).[57, 99] After formation of N-oxides by pyridine oxidation with MCPBA or *in situ* generated peracetic acid, pyridyl alcohols **78a** and **78b** were obtained after Boekelheide rearrangement[85] and subsequent hydrolysis. Oxidation under Swern conditions[100] gave the corresponding ketones **76a** and **76c** (46-50% yield over four steps). Alternatively, the same products could be obtained from ozonolysis of olefins **79a** and **79b**, which were prepared by condensation of benzaldehyde with fused bicyclic pyridines **61** as described by *R. Thummel* and co-workers.[101] The yields obtained following this second approach were up to 10% higher, as only two steps are required (scheme 3.4).

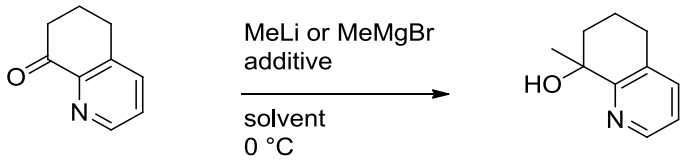


Scheme 3.4: Synthesis of pyridyl ketones **76a** and **76c**.

3.2.2 Phosphinite Ligands and Their Ir-Complexes

In order to prepare the phosphinite ligands the tertiary alcohol **80** was required. For initial experiments a racemic synthesis of **80** was conducted. Simple Grignard addition to **76c** did not lead to the product in an efficient way. Even in the presence of a Lewis acid like cerium trichloride[102] only 41% of the desired tertiary alcohol **80** was obtained. In order to improve the outcome of this transformation other reaction conditions were explored (table 3.1). The best result in terms of product yield and purity was obtained using methyl magnesium chloride in the presence of zinc chloride (entry 2).[103] Although alkylation using methyl lithium gave similar results, the isolated product contained some impurities, which were difficult to separate (entries 4-5).

Table 3.1: Optimization of the prepartion of tertiary alcohol **80**.

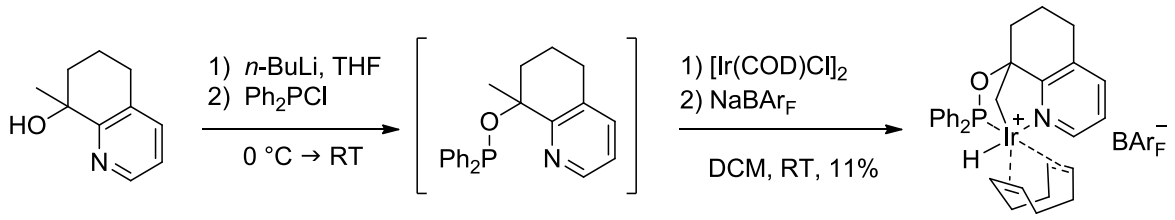


76c **80**

Entry	Reagent	Additive	Solvent	Yield [%]
1	MeMgCl (1.8 eq.)	$CeCl_3$ (1.5 eq.)	THF	41
2[103]	MeMgCl (1.5 eq.)	$ZnCl_2$ (0.1 eq.)	THF	63
3	MeMgCl (1.5 eq.)	$ZnCl_2$ (0.1 eq.) / LiBr (1.0 eq.)	THF	67
4[104]	MeLi (2.0 eq.)	LiBr (1.0 eq.)	Et_2O	76
5[105]	MeLi (1.2 eq.)	-	Et_2O / DME 1:1	79

With the tertiary alcohol **80** in hand, the preparation of the phosphinite ligand and the corresponding Ir-complex was attempted (scheme 3.5). Indeed, using a strong base (*n*-BuLi) and chlorodiphenylphosphine, the formation of the ligand was observed by ^{31}P-NMR spectroscopy. Despite of working under strictly inert conditions (degassed solvent, dry flasks) and purified reagents, several unidentified side products and decomposition products were obtained. Unfortunately, purification of the crude N,P ligand was not possible due to its decomposition on silica gel and aluminum oxide. Therefore, the use of the crude ligand **75** for the preparation of the corresponding iridium complex was investigated. Using the established procedure for the complexation of N,P ligands a complex product mixture was obtained.[36]

Analysis of the reaction mixture by ^{31}P-NMR spectroscopy revealed the formation of a complex at room temperature, but decomposition at elevated temperature (50 °C). To suppress this decomposition the complex was formed at room temperature and isolated as a pale-yellow solid. ^{31}P-NMR and MS analysis suggested formation of the expected bidentate $Ir^{(I)}$-complex, but the observed color and careful analysis of the ^{1}H-NMR shifts, revealed the presence of the cyclometalled tridentate C,N,P-derived $Ir^{(III)}$-complex **81**. The ^{31}P-NMR spectrum of **81** shows a singlet at 100.17 ppm (figure 3.4). The ^{1}H-NMR spectrum displays a doublet in the high-filed region at −15.88 ppm ($^{2}J_{PH,cis}$ = 9.2 Hz). The signals of the diastereotopic nuclei of the methylene group ($IrCH_2$) appear as a double doublet at 3.41 ppm ($^{1}J_{HH}$ = 15.2 Hz, $^{2}J_{HH}$ = 8.0 Hz) and as a double triple doublet at 2.68 ppm ($^{1}J_{HH}$ = 15.2 Hz, $^{2}J_{HH}$ = 8.0 Hz, $^{3}J_{PH}$ = 6.2 Hz). Crystal structure analysis of **81** revealed an insertion of iridium into the methyl C-H bond (for crystal structure see chapter 3.4). Such insertion reactions are generally strongly thermodynamically favored for platinum group metals, like iridium.[97] Nevertheless, this is one of the rare examples of cyclometallation into relatively inert sp^3 carbon-hydrogen bonds which lead to a formation of tridentate ligand.[106]



80 **75** **81**

Scheme 3.5: Formation of the tridentate $Ir^{(III)}$-complex **81**.

The obtained Ir-complex **81** showed no catalytic activity in the hydrogenation of (*E*)-α-methylstilbene. For this reason and the fact that other substituents on the quaternary center (*i*-Pr, *t*-Bu, Ph) should have a similar influence on cyclometallation the synthesis of these phosphinite-derived ligands was not further investigated.

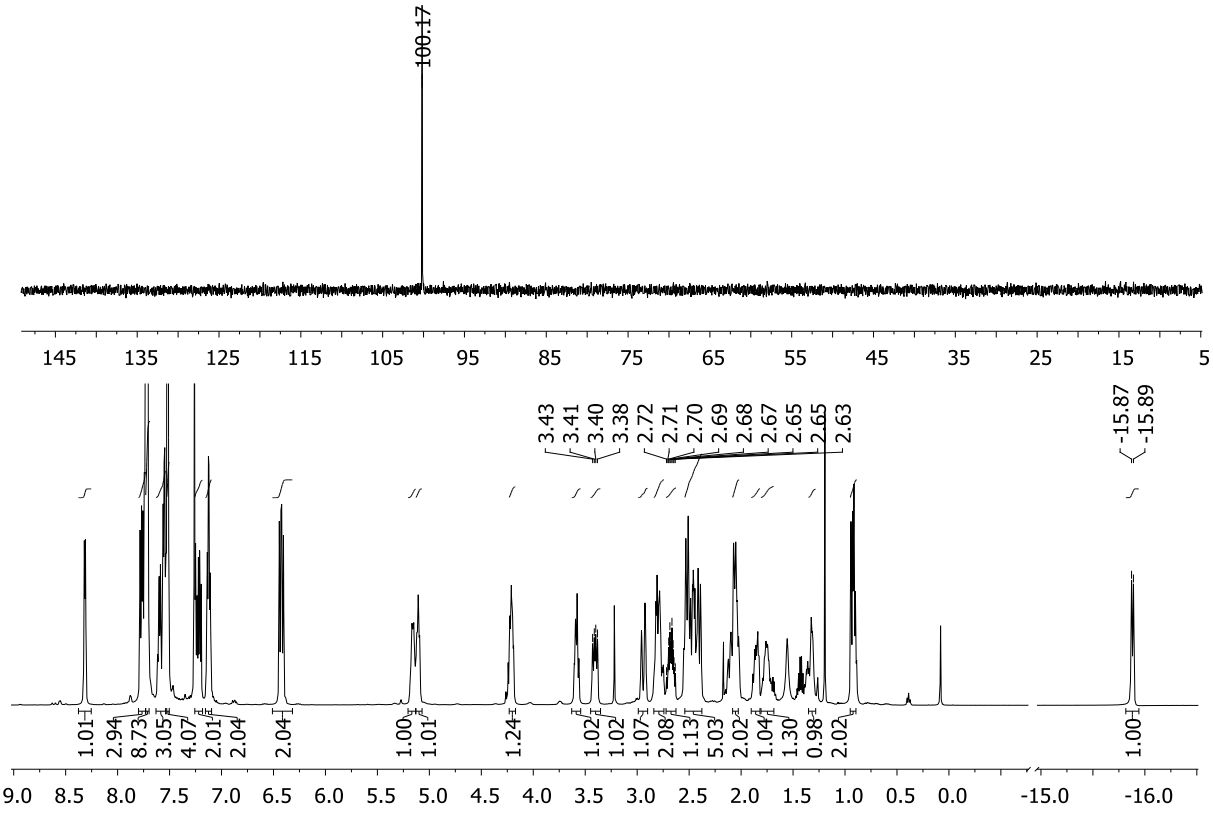


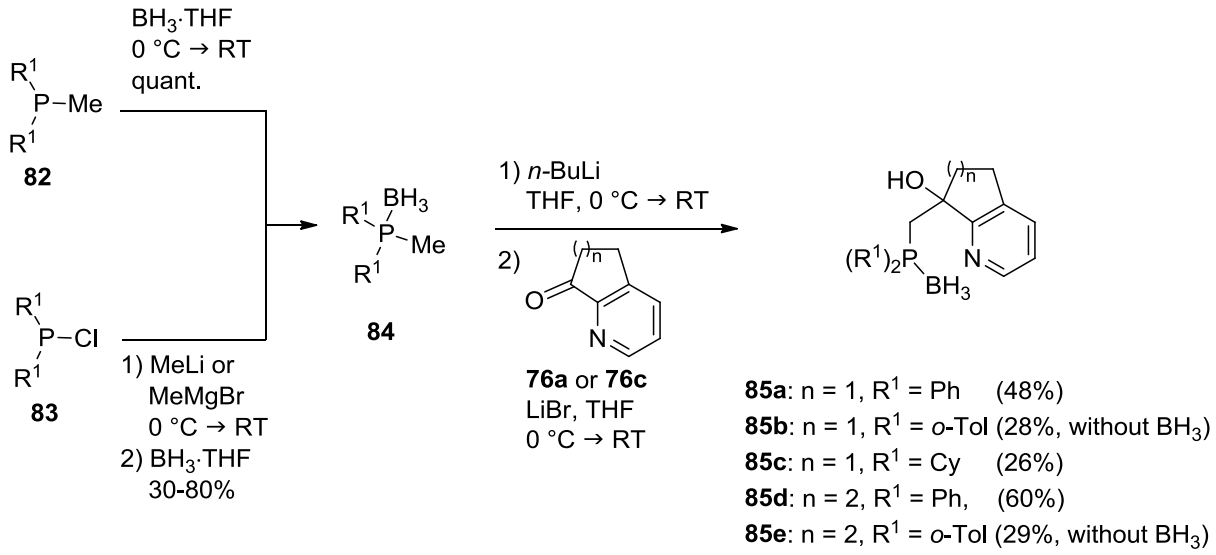
Figure 3.4: ^{31}P- and ^{1}H-NMR spectra of the cyclometallated Ir$^{(III)}$-complex **81**.

3.2.3 Phosphine Ligands and Their Ir-Complexes

A modification of the strategy was required in order to prepare the phosphine based ligands. Instead of treating the carbonyl compound **76** with a Grignard-reagent, a lithiated methyl-phosphine was added (scheme 3.6). In order to increase the acidity of the methyl group of **82**, a phosphine-BH_3-adduct was pre-formed. For this purpose commercially available diphenylmethylphosphine was treated with BH_3·THF adduct, which gave the desired product **84** in quantitative yield. All other BH_3-protected methylphosphines were prepared by reacting the chlorophosphines **83** with methyl lithium or methyl magnesium bromide and subsequent protection with BH_3·THF (scheme 3.4).

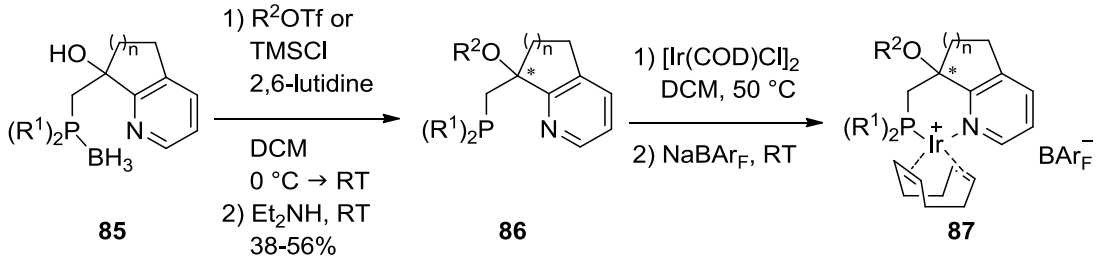
In the next step deprotonation of the methyl group of **84** and nucleophilic attack to the ketones **76a** and **76c** in the presence of LiBr gave the racemic phosphines **85**. It should be noted that the P-bound BH_3-group for *ortho*-tolyl derivatives **85b** and **85e** was removed during the work-up. All other phosphines **85** were isolated in low to moderate yield as their BH_3-adducts. The enantiopure tertiary alcohols **85** were obtained after resolution by semipreparative HPLC using a chiral stationary phase (OD). Because of the low solubility of pyridyl alcohol **85d** in apolar solvents and incomplete separation of the enantiomers of, the

BH_3-group was removed prior to the resolution. For the dicyclohexylphosphine derivative **85c**, conditions for the separation of the enantiomers by HPLC on chiral stationary phase were not found.



Scheme 3.6: Preparation of tertiary alcohols **85a-e** by nucleophilic addition to ketones **76a** and **76c**.

Table 3.2: Alcohol protection, phosphine deprotection and preparation of the Ir-complexes **87**.



Entry	Ir-complex	n	R^1	R^2	^{31}P-NMR (L) [ppm]	^{31}P-NMR [ppm]	Yield [%][a]
1	(+)-**87a**	1	Ph	TBS	–27.0	10.4	73
2	*rac.*-**87b**	2	Ph	TMS	−25.7	7.5	71
3	(+)-**87c**	2	Ph	TBS	–26.4	6.5	53
4	(−)-**87d**	2	Ph	TIPS	–25.1	7.8	70
5	(−)-**87e**	2	*o*-Tol	TBS	–49.0	11.7	76

[a]: Isolated yields of the Ir-complexes **87** after flash chromatography over silica gel.

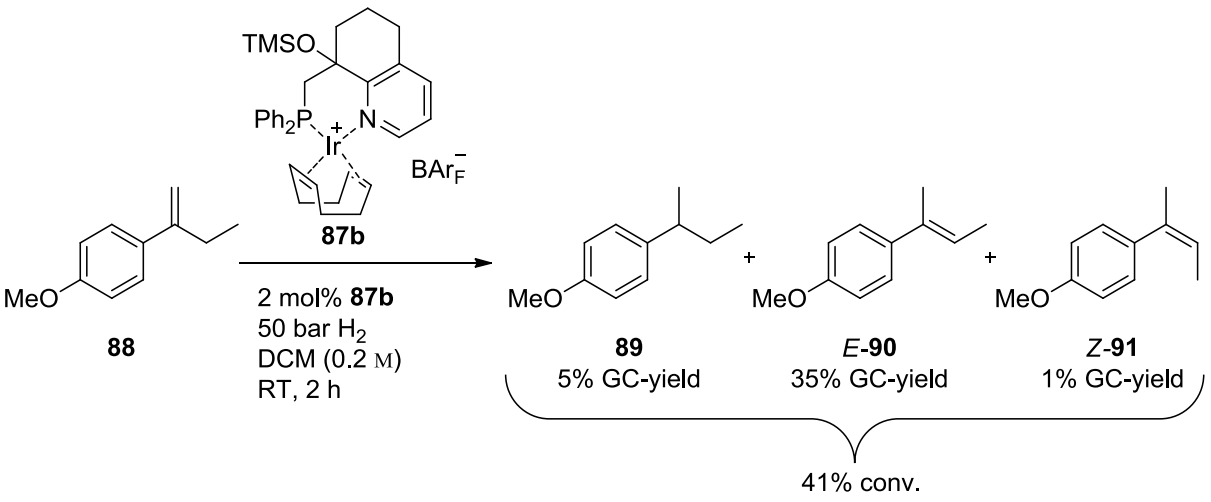
In order to prepare the iridium complexes **87** the tertiary alcohols **85** were protected as silylethers and the P-bound BH_3-groups were removed using diethyl amine. Following this

approach, five iridium complexes having different electronically and sterically properties were prepared using established conditions (table 3.2).[36] It should be mentioned, that the TMS complex **87b** was prepared in racemic form. Furthermore, complex having *ortho*-tolyl groups on the phosphorus atom **87e** was obtained as mixtures of rotamers, due to the restricted rotation of the sterically demanding groups. Preparation of Ir-complexes using the free alcohols **85d** failed.

3.3 Hydrogenation Results

3.3.1 Studies Using Racemic Catalysts

In order to evaluate the activity of the new catalysts, initial hydrogenations using the racemic TMS protected Ir-complex **87b** were performed. Using 2 mol% of catalyst loading and 50 bar hydrogen pressure, only 41% conversion for the terminal olefin **88** was observed (scheme 3.8). Furthermore, GC analysis of the reaction mixture showed only 5% of the desired product **89** and mainly isomerization to the more stable trisubstituted olefins **90** and **91**. In order to exclude pressure induced isomerization, a control experiment without the catalyst was performed. Indeed, no isomerization of the terminal C=C bond of **88** was observed at 50 bar hydrogen pressure within 24 hours.

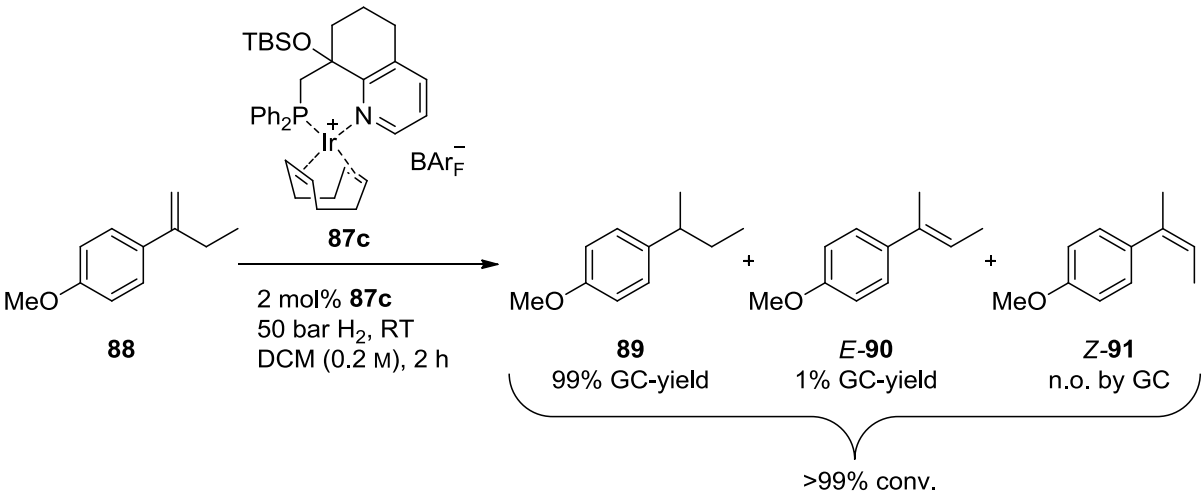


Scheme 3.7: Hydrogenation studies using terminal olefin **88** and Ir-catalyst **87b**.

One explanation for the low product formation could be found in a hampered coordination of the substrate to the iridium due to the TMS group. However, this does not explain the

isomerization of **88** to olefins **90** and **91**. A more reasonable explanation would be cleavage and decomposition of catalyst. It was independently proved by *M. Maywald*[107] and *K. Burgess* and co-workers[108] that iridium hydride species, once formed upon catalyst activation, are strong Brønsted acids. Such an acidic metal complex can lead to the cleavage of the acid labile TMS protecting group. Indeed, NMR experiments using activated Ir-complex **87b** indicated that such decomposition occurs. Furthermore, iridium hydrides themselves can promote olefin isomerization as well.

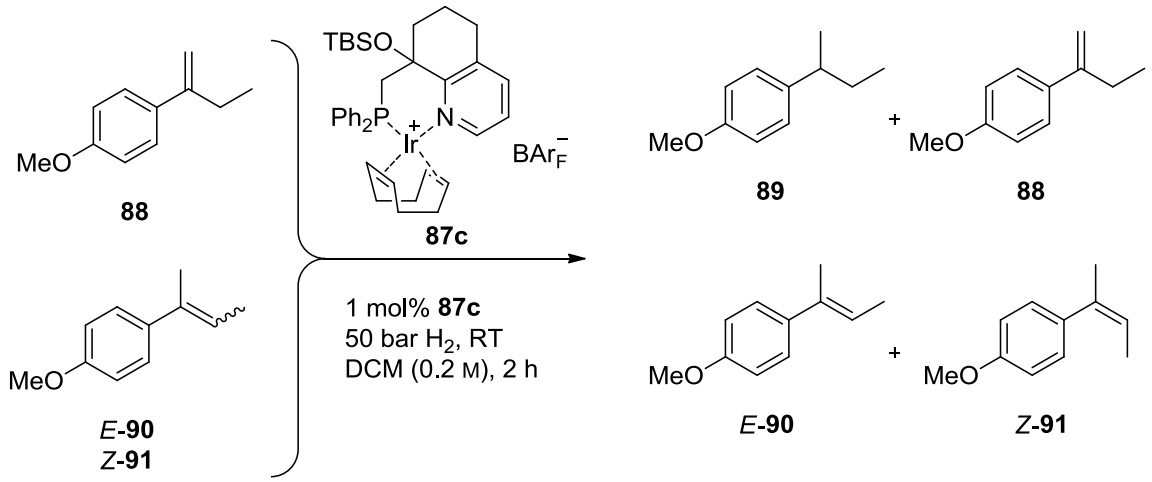
To avoid the undesired TMS cleavage, acid stable protecting groups were installed. Performing the hydrogenation experiment under the same conditions described in scheme 3.8 but now using the TBS protected Ir-catalyst **87c**, full consumption of the starting material was observed (scheme 3.9). GC analysis of the reaction mixture revealed 99% product formation and only traces of isomerization product.



Scheme 3.8: Hydrogenation studies using terminal olefin **88** and Ir-catalyst **87c**.

Hydrogenation of the trisubstituted olefins **90** and **91** would probably be slower than in the case of **88** as traces of the isomerization product were detected. To support this hypothesis, experiments using a mixture of isomeric substrates with the same catalyst were performed and analyzed by GC (see table 3.3).

Table 3.3: Hydrogenation studies using mixtures of isomeric substrates and Ir-catalyst **87c**.



Entry	Substrate mixture	**89** [%][a]	**88** [%][a]	(*E*)-**90** [%][a]	(*Z*)-**91** [%][a]
1	**88** / (*E*)-**90** 1:1	32	3	65	0
2	**88** / (*E*)-**91** 1:1	39	0	6	55
3	**88** / (*E*)-**90** / (*Z*)-**91** 1:1:1	26	0	36	38
4	(*E*)-**90** / (*Z*)-**91** 1:1	2	0	49	49

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst.

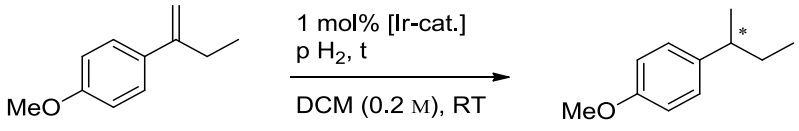
Indeed, using only 1 mol% of Ir-catalyst **87c** and a 1:1 mixture of terminal olefin **88** and (*E*)-olefin **90**, 32% of the hydrogenation product **89** was obtained (table 3.2, entry 1). While only 3% of the unreacted terminal olefin **88** remained untouched, 65% of the more stable trisubstituted olefin (*E*)-**90** was obtained. Preforming the same experiment using only olefins (*Z*)-**91** and **88** in a 1:1 ratio, again partial isomerization was observed (entry 2). Using all three isomers of the alkene in a 1:1:1 ratio only 26% hydrogenation product was obtained, while partial isomerization to both trisubstitued olefins was observed. In a last experiment only the trisubstituted olefins (*E*)-**90** and (*Z*) -**91** were mixed in a 1:1 ratio and reaction of both gave only traces of product (2%).

These results clearly showed an isomerization pathway, which is competing with the desired hydrogenation. The isomerization favors the more stable *E* olefin (thermodynamically controlled). Ir-catalyst **87c** is highly selective towards the hydrogenation of terminal C=C bonds, as only traces of hydrogenation products were obtained using a 1:1 mixture of (*E*)-**90** and (*Z*)-**91** alkenes.

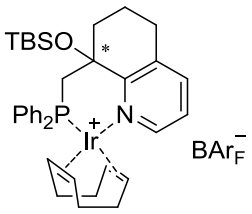
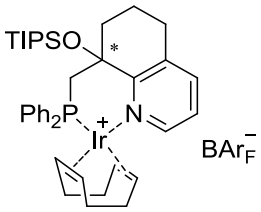
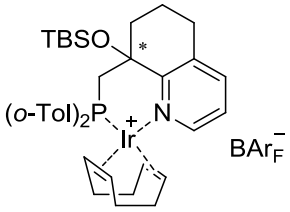
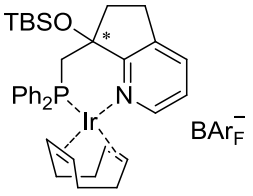
3.3.2 Asymmetric Hydrogenation of Terminal Olefins

In order to evaluate the level of enantioselectivity that could be obtained with of the newly designed Ir-catalysts, hydrogenation studies using model substrate **88** were performed. For this purpose important reaction parameters, like hydrogen pressure and reaction time, were varied. The results of this study are shown in table 3.4.

Table 3.4: Asymmetric hydrogenation of model substrate **88** using the newly developed Ir-catalysts.



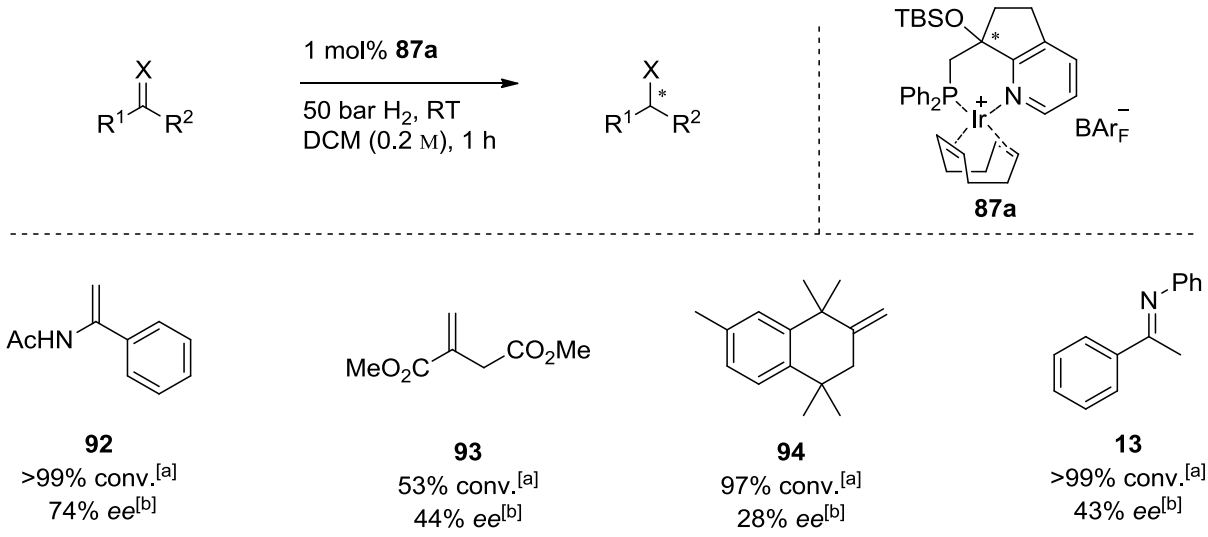
88 **89**

Entry	Ir-catalyst	p [bar]	T [h]	Conv. [%][a]	89 [%][a]	ee [%][b]	Isomerization (*E*)-**90** [%][a]	Isomerization (*Z*)-**91** [%][a]
1	 (+)-**87c**	1	1	24	5	n.d.	19	n.o.
2		5	5	98	88	75 (*R*)	10	n.o.
3		50	1	99	79	66 (*R*)	18	2
4		100	1	>99	99	*rac*.	<1	n.o.
5	 (−)-**87d**	5	5	45	42	62 (*S*)	3	n.o.
6		50	1	55	31	27 (*S*)	23	n.o.
7		100	1	>99	93	69 (*S*)	6	1
8	 (−)-**87e**	5	5	78	69	36 (*R*)	9	n.o.
9		50	1	97	54	49 (*R*)	41	1
10	 (+)-**87a**	1	1	95	95	78 (*R*)	n.o.	n.o.
11		5	5	>99	>99	45 (*R*)	n.o.	n.o.
12		50	1	>99	>99	42 (*R*)	n.o.	n.o.

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst. [b]: Determined by GC analysis on a chiral stationary phase.

The best result in terms of enantioselectivity was obtained applying lower hydrogen pressure (<5 bar). This is not very surprising as terminal olefins are known to react with higher enantioselectivity at lower pressure with iridium catalysts.[49] The highest enantiomeric excess achieved was 78% using catalyst **87a** (entry 10). The structurally similar catalyst **87c** having a six-membered fused bicycle gave a comparable *ee* of 75%, but also a significant amount of isomerization product was detected (entry 2). Increasing steric hindrance around the phosphorus atom and the oxygen atoms led to lower reactivity and enantioselectivity (entries 2, 5 and 8).

Furthermore, a preliminary study of the substrate scope with three terminal olefins having different electronic properties and the imine model substrate **13** with catalyst **87a** was performed (see scheme 3.10). Model substrates which are frequently applied in Rh-catalyzed asymmetric hydrogenations were chosen and *N*-(1-phenyl-vinyl)-acetanilide **92** gave full conversion and moderate 74% *ee*, whereas diethyl itaconate **93** was reduced with 53% conversion and 44% *ee*. The hydrogenation product of substrate **94** proceeded with almost full conversion (97%) but very low enantioselectivity (28% *ee*) were obtained. Surprisingly, catalyst **87a** showed full conversion in the hydrogenation of trisubstituted imine **13**. This results indicate that the hydrogenation of C=N bonds follows a different mechanistic pathway, which is currently under investigation.[109]



Scheme 3.9: Hydrogenation results obtained with selected terminal olefins and an imine using Ir-complex **87a**. [a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

3.4 Crystal Structure Analysis

The crystal structure of $Ir^{(III)}$-complex **81** is directly compared to the structurally similar $Ir^{(I)}$-complex **95** (figure 3.5 and table 3.4). Due to the rigid structure of **81**, different bond lengths and a different bite angle were expected. While the Ir-P bond in complex **81** is slightly shorter compared to complex **95**, the Ir-N bond is significantly longer (>0.1 Å). Nevertheless, the bite angle given by P-Ir-N atoms remains almost the same (86.2 ± 0.1°). $Ir^{(III)}$-complex **81** has as well a boat-like conformation, which is tighter when compared to **95** (0.3 Å shorter distances between Ir and benzylic carbon atom C9).

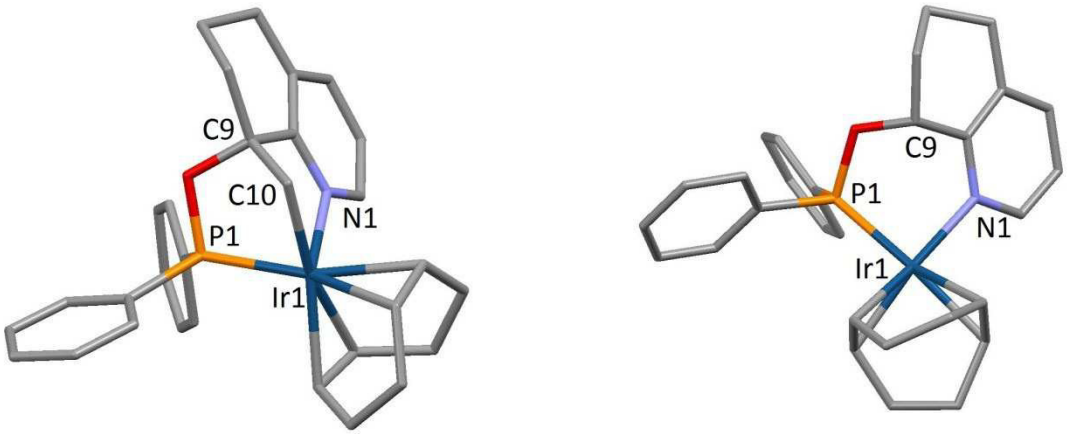
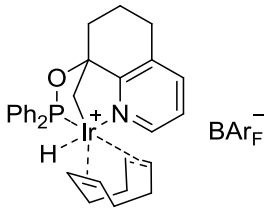
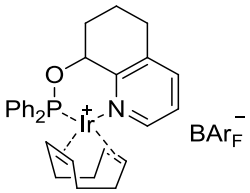


Figure 3.5: Crystal structures of **81** (left) and of **95** (right); BAr_F counterions were omitted for clarity.

Table 3.5: Selected bond lengths and bond angles of Ir-complexes **81** and **95**.

	 **81**	 **95**[57a]
Ir-P [Å]:	2.252(2)	2.2758(2)
Ir-N [Å]:	2.217(6)	2.1078(2)
P-O [Å]:	1.619(5)	1.6273(19)
Ir-C9 [Å]:	2.851	3.159
∠ P-Ir-N [°]:	86.27(7)	86.23(7)

The differences between the phosphine derived complexes **87b** and **96** are more pronounced (figure 3.6 and table 3.5). The installation of a quaternary carbon atom leads to longer coordination bonds (Ir-N and Ir-P). Therefore, the bite angle of **87b** is also larger than in the case of **96** (Δ = 2.2 °), which is close to the bite angles found in phosphinite derived complexes (see **81**). Due to the steric hindrance of the silyl group the boat conformation in **87b** is less distinctive when compared to complex **96**.

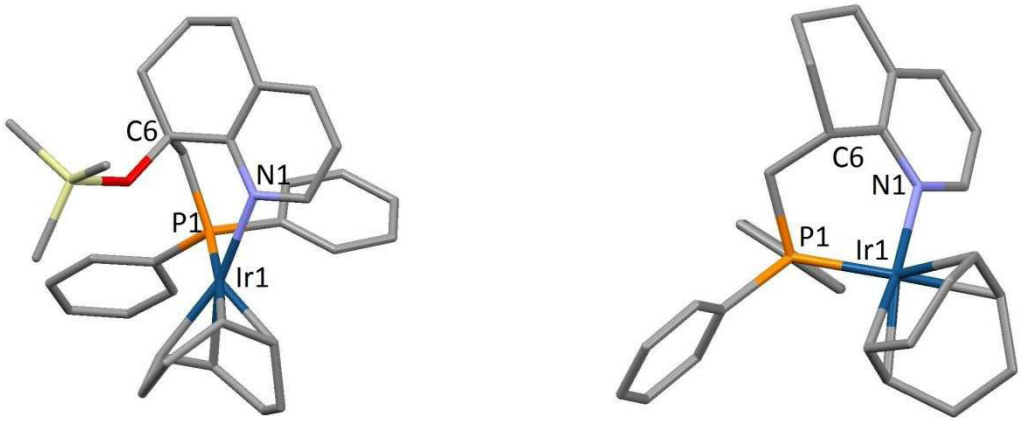
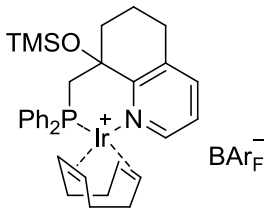
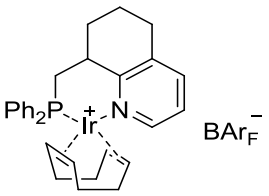


Figure 3.6: Mirror images of crystal structures of **87b** (left) and **96** (right); BAr_F counterions were omitted for clarity.

Table 3.6: Selected bond lengths and bond angles of Ir-complexes **87b** and **96**.



87b



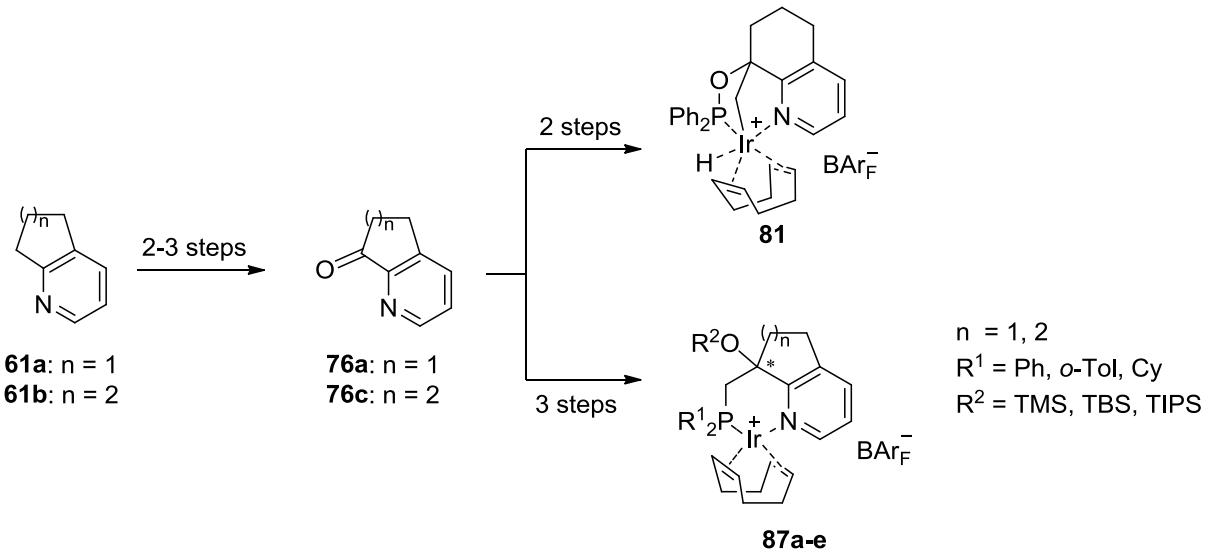
96[57a]

	87b	**96**[57a]
Ir-P [Å]:	2.306(1)	2.2869(17)
Ir-N [Å]:	2.153(4)	2.103(6)
P-C [Å]:	1.839(5)	1.836(7)
Ir-C6 [Å]:	3.346	3.278
∠ P-Ir-N [°]:	86.2(1)	83.96(16)

Although the crystal structures give some insight into the conformational preferences of the ligand complexes, direct conclusions concerning the structures of the active catalysts are not possible due to the very different coordination spheres resulting after removal of the COD group.

3.5 Summary

In summary new pyridine derived N,P ligands containing a quaternary stereogenic center were synthesized from commercially available heterocycles **61** and converted into their Ir-complexes. While the phosphinite derived N,P ligand **75** was found to undergo an irreversible cyclometalation to give an air-stable, but catalytically inactive $Ir^{(III)}$-complex **81**, the phosphine derived complexes **87** were isolated as desired $Ir^{(I)}$-complexes.



Scheme 3.10: Preparation of pyridyl ketones **76a** and **76c** for the synthesis of pyridine-phosphinite and pyridine-phosphine ligands having a quaternary stereogenic center and their Ir-complexes.

Applying these new Ir-complexes to the hydrogenation of olefins, a high selectivity towards the reduction of terminal versus tricyclic C=C bonds was found. These are first examples of Ir-complexes which are able to chemoselectivly reduce a terminal C=C bond in the presence of a trisubstitued C=C bond even at elevated pressure. However, the enatioselectivities achieved for model substrate **88** were clearly lower compared to previously developed catalysts, like Ir-TrePHOX **21**[49] or the pyrinoside based Ir-complexes **41**.[71] Furthermore, a preliminary study of the substrate scope revealed again low enantioselectivties for several terminal olefins.

Chapter 4

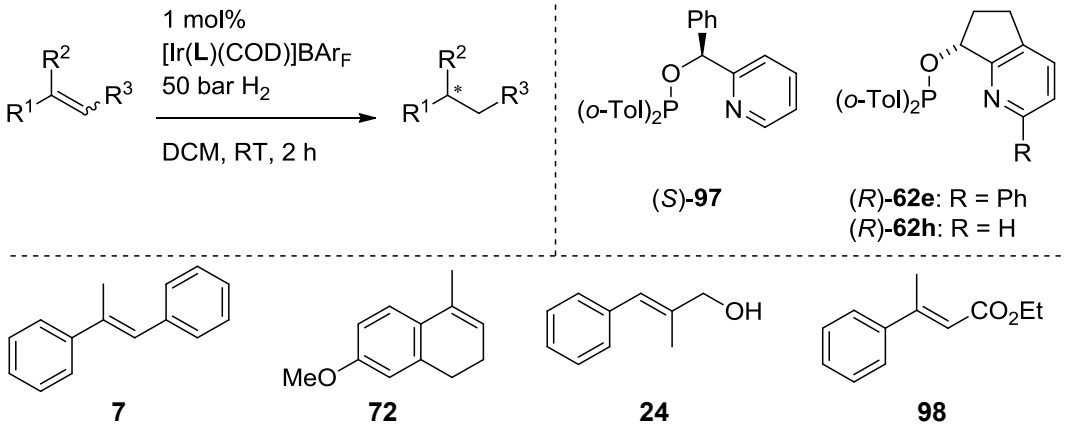
New Pyridine–Phosphinite Based Ligands for Iridium-Catalyzed Asymmetric Hydrogenation

4.1 Introduction

4.1.1 N,P Ligands without Fused Bicyclic Motif

The structural features that are important for the excellent performances of iridium complexes bearing bicyclic pyridine-phosphinite ligands **62** in the asymmetric hydrogenation of a broad range of substrates, have been discussed in previous chapters. Additionally, it should be noted, that the effect of the size of the cyclic backbone of the fused ring in the ligand scaffold was investigated as well. Ligands containing a fused ring consisting of five atoms were found to be the most active and selective for most of the tested model olefins.[57]

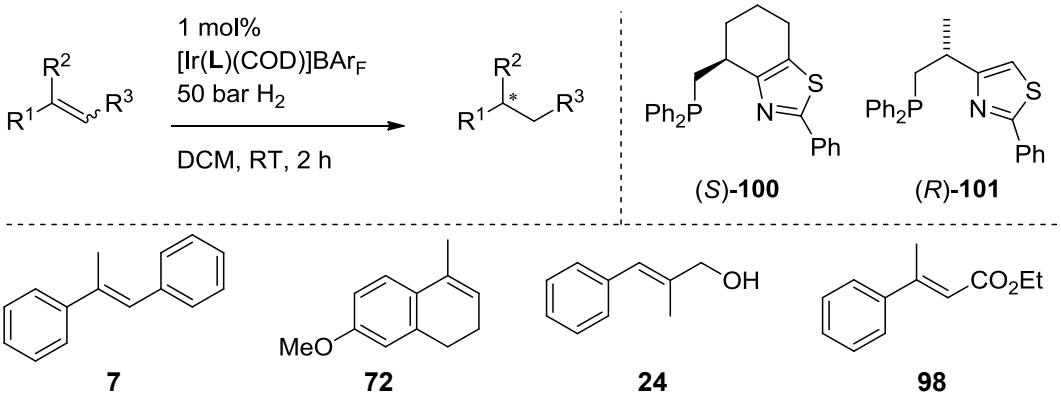
Prior to the work on bicyclic pyridine phosphinite ligands *A. Pfaltz* and co-workers investigated structurally similar bidentate N,P ligands lacking a fused ring.[110] The selectivities obtained with ligand **97** for example were higher for most of the model substrates compared to the fused bicyclic ligand **62h**. However, the installation of a phenyl group at the *ortho*-position of the pyridine ring into the ligand scaffold had a remarkably strong beneficial effect on the performance of bicyclic ligands in the hydrogenation reaction. The enantioselectivity obtained with ligand **62e** was in all cases significantly higher compared to **62h** and **97** (scheme 4.1).



	7	**72**	**24**	**98**
(*S*)-**97**	>99% conv. 95% *ee* (*S*)	>99% conv. 76% *ee* (*R*)	>99% conv. 95% *ee* (*S*)	70% conv. 22% *ee* (*S*)
(*R*)-**62h**	>99% conv. 74% *ee* (*R*)	>99% conv. 69% *ee* (*S*)	>99% conv. 92% *ee* (*R*)	>99% conv. 46% *ee* (*R*)
(*R*)-**62e**	>99% conv. >99% *ee* (*R*)	>99% conv. 87% *ee* (*S*)	>99% conv. 97% *ee* (*R*)	>99% conv. 96% *ee* (*R*)

Scheme 4.1: Comparison of selectivity of pyridine-phosphinite derived N,P ligands in the iridium-catalyzed asymmetric hydrogenation of model olefins.[57, 110]

Furthermore, as mentioned in the introduction, *P. G. Andersson* and co-workers developed N,P ligands **100** based on the rigid thiazole ligand scaffold,[67] which are enantioselective for a broad range of substrates. In later studies, they built an open-chain version of the thioazole core in order to obtain a more flexible ligand scaffold, which might be beneficial for some substrates. Applying these new N,P ligands **101** to the iridium-catalyzed asymmetric hydrogenation, similar results for many model olefins were obtained as with the rigid scaffold (scheme 4.2). Only for the cyclic olefin **72** ligand **101** led to significantly lower *ee*.[111]

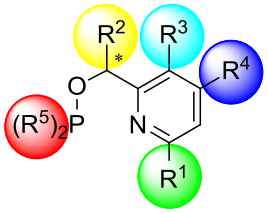


	7	**72**	**24**	**98**
(*S*)-**100**	>99% conv. >99% *ee* (*S*)	>99% conv. 93% *ee* (*R*)	>99% conv. 99% *ee* (*S*)	>99% conv. 98% *ee* (*S*)
(*R*)-**101**	>99% conv. >99% *ee* (*R*)	>99% conv. 57% *ee* (*S*)	>99% conv. 91% *ee* (*R*)	>99% conv. 98% *ee* (*R*)

Scheme 4.2: Comparison of selectivity of thiazole derived N,P ligands **100** and **101** in the iridium-catalyzed asymmetric hydrogenation of model olefins.[67, 111]

4.1.2 Objective of This Work

Here the development of pyridine-phosphinite ligands without a rigid bicyclic ring system based on structure **102** is aimed. This ligand scaffold provides a unique opportunity to study various substitution patterns. First of all, the incorporation of substituents like Me, Et or Ph at the *ortho*-position of the pyridine ring (R^1) could have beneficial stereoshielding effect, on the basis of what has been observed for the bicyclic N,P ligands **62e**. As substituents on the stereogenic center (R^2), Me and Ph groups were selected for investigation. Moreover, the orientation at this R^2-residue should be influenced by putting a Me residue at the R^3 position. By changing the R^4 substituents, the electronic properties of the N donor can be tuned. And finally, the activity and selectivity of the ligands can be tuned by employing various substituents (R^5) on the P donor.



102

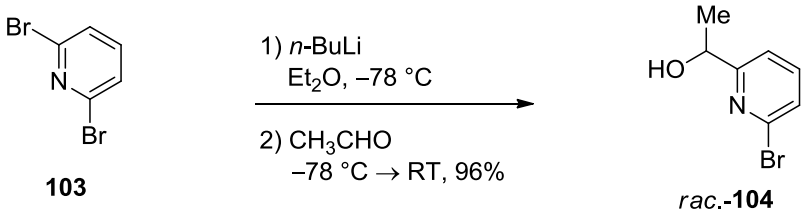
R^1: Me, Et, Ph
R^2: Me, Ph
R^3: H, Me
R^4: H, OMe
R^5: Ph, *o*-Tol, *t*-Bu

Figure 4.1: New pyridine-phosphinite based ligands **102** aimed to develop for this study.

4.2 Synthesis

4.2.1 Synthesis of Chiral Pyridyl Alcohols by Enzymatic Kinetic Resolution

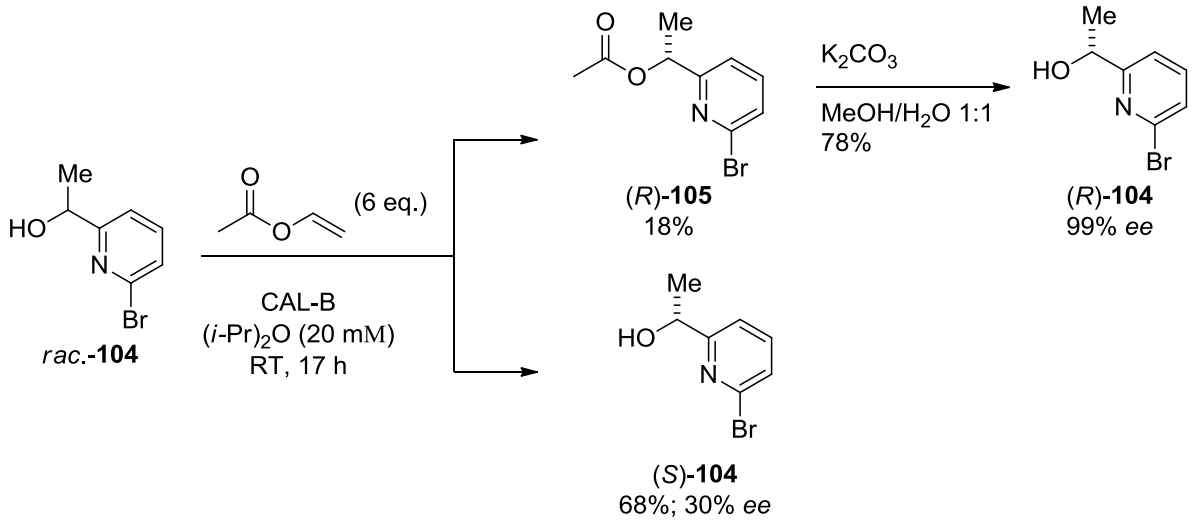
Starting from commercially available 2,6-dibromopyridine **103** the racemic pyridyl alcohol **104** was obtained after lithium-halogen exchange and subsequent trapping with acetaldehyde in excellent yield following the procedure described by *C. Bolm* and coworkers.[112]



103 *rac.*-**104**

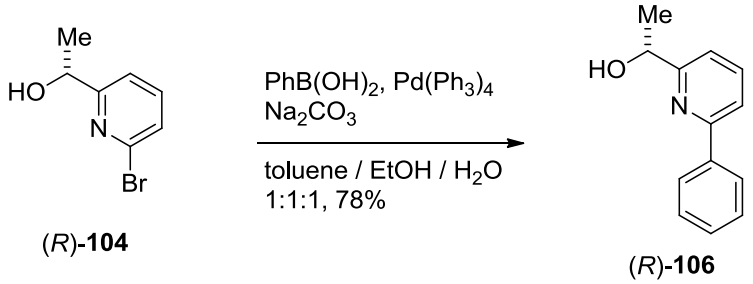
Scheme 4.3: Preparation of the racemic 6-bromo pyridyl alcohol **104**.

The enzymatic kinetic resolution of pyridyl alcohols using various lipases has been investigated by the research group of *J. Uenishi* and *K. Nakamura*.[113] Among all the systems tested CAL (*Candida antarctica* lipase) gave the best results. Under optimized conditions (6 h at 25 °C) they converted **104** into acetate (*R*)-**105** with 46% yield and 97% *ee*, whereas the recovered alcohol (*S*)-**104** was isolated in 49% yield and 93% *ee*. However, running the same reaction under the reported reaction conditions, only 18% conversion was obtained after 17 hours. Nevertheless, as sufficient quantities of enantiopure alcohol (*R*)-**104** were obtained after hydrolysis under weak basic conditions, this sequence was not further optimized.



Scheme 4.4: Enzymatic kinetic resolution of the 6-bromo pyridyl alcohol **104**.

In the next step the enantiopure pyridyl alcohol (*R*)-**104** was subjected to a Suzuki−Miyaura reaction in order to install a phenyl group onto the pyridine ring. The coupling product (*R*)-**106** was obtained in 78% yield using reported reaction conditions.[86]

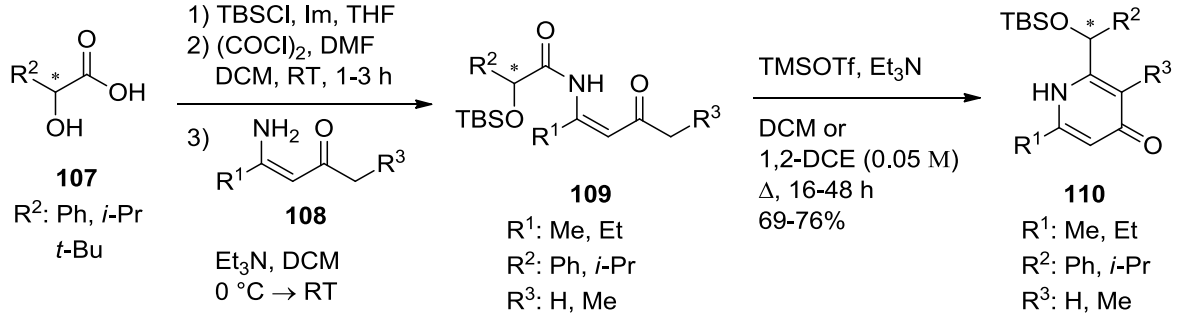


Scheme 4.5: Suzuki−Miyaura coupling to obtain (*R*)-**106**.[86]

4.2.2 Synthesis of Chiral Pyridyl Alcohols from the Chiral Pool

C. Eidamshaus and *H.-U. Reissig* recently reported a flexible and rapid approach towards highly functionalized enantiopure pyridyl alcohols.[114] Starting from readily available β-ketoenamines **108** and enantiopure α-hydroxy carboxylic acids **107** derived from the chiral pool, 4-pyridone **110** were obtained *via* a TMSOTf mediated cyclocondensation (scheme 4.6). β-Ketoenamides **109** derived from mandelic acid **107a** (R^2 = Ph) were performing best in the cyclization sequence, whereas alkyl substitued α-hydroxy carboxylic acid **107b-c** gave lower yields (R^2 = *i*-Pr) or no cyclization product **110** (R^2 = *t*-Bu). Furthermore, the cyclization was

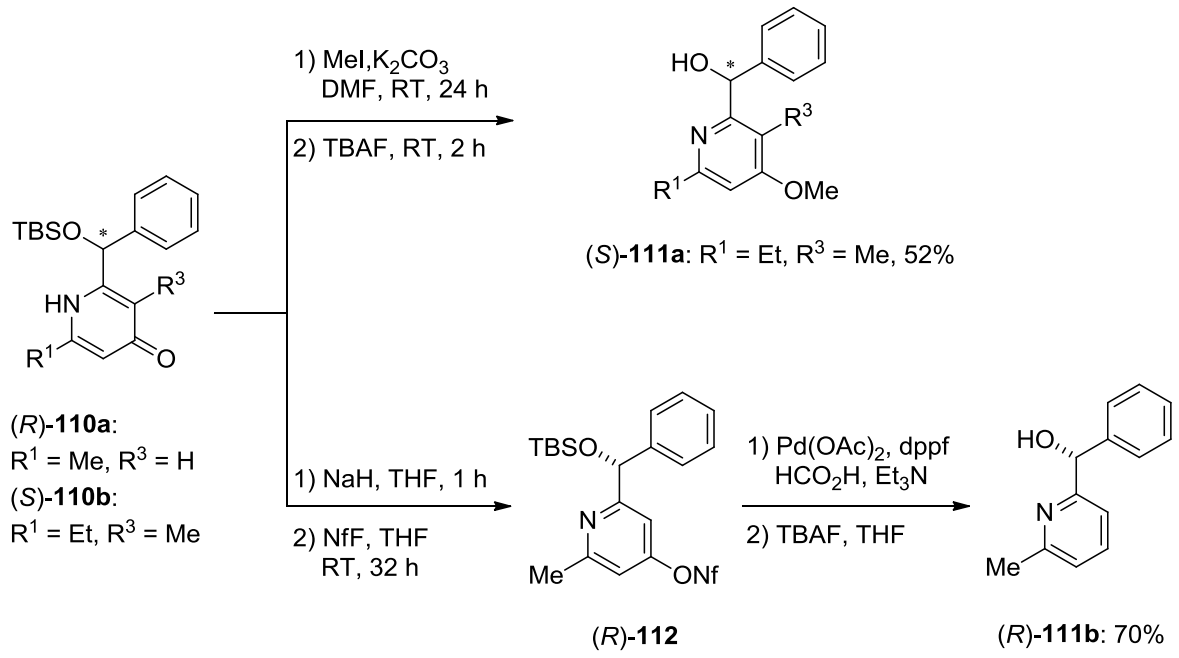
also sensitive to the steric properties of the β-ketoenamides, which allowed only small residues to be incorporated at the double bond (R^1 = Me, Et).



Scheme 4.6: *Reissig's* route to enantipure protected 4-pyridones **110**.[114]

The 4-pyridones **110** are in equilibrium with their 4-hydroxy tautomers. In this context an *O*-selective functionalization strategy was developed to obtain pyridyl alcohols **111** with different electronic and steric properties. Methylation of **110** with methyl iodide and TBS cleavage gave electron-rich pyridyl alcohols **111a** in moderate to excellent yields (scheme 4.7).

Alternatively, the formation of pyrid-4-yl nonaflate (*R*)-**112**, which is an excellent reaction partner in cross-coupling reactions, was achieved. Using (*R*)-**112** in combination with a Pd-catalyst defunctionalization towards (*R*)-**111b** was achieved in the presence of formic acid.

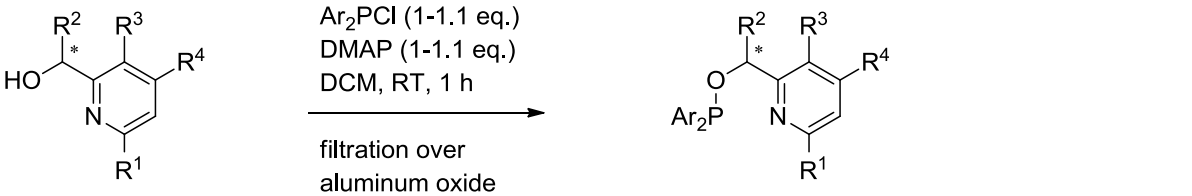


Scheme 4.7: Selective *O*-functionalization strategy to obtain pyridyl alcohols **111a-b** with different electronic and steric properties.[114]

As some of these pyridyl alcohols showed promising results in asymmetric transformations, for example in the alkylation or alkynylation of aldehydes, in the asymmetric copper-catalyzed Henry reaction and in the asymmetric allylation of benzaldehyde with allyl(trichloro) silane,[115] *C. Eidamshaus* and *H.-U. Reissig* kindly provided the enantiopure pyridyl alcohols **111a-b** for the formation of N,P ligands and their iridium complexes.

4.2.3 Formation of N,P Ligands

For the formation of the corresponding aryl phosphinite ligands the optimized conditions for the bicyclic-pyridine arylphosphinites (see chapter 2) were employed. Using enantiopure pyridyl alcohols **106** and **111a-b**, a small excess of chloro-arylphosphine (up to 1.1 eq.) and *N*,*N*-dimethylaminopyridine (up to 1.1 eq.) arylphosphinite ligands **102** were obtained after filtration over basic aluminum oxide under an inert atmosphere (scheme 4.8). The ligands were not isolated or further purified, and directly converted into the corresponding iridium complexes.

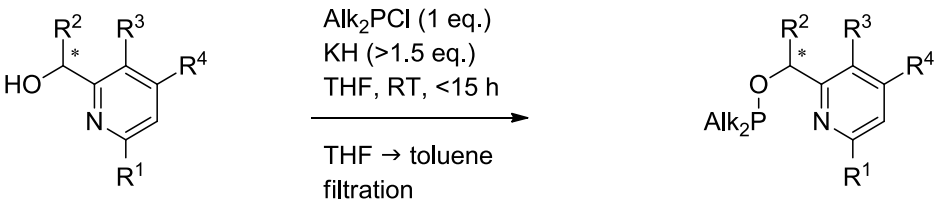


106 or **111a-b**

(*R*)-**102a**: R^1 = Ph, R^2 = Me, R^3 = H, R^4 = H, Ar = *o*-Tol
(*R*)-**102c**: R^1 = Me, R^2 = Ph, R^3 = H, R^4 = H, Ar = Ph
(*R*)-**102d**: R^1 = Me, R^2 = Ph, R^3 = H, R^4 = H, Ar = *o*-Tol
(*S*)-**102f**: R^1 = Et, R^2 = Ph, R^3 = Me, R^4 = OMe, Ar = Ph
(*S*)-**102g**: R^1 = Et, R^2 = Ph, R^3 = Me, R^4 = OMe, Ar = *o*-Tol

Scheme 4.8: Formation P-aryl phosphinite ligands **102** from monocyclic pyridyl alcohols.

For the formation of the P-alkyl phosphinite ligands a modification of the procedure described by *S. Kaiser* for the bicyclic phosphinite ligands was investigated. Instead of using sodium hydride in a THF/DMF (9:1) mixture at high dilution (0.05 M), the reaction was performed with an excess of potassium hydride in the presence of THF only but at higher concentration (0.5-0.1 M; scheme 4.9). The reaction progress was monitored by ^{31}P-NMR spectroscopy and revealed full conversion within 15 h. After complete conversion, the solvent was replaced by toluene in order to remove the excess of KH and KCl by filtration.[116] Again, the ligands were neither isolated nor purified.



106 or **111a-b**

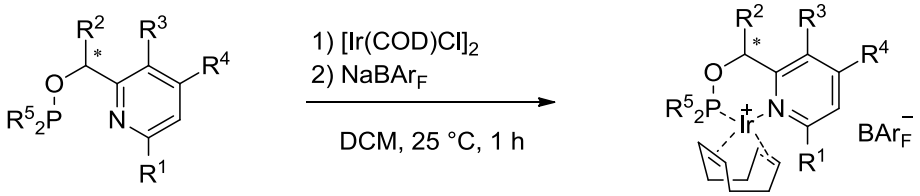
(*R*)-**102b**: R^1 = Ph, R^2 = Me, R^3 = H, R^4 = H, Alk = *t*-Bu
(*R*)-**102e**: R^1 = Me, R^2 = Ph, R^3 = H, R^4 = H, Alk = *t*-Bu
(*S*)-**102h**: R^1 = Et, R^2 = Ph, R^3 = Me, R^4 = OMe, Alk = *t*-Bu

Scheme 4.9: Formation P-alkyl phosphinite ligands **102** from monocyclic pyridyl alcohols.

4.2.4 Formation of the Iridium Complexes

The iridium complexes of N,P ligands **102** were obtained using our standard procedure.[36] Heating was not required as the formation of complex could be checked by ^{31}P-NMR. After counter ion exchange from chloride to BAr_F^- the desired iridium complexes were formed in low to good yields (table 4.1, 13-69% over two steps). It is important to mention that the complexes **113f**, **113g** and **113h** are not stable towards silica gel flash chromatography using ethereal solvent (diethyl ether or *tert*-butyl methyl ether). The best way to obtain them in high purity was using flash chromatography on basic aluminum oxide and recrystallization from diethyl ether / *n*-pentane mixture, yet still <6% of an identified impurity could be detected by ^{31}P- and by ^{1}H-NMR. This impurity is not resulting from any cyclometalation reaction of iridium with the aromatic protons, as no Ir-H signals were detected in the ^{1}H-NMR spectra in the high-field region (between −10 and −50 ppm).

Table 4.1: Formation of the iridium complexes **113** derived from monocyclic pyridine-phosphinite ligands **102**.



102 **113**

Entry	Ir-complex	R^1	R^2	R^3	R^4	R^5	^{31}P-NMR (L) [ppm]	^{31}P-NMR [ppm]	Yield [%][a] (2 steps)
1	(*R*)-**113a**	Ph	Me	H	H	*o*-Tol	94.7	96.5 (br s)	13
2	(*R*)-**113b**	Ph	Me	H	H	*t*-Bu	154.9	133.8	34
3	(*R*)-**113c**	Me	Ph	H	H	Ph	111.5	98.9	21

4	(*R*)-**113d**	Me	Ph	H	H	*o*-Tol	98.6	108.6 (br s)	53
5	(*R*)-**113e**	Me	Ph	H	H	*t*-Bu	165.6	138.3	43
6	(*S*)-**113f**	Et	Ph	Me	OMe	Ph	111.6	98.9	26[b]
7	(*S*)-**113g**	Et	Ph	Me	OMe	*o*-Tol	99.0	107.4 (br s)	69[c]
8	(*S*)-**113h**	Et	Ph	Me	OMe	*t*-Bu	167.1	140.0	46[d]

[a]: Isolated yields of the Ir-complexes **113** after flash chromatography over silica gel; [b]: contains according to ^{1}H-NMR 5% of an unidentified impurity after flash chromatography and recrystallization; [c]: contains according to ^{1}H-NMR 2% of an unidentified impurity after flash chromatography and recrystallization; [d]: contains according to ^{1}H-NMR 6% of an unidentified impurity after flash chromatography and recrystallization.

4.3 Hydrogenation Results

The new pyridine–phosphinite based ligands were evaluated in the iridium-catalyzed asymmetric hydrogenation of model substrates. The set of these model substrates includes trisubstituted unfunctionalized olefins with various substitution patterns and different double bond geometry **7**, **90** and **91**, a terminal olefin **88**, an endocyclic olefin **72**, two selected functionalized olefins (an allylic alcohol **24**, an α,β-unsaturated ester **98**) and a ketimine **13** (figure 4.2). Furthermore, their performances were compared to those of structurally similar catalysts **114** derived from ligand **97**[110] and to the best result obtained with bicyclic pyridine-phosphinite based catalysts.

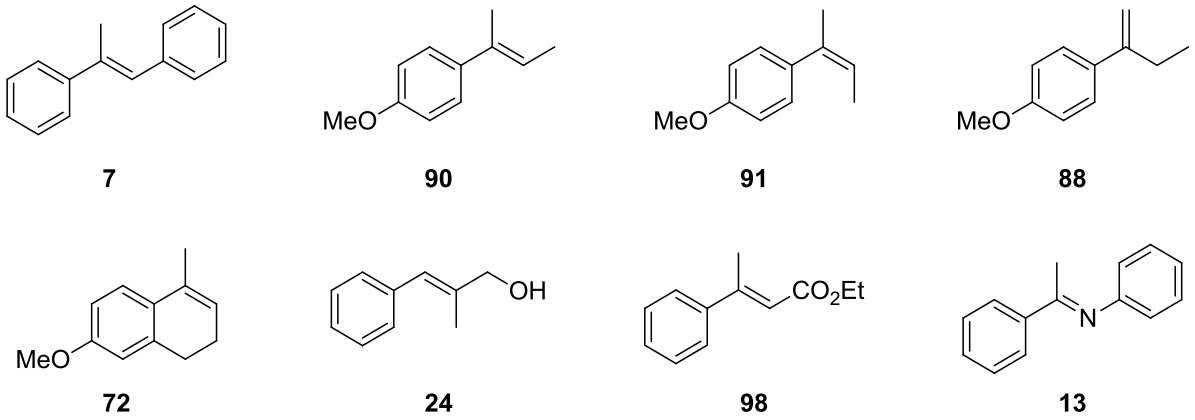
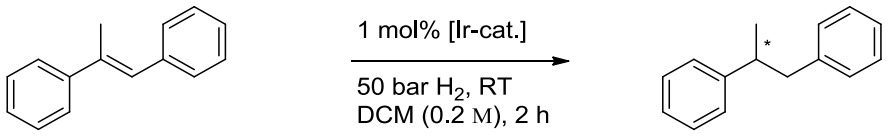
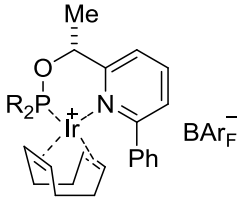
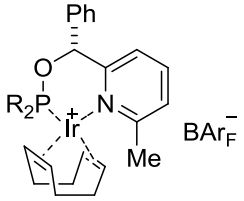
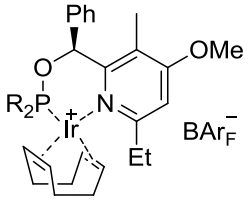
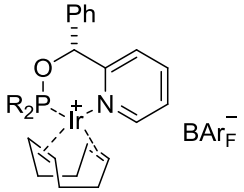
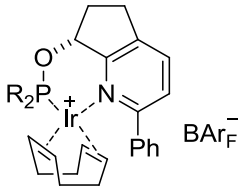


Figure 4.2: Model substrates used for the Ir-catalyzed asymmetric hydrogenation.

Table 4.2: Hydrogenation of (*E*)-α-methylstilbene (**7**).



7 **9**

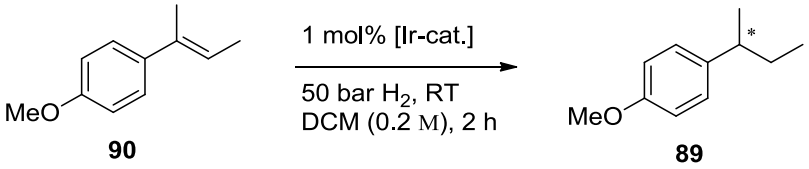
Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*R*)-**113a**	*o*-Tol	7	n.d.
2		(*R*)-**113b**	*t*-Bu	7	n.d.
3		(*R*)-**113c**	Ph	5	n.d.
4		(*R*)-**113d**	*o*-Tol	31	94 (*R*)
5		(*R*)-**113e**	*t*-Bu	>99	96 (*R*)
6		(*S*)-**113f**	Ph	7	n.d.
7		(*S*)-**113g**	*o*-Tol	2	n.d.
8		(*S*)-**113h**	*t*-Bu	12	95 (*S*)
9[110]		(*R*)-**114a**	*t*-Bu	>99	95 (*R*)
10[57]		(*R*)-**36b**	*o*-Tol	>99	>99 (*R*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

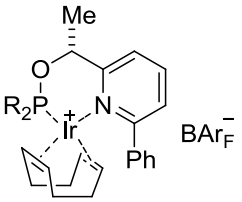
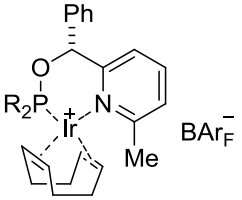
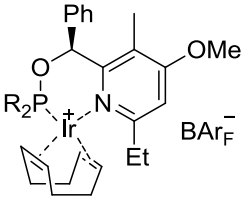
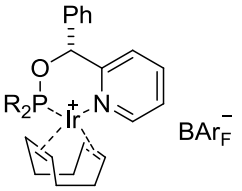
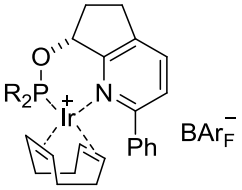
Iridium complexes (*R*)-**113a**, (*R*)-**113b** and (*R*)-**113c** with monocyclic pyridine-phosphinite ligands, proved to be not suitable for the asymmetric reduction of stilbene **7** as low conversions (<7%) were observed (table 4.2, entries 1-3). Catalyst (*R*)-**113e** having sterically bulky *tert*-butyl groups on the phosphorus atom performed best among tested complexes, providing full conversion and 96% *ee* (entry 5). On the other hand, complexes with an electron-rich pyridine ring were not very active (entries 6-8), albeit in certain cases high *ee*

could be obtained (entry 8). The results obtained are comparable to those obtained with previously known monocyclic pyridine-phosphinite iridium complexes like (*R*)-**114b** (entry 9), but they cannot compete with bicyclic pyridine-phosphinite based catalysts like (*R*)-**36b** (entry 10).

Table 4.3: Hydrogenation of (*E*)-2-(4-methoxyphenyl)-2-butene (**90**).



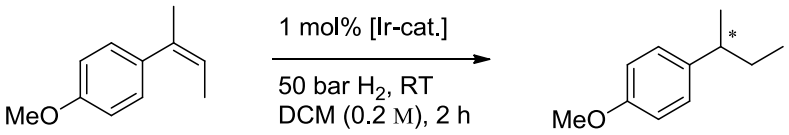
90 **89**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*R*)-**113a**	*o*-Tol	71	95 (*R*)
2		(*R*)-**113b**	*t*-Bu	82	30 (*R*)
3		(*R*)-**113c**	Ph	99	84 (*R*)
4		(*R*)-**113d**	*o*-Tol	>99	92 (*R*)
5		(*R*)-**113e**	*t*-Bu	>99	93 (*R*)
6		(*S*)-**113f**	Ph	13	6 (*R*)
7		(*S*)-**113g**	*o*-Tol	16	6 (*S*)
8		(*S*)-**113h**	*t*-Bu	69	92 (*S*)
9[110]		(*R*)-**114b**	Ph	>99	87 (*R*)
10[57]		(*R*)-**36b**	*o*-Tol	>99	>99 (*R*)

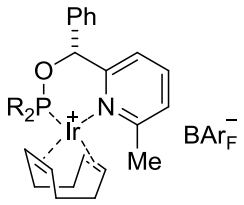
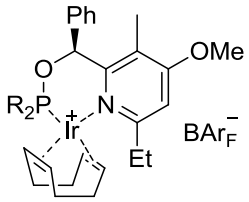
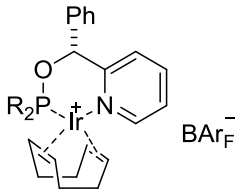
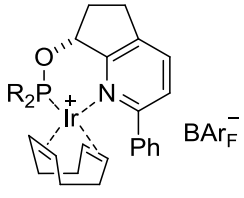
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

In the hydrogenation of trisubstituted (*E*)-olefin **90** many of the catalysts tested showed high activity (table 4.3). The best result in terms of enantioselectivity was obtained with catalyst (*R*)-**113a**, altough the reaction did not reach full conversion within two hours (entry 1). Full conversions and only slighthly lower enantioselectivities (92% and 93% respectively) were obtained with (*R*)-**113d** and (*R*)-**113e** (entries 4 and 5). As already seen in the hydrogenation of stilbene **7**, the electron-rich pyridine unit has a strong negative influence on the catalytic activity and selectivity of the iridium catalyst (entries 6-8). The best *ee* obtained with the new catalysts is higher compared to the highest previously reported values with monocyclic catalysts, like (*S*)-**114b** (entry 7). However, these values are clearly lower compared to those obtained with the rigid bicyclic ligand complex (*R*)-**36b** (entry 10).

Table 4.4: Hydrogenation of (*Z*)-2-(4-methoxyphenyl)-2-butene (**91**).



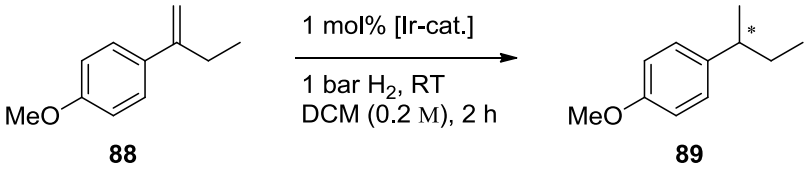
91 **89**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*R*)-**113c**	Ph	44	87 (*S*)
2		(*R*)-**113d**	*o*-Tol	85	87 (*S*)
3		(*R*)-**113e**	*t*-Bu	>99	86 (*S*)
4		(*S*)-**113f**	Ph	35	8 (*S*)
5		(*S*)-**113g**	*o*-Tol	19	*rac*.
6		(*S*)-**113h**	*t*-Bu	25	86 (*R*)
7[110]		(*R*)-**114b**	Ph	>99	90 (*S*)
8[57]		(*R*)-**36b**	*o*-Tol	>99	98 (*S*)

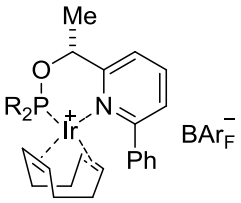
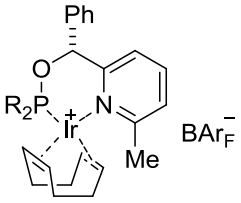
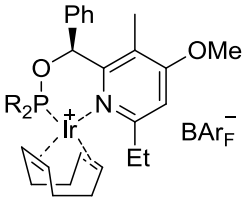
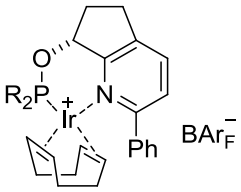
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

In general, the newly developed catalysts showed poor activity towards the hydrogenation of simple trisubstituted (*Z*)-olefin **91** (table 4.4). Only with catalyst (*R*)-**113e**, having bulky *tert*-butyl groups on phosphorus, full conversion was achieved with 86% *ee* (entry 3). Similar enationselectivites but clearly lower activities were measured for catalysts with P-aryl groups (entries 1 and 2). Catalysts having electron-rich pyridines performed poorly in terms of activity (entries 4-6). Again these catalysts gave similar enantioselectivities those obtained with previously reported monocyclic ligand complexes (*R*)-**114b** (entry 7). However, they were significantly less selective than bicyclic pyridine-phosphinite based Ir-complexes, like (*R*)-**36b** (entry 8).

Table 4.5: Hydrogenation of 2-(4-methoxyphenyl)-1-butene (**88**).



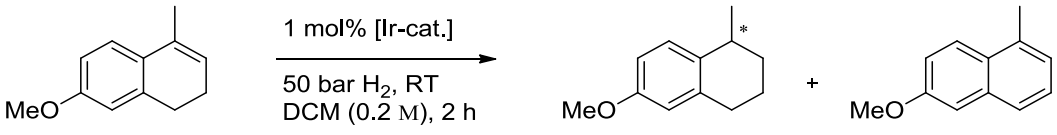
88 **89**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*R*)-**113a**	*o*-Tol	23	70 (*S*)
2		(*R*)-**113b**	*t*-Bu	38	59 (*S*)
3		(*R*)-**113c**	Ph	>99	36 (*S*)
4		(*R*)-**113d**	*o*-Tol	>99	44 (*S*)
5		(*R*)-**113e**	*t*-Bu	>99	26 (*S*)
6		(*S*)-**113f**	Ph	47	7 (*S*)
7		(*S*)-**113g**	*o*-Tol	67	17 (*R*)
8		(*S*)-**113h**	*t*-Bu	>99	40 (*R*)
9[57]		(*R*)-**36b**	*o*-Tol	>99	80 (*S*)

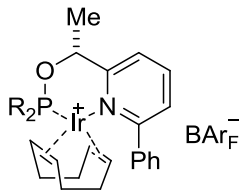
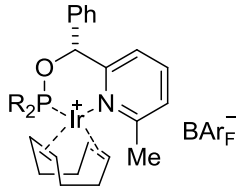
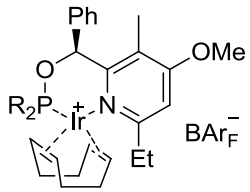
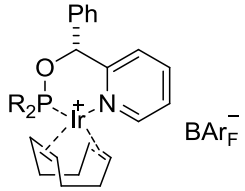
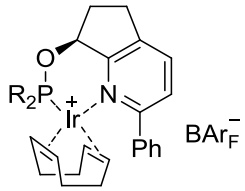
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

For the hydrogenation of the terminal double bond in substrate **88** full conversions with moderate *ee* were only achieved with catalysts (*R*)-**113c**, (*R*)-**113d**, (*R*)-**113e** and (*S*)-**113h** (table 4.5, entries 3-5 and 8). In terms of enantioselectivity, catalysts with a phenyl group at the *ortho*-position of the pyridine performed better, but they did not show high activity (entries 1 and 2). Again the results obtained cannot compete with the best results reported using catalyst (*R*)-**36b** (entry 9).

Table 4.6: Hydrogenation of 7-methoxy-1,2-dihydro-naphthalene (**72**).



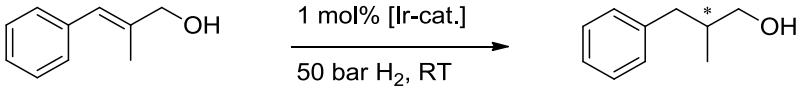
72 **73** **115**

Entry	Ir-catalyst		R	Conv. [%][a]	115 [%][a]	ee [%][b]
1		(*R*)-**113a**	*o*-Tol	89	38	56 (*S*)
2		(*R*)-**113b**	*t*-Bu	99	20	22 (*S*)
3		(*R*)-**113c**	Ph	35	n.o.	59 (*S*)
4		(*R*)-**113d**	*o*-Tol	93	2	87 (*S*)
5		(*R*)-**113e**	*t*-Bu	>99	1	86 (*S*)
6		(*S*)-**113f**	Ph	44	1	*rac*.
7		(*S*)-**113g**	*o*-Tol	46	1	3 (*R*)
8		(*S*)-**113h**	*t*-Bu	66	1	80 (*R*)
9[110]		(*R*)-**114b**	Ph	>99	n.o.	87 (*S*)
10[57]		(*S*)-**36d**	*t*-Bu	>99	n.o.	92 (*R*)

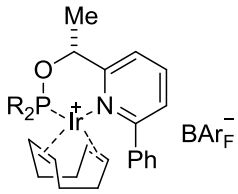
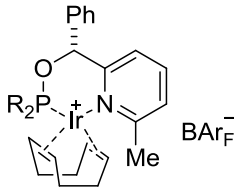
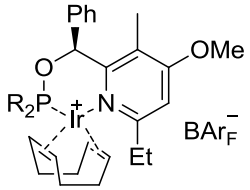
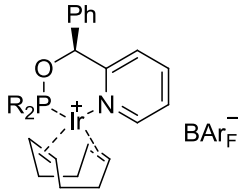
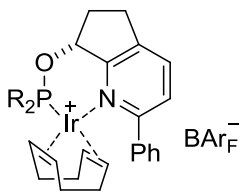
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

For substrate **72** having an endocyclic double bond, catalysts (*R*)-**113d** and (*R*)-**113e** reached high conversions with reasonably good enantioselectivities (table 4.6, entries 4 and 5). Catalysts with an electron-rich pyridine ring were not very active (entries 5-8). Surprisingly, iridium catalysts with a phenyl group at the *ortho*-position of the pyridine ring (*R*)-**113a** and (*R*)-**113b** performed poorly in terms of selectivity and a significant amount of the side product **115** was obtained (entries 1-2). Catalyst (*R*)-**113e** was as enantioselective as the previously reported catalyst (*R*)-**114b**, but both complexes performed worse than the bicyclic complex (*S*)-**36d.**

Table 4.7: Hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**24**).



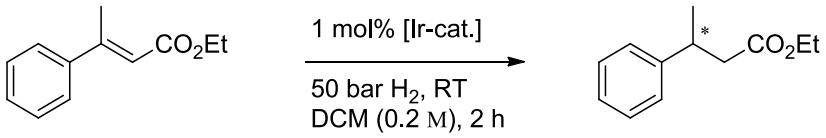
24 **25**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*R*)-**113a**	*o*-Tol	29	55 (*S*)
2		(*R*)-**113d**	*o*-Tol	76	83 (*S*)
3		(*R*)-**113e**	*t*-Bu	27	62 (*S*)
4		(*S*)-**113f**	Ph	12	*rac*.
5		(*S*)-**113g**	*o*-Tol	2	n.d.
6		(*S*)-**113h**	*t*-Bu	2	n.d.
7[110]		(*S*)-**114c**	*o*-Tol	>99	95 (*R*)
8[57]		(*R*)-**36b**	*o*-Tol	>99	97 (*S*)

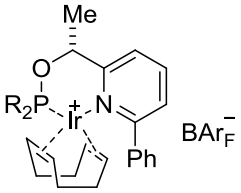
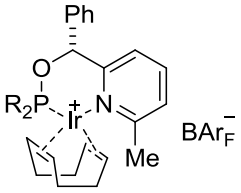
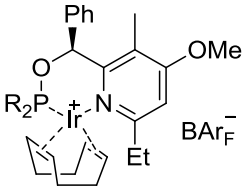
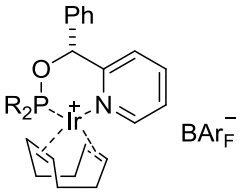
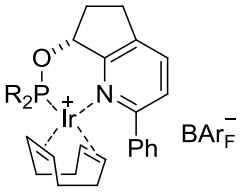
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

The newly developed iridium catalysts proved to be not particularly suitable for the hydrogenation of allylic alcohols, like **24**. Only catalyst (*R*)-**113d** gave conversion over 50% with an acceptable *ee* of 83% (table 4.7, entry 2). This is in clear contrast to the previously developed monocyclic pyridine-phosphinite catalyst (*R*)-**114c** and to the bicyclic pyridine-phosphinite catalyst (*R*)-**36b** that aforded the desired product **25** with excellent enantioselectivities of up 97% and full conversion (entries 7-8).

Table 4.8: Hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**98**).



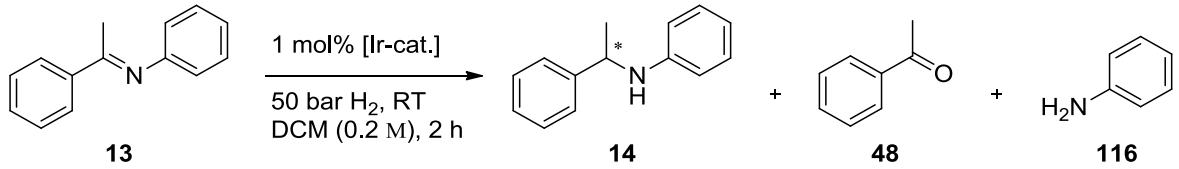
98 **99**

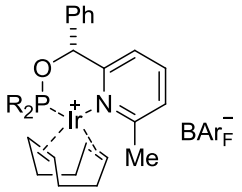
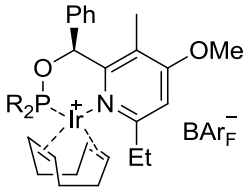
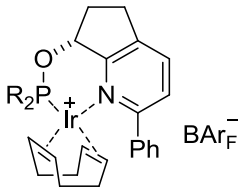
Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*R*)-**113a**	*o*-Tol	5	n.d.
2		(*R*)-**113b**	*t*-Bu	6	n.d
3		(*R*)-**113d**	*o*-Tol	19	30 (*R*)
4		(*R*)-**113e**	*t*-Bu	89	76 (*R*)
5		(*S*)-**113f**	Ph	92	12 (*R*)
6		(*S*)-**113g**	*o*-Tol	10	16 (*S*)
7		(*S*)-**113h**	*t*-Bu	31	22 (*S*)
8[110]		(*R*)-**114a**	*t*-Bu	>99	95 (*R*)
9[57]		(*R*)-**36b**	*o*-Tol	>99	96 (*R*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

The enantioselectivity of the newly developed catalysts in the hydrogenation of the α,β-unsaturated ester **98** was poor. Only catalyst (*R*)-**113e** gave a moderate 76% *ee* at 86% conversion (table 4.8, entry 4). Most of the complexes tested showed poor activity and selectivity, which is again in clear contrast to previously reported, structurally similar catalysts like (*R*)-**114a** and to the bicyclic pyridine-phosphinite catalysts like (*R*)-**36b** which gave up to 96% *ee* (entries 8-9).

Table 4.9: Hydrogenation of (*E*)-*N*-(1-phenylethylidene)aniline (**13**).



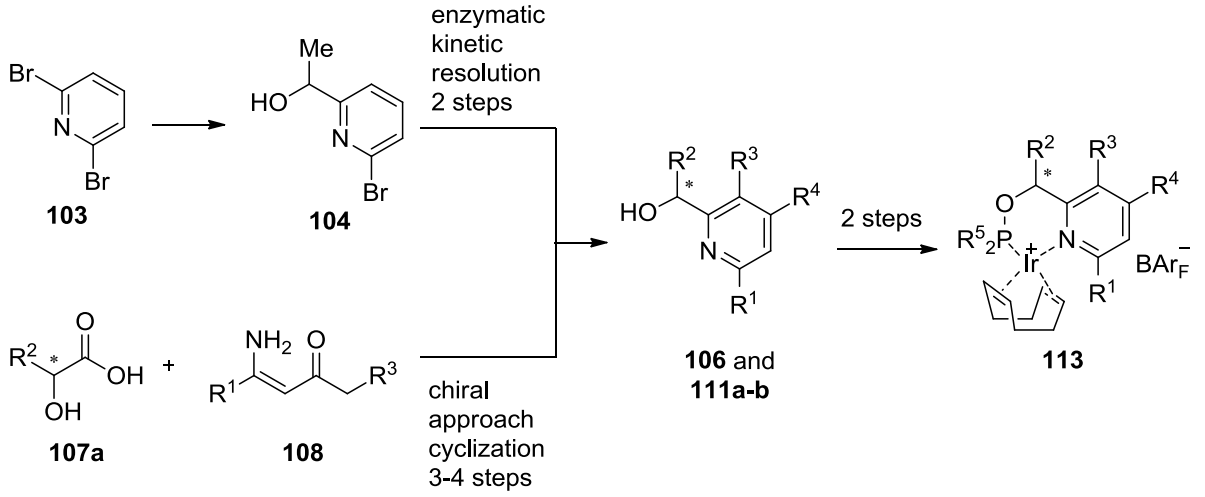
Entry	Ir-catalyst		R	Conv. [%][a]	14 [%][a]	48 + 116 [%][a]	*ee* [%][b]
1		(*R*)-**113c**	Ph	84	58	25	28 (*R*)
2		(*R*)-**113d**	*o*-Tol	97	85	11	17 (*R*)
3		(*R*)-**113e**	*t*-Bu	>99	>99	n.o.	23 (*S*)
4		(*S*)-**113f**	Ph	>99	98	1	12 (*R*)
5		(*S*)-**113g**	*o*-Tol	88	79	9	15 (*S*)
6		(*S*)-**113h**	*t*-Bu	85	44	41	*rac*.
8[57b]		(*R*)-**36b**	*o*-Tol	>99	>99	n.o.	82 (*S*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

In general, pyridine-phosphinite derived ligands showed moderate enantioselectivity towards the model substrate **13**.[57, 87] The catalysts developed in this study showed high activity but low enantioselectivity (table 4.9). For most of the developed catalysts a significant amount of hydrolysis products (acetophenone **48** and aniline **116**) was obtained.

4.5 Summary

In summary, the synthesis of differently substituted enantiopure pyridyl alcohols **106** and **111a-b** using different approaches was described (scheme 4.10). One synthetic pathway starts from commercially available 2,6-dibromopyridine **103**, which gave racemic pyridyl alcohol **104** after lithium-halogen exchange and subsequent trapping with acetaldehyde. Enzymatic kinetic resolution provided the secondary pyridyl alcohol **104**, which was further modified by Suzuki−Miyaura coupling to give **106**. Alternatively, enantiopure pyridyl alcohols **111a-b** were obtained from β-ketoenamine **108** and mandelic acid **107** by a sequence including ring cyclization and *O*-selective functionalization. Formation of N,P ligands and Ir-complexes **113** was achieved following previously established conditions.



Scheme 4.10: Synthesis of enantiopure pyridyl alcohol **106** and **111a-b** for the formation of new monocyclic pyridine-phosphinite derived iridium complexes **113** for asymmetric hydrogenation.

Applying these Ir-complexes to the asymmetric hydrogenation of unfunctionalized olefins up to 96% *ee* were obtained. Nevertheless, these complexes cannot compete with catalysts based on the rigid bicyclic framework. For partially functionalized olefins and imines low activity and selectivity were obtained

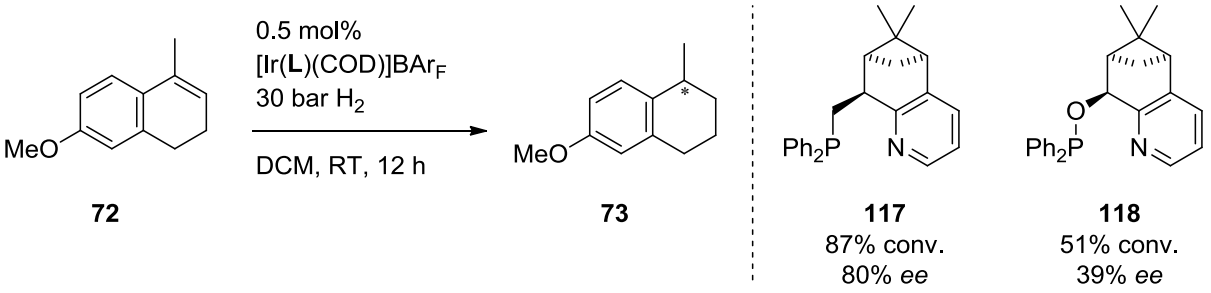
Chapter 5

New Bicyclic Pyridine Amino-Phosphine Derived Ligands for Iridium-Catalyzed Asymmetric Hydrogenations

5.1 Introduction

5.1.1 Electronic Properties of N,P Ligands

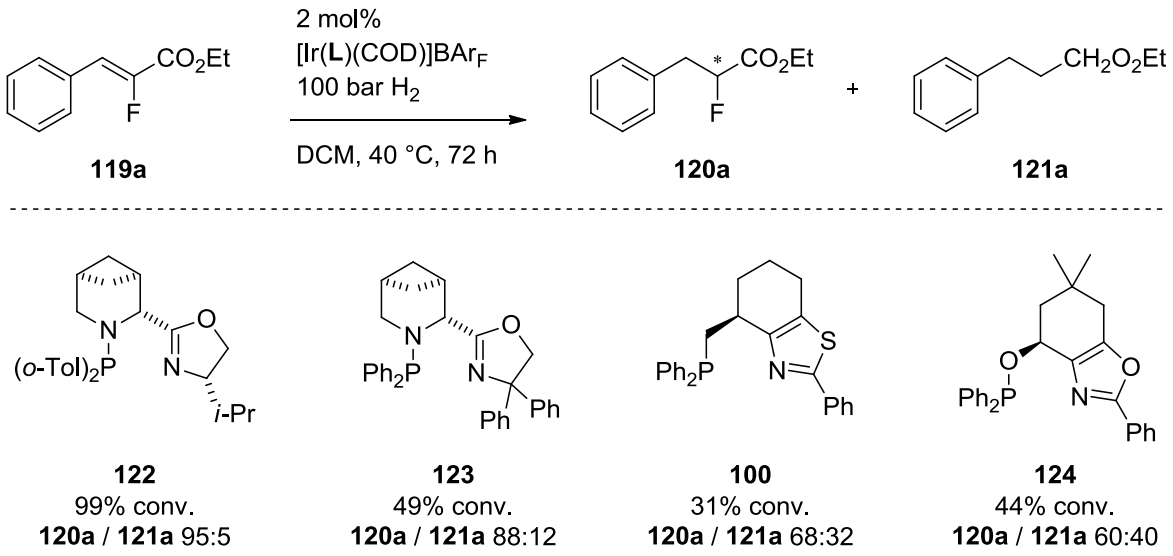
As seen in the previous chapters small changes of the ligand scaffold can have a huge impact on the enantioselectivity and conversion of asymmetric hydrogenations. For example, employing the structurally similar α-pinene derived N,P ligands **117** (phosphine) and **118** (phosphinite) in the iridium-catalyzed asymmetric hydrogenation of the cyclic olefin **72** higher activity and selectivity was obtained using the catalyst derived from **117** (scheme 5.1).[117] The only difference between the two ligands is the atom which links the P-donor to the N-donor. As both structures should have similar steric properties, their electronic properties must clearly be different.



72 **73** **117** 87% conv. 80% *ee* **118** 51% conv. 39% *ee*

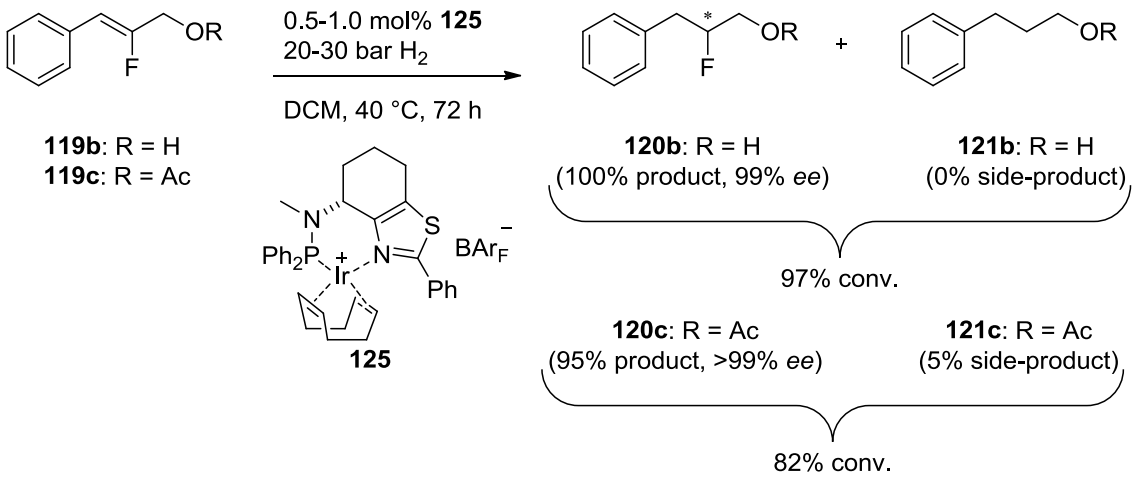
Scheme 5.1: Iridium-catalyzed asymmetric hydrogenation of model substrate **72** using structurally similar N,P ligands **117** and **118**.[117]

A further example, which demonstrates the importance of the electronic properties of a catalyst, is shown in scheme 5.2.[69] Employing Ir-complexes for the hydrogenation of vinyl fluorides **119a** an ideal catalyst should provide the hydrogenation product **120a** in high enantiomeric purity while avoiding a competitive defluorination that would afford the side-product **121a**. A preliminary screening revealed iridium complexes derived from aminophosphine-ligands **122** and **123** as the most active and chemoselective catalysts for this substrate. On the other hand iridium complexes derived from phosphine ligand **100** or phosphinite ligand **124** showed lower activities and, moreover, gave significant amounts of the side-product **121a**.



Scheme 5.2: Comparison of reactivity and chemoselectivity of selected N,P ligands in the iridium-catalyzed asymmetric hydrogenation of fluorinated olefin **119a**.[69]

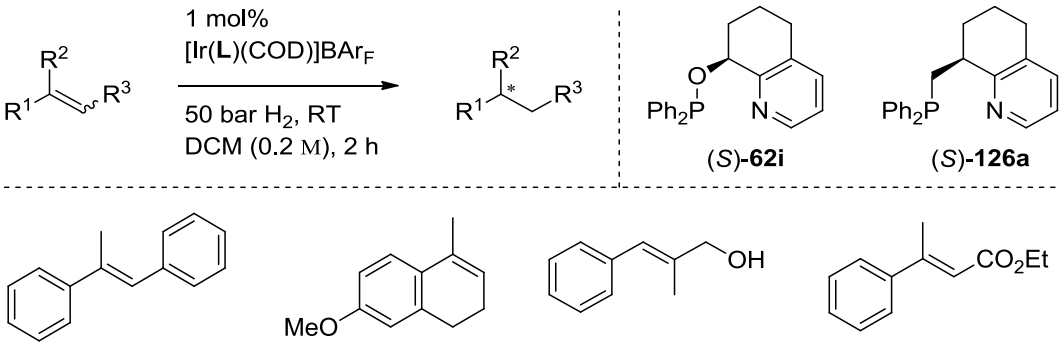
As Ir-complexes derived from ligands **100** and **124** were known to induce higher level of *ee*s for other trisubstituted olefins the authors considered to introduce an aminophosphine unit into the ligand scaffold. Therefore, they developed iridium catalyst **125** consisting of a thiazole-aminophosphine ligand which was very efficient in the hydrogenation of fluorinated allylic alcohol **119b** and allylic acetate **119c** (scheme 5.3). Only small amounts (<5%) of defluorinated side-products **121** were detected, moreover the hydrogenation products **120b** and **120c** were obtained in excellent enantiomeric excess (99%).[69]



Scheme 5.3: Asymmetric hydrogenation of fluorinated olefins **119b** and **119c** using Ir-catalyst **125**.[69]

5.1.2 Phosphine *vs.* Phosphinite Derived N,P Ligands

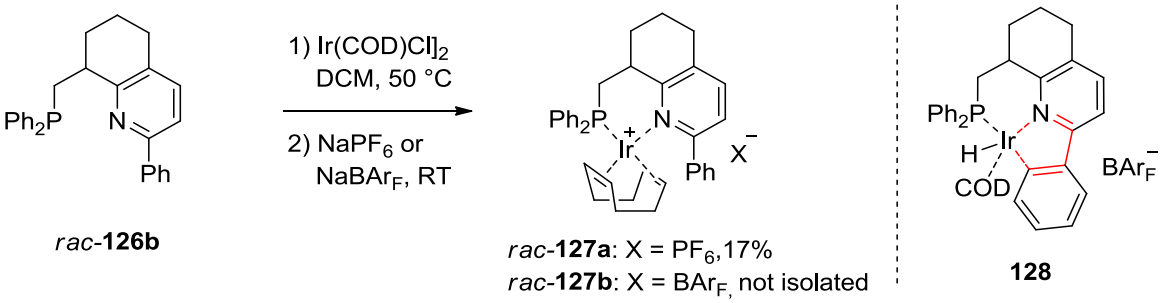
Taking into account the unrivaled success of bicyclic pyridine phosphinite ligands in asymmetric hydrogenations, structural variations of these systems would be the next logical step. Indeed, in parallel to the development of phosphinite derived ligands, *S. Kaiser* prepared as well their phosphine analogs.[57a] When the performance of both ligand structures in hydrogenation was compared, opposite trends to those observed by *J. Verendel* and *P. G. Andersson* (see scheme 5.1) were found for unfunctionalized olefins.[117] While both ligands showed comparable reactivity, the phosphinite ligand **62i** gave always higher, or at least equal, enantioselectivity compared to the phosphine ligand **126a** in the reduction of unfunctionalized olefins like **7** and **72** (Figure 5.1). However, for the functionalized alkenes like the allylic alcohol **24**, the phosphine ligand **126a** was more active but less selective, whereas for the α,β-unsaturated ester **98** ligand **126a** showed higher activity and selectivity.[57a]



	7	**72**	**24**	**98**
(*S*)-**62i**	>99% conv. 91% *ee* (*S*)	>99% conv. 78% *ee* (*R*)	26% conv. 89% *ee* (*R*)	24% conv. 26% *ee* (*R*)
(*S*)-**126a**	>99% conv. 88% *ee* (*S*)	>99% conv. 53% *ee* (*R*)	>99% conv. 79% *ee* (*R*)	>99% conv. 82% *ee* (*R*)

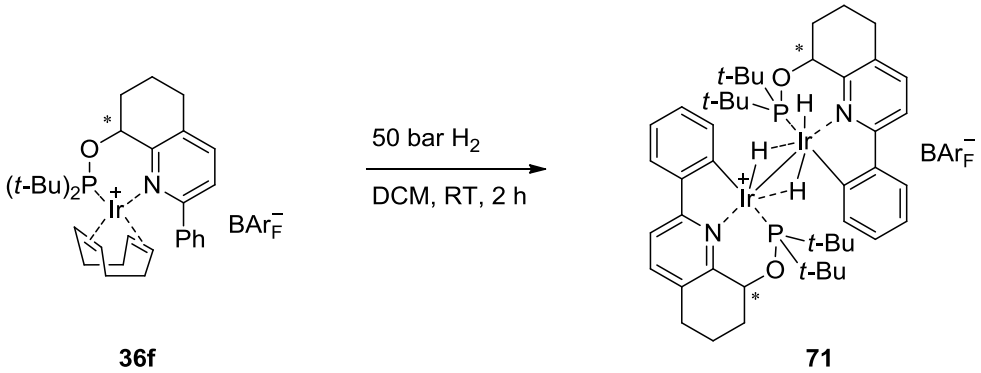
Figure 5.1: Comparison of selectivity and activity of phosphinite and phosphine derived ligand in the iridium-catalyzed asymmetric hydrogenation of selected olefins.[57a]

Encouraged by these promising results, *D. Woodmansee* attempted the synthesis of phosphine ligands having the desired aryl substitution on the pyridine ring in the scaffold. As seen in chapter 3 this substitution plays an important role, in order to obtain very high selectivity. However, ligand **126b** with a phenyl group in this position could only be converted into the corresponding iridium$^{(I)}$ complex with the PF_6^- counter ion **127a**, but not with the more active BAr_F^- anion **127b**.[87b] It was suggested that a competitive cyclometallation reaction produced a stable, but unreactive, Ir$^{(III)}$-complex **128**.



Scheme 5.4: Complexation study of bicyclic pyridine phosphine derived ligands **126**.[97]

Interestingly, as already discussed in chapter 3 (scheme 3.1), such a cyclometallation does not occur in the phosphinite derived Ir-complexes. Only under reaction conditions that lead to an irreversible removal of the COD ligand, the cyclometallated species **71** could be isolated starting from **36f** (scheme 5.5).[98]



Scheme 5.5: Cyclometallation of phosphinite derived Ir-complex **36f** occurring under hydrogenation conditions.[98]

5.1.3 Objective of This Work

Although the bicyclic pyridine-phosphinite derived iridium complexes showed high activities and selectivities over a broad range of substrates, the development of new N,P ligands is still important. In the initial part of this chapter the importance of small variations of the ligand scaffold was shown in order to obtain hydrogenation catalysts for specific substrates (vinyl fluorides). In this section the development of new bicyclic pyridine-aminophosphine derived complexes is desribed. Initially, these new N,P ligands were applied to the iridium-catalyzed hydrogenations. But ideally if these new ligands showed promising results, they might found also find application in many other metal-catalyzed asymmetric transformations. Due to the smaller bond-length between phosphorus and nitrogen atoms these ligands should also be more stable towards air and moisture, when compared to the phosphite ligands (figure 5.2).

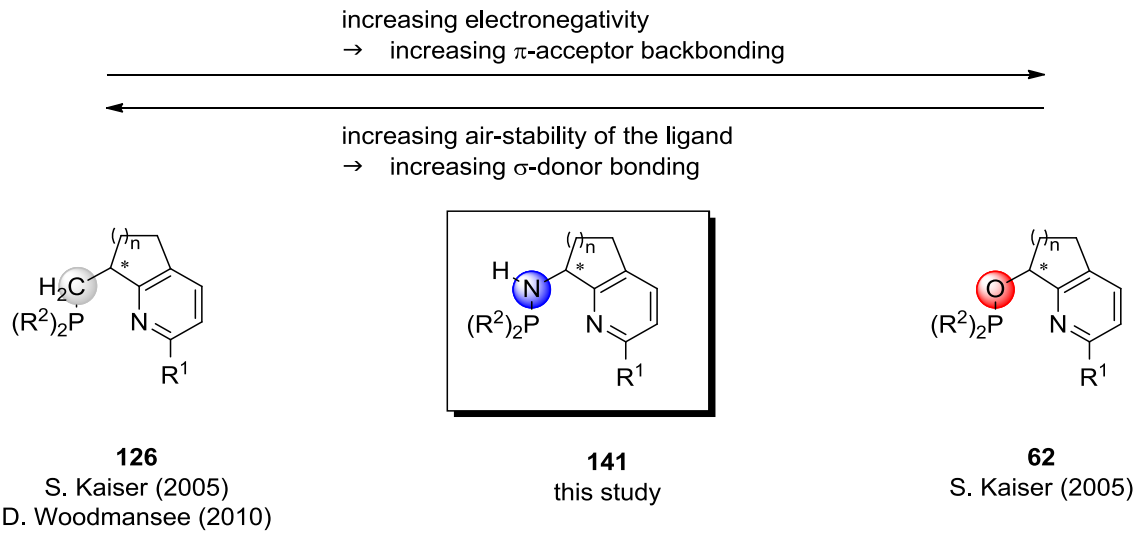


Figure 5.2: Comparison of different bicyclic pyridine derived N,P ligands.

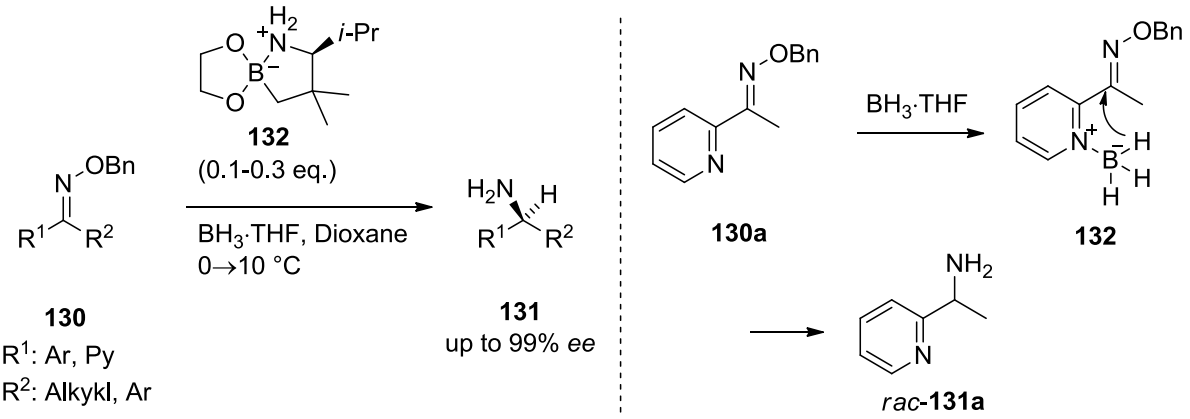
5.2 Synthesis

5.2.1 Methods Described in the Literature

Basically three different methods are available to obtain enantioenriched pyridyl amines **136**, which are required for the preparation of the aminophosphine ligands **141**:

- Reduction of oximes / imines
- Substitution of protected alcohols
- Resolution of racemic amines

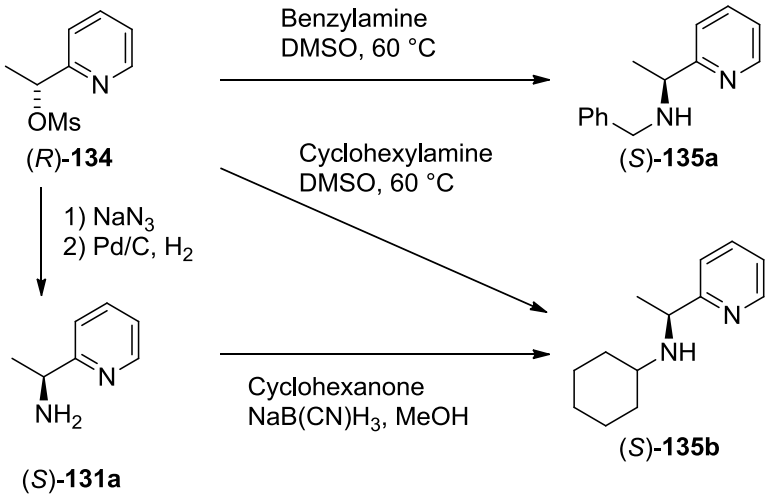
The asymmetric reduction of oximes or imines seems very attractive at first glance. The required oximes or imines could be easily obtained from the pyridyl ketones that were described in chapter 3. Several boron based catalysts were reported for the asymmetric reduction of oximes.[118] One such example is shown on the left in scheme 5.6. Ketoxime ethers **130** are reduced to the desired amines **131** using spiroborate catalyst **132**. Excellent *ee*s up to 99% were reported for several amines **131** having at least one aromatic or heteroaromatic residue. Unfortunately, the authors reported low enantioselectivities for 2-substitued pyridine oxime ether **130a** due to an uncatalyzed background reduction that takes place by hydride transfer from pyridine-borane-adduct **133**. Even using a stoichiometric amount of the catalyst, a modest result of 73% *ee* was obtained.[118b] Therefore, this approach was not used in this study.



Scheme 5.6: Synthesis of enantiopure (hetero)aromatic amines **131** by asymmetric reduction of ketoxime ethers **130** using spiroborate catalyst **132** (left); Uncatalyzed background reduction of 2-pyridine derived ketoxime ether **130a**, which gives low enantioselecitivity for this substrate (right).[118b]

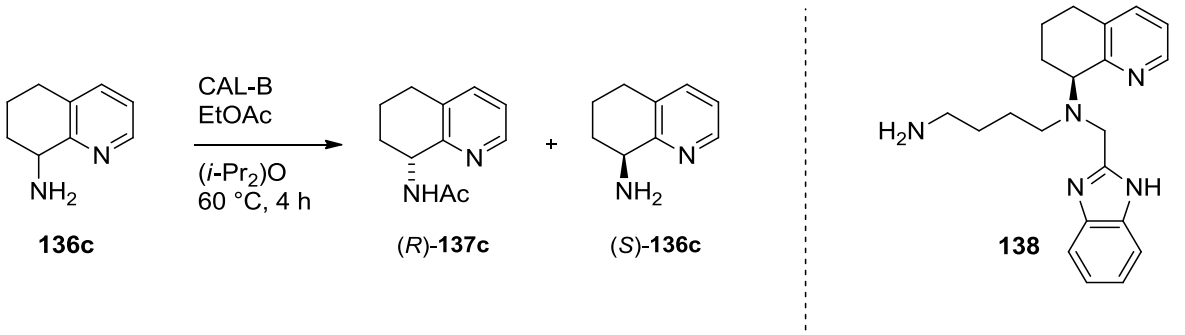
Despite the numerous reports on the asymmetric reduction of imines,[119] only one example employing pyridyl imines as substrates for this transformation was found in the literature.[120] As very low enantiomeric excess was reported for this substrate, this approach was not applied this course.

Enantiopure pyridyl amines (*S*)-**131a** or (*S*)-**135** could also be obtained by S_N2 reaction from enantiopure pyridyl alcohols using a suitable leaving group. Interestingly, *J. Uenishi* and co-workers used the enantiopure mesylate (*R*)-**134** for the preparation of primary amines **131a** and secondary amines **135** (scheme 5.7). The latter were obtained by direct substitution with benzylamine and cyclohexylamine respectivelyby whereas the primary amine **131a** was obtained by using sodium azide with subsequent reduction (scheme 5.7).[121] As the synthesis of enantiopurey bicyclic pyridyl alcohols has been investigated and optimized in the *Pfaltz* research group (chapter 2),[95-96] this strategy seems to be very attractive. But due to the explosive nature of azides this approach was not investigated.[122]



Scheme 5.7: Synthesis of enantiopure pyridyl amines by nucleophilic substitution using **134**.[121]

Probably, the fastest way to obtain enantiopure pyridyl amines **136** would be the resolution of enantiomers by semiprepartive HPLC (most likely as their acetamide derivatives) or by recrystallization of diastereomeric salts formed from cheap and readily available chiral acids (*e.g.* tartaric acid or mandelic acid).[123] However, as an asymmetric synthesis was preferred, such a resolution would only serve as a back-up plan. Enzymatic kinetic resolution of pyridyl amines is a reasonable approach in order to obtain enantioenriched pyridyl amines **136**. Indeed, the required reaction has been investigated by industrial scientists, as these important heterocyclic amines are useful building blocks in medicinal chemistry.[124] Following this approach researchers at *AnorMED* developed robust process for the synthesis of a CXCR4 chemokine receptor antagonist **138** for the treatment of HIV (scheme 5.8).[125]

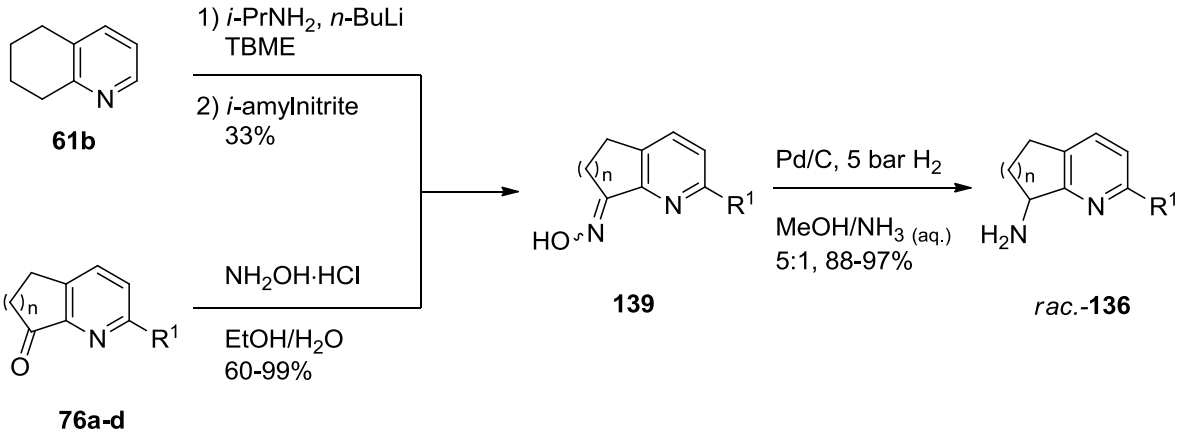


Scheme 5.8: Enzymatic kinetic resolution of pyridyl amine **136c** for the preparation of the drug **138** for treatment of HIV.[125]

5.2.2 Synthesis of Racemic Pyridyl Amines

In order to obtain racemic pyridyl amines **136** the synthesis *via* pyridyl oximes **139** was selected. The most straightforward way to obtain pyridyl oximes **139** is shown in scheme 5.9. The synthesis started from the commercially available bicyclic heterocycle **61b** and gave, after deptronation with LDA and subsequent trapping with isoamyl nitrite, the desired oxime **139c** (R^1 = H, n = 2) in moderate yield of 33%. However, isolation and purification of the product by crystallization was very difficult as it was obtained as a sticky oil.

Therefore, pyridyl oximes **139** were prepared from pyridyl ketones **76** (see chapter 3.2) by condensation using hydroxylamine. The oximes precipitated directly out of the reaction mixture and therefore their isolation was more convenient. Reduction of oximes **139** with hydrogen gas in the presence of palladium on charcoal gave racemic amine **136** in excellent yields (88-97%).

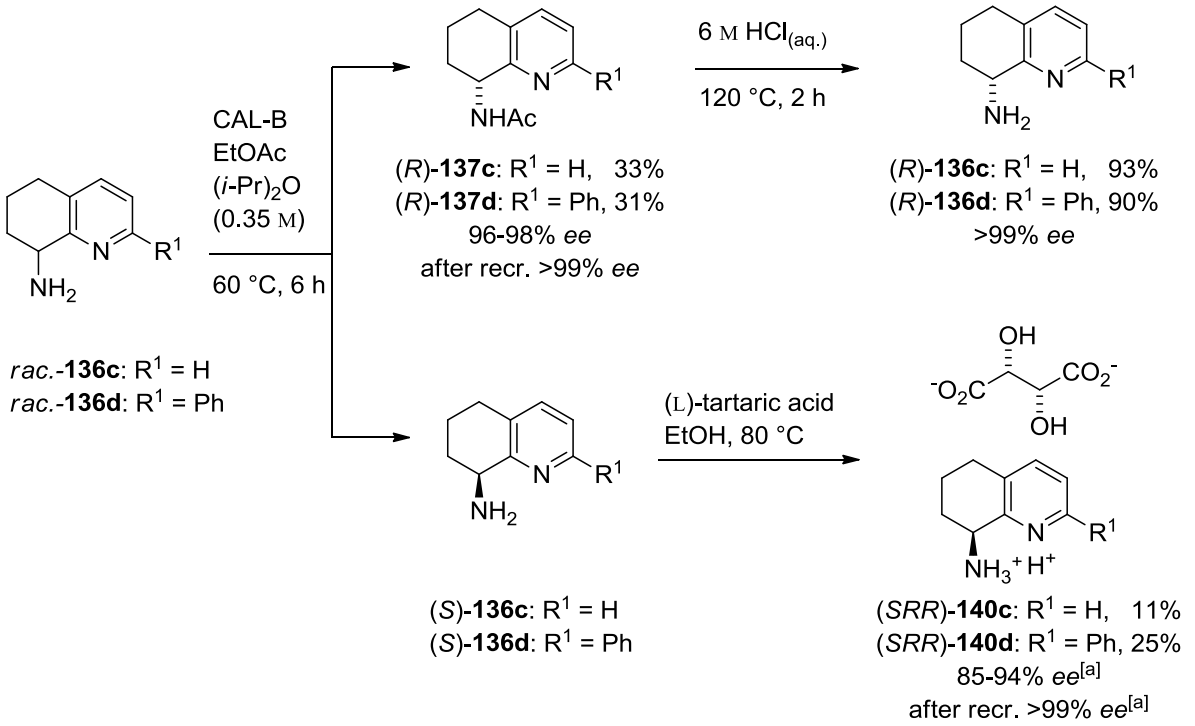


Scheme 5.9: Synthesis of racemic pyridiyl amines **136**.

5.2.3 Preparation of Enantiopure Pyridyl Amines

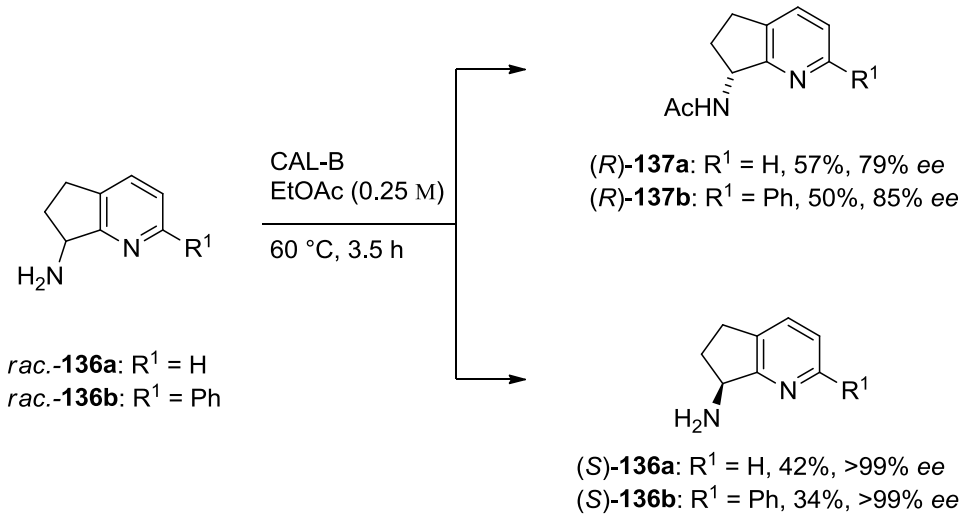
The enzymatic kinetic resolution route was selected for the preparation of the enantiomers (*S*)-**136** and (*R*)-**137** as this pathway provides both enantiomers in high enantiomeric purity using a readily available enzyme. Employing the published conditions[124] using immobilized enzyme CAL-B, ethyl acetate as acylating agent and diisopropyl ether, longer reaction times then those reported were required for substrates **136c-d** (scheme 5.8).[124] After six hours (instead of four hours) at 60 °C 50% conversion was obtained as determined by ^{1}H-NMR spectroscopy by integration of the signals of the protons at the stereogenic center (δ = 4.91 ppm for the amide and 3.99 ppm for the amine; scheme 5.10). Separation of the two products was readily achieved by flash chromatography. Under these conditions the pyridyl amides (*R*)-**137c-d** were obtained in 96-98% *ee*. Recrystallization from ethyl acetate gave the amides in perfect enantiomeric purity (>99% *ee*). Hydrolysis under acid conditions provided the pyridyl amines (*R*)-**136c-d**.

After separation from the amides (*R*)-**137c-d** the remaining amines (*S*)-**136c-d** were directly crystallized as tartaric acid salts (*SRR*)-**140c-d**. The products were found to have an *ee* between 85-94%, which was again increased by recrystallization to >99%.



Scheme 5.10: Enzymatic kinetic resolution of pyridyl amines **136c-d** with a six membered carbocyclic ring. [a] The *ee* was determined of the free amine (*S*)-**136c-d**.

The conditions described above were not applicable to the enzymatic kinetic resolution of pyridyl amines **136a-b** with a five membered carbocyclic ring (scheme 5.11) as these substrates showed low solubility in diisopropyl ether. Therefore, the reaction was run directly in ethyl acetate as solvent. Already after 3.5 hours 55-60% conversion was obtained. Therefore, the enantiomeric purity of the pyridyl amides (*R*)-**137a-b** was only moderate (75-79% *ee*). The *ee* of (*R*)-**137b** could only be increased to 85% by recrystallization. However, due to the higher conversion the *ee* of pyridyl amines (*S*)-**136a-b** was already >99%.

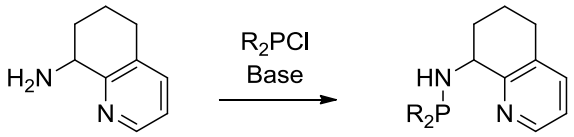


Scheme 5.11: Enzymatic kinetic resolution of pyridyl amines **136a-b** with a five membered carbocyclic ring.

5.2.4 Formation of N,P Ligands and Their Ir-Complexes

The phosphorus nitrogen bond could not be formed using the conditions applied in the synthesis of phosphinites (chapter 2). Therefore, several different conditions were investigated (table 5.1). Standard conditions for the formation of P-N bonds in toluene or THF as solvents in the presence of a weak base (triethyl amine or DIPEA) gave only small amounts of the product **141** (entries 1-3). Using stronger base (for example NaH) a higher yield of the product **141** was obtained, however a significant amount of impurities were obtained as well (entries 4-5). These impurities could not be separated by filtration through silica gel or aluminium oxide due to decomposition of the product **141**. The successful conditions employed for the formation of phosphinites (chapter 2; DCM and DMAP) led to the desired products but good yields were obtained only for the *ortho*-tolyl derivative (entries 6-9).

Table 5.1: Formation of phosphorus nitrogen bond using chlorophosphines.



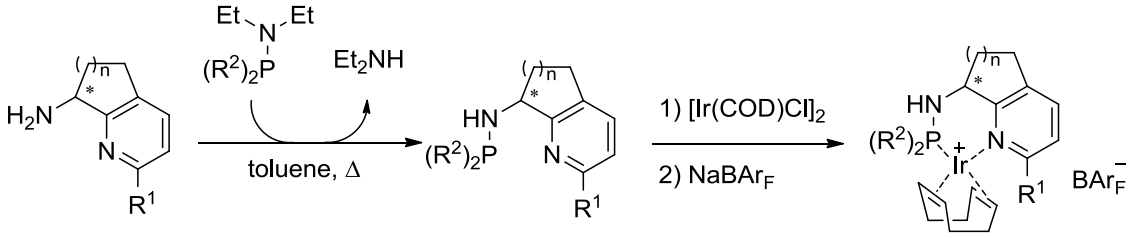
136c **141**

Entry	Solvent	Base	R_2PCl	Purification	Yield[a] [%]	Comment
1	toluene	Et_3N	Ph_2PCl	SiO_2	traces	decomposition on silica gel
2	toluene	Et_3N	Ph_2PCl	Al_2O_3	8	
3	toluene	DIPEA	Ph_2PCl	Al_2O_3	0	
4	THF/DMF 9:1	NaH	$(t\text{-Bu})_2PCl$	Al_2O_3	74	impure mixture, which also gave impure Ir-complex
5	THF/DMF 9:1	NaH	Cy_2PCl	Al_2O_3	25	
6	DCM	DMAP	Ph_2PCl	Al_2O_3	20	
7	DCM	DMAP	Ph_2PCl (>2 eq.)	Al_2O_3	n.d.	side products
8	DCM	DMAP	$(o\text{-Tol})_2PCl$	Al_2O_3	65	
9	DCM	DMAP	Cy_2PCl	Al_2O_3	20	

[a]: Isolated yield of the N,P ligand **141**.

Due to these difficulties a similar approach to that reported by *B. Breit* and *J. Wieland* was used.[126] Instead of using the commercially available chlorophosphines, diethylaminophosphines were used as phosphorus source. Diethylaminophosphines have been synthesized from the chlorophosphines and diethylamine in toluene using an excess of triethylamine.[57a, 127] Their purification was possible by distillation, which gave the desired materials in good yield and purity. Diethylaminophosphines were then used in a nucleophilic substitution with the chiral pyridyl amine **136**. The only side product formed was diethylamine, that could be removed under a stream of inert gas (argon). The ligands obtained using this method were pure and could directly be converted to their iridium complexes using our standard procedure.[36] Moreover, using this method for the formation of N,P bonds, the yields of the desired Ir-complexes were higher (entries 1-3, 6-7) compared to the approach using chlrorophosphines (entries 4 and 5). However, it should be noted that the preparation of N,P ligands having a di-*tert*-butyl-phosphino group failed as the diethylamino-di-*tert*-butyl-phosphine could not be prepared.

Table 5.2: Formation of Ir-complexes **142** using diethylaminophosphine for the prepration of N,P ligands **141**.



136 **141** **142**

Entry	Ir-complex	n	R^1	R^2	^{31}P-NMR (L) [ppm]	^{31}P-NMR [ppm]	Yield [%][a] (2 steps)
1	(*S*)-**142a**	1	Ph	Ph	33.9	49.7	70
2	(*S*)-**142b**	1	Ph	o-Tol	18.9	55.9 (br s)	67
3	(*S*)-**142c**	2	H	Ph	33.4	51.1	52
4	(*R*)-**142d**	2	H	*o*-Tol	13.5	54.7	21[b]
5	(*R*)-**142e**	2	H	Cy	45.8	61.5	11[b]
6	(*S*)-**142f**	2	Ph	Ph	34.3	40.8	42
7	(*S*)-**142g**	2	Ph	*o*-Tol	19.3	43.4	46

[a]: Isolated yields of the Ir-complexes **142** after flash chromatography over silica gel; [b]: Isolated yield of Ir-complex (*R*)-**142d** and (*R*)-**142e** where the N,P ligands were obtained from chlorophosphines (table 5.1, entries 8-9).

5.3 Crystal Structure Analysis

From the complexes (*S*)-**142a** and (*S*)-**142c** suitable crystals for X-ray analysis were obtained by overlaying a saturated ethereal solution with *n*-pentane. They were obtained as red and yellow blocks, respectively. *Mercury* sticks representations are shown in figures 5.3 and 5.4. Selected structural parameters are given in tables 5.3 and 5.4, whereas the full characterization parameters can be found in the appendix (chapter 8.9). Crystal structures of the phosphine and phosphinite derived complexes **95** and **96** obtained by the work of *S. Kaiser*[57a] are compared to the complexes obtained in this study.

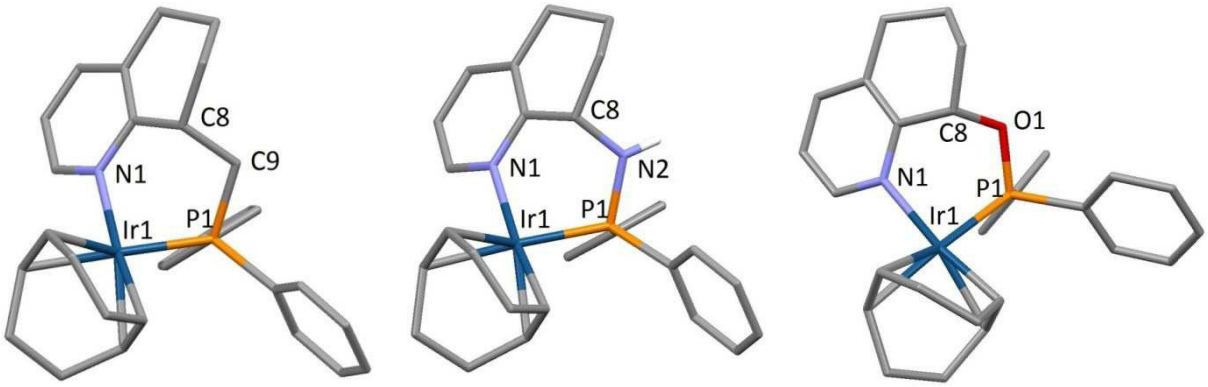
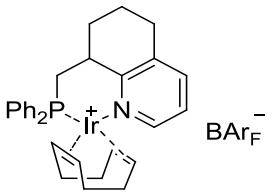
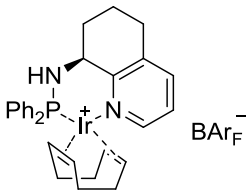
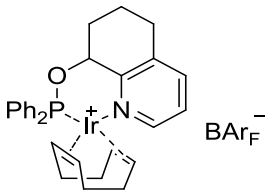


Figure 5.3: Crystal structures of various bicyclic pyridine derived Ir-complexes: **96** (left) (*S*)-**142c** (center) and mirror image of **95** (right); All BAr_F counterions were omitted for clarity.

Table 5.3: Selected bond lengths and bite angle of Ir-complexes **96**, (*S*)-**142c** and **95**.

	 **96**[57a]	 (*S*)-**142c**	 **95**[57a]
Ir-P [Å]:	2.2869(17)	2.2784(5)	2.2758(2)
Ir-N [Å]:	2.103(6)	2.103(2)	2.1078(2)
P-X [Å]:	1.836(7)	1.669(2)	1.6273(19)
Ir-C8 [Å]:	3.278	3.044	3.159
∠ P-Ir-N [°]:	83.96(16)	85.18(5)	86.23(7)

In all complexes the Ir atom adopts a square planar geometry. The Ir-P distance is slightly longer in the phosphine complex **96** (Δ0.01 Å), compared to the phosphinite **95** and aminophosphine (*S*)-**142c** complexes. As expected, the P−X distance (X = C, N or O) showed

significant differences between the three complexes. The distances decrease with the electronegativity of the neighbor atom starting from 1.84 Å (C−P), 1.67 Å (N−P) to 1.63 Å (O−P). The opposite trend can be observed for the bite angle given by the coordination atoms N-Ir-P, which increases from 84.0° (**96**), 85.2° (**142c**), to 86.2° (**95**). Somehow surprisingly, complex (*S*)-**142c** revealed a more characteristic boat conformation, which is reflected by the shortest distance found between Ir and C8.

The unit cell of (*S*)-**142a** contains two molecules (only one of them is shown in figure 5.4). Comparison of this crystal structure to those of complex (*S*)-**36a** (chapter 2.4) revealed again the similarity of these two complexes. The most significant difference is the longer distance between the phosphorus atom and its neighbor atom, which is 0.05 Å longer for the aminophosphine derived complex (*S*)-**142a**.

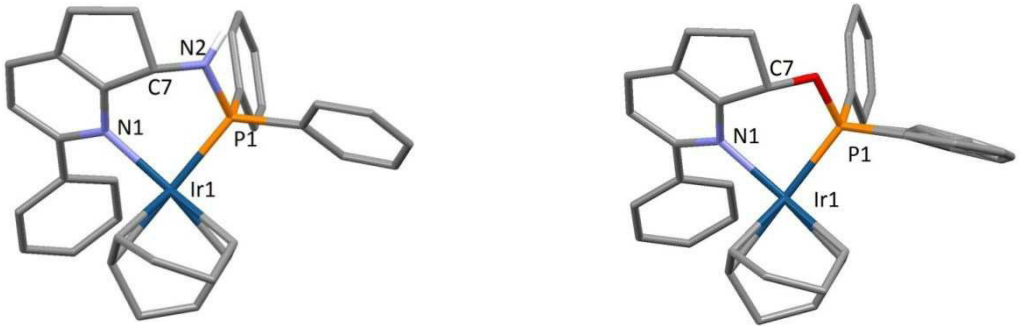
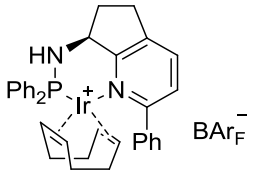
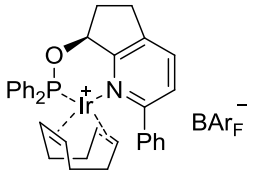


Figure 5.4: X-ray crystal structures of bicyclic pyridine derived Ir-complexes (*S*)-**142a** (left) and (*S*)-**36a** (right). Both BAr_F counterions were omitted for clarity.

Table 5.4: Selected bond lengths and bite angle of Ir-complexes having a 5-atoms-membered carbocyclic ring.



(*S*)-**142a**



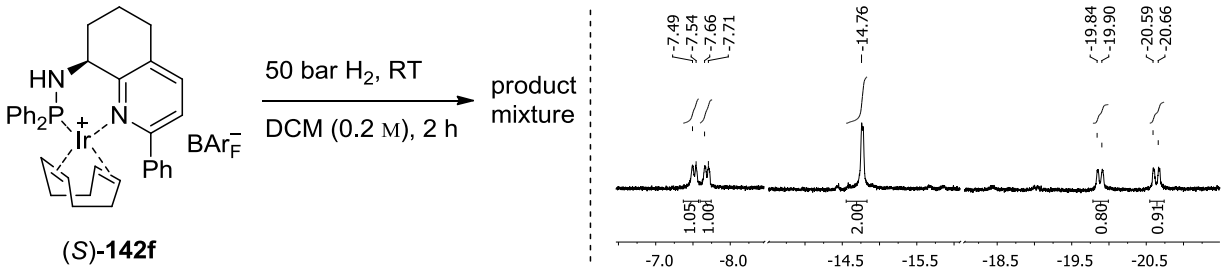
(*S*)-**36a**

	(*S*)-**142a**	(*S*)-**36a**
Ir-P [Å]:	2.2737(8) / 2.2644(7)	2.2529(9)
Ir-N [Å]:	2.111(2) / 2.148(2)	2.121(2)
P-X [Å]:	1.663(2) / 1.659(2)	1.619(2)
Ir-C7 [Å]:	3.255 / 3.226	3.221
∠ P-Ir-N [°]:	86.92(6) / 86.03(6)	86.27(7)

5.4 Hydrogenation Results

5.4.1 Potential Cyclometallation

Before starting the investigation of the new bicyclic pyridine amino-phosphine derived ligands in Ir-catalyzed asymmetric hydrogenations, potential cyclometallation of complexes (*S*)-**142f** and (*S*)-**142g** was evaluated. For this purpose the same experiment described in scheme 5.5 was performed using complex (*S*)-**142f** instead of the phosphinite derived complex **36f** (scheme 5.12).

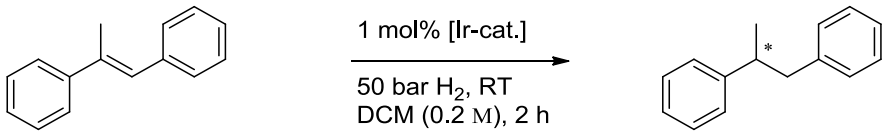


Scheme 5.12: Activation of aminophosphine derived iridium complex (*S*)-**142f** with hydrogen gas (left). High-field region of the NMR spectra obtained from the product mixture (right).

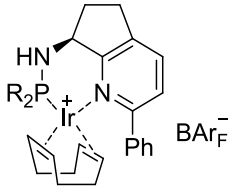
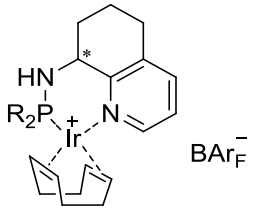
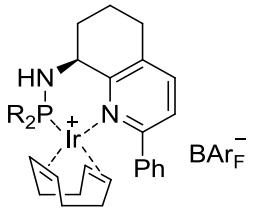
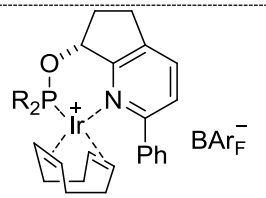
After purification by flash chromatography a mixture of at least two different components was obtained. ESI-MS analysis indicates a mixture of mononuclear, binuclear and even trinuclear iridium species. NMR data are neither in agreement with an H-bridged trinuclear complex nor with the cyclometallaed binuclear complex similar to **71**. The integration ratio of the hydride signals for the H-bridged trinuclear complex should be 1:2:2 rather than 1:1:1, and the signal observed at −7.55 ppm would be a quartet rather than a double doublet. The integral ratio of 1:1:1 would be in agreement with a binuclear complex, similar to **71**. However, the chemical shifts and the signal splittings are completely different. Unfortunately, no crystal suitable for X-ray crystal analysis could be obtained from the mixture of these components. Therefore, the nature of the degradation products remains unclear.

5.4.2 Hydrogenation of Model Substrates

Table 5.5: Hydrogenation of (*E*)-α-methylstilbene (**7**).



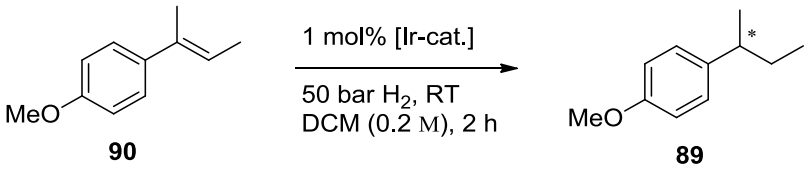
7 **9**

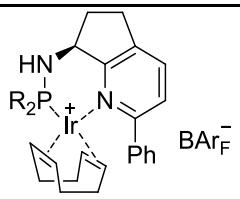
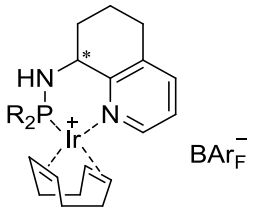
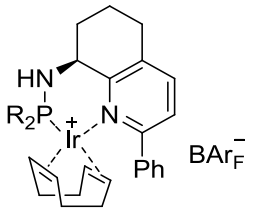
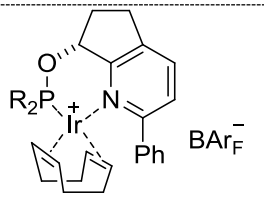
Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	>99	98 (*S*)
2		(*S*)-**142b**	*o*-Tol	>99	98 (*S*)
3		(*S*)-**142c**	Ph	96	86 (*S*)
4		(*R*)-**142d**	*o*-Tol	>99	77 (*R*)
5		(*R*)-**142e**	Cy	>99	91 (*R*)
6		(*S*)-**142f**	Ph	1	n.d.
7		(*S*)-**142g**	*o*-Tol	10	17 (*R*)
8[57b]		(*R*)-**36b**	*o*-Tol	>99	>99 (*R*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

Most of the aminophosphine pyridine derived iridium complexes that were tested proved to be very active in the hydrogenation of methylstilbene **7**. Only catalysts (*S*)-**142f** and (*S*)-**142g** gave very low conversions (table 5.5, entries 6 and 7). Catalyst (*R*)-**142e** provided a respectable 91% *ee* (entry 5). However, the most selective catalysts are (*S*)-**142a** and (*S*)-**142b**, giving the hydrogenation product with 98% *ee* (entries 1 and 2). This is close to the *ee* achieved with the best phosphinite derived Ir-complex (*R*)-**36b** (entry 8).

Table 5.6: Hydrogenation of (*E*)-2-(4-methoxyphenyl)-2-butene (**90**).

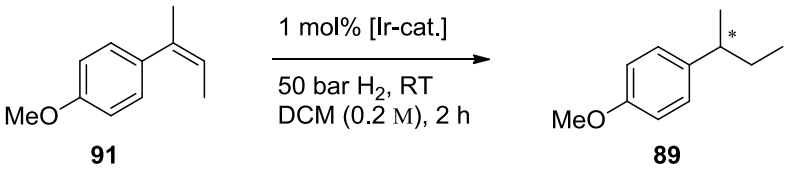


Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	>99	94 (*S*)
2		(*S*)-**142b**	*o*-Tol	>99	86 (*S*)
3		(*S*)-**142c**	Ph	>99	77 (*S*)
4		(*R*)-**142d**	*o*-Tol	>99	64 (*R*)
5		(*R*)-**142e**	Cy	>99	58 (*R*)
6		(*S*)-**142f**	Ph	68	90 (*S*)
7		(*S*)-**142g**	*o*-Tol	>99	38 (*S*)
8[57b]		(*R*)-**36b**	*o*-Tol	>99	>99 (*R*)

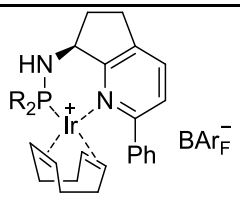
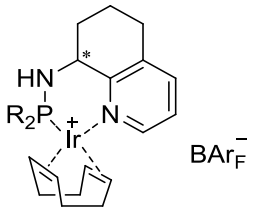
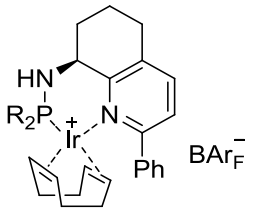
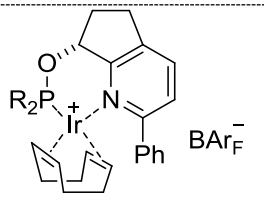
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

Again almost all the Ir-complexes showed high activity in the hydrogenation of the (*E*)-olefin **90**. In terms of enantioselectivity catalyst (*S*)-**142a** performed best, giving the product with 94% *ee* (table 5.6, entry 1). However, this is clearly lower, compared to the structurally similar phosphinite derived catalyst (*R*)-**36b** which gave >99% *ee* (entry 8). In contrast to the trend observed with the phosphinite-derived catalyst, the sterically more demanding *ortho*-tolyl groups gave in this case lower enantioselectivities (entries 1 *vs.* 2, 3 *vs.* 4, 6 *vs.* 7).

Table 5.7: Hydrogenation of (*Z*)-2-(4-methoxyphenyl)-2-butene (**91**).



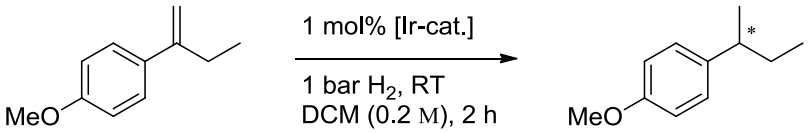
91 **89**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	>99	96 (*R*)
2		(*S*)-**142b**	*o*-Tol	>99	87 (*R*)
3		(*S*)-**142c**	Ph	82	76 (*R*)
4		(*R*)-**142d**	*o*-Tol	>99	80 (*S*)
5		(*R*)-**142e**	Cy	>99	37 (*S*)
6		(*S*)-**142f**	Ph	60	86 (*R*)
7		(*S*)-**142g**	*o*-Tol	73	32 (*R*)
8[57b]		(*R*)-**36b**	*o*-Tol	>99	98 (*S*)

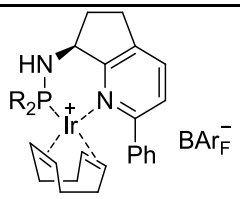
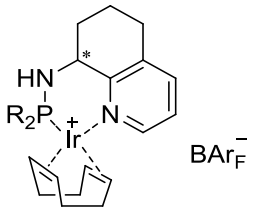
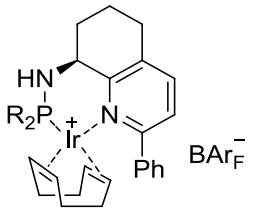
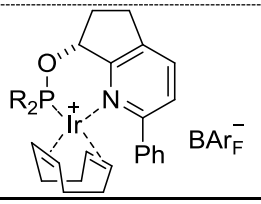
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

Catalysts (*S*)-**142c**, (*S*)-**142f** and (*S*)-**142g** did not give full conversion in the hydrogenation of the (*Z*)-alkene **91** (table 5.7, entries 3, 6 and 7). In terms of enantioselectivity again catalyst (*S*)-**142a** performed best (entry 1). The *ee* of 96% is very close to the best result obtained with the phosphinite catalyst (*R*)-**36b** (entry 8). This time a clear trend in the influence of the P-substituents was not observed. While (*R*)-**142d** bearing *ortho*-tolyl groups gave higher *ee* than (*S*)-**142c** (entries 3 *vs.* 4), catalyst (*S*)-**142b** was performing worse than (*S*)-**142a** (entries 1 *vs.* 2).

Table 5.8: Hydrogenation of 2-(4-methoxyphenyl)-1-butene (**88**).



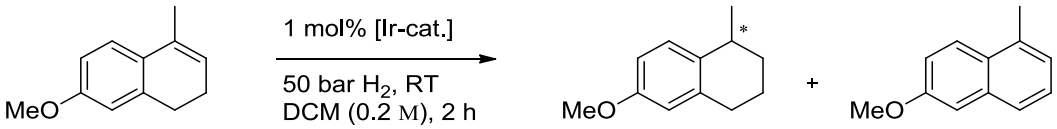
88 **89**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	>99	10 (*R*)
2		(*S*)-**142b**	*o*-Tol	>99	24 (*R*)
3		(*S*)-**142c**	Ph	>99	32 (*R*)
4		(*R*)-**142d**	*o*-Tol	>99	25 (*S*)
5		(*R*)-**142e**	Cy	>99	38 (*S*)
6		(*S*)-**142f**	Ph	>99	55 (*S*)
7		(*S*)-**142g**	*o*-Tol	>99	rac.
8[57b]		(*R*)-**36b**	*o*-Tol	>99	80 (*S*)

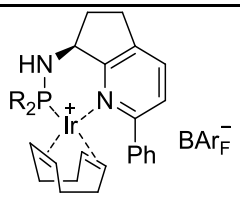
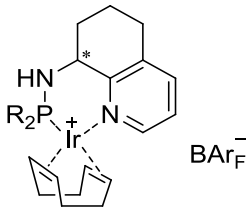
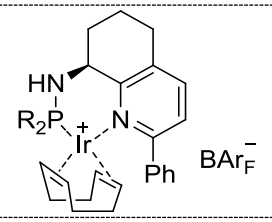
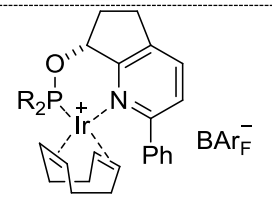
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

Although all the aminophosphine derived catalysts showed high activity in the hydrogenation of terminal olefin **88**, enantioselectivities were only low to moderate (table 5.8). Surprisingly, the best result (55% *ee*, entry 6) was achieved using catalyst (*S*)-**142f** which performed poorly with the previously tested olefins. Electronic effects seem to play a crucial role for the selectivity. While the phosphinite derived catalyst (*R*)-**36b** produced 80% *ee* (entry 8), the aminophosphine catalyst (*S*)-**142b** gave only 24% *ee* (entry 2).

Table 5.9: Hydrogenation of 7-methoxy-1,2-dihydro-naphthalene (**72**).



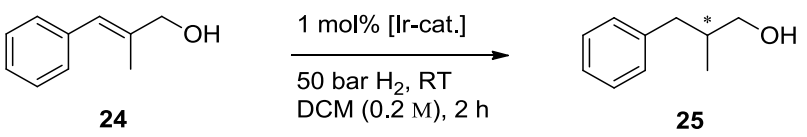
72 **73** **115**

Entry	Ir-catalyst		R	Conv. [%][a]	21 [%]	ee [%][b]
1		(*S*)-**142a**	Ph	>99	n.o.	89 (*R*)
2		(*S*)-**142b**	*o*-Tol	>99	n.o.	87 (*R*)
3		(*S*)-**142c**	Ph	98	3	60 (*R*)
4		(*R*)-**142d**	*o*-Tol	>99	n.o.	60 (*S*)
5		(*R*)-**142e**	Cy	>99	n.o.	27 (*S*)
6		(*S*)-**142f**	Ph	41	6	22 (*R*)
7		(*S*)-**142g**	*o*-Tol	71	18	19 (*R*)
8[57b]		(*R*)-**36b**	*o*-Tol	>99	n.o.	87 (*S*)

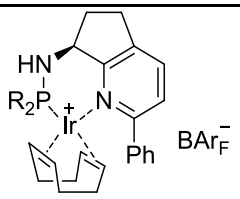
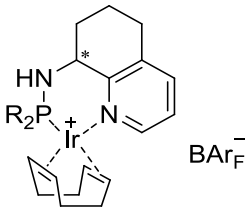
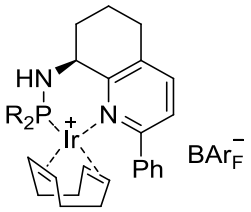
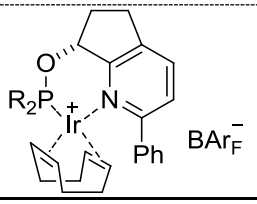
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

As seen already in the previous chapters (for example chapter 4), the cyclic olefin **72** can be a very challenging substrate because it is prone to oxidation leading to the aromatic naphthalene derivative **115**. This side reaction was only observed for catalysts that showed poor activity (table 5.9, entries 3, 6 and 7). All the other catalysts gave selectively the hydrogenation product. The best enantioselectivity was again achieved with catalyst (*S*)-**142a** (89% *ee*, entry 1). The enantioselectivity is even higher *ee* than that previously obtained with the phosphinite derived catalyst (*R*)-**36b** (entry 8).

Table 5.10: Hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**24**).



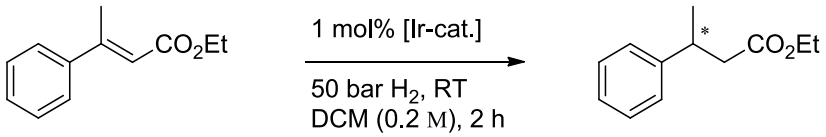
24 **25**

Entry	Ir-catalyst		R	Conv. [%][a]	Product [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	>99	>99	84 (*R*)
2		(*S*)-**142b**	*o*-Tol	>99	>99	86 (*R*)
3		(*S*)-**142c**	Ph	>99	85	60 (*R*)
4		(*R*)-**142d**	*o*-Tol	>99	>99	81 (*S*)
5		(*R*)-**142e**	Cy	>99	88	49 (*S*)
6		(*S*)-**142f**	Ph	90	50	27 (*R*)
7		(*S*)-**142g**	*o*-Tol	>99	75	8 (*R*)
8[57b]		(*R*)-**36b**	*o*-Tol	>99	>99	97 (*S*)

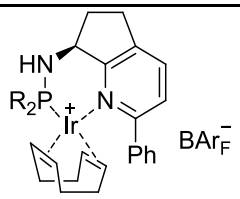
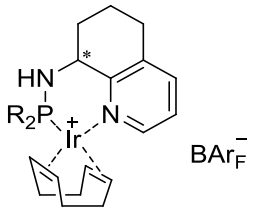
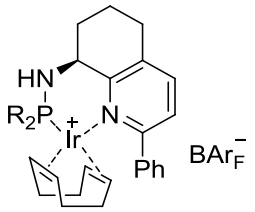
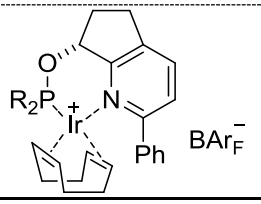
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

The allylic alcohol **24** is a challenging substrate too, as often unpredictable side reactions (oxidation, isomerization, polymerization) can occur. Therefore, the yield of product that was determined by GC is given in the column next to the conversion in table 5.10, whereas conversion is termed to the consumption of starting material. Again the less reactive complexes gave also significant amount of side products (not identified) whereas the more active catalysts led to clean hydrogenation. In contrast to the previously described substrates, the most selective catalyst in this case was (*S*)-**142b** with the *ortho*-tolyl groups on phosphorus atom (entry 2). However, the enantioselectivity obtained with this catalyst is clearly lower than the value achieved with the structurally related phosphinite derived catalyst (*R*)-**36b** (entry 2 *vs.* 8).

Table 5.11: Hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**98**).



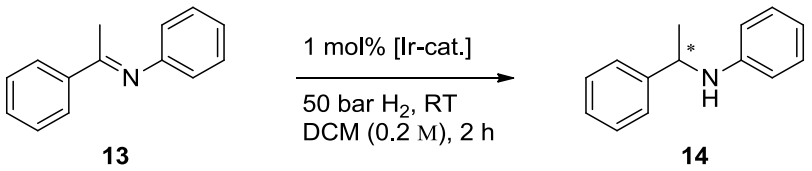
98 **99**

Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	>99	46 (*S*)
2		(*S*)-**142b**	*o*-Tol	>99	86 (*S*)
3		(*S*)-**142c**	Ph	40	41 (*S*)
4		(*R*)-**142d**	*o*-Tol	93	76 (*R*)
5		(*R*)-**142e**	Cy	>99	92 (*R*)
6		(*S*)-**142f**	Ph	1	n.d.
7		(*S*)-**142g**	*o*-Tol	16	25 (*S*)
8[57b]		(*R*)-**36b**	*o*-Tol	>99	96 (*R*)

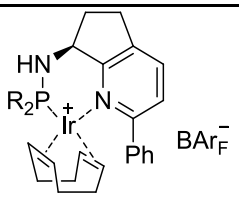
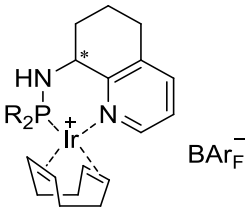
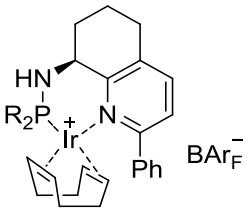
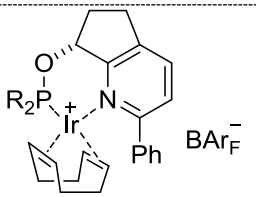
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

In the hydrogenation of the α,β-unsaturated ester **98** catalysts (*S*)-**142f** and (*S*)-**142g** showed poor activity (table 5.11, entries 6 and 7). Only three of the eight complexes tested gave full conversion. The best result in terms of enantioselectivity was obtained with catalyst (*R*)-**142e**, which provided the product with 92% *ee* (entry 5). For this substrate the sterically more demanding bis-*ortho*-tolyl phosphine induced as well significantly higher enantioselectivities than the diphenylphosphine ligands (entries 1 *vs.* 2, and 3 *vs.* 4).

Table 5.12: Hydrogenation of (*E*)-*N*-(1-phenylethylidene)aniline (**13**).



13 **14**

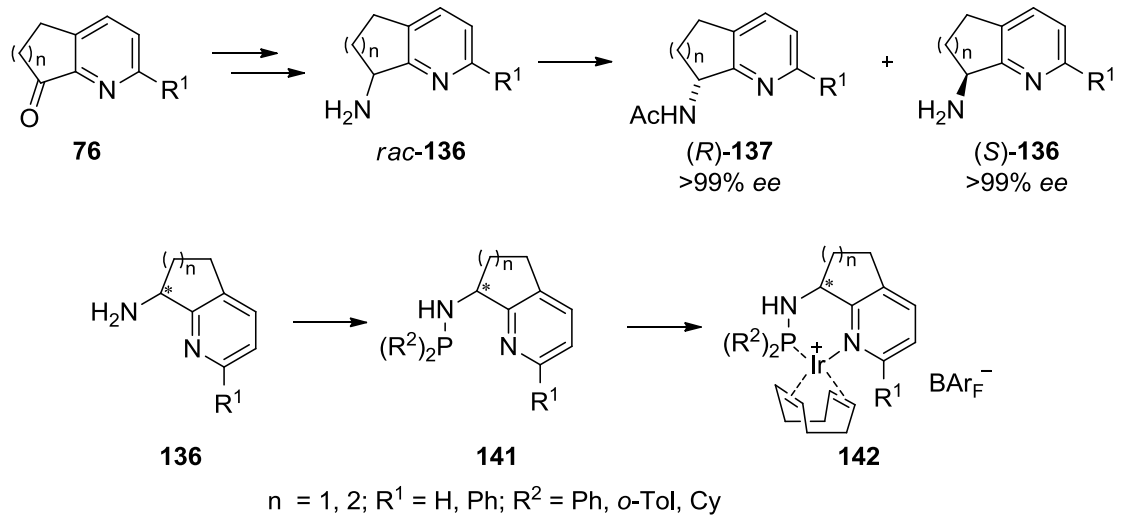
Entry	Ir-catalyst		R	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**142a**	Ph	51	19 (*R*)
2		(*S*)-**142b**	*o*-Tol	31	63 (*R*)
3		(*S*)-**142c**	Ph	51	4 (*R*)
4		(*R*)-**142d**	*o*-Tol	44	rac.
5		(*R*)-**142e**	Cy	>99	39 (*R*)
6		(*S*)-**142f**	Ph	5	n.d.
7		(*S*)-**142g**	*o*-Tol	1	n.d.
8[57b]		(*R*)-**36b**	*o*-Tol	>99	82 (*S*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

In the hydrogenation of imine **13** most of the applied catalysts did not lead to reach full conversion within the given reaction time (2 hours, table 5.12) and the chiral amine **14** was obtained with a maximum *ee* of 63% (entry 2).

5.5 Summary and Outlook

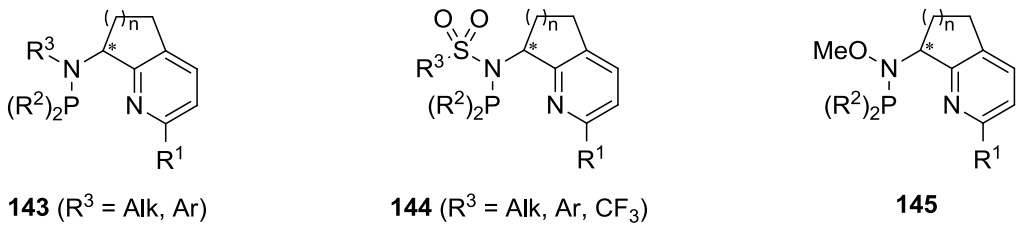
In summary, a synthetic route towards enantiopure pyridyl amines **136** was developed. The key step, to obtain enantiomerically pure ligands, was an enzymatic kinetic resolution of primary pyridyl amines (scheme 5.11). Furthermore, an efficient approach for the formation of N,P ligands was developed. After complexation to iridium seven different air-stable complexes with various electronic and steric properties were obtained (Scheme 5.13).



Scheme 5.13: Synthesis of aminophosphine derived iridium precatalyst **142** for the asymmetric hydrogenations.

Applying these complexes to the asymmetric hydrogenation of several model substrates excellent enatioselectivies were obtained for weakly functionalized olefins (up to 98% *ee*). For olefins with coordinating groups (like carbonyl) very good enantioselectivies (up to 92% *ee*) were obtained, whereas these catalysts performed poorly in the hydrogenation of acetophenone imine.

Future work might be dedicated to the development of N,P ligands **143**, **144** and **145**. By installing various substituents on the P-bound nitrogen atom, a more direct approach to control the electronic properties of the ligands could be achieved (Scheme 5.14).



Scheme 5.14: Proposed ligands **143**, **144** and **145** for Ir-catalyzed asymmetric hydrogenation.

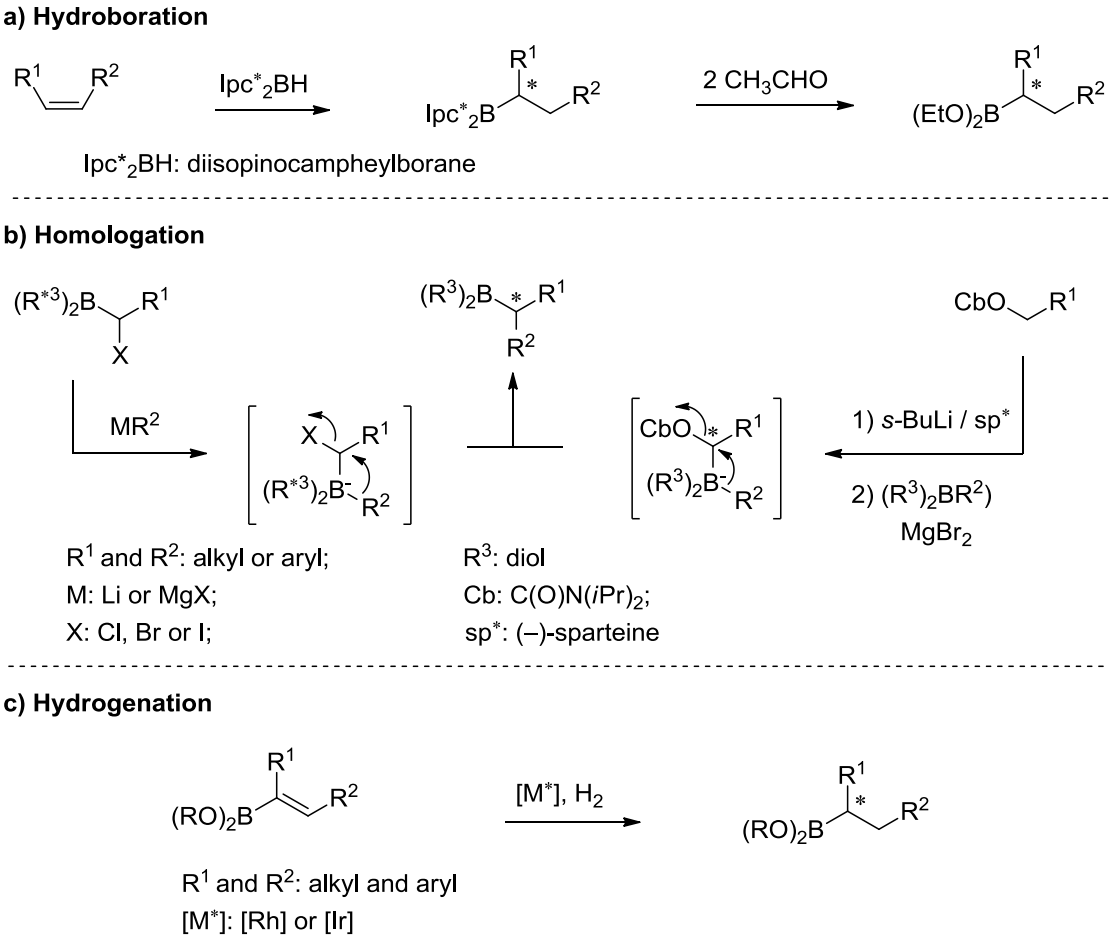
Chapter 6

Iridium-Catalyzed Enantioselective Hydrogenation of Alkenylboronic Esters

6.1 Introduction

6.1.1 Chiral Boronic Acids and Esters

Chiral boronic acids are highly versatile building blocks in organic synthesis,[128] since carbon-boron bonds can be readily converted into C–O, C–N and C–C bonds in a stereospecific manner.[129] Furthermore, boronic acids can act as surrogates of carboxylic acids[128] and are thus interesting motifs for drug design.[130] For example, α-amino boronic acids serve as building blocks for unnatural peptides, which are getting increasing attention as new anti-cancer drugs.[131] Hence, enantioselective routes to these compounds are of great value. The most widely used method for the synthesis of enantioenriched chiral boronic esters is the hydroboration of C=C bonds with chiral hydroboranes pioneered by *H. Brown* (scheme 6.1a).[132] The method works particularly well with 1,2-disubstituted *cis* olefins, while the corresponding *trans* isomers and trisubstituted olefins usually react with much lower enantioselectivity.[129a-c]



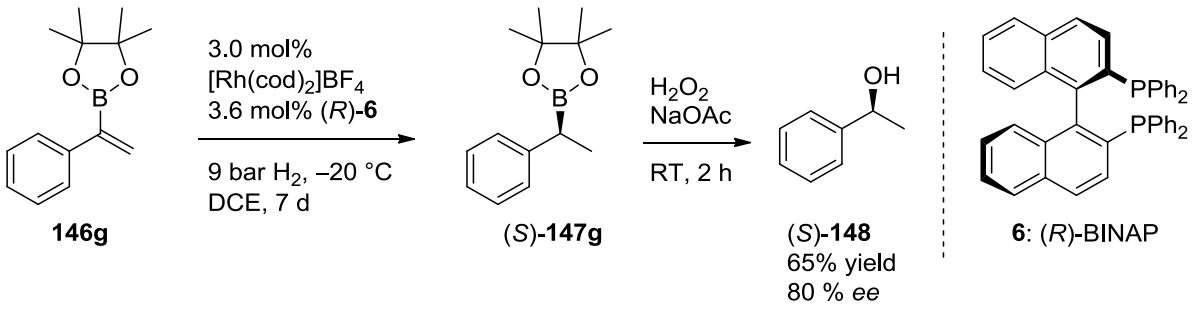
Scheme 6.1: Enantioselective routes to chiral secondary alkyl boronates.

On the other hand, the homologation reaction involving a stereoselective migration-displacement process, originally developed by *D. Matteson*[133] and further investigated by *V. Aggarwal*,[134] yields chiral secondary boron compounds directly from α-haloboronic esters or primary alcohols (scheme 6.1b).

Although these approaches have proved very useful in complex molecule synthesis, it was desirable to develop catalytic methods that do not require stoichiometric quantities of chiral reagents. The discovery of *D. Männig* and *H. Nöth* that rhodium complexes catalyze the addition of catecholborane to alkenes paved the way toward enantioselective catalytic hydroboration.[135] Subsequently, rhodium,[136] and to a lesser extent other transition metal complexes with chiral ligands have been successfully used as catalysts to prepare chiral organoboranes in high enantiomeric purity.[129d, 137] However, the substrate scope of these reactions is still limited. With few exceptions, high enantio- and regioselectivities are only obtained with aryl-substituted alkenes.

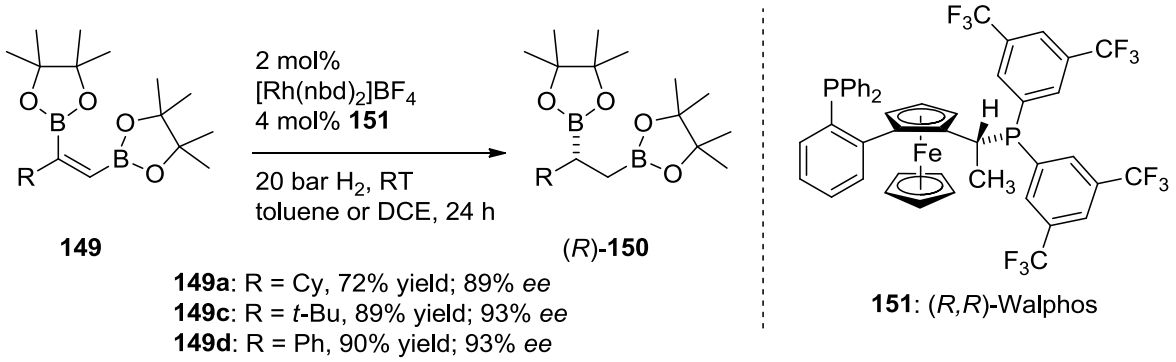
6.1.2 Hydrogenation of Boronic Esters Described in the Literature

The asymmetric hydrogenation of alkenylboronic esters is attractive, because it avoids the regioselectivity problems often encountered in catalytic and stoichiometric hydroborations. Moreover, asymmetric hydrogenation is one of the best established reactions in organic synthesis with a wide range of potential catalysts available. The first report using alkenylboronic ester **146g** for asymmetric hydrogenation was published in 2002 by *N. Miyaura* and co-workers. The chiral boronate (*S*)-**147g** was not isolated, but rather oxidized to 1-phenyl-1-ethanol (**148**). Using Rh-complexes in combination with diphosphine ligands in general low catalytic activity and selectivity were achieved. The highest *ee* (80%) was obtained using BINAP **6** as chiral ligand after seven days reaction time (scheme 6.2).[138]



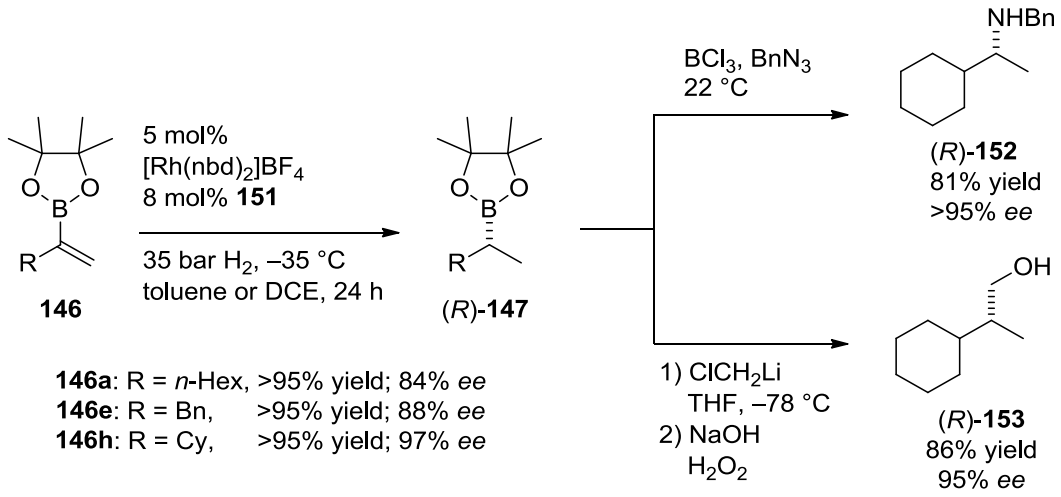
Scheme 6.2: First reported Rh-BINAP mediated asymmetric hydrogenation of alkenylboronic ester **146g**.[138]

Two years later *J. Morgan* and *J. Morken* reported on the enantioselective Rh-catalyzed hydrogenation of 1,2-bis(boronates) **149** mediated by bisphosphine ligands.[139] The best results in terms of activity and selectivity were achieved using Walphos[140] ligand **151** (scheme 6.3). It should be mentioned that the hydrogenation products **150** were again directly oxidized to the enantioenriched diols rather than isolated. However, a relatively narrow substrate scope was reported, but nevertheless high enantioselectivities (86-93%) were achieved for various residues.



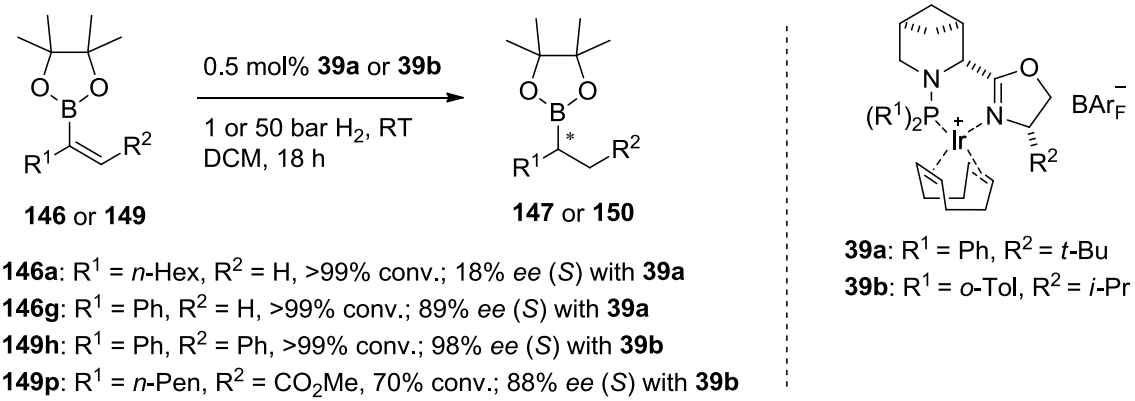
Scheme 6.3: Rh-Walphos-catalyzed asymmetric hydrogenation of alkenyl-1,2-bis(boronates) **149**.[139]

Two years later and *W. Moran* and *J. Morken* successfully employed alkenyl boronic esters **146** for the Rh-catalyzed asymmetric hydrogenation, using again Walphos ligand **151** (scheme 6.4).[141] In general, full conversions and high *ee*s (81-97%) for several alkenyl boronic esters were achieved. However, relatively high catalyst loading loadings of 5 mol% and long reaction times were required. Furthermore, the authors demonstrated the usefulness of the hydrogenation products (*R*)-**147**. For example chiral secondary amine (*R*)-**152** could be obtained after a sequence involving the cleavage of the pinacole group, treatment with benzyl azide and subsequent rearrangement with release of nitrogen gas. On the other hand, they obtained the chiral primary alcohol (*R*)-**153** after homologenation with lithiated chloromethane and oxidation with hydrogen peroxide.



Scheme 6.4: Rh-Walphos-catalyzed asymmetric hydrogenation of alkenylboronate **146** and potential applications of the hydrogenation product (*R*)-**147h**.[141]

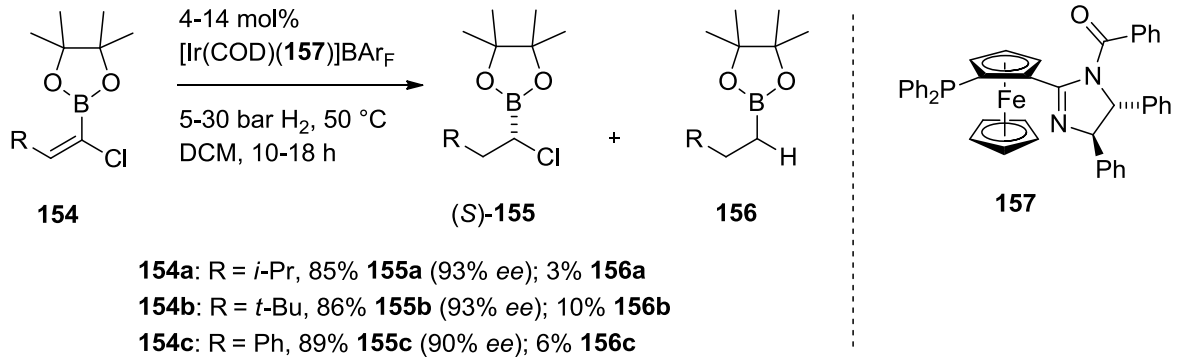
More recently, *P. G. Andersson* and co-workers found that iridium complexes with chiral N,P ligands are more active catalysts in reactions of this type, giving full conversion with only 0.5 mol% catalyst loading (scheme 6.5). With certain alkenylboronates, for example **146g**, **149h** and **149p**, high *ee*s were achieved, while analogous alkyl-substituted substrates, like **146a** gave unsatisfactory enantiomeric excesses.[64, 71a]



Scheme 6.5: First reported Ir-catalyzed asymmetric hydrogenation of alkenyl boronic esters hydrogenation **146** or **149**.[64, 71a]

Parallel to the studies described herein, a new report on the Ir-catalyzed asymmetric hydrogenation of alkenyl boronic esters was published recently (scheme 6.6).[142] In this case, the authors achieved the challenging hydrogenation of boronic esters **154**, which have a chlorine atom at the vinylic position. In analogy to the hydrogenation of vinyl fluorides described in chapter 5.1, the challenge with substrates **154** is to find efficient hydrogenation conditions, while avoiding dehalogenation to the side-product **156**. The valuable

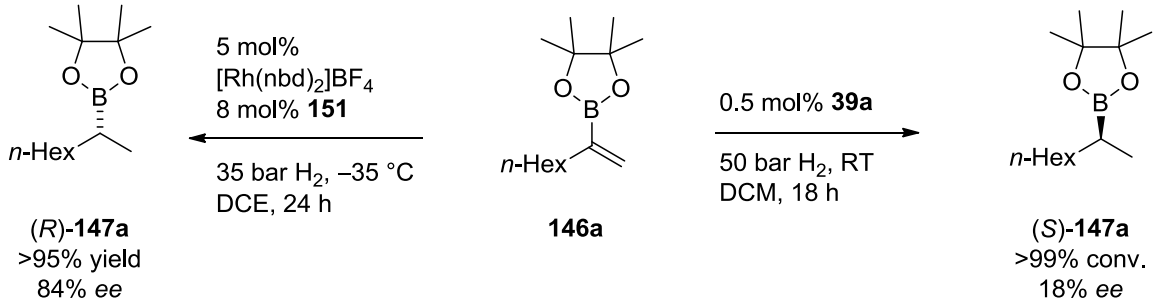
hydrogenation products **155** were obtained using an Ir-catalyst derived from ferrocenyl imidazoline N,P ligand **157**.



Scheme 6.6: Ir-catalyzed asymmetric hydrogenation of (1-chloro-1-alkenyl) boronic esters **154**.[142]

6.1.3 Objective of This Study

Overall, the scope of these Rh- and Ir-catalyzed hydrogenations is still limited, so the search for other catalysts that enhance the application range will continue. The hydrogenation of the aliphatic boronate **146a**, which so far had given unsatisfactory results with Ir-catalysts, served as a starting point for this study (scheme 6.7).



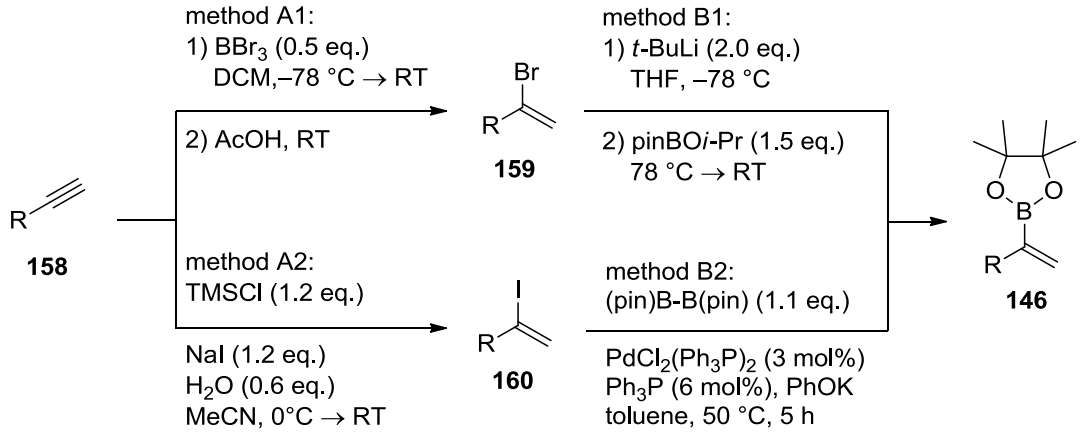
Scheme 6.7: Results obtained in Rh- and Ir-catalyzed asymmetric hydrogenations of alkyl substituted vinylic boronic esters **146a**.[64, 71a, 141]

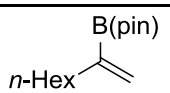
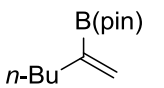
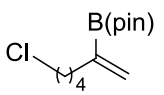
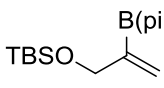
6.2 Synthesis of Substrates

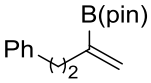
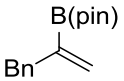
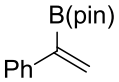
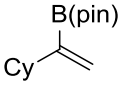
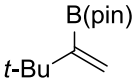
6.2.1 Synthesis of Terminal Boronic Esters

The boronic ester substrates bearing a terminal double bond were obtained by two different procedures both starting from commercially available alkynes **157** (table 6.1). Addition of boron tribromide to alkynes led to 2-bromo-alkenylboranes, which were hydrolyzed in the presence of acetic acid to give 2-bromo-alkenyl intermediates **159**. Lithium halogen exchange from **159** with *t*-BuLi and subsequent trapping with (pin)BO(*i*-Pr) provided access to most of the substrates **146** (entries 1-2 and 5-8).[141] Since substrates **146c**, **146d** and **146i** could not be obtained by this approach, they were synthesized *via* the corresponding vinyl iodides **160** as described by *Y. Ishii et al.*[143] By using a mixture of TMSCl, NaI and water, hydrogen iodide was generated *in situ*. Under these conditions HI adds to the C≡C bond with complete *cis*-selectivity in a Markovnikov fashion, to give **160**. Vinyl iodides **160** were used with bis(pinacolato)diboron for C−B Miyaura-coupling-reaction, to obtain vinyl boronates **146c**, **146d** and **146i** (entries 3, 4 and 9).[144] Both approaches provide the substrates in poor to moderate yields (14-56%).

Table 6.1: Preparation of terminal alkenyl boronic esters **146**.



Entry	Alkyne	Methods used	Intermediate	Substrate		Yield[a] [%]
1	1-octyne (**158a**)	A1 & B1	**159a**		**146a**	31
2	1-hexyne (**158b**)	A1 & B1	**159b**		**146b**	29
3	6-chloro-1-hexyne (**158c**)	A1 & B2	**159c**		**146c**	26
4	propargyl alcohol (**158d**)	A2 & B2	**160a**		**146d**[a]	58

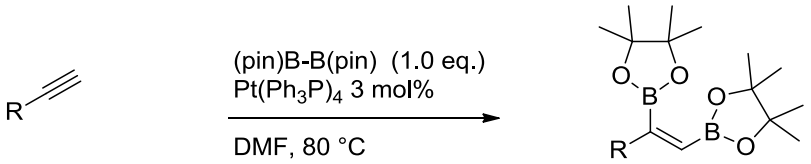
5	4-phenyl-1-butyne (**158e**)	A1 & B1	**159d**		**146e**	36
6	3-phenyl-1-propyne (**158f**)	A1 & B1	**159e**		**146f**	14
7	---	---	---		**146g**	---[b]
8	cyclohexylacetylene (**158g**)	A1 & B1	**159f**		**146h**	24
9	3,3-dimethyl-1-butyne (**158h**)	A2 & B2	**160b**		**146i**	36

[a] The TBS protecting group was not stable under the reaction conditions applied for methods A1 and A2, but had to be introduced prior installation of the boron group.[145] Therefore, the free alcohol was protected using TBSCl (1.1 eq.) and DMAP (1.1 eq.) in DCM (0.1 M) solution after halogenation. [b] 1-Phenylvinylboronic acid pinacol ester (**146g**) was purchased from Aldrich (659193).

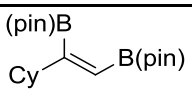
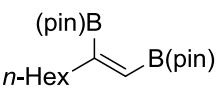
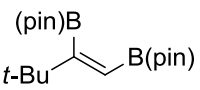
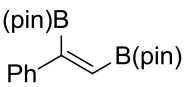
6.2.2 Synthesis of Trisubstituted Boronic Esters

In order to achieve high levels of enantioselectivities, the synthesis of substrates with perfect *E* and *Z* selectivity is important. Therefore alkynes were reacted with bis-pinacolato diboron using a platinum catalyst to obtain trisubstited *cis*-1,2-bis(boryl)alkenes **149a-c** obtained in good yields 74-83% (table 6.2, entries 1-3). 1,2-Bis-boronates **149a-d** were used as substrates for the hydrogenation.

Table 6.2: Preparation of trisubstitued *cis*-1,2-bis(boryl)alkenes **149a-d**.



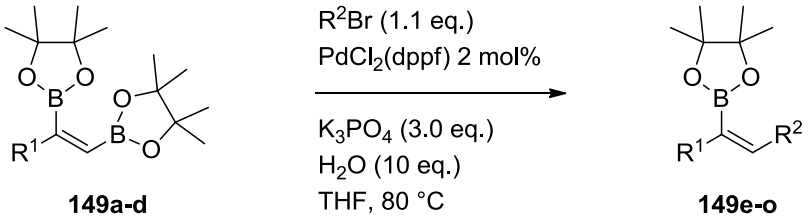
158 **149a-d**

Entry	Alkyne	Products		Yield [%]
1	cyclohexylacetylene (**158g**)		**149a**	83
2	1-octyne (**158a**)		**149b**	74
3	3,3-dimethyl-1-butyne (**158h**)		**149c**	83
4	---		**149d**	---[a]

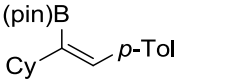
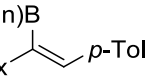
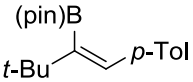
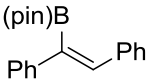
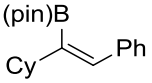
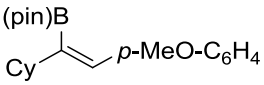
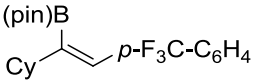
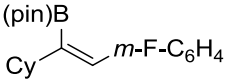
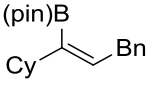
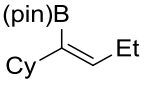
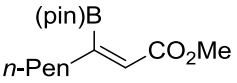
[a] (*E*)-α,β-Styrenediboronic acid bis(pinacol) ester (**149d**) was purchased from *Alfa Aesar* (L19651) and used as received.

Furthermore, they are also versatile precursors for the preparation of alkenyl-monoboronic esters with a trisubstituted C=C bond by Suzuki−Miyaura coupling occurring selectively at the more reactive terminal boronate group.[146] In this way a series of alkenylboronates **149e-n**, in which the terminal boron substituent had been replaced by different groups (table 6.3, entries 1-9) was prepared in generally good yield (60-73%). Only for the purely alkyl substituted alkenylboronate **149n** the yield dropped down to 19% (entry 10).

Table 6.3: Preparation of trisubstitued alkenyl boronic esters **149e-o**.

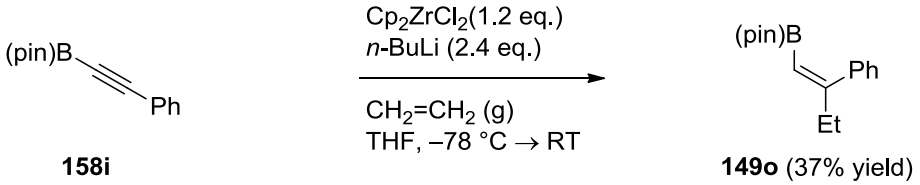


149a-d **149e-o**

Entry	1,2-bis(boryl)alkenes	R^2-Br	Substrate		Yield [%]
1	**149a**	4-bromotoluene		**149e**	60
2	**149b**	4-bromotoluene		**149f**	62
3	**149c**	4-bromotoluene		**149g**	66
4	---	---		**146h**	---[a]
5	**149a**	bromobenzene		**149i**	73
6	**149a**	4-bromoanisole		**149j**	64
7	**149a**	4-bromo-trifluorotoluene		**149k**	64
8	**149a**	1-bromo-3-fluorobenzene		**149l**	75
9	**149a**	benzyl bromide		**149m**	78
10	**149a**	ethyl bromide		**149n**	19
11	---	---		**146p**	---[a]

[a] Stilbeneboronic acid pinacol ester (**146h**) and Methyl (*E*)-oct-2-enoate-3-boronic acid pinacol ester (**146p**) were purchased from *Alfa Aesar* (L19651) respectively from *Aldrich* (540625) used as received.

Finally, substrate **149o** was obtained by a zirconocene-mediated regioselective coupling with ethylene gas from 2-phenyl-1-ethynylboronic acid pinacol ester **158** in moderate yield (scheme 6.8).

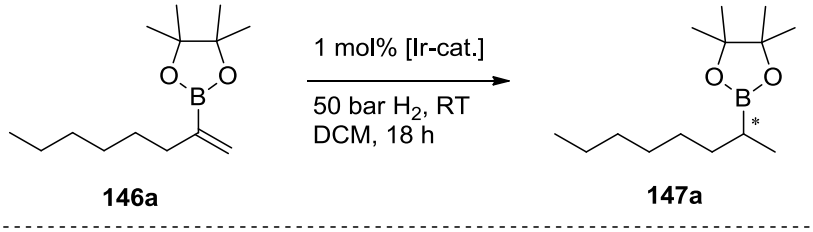


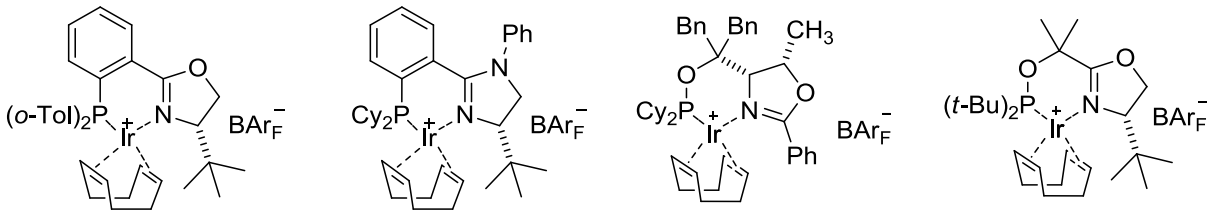
Scheme 6.8: Zirconocene mediated regioselective preparation of substrate **149o**.[142]

6.3 Hydrogenation Results

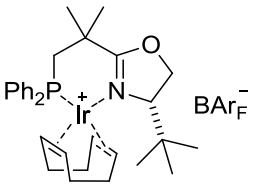
6.3.1 Hydrogenation of Terminal Boronic Esters

As already mentioned the hydrogenation of the aliphatic boronate **146a**, which so far had given unsatisfactory results with Ir-catalysts, served as a starting point for this study. In a series of chiral N,P ligand complexes that were screened in this reaction,[38b] complex **162c** derived from an imidazoline-phosphinite ligand stood out as the most promising catalyst, providing an enantiomeric excess of 68% at 50 bar hydrogen pressure (scheme 6.9).[147]

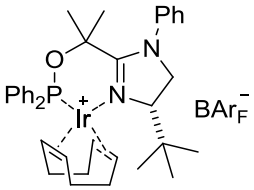




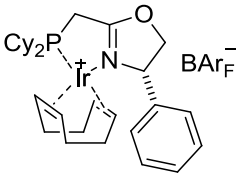
15e	**161**	**21b**	**26k**
>99% conv.[a]	>99% conv.[a]	>99% conv.[a]	>99% conv.[a]
14% *ee* (*S*)[b]	34% *ee* (*S*)[b]	34% *ee* (*S*)[b]	12% *ee* (*S*)[b]



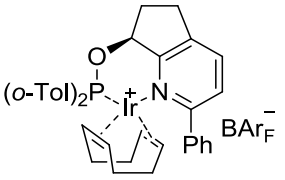
30b
>99% conv.[a]
5% *ee* (*S*)[b]



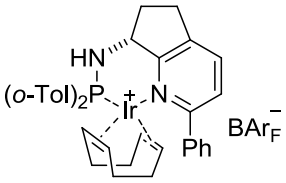
162c
>99% conv.[a]
68% *ee* (*S*)[b]



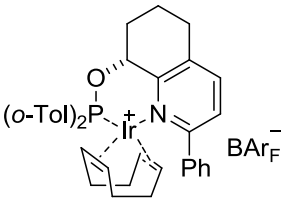
33b
>99% conv.[a]
9% *ee* (*S*)[b]



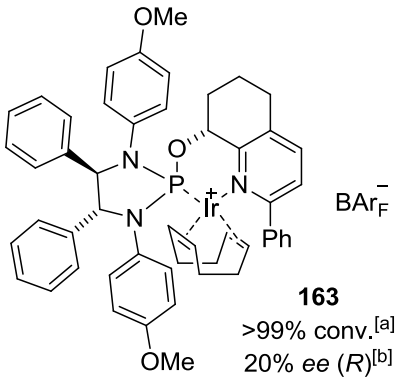
36b
>99% conv.[a]
16% *ee* (*S*)[b]



142b
>99% conv.[a]
14% *ee* (*R*)[b]



36e
>99% conv.[a]
15% *ee* (*R*)[b]



163
>99% conv.[a]
20% *ee* (*R*)[b]

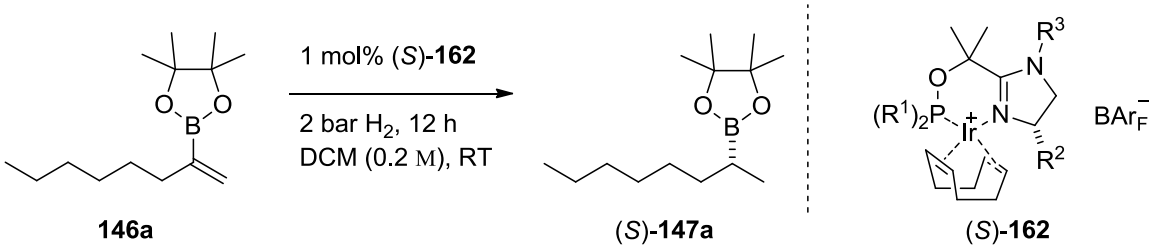
Scheme 6.9: Catalyst screening for the hydrogenation of boronic ester **146a**.
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

In a next step important reaction parameters were systematically varied, in order to increase the enantioselectivity. Since terminal olefins are known to react with higher enantioselectivity at lower pressure with iridium catalysts of this type,[49] the hydrogenation of **146a** was performed at 2 bar hydrogen pressure. Indeed, the *ee* increased to 86% while full conversion was still achieved. The reaction was also proceeding with a standard hydrogen ballon with the same enantioselectivity, but somehow slower reaction rate. Therefore, the pressure of 2 bar H_2 was kept, in order to achieve full conversion. Furthermore, the solvent influence was investigated, since hydrogenation with rhodium complexes showed a remarkably high solvent dependence for substrates of this type.[141] However, in this case the solvent influence proved to be weak. In DCM, DCE, toluene and chlorobenzene an *ee* of 86% was obtained, while only slightly lower enantioselectivities were recorded in more polar solvents like cyclopentyl methyl ether (83% *ee*), ethyl aceate (81% *ee*) or trifluoroethanol (78% *ee*). No special precautions to exclude oxygen and moisture were found to be necessary when setting up the hydrogenation, so the reaction solutions could be conveniently prepared in the laboratory atmosphere without rigorous purification of the solvents.

Next, the steric and electronic effects of the substituents at the stereogenic center and the nitrogen atom of the imidazoline ring and at the phosphorus atom of the ligand were studies. As shown in table 6.4 the sterically demanding *tert*-butyl group on the imidazole ring is

necessary for achieving high enantioselectivity (entry 1 *vs.* 2). The introduction of electron donor or acceptor substituents in the N-phenyl group led to lower *ee* values (entries 3-5). Replacement of the P-phenyl groups by P-*ortho*-tolyl groups also lowered the enantioselectivity (entry 6), whereas the more electron-donating dicyclohexylphosphino group improved the *ee* to 91% (entry 7). The sterically more demanding di-*tert*-butylphosphino group, on the other hand, caused a decrease of the *ee* to 77% (entry 8). Thus, catalyst **162h** that seemed to have an optimal balance between electronic and steric properties was selected for further studies.

Table 6.4: Catalyst optimization performed in the hydrogenation of vinyl boronate **146a**.



146a (*S*)-**147a** (*S*)-**162**

Entry	[Ir-cat.]	R^1	R^2	R^3	Conv. [%][b]	*ee* [%][b]
1	(*R*)-**162a**	Ph	*i*-Pr	Ph	>99	46 (*R*)
2	**162c**	Ph	*t*-Bu	Ph	>99	86
3	**162d**	Ph	*t*-Bu	*o*-Tol	>99	79
4	**162e**	Ph	*t*-Bu	*p*-F_3C-C_6H_4	>99	80
5	**162f**	Ph	*t*-Bu	3,5-$(MeO)_2$-C_6H_3	>99	59
6	**162g**	*o*-Tol	*t*-Bu	Ph	>99	81
7	**162h**	Cy	*t*-Bu	Ph	>99	91
8	**162i**	*t*-Bu	*t*-Bu	Ph	>99	77

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

The enantioselectivity of catalyst **162h** could be further improved by lowering the temperature. The best result was achieved at –20 °C with an *ee* of 96%, while still maintaining full conversion (table 6.5 and figure 6.1). For the di-*tert*-butylphosphino-imidazoline ligand complex **162i** the temperature had a similar effect with an increase in *ee* from 68% at 40 °C to 81% at –20 °C. Remarkably, the di-*ortho*-tolyl analogue **162g** showed a strikingly different behavior. In this case, the enantioselectivity dropped from 81% *ee* to 15% *ee* when the temperature was lowered from 25 °C to –20 °C. The enantioselectivity of the

corresponding catalyst **162a** with a diphenylphosphino group, on the other hand, remained in a narrow range of 80 to 85% *ee* between –20 and 40 °C.

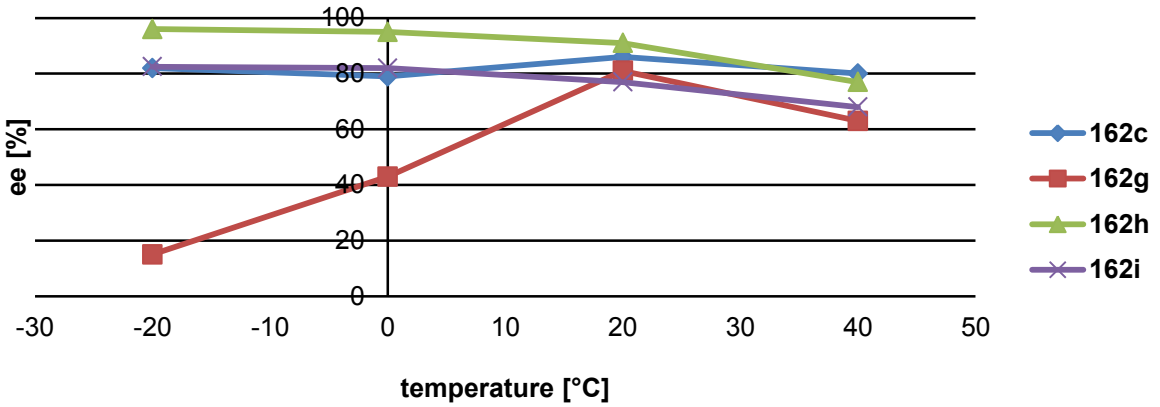
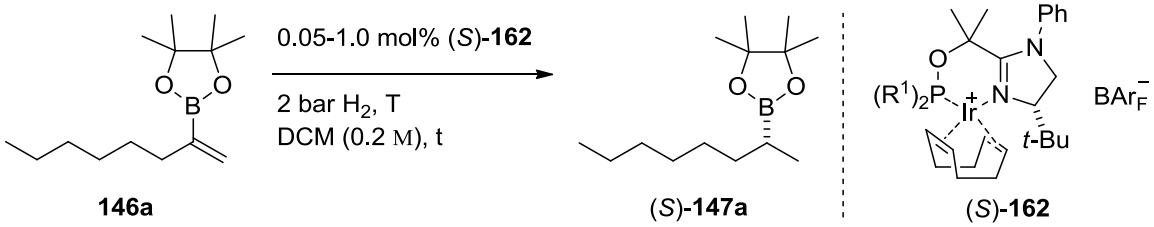


Figure 6.1: Temperature influence in the hydrogenation of terminal vinyl boronate **146a** using phosphinite-imidazoline derived catalyst **162c** and 1**62g-i**.

A series of experiments at different catalyst loadings and a reaction time of 4 h demonstrated that 0.1 mol% catalyst are sufficient to achieve full conversion and retain the *ee* at 96% (table 6.5, entries 17-20). Lower catalyst loadings led to incomplete conversion although the enantioselectivity was not affected (entry 21).

Table 6.5: Reaction parameters optimization performed in the hydrogenation of vinyl boronate **146a**.

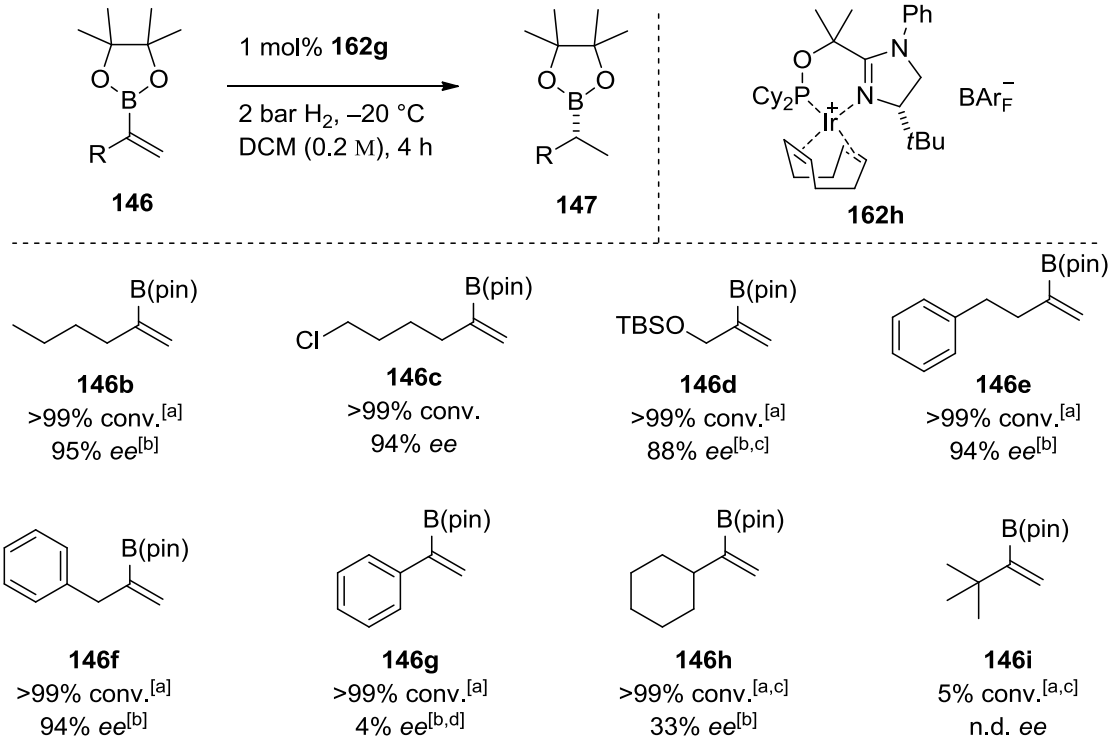


Entry	[Ir-cat]	R^1	Ir-cat. [mol%]	Time [h]	T [°C]	Conv. [%][a]	*ee* [%][b]
1	**162c**	Ph	1.00	12	40	>99	80
2	**162c**	Ph	1.00	12	25	>99	86
3	**162c**	Ph	1.00	12	0	>99	79
4	**162c**	Ph	1.00	12	−20	>99	82
5	**162g**	*o*-Tol	1.00	12	40	>99	63
6	**162g**	*o*-Tol	1.00	12	25	>99	81
7	**162g**	*o*-Tol	1.00	12	0	>99	42
8	**162g**	*o*-Tol	1.00	12	−20	>99	15
9	**162h**	Cy	1.00	12	40	>99	77
10	**162h**	Cy	1.00	12	25	>99	91
11	**162h**	Cy	1.00	12	0	>99	95
12	**162h**	Cy	1.00	12	−20	>99	96
13	**162i**	*t*-Bu	1.00	12	40	>99	68

14	**162i**	*t*-Bu	1.00	12	25	>99	77
15	**162i**	*t*-Bu	1.00	12	0	>99	82
16	**162i**	*t*-Bu	1.00	12	−20	>99	83
17	**162h**	Cy	1.00	4	−20	>99	96
18	**162h**	Cy	0.50	4	−20	>99	96
19	**162h**	Cy	0.25	4	−20	>99	96
20	**162h**	Cy	0.10	4	−20	>99	96
21	**162h**	Cy	0.05	4	−20	58	96

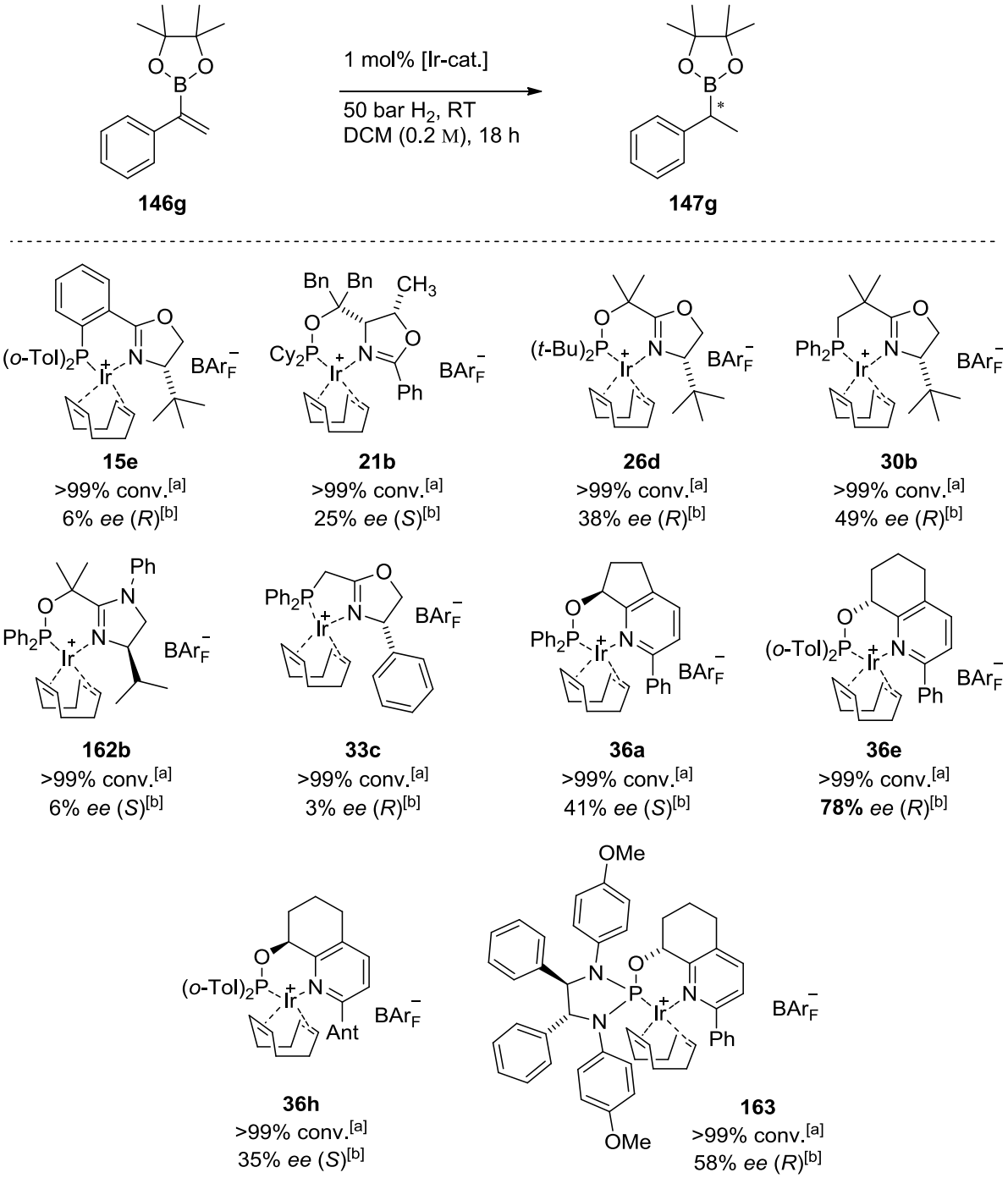
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

Having established the optimal conditions for substrate **146a**, the scope of catalyst **162h** in the hydrogenation of boronic esters with a terminal C=C bond was investigated (scheme 6.10). All substrates having a CH_2 group next to the double bond were well tolerated. Excellent activity and enantioselectivity were obtained for a variety of different substrates having additional functional groups (chloride **146c**, OTBS **146d** or phenyl groups **146e-f**). Sterically more demanding substituents next to the C=C bond (**146g-i**) required higher catalyst loadings (1 mol%) and longer reaction times (>12 h) to achieve full conversion, and a dramatic drop in enantioselectivity was observed. In this respect, catalyst **162h** strongly differed from *Andersson's* Ir-catalysts **39a** that gave 89% *ee* with substrate **146g**, but only 18% *ee* with **146a**.[64]



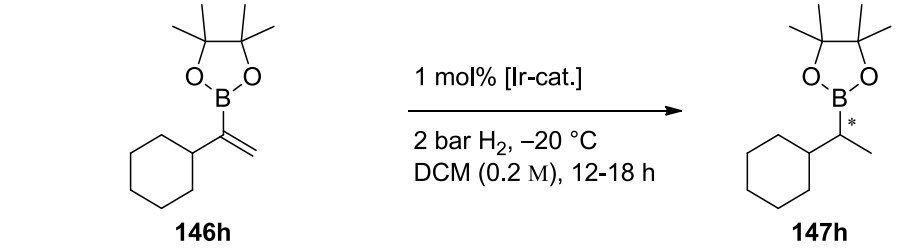
Scheme 6.10: Substrate scope of the hydrogenation of terminal boronic esters **146**.
[a] Determined by GC analysis of the reaction mixture after removal of the catalyst; [b] Determined by GC analysis on a chiral stationary phase; [c] Reaction time 12 hours.

In order to figure out which catalysts might provide reasonable *ee*s in the hydrogenation aromatic and branched substrates **146g** and **146h**, more catalyst screenings were performed. For the styrene-based substrate **146g** the best result was obtained using the bicyclic pyridine-phosphinite derived Ir-catalyst **36e** (scheme 6.11, 78% *ee*). However, all attempts to further increase the selectivity by variation of the catalyst structure or by changing the reaction conditions failed.

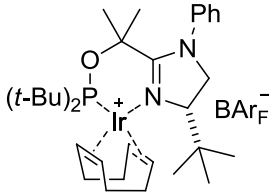


Scheme 6.11: Catalyst screening for the hydrogenation of boronic ester **146g**.
[a] Determined by GC analysis of the reaction mixture after removal of the catalyst; [b] Determined by HPLC analysis on a chiral stationary phase.

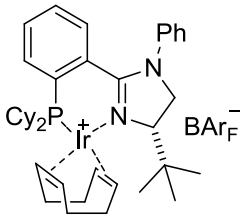
For the cyclohexyl-substituted olefin **146h** the optimized reaction conditions (2 bar, and −20 °C) for the hydrogenation of **146a** were applied. As shown in scheme 6.10, the imidazolyl-dicyclohexyl-phosphinite-catalyst **162h** gave only 33% *ee* (scheme 6.10). However, using the sterically more demanding imidazolyl-di-*tert*-butyl-phosphinite-catalyst **162i** an *ee* of 67% could be achieved (scheme 6.12). This is approximately in the same range as the values obtained with one of the ThrePHOX derived Ir-catalysts **21b** (69% *ee*), but lower than that achieved with one member of the Ir-NeoPHOX family **30b** (85% *ee*). However, the best results (91% *ee*) for the hydrogenation of substrate **146h** was achieved using a phosphanyl-methyl-oxazoline derived catalyst **33d**. Nevertheless, this value is still clearly lower than the one reported with Rh-Walphos catalyst.[141]



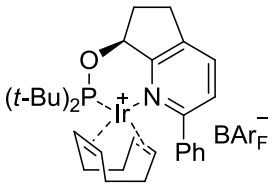
146h **147h**



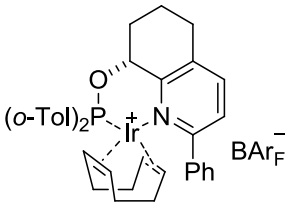
162i
>99% conv.[a]
67% *ee* (*S*)[b]



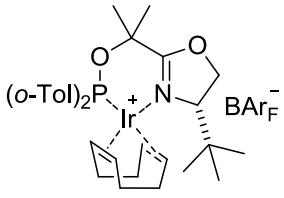
161
>99% conv.[a]
23% *ee* (*S*)[b]



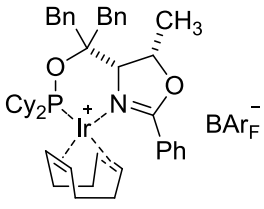
36d
>99% conv.[a]
52% *ee* (*R*)[b]



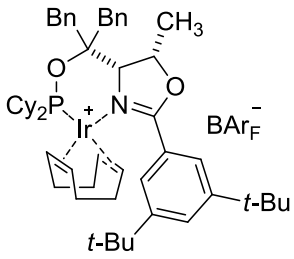
36e
>99% conv.[a]
16% *ee* (*S*)[b]



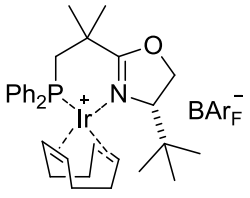
26b
>99% conv.[a]
38% *ee* (*S*)[b]



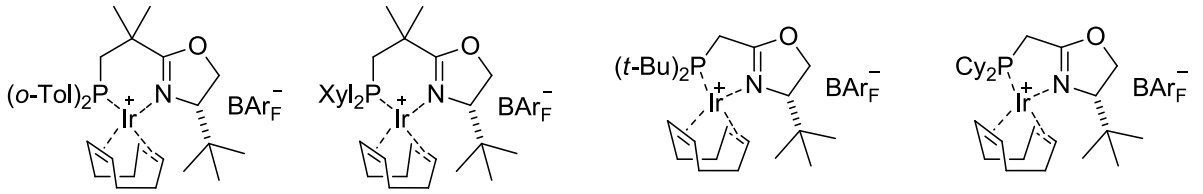
21b
>99% conv.[a]
69% *ee* (*R*)[b]



21c
>99% conv.[a]
63% *ee* (*R*)[b]



30b
>99% conv.[a]
62% *ee* (*S*)[b]



30a
>99% conv.[a]
85% *ee* (*S*)[b]

30c
>99% conv.[a]
53% *ee* (*S*)[b]

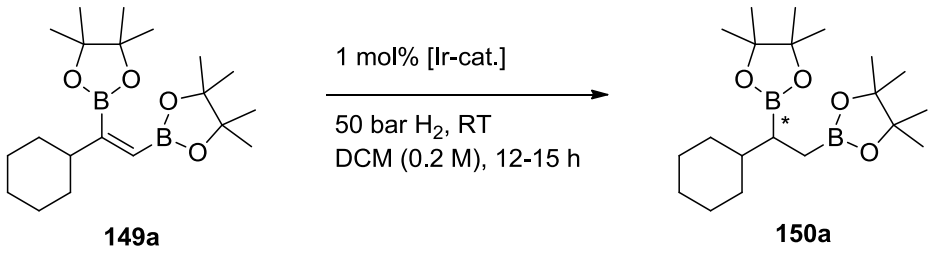
33d
>99% conv.[a]
91% *ee* (*S*)[b]

33e
>99% conv.[a]
65% *ee* (*S*)[b]

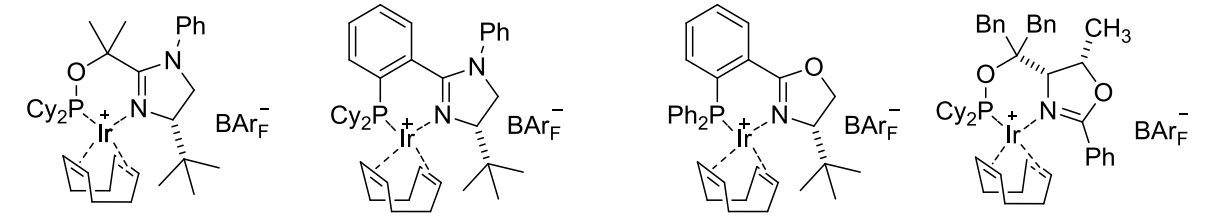
Scheme 6.12: Catalyst screening for the hydrogenation of boronic ester **146h**.
[a] Determined by GC analysis of the reaction mixture after removal of the catalyst; [b] Determined by GC analysis on a chiral stationary phase.

6.3.2 Hydrogenation of Trisubstituted Boronic Esters

The next substrates targeted were bisboronic esters **149a-d** (table 6.2, entries 1-4). However, for this substrate class the phosphinite-imidazoline ligand complex **162h** gave poor enantioselectivities (only 13% *ee* for substrate **149a**). In a brief catalyst screening (scheme 6.13) the pyridine-phosphinite complexes[56, 57b] **36d** and **36e** emerged as the most promising catalysts for substrates of this type.



149a **150a**

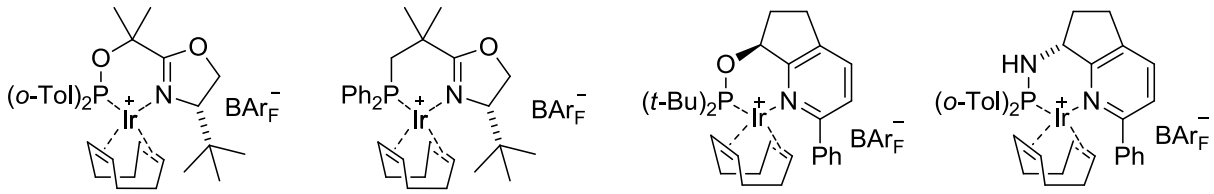


162g
>99% conv.[a]
16% *ee* (–)[b]

161
>99% conv.[a]
16% *ee* (–)[b]

15f
>99% conv.[a]
20% *ee* (–)[b]

21a
>99% conv.[a]
34% *ee* (–)[b]

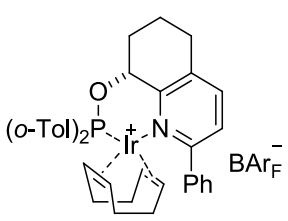


26b
>99% conv.[a]
66% *ee* (–)[b]

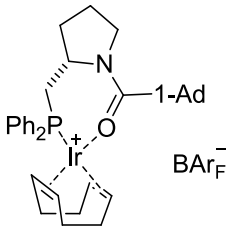
30b
>99% conv.[a]
32% *ee* (+)[b]

36d
>99% conv.[a]
95% *ee* (+)[b]

142b
>99% conv.[a]
80% *ee* (–)[b]



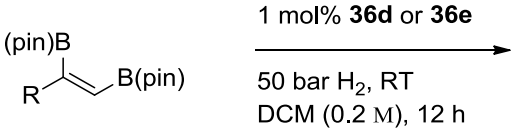
36e
>99% conv.[a]
97% *ee* (–)[b]



164
>99% conv.[a]
55% *ee* (+)[b]

Scheme 6.13: Catalyst screening for the hydrogenation of bis-boronic ester **149a**.
[a] Determined by GC analysis of the reaction mixture after removal of the catalyst; [b] Determined by GC analysis on a chiral stationary phase.

Catalyst **36e** having a 6-membered carbocyclic ring showed higher *ee* for substrate **149a** than the more rigid catalyst **36d**. But the activity of catalyst **36d** in the hydrogenation of different 1,2-bisboronic esters **149a-d** showed a broader substrate scope (scheme 6.14). Various substituents (cyclohexyl, *n*-hexyl, *tert*-butyl, and phenyl) at the C=C bond were tolerated, giving high conversions for all substrates. The cyclohexyl- and phenyl-substitued bisboronates **149a** and **149d** reacted with excellent enantioselectivities of 95 and 98% *ee*, while the sterically less demanding *n*-hexyl derivative gave 72% *ee*. On the other hand, catalyst **36e** gave even higher *ee* for substrate **149d**, but clearly lower activity for **149c** and lower selectivity for **149c.**

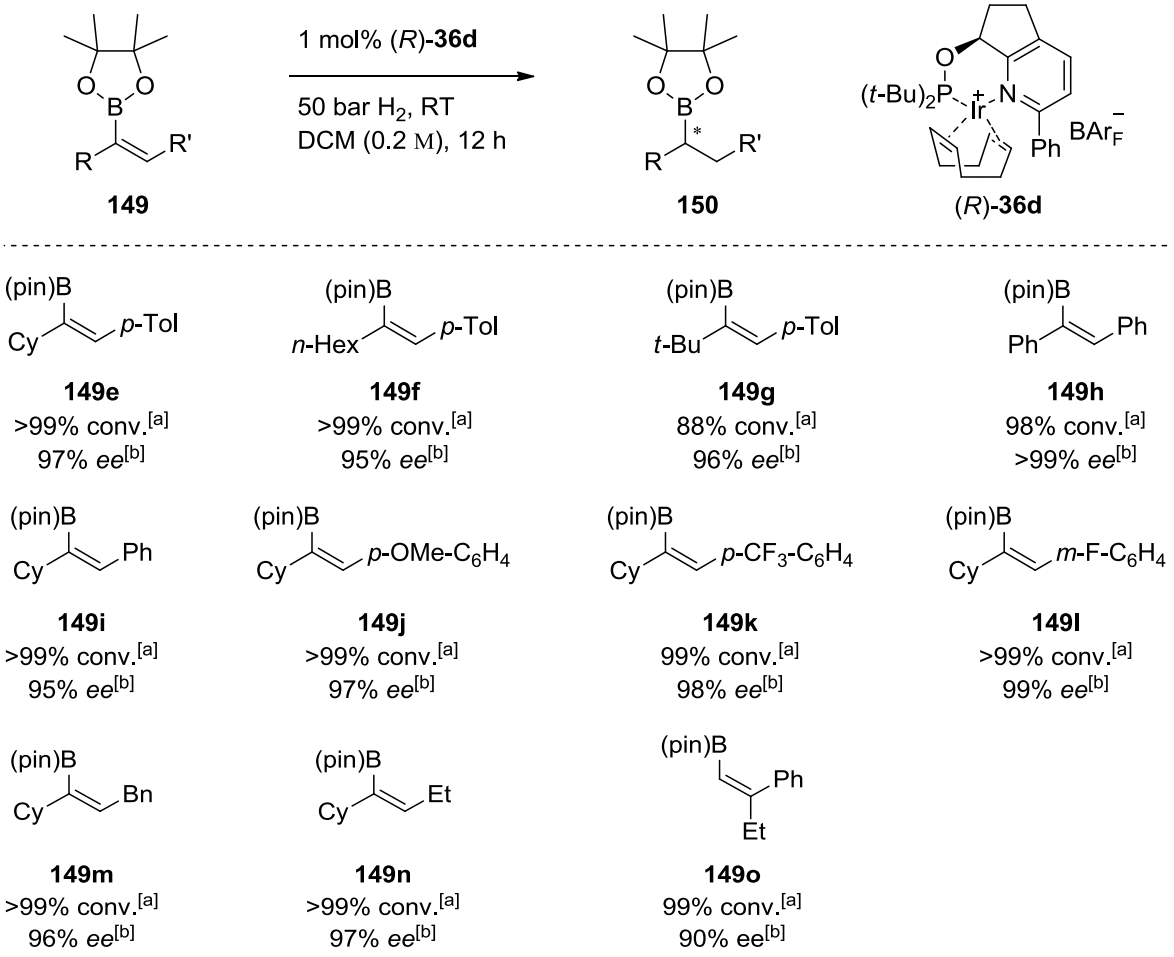


	149b	**149c**	**149c**
(*S*)-**36d**	>99% conv. 72% *ee* (+)	97% conv. 85% *ee* (+)	>99% conv. 98% *ee* (+)
(*R*)-**36e**	>99% conv. 59% *ee* (−)	20% conv. n.d. *ee* (−)	>99% conv. >99% *ee* (−)

Scheme 6.14: Comparison of selectivity and activity of pyridine-phosphinite derived Ir-complexes **36d** and **36e** for the asymmetric hydrogenation of 1,2-bisboronic esters **149b-d**.

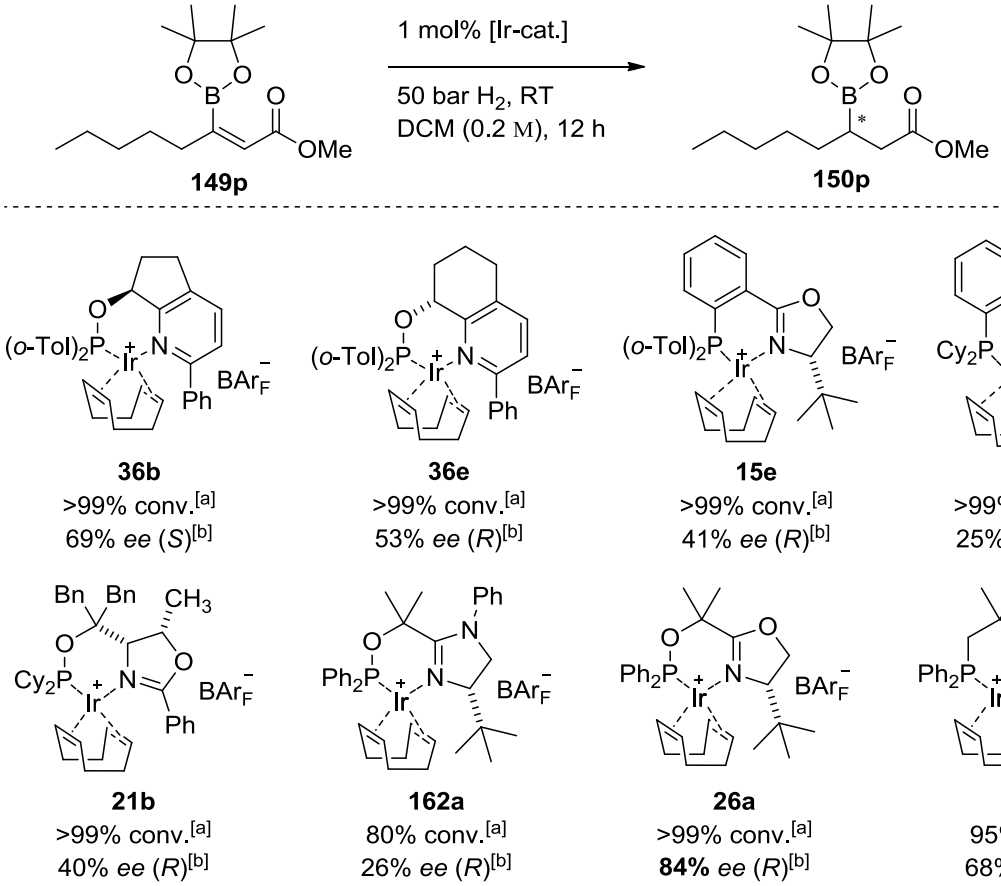
Therefore, the hydrogenation of trisubstitued mono boronic esters **149e-p** was performed using iridium catalyst **36d**. Generally, excellent selectivities from 95% up to >99% *ee* were achieved. With the exception of the sterically demanding *tert*-butyl derivative **149g**, all other

substrates gave >98% conversion. Electron donor or acceptor groups at the aryl substituent had no significant effect on *ee* and conversion. Aryl substituents at the C=C bond are not essential for achieving high enantioselectivity, as shown by the hydrogenation of the merely alkyl-substituted substrates **149m** and **149n**. Substrate **149o**[148] bearing a boronic ester residue at the less substituted olefinic C atom reacted with lower, but still very good enantioselectivity yielding the corresponding primary alkylboronate with full conversion and 90% *ee*.



Scheme 6.15: Substrate scope of the hydrogenation of trisubstitued boronic esters **149**.
[a] Determined by GC analysis of the reaction mixture after removal of the catalyst; [b] Determined by GC or HPLC analysis on a chiral stationary phase.

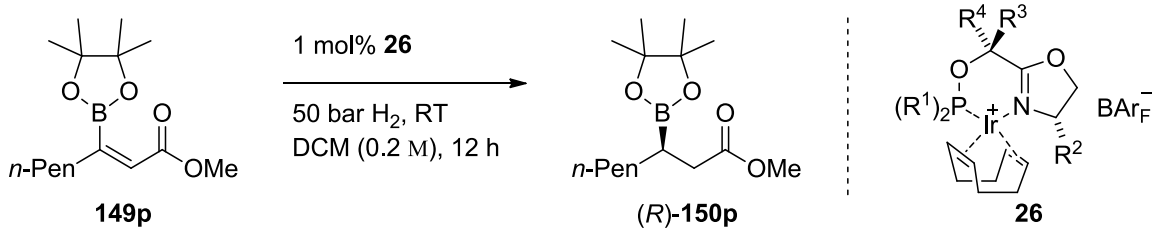
Furthermore, the hydrogenation of substrate **146p** which has a coordinating carbonyl group adjacent to the C=C bond was investigated. Initial screening revealed complex **26a** derived from SimplePHOX ligand as the most promising catalyst for this substrate (84% *ee*; scheme 6.16).



Scheme 6.16: Catalyst screening for the hydrogenation of trisbustituted boronic ester **146p** having a coordinating carbonyl group adjacent on the C=C bond.
[a] Determined by GC analysis of the reaction mixture after removal of the catalyst; [b] Determined by GC analysis on a chiral stationary phase.

In a next step, variation of the catalyst structure **26** was investigated in order to improve the enantioselectivity for this substrate. For this purpose the substituent on phosphorus, on the oxazoline moiety and the bridging unit were modified (table 6.6). This variation revealed that phenyl and cyclohexyl groups were well tolerated as substituents on the phosphorus atom, while *o*-Tol, *t*-Bu or 3,5-CF_3-C_6H_3 groups gave significantly lower *ee*s (entries 1-6). Modification of the bridging unit, which allows the installation of an additional stereogenic center,[98] did not give any improvement in *ee* (entries 7-9). Finally, by replacing the substituent on the oxazoline to phenyl the highest *ee* of 90% was obtained (entry 13).

Table 6.6: Catalyst structure optimization performed for the hydrogenation of trisbustituted boronic ester **149p**.



Entry	[Ir-cat]	R^1	R^2	R^3	R^4	Conv. [%][a]	*ee* [%][b]
1	**26a**	Ph	*t*-Bu	CH_3	CH_3	>99	84
2	**26a**	Ph	*t*-Bu	CH_3	CH_3	70[c]	83
3	**26b**	*o*-Tol	*t*-Bu	CH_3	CH_3	41[c]	60
4	**26j**	Cy	*t*-Bu	CH_3	CH_3	>99[c]	82
5	**26k**	*t*-Bu	*t*-Bu	CH_3	CH_3	>99[c]	55
6	**26d**	3,5-CF_3-C_6H_3	*t*-Bu	CH_3	CH_3	78[d]	20
7	**26e**[e]	Ph	*t*-Bu	Ph	H	>99	78
8	**26f**[e]	Ph	*t*-Bu	H	Ph	>99	19
9	**26g**[e]	*o*-Tol	*t*-Bu	Ph	H	>99	70
10	**26c**	Ph	*i*-Pr	CH_3	CH_3	>99	86
11	**26l**	Cy	*i*-Pr	CH_3	CH_3	>99	79
12	**26m**	*t*-Bu	*i*-Pr	CH_3	CH_3	>99	77
13	**26h**	Ph	Ph	CH_3	CH_3	>99	90
14	**26i**	Ph	Bn	CH_3	CH_3	>99	86

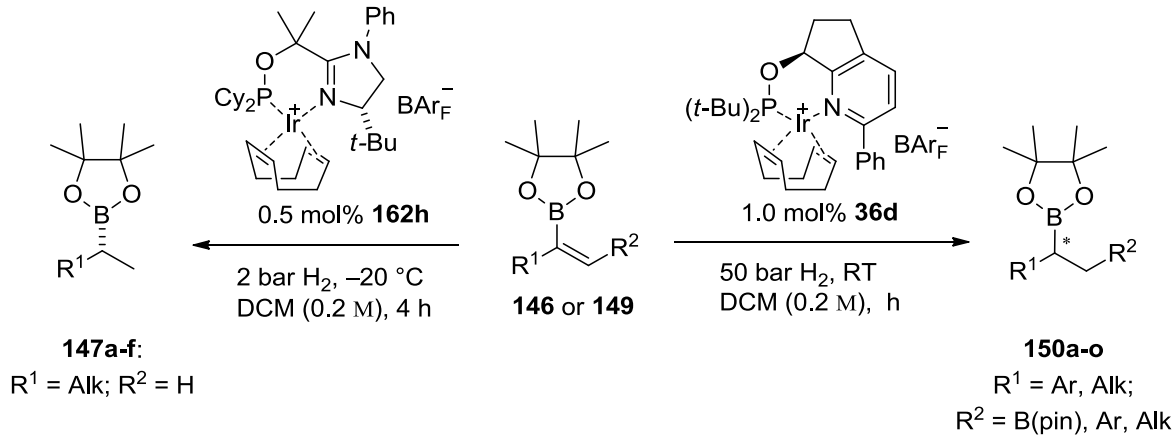
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase; [c]: Experiment performed at 5 bar H_2 pressure; [d]: Experiment performed using 2 mol% [Ir-cat.]; [e] Ir-complexes **26e-g** were kindly provided by *A. Schumacher*.[98]

6.4 Summary and Outlook

In summary, the preparation of terminal vinyl boronates **146** from commercially available alkynes was achieved in acceptable yields. Furthermore, starting from alkynes, 1,2-bisboronic ester **149a-d** were obtained by Pt-catalyzed addition of bis(pinacolato)diboron in good yields. Those 1,2-bisboronic esters **149a-d** were then used for the chemoselective preparation of trisubstited mono-boronic esters **149a-o**.

The alkenyl boronic acid esters obtained were applied in the Ir-catalyzed asymmetric hydrogenation. While an Ir-complex derived from phosphinoimidazoline ligand **162h** was identified as highly efficient for the enantioselective hydrogenation of terminal vinyl boronic esters **146**, trisubstituted bis- and monoboronates **149** could be reduced with high activity and excellent selectivity employing a pyridine-phosphinite derived Ir-complex **36d**. Furthermore, alkenyl boronic esters which gave low selectivity with these two catalysts could also be

efficiently reduced by other Ir-complexes, but required additional screening and optimization studies (scheme 6.17).



Scheme 6.17: Ir-catalyzed asymmetric hydrogenation of alkenyl boronic eter **146** and **149**.

Future work might be dedicated to the development of asymmetric hydrogenation of tetrasubstitued boronic esters. This would allow installing two stereogenic centers in one step and would therefore have a very high synthetic relevance. Tetrasubstituted bis-boronic esters could be obtained from symmetrical alkynes and then modified by Suzuki−Miyaura coupling to target substrates.

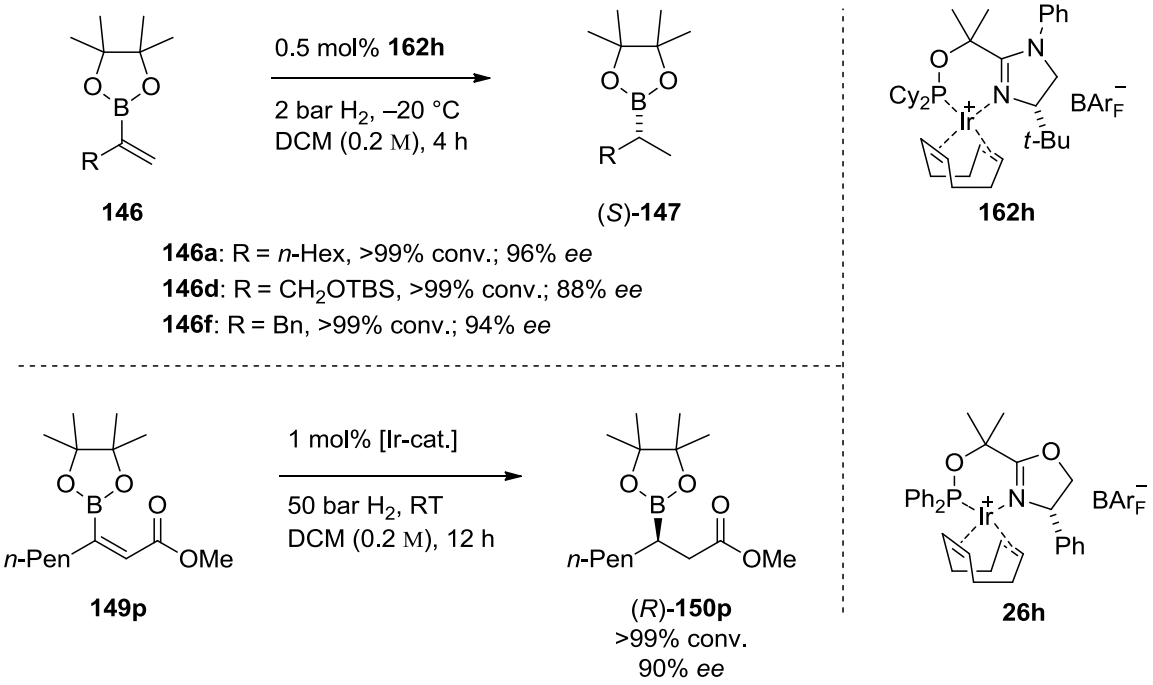
Chapter 7

P-Alkyl SimplePHIM Derived Ir-Complexes and Modification of SimplePHOX Derived Ir- Complexes for Asymmetric Hydrogenation

7.1 Introduction

7.1.1 Objective of This Work

During the investigations on the asymmetric hydrogenation of alkenyl boronic esters (chapter 6) a SimplePHIM Ir-complex **162h** bearing cyclohexyl groups at the phosphorus atom, was identified as the most suitable catalyst for terminal vinyl boronates **146**. Furthermore regarding the asymmetric hydrogenation of trisubstituted boronic esters substrate **146p** having a carbonyl group adjacent to the C=C bond, the best *ee* of 90% was obtained using Ir-SimplePHOX derived catalyst **26h** (scheme 7.1). These two complexes are examples of Ir-catalysts, which were synthesized for specific substrates in order to optimize the enantioselectivity. Therefore, the aim of this study was to develope the synthesis of those Ir-complexes and to explore the general potential for the asymmetric hydrogenation of olefins.

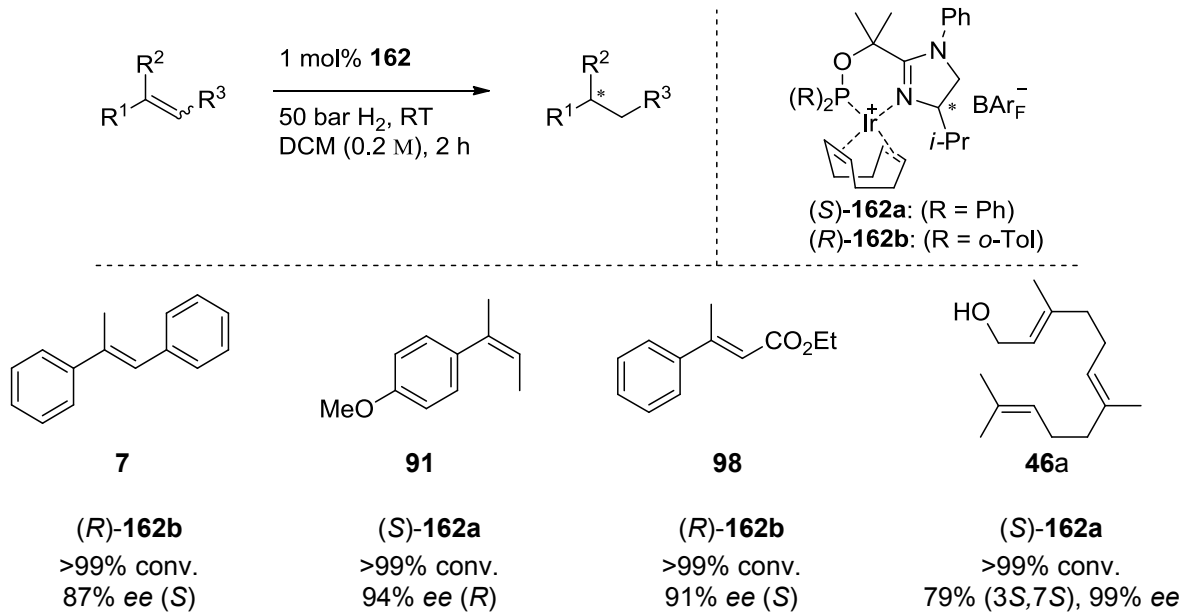


Scheme 7.1: Selected results obtained in Iridium-catalyzed asymmetric hydrogenation of alkenyl boronic esters.

7.1.2 Ir-SimplePHIM Complexes Prior to This Work

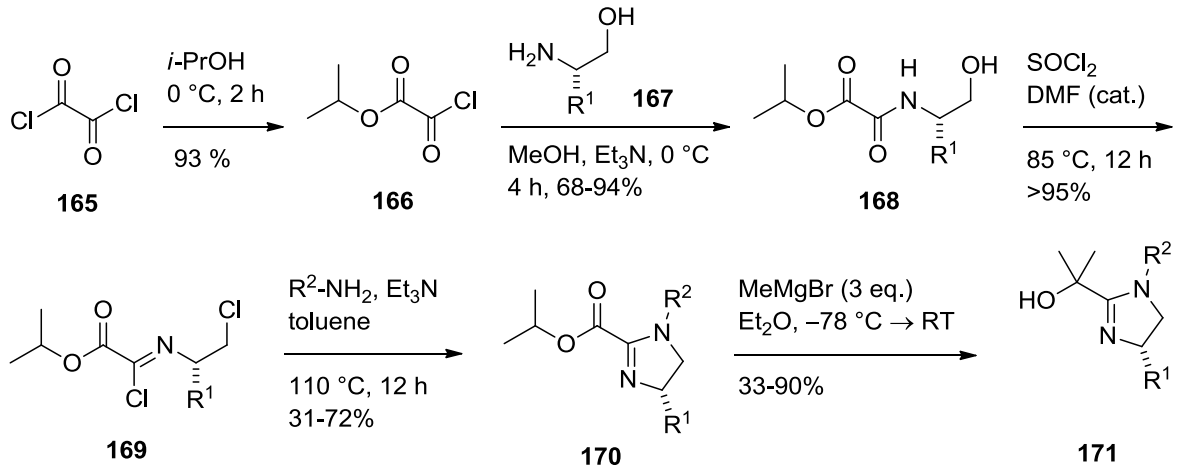
Complex **162h** belongs to the structural family of Ir-SimplePHIM complexes previously developed by *F. Menges*.[147] However, prior to the work on asymmetric hydrogenation of alkenyl boronic esters only P-aryl derived Ir-SimplePHIM complexes **162a-g** were known. Complexes **162a-g** showed encouraging results in the asymmetric hydrogenation of model

olefins, like α-methylstilbene **7**, (*Z*)-olefin **91** and α,β-unsaturated ester **98** and in the hydrogenation of farnesol **46a** (scheme 7.2).[84, 147]



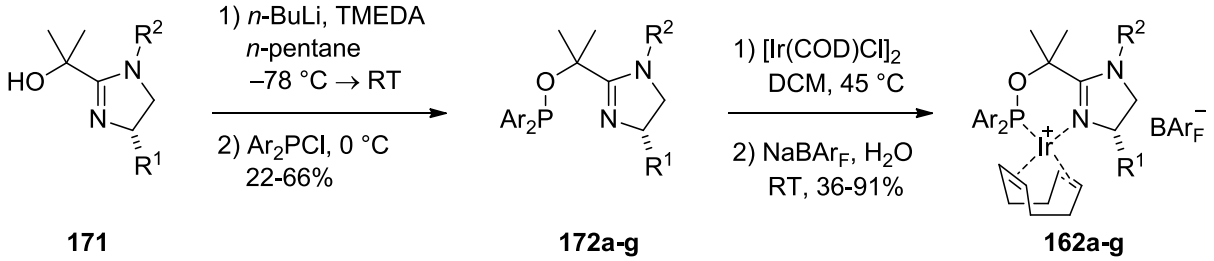
Scheme 7.2: Ir-SimplePHIM complexes **162a-b** previously used in the asymmetric hydrogenation.[84, 147]

The synthetic route towards the P-aryl SimplePHIM Ir-complexes **162a-g** starts with the esterfication of oxalyl chloride **165** with isopropanol. Coupling of **166** with amino alcohols **167** gave amides **168**, which were converted to the β-chloroimidoyl chloride **169** using thionyl chloride. The subsequent cyclization with anilines afforded imidazolinyl esters **170**, which gave upon addition of methyl Grignard reagent tertiary alcohols **171**.



Scheme 7.3: Synthesis of imidazolyl alcohols **171**.[147]

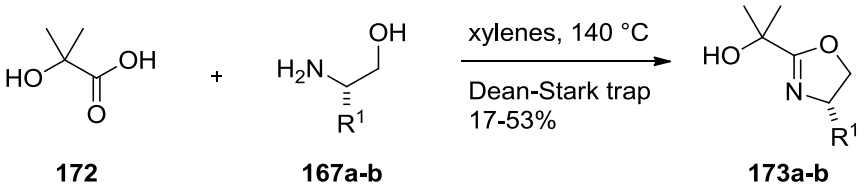
These imidazolinyl alcohols **171** served as starting materials for the preparation of arylphosphinites **172a-g** and the corresponding Ir-complexes **162a-g**.[147]



Scheme 7.4: Synthesis of P-aryl Ir-SimplePHIM complexes **162a-g**.[147]

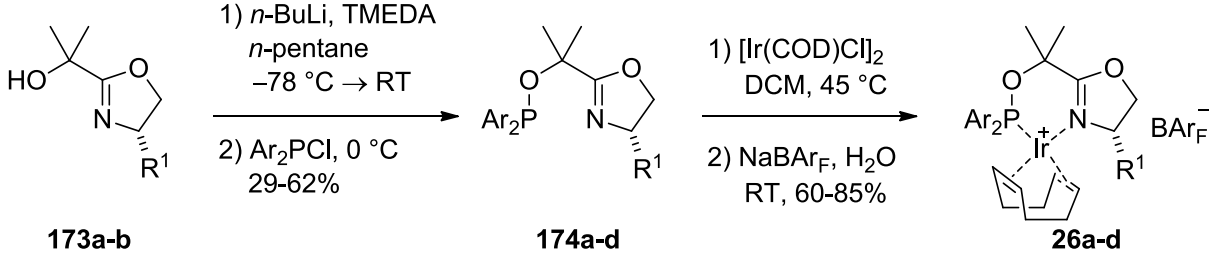
7.1.3 Ir-SimplePHOX Complexes Prior to This Work

In contrast to Ir-SimplePHIM complexes, the Ir-SimplePHOX complex family is based on the oxazoline as N-donor. P-aryl complexes **26a-d** were first investigated by *S. Smidt* and *F. Menges*,[51] while *M. Schrems* reported the synthesis of P-alkyl Ir-SimplePHOX complexes **26j-m**.[53] In general, the synthetic sequence leading to complexes **26** is simple and short. Condensation of 2-hydroxyisobutyric acid **172** with amino alcohols **167a-b** provides the oxazolinyl alcohols **173a-b** in low yield (scheme 7.5).



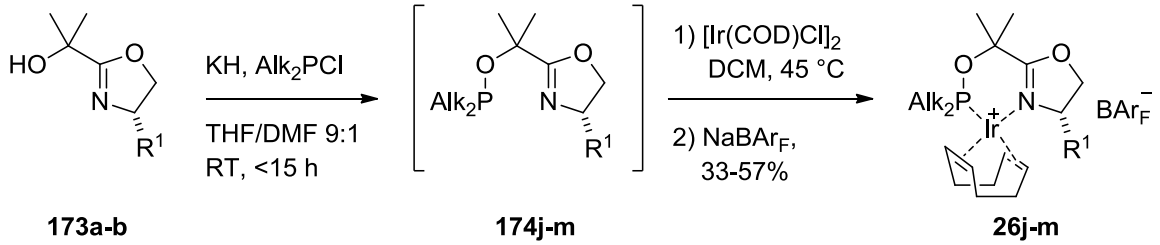
Scheme 7.5: Synthesis of oxazolyl alcohol **173a-b**.[51]

Deprotonation of the alcohols **173a-b** using *n*-BuLi and subsequent trapping with aryl-chlorophosphines furnishes P-aryl ligands **174a-d**, which can be directly converted to the Ir-complexes **26a-d** (scheme 7.6).[51]



Scheme 7.6: Synthesis of P-aryl Ir-SimplePHOX complexes **26a-d**.[51]

On the other hand, P-alkyl Ir-SimplePHOX complexes **26j-m** were prepared using sodium hydride in concentrated solution of THF/DMF 9:1 (scheme 7.7). Both P-Aryl and P-Alkyl Ir-SimplePHOX complexes showed high activity and selectivity in the hydrogenation of C=C and C=N bonds.[51, 116]



173a-b **174j-m** **26j-m**

Scheme 7.7: Synthesis of P-Alkyl Ir-SimplePHOX complexes **26j-m**.[116]

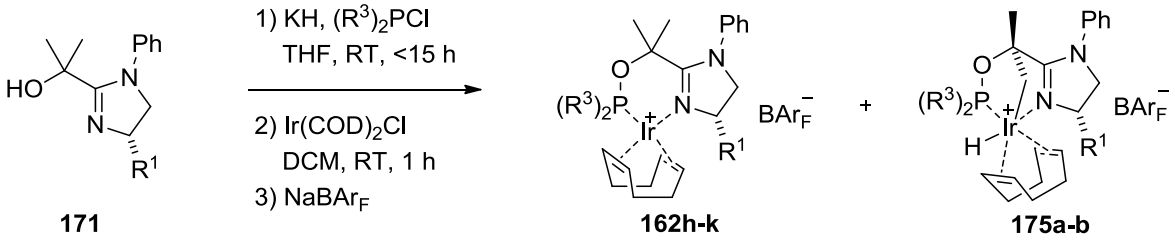
However, Ir-SimplePHOX complexes having aromatic R^1 gropus on the oxazoline ring have not been reported so far. As such residues were required for the hydrogenation of trisubstitued boronic esters, their synthesis and performance in the asymmetric hydrogenation of model olefins is described herein.

7.2 Synthesis

7.2.1 P-Alkyl Ir-SimplePHIM Complexes

Imidazolinyl alcohols **171** were required for the formation of P-alkyl Ir-SimplePHIM complexes. They were obtained following the same procedure as described by *F. Menges* (scheme 7.3).[147] The formation of P-alkyl Ir-SimplePHIM complexes **162h-k** was achieved in 24-62% yield (table 7.1, entries 1-4) employing similar conditions as implemented by *M. Schrems* for **26j-m** (scheme 7.7).[116] Rather than using sodium hydride in THF/DMF 9:1, an excess of potassium hydride in pure THF was used.

Table 7.1: Formation of Ir-complexes **162h-k** starting from imidazolyl alcohols **171**.



171 **162h-k** **175a-b**

Entry	R^1	R^3	Ir-complex	^{31}P-NMR (L) [ppm]	^{31}P-NMR **126h-k** [ppm]	^{31}P-NMR **175** [ppm]	Ratio **162 : 175**	**Yield** [%] (2 steps)
1	*t*-Bu	Cy	(*S*)-**162h**	129.8	109.2	n.o.	--	25
2	*t*-Bu	*t*-Bu	(*S*)-**162i**	144.2	138.7	n.o.	--	55
3	*i*-Pr	Cy	(*S*)-**162j**	122.3	112.9	145.8 (**175a**)	2.3:1[a]	24[b]
4	*i*-Pr	*t*-Bu	(*S*)-**162k**	143.8	133.2	146.0 (**175b**)	1:1.9[a]	62[b]

[a]: The ratio between both Ir-species formed was calculated from the inegrals of ^{31}P-NMR signals; [b]: Isolated yields of the mixture of Ir-complex **162j-k** and **175a**-b after flash chromatography over silica gel.

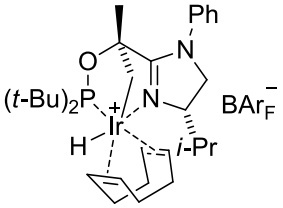
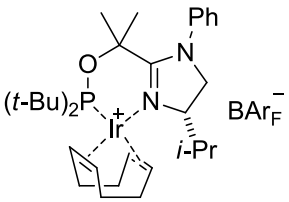
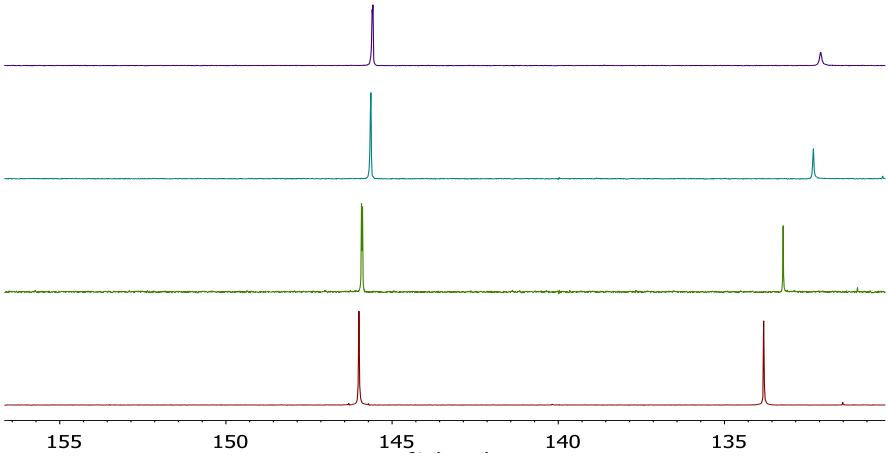
7.2.2 Cyclometalled P-Alkyl Ir-SimplePHIM Complexes

Complexes **162j** and **162k** containing isopropyl residues on the imidazoline ring were isolated as a mixture of two different Ir-species. Both species were inseparable by flash chromatography or recrystallization. NMR analysis showed signals in the high field region (between −15 and −20 ppm) which are characteristic for Ir-hydrides, similar to those described in chapter 3. Indeed a more detailed investigation revealed an unusual insertion of the iridium into one of the sp^3 C−H bonds of the geminal methyl group. The extent of cyclometallation depends on the substitution of the P-donor as ^{31}P-NMR spectra revealed a 2:1 ratio in favour of the non-cyclometallated form for **162k**, while the cyclometalled form **175b** was predominantly found in complex **162k** (1:2 ratio). Furthermore, crystals suitable for X-ray diffraction analysis were obtained from the cyclometallated **175b** (see chapter 7.3 for crystal structure analysis). Taking the obtained crystals of **175b** back again in solution a ratio of 1:2 between **162k** and **175b** was observed by ^{31}P-NMR. This indicates a reversible formation of both complexes in solution, whereas the cyclometalled form **175b** is more favored in solid structure.

The tendency to undergo cyclometallation depends also on the substitution pattern at the N-donor, as cyclometallation does not occur for complexes **162h** and **162i**, which bear a *tert*-

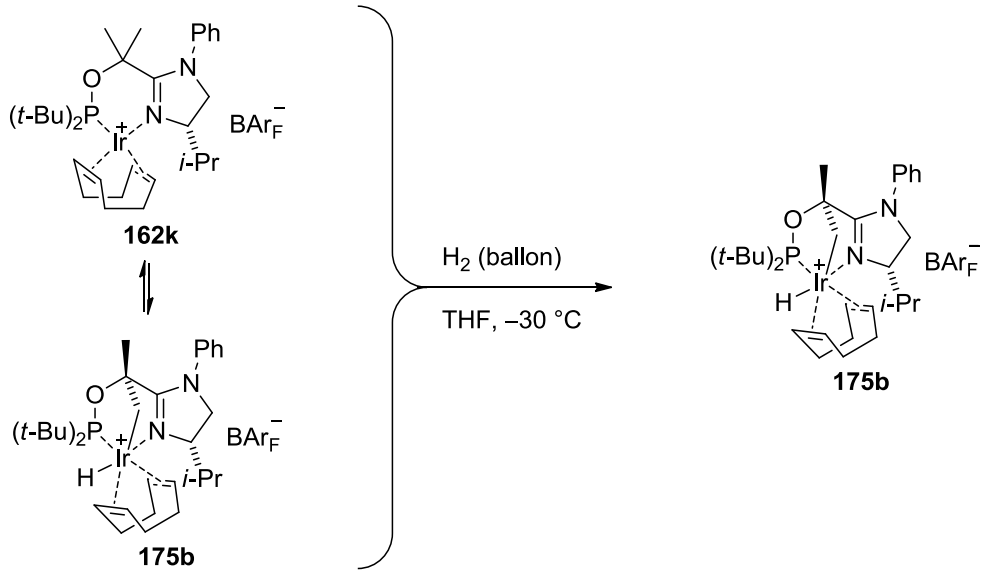
butyl group on the imidazoline ring. Cyclometallated species derived from complexes **162a-b**, which have the isopropyl group on the imidazoline part, but contain aromatic groups on the phosphorus atom are also not found. Structurally similar P-alkyl Ir-SimplePHOX complexes **26j-m** as well showed no tendency to form cyclometalled species.

Table 7.2: Temperature dependence on the equilibrium between the Ir-SimplePHIM complex **162k** and its cyclometalled form **175b**.

 **175b**		 **162k**	**T** [°C]	**Ratio 175b : 162k**
			−60	2.4 : 1
			−40	2.3 : 1
			25	1.9 : 1
			60	1.3 : 1

The reversibility of the C−H insertion observed in complex **162k** was also confirmed by ^{31}P-NMR spectra recorded at different temperatures. While at elevated temperature (60 °C) the ratio of both components **162k** and **175b** is close to 1:1, at rt and lower temperatures the cyclometallated species **175b** predominates over **162k** (>2:1).

Interestingly, upon treating the mixture of **162k** and **175b** in a sealed NMR tube at −30 °C in d_8-THF with dihydrogen gas for 16 h, clean formation of only the cyclometalled form **175b** was observed (scheme 7.8 and figure 7.1). The NMR spectra remained nearly unchanged when the sample was left to reach room temperature (only traces of addition Ir-H signals were found).



Scheme 7.8: Reaction of equilibrium mixture of Ir-SimplePHIM complex **162k** and its cyclometalled form **175b** with dihydrogen.

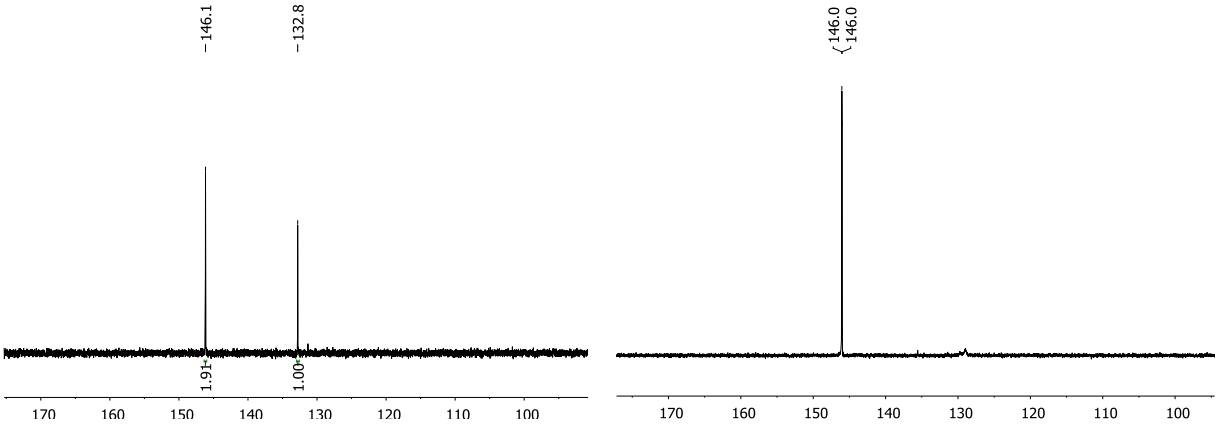
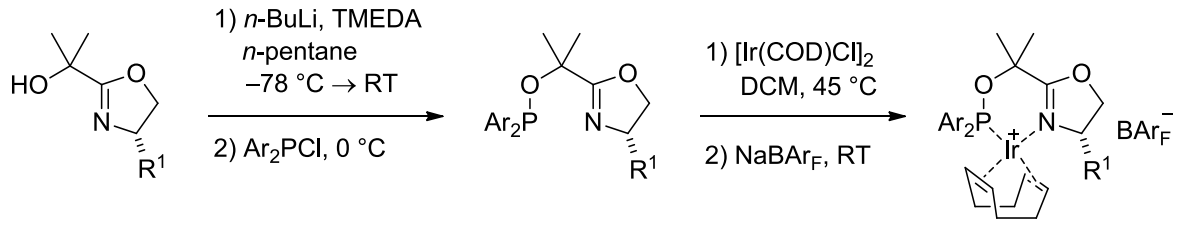


Figure 7.1: ^{31}P-NMR spectra recorded before (left) and after (right) reaction of Ir-SimplePHIM complex **162k** and its cyclometalled form **175b** with dihydrogen.

7.2.3 SimplePHOX Derived Complexes

The required oxazolinyl alcohols (**173b**, R^1 = *t*-Bu) and **173c**, R^1 = Ph) were kindly provided by *E. Hörmann* or they were obtained (**173d**, R^1 = Bn) by condensation hydroxy-isobutyric acid **172** with amino alcohol **167d** (R^1 = Bn) following the described procedure (scheme 7.5). The N,P ligands and their Ir-complexes **26d** and **26h-i** were formed in low to moderate yields applying the outlined conditions.[51] In this case no cyclometallation was observed.

Table 7.3: Synthesis of Ir-SimplePHOX complexes **26d** and **26h-i**.[51]



173 **174** **26d** and **26h-i**

Entry	R^1	Ar	Ir-Complex	^{31}P-NMR (L) [ppm]	Yield [%]	^{31}P-NMR [ppm]	Yield [%] (2nd steps)
1	*t*-Bu	3,5-CF_3-C_6H_3	(*S*)-**26d**	83.3	38	96.6	67
2	Ph	Ph	(*S*)-**26h**	95.5	8	101.8	45
3	Bn	Ph	(*S*)-**26i**	94.8	9	102.0	98

7.3 Crystal Structure Analysis

The crystal structure of the cyclometallated form of $Ir^{(III)}$-complex **175b** was obtained by overlaying an etheral solution of **162k** and **175b** with *n*-pentane. The cyclometallated species appears to be the more stable form of the P-alkyl Ir-SimplePHIM complexes in the crystalline state and thus crystalizes preferentially.

This crystal structure is compared to two previously obtained structures of Ir-SimplePHIM complexes **162l** and Ir-SimplePHOX complex **26m** (figure 7.2 and table 7.4). Complex **162l** was selected to get insights into the coordination sphere of the $Ir^{(I)}$-SimplePHIM complexes. In respect of steric and electronic properties complex **162l** significantly differs from the obtained $Ir^{(III)}$-complex **175b**. On the hand Ir-SimplePHOX complex **26m** is closely matching the steric properties found in the non-cyclometalled complex **162k**.

The substituents on the P-donor and the N-donor were found to orientate almost in parallel fashion in $Ir^{(I)}$-complexes **162l** and **26m** in contrary to the cyclometallated $Ir^{(III)}$-complex **175b**. In this case a switch of the boat chelating conformation is pushing these substitutes away from each other.

Although this crystal structure gives some insights in the complex geometry of the cyclometallated species **175b** the coordination in solution might be completely different, since an equilibrium is observed between **162k** and **175b**. Therefore, direct conclusions concerning the structures of the active catalyst are not possible due to the very different coordination spheres resulting after removal of the COD ligand.

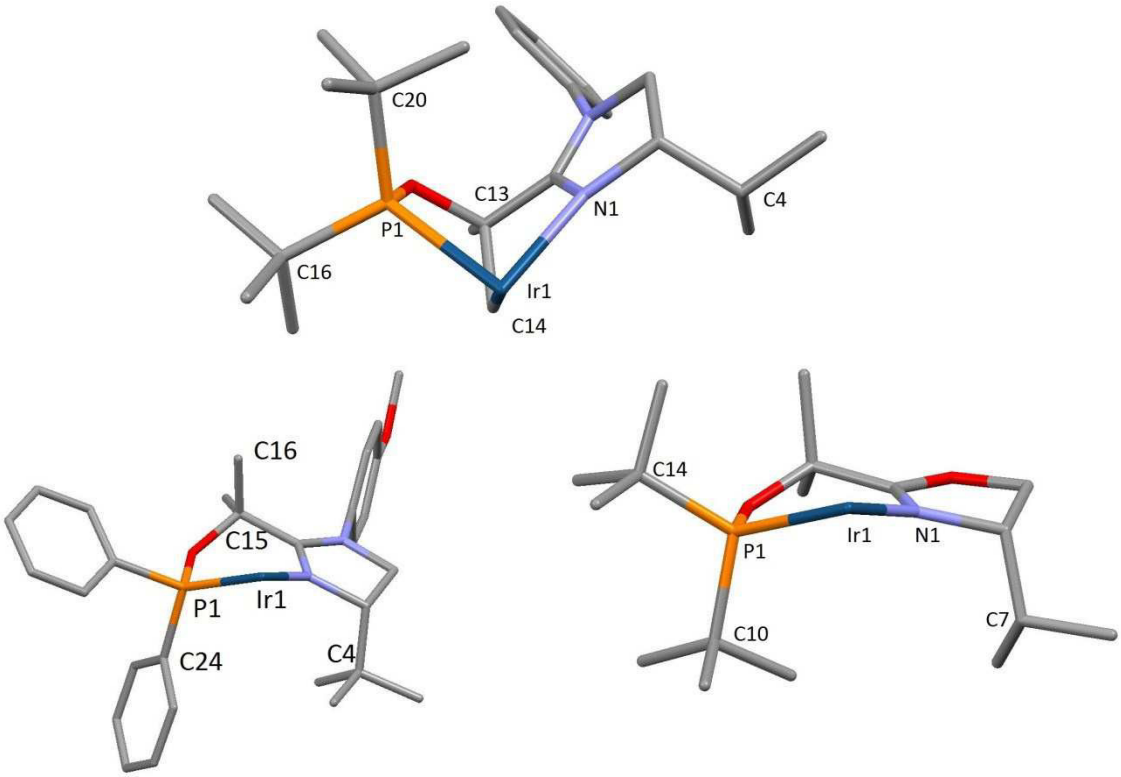
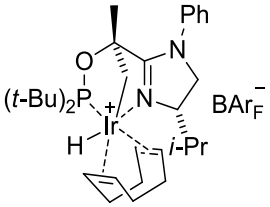
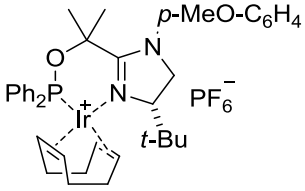
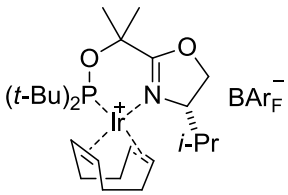


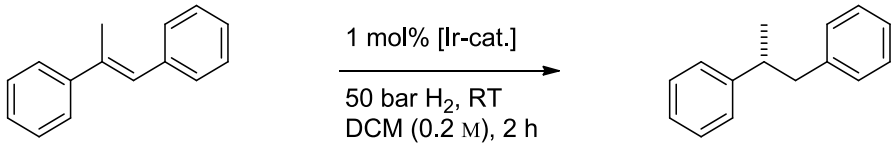
Figure 7.2: Crystal structures of complexes **175b**, **162l** and **26m**; all COD ligands and counterions were omitted for clarity.

Table 7.4: Selected bond lengths and bond angles of Ir-complexes **175b**, **162l** and **26m**.

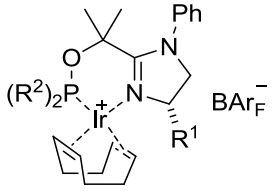
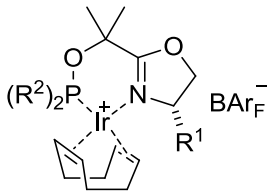
	 **175b**	 **162l**[147a]	 **26m**[116]
Ir-P [Å]:	2.311(1) / 2.310(1)	2.2348(15)	2.3033(8)
Ir-N [Å]:	2.212(4) / 2.210(5)	2.088(5)	2.107(2)
∠ P-Ir-N [°]	87.6(1) / 87.3(1)	85.2(1)	88.74(7)

7.4 Hydrogenation Results

Table 7.5: Hydrogenation of (*E*)-α-methylstilbene (**7**).



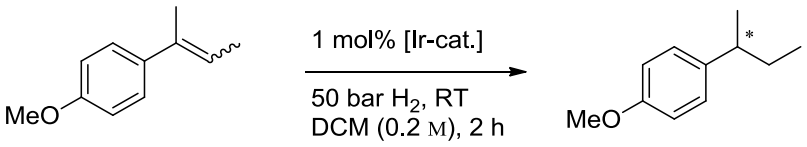
7 **8**

Entry	Ir-catalyst		R^1	R^2	Conv. [%][a]	ee [%][b]
1		(*S*)-**162h**	*t*-Bu	Cy	36	55 (*R*)
2		(*S*)-**162i**	*t*-Bu	*t*-Bu	22	29 (*R*)
3		(*S*)-**162j**	*i*-Pr	Cy	96	91 (*R*)
4		(*S*)-**162k**	*i*-Pr	*t*-Bu	>99	95 (*R*)
5[147a]		(*R*)-**162b**	*i*-Pr	*o*-Tol	>99	87 (*S*)
6		(*S*)-**26h**	Ph	Ph	>99	51 (*R*)
7		(*S*)-**26i**	Bn	Ph	98	89 (*R*)
8		(*S*)-**26d**	*t*-Bu	3,5-CF_3-C_6H_3	>99	88 (*R*)
9[116]		(*S*)-**26k**	*t*-Bu	*t*-Bu	>99	>99 (*R*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

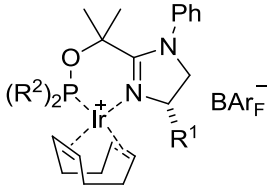
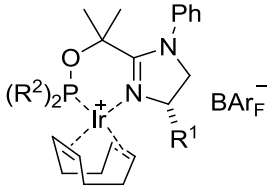
Ir-SimplePHIM complexes bearing *tert*-butyl groups on imidazoline scaffold provided poor activity in the hydrogenation of methylstilbene **7** (table 7.5, entries 1-2). Complexes (*S*)-**162j** and (*S*)-**162k** derived from the less expensive valinol scaffold displayed higher activities and selectivies (entries 3 and 4). The same trend was also previously observed for the P-Aryl SimplePHIM complexes **162a-g**.[147a] The best result was achieved using catalyst (*S*)-**162k** (entry 4), which is superior to complex (*R*)-**162b**. Variations of the SimplePHOX scaffold led to a decrease in selectivity, when compared to the best reported value (entries 6-9).

Table 7.6: Hydrogenation of (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**90** and **91**).



(*E*)-**90**
(*Z*)-**91**

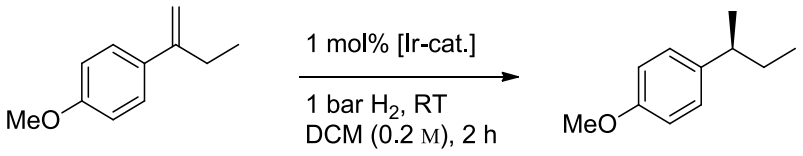
89

Entry	Substrate	Ir-catalyst		R^1	R^2	Conv. [%][a]	*ee* [%][b]
1	(*E*)-**90**		(*S*)-**162h**	*t*-Bu	Cy	83	72 (*R*)
2	(*E*)-**90**		(*S*)-**162i**	*t*-Bu	*t*-Bu	>99	81 (*R*)
3	(*E*)-**90**		(*S*)-**162j**	*i*-Pr	Cy	>99	88 (*R*)
4	(*E*)-**90**		(*S*)-**162k**	*i*-Pr	*t*-Bu	>99	90 (*R*)
5[147a]	(*E*)-**90**		(*R*)-**162b**	*i*-Pr	*o*-Tol	>99	91 (*S*)
6	(*Z*)-**91**		(*S*)-**162h**	*t*-Bu	Cy	60	71 (*S*)
7	(*Z*)-**91**		(*S*)-**162i**	*t*-Bu	*t*-Bu	13	*rac*.
8	(*Z*)-**91**		(*S*)-**162j**	*i*-Pr	Cy	>99	85 (*S*)
9	(*Z*)-**91**		(*S*)-**162k**	*i*-Pr	*t*-Bu	95	80 (*S*)
10[147a]	(*Z*)-**91**		(*S*)-**162a**	*i*-Pr	Ph	>99	94 (*S*)

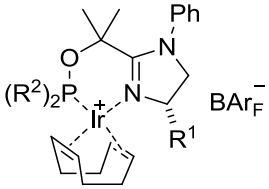
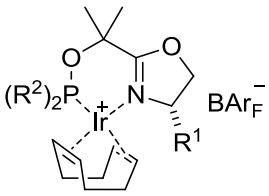
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase.

In the hydrogenation of the (*E*)-olefin **90** and (*Z*)-olefin **91** complexes derived from the less expensive valinol scaffold performed better than the *tert*-leucinol derivatives (table 7.6, entries 1-2 *vs.* 3-4, 6-7 *vs.* 8-9). Moderate enantioselectivities (up to 90%) were achieved using the newly developed P-alkyl Ir-SimplePHIM complexes. These values are lower, when compared to the P-aryl derived complexes.

Table 7.7: Hydrogenation of 2-(4-methoxyphenyl)-1-butene (**88**).



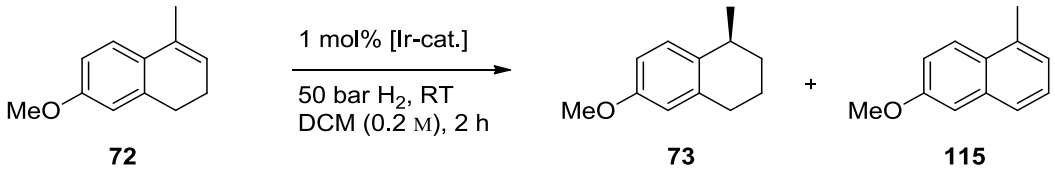
88 **89**

Entry	Ir-catalyst		R^1	R^2	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**162h**	*t*-Bu	Cy	>99	39 (*S*)
2		(*S*)-**162i**	*t*-Bu	*t*-Bu	>99	83 (*S*)
3		(*S*)-**162j**	*i*-Pr	Cy	>99	47 (S)
4		(*S*)-**162k**	*i*-Pr	*t*-Bu	>99	80 (R)
5[147a]		(*S*)-**162a**	*i*-Pr	Ph	>99	44 (*S*)[c]
6		(*S*)-**26h**	Ph	Ph	>99	45 (*S*)
7		(*S*)-**26i**	Bn	Ph	>99	52 (*S*)
8		(*S*)-**26d**	*t*-Bu	3,5-CF_3-C_6H_3	99	86 (*S*)
9[51]		(*S*)-**26a**	*t*-Bu	Ph	>99	78 (*S*)

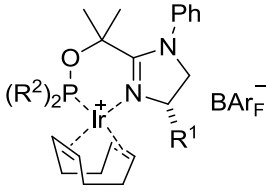
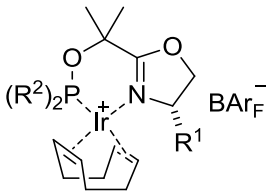
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by GC analysis on a chiral stationary phase; [c]: Result obtained at 50 bar H_2 pressure.

In contrast to the trisubstited olefins **90** and **91** the installation of electron-rich phosphinites (P-alkyl residues) had a beneficial effect on the enantioselectivity in the hydrogenation of terminal C=C bond, found in **88**. The best result of 83% *ee* was achieved using catalyst (*S*)-**162j** (table 7.7, entry 2). Furthermore, the electron-poor phosphinite unit found in SimplePHOX-complex (*S*)-**26d** showed also a positive influence on the hydrogenation of terminal olefin **88**. In this case an *ee* of 86% was achieved (entry 8), which is clearly higher than previously reported (entry 9).

Table 7.8: Hydrogenation of 7-methoxy-1,2-dihydro-naphthalene (**72**).



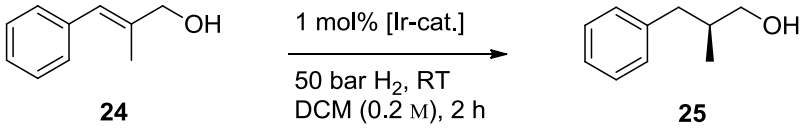
72 **73** **115**

Entry	Ir-catalyst		R^1	R^2	Conv. [%][a]	115 [%][a]	*ee* [%][b]
1		(*S*)-**162h**	*t*-Bu	Cy	57	1	86 (*S*)
2		(*S*)-**162i**	*t*-Bu	*t*-Bu	14	1	77 (*S*)
3		(*S*)-**162j**	*i*-Pr	Cy	78	1	78 (*S*)
4		(*S*)-**162k**	*i*-Pr	*t*-Bu	98	1	79 (*S*)
5[147a]		(*S*)-**162a**	*i*-Pr	Ph	>99	n.o.	88 (*S*)
6		(*S*)-**26h**	Ph	Ph	42	3	86 (*S*)
7		(*S*)-**26i**	Bn	Ph	24	6	75 (*S*)
8		(*S*)-**26d**	*t*-Bu	3,5-CF_3-C_6H_3	44	19	n.d.
9[51]		(*S*)-**25b**	*t*-Bu	*o*-Tol	>99	n.o.	95 (*R*)

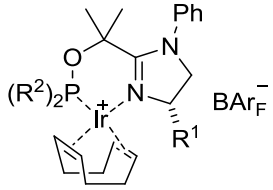
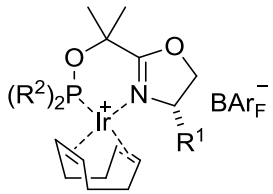
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

For the challenging cyclic substrate **72** none of the newly obtained complexes gave full conversion within two hours (table 7.8). While the most active complex (*S*)-**162k** gave moderate 79% *ee* (entry 4), the less active complex (*S*)-**162h** provided 86% *ee*. All of the new SimplePHOX complexes displayed poor activity and moderate selectivity (entries 6-8).

Table 7.9: Hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**24**).



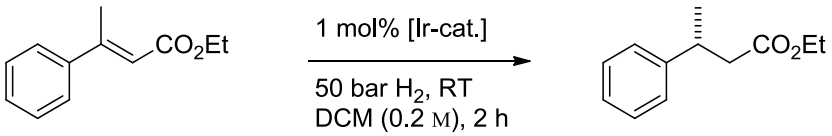
24 **25**

Entry	Ir-catalyst		R^1	R^2	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**162h**	*t*-Bu	Cy	>99	62 (*S*)
2		(*S*)-**162i**	*t*-Bu	*t*-Bu	>99	7 (*S*)
4[147a]		(*S*)-**162a**	*i*-Pr	Ph	>99	96 (*S*)
4		(*S*)-**26h**	Ph	Ph	98	81 (*S*)
5		(*S*)-**26i**	Bn	Ph	98	89 (*S*)
6		(*S*)-**26d**	*t*-Bu	3,5-CF_3-C_6H_3	>99	77 (*S*)
7[51]		(*S*)-**25b**	*t*-Bu	*o*-Tol	>99	97 (*S*)

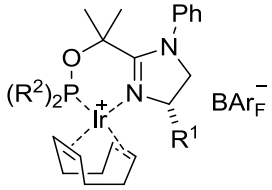
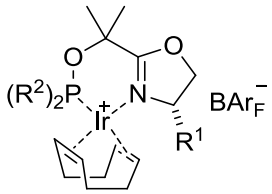
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

In general, low enantioselectivities were obtained using P-alkyl Ir-SimplePHIM complexes in the hydrogenation of allylic alcohol **24** (Table 7.9, entries 1-2). On the other hand SimplePHOX derived catalysts led to full conversion, but no improvement in enantioselectivity compared to the previously reported complexes (entries 4-6 *vs.* 7).

Table 7.10: Hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**98**).



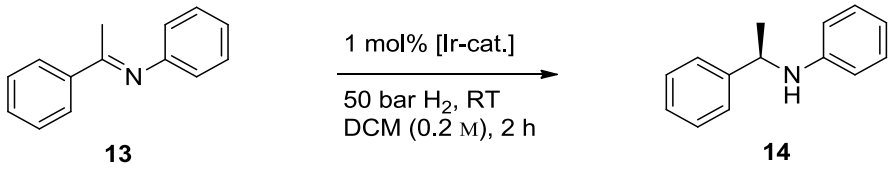
98 **99**

Entry	Ir-catalyst		R^1	R^2	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**162h**	*t*-Bu	Cy	>99	5 (*R*)
2		(*S*)-**162i**	*t*-Bu	*t*-Bu	46	42 (*R*)
3		(*S*)-**162j**	*i*-Pr	Cy	98	40 (*R*)
4		(*S*)-**162k**	*i*-Pr	*t*-Bu	>99	83 (*R*)
5[147a]		(*R*)-**162b**	*i*-Pr	*o*-Tol	>99	91 (*S*)
6		(*S*)-**26h**	Ph	Ph	>99	82 (*R*)
7		(*S*)-**26i**	Bn	Ph	75	85 (*R*)
8		(*S*)-**26d**	*t*-Bu	3,5-CF_3-C_6H_3	9	77 (*R*)
9[116]		(*S*)-**26k**	*t*-Bu	*t*-Bu	>99	>99 (*R*)

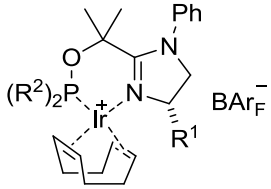
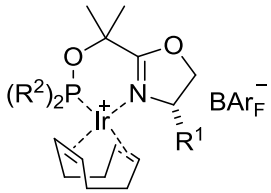
[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

The introduction of P-alkyl residues did not give any improvement in *ee* in the hydrogenation of the α,β-unsaturated ester **98** (table 7.10, entries 1-4). However, these complexes demonstrate the beneficial effect of an isopropyl residue compared to *tert*-butyl group on the imidazoline ring (entries 1 *vs.* 3, 2 *vs.* 4). The new SimplePHOX (*S*)-**26h-i** complexes showed moderate enantioselectivities (entries 6-8). Furthermore, the installation of electron-poor phosphinite (**26k**) reduced the activity significantly (entry 8).

Table 7.11: Hydrogenation of (*E*)-*N*-(1-phenylethylidene)aniline (**13**).



13 **14**

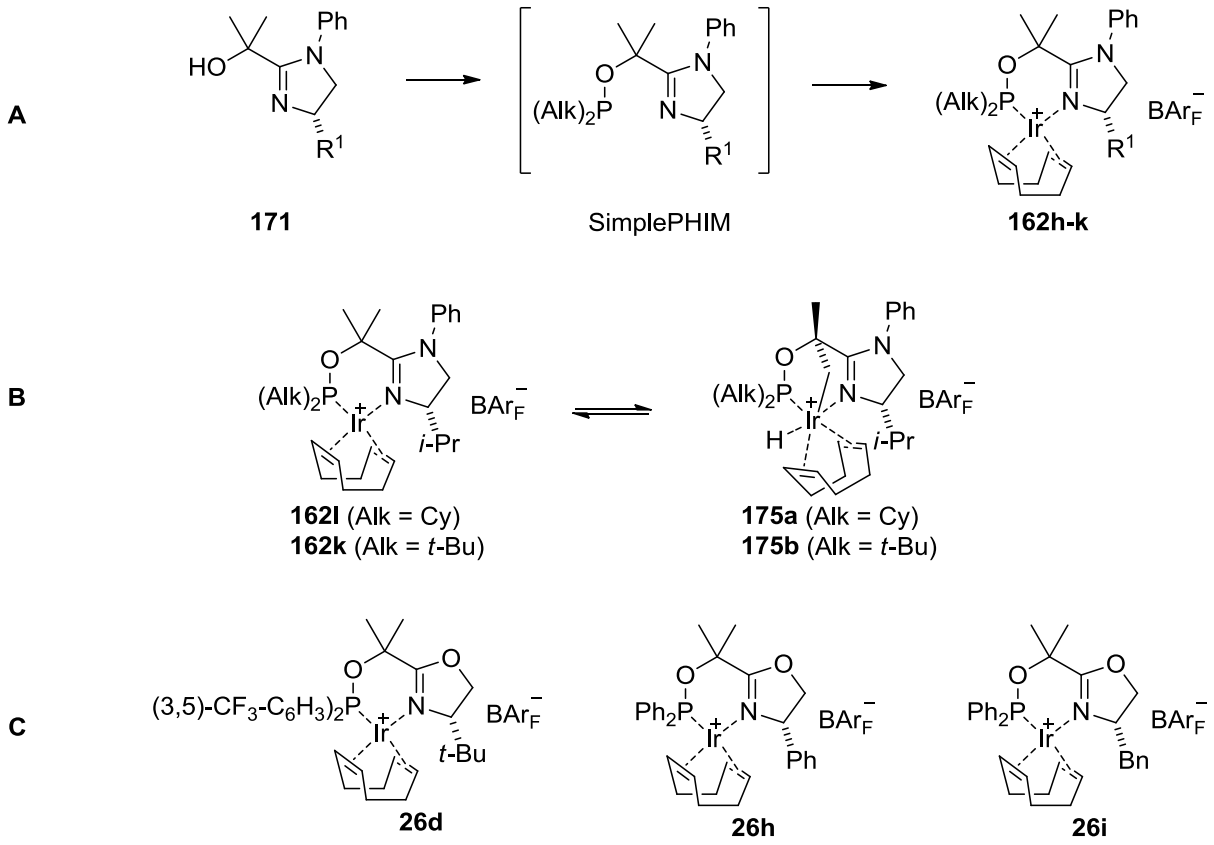
Entry	Ir-catalyst		R^1	R^2	Conv. [%][a]	*ee* [%][b]
1		(*S*)-**162h**	*t*-Bu	Cy	16	61 (*R*)
2		(*S*)-**162i**	*t*-Bu	*t*-Bu	30	25 (*R*)
3		(*S*)-**162j**	*i*-Pr	Cy	>99	85 (*R*)
4		(*S*)-**162k**	*i*-Pr	*t*-Bu	85	64 (*R*)
5		(*S*)-**26h**	Ph	Ph	>99	44 (*R*)
6		(*S*)-**26i**	Bn	Ph	>99	32 (*R*)
7		(*S*)-**26d**	*t*-Bu	3,5-CF_3-C_6H_3	>99	45 (*R*)
8[116]		(*S*)-**26l**	Cy	*i*-Pr	>99	88 (*R*)

[a]: Determined by GC analysis of the reaction mixture after removal of the catalyst; [b]: Determined by HPLC analysis on a chiral stationary phase.

Beside complex (*S*)-**162j**, most of the newly Ir-SimplePHIM complexes did not reach full conversion in the hydrogenation of acetophenone imine **13**. However, the most active catalyst (*S*)-**162j** provided a respectable 85% *ee*. All of the SimplePHOX derivatives gave full conversion, but significantly lower *ee* (entries 5-7), as obtained with best complex of this family (entry 8).

7.5 Summary

In summary, the synthesis of P-alkyl Ir-SimplePHIM complexes **162h-k** starting from imidazolinyl alcohol **171** is described (scheme 7.9A). Complexes having P-Alkyl substituents and an isopropyl group on the imidazoline were found to undergo a reversible cyclomellation reaction, furnishing a tridentate C,N,P complex **175a-b** (scheme 7.9B). Furthermore, the Ir-SimplePHOX family was extended with three new members **26d**, **26h** and **26i** (scheme 7.9C).



Scheme 7.9: Synthesis of P-alkyl SimplePHIM derived Ir-complexes **162h-k** and three new members of the Ir-SimplePHOX family.

Applying these new complexes in the hydrogenation of model olefins high activities but moderate enantioselectivities were obtained. For methylstilbene and acetophenone imine the obtained enantioselectivities were higher compared to those previously reported for P-aryl SimplePHIM complexes **162a-g**. Although the P-alkyl Ir-SimplePHIM complexes **162l-k** bearing isopropyl group on imidazoline were found to stay in equilibrium with their cyclometallated form **175a-b**, they were more active in the hydrogenation compared to the complexes having *tert*-butyl groups on the N-donor. The newly obtained Ir-SimplePHOX complexes (**26d**, **26h** and **26i**) did not provide any significantly improved enantioselectivity compared to previously prepared SimplePHOX catalysts.

Chapter 8

Experimental Part

8.1 Working Techniques

Commercially available reagents were purchased from Acros, Aldrich, Alfa-Aesar, Fluka, Frontier Scientific, Strem or TCI and used as received. The solvents were collected from a purification column system (PureSolv, Innovative Technology Inc.)[149] or purchased from Aldrich or Fluka in sure/sealedTM bottles over molecular sieves. Column chromatographic purifications were performed on Merck silica gel 60 (particle size 40-63 nm) according to the procedure published by *Still* and *Mitra*.[150] The eluents were of technical grade and distilled prior to use. The hydrogenation experiments were obtained in air.

8.2 Analytical Methods

Thin Layer Chromatography (TLC): TLC plates were obtained from *Macherey-Nagel* (Polygram SIL/UV254, 0.2 mm silica with fluorescence indicator). UV light (254 nm) or basic permanganate solution were used to visualize the respective compounds.

NMR-Spectroscopy: NMR spectra were measured either on a Bruker DPX-NMR (400 MHz), on a Bruker BZH-NMR (250 MHz) or a Bruker Avance DRX-NMR (500 MHz) spectrometer equipped with BBO broadband probe heads. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent peaks and coupling constants (J) are reported in Hertz (Hz). Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc. (Andover, MA, USA). The measurements were performed at 25 °C, if nothing else is reported. The chemical shift δ values were corrected to 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR) for $CHCl_3$, 5.32 ppm (^{1}H NMR) and 54.0 ppm (^{13}C NMR) for CH_2Cl_2.^{19}F NMR spectra relative to $CFCl_3$ (δ = 0 ppm) and ^{11}B NMR spectra relative to $BF_3 \cdot OEt_2$ (δ = 0 ppm) as external standards. ^{13}C, ^{19}F and spectra were recorded ^{1}H-decoupled. Carbon atoms directly attached to the boron were not detected in ^{13}C spectra (quadrupole relaxation) for the alkynyl boronic esters.[141, 151] The assignment of ^{1}H and ^{13}C signals was partly made by 2D-NMR, namely COSY, HMQC, HMBC and NOSY. Multiplicities are reported as follows: s=singlet, d=doublet, t=triplet, q=quartet, quin=quintet, m=multiplet and b=broad.

Mass Spectrometry (MS): Mass spectra were measured by Dr. H. Nadig (Department of Chemistry, University of Basel) on a VG70-250 (electron ionization (EI)) mass spectrometer or a MAR 312 (fast atom bombardment (FAB)) mass spectrometer. FAB was performed with

3-nitrobenzyl alcohol (NBA) as matrix. The signals are given in mass to charge ratio (*m/z*). The fragment and intensities are given in brackets. All values are rounded to the nearest whole number.

High Resolution Mass Spectrometry (HRMS): High Resolution Mass spectra were measured by the group of Dr. Xiangyang Zhang (Department of Chemistry, ETH Zürich) on a Micromass (Waters) AutoSpec Ultima.

Infrared Spectroscopy (IR): The IR spectra were recorded on a Shimadzu FTIR-8400S Fourier Transform spectrometer with ATR/Golden Gate technology. The absorption bands are given in wave numbers ϑ (cm−1). The peak intensity is assigned with s (strong), m (medium) and w (weak). The index br stands for broad.

Optical Rotations ($[\alpha]_D^{20}$): Optical rotations were measured on a Perkin Elmer Polarimeter 341 (1 dm cylindrical cell) or on a Jasco P-2000 Polarimeter (1 dm cylindrical cell) at 589 nm. The concentration (*c*) is given in g/100 mL.

Elemental Analysis (EA): Elemental analyses were measured by Mr. W. Kirsch and Sylvie Mittelheiser (Department of Chemistry, University of Basel) on a Leco CHN-900 or a Vario Micro Cube by Elementar (C-, H-, N-detection). The data are indicated in mass percent.

Melting Points (m.p.): Melting points were determined on a Büchi B-545 apparatus and were not corrected.

High Performance Liquid Chromatography (HPLC): HPLC analysis was measured on Shimadzu Class-VP Version 5.0 systems with SCL-10A system controller, LC-10AD pump system, SIL-10AD auto injector, CTO-10AC column oven, DGU-14A degasser and SPD-M10A diode array- or UV/VIS detector or on Shimadzu LC-20A prominence with LC-20AD pump system, SIL-20AHT auto injector, CTO-10AS column oven, SPD-M20A diode array, DGU-20A3 degasser. Chiral columns *Chiralcel* AD-H, IC, OD-H, or OJ-H (4.6 mm × 250 mm) from Daicel Chemical Industries were used.

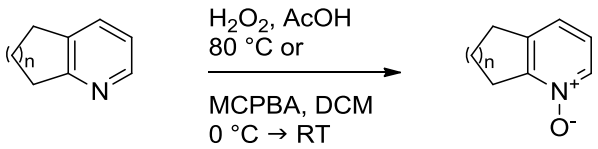
Gas Chromatography (GC): Gas chromatograms were recorded on a Carlo Erba HRGC Mega2 Series 800 (HRGS Mega2) or a GC-2010 Plus von Shimadzu instruments. Achiral separations were performed on a *Restek* Rtx®-1701 column (30 m × 0.25 mm × 0.25 μm) using helium as carrier gas. For the separations of enantiomers *Chiraldex G-TA*, γ–cyclodextrin TFA column (30 m × 0.25 mm × 0.25 μm), *Macherey-Nagel* Hydrodex-ß-3P (25 m × 0.25 mm × 0.25 μm), *Brechbühler SE54* ß-cyclodextrin DEtTButSil (25 m × 0.25

mm × 0.25 µm), *Varian* CP-Chiralsil-dex CB (25 m × 0.25 mm × 0.25 µm) *Varian* CP-Sil 88 (25 m × 0.25 mm × 0.25 µm) were used with H_2 as carrier gas.

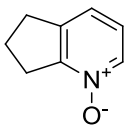
Gas Chromatography-Mass Spectrometry (GC-MS): The GC-MS spectra were recorded on a HP5890 gas chromatograph with a HP5970A detector equipped with a Macherey and Nagel Optima5 (5% polyphenylmethylsiloxane column, 25 m × 0.2 mm × 35 µm), a HP5890 gas chromatograph with a HP5971 detector equipped with a Agilent HP1 (1% dimethylsiloxane column, 15 m × 0.2 mm × 33 µm). For both instruments the flow was set to 1 mL/min with 20:1 split ratio. A Shimadzu GCMS-QP2010 SE equipped with a *Restek* Rtx®-5MS (30 m × 0.2 mm × 0.2 µm) was used too. For this instrument the carrier pressure (He) was set to 100 kPa with 40:1 split ratio.

8.3 Development of a New Synthetic Route to Bicyclic Pyridine-Phosphinite Ligands and Their Corresponding Ir-Complexes

8.3.1 Formation of N-Oxides



6,7-Dihydro-*5H*-cyclopenta[1]pyridine-*N*-oxide (69a)

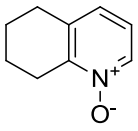


6,7-dihydro-5*H*-cyclopenta[1]pyridine (10.0 g, 83.9 mmol, 1.0 eq.) was added to a solution of MCPBA (24.8 g, 101 mmol, 1.2 eq.) in DCM (100 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirring was continued for additional 1.5 h. The reaction mixture was again cooled down to 0 °C and NaOH 2 M aq. solution (100 mL) was added. The layers were separated and the aq. phase was extracted with with DCM (5×250 mL). Combined organic layers were washed with brine (200 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The obtained crude N-oxide was purified by recrystallization from a boiling mixture of *n*-heptane (7 mL) and toluene (4 mL) to obtain the title compound **69a** as a pale yellow solid (8.16 g, 60.4 mmol, 72%). The analytical data match the reported values.[57b]

C_8H_9NO (135.16 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.05 (dd, *J* = 7.3, 1.8 Hz, 1H, H_{Ar}), 7.13 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.08 (dd, *J* = 7.3, 7.8 Hz, 1H, H_{Ar}), 3.18 (t, *J* = 7.6 Hz, 2H, CH_2), 3.03 (t, *J* = 7.6 Hz, 2H, CH_2), 2.19 (pentet, *J* = 7.6 Hz, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 153.5 (C_{Ar}), 142.6 (C_{Ar}), 137.7 (HC_{Ar}), 124.2 (HC_{Ar}), 122.9 (HC_{Ar}), 32.0 (CH$_2$), 29.9 (CH$_2$), 22.4 (CH$_2$) ppm. **m.p.**: 119–120°C; lit. 117 °C.[57b]

5,6,7,8-Tetrahydroquinoline-*N*-oxide (69b)

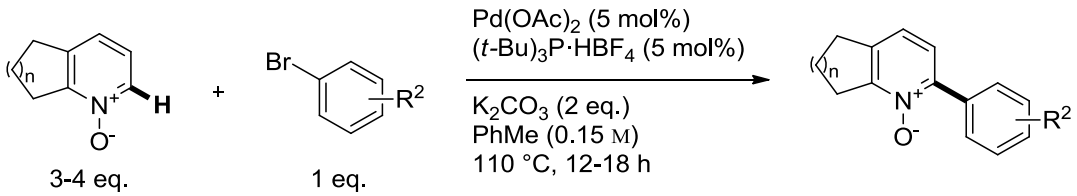


Hydrogen peroxide 30 w% solution (26.0 mL, 23.5 g, 255 mmol, 3.4 eq), was added to a solution of 5,6,7,8-tetrahydroquinoline (10.3 mL, 10.0 g, 75.1 mmol, 1.0 eq.) and acetic acid (48.5 mL, 50.9 g, 847 mmol, 11.3 eq.). The reaction mixture was stirred at 80 °C for 18 h. The reaction mixture was cooled down to 0 °C and NaOH 3 M aq. solution (200 mL) was added. The mixture was extracted with DCM (5×250 mL). The combined organic layers were washed with brine (200 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The obtained crude N-oxide was purified by flash chromatography (SiO_2, 6 cm × 10 cm, cyclohexane / ethyl acetate 1:4) to obtain the title compound **69b** as a pale yellow solid (9.10 g, 61.0 mmol, 81%). The analytical data match the reported values.[57b]

$C_9H_{11}NO$ (149.19 g/mol):

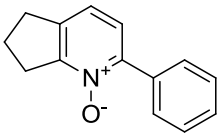
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 7.5 Hz, 1H, H_{Ar}), 7.02–6.96 (m, 2H, H_{Ar}), 2.90 (t, *J* = 6.2 Hz, 2H, CH_2), 2.73 (t, *J* = 6.2 Hz, 2H, CH_2), 1.91–1.81 (m, 2H, CH_2), 1.79–1.68 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 147.2 (C_{Ar}), 137.3 (C_{Ar}), 136.8 (HC_{Ar}), 126.7 (HC_{Ar}), 122.4 (HC_{Ar}), 29.0 (CH$_2$), 25.1 (CH$_2$), 22.2 (CH$_2$), 22.0 (CH$_2$) ppm. **m.p.**: 80–81 °C; lit. 83 °C.[57b] **TLC** (SiO_2, cyclohexane / ethyl acetate 1:4): R_f = 0.10.

8.3.3 Arylations of N-oxides



General Procedure A: A solution of aryl bromide (1.0 eq.) in toluene (0.3 M) was slowly added to a mixture of N-oxide (3.0 eq.), $Pd(OAc)_2$ (5 mol%), $(t\text{-Bu})_3P{\cdot}HBF_4$ (5 mol%), K_2CO_3 (2.0 eq.) in toluene (0.3 M). The reaction mixture was stirred for 15-18 hours at 125 °C. After cooling down to rt the reaction mixture was filtered over a pad of *Celite*® and rinsed with DCM (50-150 mL). Water (100 mL) was added to the obtained filtrated and the mixture was extracted with DCM (5×100-150 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography.

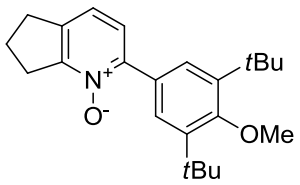
2-Phenyl-6,7-dihydro-*5H*-cyclopenta[1]pyridine-*N*-oxide (53a)



The title compound **53a** was obtained following the general procedure **A** using phenyl bromide (388 mg, 2.47 mmol, 1.0 eq) in toluene (8.0 mL), **69a** (1.00 g, 7.40 mmol, 3.0 eq.), $Pd(OAc)_2$ (27.7 mg, 123 µmol, 5 mol%), $(t\text{-Bu})_3P{\cdot}HBF_4$ (35.8 mg, 123 µmol, 5 mol%), K_2CO_3 (682 mg, 4.93 mmol, 2.0 eq.) in toluene (8.0 mL) and after purification by flash chromatography (SiO_2, 3 cm × 15 cm, ethyl acetate) as a pale yellow solid (285 mg, 1.35 mmol, 55%). The analytical data match the reported values.[57b]

$C_{14}H_{13}NO$ (211.26 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.73 (dd, *J* = 7.7, 1.1 Hz, 2H, H_{Ar}), 7.40–7.34 (m, 3H, H_{Ar}), 7.18 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.07 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 3.14 (t, *J* = 7.1 Hz, 2H, CH_2), 2.99 (t, *J* = 7.1 Hz, 2H, CH_2), 2.20–2.10 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 154.2 (C_{Ar}), 148.0 (C_{Ar}), 141.9 (C_{Ar}), 133.4 (C_{Ar}), 129.8 (HC_{Ar}), 129.5 (HC_{Ar}), 128.5 (HC_{Ar}), 125.7 (HC_{Ar}), 122.5 (HC_{Ar}), 32.1 (CH_2), 30.5 (CH_2), 22.7 (CH_2) ppm. **m.p.**: 123–124 °C; lit. 125 °C.[57b] **TLC** (SiO_2, ethyl acetate): R_f = 0.15.

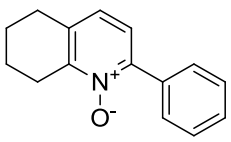
2-(3,5-Di-*tert*-butyl-4-methoxyphenyl)-6,7-dihydro-*5H*-cyclopenta[1]pyridine-*N*-oxide (53c)



The title compound **53c** was obtained following the general procedure **A** using 5-bromo-1,3-di-*tert*-butyl-2-methoxybenzene (2.20 g, 7.66 mmol, 1.0 eq.), **69a** (3.11 g, 23.0 mmol, 3.0 eq.), $Pd(OAc)_2$ (86.1 mg, 390 µmol, 5 mol%), $(t\text{-Bu})_3P{\cdot}HBF_4$ (111 mg, 390 µmol, 5 mol%), K_2CO_3 (2.12 g, 15.3 mmol, 2.0 eq.) in toluene (50 mL) and after purification by flash chromatography (SiO_2, 3 cm × 19 cm, DCM → DCM / MeOH 98:2) as a black solid (960 mg, 2.72 mmol, 36%).

$C_{23}H_{31}NO_2$ (353.50 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.67 (s, 2H, H_{Ar}), 7.18 (d, J = 7.3 Hz, 1H, H_{Ar}), 7.06 (d, J = 7.3 Hz, 1H, H_{Ar}), 3.65 (s, 3H, OCH_3), 3.16 (t, J = 7.5 Hz, 2H, CH_2), 2.98 (t, J = 7.5 Hz, 2H, CH_2), 2.15 (pentet, J = 7.5 Hz, 2H, CH_2), 1.38 (s, 18H, $(CH_3)_3C$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 160.7 (C_{Ar}), 154.1 (C_{Ar}), 148.2 (C_{Ar}), 143.5 (C_{Ar}), 140.1 (C_{Ar}), 128.6 (HC_{Ar}), 127.5 (C_{Ar}), 125.6 (HC_{Ar}), 122.5 (HC_{Ar}), 64.7 (OCH_3), 36.3 $(CH_3)_3C$), 32.5 $(CH_3)_3C$), 32.1 (CH_2), 30.6 (CH_2), 22.7 (CH_2) ppm. **TLC** (SiO_2, DCM / MeOH 98:2): R_f = 0.26.

2-Phenyl-5,6,7,8-tetrahydroquinoline-*N*-oxide (53b)

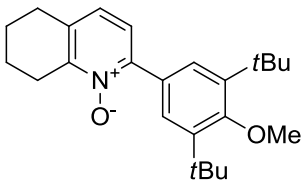


The title compound **53b** was obtained following the general procedure **A** using 5-bromo-1,3-di-*tert*-butyl-2-methoxybenzene (2.20 g, 7.66 mmol, 1.0 eq.), **69b** (3.43 g, 23.0 mmol, 3.0 eq.), $Pd(OAc)_2$ (27.7 mg, 123 µmol, 5 mol%), $(t\text{-Bu})_3P{\cdot}HBF_4$ (35.8 mg, 123 µmol, 5 mol%), K_2CO_3 (682 mg, 4.93 mmol, 2.0 eq.) in toluene (50 mL) and after purification by flash chromatography (SiO_2, 3 cm × 16 cm, ethyl acetate) as a pale yellow solid (184 mg, 0.817 mmol, 33%). The analytical data match the reported values.[57b]

$C_{15}H_{15}NO$ (225.28 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.70 (dd, J = 7.1, 1.2 Hz, 2H, H_{Ar}), 7.40–7.28 (m, 3H, H_{Ar}), 7.14 (d, J = 7.1 Hz, 1H, H_{Ar}), 6.97 (d, J = 7.1 Hz, 1H, H_{Ar}), 2.92 (t, J = 7.8 Hz, 2H, CH_2), 2.74 (t, J = 7.8 Hz, 2H, CH_2), 1.90–1.82 (m, 2H, CH_2), 1.74–1.68 (m, 2H, CH_2) ppm.

^{13}C{^{1}H}-NMR (101 MHz, $CDCl_3$): δ = 149.7 (C_{Ar}), 147.1 (s, C_{Ar}),135.3 (C_{Ar}), 134.1 (C_{Ar}), 129.8 (HC_{Ar}), 129.4 (HC_{Ar}), 128.5 (HC_{Ar}), 126.1 (HC_{Ar}), 123.8 (HC_{Ar}), 29.1 (CH_2), 25.6 (CH_2), 22.5 (CH_2), 22.1 (CH_2) ppm. **m.p.**: 129–130 °C; lit. 137 °C.[57b] **TLC** (SiO_2, ethyl acetate): R_f = 0.25.

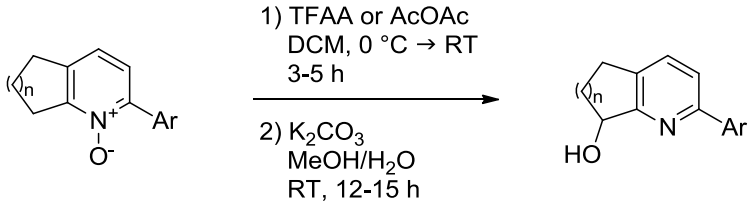
2-(3,5-Di-*tert*-butyl-4-methoxyphenyl)-5,6,7,8-tetrahydroquinoline-*N*-oxide (53d)



The title compound **53d** was obtained following the general procedure **A** using phenyl bromide (388 mg, 2.47 mmol, 1.0 eq) in toluene (8.0 mL), **69b** (1.10 g, 7.40 mmol, 3.0 eq.), $Pd(OAc)_2$ (27.7 mg, 123 µmol, 5 mol%), (t-Bu)$_3$P·HBF_4 (35.8 mg, 123 µmol, 5 mol%), K_2CO_3 (2.12 g, 15.3 mmol, 2.0 eq.) in toluene (50 mL) and after purification by flash chromatography (SiO_2, 3 cm × 18 cm, cyclohexane / DCM 1:1 → cyclohexane / DCM / ethyl acetate 5:5:2) as a black solid (184 mg, 0.817 mmol, 33%).

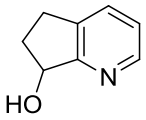
$C_{24}H_{33}NO_2$ (367.52 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.70 (s, 2H, H_{Ar}), 7.21 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.01 (d, J = 7.7 Hz, 1H, H_{Ar}), 3.72 (s, 3H, OCH_3), 3.05–2.94 (m, 2H, CH_2), 2.82–2.74 (m, 2H, CH_2), 1.93–1.87(m, 2H, CH_2), 1.85–1.76 (m, 2H, CH_2), 1.45 (s, 18H, $(CH_3)_3C$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 160.6 (C_{Ar}), 149.5 (C_{Ar}), 147.5 (C_{Ar}), 143.5 (C_{Ar}), 134.3 (C_{Ar}), 128.6 (HC_{Ar}), 128.2 (HC_{Ar}), 126.1 (HC_{Ar}), 123.7 (HC_{Ar}), 64.7 (OCH_3), 36.3 $(CH_3)_3C$), 32.5 $(CH_3)_3C$), 29.1 (CH_2), 25.7 (CH_2), 22.6 (CH_2), 22.1 (CH_2) ppm. **TLC** (SiO_2, cyclohexane / DCM / ethyl acetate 5:5:2): R_f = 0.20.

8.3.4 Boekelheide Rearrangement and Hydrolysis



General Procedure B: Trifluoroacetic anhydride (2.5 eq.) or acetic anhydride (2.5 eq.) was slowly added to a solution of the N-oxide (1 eq.) in DCM (0.9–1.0 M) at 0 °C. After stirring for 3-12 h at RT, the volatiles were removed under in *vacuo*. The crude acetate was dissolved in MeOH / water 1:1 mixture (0.3 M) and hydrolyzed with K_2CO_3 (>2.5 eq.). After stirring for additional 12-16 h at RT, the reaction mixture was extracted with DCM (3×20-50 mL). Combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography or by recrystallization.

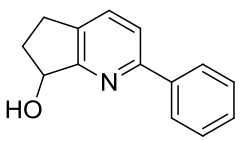
6,7-Dihydro-*5H*-cyclopenta[1]pyridin-7-ol (78a)



The title compound **78a** was obtained following the general procedure **B** using **69a** (1.18 g, 8.73 mmol, 1.0 eq.) in DCM (10 mL), acetic anhydride (2.0 mL, 2.16 g, 21.2 mmol, 2.5 eq.) during 4 h; subsequent hydrolysis using K_2CO_3 (2.80 g, 20.3 mmol, 2.4 eq.) in MeOH / water 1:1 (30 mL) during 16 h at rt and purification by flash chromatography (SiO_2, 3.5 cm × 40 cm, ethyl acetate / cyclohexane 20:1→ 1:0) as a slightly yellow solid (325 mg, 2.40 mmol, 28%). The analytical data match the reported values.[57b]

C_8H_9NO (135.16 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.44–7.42 (m, 1H, H_{Ar}), 7.57 (dd, J = 7.6, 1.1 Hz, 1H, H_{Ar}), 7.15 (dd, J = 7.6, 4.9 Hz, 1H, H_{Ar}), 5.24 (t, J = 6.8 Hz, 1H, C*H*), 4.49 (br s, 1H, O*H*), 3.09–3.02 (m, 1H, CH_2), 2.87–2.80 (m, 1H, CH_2), 2.60–2.52 (m, 1H, CH_2CH(OH)), 2.11–2.02 (m, 1H, CH_2CH(OH)) ppm.

2-Phenyl-6,7-dihydro-*5H*-cyclopenta[1]pyridin-7-ol (54a)

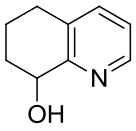


The title compound **54a** was obtained following the general procedure **B** using **53a** (280 mg, 1.33 mmol, 1.0 eq.), DCM (5.0 mL), TFAA (443 µL, 696 mg, 3.31 mmol, 2.5 eq.); subsequent hydrolysis using MeOH (2.0 mL) and K_2CO_3 1 M aq. solution (20 mL) and purification by flash chromatography (SiO_2, 1.5 cm × 19 cm, cyclohexane / ethyl acetate 1:1) as a slightly yellow solid (220 mg, 1.04 mmol, 79%). The analytical data match the reported values.[57b]

$C_{14}H_{13}NO$ (211.26 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.95 (dd, *J* = 7.2 Hz, 1.3 Hz, 2H, H_{Ar}), 7.65–7.58 (m, 2H, H_{Ar}), 7.47–7.35 (m, 3H, H_{Ar}), 5.29–5.21 (m, 1H, C*H*), 3.60 (br s, 1H, O*H*), 3.05–2.99 (m, 1H, CH_2), 2.85–2.70 (m, 1H, CH_2), 2.54–2.48 (m, 1H, CH_2), 2.12–1.97 (m, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 165.1 (C_{Ar}), 157.0 (C_{Ar}), 139.9 (C_{Ar}), 135.2 (C_{Ar}), 134.2 (HC_{Ar}), 129.1 (HC_{Ar}), 127.4 (HC_{Ar}), 120.5 (HC_{Ar}), 75.2 (*C*H), 33.5 (*C*H_2), 27.6 (*C*H_2) ppm. **m.p.**: 118–119°C; lit. 119 °C.[57b] **TLC** (SiO_2, cyclohexane / ethyl acetate 1:1): R_f = 0.70.

5,6,7,8-Tetrahydroquinolin-8-ol (78b)

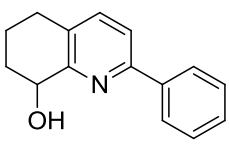


The title compound **78b** was obtained following the general procedure **B** using **69b** (7.93 g, 53.2 mmol, 1.0 eq.), DCM (100 mL), TFAA (20 mL, 29.6 g, 141 mmol, 2.6 eq.); subsequent hydrolysis using K_2CO_3 (14.0 g, 101 mmol, 1.9 eq.) in MeOH / water 1:1 mixture (150 mL) and purification by recrystallization from boiling TBME (10 mL) as a pale yellow solid (5.46 g, 36.6 mmol, 69%). The analytical data match the reported values.[57b]

$C_9H_{11}NO$ (149.19 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.45–8.34 (m, 1H, H_{Ar}), 7.44–7.38 (m, 1H, H_{Ar}), 7.12 (dd, *J* = 7.7, 4.8 Hz, 1H, H_{Ar}), 4.71 (t, *J* = 7.0 Hz, 1H, C*H*), 4.21 (s, 1H, O*H*), 2.89–2.73 (m, 2H, CH_2), 2.33–2.22 (m, 1H, CH_2), 2.06–1.95 (m, 1H, CH_2), 1.87–1.74 (m, 2H, CH_2) ppm. **MS** (FAB NBA) *m/z* (%): 150 ([M+H]$^+$, 100, 132 (34). **EA**: calc. (%) C 72.46, H 7.43, N 9.39; found C 72.23, H 7.30, N 9.41. **m.p.**: 67–68°; lit. 65 °C.[57b]

2-Phenyl-5,6,7,8-tetrahydroquinolin-8-ol (54b)

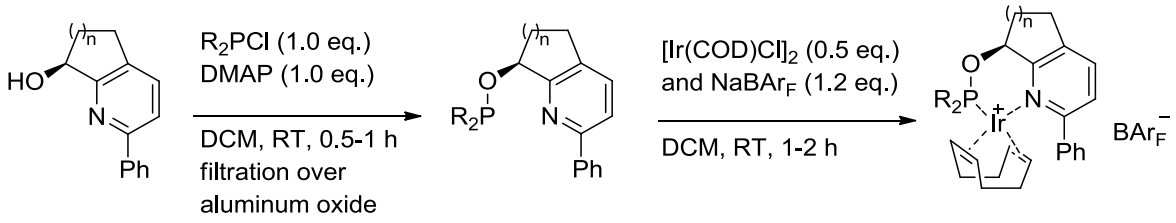


The title compound **54b** was obtained following the general procedure **B** using **53b** (180 mg, 800 µmol, 1.0 eq.), DCM (5 mL), TFAA (279 µL, 421 mg, 2.00 mmol, 2.5 eq.); subsequent hydrolysis using MeOH (2.0 mL) and K_2CO_3 1 M aq. solution (20 mL) and purification by by flash chromatography (SiO_2, 1.5 cm × 16 cm, cyclohexane / ethyl acetate 1:1) as a slightly yellow solid (112 mg, 497 µmol, 62%). The analytical data match the reported values.[57b]

$C_{15}H_{15}NO$ (225.28 g/mol):

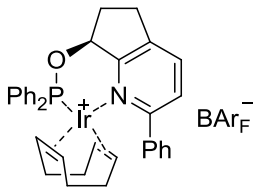
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 7.1, 1.2 Hz, 2H, H_{Ar}), 7.50 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.42–7.35 (m, 3H, H_{Ar}), 7.34–7.30 (m, 1H, H_{Ar}), 4.68–4.65 (m, 1H, C*H*), 4.26 (s, 1H, O*H*), 2.79–2.72 (m, 2H, CH_2), 2.32–2.25 (m, 1H, CH_2), 1.96–1.89 (m, 1H, CH_2) 1.87–1.75 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 158.1 (C_{Ar}), 154.7 (C_{Ar}), 139.3 (C_{Ar}), 138.1 (HC_{Ar}), 130.3 (C_{Ar}), 129.3 (HC_{Ar}), 129.1 (HC_{Ar}), 127.1 (HC_{Ar}), 119.6 (HC_{Ar}), 69.6 (*C*H), 31.1 (*C*H_2), 28.4 (*C*H_2), 20.1 (*C*H_2) ppm. **m.p.**: 80–81 °C; lit. 82 °C.[57b] **TLC** (SiO_2, cyclohexane / ethyl acetate 1:1): R_f = 0.54.

8.3.5 Formation of N,P Ligands From Pyridyl Alcohols and Subsequent Complexation with Iridium



General Procedure C: A *Schlenk* flask was charged with pyridyl alcohol (1.0 eq.) and 4-dimethylaminopyridine (1.0 eq.). The Schlenk flask was evacuated three times and each time backfilled with argon. The mixture was dissolved in DCM (0.5 mL) and was treated with the corresponding chlorophosphine (1.0 eq.). The reaction was stirred at room temperature for 30-60 minutes, until ^{31}P-NMR shows full conversion. A second *Schlenk* flask was filled with $[Ir(COD)Cl]_2$ (0.5 eq.), $NaBAr_F$ (1.2 eq.) and assembled with a *Schlenk* fritt. The *Schlenk* fritt was charged with basic aluminum oxide (brockman activity 1, d×h, 2 cm × 1 cm). The equipment was evacuated three times and each time backfilled with argon. The ligand containing solution was filtered over the aluminum oxide layer and rinsed with DCM (5-10 mL). The new obtained reaction mixture was stirred at room temperature for 1-2 hours until ^{31}P-NMR shows full conversion. Afterwards the solvent was removed under reduced pressure. The crude Ir-complex was purified by flash chromatography. First side products were separated by elution with TBME and then the desired Ir-complex was washed down with DCM (collecting the orange-red band). If required the Ir-complex was recrystallized by overlaying a saturated etheral solution with *n*-pentane.

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-7-(2-phenyl-6,7-dihydro-*5H*-[1]pyrindine)-diphenylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate (36a)



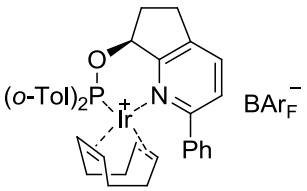
Ir-complex **36a** was obtained following the general procedure **C** using pyridyl alcohol (*S*)-**54a** (29.4 mg, 139 µmol, 1.0 eq.), DMAP (17.0 mg, 139 µmol, 1.0 eq.), chlorodiphenylphosphine (25.0 µL, 30.7 mg, 139 µmol, 1.0 eq.), DCM (0.5 mL), $[Ir(COD)Cl]_2$ (47.0 mg, 70.0 µmol, 0.5 eq.), $NaBAr_F$ (148 mg, 167 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 20 cm) and recrystallization from diethyl ether (2 mL) / *n*-petane (50 mL) as an orange solid (137 mg, 87.8 µmol, 63%). Suitable crystals for X-ray analysis were obtained by overlaying a concentrated etheral solution with *n*-pentane.

^{31}P{^{1}H}-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 108.5 (s) ppm.

$C_{66}H_{46}BF_{24}IrNOP$ (1559.06 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.88 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.82–7.74 (m, 10H, BAr_F-*H*, H_{Ar}), 7.73–7.67 (dd, *J* = 11.4 Hz, 7.6, 3H, H_{Ar}), 7.65 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.63–7.55 (m, 6H, BAr_F-*H*, H_{Ar}), 7.55–7.41 (m, 8H, H_{Ar}), 6.43–6.46 (m, 1H, C*H*OP), 4.69–4.59 (br s, 1H, C*H* COD), 4.37 (m_c, *J* = 2.7 Hz, 1H, C*H* COD), 3.32–3.20 (m, 1H, Ar-CH_2), 3.18–3.07 (m, 2H, Ar-CH_2, CH_2CH_2CH), 3.04–2.90 (m, 2H, C*H* COD), 2.70–2.57 (m, 1H, CH_2CH_2CH), 2.32–2.23 (m, 2H, CH_2 COD), 2.18 (ddd, *J* = 16.4, 10.0, 5.3 Hz, 1H, CH_2 COD), 2.07 (dd, *J* = 15.4, 7.8 Hz, 1H, CH_2 COD), 1.89 (dt, *J* = 13.6, 9.2 Hz, 1H, CH_2 COD), 1.43–1.16 (m, 3H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.4 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 161.5 (d, J_{PC} = 4 Hz, C_{Ar}), 161.3 (s, C_{Ar}), 139.3 (d, J_{PC} = 14 Hz, C_{Ar}), 137.7 (s, HC_{Ar}), 136.3 (s, C_{Ar}), 135.8 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.7 (d, J_{PC} = 2 Hz, HC_{Ar}), 132.3 (s, HC_{Ar}), 131.8 (s, C_{Ar}), 130.9 (d, J_{PC} = 14 Hz, HC_{Ar}), 130.1 (s, HC_{Ar}), 130.0 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.8 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.6 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 128.1 (s, HC_{Ar}), 127.7 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 100.4 (d, J_{PC} = 10 Hz, *C*H COD), 91.8 (d, J_{PC} = 14 Hz, *C*H COD), 86.0 (s, *C*HOP), 70.0 (s, *C*H COD), 63.6 (s, *C*H COD), 37.1 (s, CH_2 COD), 34.4 (s, CH_2 COD), 30.7 (d, J_{PC} = 10 Hz, CH_2CH_2CH), 28.9 (s, CH_2 COD), 28.1 (s, Ar-CH_2), 25.2 (s, CH_2 COD) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, CD_2Cl_2): δ = 99.5 (s) ppm. **MS** (FAB NBA) *m/z* (%):

696 ([Ir(L)(COD)]$^+$, 100), 586 (19) **EA**: calc. (%) C 50.85, H 2.97, N 0.90; found C 50.70, H 3.06, N 0.78. **m.p.**: 152–153 °C. **$[\alpha]_D^{20}$**: +23 (*c* = 1.19, $CHCl_3$).

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-7-(2-phenyl-6,7-dihydro-*5H*-[1]pyrindine)di-(*ortho*-tolyl)phosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate (36b)



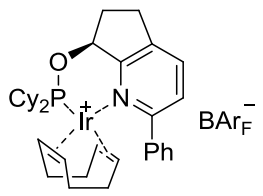
Ir-complex **36b** was obtained following the general procedure **C** using pyridyl alcohol (*S*)-**54a** (106 mg, 500 µmol, 1.0 eq.), DMAP (61.1 mg, 500 µmol, 1.0 eq.), chloro-di-*ortho*-tolyl-phosphine (124 mg, 500 µmol, 1.0 eq.), DCM (1.0 mL), $[Ir(COD)Cl]_2$ (168 mg, 250 µmol, 0.5 eq.), $NaBAr_F$ (532 mg, 600 µmol, 1.2 eq.) and after purification by flash chromatography (SiO_2, 3 cm × 12 cm) and recrystallization from diethyl ether (2 mL) and *n*-petane (50 mL) as an orange solid (479 mg, 302 µmol, 60%). Suitable crystals for X-ray analysis were obtained by overlaying a concentrated etheral solution with *n*-pentane. The analytical data match the reported values.[57b]

^{31}P{^{1}H}-NMR of (*o*-Tol)$_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 101.3 (s) ppm.

$C_{68}H_{50}BF_{24}IrNOP$ (1587.11 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.08 (br s, 1H, H_{Ar}), 7.91 (br s, 2H, H_{Ar}), 7.84 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.78 (br s, 8H, BAr_F-*H*), 7.73 (m_c, *J* = 7.4 Hz, 1H, H_{Ar}), 7.67 (m_c, *J* = 7.3 Hz, 2H, H_{Ar}), 7.63 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.59 (br s, 4H, BAr_F-*H*), 7.48–7.37 (m, 4H, H_{Ar}), 7.36–7.27 (br s, 1H, H_{Ar}), 7.15 (m_c, *J* = 2.1 Hz, 1H, H_{Ar}), 6.71 (m_c, *J* = 8.0 Hz, 1H, H_{Ar}), 6.36 (m_c, *J* = 8.6 Hz, 1H, C*H*OP), 4.73 (br s, 1H, C*H* COD), 4.22 (br s, 1H, C*H* COD), 3.26–3.14 (m, 1H, Ar-CH_2), 3.12–2.95 (m, 3H, Ar-CH_2, CH_2CH_2CH, C*H* COD), 2.84 (br s, 4H, Ar-CH_3, C*H* COD) 2.56–2.17 (m, 6H, CH_2CH_2CH, Ar-CH_3, CH_2 COD), 2.13 (m_c, *J* = 15.0, 7.9 Hz, 1H, CH_2 COD), 2.07–1.90 (m, 2H, CH_2 COD), 1.44–1.26 (m, 2H, CH_2 COD), 1.25–1.16 (m, 1H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.4 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 161.5 (s, C_{Ar}), 161.3 (d, J_{PC} = 3 Hz, C_{Ar}), 141.5 (d, J_{PC} =8 Hz, C_{Ar}), 139.2 (d, J_{PC} = 9 Hz, C_{Ar}), 137.4 (s, HC_{Ar}), 135.2 (s, HC_{Ar} BAr_F), 135.1 (s, C_{Ar}), 134.7 (s, C_{Ar}), 133.3 (d, J_{PC} = 7 Hz, HC_{Ar}), 133.0 (s, HC_{Ar}), 132.5 (s, HC_{Ar}), 132.4 (s, HC_{Ar}), 131.9 (s, HC_{Ar}), 131.6 (s, HC_{Ar}), 131.4 (s, HC_{Ar}), 129.7 (s, HC_{Ar}), 129.3 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 128.3

(s, HC_{Ar}), 126.7 (d, J_{PC} = 11 Hz, HC_{Ar}), 125.0 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 117.9 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 99.1 (br s, *C*H COD), 90.0 (br s, *C*H COD), 83.9 (s, *C*HOP), 69.0 (s, *C*H COD), 67.1 (br s, *C*H COD), 36.7 (s, *C*H_2 COD), 34.4 (s, *C*H_2 COD), 30.5 (d, J_{PC} = 9 Hz, CH_2CH_2CH), 28.4 (s, *C*H_2 COD), 27.5 (s, Ar-*C*H_2), 24.9 (s, *C*H_2 COD), 23.2 (d, J_{PC} = 5 Hz, Ar-*C*H_3), 22.7 (br s, Ar-*C*H_3) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 113.6 (br s) ppm. **MS** (FAB NBA) *m/z* (%): 724 ([Ir(L)(COD)]$^+$, 100), 612 (35), 194 (14). **EA**: calc. (%) C 51.46, H 3.18, N 0.88; found C 51.46, H 3.18, N 0.84. **m.p.**: 131–132 °C; lit. 84 °C.[57b]. **[α]$_D^{20}$**: +21 (*c* = 1.01, $CHCl_3$); lit. −10 (*c* = 1.01, $CHCl_3$) for (*R*)-enantiomere.[57b]

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-7-(2-phenyl-6,7-dihydro-*5H*-[1]pyrindine)-dicyclohexyl-phosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate (36c)



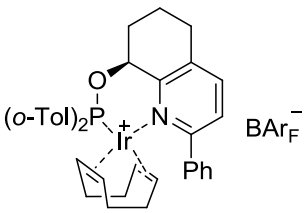
Ir-complex **36c** was obtained following the general procedure C using pyridyl alcohol (*S*)-**54a** (95.7 mg, 453 µmol, 1.0 eq.), DMAP (55.3 mg, 453 µmol, 1.0 eq.), chlorodicyclohexylphosphine (100 µL, 105 mg, 453 µmol, 1.0 eq.), DCM (1.0 mL), $[Ir(COD)Cl]_2$ (152 mg, 226 µmol, 0.5 eq.), $NaBAr_F$ (482 mg, 544 µmol, 1.2 eq.) and after purification by flash chromatography (SiO_2, 3 cm × 12 cm) and recrystallization from diethyl ether (2 mL) and *n*-pentane (50 mL) as an orange solid (469 mg, 299 µmol, 66%). Suitable crystals for X-ray analysis were obtained by overlaying a concentrated etheral solution with *n*-pentane. The analytical data match the reported values.[57b]

^{31}P{^{1}H}-NMR of Cy_2PCl (162 MHz, CD_2Cl_2): δ = 126.7 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 147.6 (s) ppm.

$C_{66}H_{58}BF_{24}IrNOP$ (1571.16 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.32 (d, *J* = 7.4 Hz, 2H, *H*$_{Ar}$), 7.89 (d, *J* = 8.0 Hz, 1H, *H*$_{Ar}$), 7.80–7.70 (m, 10H, BAr_F-*H*, *H*$_{Ar}$), 7.68 (t, *J* = 7.5 Hz, 2H, *H*$_{Ar}$), 7.56 (m, 4H, BAr_F-*H*), 5.80–5.74 (m, 1H, C*H*OP), 4.89–4.82 (m, 1H, C*H* COD), 4.66–4.59 (m, 1H, C*H* COD), 3.58–3.48 (m, 1H, C*H* COD), 3.18–3.09 (m, 1H, Ar-CH_2), 3.05–2.95 (m, 1H, Ar-CH_2), 2.85–2.75 (m, 1H, CH_2CH_2CH), 2.68–2.58 (m, 1H, C*H* COD), 2.49–2.02 (m, 7H, CH_2), 2.01–1.74 (m, 7H, CH_2), 1.72–1.20 (m, 12H, CH_2), 1.17–0.98 (m, 4H, CH_2), 0.63–0.49 (m, 1H, CH_2) ppm.
^{13}C{^{1}H}-NMR (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 162.0 (d, J_{PC} = 3

Hz, C_{Ar}), 160.3 (s, C_{Ar}), 139.1 (s, C_{Ar}), 139.0 (s, C_{Ar}), 137.6 (s, HC_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.3 (s HC_{Ar}), 130.3 (s, HC_{Ar}), 129.4 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 128.8 (s, HC_{Ar}), 127.4 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 95.6 (d, J_{PC} = 8 Hz, *C*H COD), 85.4 (d, J_{PC} = 15 Hz, *C*H COD), 85.2 (s, *C*HOP), 69.6 (s, *C*H COD), 66.2 (s, *C*H COD), 39.2 (d, J_{PC} = 31 Hz, *C*H Cy), 37.8 (d, J_{PC} = 3 Hz, CH_2), 36.8 (d, J_{PC} = 31 Hz, *C*H Cy), 35.4 (s, CH_2), 30.1 (d, J_{PC} = 9 Hz, CH_2CH_2CH), 28.7 (s, CH_2), 28.3 (s, CH_2), 28.2 (s, CH_2), 27.4 (s, Ar-CH_2), 27.3 (d, J_{PC} = 3 Hz, CH_2), 27.2 (s, CH_2), 27.1 (s, CH_2), 27.0 (s, CH_2), 26.7 (s, CH_2), 26.6 (d, J_{PC} = 2 Hz, CH_2), 26.5 (s, CH_2), 26.4 (s, CH_2), 26.3 (s, CH_2), 25.5 (s, CH_2), 24.5 (d, J_{PC} = 2 Hz, CH_2) ppm. **$^{31}P\{^1H\}$-NMR** (202 MHz, CD_2Cl_2): δ = 121.8 (s) ppm. **MS** (FAB NBA) *m/z* (%): 708 ($[Ir(L)(COD)]^+$, 100), 596 (25), 432 (16), 194 (13). **EA**: calc. (%) C 50.45, H 3.72, N 0.89; found C 50.60, H 3.71, N 0.71. **m.p.**: 169–171 °C; lit. 175 °C.[57b]. **$[\alpha]_D^{20}$**: −44 (*c* = 1.04, $CHCl_3$); lit. +41 (*c* = 1.09, $CHCl_3$) for (*R*)-enantiomere.[57b]

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-8-(2-phenyl-5,6,7,-tetrahydrochinolinyl)-di-(*ortho*-tolyl)phosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate (36e)



Ir-complex **36e** was obtained following the general procedure **C** using pyridyl alcohol (*S*)-**54c** (25 mg, 111 µmol, 1.0 eq.), DMAP (13.6 mg, 111 µmol, 1.0 eq.) chloro-di-*ortho*-tolyl-phosphine (27.6 mg, 111 µmol, 1.0 eq.), DCM (0.5 mL), $[Ir(COD)Cl]_2$ (37.3 mg, 55.5 µmol, 0.5 eq.) and $NaBAr_F$ (118 mg, 133 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) and recrystallization from diethyl ether (2 mL) and *n*-pentane (50 mL) was isolated as an orange solid (118 mg, 73.4 µmol, 66%). Suitable crystals for X-ray analysis were obtained by overlaying a concentrated etheral solution with *n*-pentane. The analytical data match the reported values.[57b]

$^{31}P\{^1H\}$-NMR of (*o*-Tol) $_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
$^{31}P\{^1H\}$-NMR of the Ligand (162 MHz, CD_2Cl_2): δ = 99.8 (s) ppm.

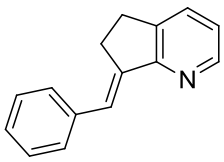
$C_{69}H_{52}BF_{24}IrNOP$ (1601.14 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.90–7.65 (m, 12H, H_{Ar}, BAr_F-*H*), 7.65–7.50 (m, 7H, H_{Ar}, BAr_F-*H*), 7.48–7.39 (m, 3H, H_{Ar}), 7.39–7.31 (m, 2H, H_{Ar}), 7.29–7.23 (m, 1H, H_{Ar}), 7.20 (t, *J*

= 6.3 Hz, 1H, H_{Ar}), 6.96–6.85 (m, 1H, H_{Ar}), 6.31–6.24 (m, 1H, C*H*OP), 4.71 (br s, 1H, C*H* COD), 4.49 (br s, 1H, C*H* COD), 3.24 (br s, 1H, C*H* COD), 3.06–2.96 (m, 1H, CH_2), 2.89 (s, 3H, Ar-CH_3), 2.87–2.74 (m, 2H, C*H* COD, CH_2), 2.68–2.59 (m, 1H, CH_2), 2.49 (s, 3H, Ar-CH_3), 2.45–2.30 (m, 2H, CH_2), 2.16–1.95 (m, 3H, CH_2), 1.93–1.79 (m, 3H, CH_2), 1.42–1.31 (m, 1H, CH_2), 1.30–1.18 (m, 1H, CH_2), 1.15–1.04 (m, 1H, CH_2) ppm. **$^{13}C\{^1H\}$-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.8 (s, C_{Ar}), 141.5 (s, HC_{Ar}), 139.6 (s, C_{Ar}), 136.7 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 134.8 (s, C_{Ar}), 134.4 (s, C_{Ar}), 133.0 (d, J_{PC} = 8 Hz, HC_{Ar}), 132.8 (s, HC_{Ar}), 132.7 (s, HC_{Ar}), 132.1 (s, HC_{Ar}), 132.0 (d, J_{PC} = 14 Hz, HC_{Ar}), 130.4 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 128.2 (s, HC_{Ar}), 127.0 (d, J_{PC} = 11 Hz, HC_{Ar}), 126.4 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 94.8 (br s, *C*H COD), 83.1 (br s, *C*H COD), 76.7 (s, *C*HOP), 70.4 (s, *C*H COD), 70.2 (br s, *C*H COD), 36.5 (d, J_{PC} = 2 Hz, CH_2), 35.2 (s, CH_2), 31.2 (d, J_{PC} = 10 Hz, CH_2), 29.3 (s, CH_2), 29.0 (s, CH_2), 24.2 (s, CH_2), 23.3 (d, J_{PC} = 7 Hz, Ar-CH_3), 22.5 (d, J_{PC} = 57 Hz, Ar-CH_3), 19.0 (s, CH_2) ppm. **$^{31}P\{^1H\}$-NMR** (162 MHz, CD_2Cl_2): δ = 99.3 (br s) ppm. **MS** (FAB NBA) *m/z* (%): 738 ($[Ir(L)(COD)]^+$, 100), 628 (58), 534 (11), 419 (11), 218 (16). **EA**: calc. (%) C 51.76, H 3.27, N 0.87; found C 51.92, H 3.30, N 0.71. **m.p.**: 158–159 °C; lit. 163 °C.[57b] **$[\alpha]_D^{20}$**: +33 (*c* = 0.985, $CHCl_3$); lit. +41 (*c* = 1.0, $CHCl_3$).[57b]

8.4 New N,P Ligands with a Quaternary Stereogenic Center and Their Iridium-Complexes

8.4.1 Preparation of Ligand Precursors

(*E*)-7-benzylidene-6,7-dihydro-*5H*-cyclopenta[1]pyridine (79a)

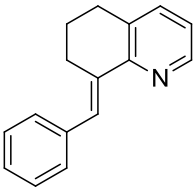


A mixture of 6,7-dihydro-5*H*-cyclopenta[1]pyridine (5.0 mL, 5.15 g, 43.2 mmol), benzaldehyde (6.6 mL, 6.93 g, 65.3 mmol, 1.5 eq.) and acetic anhydride (7.8 mL, 8.42 g, 82.5 mmol, 1.9 eq.) was stirred at 180 °C for 13 h. All volutiles were then removed under reduced pressure at 100 °C. Ice cold water (40 mL) was added to the obtained black residue and the mixture was made basic (pH > 10) with aqueous NaOH 2 M solution (40 mL) and then extracted with DCM (4×50 mL). Combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified by *Kugelrohr* distillation (150–160 °C / 0.2 mbar). Recrystallization from *n*-hexanes (10 mL) gave the title compound **79a**

(6.60 g, 31.8 mmol, 74%) as a colorless solid. The analytical data match the reported values.[101a]

$C_{15}H_{13}N$ (207.27 g/mol):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 4.7 Hz, 1H, H_{Ar}), 7.51–7.47 (m, 3H, H_{Ar}), 7.44 (s, 1H, C*H*), 7.32 (t, *J* = 7.7 Hz, 2H, H_{Ar}), 7.18 (t, *J* = 7.4 Hz, 1H, H_{Ar}), 7.02 (dd, *J* = 7.5, 4.9 Hz, 1H, H_{Ar}), 3.09–3.08 (m, 2H, CH_2), 3.03–3.00 (m, 2H, Ar-CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 160.7 (C_{Ar}), 148.4 (HC_{Ar}), 141.2 (*C*=CH), 138.9 (C_{Ar}), 137.6 (C_{Ar}), 133.0 (HC_{Ar}), 129.0 (HC_{Ar}), 128.4 (HC_{Ar}), 126.9 (HC_{Ar}), 122.3 (HC_{Ar}), 122.1 (C=*C*H), 28.7 (*C*H_2), 28.2 (Ar-*C*H_2) ppm. **MS**: (FAB NBA) *m/z* (%): 208 ($[M+H]^+$, 100), 130 (5), 117 (6), 91 (9), 77 (109, 63 (5), 51 (6), 39 (7). **IR**: $\tilde{\nu}$ = 2986 (w), 2938 (w), 1596 (w), 1575 (m), 1490 (m), 1446 (m), 1430 (s), 1415 (s), 1263 (m), 1202 (w), 1163 (m), 1106 (w), 1079 (s), 1006 (m), 965 (w), 916 (s), 881 (m), 817 (m), 798 (s), 774 (m), 750 (s), 692 (s) cm^{-1}. **EA**: calc. (%) C 86.92, H 6.32, N 6.76; found C 86.72, H 6.37, N 6.82. **m.p.**: 75–76 °C; lit. 74–75 °C.[101a]

(*E*)-8-Benzylidene-5,6,7,8-tetrahydroquinoline (79b)

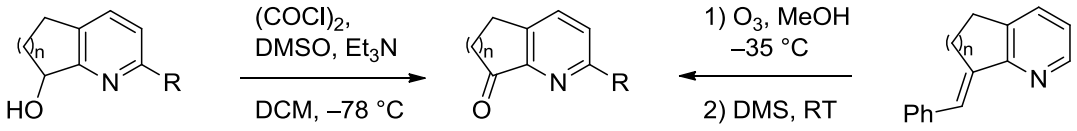


A mixture of 5,6,7,8-tetrahydroquinoline (5.0 mL, 5.15 g, 38.7 mmol), benzaldehyde (6.0 mL, 6.30 g, 59.4 mmol, 1.5 eq.) and acetic anhydride (7.0 mL, 7.56 g, 74.1 mmol, 1.9 eq.) was stirred at 180 °C for 15 h. The volutiles were removed under reduced pressure at 100 °C. Ice cold water (40 mL) was added to the obtained black residue and the mixture was made distinctly basic (pH > 10) with aq. NaOH 2 M solution (5 mL) and then extracted with DCM (4×50 mL). Combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified by *Kugelrohr* distillation (150–160 °C / 0.2 mbar). Recrystallization from *n*-hexane (25 mL) gave the title compound **79b** (6.40 g, 28.9 mmol, 75%) as a colorless solid. The analytical data match the reported values.[101a]

$C_{16}H_{15}N$ (221.30 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.48 (dt, *J* = 4.4, 0.8 Hz, 1H, H_{Ar}), 7.98 (s, 1H, C*H*), 7.36–7.46 (m, 5H, H_{Ar}), 7.26 (tt, *J* = 7.2, 1.2 Hz, 1H, H_{Ar}), 7.09 (dd, *J* = 7.6, 4.6 Hz, 1H, H_{Ar}), 2.90–2.93 (m, 2H, ArCH_2), 2.86 (t, *J* = 6.2 Hz, 2H, CH_2C(O)), 1.86 (p, *J* = 6.2 Hz, 2H, $CH_2CH_2CH_2$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 152.9 (C_{Ar}), 147.2 (HC_{Ar}), 137.9

(*C*=CH), 136.9 (*C*H), 135.3 (C_{Ar}), 132.6 (C_{Ar}), 129.6 (HC_{Ar}), 128.0 (HC_{Ar}), 126.9 (HC_{Ar}), 126.7 (HC_{Ar}), 121.9 (HC_{Ar}), 29.8 (CH_2), 28.0 (CH_2), 22.7 (CH_2) ppm. **MS** (EI, 70 eV, ca. 50 °C) *m/z* (%): 220 ($[M]^+$, 100). **IR**: $\tilde{\nu}$ = 2946 (m), 2928 (w), 2915 (w), 2834 (w), 1580 (w), 1563 (m), 1485 (m), 1456 (w), 1435 (s), 1419 (m), 1182 (w), 1116 (m), 1072 (w), 1057 (w), 1029 (w), 926 (s), 918 (w), 901 (w), 887 (m), 864 (m), 847 (w), 832 (m), 826 (w), 792 (s), 772 (s), 757 (s), 715 (m), 699 (s) cm^{-1}. **EA**: calc. (%) C 86.84, H 6.83, N 6.33; found C 86.70, H 6.92, N 6.23. **m.p.**: 66–67 °C; lit. 62–64 °C.[101a]

8.4.2 Preparation Pyridyl Ketones



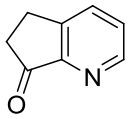
Swern Oxidation, **General Procedure D**:

A solution of DMSO (2.5 eq.) in DCM (2.5–5 M) was slowly added to a solution of oxalyl chloride (1.2 eq.) in DCM (0.5–0.6 M) at –78 °C. After stirring for 15 min, a solution of pyridyl alcohol (1.0 eq.) in DCM (1 M) was slowly added. After stirring for additional 20 min, triethylamine (>5 eq.) was added to the reaction mixture. The cooling bath was removed and the reaction mixture was allowed to reach RT. The volutiles were removed in *vacuo*. The residue was dissolved in DCM (20 mL), and washed with water (10 mL) and with brine (10 mL). After drying over $MgSO_4$, the solvent was removed under reduced pressure. The obtained ketone was purified by flash chromatography or by *Kugelrohr* distillation.

Ozonolysis, **General Procedure E**:

A solution of olefin (1.0 eq.) in MeOH (0.2 M) was treated with ozone (40 L / min) at –40 °C for 2 h. Afterwards the reaction mixture was purged with N_2. Dimethyl sulfide (3.0 eq.) was then added. The mixture was stirred for 0.5 h at –40 °C, before it was allowed to warm to rt overnight. The solvent was removed under reduced pressure. The obtained ketone was purified by flash chromatography or by *Kugelrohr* distillation.

5*H*-Cyclopenta[1]pyridin-7(6*H*)-one (76a)



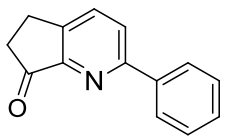
The title compound **76a** was obtained following the general procedure **D** using oxalyl chloride (0.29 mL, 429 mg, 3.38 mmol, 1.2 eq.), DCM (7.5 mL), DMSO (0.53 mL, 583 mg, 7.37 mmol, 2.5 eq.), DCM (3.0 mL), **78a** (393 mg, 2.91 mmol, 1.0 eq.), DCM (3.0 mL), triethylamine (2.1 mL, 1.53 g, 15.1 mmol, 5.2 eq.), after purification by flash chromatography (SiO_2, 3 cm × 10 cm, TBME / cyclohexane 1:1 → 1:0) and by *Kugelrohr* distillation (125–130 °C, 0.1 mbar) as a slightly yellow solid (297 mg, 2.23 mmol, 77%).

Alternativly the title compound **76a** was prepared following the general procedure **E** using **79a** (9.45 g, 45.6 mmol, 1.0 eq.), MeOH (200 mL), ozone, dimethyl sulfide (10 mL, 8.40 g, 135 mmol, 3.0 eq.), after purification by *Kugelrohr* distillation (125–130 °C, 0.1 mbar) as brown solid (4.34 g, 32.6 mmol, 72%). The analytical data match the reported values.[101a]

C_8H_7NO (133.05 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.77–8.76 (m, 1H, H_{Ar}), 7.90–7.87 (m, 1H, H_{Ar}), 7.44 (dd, J = 7.9 Hz, 4.5 Hz, 1H, H_{Ar}), 3.17 (m, 2H, CH_2CO), 2.78–2.75 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 205.3 (C=O), 154.0 (C_{Ar}), 150.6 (HC_{Ar}), 149.5 (C_{Ar}), 135.3 (HC_{Ar}), 127.3 (HC_{Ar}), 34.8 (CH$_2$C(O)), 23.4 (ArCH$_2$) ppm. **MS** (EI, 70 eV, RT) *m/z* (%): 133 ([M]$^+$, 100), 104 (57), 78 (23), 51 (10). **IR**: $\tilde{\nu}$ = 3185 (m br), 2963 (w), 2925 (w), 2876 (w), 1578 (s), 1449 (m), 1426 (m), 1331 (m), 1289 (m), 1187 (w), 1117 (w), 1082 (s), 1053 (m), 1001 (s), 969 (s), 949 (m), 884 (m), 830 (m), 799 (s,) 780 (m), 724 (w), 689 (s br) cm^{-1}. **EA**: calc. (%) C 72.17, H 5.30, N 10.52; found C 72.08, H 5.39, N 10.51. **m.p.**: 117–118 °C; lit. 118–120 °C.[101a]

2-Phenyl-5,6,7,8-tetrahydroquinolin-8-on (76b)

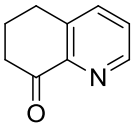


The title compound **76b** was obtained following the general procedure **D** using oxalyl chloride (1.0 mL, 1.48 g, 11.6 mmol, 1.2 eq.), DCM (30 mL), DMSO (1.8 mL, 1.98 g, 25.4 mmol, 2.3 eq.), DCM (10 mL), **54a** (2.30 g, 10.9 mmol, 1.0 eq.), DCM (10 mL), triethylamine (7.7 mL, 5.54 g, 54.8 mmol, 5.0 eq.), after purification by flash chromatography (SiO_2, 3 cm × 20 cm, DCM / cyclohexane 1:1 → 1:0) as

pale greenish solid (422 mg, 1.90 mmol, 90%). The analytical data match the reported values.[152]

$C_{14}H_{11}NO$ (209.24 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.13–7.99 (m, 2H, H_{Ar}), 7.89 (q, J = 8.2 Hz, 2H, H_{Ar}), 7.50–7.34 (m, 3H, H_{Ar}), 3.19–3.10 (m, 2H, CH_2), 2.81–2.73 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 205.8 (*C*O), 158.7 (C_{Ar}), 154.2 (C_{Ar}), 148.4 (C_{Ar}), 138.4 (C_{Ar}), 136.1 (HC_{Ar}), 129.7 (HC_{Ar}), 128.9 (HC_{Ar}), 127.5 (HC_{Ar}), 124.8 (HC_{Ar}), 35.5 (*C*H_2), 23.4 (*C*H_2) ppm. **MS** (EI, 70 eV, ca. 200 °C) *m/z* (%): 209 ([M]$^+$, 100), 180 (42), 152 (6), 140 (11), 115 (8), 77 (6). **EA**: calc. (%) C 80.36, H 5.30, N 6.69; found C 80.83, H 5.54, N 6.67. **m.p.**: 172–174 °C (dec.); lit. 167–168 °C.[152] **TLC** (SiO_2, DCM): R_f = 0.10.

5,6,7,8-Tetrahydroquinolin-8-on (76c)

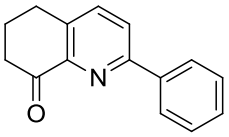


The title compound **76c** was obtained following the general procedure **D** using oxalyl chloride (1.0 mL, 1.48 g, 11.7 mmol, 1.1 eq.), DCM (20 mL), DMSO (1.8 mL, 1.98 g, 25.0 mmol, 2.4 eq.), DCM (5.0 mL), **78b** (1.51 g, 10.6 mmol, 1.0 eq.), DCM (10 mL), triethylamine (7.5 mL, 5.48 g, 54.1 mmol, 5.1 eq.), after purification by *Kugelrohr* distillation (150–160 °C, 0.1 mbar) to give the title compound **76c** as a slightly yellow solid (1.50 g, 10.2 mmol, 96%).
Alternativly the title compound **76c** was prepared following the general procedure **E** using **79b** (10.0 g, 47.0 mmol, 1.0 eq.), MeOH (170 mL), ozone, dimethyl sulfide (10.3 mL, 8.76 g, 141 mmol, 3.0 eq.), after purification by recrystallization from a mixture of diisopropyl ether (55 mL) and acetone (10 mL) as a slightly yellow solid (4.50 g, 31 mmol, 66%). The analytical data match the reported values.[101a]

C_9H_9NO (147.07 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.70 (dd, J = 4.5, 0.8 Hz, 1H, H_{Ar}), 7.65 (dd, J = 7.8, 0.8 Hz, 1H, H_{Ar}), 7.38 (dd, J = 7.8, 4.5 Hz, 1H, H_{Ar}), 3.03 (t, J = 6.1 Hz, 2H, ArCH_2), 2.81 (t, J = 6.6 Hz, 2H, CH_2C(O)), 2.20 (p, J = 2.4 Hz, 2H, $CH_2CH_2CH_2$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 196.7 (*C*O), 149.0 (HC_{Ar}), 148.1 (C_{Ar}), 140.7 (C_{Ar}), 137.5 (HC_{Ar}), 126.9 (HC_{Ar}), 39.6 (CH_2C=O), 29.0 (ArCH_2), 22.6 ($CH_2CH_2CH_2$) ppm. **MS** (EI, 70 eV, ca. 50 °C) *m/z* (%): 147 ([M]$^+$, 73), 118 (39), 91 (100), 64 (18), 55 (28), 51 (11), 39 (21). **IR**: $\tilde{\nu}$ =

3354 (w), 3165 (w), 3049 (w), 2941 (m), 2880 (w), 1686 (s), 1582 (w), 1562 (m), 1435 (w), 1421 (m), 1350 (w), 1329 (m), 1294 (s), 1271 (w), 1196 (m), 1184 (m), 1148 (w), 1111 (m), 1088 (m), 1055 (w), 1036 (m), 1001 (w), 906 (m), 897 (s), 862 (m), 818 (m), 800 (s), 773 (w), 704 (w), 689 (m), 648 (m) cm^{-1}. **EA**: calc. (%) C 73.45, H 6.16, N 9.52; found C 73.06, H 6.24, N 9.45. **m.p.**: 82–87 °C; lit: 98–100 °C.[101a]

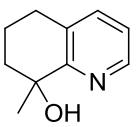
2-Phenyl-5,6,7,8-tetrahydroquinolin-8-on (76d)



The title compound **76d** was obtained following the general procedure **D** using oxalyl chloride (0.20 mL, 296 mg, 2.33 mmol, 1.1 eq.), DCM (5.0 mL), DMSO (0.35 mL, 385 mg, 2.33 mmol, 2.3 eq.), DCM (1.0 mL), **54b** (478 mg, 2.12 mmol, 1.0 eq.), DCM (2.0 mL), triethylamine (1.5 mL, 1.10 g, 10.8 mmol, 5.1 eq.) after purification by flash chromatography (SiO_2, 3 cm × 15 cm, ethyl acetate / cyclohexane 1:4 → 1:1 → 1:0) as a colorless solid (422 mg, 1.90 mmol, 90%). The analytical data match the reported values.[152]

$C_{15}H_{13}NO$ (223.27 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.06–8.03 (m, 2H, H_{Ar}), 7.81 (d, J = 8.1 Hz, 1H, H_{Ar}), 7.70 (br d, J = 8.2 Hz, 1H, H_{Ar}), 7.48–7.38 (m, 3H, H_{Ar}), 3.03 (t, J = 6.1 Hz, 2H, ArCH_2), 2.84–2.79 (m, 2H, CH_2C(O)), 2.20 (t, J = 6.4 Hz, 2H, $CH_2CH_2CH_2$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 196.8 (*C*O), 156.8 (C_{Ar}), 148.0 (C_{Ar}), 139.3 (C_{Ar}), 138.6 (C_{Ar}), 138.5 (HC_{Ar}), 129.4 (HC_{Ar}), 128.8 (HC_{Ar}), 127.3 (HC_{Ar}), 124.0 (HC_{Ar}), 40.0 (CH_2C=O), 29.1 (ArCH_2), 22.8 ($CH_2CH_2CH_2$) ppm. **MS** (EI, 70 eV, ca. 150 °C) *m/z* (%): 223 (100, $[M]^+$), 194 (40), 167 (66). **EA**: calc. (%) C 80.69, H 5.87, N 6.27; found C 80.68, H 5.86, N 6.17. **m.p.**: 135–137 °C; lit. 145–146 °C.[152] **TLC** (SiO_2, EtOAc): R_f = 0.67.

8-Methyl-5,6,7,8-tetrahydroquinolin-8-ol (80)



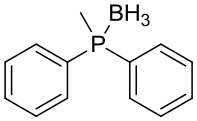
Methylmagnesium chloride 3 M solution in THF (3.0 mL, 9.0 mmol, 1.3 eq.) was slowly added to a suspension of zinc chloride (100 mg, 734 µmol, 0.1 eq.) and **76c** (1.02 g, 6.92 mmol, 1.0 eq.) in THF (20 mL) at 0 °C. After stirring for 2 h under ice bath control, the reaction was quenched by addition of a ½-sat. aq. NH_4Cl solution

(50 mL). Extraction with DCM (3×50 mL), drying with $MgSO_4$ and evaporation of solvent under reduced pressure offered the crude product. Purification by flash chromatography (SiO_2, 1.5 cm × 12 cm, cyclohexane / TBME 10:1) gave the title compound **80** (712 mg, 4.36 g, 63%) as a colorless solid. The analytical data match the reported values.[104]

$C_{10}H_{13}NO$ (163.22 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.40 (dd, *J* = 4.7, 0.7 Hz, 1H, H_{Ar}), 7.36 (dd, *J* = 7.7, 0.7 Hz, 1H, H_{Ar}), 7.07 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 3.93 (s, 1H, O*H*), 2.85–2.72 (m, 2H, ArCH_2), 2.07–1.91 (m, 3H, CH_2CH_2C(OH)), 1.86–1.76 (m, 1H, CH_2C(OH)), 1.53 (s, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 160.9 (C_{Ar}), 147.0 (HC_{Ar}), 136.8 (HC_{Ar}), 130.5 (C_{Ar}), 122.1 (HC_{Ar}), 70.7 (*C*(OH)), 36.8 (*C*H$_2$), 30.5 (*C*H$_3$), 28.7 (*C*H$_2$), 19.7 (*C*H$_2$) ppm. **MS** (FAB NBA) *m/z* (%): 164 ([M+H]$^+$, 100), 146 (66), 136 (9), 107 (8), 89 (10), 77 (14), 51 (8); (FAB NBA + KCl) *m/z* (%): 202 ([M+K]$^+$, 12), 164 ([M+H]$^+$, 100), 146 (6), 107 (10), 89 (10), 77 (19), 63 (9), 51 (10). **IR**: $\tilde{\nu}$ = 3292 (w br), 3053 (w), 2935 (m) , 2866 (w), 1576 (m), 1454 (m), 1441 (s), 1421 (m), 1389 (m), 1364 (m), 1329 (m), 1294 (m), 1269 (w), 1200 (m), 1190 (m), 1177 (w), 1144 (s), 1107 (m), 1077 (s), 1055 (w), 1047 (m), 1016 (w), 995 (w), 984 (w), 972 (w), 935 (s), 899 (w), 870 (w), 847 (m), 837 (m), 816 (m), 799 (s), 719 (w), 682 (s), 669 (m), 621 (w) cm^{-1}. **EA**: calc. (%) C 73.59, H 8.03, N 8.03, O 9.80; found C 73.36, H 7.79, N 8.40. **m.p.**: 58–60 °C; lit: 72–73 °C.[104]

8.4.3 Preparation Methyl-Phosphines-BH_3-Adducts

Diphenyl-methyl-phosphine-borane adduct (84a)

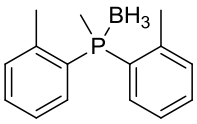


BH_3-THF-adduct 1 M solution (16.0 mL, 6.00 mmol, 1.2 eq.) was slowly added to a solution of methyldiphenylphosphine (1.00 g, 4.99 mmol, 1.0 eq.) in THF (15 mL) at 0 °C. The reaction mixture was stirred for 2 h at RT. All volatiles were removed in *vacuo* to obtain the title compound **84a** (1.08 g, 5.06 mmol, quant.) as a colorless solid. The analytical data match the reported values.[153]

$C_{13}H_{16}BP$ (214.05 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.68–7.64 (m, 4H, H_{Ar}), 7.52–7.42 (m, 6H, H_{Ar}), 1.87 (d, J_{PH} = 10.1 Hz, 3H, PCH_3), 0.99 (br q, J_{BH} = 85 Hz, 3H, BH_3) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 7.3 (q, J_{BP} = 51 Hz) ppm. **m.p.**: 48–49°C; lit 55 °C.[153]

Methyl-di-*ortho*-tolylphosphine-borane adduct (84b)

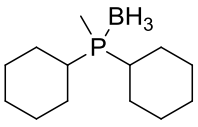


Methyllithium 1.6 M solution in diethyl ether (5.0 mL, 8.00 mmol, 1.0 eq.) was added to a solution of chloro-methyl-di-*ortho*-tolylphosphine (1.99 g, 8.00 mmol, 1.0 eq.) in diethyl ether (15 mL) at 0 °C. The reaction mixture was stirred overnight at RT. BH_3·THF 1 M solution (10 mL, 10.0 mmol, 1.3 eq.) was added at 0 °C, and the reaction mixture was stirred for additional 5 h at RT. The reaction mixture was quenched with ½-sat. aq. NH_4Cl-solution (20 mL) at 0 °C and extracted with DCM (3×15 mL). The combined organic layers were washed with water (20 mL), brine (20 mL) and dried over $MgSO_4$. After removing the solvent under reduced pressure the title compound **84b** (0.782 g, 3.23 mmol, 40%) was obtained as a colorless solid.

$C_{15}H_{20}BP$ (242.10 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.85–7.74 (m, 2H, H_{Ar}), 7.39 (tt, J = 7.5, 1.6 Hz, 2H, H_{Ar}), 7.31 (t, J = 7.5 Hz, 2H, H_{Ar}), 7.16 (dd, J = 7.5, 3.6 Hz, 2H, H_{Ar}), 2.10 (s, 6H, ArCH_3), 1.93 (d, J_{PH} = 9.8 Hz, 3H, PCH_3), 1.38 (br q, J_{BH} = 85 Hz, 3H, BH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 142.0 (d, J_{CP} = 6 Hz, C_{Ar}), 132.7 (d, J_{CP} = 13 Hz, HC_{Ar}), 131.8 (d, J_{CP} = 8 Hz, HC_{Ar}), 128.8 (d, J_{CP} = 53 Hz, C_{Ar}), 126.6 (d, J_{CP} = 11 Hz, HC_{Ar}), 21.6 (d, J_{CP} = 5 Hz, ArCH$_3$), 12.1 (d, J_{CP} = 42 Hz, CH$_3$P) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 6.90 (q, J_{BP} = 36 Hz) ppm. **m.p.**: 118–119 °C.

Dicyclohexyl-(methyl)-phosphine-BH_3-adduct (84c)

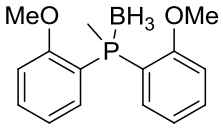


Methylmagnesium chloride 3.0 M solution in THF (3.0 mL, 8.0 mmol, 1.0 eq.) was added to a solution of chloro-dicyclohexyl-methylphosphine (1.86 g, 8.00 mmol, 1.0 eq.) in THF (7 mL) at 0 °C. The reaction mixture was stirred for 4 hours at RT. BH_3·THF 1 M solution (10 mL, 10.0 mmol, 1.3 eq.) was added at 0 °C, and the reaction mixture was stirred overnight at RT. The reaction mixture was

quenched with ½-sat. aq. NH_4Cl-solution (10 mL) at 0 °C and extracted with DCM (3×25 mL). The combined organic layers were washed with water (20 mL), brine (20 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 1.5 cm × 25 cm, cyclohexane / ethyl acetate 9:1) to obtain the title compound **84c** (1.45 g, 6.41 mmol, 80%) as a colorless solid.

$C_{13}H_{28}BP$ (226.15 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.94–1.77 (m, 6H, Cy), 1.72–1.61 (m, 6H, Cy), 1.41–1.14 (m, 10H, Cy), 1.10 (d, J_{PH} = 9.8 Hz, 3H, PCH_3), 0.76–0.20 (br q, J_{BH} = 86 Hz, 3H, BH_3). **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 31.4 (d, J_{CP} = 34 Hz, *C*H), 27.0 (*C*H_2), 26.9 (d, J_{CP} = 2 Hz, *C*H_2), 26.7 (*C*H_2), 26.3 (d, J_{CP} = 3 Hz, *C*H_2), 26.2 (d, J_{CP} = 1 Hz, *C*H_2), 3.8 (d, J_{CP} = 35 Hz, *C*H_3P) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 17.6 (q, J_{BP} = 55 Hz) ppm. **m.p.**: 77–78 °C. **TLC** (SiO_2, cyclohexane / ethyl acetate 9:1): R_f = 0.72.

Di-*ortho*-methoxyphenyl-methyl-phosphan-BH_3-adduct (84d)

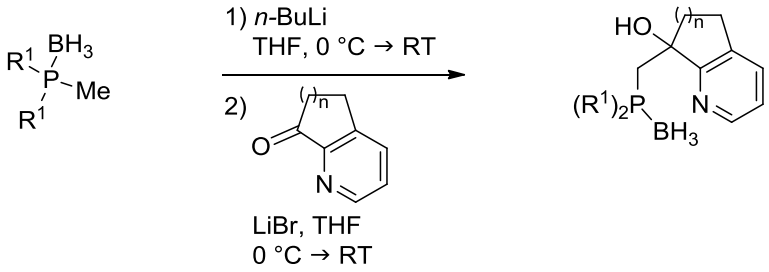


Methyllithium 1.6 M solution in diethyl ether (5.0 mL, 8.00 mmol, 1.0 eq.) was slowly added to a solution of chloro-di-*ortho*-methoxyphenyl-methyl-phosphine (3.98 g, 14.2 mmol, 1.0 eq.) in diethyl ether (20 mL) at 0 °C. The reaction mixture was stirred overnight at RT. BH_3·THF 1 M solution (10 mL, 10.0 mmol, 1.3 eq.) was added at 0 °C, and the reaction mixture was stirred overnight at RT. The reaction mixture was quenched with ½-sat. aq. NH_4Cl-solution (20 mL) at 0 °C and extracted with DCM (3×15 mL). The combined organic layers were washed with water (20 mL), brine (20 mL) and dried over $MgSO_4$. After removing the solvent under reduced pressure the crude product was purified by flash chromatography (SiO_2, 1.5 cm × 25 cm, cyclohexane / ethyl acetate 3:1) to obtain the title compound **84d** (1.15 g, 3.23 mmol, 30%) as a colorless solid.

$C_{15}H_{20}BO_2P$ (274.10 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.59 (ddd, *J* = 13.1, 7.6, 1.6 Hz, 2H, H_{Ar}), 7.48–7.41 (m, 2H, H_{Ar}), 7.00 (tdd, *J* = 7.5, 1.7, 1.0 Hz, 2H, H_{Ar}), 6.88 (dd, *J* = 8.1, 3.8 Hz, 2H, H_{Ar}), 3.69 (s, 6H, ArCH_3), 1.96 (d, J_{PH} = 10.8 Hz, 3H, PCH_3), 1.38 (br q, J_{BH} = 87 Hz, 3H, BH_3). **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 161.4 (C_{Ar}), 134.3 (d, J_{CP} = 11 Hz, HC_{Ar}), 132.8 (HC_{Ar}), 120.9 (d, J_{CP} = 11 Hz, HC_{Ar}), 118.7 (d, J_{CP} = 58 Hz, C_{Ar}), 111.4 (d, J_{CP} = 5 Hz, HC_{Ar}),

55.6 (s, O*C*H$_3$), 11.2 (d, J_{CP} = 43 Hz, *C*H$_3$P) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CDCl$_3$): δ = 7.44 (q, J_{BP} = 41 Hz) ppm.

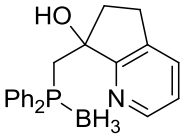
8.4.4 Addition of Phosphines



General Procedure F: A 1.6 M solution of *n*-BuLi (1.1 eq.) was added to a solution of phosphine-borane adduct (1.1 eq.) in THF (0.3-0.4 M) at 0 °C. The reaction mixture was stirred for 1-2 h at RT. A mixture of ketone (96.8 mg, 727 µmol, 1.0 eq.), lithium bromide (63.2 mg, 727 µmol, 1.0 eq.) and THF (0.6-0.7 M) was slowly added to the reaction mixture at 0 °C. The reaction mixture was stirred overnight at RT. The reaction mixture was quenched by the addition of ½-sat. aq. NH_4Cl-solution (5-10 mL) and it was extracted with TBME (2×5-10 mL). The combined organic layers were washed with water (5-10 mL), and brine (5-10 mL), and dried over $MgSO_4$. The crude product was purified by flash chromatography or by recrystallization.

Note: For phosphines having *ortho*-tolyl residues the BH_3 protecting group was removed during the work-up.

7-((Diphenylphosphino)methyl)-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-ol-BH$_3$-adduct (85a)

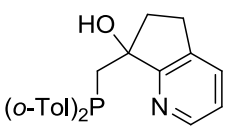


The title compound **85a** was obtained following the general procedure **F** using **84a** (171 mg, 800 µmol, 1.1 eq.), THF (2.0 mL), *n*-BuLi (0.5 mL, 800 µmol, 1.1 eq.), ketone **76a** (96.8 mg, 727 µmol, 1.0 eq.), LiBr (63.2 mg, 727 µmol, 1.0 eq.), THF (1.0 mL) and after purification by flash chromatography (SiO_2, 1.5 cm × 25 cm, cyclohexane / ethyl acetate 1:1) as a colorless solid (120 mg, 346 µmol, 48%). Enantiomers were separated by semi-preparative HPLC (chiral,

Daicel Chiracel OD (2 cm × 25 cm), *n*-hexane: *i*-PrOH 97:3, 6.0 mL / min, T_c: 40 °C, 20 mg loading, t_R 56–62 min (+) and 67–78 min (−)).

$C_{21}H_{23}BNOP$ (347.20 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.40 (dd, *J* = 4.8, 0.6 Hz, 1H, H_{Ar}), 7.79–7.73 (m, 4H, H_{Ar}), 7.53 (dd, *J* = 7.6, 0.9 Hz, 1H, H_{Ar}), 7.50–7.40 (m, 6H, H_{Ar}), 7.13 (dd, *J* = 7.6, 4.9 Hz, 1H, H_{Ar}), 3.49 (dd, *J* = 15.0, 9.9 Hz, 1H, CH_2P), 3.33 (br s, 1H, O*H*), 3.04–2.96 (m, 1H, ArCH_2), 2.69–2.67 (m, 2H, CH_2P, ArCH_2), 2.29 (ddd, *J* = 13.6, 8.1 Hz, 4.2 Hz, 1H, CCH_2CH$_2$),), 2.15 (ddd, *J* = 13.8, 8.4, 6.9 Hz, 1H, CCH_2CH$_2$), 1.70–0.70 (br s, 3H, BH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 164.7 (d, J_{CP} = 10 Hz, C_{Ar}), 146.1 (HC_{Ar}), 136.1 (C_{Ar}), 133.3 (HC_{Ar}), 132.4 (d, J_{CP} = 9 Hz, HC_{Ar}), 131.9 (d, J_{CP} = 9 Hz, HC_{Ar}), 131.3 (d, J_{CP} = 3 Hz, HC_{Ar}), 131.0 (d, J_{CP} = 2 Hz, HC_{Ar}), 130.2 (d, J_{CP} = 37 Hz, C_{Ar}), 129.7 (d, J_{CP} = 35 Hz, C_{Ar}), 128.9 (d, J_{CP} = 6 Hz, HC_{Ar}), 128.8 (d, J_{CP} = 6 Hz, HC_{Ar}), 123.4 (HC_{Ar}), 80.6 (*C*(OH)), 38.2 (d, J_{CP} = 2 Hz, C*C*H$_2$CH$_2$), 36.2 (d, J_{CP} = 34 Hz, *C*H$_2$P), 27.3 (Ar*C*H$_2$). **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 6.1 (br d, J_{PB} = 62 Hz) ppm. **MS** (FAB NBA) *m/z* (%): 348 ([M+H]$^+$, 57), 334 ([M-H-BH_3]$^+$, 40), 316 (41), 185 (100), 132 (61), 107 (21), 89 (30), 77 (40), 69 (26), 57 (42), 51 (21), 39 (33). **IR**: $\tilde{\nu}$ = 3148 (w br), 2835 (m), 1590 (w), 1483 (w), 1437 (s), 1410 (m), 1313 (w), 1246 (w), 1180 (w), 1105 (m), 1085 (m), 1064 (w), 1054 (s), 1001 (m), 969 (m), 953 (m), 821 (m), 800 (s), 763 (w), 747 (m), 731 (s), 703 (s), 689 (s br), 670 (w). **EA**: calc. (%) C 72.65, H 6.68, N 4.03; found C 72.47, H 6.67, N 3.84. **m.p.**: 122–123 °C (dec.). **TLC** (SiO_2, cyclohexane / ethyl acetate 1:1): R_f = 0.18. **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane / *i*-PrOH, 0.9 mL/min, 40 °C): t_R = 24.7 min (+), 28.6 min (−). **[α]$_D^{20}$**: +10.2 (*c* = 1.02, $CHCl_3$), −9.7 (*c* = 1.03, $CHCl_3$).

7-((Di-*ortho*-tolylphosphino)methyl)-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-ol (85b)

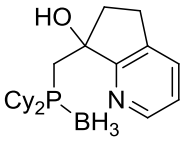


The title compound **85b** was obtained following the general procedure **F** using **84b** (310 mg, 1.28 mmol, 1.1 eq.), THF (4.0 mL), *n*-BuLi (0.8 mL, 1.28 mmol, 1.1 eq.), **76a** (155 mg, 1.16 mmol, 1.0 eq.), LiBr (101 mg, 1.16 mmol, 1.0 eq.), THF (5.0 mL), after purification by flash chromatography (SiO_2, 1.5 cm × 23 cm, cyclohexane / ethyl acetate 1:1) as a slightly reddish oil (118 mg, 0.326 mmol, 28%).

$C_{23}H_{24}NOP$ (361.42 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.38 (dd, *J* = 5.7 Hz, 1H, H_{Ar}), 7.75 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.32–7.27 (m, 1H, H_{Ar}), 7.22–6.90 (m, 8H, H_{Ar}), 5.55 (dd, *J* = 7.9, 4.2 Hz, 1H, CH_2P), 4.12 (br s, 1H, O*H*) 3.24–3.10 (m, 1H, CH_2P), 2.84–2.70 (m, 2H, ArCH_2), 2.43 (s, 3H, ArCH_3), 2.39 (s, 3H, ArCH_3), 2.33–2.08 (m, 2H, CH_2) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = –51.1 ppm. **MS** (EI, 70 eV, ca. 200 °C) *m/z* (%): 361 ([M]$^+$, 23), 343 (93), 328 (18), 252 (53), 227 (100), 220 (28), 213 (50), 207 (21), 196 (18), 179 (17), 165 (23), 148 (19), 130 (56), 121 (17), 105 (14), 91 (21), 78 (24). **TLC** (SiO_2, cyclohexane / ethyl acetate 1:1): R_f = 0.13.

7-((Dicyclohexylphosphino)methyl)-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-ol (85c)



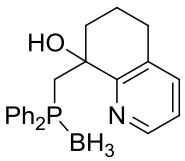
The title compound **85c** was obtained following the general procedure **F** using **84c** (289 mg, 1.28 mmol, 1.1 eq.), THF (5.0 mL), *n*-BuLi (0.8 mL, 1.28 mmol, 1.1 eq.), ketone **76a** (155 mg, 1.16 mmol, 1.0 eq.), LiBr (101 mg, 1.16 mmol, 1.0 eq.), THF (2.0 mL), after purification by flash chromatography (SiO_2, 1.5 cm × 22 cm, cyclohexane / ethyl acetate 1:1) as a slightly red solid (108 mg, 0.301 mmol, 26%).

$C_{21}H_{35}BNOP$ (359.29 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.42 (dd, *J* = 4.9, 0.7 Hz, 1H, H_{Ar}), 7.54 (dd, *J* = 7.4, 0.6 Hz, 1H, H_{Ar}), 7.12 (dd, *J* = 7.6, 4.9 Hz, 1H, H_{Ar}), 3.42 (br s, 1H, O*H*), 3.03 (td, *J* = 15.2, 7.5 Hz, 1H, ArCH_2), 2.82–2.70 (m, 2H, ArCH_2, CH_2P), 2.49 (ddd, *J* = 13.5, 8.1, 4.2 Hz, 1H, CH_2C), 2.35 (ddd, *J* = 13.8, 8.3, 7.0, 1H, CH_2C), 2.02–1.69 (m, 13H, Cy, CH_2P), 1.51–1.37 (m, 2H, Cy), 1.29–1.14 (m, 8H, Cy), 1.10–0.10 (br d, *J* = 114 Hz, 3H, BH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 165.0 (d, J_{CP} = 10 Hz, C_{Ar}), 148.2 (HC_{Ar}), 136.2 (C_{Ar}), 133.3 (HC_{Ar}), 123.2 (HC_{Ar}), 80.4 (*C*(OH)), 39.7 (*C*H$_2$C), 33.0 (d, J_{CP} = 34 Hz, CH Cy), 32.6 (d, J_{CP} = 34 Hz, CH Cy), 27.0 (d, *J* = 8 Hz, *C*H$_2$P), 26.8 (d, *J* = 4 Hz, CH$_2$ Cy), 26.7 (d, *J* = 12 Hz, CH$_2$ Cy), 26.4 (s, CH$_2$ Cy), 26.3 (d, *J* = 3 Hz, CH$_2$ Cy), 25.9 (Ar*C*H$_2$) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 16.4 (br d, J_{PB} = 58 Hz) ppm. **MS** (EI, 70 eV, ca. 150 °C) *m/z* (%): 359 ([M]$^+$, 6), 345 (5), 328 (10), 262 (100), 244 (10), 199 (8), 180 (36), 162 (27), 132 (45), 83 (6), 55 (12), 41 (6); (FAB NBA + KCl) *m/z* (%): 398 ([M+K]$^+$, 42), 356 (100), 346 (34), 328 (59), 262 (23), 180 (18), 162 (15), 132 (80), 115 (25), 81 (24), 77 (12),

55 (35), 39 (26). **IR**: $\tilde{\nu}$ = 3475 (w), 2922 (s), 2851 (s), 2381 (s br), 1740 (w), 1586 (m), 1443 (s), 1420 (m), 1363 (w), 1320 (w), 1220 (w), 1190 (w), 1142 (w), 1064 (s), 1041 (m), 1000 (m), 930 (w), 891 (m), 853 (m), 830 (w), 795 (m), 750 (w). **EA**: calc. (%) C 70.20, H 9.82, N 3.90; found C 69.91, H 9.64, N 3.72. **TLC** (SiO_2, cyclohexane / ethyl acetate 1:1): R_f = 0.26.

8-((Diphenylphosphino)methyl)-5,6,7,8-tetrahydroquinolin-8-ol-BH_3-adduct (85d-BH_3)



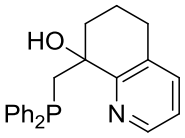
The title compound **85d-BH_3** was obtained following the general procedure **F** using diphenyl-methyl-phosphine-borane adduct **84a** (310 mg, 1.45 mmol, 1.1 eq.), THF (5.0 mL), *n*-BuLi (0.5 mL, 800 µmol, 1.1 eq.), **76c** (193 mg, 1.31 mmol, 1.0 eq.), LiBr (114 mg, 1.31 mmol, 1.0 eq.), THF (2.0 mL), after recrystallization from boiling acetone (7.0 mL) as a colorless solid (285 mg, 0.79 mmol, 60%).

$C_{22}H_{25}BNOP$ (361.18 g/mol):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.26 (dd, *J* = 3.5, 1.0 Hz, 1H, H_{Ar}), 7.85–7.81 (m, 2H, H_{Ar}), 7.62–7.59 (m, 2H, H_{Ar}), 7.48–7.42 (m, 3H, H_{Ar}), 7.40 (dd, *J* = 7.2, 1.4 Hz, 1H, H_{Ar}), 7.36–7.33 (m, 3H, H_{Ar}), 7.05 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 3.39 (br s, 1H, O*H*), 3.26 (dd, *J* = 14.8, 11.9 Hz, 1H, CH_2P), 2.93 (dd, *J* = 14.8, 10.8 Hz, 1H, CH_2P), 2.79–2.69 (m, 2H, ArCH_2), 2.33–2.27 (m, 1H, CH_2C), 2.08–2.04 (m, 1H, CH_2C), 1.93–1.85 (m, 1H, $CH_2CH_2CH_2CH_2$), 1.79–1.71 (m, 1H, $CH_2CH_2CH_2CH_2$), 1.50–0.60 (br s, 3H, BH_3) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$): δ = 158.3 (d, J_{CP} = 6 Hz, C_{Ar}), 148.4 (HC_{Ar}), 147.1 (HC_{Ar}), 137.1 (HC_{Ar}), 132.2 (d, J_{CP} = 9 Hz, HC_{Ar}), 132.1 (d, J_{CP} = 9 Hz, HC_{Ar}), 131.8 (C_{Ar}), 130.9 (d, J_{CP} = 40 Hz, C_{Ar}), 130.8 (d, J_{CP} = 3 Hz, HC_{Ar}), 130.7 (d, J_{CP} = 2 Hz, HC_{Ar}), 130.4 (d, J_{CP} = 57 Hz, C_{Ar}), 128.6 (d, J_{CP} = 10 Hz, HC_{Ar}), 128.5 (d, J_{CP} = 10 Hz, HC_{Ar}), 122.9 (HC_{Ar}), 72.7 (d, J_{CP} = 1 Hz, *C*(OH)), 38.2 (d, J_{CP} = 32 Hz, *C*H_2P), 35.5 (d, J_{CP} = 2 Hz, *C*H_2C), 27.3 (Ar*C*H_2), 19.1 (*C*H_2) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, $CDCl_3$): δ = 9.5 (br d, J_{PB} = 66 Hz) ppm. **MS** (FAB NBA) *m/z* (%): 362 ($[M+H]^+$, 65), 348 (50), 330 (13), 270 (11), 252 (12), 199 (42), 185 (62), 176 (19), 165 (10), 155 (10), 146 (100), 136 (32), 124 (14), 115 (11), 107 (27), 91 (29), 77 (39), 65 (19), 51 (10), 39 (10). **IR**: $\tilde{\nu}$ = 3194 (w br), 3066 (w), 2941 (w), 2940 (w), 2915 (w), 2397 (m), 2380 (m), 1580 (w), 1575 (w,) 1447 (m), 1434 (s), 1409 (m) 1386 (w), 1333 (w), 1302 (w), 1278 (w), 1234 (m), 1184 (w), 1134 (w), 1103 (s), 1093 (s), 1062 (s), 1039 (w), 1023 (s), 976 (s),

944 (w), 908 (m), 888 (s), 859 (m), 813 (s), 801 (s), 775 (w), 762 (w), 748 (s), 738 (s), 698 (s), 688 (s) cm^{-1}. **m.p.**: 140–141 °C (dec.). **TLC** (SiO_2, cyclohexane / DCM 1:1): R_f = 0.31.

Note: The BH_3 protecting group of **85d-BH$_3$** was removed prior the silylation of the alcohol, because of the better separation of enanatiomers by semi-preparative HPLC.

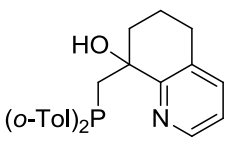
8-((Diphenylphosphino)methyl)-5,6,7,8-tetrahydroquinolin-8-ol (85d)



A solution of **85d-BH$_3$** (52 mg, 144 µmol, 1.0 eq.) in diethyl amine (2 mL, 1.42 g, 19.3 mmol, 134 eq.) was stirred for 2 h. After complete converstion, the volatiles were removed in *vacuo* to give the title compound **85d** (44.0 mg, 144 µmol, 88%). Enantiomers were separated by semi-preparative HPLC (chiral, Daicel Chiracel OD (2 cm × 25 cm), *n*-hexane : *i*-PrOH 95:5, 6.0 mL/min, T_c: 25 °C, 5 mg loading, t_R 38–48 min (+) and 52–63 min (−).

$C_{22}H_{22}NOP$ (347.39 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.34–8.26 (m, 1H, H_{Ar}), 7.53–7.45 (m, 2H, H_{Ar}), 7.41–7.23 (m, 9H, H_{Ar}), 7.02 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 3.64 (br s, 1H, O*H*), 2.94 (dd, *J* = 14.4, 3.8 Hz, 1H, CH_2P), 2.77 (t, *J* = 6.1 Hz, 2H, ArCH_2), 2.67 (dd, *J* = 14.4, 2.2 Hz, 1H, CH_2P), 2.49–2.30 (m, 1H, CH_2C), 2.11–1.96 (m, 1H, CH_2C), 1.91–1.77 (m, 2H, CH_2) ppm. **^{31}P{^{1}H}-NMR** (1622 MHz, $CDCl_3$): δ = −28.9 (s) ppm. **m.p.**: 112–113 °C. **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane / *i*-PrOH 95:5, 0.5 mL/min, 20 °C): t_R = 18.2 min (+), 23.6 min (−). **[α]$_D^{20}$**: +21.2 (*c* = 1.25, $CHCl_3$), −18.0 (*c* = 1.20, $CHCl_3$).

8-((Di-*ortho*-tolylphosphino)methyl)-5,6,7,8-tetrahydroquinolin-8-ol (85e)



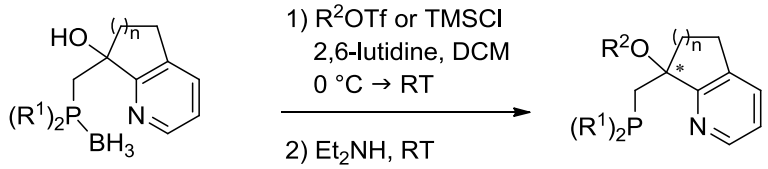
The title compound **85e** was obtained following the general procedure **F** using **84b** (348 mg, 1.44 mmol, 1.1 eq.), THF (5.0 mL), *n*-BuLi (0.9 mL, 1.44 mmol, 1.1 eq.), **76c** (193 mg, 1.31 mmol, 1.0 eq.), LiBr (114 mg, 1.31 mmol, 1.0 eq.), THF (2.0 mL), after purification by flash chromatography (SiO_2, 1.5 cm × 22 cm, cyclohexane / DCM 5:1 → 1:1 → 0:1) and by recrystallization from boiling *iso*-propanol (1.0 mL) as a yellow solid (143 mg, 0.38 mmol, 29%). Enantiomers were separated

by semi-preparative HPLC (chiral, Daicel Chiracel OD (2 cm × 25 cm), *n*-hexane : *i*-PrOH 98:2, 6.0 mL/min, T_c: 35 °C, 30 mg loading, t_R 34–40 min (+) and 42–51 min (−).

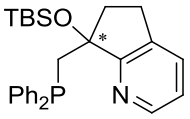
$C_{24}H_{26}NOP$ (375.44 g/mol):

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 4.6 Hz, 1H, H_{Ar}), 7.45–7.42 (m, 1H, H_{Ar}), 7.40 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.23–7.08 (m, 6H, H_{Ar}), 7.05–7.01 (m, 2H, H_{Ar}), 3.72 (br s, 1H, O*H*), 2.93 (dd, *J* = 14.7 Hz, *J* = 3.0 Hz, 1H, CH_2P), 2.81–2.78 (m, 2H, ArCH_2), 2.51–2.44 (m, 5H, CH_2C, CH_2P, ArCH_3), 2.37 (s, 3H, ArCH_3), 2.09–2.04 (m, 1H, CH_2C), 1.94–1.87 (m, 1H, $CH_2CH_2CH_2$), 1.86–1.77 (m, 1H, $CH_2CH_2CH_2$) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$): δ = 160.2 (d, J_{CP} = 3 Hz, C_{Ar}), 147.0 (HC_{Ar}), 142.3 (d, J_{CP} = 24 Hz, C_{Ar}), 142.0 (d, J_{CP} = 25 Hz, C_{Ar}), 137.9 (d, J_{CP} = 13 Hz, C_{Ar}), 137.5 (d, J_{CP} = 13 Hz, C_{Ar}), 137.0 (HC_{Ar}), 132.4 (HC_{Ar}), 131.1 (C_{Ar}), 131.0 (HC_{Ar}), 130.1 (d, J_{CP} = 5 Hz, HC_{Ar}), 130.0 (d, J_{CP} = 5 Hz, HC_{Ar}), 128.3 (HC_{Ar}), 128.1 (HC_{Ar}), 126.0 (HC_{Ar}), 125.9 (HC_{Ar}), 122.4 (HC_{Ar}), 72.7 (d, J_{CP} = 14 Hz, *C*(OH)), 41.3 (d, J_{CP} = 17 Hz, *C*H_2P), 35.4 (d, J_{CP} = 10 Hz, *C*H_2C), 28.9 (Ar*C*H_2), 21.5 (d, J_{CP} = 2 Hz, Ar*C*H_3), 21.3 (Ar*C*H_3), 19.5 ($CH_2CH_2CH_2$) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, $CDCl_3$): δ = –48.1 ppm. **MS** (EI, 70 eV, ca. 150 °C) *m/z* (%): 375 ($[M]^+$, 1), 285 (11), 266 (7), 227 (21), 213 (8), 146 (100), 91 (5); (FAB NBA) *m/z* (%):414 ($[M+K]^+$, 6), 376 ($[M+H]^+$, 26), 213 (19), 39 (12). **EA**: calc. (%) C 76.78, H 6.98, N 3.73; found C 72.42, H 6.97, N 3.60. **m.p.**: 110–111 °C. **TLC** (SiO_2, cyclohexane / DCM 5:1): R_f = 0.31. **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane / *i*-PrOH 98:2, 0.5 mL / min, 25 °C): t_R = 19.4 min (+), 25.4 min (−). **$[\alpha]_D^{20}$**: +19.7 (*c* = 0.80, $CHCl_3$), −20.3 (*c* = 1.02, $CHCl_3$).

8.4.5 Silylation of the Alcohol and Deprotection of Phosphine



(+)-7-((*tert*-Butyldimethylsilyl)oxy)-7-((diphenylphosphino)methyl)-6,7-dihydro-*5H*-cyclopenta[*1*]pyridine (86a)

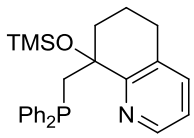


Tert-butyldimethylsilyl trifluoromethanesulfonate (20 µl, 23 mg, 87 µmol, 3.8 eq.) was slowly added to a solution of **85a** (8.0 mg, 23 µmol, 1.0 eq.) and 2,6-lutidine (20 µl, 18 mg, 172 µmol, 7.5 eq.) in DCM (0.5 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirring was continued for 2 h at RT. Water (1.0 mL) was added to the reaction mixture, fallowed by extraction with DCM (2×1.0 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Diethyl amine (1 mL) was added to the crude product and the reaction mixture was stirred overnight at RT. All volatiles were removed in *vacuo* and the crude product was purified by flash chromatography (SiO_2, 0.5 cm × 5 cm, cyclohexane / TBME 19:1) to obtain the title compound **86a** as a colorless solid (8 mg, 92.3 µmol, 56%).

$C_{27}H_{34}NOPSi$ (447.62g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.44 (dd, *J* = 4.8, 0.7 Hz, 1H, H_{Ar}), 7.57–7.53 (m, 2H, H_{Ar}), 7.48 (dd, *J* = 7.6, 0.7 Hz, 1H, H_{Ar}), 7.42–7.38 (m, 2H, H_{Ar}), 7.32–7.24 (m, 6H, H_{Ar}), 7.10 (dd, *J* = 7.6, 4.9 Hz, 1H, H_{Ar}), 3.18 (dd, *J* = 14.3, 3.2 Hz, 1H, CH_2P), 2.91–2.98 (m, 1H, ArCH_2), 2.72 (ddd, *J* = 16.3, 8.5, 4.5 Hz, 1H, ArCH_2), 2.55 (dd, *J* = 14.3, 3.5 Hz, 1H, CH_2P), 2.36–2.28 (m, 1H, CCH_2CH$_2$), 2.23–2.17 (m, 1H, CCH_2CH$_2$), 0.74 (s, 9H, (CH_3)$_3$CSi), –0.05 (s, 3H, CH_3Si), –0.54 (s, 3H, CH_3Si) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 165.8 (d, J_{CP} = 4 Hz, C_{Ar}), 148.2 (HC_{Ar}), 140.6 (d, J_{CP} = 13 Hz, C_{Ar}), 139.8 (d, J_{CP} = 13 Hz, C_{Ar}), 133.4 (d, J_{CP} = 20 Hz, HC_{Ar}), 136.9 (C_{Ar}), 133.0 (HC_{Ar}), 132.9 (d, J_{CP} = 21 Hz, HC_{Ar}), 128.4 (dd, J_{CP} = 7 Hz, 4 Hz HC_{Ar}), 123.1 (HC_{Ar}), 128.2 (HC_{Ar}), 84.1 (d, J_{CP} = 16 Hz, *C*(OH)), 41.3 (d, J_{CP} = 16 Hz, *C*H$_2$P), 39.8 (d, J_{CP} = 9 Hz, C*C*H$_2$CH$_2$), 27.3 (ArCH$_2$), 26.0 (*C*H$_3$)$_3$CSi), 18.2 ((CH$_3$)$_3$*C*Si), –2.8 (*C*H$_3$Si), –3.9 (*C*H$_3$Si) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = –27.0 ppm. **TLC** (SiO_2, cyclohexane / TBME 19:1): R_f = 0.27. **$[\alpha]_D^{20}$**: = +22.6 (*c* = 1.40, $CHCl_3$).

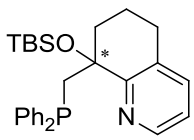
8-((Diphenylphosphino)methyl)-8-((trimethylsilyl)oxy)-5,6,7,8-tetrahydroquinoline (86b)



Trimethylsilyl chloride (30 µl, 25.7 mg, 236 µmol, 1.4 eq.) was added to a solution of alcohol **85d** (58 mg, 166 µmol, 1.0 eq.), triethyl amine (35 µl, 24 mg, 236 µmol, 1.4 eq.) and potassium iodide (5.0 mg, 30.0 µmol, 0.2 eq.) in THF (1.0 mL) at 0 °C. After stirring for overnight at RT, water (1 mL) was added. The reaction mixture was extracted with TBME (3×1 mL). Combined organic layers were dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 0.5 cm × 5 cm, DCM / cyclohexane 2:1) to give the title compound **86b** (40 mg, 92.3 µmol, 56%) as a colorless solid.

$C_{25}H_{30}NOPSi$ (419.57 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.43 (dd, *J* = 4.6, 1.6 Hz, 1H, H_{Ar}), 7.61 (dt, *J* = 7.7, 1.7 Hz, 2H, H_{Ar}), 7.42–7.31 (m, 6H, H_{Ar}), 7.29–7.20 (m, 3H, H_{Ar}), 7.09 (dd, *J* = 7.7, 4.6 Hz, 1H, H_{Ar}), 3.16 (dd, *J* = 14.0, 5.4 Hz, 1H, CH_2P), 3.06 (dd, *J* = 14.1, 3.1 Hz, 1H, CH_2P), 2.79–2.75 (m, 2H, ArCH_2), 2.13–2.06 (m, 2H, $CH_2CH_2CH_2$), 2.04–1.93 (m, 1H, CH_2C), 1.76–1.68 (m, 1H, CH_2C), 0.21 (s, 9H, CH_3Si) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 159.9 (d, J_{CP} = 3 Hz, C_{Ar}), 147.0 (HC_{Ar}), 139.8 (d, J_{CP} = 12 Hz, C_{Ar}), 139.3 (d, J_{CP} = 12 Hz, C_{Ar}), 136.8 (HC_{Ar}), 133.1 (HC_{Ar}), 132.9 (HC_{Ar}), 132.8 (HC_{Ar}), 132.6 (HC_{Ar}), 131.1 (C_{Ar}), 128.27 (HC_{Ar}), 128.24 (HC_{Ar}), 128.21 (HC_{Ar}), 128.19 (HC_{Ar}), 128.16 (HC_{Ar}), 122.6 (HC_{Ar}), 76.3 (d, J_{CP} = 19 Hz, *C*(OSi)), 42.4 (d, J_{CP} = 15 Hz, *C*H$_2$P), 38.1 (d, J_{CP} = 12 Hz, *C*H$_2$C), 26.9 (Ar*C*H$_2$), 18.6 ($CH_2CH_2CH_2$), 1.6 (*C*H$_3$Si) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = −25.7 ppm. **TLC** (SiO_2, DCM / cyclohexane 2:1): R_f = 0.20.

8-(*tert*-Butyldimethylsilyloxy)-8-((diphenylphosphino)methyl)-5,6,7,8-tetrahydroquinoline (86c)



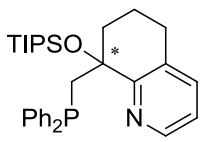
Tert-butyldimethylsilyl trifluoromethanesulfonate (66 µl, 76.1 mg, 288 µmol, 4.0 eq.) was slowly added to a solution of **85d** (25.0 mg, 72.0 µmol, 1.0 eq.) and 2,6-lutidine (50 µl, 46.2 mg, 432 µmol, 6.0 eq.) in DCM (1.0 mL). The reaction mixture was allowed to warm to rt and stirring was continued for 1.5 h at RT. Afterwards all volutiles were removed under reduced pressure. The crude product was purified by flash chromatography using a *Schlenk* fritt (SiO_2, 2 cm × 4 cm, cyclohexane /

ethyl acetate 4:1) to obtain the title compound **86c** as a colorless solid (23.0 mg, 49.8 µmol, 69%).

$C_{28}H_{36}NOPSi$ (461.65 g/mol):

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 8.39 (dd, *J* = 4.5, 0.9 Hz, 1H, H_{Ar}), 7.55 (dt, *J* = 7.5, 1.6 Hz, 2H, H_{Ar}), 7.39–7.29 (m, 6H, H_{Ar}), 7.23–7.21 (m, 3H, H_{Ar}), 7.09 (dd, *J* = 7.7, 4.6 Hz, 1H, H_{Ar}), 3.14 (dd, *J* = 14.0, 3.8 Hz, 1H, CH_2P), 3.00 (dd, *J* = 14.0, 4.9 Hz, 1H, CH_2P), 2.78–2.72 (m, 2H, ArCH_2), 2.03–1.91 (m, 3H, CH_2C, $CH_2CH_2CH_2$), 1.68–1.62 (m, 1H, CH_2C), 0.77 (s, 9H, (CH_3)$_3$CSi), 0.08 (s, 3H, CH_3Si), –0.70 (s, 3H, CH_3Si) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 158.5 (d, J_{CP} = 2 Hz, C_{Ar}), 146.7 (HC_{Ar}), 141.2 (d, J_{CP} = 14 Hz, C_{Ar}), 140.2 (d, J_{CP} = 13 Hz, C_{Ar}), 137.0 (HC_{Ar}), 133.4 (d, J_{CP} = 20 Hz, HC_{Ar}), 132.9 (d, J_{CP} = 2 Hz, C_{Ar}), 132.8 (d, J_{CP} = 19 Hz, HC_{Ar}), 128.9 (HC_{Ar}), 128.4 (d, J_{CP} = 3 Hz, HC_{Ar}), 128.2 (d, J_{CP} = 7 Hz, HC_{Ar}), 127.9 (HC_{Ar}), 122.7 (HC_{Ar}), 76.2 (d, J_{CP} = 21 Hz, *C*(OSi)), 42.2 (d, J_{CP} 15 Hz, *C*H_2P), 38.5 (d, J_{CP} = 10 Hz, *C*H_2C), 29.3 (Ar*C*H_2), 25.8 (*C*H_3)$_3$CSi), 18.7 (CH_2*C*H_2CH_2), 18.2 (d, J_{CP} = 20 Hz, (CH_3)$_3$*C*Si), –2.8 (*C*H_3Si), –4.5 (*C*H_3Si) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = –26.4 ppm.

8-((Diphenylphosphino)methyl)-8-(tri-*iso*-propylsilyloxy)-5,6,7,8-tetrahydroquinoline (86d)



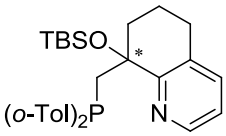
Tri-*iso*-propylsilyl trifluoromethanesulfonate (80 µl, 91.2 mg, 297 µmol, 4.1 eq.) was slowly added to a solution of alcohol **85d** (25.0 mg, 72.0 µmol, 1.0 eq.) and 2,6-lutidine (50 µl, 46.2 mg, 432 µmol, 6.0 eq.) in DCM (1.0 mL) and. The reaction mixture was allowed to warm to rt and stirring was continued for 2 h at RT. Afterwards the volatiles were removed under reduced pressure. The crude product was purified by flash chromatography using a *Schlenk* fritt (SiO_2, 2 cm × 5 cm, cyclohexane / ethyl acetate 5:1) to obtain the title compound **86d** (14.0 mg, 27.0 µmol, 38%) as a colorless oil.

$C_{31}H_{42}NOPSi$ (503.73 g/mol):

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 8.36–8.35 (m, 1H, H_{Ar}), 7.58–7.53 (m, 2H, H_{Ar}), 7.41–7.34 (m, 6H, H_{Ar}), 7.28–7.23 (m, 3H, H_{Ar}), 7.09 (dd, *J* = 7.7, 4.6 Hz, 1H, H_{Ar}), 3.52 (dd, *J* = 13.5, 4.1 Hz, 1H, CH_2P), 2.87 (dd, *J* = 13.5, 5.1 Hz, 1H, CH_2P), 2.80–2.76 (m, 2H,

ArCH_2), 2.10–2.02 (m, 2H, $CH_2CH_2CH_2$), 1.93–1.89 (m, 1H, CH_2C), 1.71–1.61 (m, 1H, CH_2C), 1.08–0.91 (m, 21H, CH(CH_3)$_3$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 158.5 (d, J_{CP} = 2 Hz, C_{Ar}), 146.7 (HC_{Ar}), 141.2 (d, J_{CP} = 14 Hz, C_{Ar}), 140.2 (d, J_{CP} = 13 Hz, C_{Ar}), 137.0 (HC_{Ar}), 133.4 (d, J_{CP} = 20 Hz, HC_{Ar}), 132.9 (d, J_{CP} = 2 Hz, C_{Ar}), 132.8 (d, J_{CP} = 19 Hz, HC_{Ar}), 128.9 (HC_{Ar}), 128.4 (d, J_{CP} = 3 Hz, HC_{Ar}), 128.2 (d, J_{CP} = 7 Hz, HC_{Ar}), 127.9 (HC_{Ar}), 122.7 (HC_{Ar}), 76.2 (d, J_{CP} = 21 Hz, C(OSi)), 42.2 (d, J_{CP} 16 Hz, CH$_2$P), 38.5 (d, J_{CP} = 9 Hz, CH$_2$C), 29.3 (ArCH$_2$), 18.7 ($CH_2CH_2CH_2$), 13.6 ((CH_3)$_2C$HSi), 13.5 ((CH$_3$)$_2$CHSi) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = –25.1 ppm.

8-((*tert*-Butyldimethylsilyl)oxy)-8-((di-*ortho*-tolylphosphino)methyl)-5,6,7,8-tetrahydroquinoline (86e)

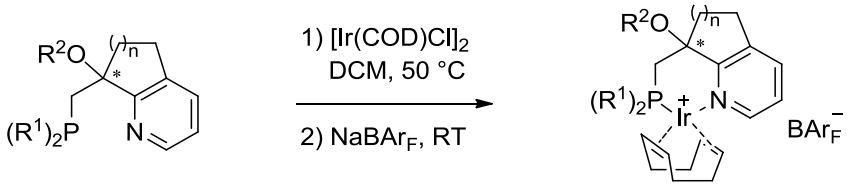


Tert-butyldimethylsilyl trifluoromethanesulfonate (100 µl, 115 mg, 435 µmol, 3.9 eq.) was added to a solution of **85e** (42.0 mg, 112 µmol, 1.0 eq.) and 2,6-lutidine (80 µl, 73.8 mg, 689 µmol, 6.1 eq.) in DCM (1.0 mL). The reaction mixture was allowed to warm to rt and stirring was continued for 2 h at RT. Afterwards the volatiles were removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 0.5 cm × 5 cm, cyclohexane / ethyl acetate 19:1) to obtain the title compound **86e** (36.0 mg, 73.5 µmol, 66%) as a colorless solid.

$C_{30}H_{40}NOPSi$ (489.70 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.40 (dd, J = 4.5, 1.4 Hz, 1H, H_{Ar}), 7.82 (ddd, J = 7.4, 3.8, 1.0 Hz, 1H, H_{Ar}), 7.34–7.27 (m, 2H, H_{Ar}), 7.23 (dt, J = 7.4, 1.4 Hz, 1H, H_{Ar}), 7.14–6.99 (m, 6H, H_{Ar}), 3.04 (dd, J = 14.3 Hz, 3.9 Hz, 1H, CH_2P), 2.86–2.82 (m, 1H, CH_2P), 2.76–2.73 (m, 2H, ArCH_2), 2.46 (s, 3H, ArCH_3), 2.25 (s, 3H, ArCH_3), 2.23–2.17 (m, 1H, CH_2C), 2.05–1.93 (m, 2H, $CH_2CH_2CH_2$, CH_2C), 1.75–1.67 (m, 1H, $CH_2CH_2CH_2$), 0.75 (s, 9H, (CH_3)$_3$CSi), 0.09 (s, 3H, CH_3Si), –0.70 (s, 3H, CH_3Si) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 159.0 (C_{Ar}), 147.0 (HC_{Ar}), 142.1 (d, J_{CP} = 6 Hz, C_{Ar}), 141.9 (d, J_{CP} = 4 Hz, C_{Ar}), 138.9 (d, J_{CP} = 14 Hz, C_{Ar}), 138.0 (d, J_{CP} = 14 Hz, C_{Ar}), 136.7 (HC_{Ar}), 132.9 (HC_{Ar}), 132.5 (C_{Ar}), 132.0 (HC_{Ar}), 129.8 (dd, J_{CP} = 9 Hz, 5 Hz, HC_{Ar}), 128.3 (HC_{Ar}), 128.0 (HC_{Ar}), 127.9 (HC_{Ar}), 125.8 (HC_{Ar}), 122.5 (HC_{Ar}), 76.3 (d, J_{CP} = 19 Hz, C(OH)), 40.2 (d, J_{CP} = 17 Hz, CH$_2$P), 38.5 (d, J_{CP} = 10 Hz, CH$_2$C), 29.6 (ArCH$_2$), 26.0 (CH$_3$)$_3$CSi), 21.5 (d, J_{CP} = 20 Hz, ArCH$_3$), 21.3 (d, J_{CP} = 19 Hz, ArCH$_3$), 19.3 ($CH_2CH_2CH_2$), 18.5 ((CH_3)$_3C$Si), –2.8 (CH$_3$Si), –4.2 (CH$_3$Si) ppm.

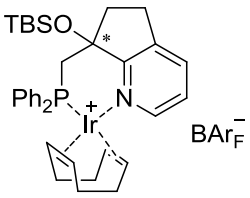
^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ = –49.0 ppm. **MS** (EI, 70 eV, ca. 150 °C) *m/z* (%): 489 ($[M]^+$, 11), 432 (100), 398 (68), 357 (9), 276 (13), 262 (34), 227 (53), 213 (19), 205 (32), 148 (8), 133 (5), 105 (5), 73 (15). **EA**: calc. (%) C 73.58, H 8.23, N 2.86; found 72.67, 8.17, 2.63. **m.p.**: 119–121°C. **TLC** (SiO_2, cyclohexane / TBME 9:1): R_f = 0.56.

8.4.6 Preparation of the Ir-complexes



General Procedure G: A solution of the N,P ligand (1.0 eq.) in DCM (0.02 M) was slowly added to a solution of $[Ir(COD)Cl]_2$ (0.5 eq.) in DCM (0.04-0.05 M). The reaction mixture was stirred for 1 h at 50 °C. $NaBAr_F$ (>1.1 eq.) was added after cooling down to RT. The reaction mixture was vigorously stirred for 0.5 h. Afterwards the solvent was removed under reduced pressure. The crude Ir-complex was purified by flash chromatography. First side products were separated by elution with TBME and then the desired Ir-complex was washed down with DCM (collecting the orange-red band). If necessary the Ir-complex was recrystallized by from DCM / *n*-pentane or diethyl ether / *n*-pentane.

(+)-[η^4-1,5-Cyclooctadiene-7-((*tert*-butyldimethylsilyl)oxy)-7-((diphenylphosphino)methyl)-6,7-dihydro-*5H*-cyclopenta[*1*]pyridine-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate (87a)

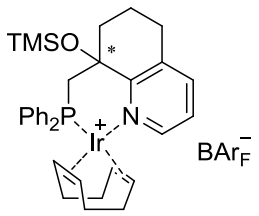


The title compound **87a** was obtained following the general procedure **G** using $[Ir(COD)Cl]_2$ (11.6 mg, 17.2 µmol, 0.5 eq.), DCM (0.5 mL), ligand **86a** (14.0 mg, 31.3 µmol, 1.0 eq.), DCM (1 mL), $NaBAr_F$ (30.5 mg, 34.4 µmol, 1.1 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) as an orange solid (37.0 mg, 23.0 µmol, 73%).

$C_{67}H_{58}BF_{24}IrNOPSi$ (1611.23 g/mol):

^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.46 (d, *J* = 5.7 Hz, 1H, H_{Ar}), 7.86–7.79 (m, 2H, H_{Ar}), 7.77 (dd, *J* = 7.7, 0.8 Hz, 1H, H_{Ar}), 7.75 (s, 8H, BAr_F-*H*), 7.56 (s, 4H, BAr_F-*H*), 7.50–7.38 (m, 6H, H_{Ar}), 7.38–7.30 (m, 3H, H_{Ar}), 4.98 (p, *J* = 7.3 Hz, 1H, C*H* COD), 4.76 (q, *J* = 6.3 Hz, 1H, C*H* COD), 3.67–3.59 (m, 1H, C*H* COD), 3.18–3.09 (m, 1H, CH_2), 2.96 (dd, *J* = 15.3, 9.1 Hz, 1H, CH_2P), 2.92–2.83 (m, 1H, CH_2) 2.80–2.70 (m, 2H, CH_2 1H, C*H* COD 1H), 2.66–2.49 (m, 4H, CH_2 1H, CH_2 COD 3H), 2.38 (dd, *J* = 15.3, 10.5 Hz, 1H, CH_2P), 2.37–2.29 (m, 1H, CH_2 COD), 2.27–2.19 (m, 1H, CH_2 COD), 2.05–1.92 (m, 1H, CH_2 COD), 1.69–1.57 (m, 1H, CH_2 COD), 1.45–1.33 (m, 1H, CH_2 COD), 0.96 (s, 9H, $(CH_3)_3$CSi), 0.36 (s, 3H, CH_3Si), 0.26 (s, 3H, CH_3Si) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 164.6 (d, J_{PC} = 5 Hz, C_{Ar}), 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 149.5 (s, HC_{Ar}), 139.8 (s, C_{Ar}), 138.4 (s, HC_{Ar}), 135.6 (d, J_{PC} = 13 Hz, HC_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 133.2 (d, J_{PC} = 54 Hz, C_{Ar}), 132.7 (d, J_{PC} = 10 Hz, HC_{Ar}), 132.6 (d, J_{PC} = 2 Hz, HC_{Ar}), 131.6 (d, J_{PC} = 2 Hz, HC_{Ar}), 129.9 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.5 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.1 (d, J_{PC} = 10 Hz, HC_{Ar}), 128.5 (d, J_{PC} = 54 Hz, C_{Ar}), 127.0 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 96.9 (d, J_{PC} = 12 Hz, *C*H COD), 89.5 (d, J_{PC} = 12 Hz, *C*H COD), 86.2 (s, *C*OSi), 63.1 (s, *C*H COD), 63.0 (s *C*H COD), 41.4 (s, *C*H_2), 40.3 (s, *C*H_2 COD), 38.8 (d, J_{PC} = 30 Hz, *C*H_2P), 36.9 (d, J_{PC} = 4 Hz, *C*H_2 COD), 31.9 (d, J_{PC} = 2 Hz, *C*H_2 COD), 29.3 (d, J_{PC} = 3 Hz, *C*H_2 COD), 27.4 (s, $(CH_3)_3C$), 27.3 (s, *C*H_2), 19.4 (s, $(CH_3)_3C$), −0.9 (s, *C*H_3Si), −1.6 (s, *C*H_3Si) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 10.4 ppm. **MS** (FAB NBA) *m/z* (%): 748 ($[Ir(L)(COD)]^+$, 100), 668 (13), 568 (10). **EA**: calc. (%) C 49.94, H 3.63, N 0.87; found C 49.16, H 3.53, N 0.83. **m.p.**: 153–154 °C. **$[\alpha]_D^{20}$**: +7.0 (*c* = 0.69, $CHCl_3$).

(±)-[η^4-1,5-Cyclooctadiene-8-((diphenylphosphino)methyl)-8-(trimethylsilyloxy)-5,6,7,8-tetrahydroquinoline-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borat (87b)

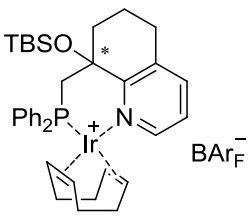


The title compound **87b** was obtained following the general procedure **G** using $[Ir(COD)Cl]_2$ (26.4 mg, 39.3 µmol, 0.5 eq.), DCM (2 mL), ligand **86b** (33.0 mg, 78.7 µmol), DCM (1 mL), $NaBAr_F$ (69.7 mg, 78.7 µmol, 1.0 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 10 cm) as an orange solid (88.0 mg, 55.6 µmol, 71%). Crystals suitable for X-ray analysis were obtained by overlaying a concentrated etheral solution with *n*-pentane.

$C_{65}H_{54}BF_{24}IrNOPSi$ (1583.18 g/mol):

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 8.67 (d, *J* = 5.6 Hz, 1H, H_{Ar}), 7.91–7.83 (m, 2H, H_{Ar}), 7.75 (s, 8H, BAr_F-*H*), 7.59 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.57 (s, 4H, BAr_F-*H*), 7.52–7.40 (m, 6H, H_{Ar}), 7.29 (ddd, *J* = 9.8, 6.6, 3.0 Hz, 2H, H_{Ar}), 7.24 (dd, *J* = 7.7, 5.7 Hz, 1H, H_{Ar}), 4.79–4.67 (m, 1H, C*H* COD), 4.55 (q, *J* = 6.1 Hz, 1H, C*H* COD), 3.56 (q, *J* = 6.3 Hz, 1H, C*H* COD), 2.93 (ddd, *J* = 16.2, 10.1, 5.5 Hz, 1H, CH_2), 2.81–2.72 (m, 2H, CH_2P 1H, CH_2 1H), 2.67–2.43 (m, 6H, CH_2P 1H, CH_2 1H, C*H* COD 1H, CH_2 COD 3H), 2.35 (dd, *J* = 12.6, 6.6 Hz, 1H, CH_2), 2.33–2.20 (m, 2H, CH_2 COD), 2.14–1.92 (m, 2H, CH_2 COD 1H, CH_2 1H), 1.84–1.66 (m, 1H, CH_2), 1.67–1.54 (m, 1H, CH_2 COD), 1.43–1.31 (m, 1H, CH_2 COD), 0.38 (s, 9H, CH_3Si) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.2 (d, J_{PC} = 3 Hz, C_{Ar}), 150.5 (s, HC_{Ar}), 142.0 (s, HC_{Ar}), 136.7 (s, C_{Ar}), 135.5 (d, J_{PC} = 13 Hz, HC_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.8 (d, J_{PC} = 10 Hz, HC_{Ar}), 131.7 (s, C_{Ar}), 131.5 (d, J_{PC} = 2 Hz, HC_{Ar}), 131.2 (s, C_{Ar}), 129.8 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.5 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.1 (d, J_{PC} = 11 Hz, HC_{Ar}), 125.7 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 97.1 (d, J_{PC} = 11 Hz, *C*H COD), 85.0 (d, J_{PC} = 5 Hz, *C*H COD), 78.2 (s, *C*OSi), 61.2 (s, *C*H COD), 57.8 (s, *C*H COD), 41.8 (d, J_{PC} = 8 Hz, *C*H_2), 40.5 (d, J_{PC} = 32 Hz, *C*H_2P), 36.8 (d, J_{PC} = 3 Hz, *C*H_2 COD), 31.5 (d, J_{PC} = 2 Hz, *C*H_2 COD), 30.8 (s, *C*H_2), 29.5 (d, J_{PC} = 3 Hz, *C*H_2 COD), 27.8 (s, *C*H_2 COD), 20.8 (s, *C*H_2), 3.6 (s, *C*H_3) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 7.5 ppm. **MS** (ESI, *c* = 0.05 mg/mL, 50 °C, 15 µL/min) *m/z* (%): 720 ($[Ir(L)(COD)]^+$, 100). **IR**: $\tilde{\nu}$ = 2961 (w br), 1602 (w), 1440 (w), 1354 (s), 1272 (s), 1181 (w), 1154 (m), 1116 (s br), 1074 (m), 1054 (m), 1034 (w), 1028 (w), 996 (w), 897 (w), 886 (m), 838 (m), 743 (m), 715 (m), 696 (m), 682 (m) cm^{-1}. **m.p.**: 163–164°C.

(+)-[η^4-1,5-Cyclooctadiene-8-(*tert*-butyldimethylsilyloxy)-8-((diphenylphosphino)methyl)-5,6,7,8-tetrahydroquinoline-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate (87c)

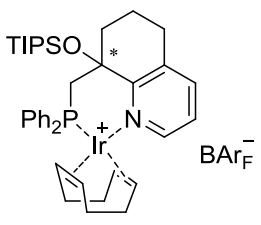


The title compound **87c** was obtained following the general procedure **G** using $[Ir(COD)Cl]_2$ (25.5 mg, 37.9 µmol, 0.5 eq.), DCM (2 mL), ligand **86c** (35.0 mg, 75.8 µmol, 1.0 eq.), DCM (1 mL), $NaBAr_F$ (67.2 mg, 83.4 µmol, 1.1 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) as an orange solid (65.0 mg, 40.0 µmol, 53%).

$C_{68}H_{60}BF_{24}IrNOPSi$ (1625.26 g/mol):

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 8.67 (d, *J* = 5.4 Hz, 1H, H_{Ar}), 7.90–7.79 (m, 2H, H_{Ar}), 7.75 (s, 8H, BAr_F-*H*), 7.58 (s, 4H, BAr_F-*H*), 7.55 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.49–7.35 (m, 6H, H_{Ar}), 7.27–7.15 (m, 3H, H_{Ar}), 4.91–4.77 (m, 2H, C*H* COD), 3.47 (q, *J* = 6.0 Hz, 1H, C*H* COD), 2.96–2.81 (m, 2H, CH_2P 1H, CH_2 1H), 2.78–2.61 (m, 4H, CH_2P 1H, CH_2 1H, C*H* COD 1H, CH_2 COD 1H), 2.60–2.42 (m, 4H, CH_2 2H, CH_2 COD 2H), 2.36–2.19 (m, 2H, CH_2 1H, CH_2 COD 1H,), 2.17–1.97 (m, 2H, CH_2 COD 1H, CH_2 1H), 1.69–1.51 (m, 2H, CH_2 COD), 1.46–1.30 (m, 1H, CH_2 COD), 0.87 (s, 9H, (CH_3)$_3$CSi), 0.53 (s, 3H, (CH_3Si)), 0.51 (s, 3H, (CH_3Si)) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 162.4 q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.0 (d, J_{PC} = 4 Hz, C_{Ar}), 150.6 (s, HC_{Ar}), 142.2 (s, HC_{Ar}), 136.7 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 135.3 (s, HC_{Ar}), 132.6 (d, J_{PC} = 2 Hz, HC_{Ar}), 132.5 (d, J_{PC} = 10 Hz, HC_{Ar}), 131.6 (d, J_{PC} = 2 Hz, HC_{Ar}), 131.5 (s, C_{Ar}), 131.0 (s, C_{Ar}), 129.8 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.5 (qq, J_{FC}=32, J_{BC}=3, C_{Ar} BAr_F), 129.3 (d, J_{PC} = 10 Hz, HC_{Ar}), 125.6 (s, HC_{Ar}), 125.2 (q, J_{FC}=272, *C*F$_3$ BAr_F), 118.1 (septett, J_{FC}=4, HC_{Ar} BAr_F), 99.1 (d, J_{PC} = 11 Hz, *C*H COD), 87.3 (d, J_{PC} = 14 Hz, *C*H COD), 78.5 (s, *C*OSi)), 60.6 (s, *C*H COD), 57.2 (s, *C*H COD), 42.1 (d, J_{PC} = 9 Hz, *C*H$_2$ COD), 40.6 (d, J_{PC} = 32 Hz, *C*H$_2$P), 36.7 (d, J_{PC} = 4 Hz, *C*H$_2$ COD), 31.4 (d, J_{PC} = 4 Hz, *C*H$_2$), 30.4 (s, *C*H$_2$), 29.6 (s, *C*H$_2$), 27.8 (s, *C*H$_2$), 27.5 (s, (CH$_3$)$_3$*C*), 21.2 (s, *C*H$_2$), 19.8 (s, (*C*H$_3$)$_3$C), 1.5 (s, *C*H$_3$Si), 0.3 (s, *C*H$_3$Si) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 6.5 ppm. **MS** (ESI, *c* = 0.05 mg/mL, 50 °C, 20 µL/min) *m/z* (%): 762 ([Ir(L)(COD)]$^+$, 100). **IR**: $\tilde{\nu}$ = 2967 (w br), 2874 (w), 1611 (w), 1471 (w), 1436 (w), 1353 (s), 1272 (s), 1170 (m), 1115 (s br), 1078 (m), 1054 (m), 1034 (m), 999 (w), 885 (m), 839 (m), 805 (w), 783 (w), 743 (w), 712 (m), 681 (s), 669 (m) cm^{-1}. **EA**: calc. (%) C 50.25, H 3.72, N 0.86; found C 50.29, H 3.70, N 0.77. **m.p.**: 169–171°C. **$[\alpha]_D^{20}$**: +12.8 (*c* = 0.35, CH_2Cl_2).

(−)-[η^4-1,5-Cyclooctadiene-8-((diphenylphosphino)methyl)-8-(tri-*iso*-propylsilyloxy)-5,6,7,8-tetrahydroquinoline-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate (87d)

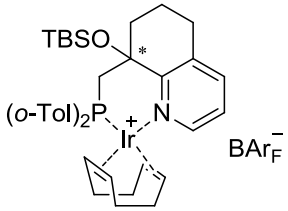


The title compound **87d** was obtained following the general procedure **G** using $[Ir(COD)Cl]_2$ (8.0 mg, 11.9 µmol, 0.5 eq.), DCM (1 mL), ligand **86d** (12.0 mg, 23.8 µmol, 1.0 eq.), DCM (0.5 mL), $NaBAr_F$ (23.2 mg, 26.2 µmol, 1.1 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 10 cm) as an orange solid (28.0 mg, 17.8 µmol, 70%).

$C_{71}H_{66}BF_{24}IrNOPSi$ (1667.34 g/mol):

^{1}H-NMR (400 MHz, CD_2Cl_2[M+H]): δ = 8.68 (d, *J* = 5.6 Hz, 1H, H_{Ar}), 7.83–7.75 (m, 2H, H_{Ar}), 7.72 (s, 8H, BAr_F-*H*), 7.55 (s, 4H, BAr_F-*H*), 7.53 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.50–7.34 (m, 6H, H_{Ar}), 7.28–7.18 (m, 3H, H_{Ar}), 4.96–4.81 (m, 2H, C*H* COD), 3.47 (q, *J* = 6.3 Hz, 1H, C*H* COD), 3.02 (dd, *J* = 15.3, 12.4 Hz, 1H, CH_2), 2.90 (ddd, *J* = 18.1, 12.9, 5.7 Hz, 1H, CH_2P), 2.84–2.76 (m, 1H, C*H* COD), 2.74–2.63 (m, 2H, CH_2P 1H, CH_2 COD 1H), 2.62–2.33 (m, 5H, CH_2 2H, CH_2 COD 3H), 2.33–2.18 (m, 2H, CH_2 1H, CH_2 COD 1H), 2.13–1.98 (m, 2H, CH_2 1H, CH_2 COD 1H), 1.68–1.56 (m, 2H, CH_2 1H, CH_2 COD 1H), 1.44–1.32 (m, 4H, CH_2 COD 1H, $((CH_3)_2CH)_3Si$ 3H), 1.12 (d, *J* = 6.4 Hz, 9H, $((CH_3)_2CH)_3Si$), 1.12 (d, *J* = 7.5 Hz, 9H, $((CH_3)_2CH)_3Si$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 162.4 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 157.3 (s, C_{Ar}), 150.5 (s, HC_{Ar}), 142.3 (s, HC_{Ar}), 137.0 (s, C_{Ar}), 135.3 (s, HC_{Ar} BAr_F), 135.2 (d, J_{PC} = 12 Hz, HC_{Ar}), 132.6 (d, J_{PC} = 5 Hz, HC_{Ar}), 132.5 (d, J_{PC} = 3 Hz, HC_{Ar}), 131.7 (d, J_{PC} = 3 Hz, C_{Ar}), 130.9 (s, C_{Ar}), 129.8 (d, J_{PC} = 11 Hz, HC_{Ar}), 129.5 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.2 (d, J_{PC} = 11 Hz, HC_{Ar}), 125.6 (s, HC_{Ar}), 125.1 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 99.4 (d, J_{PC} = 11 Hz, *C*H COD), 87.8 (d, J_{PC} = 14 Hz, *C*H COD), 77.7 (s, *C*OSi), 61.5 (s, *C*H COD), 57.6 (s, *C*H COD), 40.8 (d, J_{PC} = 9 Hz, CH_2P), 40.0 (d, J_{PC} = 1 Hz, CH_2), 36.4 (d, J_{PC} = 3 Hz, CH_2 COD), 31.0 (d, J_{PC} = 2 Hz, CH_2 COD), 30.4 (s, CH_2), 29.7 (d, J_{PC} = 2 Hz, CH_2 COD), 27.7 (s, CH_2 COD), 21.1 (s, CH_2), 19.0 (s, $(CH_3)_2CHSi$), 18.9 (s, $(CH_3)_2CHSi$), 15.4 (s, $(CH_3)_2CHSi$) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 7.8 ppm. **MS** (ESI, *c* = 0.05 mg / mL, 50 °C, 15 µL / min) *m/z* (%): 804 ($[Ir(L)(COD)]^+$, 100). **IR**: $\tilde{\nu}$ = 2944 (w br), 2863 (w), 1610 (w), 1470 (w), 1437 (w), 1352 (s), 1272 (s), 1158 (m), 1119 (s br), 1102 (s), 1055 (m), 1047 (w), 1017 (w), 1000 (w), 896 (w), 884 (m), 839 (m), 805 (w), 741 (w), 722 (w), 716 (m), 693 (w), 681 (s), 668 (s) cm^{-1}. **EA**: calc. (%) C 51.72, H 4.16, N 0.83; found C 49.67, H 3.90, N 0.60. **m.p.**: 103–104 °C. **$[\alpha]_D^{20}$**: −11.7 (*c* = 0.33, CH_2Cl_2).

(−)-[η^4-1,5-Cyclooctadiene-8-(*tert*-butyldimethylsilyloxy)-8-((di-*ortho*-tolylphosphino)methyl)-5,6,7,8-tetrahydroquinoline-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate (87e)

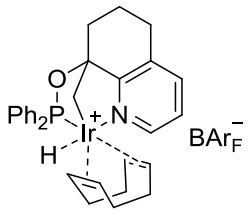


The title compound **87e** was obtained following the general procedure **G** using $[Ir(COD)Cl]_2$ (31.5 mg, 47.0 µmol, 0.5 eq.), DCM (2 mL), ligand **86e** (46.0 mg, 93.9 µmol, 1.0 eq.), DCM (1 mL), $NaBAr_F$

(91.6 mg, 103 µmol, 1.1 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 22 cm) as an orange solid (119 mg, 72.0 µmol, 76%). This compound consists as a mixture of rotamers. The experimental data given below are given for the main diastereomer.

$C_{70}H_{64}BF_{24}IrNOPSi$ (1653.31 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 9.08 (br s, 1H, H_{Ar}), 8.67 (dd, *J* = 5.4 Hz, 1H, H_{Ar}), 7.90–7.79 (m, 2H, H_{Ar}), 7.75 (s, 8H, BAr_F-*H*), 7.58 (s, 4H, BAr_F-*H*), 7.55 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.49–7.35 (m, 6H, H_{Ar}), 7.27–7.15 (m, 3H, H_{Ar}), 4.91–4.77 (m, 2H, CH_2 COD), 3.47 (q, *J* = 6.0 Hz, 1H, CH_2 COD), 2.96–2.81 (m, 2H, CH_2), 2.78–2.59 (m, 4H, CH_2), 2.69–2.42 (m, 4H, CH_2), 2.61–2.36 (m, 3H, CH_2), 2.36–2.19 (m, 2H, CH_2), 2.17–1.97 (m, 2H, CH_2), 1.69–1.51 (m, 2H, CH_2), 1.46–1.30 (m, 1H, CH_2), 0.87 (s, 9H, (CH_3)$_3$CSi), 0.53 (s, 3H, (CH_3Si)), 0.51 (s, 3H, (CH_3Si)) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 11.7 ppm (rotamer 2.4 ppm). **MS** (FAB NBA) *m/z* (%): 790 ([Ir(L)(COD)]$^+$, 100), 606 (28), 546 (10), 202 (16), 146 (11). **IR**: $\tilde{\nu}$ = 2962 (w br), 2893 (w), 1610 (w), 1481 (w), 1447 (w), 1352 (s), 1272 (s), 1159 (m), 1115 (s br), 1070 (m), 1051 (m), 1032 (m), 1005 (w), 886 (m), 820 (w), 807 (w), 786 (w), 744 (m), 723 (w), 710 (s), 681 (s), 668 (m) cm^{-1}. **EA**: calc. (%) C 50.85, H 3.90, N 0.85; found C 50.87, H 3.85, N 0.69. **m.p.**: 83–84 °C. **$[\alpha]_D^{20}$**: −0.9 (*c* = 0.42, $CHCl_3$).

(±)-[η^4-1,5-Cyclooctadiene-8-methyl-8-(5,6,7,8-tetrahydoquinolinyl)diphenylphosphinite-hydrido-iridium(III)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]-borate (81)



To a solution of **80** (95.0 mg, 582 µmol, 1.0 eq.) in THF (2.0 mL) was added a *n*-BuLi 1.6 M solution in hexanes (0.4 mL, 640 µmol, 1.1 eq.) at –78 °C. The reaction mixture was stirred at 0 °C for 1 h, fallowed by slow addition of a solution of chlorodiphenylphosphine (120 µL, 140 mg, 639 µmol, 1.0 eq.) in THF (1.0 mL). The cooling bath was removed and the reaction mixture was stirred for additional 2 h at RT. The solvent was removed under reduce pressure, following by addition of DCM (5.0 mL) and filtration through a HPLC syringe filter (*CHROMAFIL*® O-20/15 MS, pore size 20 µm). The syringe filter was purged with DCM (1.0 mL). The obtained solution was added to a solution of $[Ir(COD)Cl]_2$ (97.0 mg, 145 µmol, 0.25 eq.) in DCM (1.0 mL) at 0 °C and stirred for an additional 1 h at 0 °C. $NaBAr_F$ (284 mg, 321 µmol, 0.55 eq.) was added and stirring was continued for additional 30 min. The reaction mixture was washed with water (5.0 mL) and the aq. phase was re-extracted with DCM (5.0 mL). Combined organic layers were dried over

$MgSO_4$, filtered and the solvent was removed under reduced pressure. Purification by flash chromatography (SiO_2, 1.5 cm × 25 cm, TBME → DCM / cyclohexane 2:1) gave the title compound **81** (100 mg, 66.2 µmol, 11%) as pale grey solid.

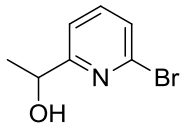
$^{31}P\{^1H\}$-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.
$^{31}P\{^1H\}$-NMR of the ligand (162 MHz, C_6D_6): δ = 86.9 (s) ppm.

$C_{62}H_{46}BF_{24}IrNOP$ (1511.00 g/mol):
^1H-NMR (500 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 5.2 Hz, 1H, H_{Ar}), 7.76 (dd, *J* = 13.3, 7.6 Hz, 3H, H_{Ar}), 7.72 (s, 8H, BAr_F-*H*), 7.64–7.53 (m, 3H, H_{Ar}), 7.52 (s, 4H, BAr_F-*H*), 7.26–7.18 (m, 2H, H_{Ar}), 7.12 (td, *J* = 7.7, 2.4 Hz, 2H, H_{Ar}), 6.42 (dd, *J* = 11.5, 7.7 Hz, 2H, H_{Ar}), 5.23–5.14 (m, 1H, C*H* COD), 5.11 (t, *J* = 6.7 Hz, 1H, C*H* COD), 4.26–4.16 (m, 1H, C*H* COD), 3.58 (q, *J* = 7.2 Hz, 1H, C*H* COD), 3.41 (dd, *J* = 15.2, 8.0 Hz, 1H, CH_2Ir), 2.99–2.90 (m, 1H, CH_2), 2.86–2.74 (m, 2H, CH_2 1H, CH_2 COD 1H), 2.68 (dtd, 1H, *J* = 15.2, 8.0, 6.2 Hz, 1H, CH_2Ir), 2.60–2.36 (m, 4H, CH_2 COD 3H, CH_2 1H), 2.15–1.99 (m, 2H, CH_2 2H), 1.90–1.82 (m, 1H, CH_2 COD), 1.81–1.70 (m, 1H, CH_2 COD), 1.39–1.28 (m, 1H, CH_2 COD), 0.96–0.87 (m, 2H, CH_2 COD 1H, CH_2 1H), −15.88 (d, *J* = 9.2 Hz, 1H, Ir-H) ppm. **$^{13}C\{^1H\}$-NMR** (126 MHz, $CDCl_3$): δ = 161.8 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 161.7 (d, J_{PC} = 2 Hz, C_{Ar}), 150.5 (s, HC_{Ar}), 140.4 (s, HC_{Ar}), 136.9 (s, C_{Ar}), 134.9 (s, HC_{Ar} BAr_F), 133.5 (d, J_{PC} = 2 Hz, HC_{Ar}), 132.7 (d, J_{PC} = 15 Hz, C_{Ar}), 132.1 (s, HC_{Ar}), 132.04 (d, J_{PC} = 23 Hz, HC_{Ar}), 132.00 (s, HC_{Ar}), 131.8 (d, J_{PC} = 2 Hz, HC_{Ar}), 131.4 (d, J_{PC} = 47 Hz, C_{Ar}), 129.4 (d, J_{PC} = 12 Hz, HC_{Ar}), 129.1 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.0 (d, J_{PC} = 11 Hz, HC_{Ar}), 127.9 (d, J_{PC} = 11 Hz, HC_{Ar}), 126.3 (s, HC_{Ar}), 124.7 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 117.6 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 96.8 (s, *C*O), 90.6 (d, J_{PC} = 11 Hz, *C*H COD), 90.4 (d, J_{PC} = 16 Hz, *C*H COD), 86.2 (s, *C*H COD), 83.7 (s, *C*H COD), 39.7 (d, J_{PC} = 8 Hz, *C*H_2Ir), 36.2 (d, J_{PC} = 10 Hz, *C*H_2 COD), 31.1 (s, *C*H_2 COD), 28.8 (s, *C*H_2), 27.9 (s, *C*H_2 COD), 25.7 (s, *C*H_2 COD), 24.2 (d, J_{PC} = 4 Hz, *C*H_2), 20.9 (s, *C*H_2) ppm. **$^{31}P\{^1H\}$-NMR** (202 MHz, $CDCl_3$): δ = 100.2 ppm. **MS** (FAB NBA) *m/z* (%): 648 ($[Ir(L)(COD)]^+$, 89), 538 (19), 444 (30), 384 (21), 258 (20), 245 (20), 230 (21), 166 (23), 149 (45), 107 (68), 89 (98), 77 (100), 65 (41), 51 (38), 39 (63). **IR**: $\tilde{\nu}$ = 2967 (w br), 1609 (w), 1438 (w), 1353 (s), 1271 (s), 1090 (s br), 999 (w), 897 (w), 885 (m), 863 (w), 852 (w), 838 (m), 811 (w), 788 (m), 768 (m), 743 (m), 714 (s), 708 (m), 681 (s), 667 (m) cm^{-1}. **EA**: calc. (%) C 49.28, H 3.07, N 0.93; found C 49.64, H 3.32, N 0.79.

8.5 New Pyridine–Phosphinite Based Ligands for Iridium-Catalyzed Asymmetric Hydrogenation

8.5.1 Preparation of the Ligand Precursers

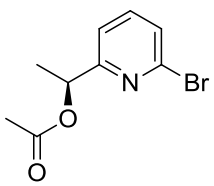
1-(6-Bromopyridin-2-yl)ethanol (104)



A *n*-BuLi 1.6 M solution (5.0 mL, 8.00 mmol, 1.0 eq.) was slowly added to a solution of 2,5-dibromopyridine (1.90 g, 8.00 mmol, 1.0 eq.) in diethyl ether (40 mL) at −78 °C. After stirring for 1.5 h at −78 °C, acetaldehyde (1 mL, 0.78 g, 17.7 mmol, 2.2 eq.) was added. The reaction mixture was stirred for 2 h at −78 °C, afterwards it was allowed to warm to RT. HCl 1 M aq. solution (15 mL) was added and the biphasic mixture was separated. The aqueous layer was extracted with TBME (3×10 mL). Combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The title compound **104** was obtained after purification by *Kugelrohr* distillation (110–115 °C / 0.1 mbar) as a colorless oil (1.56 g, 7.72 mmol, 96%). The analytical data match the reported values.[112]

C_7H_8BrNO (202.05 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.52 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.35 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.28 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 4.84 (q, *J* = 6.4 Hz, 1H, C*H*), 3.69 (br s, 1H, O*H*), 1.47 (d, *J* = 6.4 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 165.2 (C_{Ar}), 142.1 (C_{Ar}), 139.2 (HC_{Ar}), 126.6 (HC_{Ar}), 118.5 (HC_{Ar}), 79.1 (*C*H), 24.1 (*C*H_3) ppm. **MS** (EI, 70 eV, rt, *m/z* (%): 202 (5, [M^+]), 186 (100), 158 (31), 106 (19), 78 (45), 51 (11). **b.p.**: 110–115 °C / 0.1 mbar).

(*R*)-1-(6-Bromopyridin-2-yl)ethyl acetate (105)

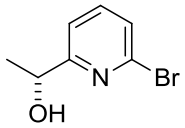


Vynyl acetate (2.0 mL, 1.89 mg, 21.7 mmol, 5.8 eq.) was added to a mixture of pyridyl alcohol **104** (750 mg, 3.71 mmol, 1.0 eq.) and CAL-B (300 mg) in diisopropyl ether (200 mL). The reaction mixture was stirred for 17 h at RT. The reaction mixture was filtered and washed with ethyl acetate (100 mL). The solvents were removed under reduced pressure. Separation of the two products was chieved by MPLC (SiO_2, cyclohexane / ethyl acetate 95:5). The title compound

(*R*)-**105** (165 mg, 682 µmol, 18%) was obtained as a colorless oil. The analytical data match the reported values.[112]

$C_9H_{10}BrNO_2$ (242.09 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.53 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.38 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.28 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 5.85 (q, *J* = 6.8 Hz, 1H, C*H*), 2.12 (s, 3H, CCH_3), 1.57 (d, *J* = 6.4 Hz, 3H, CHCH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.1 (*C*=O), 161.9 (C_{Ar}), 141.6 (C_{Ar}), 138.9 (HC_{Ar}), 127.1 (HC_{Ar}), 119.0 (HC_{Ar}), 72.4 (*C*H), 21.2 (*C*H_3), 20.6 (*C*H_3) ppm. **MS** (EI, 70 eV, RT, *m/z* (%): 243 ([M^+], 0.2), 200 (100), 186 (23), 158 (8), 104 (46), 78 (24), 43 (78). **TLC**: (SiO_2, cyclohexane / ethyl acetate 95:5): R_f = 0.15. **$[\alpha]_D^{20}$**: +74.2 (*c* = 0.93, $CHCl_3$); lit. +72 (*c* = 1.49, $CHCl_3$).[112]

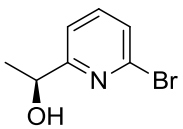
(*S*)-1-(6-Bromopyridin-2-yl)ethanol ((*S*)-104)



The title compound (*S*)-**104** was obtained by enzymatic kinetic resolution after the separation of the product by MPLC (SiO_2, cyclohexane / ethyl acetate 95:5) as a colorless oil (507 mg, 2.51 mmol, 68%).

TLC: (SiO_2, cyclohexane / ethyl acetate 95:5) : R_f = 0.10. **HPLC** (chiral, Daicel Chiracel OD-H, (4.6 mm × 250 mm), *n*-heptane / *i*-PrOH 98:2, 0.5 mL / min, 25 °C: t_R = 32.0 min (*S*), 34.4 min (*R*), 30% *ee*. **$[\alpha]_D^{20}$**: −3.3 (*c* = 1.07, $CHCl_3$); lit. −10.8 (*c* = 2.75, $CHCl_3$).[112].

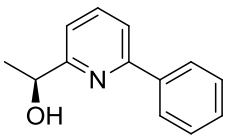
(*R*)-1-(6-Bromopyridin-2-yl)ethanol ((*R*)-104)



Water (5 mL) and K_2CO_3 (200 mg, 1.45 mmol, 2.1 eq.) were added to a solution of acetate (*R*)-**105** (165 mg, 682 µmol, 1.0 eq.) in methanol (5 mL) and the reaciton mixture was stirred at rt over night. The reaction mixture was extracted with DCM (3×5 mL). Combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The title compound (*R*)-**104** (108 mg, 535 µmol, 78%) was obtained as a colorless oil.

HPLC (chiral, Daicel Chiracel OD-H, (4.6 mm × 250 mm), *n*-heptane / *i*-PrOH 98:2, 0.5 mL / min, 25 °C: t_R = 33.0 min (*S*), 34.4 min (*R*), >99% *ee*. **[α]$_D^{20}$**: +7.1 (*c* = 0.78, $CHCl_3$); lit. +11.0 (*c* = 1.49, $CHCl_3$).[112]

(*R*)-1-(6-Bromopyridin-2-yl)ethanol ((*R*)-106)



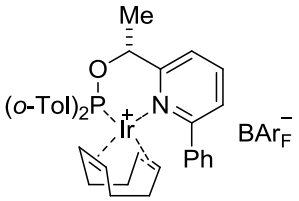
A degassed solution of phenylboronic acid (80.2 mg, 658 µmol, 1.2 eq.) in ethanol (1.5 mL) and a degassed solution of Na_2CO_3 (113 mg, 1.07 mmol, 2.0 eq.) in water (1.5 mL) were added to a degassed solution of $Pd(PPh_3)_4$ (6.50 mg, 5.63 µmol, 1 mol%) and pyridyl alcohol (*R*)-**104** (108 mg, 535 µmol, 1.0 eq.) in toluene (1.5 mL). The reaction mixture was stirred for 15 h at 85 °C. After cooling down to RT, the layers were separated. The aquoues layer was extracted with DCM (2×1 mL). The combined organic layers were dried over over $MgSO_4$, filtered and evaporated under reduced pressure. Purification by flash chromatography (SiO_2, cyclohexane / ethyl acetate 4:1) gave the title compound (*R*)-**106** as pale yellow oil (102 mg, 512 µmol, 96%).

$C_{13}H_{13}BrNO$ (199.25 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.04–8.02 (m, 2H, H_{Ar}), 7.38 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.65 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.51–43 (m, 3H, H_{Ar}), 7.20 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 4.95 (dd, *J* = 4.8, 1.6 Hz, 1H, C*H*), 4.77 (d, *J* = 4.4 Hz, 1H, O*H*), 1.55 (d, *J* = 6.4 Hz, 3H, CHCH_3) ppm. **TLC**: (SiO_2, cyclohexane / ethyl acetate 4:1): R_f = 0.30. **HPLC** (chiral, Daicel Chiracel OD-H, (0.46 cm × 25 cm), heptane / *i*-PrOH 90:10, 0.5 mL / min, 25 °C: t_R = 15.8 min (*S*), 19.2 min (*R*), >99% *ee*. **[α]$_D^{20}$**: −27.5 (*c* = 1.20, $CHCl_3$).

8.5.2 Preparation of Ir-complexes

(*R*)-[η^4-1,5-Cyclooctadiene-2-(ethyl-6-phenylpyridyl)-1-di-*ortho*-tolylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*R*)-113a)

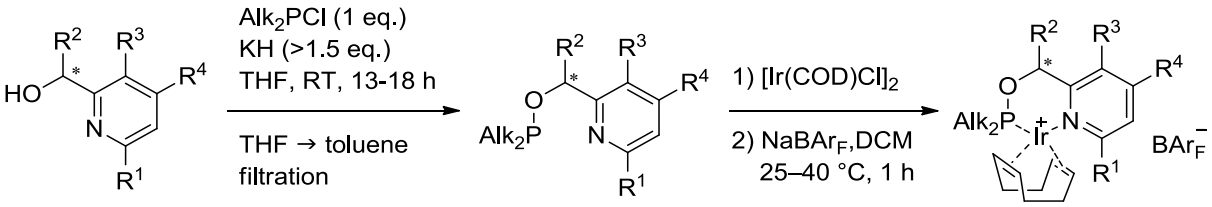


The intermediate N,P ligand (*R*)-**102a** was obtained following the general procedure **C** using pyridyl alcohol (*R*)-**106** (40 mg, 201 µmol, 1.0 eq.), DMAP (25.0 mg, 201 µmol, 1.0 eq.), chloro-diphenylphosphine (50.0 mg, 201 µmol, 1.0 eq.), THF (1.0 mL) and after filtration over silica gel SiO_2, 1.5 cm × 5 cm, cyclohexane / TBME 5:1, degassed) under innert conditions as a colorless foam (24.0 mg, 58.3 µmol, 29%). The title compound (*R*)-**113a** was obtained following general procedure **G** using the N,P ligand (*R*)-**102a**, $[Ir(COD)Cl]_2$ (20.0 mg, 29.8 µmol, 0.5 eq.), DCM (1.5 mL) and $NaBAr_F$ (58.0 mg, 65.5 µmol, 1.2 eq.) after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm, TBME then DCM) was isolated as an orange foam (40 mg, 25.3 µmol, 13% over two steps).

^{31}P{^{1}H}-NMR of (*o*-Tol)$_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 94.7 (s) ppm.

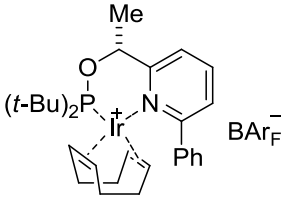
$C_{67}H_{50}BF_{24}IrNOP$ (1575.08 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.00 (t, *J* = 7.9 Hz, 1H, H_{Ar}), 7.76–7.68 (m, 11H, BAr_F-*H*, H_{Ar}), 7.68–7.59 (m, 3H, H_{Ar}), 7.56 (s, 4H, BAr_F-*H*), 7.52–7.39 (m, 4H, H_{Ar}), 7.38–7.34 (m, 2H, H_{Ar}), 7.25–7.18 (m, 2H, H_{Ar}), 6.94 (dd, *J* = 12.5, 8.0 Hz, 1H, H_{Ar}), 6.33 (p, *J* = 6.6 Hz, 1H, C*H*OP), 4.63–4.57 (m, 1H, C*H* COD), 4.52 (t, *J* = 6.3 Hz, 1H, C*H* COD), 3.38–3.24 (m, 1H, C*H* COD), 2.93 (s, 3H, CH_3), 2.79 (p, *J* = 7.4 Hz, 1H, C*H* COD), 2.49 (s, 3H, CH_3), 2.36 (ddd, *J* = 16.9, 10.9, 6.3 Hz, 1H, CH_2 COD), 2.10 (d, *J* = 6.5 Hz, 3H, CHCH_3), 1.92–1.71 (m, 5H, CH_2 COD), 1.41–1.32 (m, 1H, CH_2 COD), 1.26–1.19 (m, 1H, CH_2 COD) ppm.
^{31}P{^{1}H}-NMR (162 MHz, CD_2Cl_2): δ = 96.5 (br s) ppm.

Formation of P-alkyl N,P Ligands and Subsequent Complexation with Iridium



General Procedure H: A *Schlenk* flask was charged with the pyridyl alcohol (1.0 eq.) and the corresponding chloro-alkylphosphine (>1 eq.). THF (>0.5 M) and KH (dry, >1 eq.) were added. The reaction mixture was stirred at rt until ^{31}P-NMR revealed full conversion of the chlorophosphine (usually >12 h). After reaching full conversion the solvent was removed in *vacuo*. Toluene (1 mL) was added and the suspension was filtered over a plug of *Celite*® using a *Schlenk* (d×h, 2 cm × 1 cm). Toluene (2×1 mL) was used for purging. The obtained N,P ligands was converted to the corresponding Ir-complex following general procedure **G**.

(*R*)-[η^4-1,5-Cyclooctadiene-2-(ethyl-6-phenylpyridyl)-1-di-*tert*-butylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*R*)-113a)



The intermediate N,P ligand (*R*)-**102b** was obtained following the general procedure **H** using pyridyl alcohol (*R*)-**106** (42.0 mg, 211 µmol, 1.0 eq.), chloro-di-*tert*-butylphosphine (40 µL, 38.0 mg, 211 µmol, 1.0 eq.), KH (10.2 mg, 253 µmol, 1.2 eq.), THF (1.0 mL) as a colorless foam (65.0 mg, 189 µmol, 90%).

The title compound (*R*)-**113a** was obtained following the general procedure **G** using (*R*)-**106b** (65.0 mg, 189 µmol, 90%). $[Ir(COD)Cl]_2$ (63.6 mg, 94.6 µmol, 0.5 eq.), DCM (3 mL), $NaBAr_F$ (185 mg, 208 µmol, 1.1 eq.) and after purification by flash chromatography (SiO_2, 1.5 cm × 20 cm, TBME then DCM) as an orange solid (107 mg, 71.0 µmol, 34% over two steps).

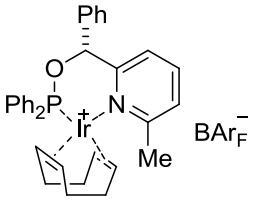
^{31}P{^{1}H}-NMR of $(t\text{-Bu})_2PCl$ (162 MHz, C_6D_6): δ = 146.4 (s) ppm.

^{31}P{^{1}H}-NMR of the ligand (162 MHz, C_6D_6): δ = 154.9 (s) ppm.

$C_{61}H_{54}BF_{24}IrNOP$ (1507.05 g/mol):

^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.27 (d, *J* = 7.4 Hz, 2H, H_{Ar}), 8.02 (t, *J* = 7.9 Hz, 1H, H_{Ar}), 7.79 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 7.76–7.68 (m, 11H, BAr_F-*H*, H_{Ar}), 7.63 (dd, *J* = 7.8, 1.0 Hz, 1H, H_{Ar}), 7.56 (s, 4H, BAr_F-*H*), 5.82 (dq, *J* = 9.6, 6.5 Hz, 1H, C*H*OP), 5.23 (t, *J* = 6.7 Hz, 1H, C*H* COD), 4.41 (t, *J* = 5.5 Hz, 1H, C*H* COD), 4.21 (p, *J* = 8.6 Hz, 1H, C*H* COD), 2.42 (p, *J* = 8.0 Hz, 1H, C*H* COD), 2.24–2.13 (m, 2H, CH_2 COD), 2.05–1.92 (m, 2H, CH_2 COD), 1.92 (d, *J* = 6.5 Hz, 3H, CH_3), 1.71–1.61 (m, 2H, CH_2 COD), 1.60 (br s, 9H, C(CH_3)$_2$), 1.05 (d, *J* = 14.4 Hz, 9H C(CH_3)$_2$), 0.96–0.82 (m, 2H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.4 (d, J_{PC} = 3 Hz, C_{Ar}), 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.0 (s, C_{Ar}), 140.8 (s, HC_{Ar}), 139.9 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.3 (s HC_{Ar}), 130.6 (s, HC_{Ar}), 129.7 (s, HC_{Ar}), 129.4 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 126.6 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, *C*F_3 BAr_F), 121.2 (s, HC_{Ar}), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 88.7 (d, J_{PC} = 5 Hz, *C*H COD), 79.3 (s, *C*HOP), 77.7 (d, J_{PC} = 19 Hz, *C*H COD), 74.8 (s, *C*H COD), 63.6 (s, *C*H COD), 41.6 (d, J_{PC} = 18 Hz, *C*(CH$_3$)$_2$), 40.2 (d, J_{PC} = 19 Hz, *C*(CH$_3$)$_2$), 37.1 (s, *C*H$_2$ COD), 35.7 (s, *C*H$_2$ COD), 28.64 (s, C(*C*H$_3$)$_2$), 28.59 (s, C(*C*H$_3$)$_2$), 28.3 (s, *C*H$_2$ COD), 23.9 (s, *C*H$_2$ COD), 19.0 (d, J_{PC} = 8 Hz, *C*H$_3$) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, CD_2Cl_2): δ = 133.8 (s) ppm.

(*R*)-(−)-[η^4-1,5-Cyclooctadiene-((phenyl)methyl)-(6-methylpyridyl)-diphenylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*R*)-113c)



The intermediate N,P ligand (*R*)-**102c** was obtained following the general procedure **C** using (*R*)-(6-methylpyridin-2-yl)(phenyl)methanol (19.9 mg, 100 µmol, 1.0 eq.), DMAP (12.2 mg, 100 µmol, 1.0 eq.), chloro-diphenylphosphine (18 µL, 22.1 mg, 100 µmol, 1.0 eq.), DCM (1.0 mL), after filtration over aluminum oxide (d×h, 2 cm × 2 cm) and washing with DCM (10 mL). The N,P ligand solution was concentrated in *vacuo* up to 1 mL. The title compound (*R*)-**113c** was obtained following the general procedure **G** using the N,P ligand solution, $[Ir(COD)Cl]_2$ (33.6 mg, 50 µmol, 0.5 eq.), DCM (2 mL), $NaBAr_F$ (99.0 mg, 112 µmol, 1.1 eq.), after purification by flash chromatography (SiO_2, 3 cm × 10 cm, TBME then DCM) as an orange solid (33 mg, 21.3 µmol, 21% over two steps).

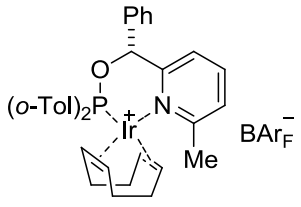
^{31}P{^{1}H}-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.

^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 111.5 (s) ppm.

$C_{65}H_{46}BF_{24}IrNOP$ (1547.03 g/mol):

^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.84 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.76 (s, 8H, BAr_F-*H*), 7.64 (ddt, , *J* = 9.5, 5.1, 3.8 Hz, 7H, H_{Ar}), 7.60 (m, 4H, BAr_F-*H*), 7.52–7.42 (m, 6H, H_{Ar}), 7.35–7.29 (m, 2H, H_{Ar}), 7.22 (dd, *J* = 7.9, 1.0 Hz, 2H, H_{Ar}), 6.76 (d, *J* = 7.7 Hz, 1H, C*H*OP), 5.27 (d, *J* = 8.4 Hz, 1H, C*H* COD), 4.59 (t, *J* = 6.5 Hz, 1H, C*H* COD), 4.40 (p, *J* = 7.5 Hz, 1H, C*H* COD), 3.15–3.10 (m, 1H, C*H* COD), 3.08 (s, 3H, CH_3), 2.36 (ddt, *J* = 15.9, 10.1, 5.0 Hz, 1H, CH_2 COD), 2.51–2.43 (m, 1H, CH_2 COD), 2.35 (dd, *J* = 15.7, 7.8 Hz, 1H, CH_2 COD), 2.31–2.21 (m, 1H, CH_2 COD), 2.11–2.00 (m, 1H, CH_2 COD), 1.98–1.86 (m, 1H, CH_2 COD), 1.77–1.58 (m, 2H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.9 (s, C_{Ar}), 160.3 (s, C_{Ar}), 140.4 (s, HC_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 133.2 (s HC_{Ar}), 132.5 (s HC_{Ar}), 132.0 (d, J_{PC} = 16 Hz, HC_{Ar}), 130.5 (s, HC_{Ar}), 129.9 (s, HC_{Ar}), 129.8 (s, HC_{Ar}), 129.4 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 127.8 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 123.4 (s, HC_{Ar}), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 102.7 (d, J_{PC} = 9 Hz, *C*H COD), 92.17 (d, J_{PC} = 14 Hz, *C*H COD), 85.2 (s, *C*HOP), 69.5 (s, *C*H COD), 66.5 (s, *C*H COD), 37.6 (s, CH_2 COD), 34.6 (s, CH_2 COD), 29.1 (s, CH_3), 28.3 (s, CH_2 COD), 25.9 (s, CH_2 COD) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, CD_2Cl_2): δ = 98.9 (s) ppm. **MS** (FAB NBA) *m/z* (%): 684 ([Ir(L)(COD)]$^+$, 100), 576 (22), 498 (12), 182 (31). **EA**: calc. (%) C 50.47, H 3.00, N 0.91; found C 50.46, H 2.92, N 1.01. **m.p.**: 134–135 °C. **$[\alpha]_D^{20}$**: −16.0 (*c* = 0.53, $CHCl_3$).

(*R*)-(+)-[η^4-1,5-Cyclooctadiene-((phenyl)methyl)-(6-methylpyridyl)-di-*ortho*-tolylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*R*)-113d)

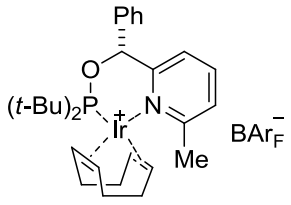


The intermediate N,P ligand (*R*)-**102d** was obtained following the general procedure **C** using (*R*)-(6-methylpyridin-2-yl)(phenyl)-methanol (39.9 mg, 200 µmol, 1.0 eq.), DMAP (25.7 mg, 210 µmol, 1.06 eq.), chloro-di-*ortho*-tolylphosphine (52.2 mg, 210 µmol, 1.05 eq.), DCM (1.0 mL), after purification by flash chromatography (SiO_2, 2 cm × 10 cm, pentane / diethyl ether 10:1, Argon degassed). The filtrate was concentrated in *vacuo* to obtain the intermediate ligand (48 mg, 117 µmol, 58%) as a colorless solid. The title compound (*R*)-**113d** was obtained following the general procedure **G** using the N,P ligand (48 mg, 117 µmol, 58%), $[Ir(COD)Cl]_2$ (39.2 mg, 58.3 µmol, 0.5 eq.), DCM (3 mL), $NaBAr_F$ (120 mg, 136 µmol, 1.2 eq.), purification by flash chromatography (SiO_2, 3 cm × 10 cm, TBME then DCM) as a red solid (166 mg, 105 µmol, 53% over two steps).

^{31}P{^{1}H}-NMR of (*o*-Tol)$_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 98.6 (s) ppm.

$C_{67}H_{50}BF_{24}IrNOP$ (1575.08 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 7.98 (br s, 1H, H_{Ar}), 7.83–7.71 (m, 9H, BAr_F-*H*, H_{Ar}), 7.62–7.49 (m, 10H, BAr_F-*H*, H_{Ar}), 7.45–7.36 (m, 2H, H_{Ar}), 7.35–7.28 (m, 2H, H_{Ar}), 7.27–7.20 (m, 2H, H_{Ar}), 7.16 (t, *J* = 7.3 Hz, 1H, H_{Ar}), 6.86–6.63 (m, 1H, H_{Ar}), 5.29 (br s, 1H, C*H*OP), 4.51 (br s, 1H, C*H* COD), 4.19 (br s, 1H, C*H* COD), 3.23 (br s, 3H, Ar-CH_3), 3.19–3.17 (m, 1H, C*H* COD), 2.90 (br s, 1H, CH_2 COD), 2.77–2.74 (m, 1H, CH_2 COD), 2.52 (br s, 3H, Ar-CH_3), 2.44 (dd, *J* = 15.8, 9.2 Hz, 2H, CH_2 COD), 2.35–2.17 (m, 5H, CH_2 COD 2H, Ar-CH_3), 2.16–2.02 (m, 1H, CH_2 COD), 1.92–1.79 (m, 1H, CH_2 COD), 1.72–1.59 (m, 1H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 162.4 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.8 (s, C_{Ar}), 160.3 (s, C_{Ar}), 141.4 (d, J_{PC} = 11 Hz, C_{Ar}), 140.4 (s, HC_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 134.9 (d, J_{PC} = 11 Hz, C_{Ar}), 134.4 (s, C_{Ar}), 133.8 (s, C_{Ar}), 133.7 (s, HC_{Ar}), 133.2 (s, HC_{Ar}), 132.9 (s, HC_{Ar}), 132.7 (s, HC_{Ar}), 132.6 (s, HC_{Ar}), 131.0 (s, HC_{Ar}), 130.9 (s, HC_{Ar}), 130.4 (s, HC_{Ar}), 130.0 (s, HC_{Ar}), 129.6 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 128.4 (s, HC_{Ar}), 127.9 (s HC_{Ar}), 127.1 (d, J_{PC} = 12 Hz, HC_{Ar}), 126.1 (d, J_{PC} = 17 Hz, HC_{Ar}), 125.3 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 123.7 (s, HC_{Ar}), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 101.1 (br s, *C*H COD), 89.5 (br d, J_{PC} = 12 Hz, *C*H COD), 84.2 (s *C*HOP), 69.6 (s, 2 × *C*H COD), 37.9 (s, *C*H_2 COD), 35.1 (s, *C*H_2 COD), 28.8 (s, *C*H_2 COD), 28.6 (s, *C*H_3), 25.6 (s, *C*H_2 COD), 22.4 (s, *C*H_3), 22.3 (s, *C*H_3) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 108.6 (br s) ppm. **MS** (FAB NBA) *m/z* (%): 712 ([Ir(L)(COD)]$^+$, 100), 602 (21), 182 (28). **EA**: calc. (%) C 51.09, H 3.20, N 0.89; found C 51.18, H 3.14, N 1.02. **$[\alpha]_D^{20}$**: +20.0 (*c* = 1.02, $CHCl_3$).

(*R*)-(+)-[η^4-1,5-Cyclooctadiene-((phenyl)methyl)-(6-methylpyridyl)-di-*tert*-butylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*R*)-113e)



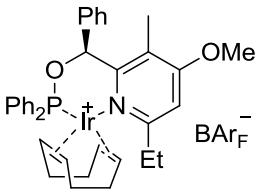
The intermediate N,P ligand (*R*)-**102e** was obtained following the general procedure **H** using (*R*)-(6-ethyl-4-methoxy-3-methylpyridin-2-yl)(phenyl)methanol (60 mg, 233 µmol, 1.0 eq.), chloro-di-*tert*-butylphosphine (20 µL, 19.0 mg, 210 µmol, 1.1 eq.), KH (20.0 mg, 499 µmol, 2.5 eq.), THF (0.5 mL) as a sticky oil (60.0 mg, 175 µmol, 87%).The title compound (*R*)-**113e** was obtained following the general procedure **G** using the

N,P ligand (60.0 mg, 175 µmol, 87%), $[Ir(COD)Cl]_2$ (63.6 mg, 94.6 µmol, 0.5 eq.), DCM (3 mL),$NaBAr_F$ (185 mg, 208 µmol, 1.1 eq.), after purification by flash chromatography (SiO_2, 2 cm × 18 cm, TBME then DCM) and recrystallization form diethyl ether (1 mL) and *n*-pentane (25 mL) as a red solid (113 mg, 75.0 µmol, 43% over two steps).

$^{31}P\{^1H\}$-NMR of $(t\text{-Bu})_2PCl$ (162 MHz, C_6D_6): δ = 146.4 (s) ppm.
$^{31}P\{^1H\}$-NMR of the ligand (162 MHz, C_6D_6): δ = 165.6 (s) ppm.

$C_{61}H_{54}BF_{24}IrNOP$ (1507.05 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 7.79 (s, 8H, BAr_F-*H*), 7.64–7.40 (m, 9H, BAr_F-*H*, H_{Ar}), 7.34 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.05 (d, *J* = 9.9 Hz, 1H, H_{Ar}), 6.68 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 5.44–5.37 (m, 1H, C*H*OP), 4.95 (t, *J* = 8.4 Hz, 1H, C*H* COD), 4.22 (q, *J* = 8.5 Hz, 1H, C*H* COD), 3.36–3.26 (m, 4H, CH_3, 1H, C*H* COD), 2.64 (dtd, *J* = 15.9, 10.2, 5.7 Hz, 1H, CH_2 COD), 2.48–2.30 (m, 2H, C*H* COD 1H, CH_2 COD 1H), 2.22 (dt, *J* = 13.8, 9.3 Hz, 1H, CH_2 COD), 2.13–1.95 (m, 2H, CH_2 COD), 1.72–1.62 (m, 1H, CH_2 COD), 1.61–1.50 (m, 2H, CH_2 COD), 1.41 (d, *J* = 13.8 Hz, 9 H, $(CH_3)_3C$), 1.06 (d, *J* = 14.9 Hz, 9 H, $(CH_3)_3C$) ppm. **$^{31}P\{^1H\}$-NMR** (202 MHz, CD_2Cl_2): δ = 138.3 (s) ppm. **MS** (FAB NBA) *m/z* (%): 644 ($[Ir(L)(COD)]^+$, 100), 422 (22), 182 (14). **EA**: calc. (%) C 48.62, H 3.61, N 0.93; found C 48.55, H 3.56, N 1.08. **$[\alpha]_D^{20}$**: +37.6 (*c* = 0.52, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-((phenyl)methyl)-(6-ethyl-4-methoxy-3-methylpyridyl)-diphenylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-113f)



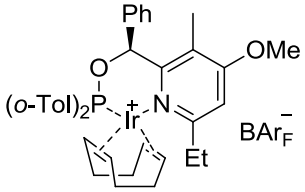
The intermediate ligand (*S*)-**102f** was obtained following the general procedure **C** using (*S*)-(6-methylpyridin-2-yl)(phenyl)methanol (34.0 mg, 132 µmol, 1.0 eq.), DMAP (17.8 mg, 145 µmol, 1.1 eq.), chloro-diphenylphosphine (26 µL, 32.0 mg, 145 µmol, 1.0 eq.), DCM (1.0 mL), after filtration over aluminum oxide (Al_2O_3, 2 cm × 2 cm) as a colorless oil (21 mg, 47.6 mmol, 36%). The title compound (*S*)-**113f** was obtained following the general procedure **G** using the N,P ligand (*S*)-**102f** (21 mg, 47.6 mmol, 36%), $[Ir(COD)Cl]_2$ (16.0 mg, 23.4 µmol, 0.5 eq.), DCM (1.5 mL), $NaBAr_F$ (45.0 mg, 50.8 µmol, 1.1 eq.), after purification by flash chromatography (Al_2O_3, 2 cm × 10 cm, only DCM) and

recrystallization from diethyl ether (1 mL) and *n*-pentane (25 mL) as an orange solid (56.0 mg, 34.9 µmol, 26% over two steps).

^{31}P{^{1}H}-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 111.6 (s) ppm.

$C_{68}H_{52}BF_{24}IrNO_2P$ (1605.11 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 8H, BAr_F-*H*), 7.59–7.49 (m, 9H, H_{Ar}, BAr_F-*H*), 7.48–7.40 (m, 4H, H_{Ar}), 7.34–7.28 (m, 4H, H_{Ar}), 6.62 (s, 1H, H_{Ar}), 6.86 (d, *J* = 27.5 Hz, 1H, H_{Ar}), 6.62 (s, 1H, H_{Ar}), 4.50–4.32 (m, 2H, C*H*OP, C*H* COD), 4.15 (dq, *J* = 11.2, 4.2 Hz, 1H, C*H* COD), 3.84 (s, 3H, OCH_3), 3.42–3.24 (m, 1H, C*H* COD), 3.12 (dq, *J* = 14.8, 7.4 Hz, 1H, CH_2 COD), 2.98 (tt, *J* = 6.8, 3.1 Hz, 1H, CH_2 COD), 2.46–2.33 (m, 1H, CH_2 COD), 2.29 (s, 3H, ArCH_3), 2.23–2.08 (m, 1H, CH_2 COD), 1.99–1.78 (m, 2H, C*H* COD, CH_2 COD), 1.49–1.21 (m, 4H, CH_2 COD), 0.90–0.82 (m, 1H, CH_2 COD), 0.79 (t, *J* = 7.5 Hz, 3H, CH_2CH_3) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, $CDCl_3$): δ = 98.9 (s) ppm. **MS** (FAB NBA) *m/z* (%): 742 ([Ir(L)(COD)]$^+$, 71), 634 (20), 458 (12), 240 (100). **EA**: calc. (%) C 50.88, H 3.27, N 0.87; found C 51.01, H 4.15, N 1.04. **m.p.**: 177–178 °C. **$[\alpha]_D^{20}$**: −69.0 (*c* = 0.26, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-((phenyl)methyl)-(6-ethyl-4-methoxy-3-methylpyridyl)-di-*ortho*-tolylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-113g)

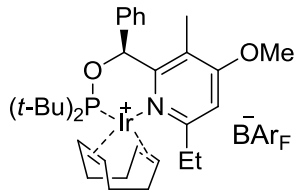


The intermediate ligand (*S*)-**102g** was obtained following the general procedure **C** using (*S*)-(6-methylpyridin-2-yl)(phenyl)methanol (40.0 mg, 155 µmol, 1.0 eq.), DMAP (21.2 mg, 173 µmol, 1.1 eq.), chloro-di-*ortho*-tolylphosphine (40.0 mg, 161 µmol, 1.05 eq.), DCM (1.0 mL), after filtration over aluminum oxide (Al_2O_3, 2 cm × 2 cm, DCM) as colerless foam (68 mg, 145 µmol, 94%). The title compound (*S*)-**113g** was obtained following general procedure **G** using the N,P ligand (*S*)-**102g** (68 mg, 145 µmol, 94%), $[Ir(COD)Cl]_2$ (49.0 mg, 72.9 µmol, 0.5 eq.), DCM (3 mL), $NaBAr_F$ (137 mg, 155 µmol, 1.1 eq.), after purification by flash chromatography (Al_2O_3, 2 cm × 20 cm, only DCM) and by recrystilliazation form diethyl ether (1 mL) with *n*-pentane (25 mL) as a orange foam (175 mg, 107 µmol, 69% over two steps).

^{31}P{^{1}H}-NMR of (*o*-Tol)$_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 99.0 (s) ppm.

$C_{70}H_{56}BF_{24}IrNO_2P$ (1633.16 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = (500 MHz, CD_2Cl_2): δ = 8.25 (d, *J* = 7.9 Hz, 1H, C*H*OP), 7.73 (s, 8H, BAr_F-*H*), 7.56 (s, 4H, BAr_F-*H*), 7.54–7.51 (m, 1H), 7.50–7.43 (m, 3H), 7.39 (t, *J* = 7.3 Hz, 3H), 7.32–7.26 (m, 3H), 7.24–7.18 (m, 2H), 7.16–7.08 (m, 1H), 6.69 (br s, 1H, H_{Ar}), 5.45–5.35 (m, 1H, C*H* COD), 4.45–4.30 (m, 1H, C*H* COD), 4.20–4.09 (m, 1H, C*H* COD), 3.77 (m, 3H, OCH_3), 3.55–3.35 (m, 1H, C*H* COD), 2.70–2.55 (m, 1H, CH_2 COD), 2.50–2.14 (m, 11H, CH_2 COD 6H, CH_2CH$_3$ 2H, Ar-CH_3 3H), 1.81–1.72 (m, 1H, CH_2 COD), 1.60–1.17 (m, 9H, CH_3, CH$_2$CH_3, Ar-CH_3) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 168.4 (s, C_{Ar}), 164.2 (s, C_{Ar}), 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 155.0 (s, C_{Ar}), 137.2 (d, J_{PC} = 7 Hz, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 133.6 (s, HC_{Ar}), 133.3 (br s, HC_{Ar}), 133.1 (s, HC_{Ar}), 132.8 (s, HC_{Ar}), 132.6 (s, HC_{Ar}), 132.1 (d, J_{PC} = 16 Hz, C_{Ar}), 131.1 (br s, HC_{Ar}), 130.2 (br s, HC_{Ar}), 130.1 (s, HC_{Ar}), 129.6 (s, HC_{Ar}), 129.4 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 126.7 (d, J_{PC} = 11 Hz, C_{Ar}), 125.2 (q, J_{FC} = 272 Hz, *C*F$_3$ BAr_F), 123.6 (s, C_{Ar}), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 107.4 (s, HC_{Ar}), 100.1 (br s, *C*H COD), 88.4 (s, *C*H COD), 85.7 (s, *C*HOP), 67.5 (br s, *C*H COD), 67.0 (br s, *C*H COD), 57.0 (s, O*C*H$_3$), 38.1 (d, J_{PC} = 3 Hz, *C*H$_2$ COD), 35.5 (d, J_{PC} = 3 Hz, *C*H$_2$ COD), 35.3 (s, *C*H$_2$CH$_3$), 28.7 (s, Ar-*C*H$_3$), 25.4 (s, *C*H$_2$ COD), 22.03 (s, *C*H$_2$ COD), 21.98 (s, Ar-*C*H$_3$), 14.3 (CH$_2$*C*H$_3$), 11.3 (s, *C*H$_3$) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, CD_2Cl_2): δ = 107.4 (br s) ppm. **MS** (FAB NBA) *m/z* (%): 770 ([Ir(L)(COD)]$^+$, 65), 662 (22), 240 (100). **EA**: calc. (%) C 51.48, H 3.46, N 0.86; found C 50.33, H 3.60, N 1.09. **m.p.**: 83–84 °C. **[α]$_D^{20}$**: −39.7 (*c* = 0.70, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-((phenyl)methyl)-(6-ethyl-4-methoxy-3-methylpyridyl))-di-*tert*-butylphosphinite-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-113h)



The intermediate ligand (*S*)-**102h** was obtained following the general procedure **H** using (*S*)-(6-methylpyridin-2-yl)(phenyl)-methanol (60 mg, 233 µmol, 1.0 eq.), chloro-di-*tert*-butylphosphine (44 µL, 42.1 mg, 233 µmol, 1.0 eq.), KH (14. 0 mg, 349 µmol, 1.5 eq.), THF (1.0 mL) as a colorless foam (68.0 mg, 169 µmol, 73%). The

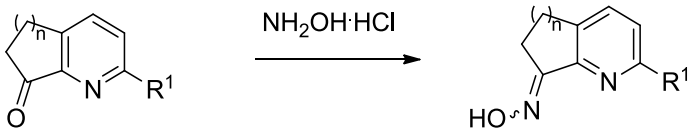
title compound (*S*)-**113h** was obtained following general procedure **G** using the N,P ligand (68.0 mg, 169 µmol, 73%), $[Ir(COD)Cl]_2$ (57.36 mg, 85.3 µmol, 0.5 eq.) in DCM (3 mL), $NaBAr_F$ (160 mg, 181 µmol, 1.1 eq.), after purification by flash chromatography (Al_2O_3, 3 cm × 14 cm, cyclohexane / DCM 2:1) and recrystallization from diethyl ether solution (1 mL) and *n*-pentane (25 mL) as a red solid (170 mg, 108 µmol, 46% over two steps).

$^{31}P\{^1H\}$-NMR of $(t\text{-Bu})_2PCl$ (162 MHz, C_6D_6): δ = 146.4 (s) ppm.
$^{31}P\{^1H\}$-NMR of the ligand (162 MHz, C_6D_6): δ = 167.1 (s) ppm.

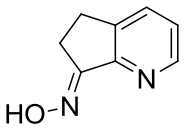
$C_{64}H_{60}BF_{24}IrNO_2P$ (1565.13 g/mol):
^1H-NMR (500 MHz, CD_2Cl_2): δ = 7.73 (s, 8H, BAr_F-*H*), 7.57 (s, 4H, BAr_F-*H*), 7.56–7.05 (m 5H, H_{Ar}), 6.87 (s, 1H, H_{Ar}), 5.28–5.21 (m, 1H, C*H* COD), 5.05–4.98 (m, 1H, C*H* COD), 4.04 (d, *J* = 7.5 Hz, 1H, C*H* COD), 3.96 (dq, *J* = 14.9, 7.4 Hz, 1H, CH_2CH_3), 3.88 (m, 3H, OCH_3), 3.51 (dq, *J* = 14.9, 7.4 Hz, 1H, CH_2CH_3), 3.29 (p, *J* = 7.4 Hz, 1H, C*H* COD), 2.59 (dtd, *J* = 15.9, 10.6, 5.7 Hz, 1H, CH_2 COD), 2.31 (ddt, *J* = 15.3, 9.8, 5.3 Hz, 1H, CH_2 COD), 2.23 (ddt, *J* = 15.7, 8.0 Hz, 1H, CH_2 COD), 2.14 (dt, *J* = 13.9, 9.3 Hz, 1H, CH_2 COD), 2.08–1.94 (m, 2H, CH_2 COD), 1.62–1.53 (m, 1H, CH_2 COD), 1.56 (t, *J* = 7.4 Hz, 3H, CH_2CH_3), 1.50–1.40 (m, 2H, CH_2 COD), 1.39–1.31 (m, 12H, CH_3, $(CH_3)_3C$), 1.01 (d, *J* = 14.8 Hz, 9H, $(CH_3)_3C$) ppm. **$^{13}C\{^1H\}$-NMR** (126 MHz, CD_2Cl_2): δ = 168.6 (s, C_{Ar}), 164.3 (s, C_{Ar}), 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 155.4 (s, C_{Ar}), 137.2 (d, J_{PC} = 7 Hz, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 130.1 (br s, HC_{Ar}), 129.7 (s, HC_{Ar}), 129.4 (qq, J_{FC} = 32 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 126.6 (s, C_{Ar}), 125.2 (q, J_{FC} = 272 Hz, CF_3 BAr_F), 123.6 (s, C_{Ar}), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 107.5 (s, HC_{Ar}), 93.5 (d, J_{PC} = 6 Hz, *C*H COD), 87.4 (s, *C*HOP), 82.1 (d, J_{PC} = 18 Hz, *C*H COD), 71.8 (s, *C*H COD), 59.9 (s, *C*H COD), 57.1 (s, OCH_3), 41.3 (d, J_{PC} = 19 Hz, $(CH_3)_3C$), 40.0 (d, J_{PC} = 19 Hz, $(CH_3)_3C$), 39.2 (d, J_{PC} = 3 Hz, CH_2 COD), 35.9 (s, CH_2 COD), 35.4 (s, CH_2CH_3), 29.0 (s, $(CH_3)_3C$), 28.9 (s, $(CH_3)_3C$), 28.5 (s, CH_2 COD), 24.3 (d, J_{PC} = 3 Hz, CH_2 COD), 13.7 (CH_2CH_3), 11.0 (s, CH_3) ppm. **$^{31}P\{^1H\}$-NMR** (162 MHz, CD_2Cl_2): δ = 140.0 (s) ppm. **MS** (FAB NBA) *m/z* (%): 702 ($[Ir(L)(COD)]^+$, 100), 594 (11), 538 (28), 478 (33), 431 (14), 240 (50). **EA**: calc. (%) C 49.11, H 3.86, N 0.89; found C 47.97, H 3.80, N 1.22. **m.p.**: 123–124 °C. **$[\alpha]_D^{20}$**: −40.1 (*c* = 0.50, $CHCl_3$).

8.6 New Bicyclic Pyridine Amino-Phosphine Derived Ligands for Iridium-Catalyzed Asymmetric Hydrogenations

8.6.1 Formation of N-Oximies



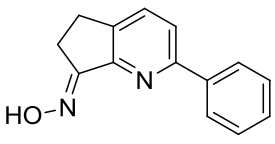
5*H*-Cyclopenta[1]pyridin-7(6*H*)-one oxime (139a)



A mixture of ketone **76a** (1.29 g, 9.69 mmol, 1.0 eq.), hydoxylamine hydrochloride (1.36 g, 19.6 mmol, 2.0 eq.), sodium acetate (2.76 g, 33.6 mmol, 3.5 eq.), MeOH (15 mL) and water (5 mL) was stirred for 14 hours at RT. A precipitate is formed, which was separated by filtration, followed by washing with water (10 mL) and pentane (10 mL). The title compound **139a** (1.08 g, 7.29 mmol, 75%) was isolated as a colorless solid.

$C_8H_8N_2O$ (148.16 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 11.25 (s, 1H, N-O*H*), 8.47 (d, *J* = 3.1 Hz, 1H, H_{Ar}), 7.78 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.30 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 3.04–2.88 (m, 2H, CH_2), 2.87–2.64 (m, 2H, CH_2) ppm.**^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 159.6 (*C*=N), 155.2 (C_{Ar}), 149.9 (HC_{Ar}), 141.9 (C_{Ar}), 133.8 (HC_{Ar}), 123.8 (HC_{Ar}), 25.4 (CH_2), 24.4 (CH_2) ppm. **MS** (EI, 70 eV, ca. 200°C, *m/z* (%): 148 (97, [M^+]), 130 (76), 117 (100), 104 (34), 91 (31), 79 (18), 63 (13), 51 (16), 39 (14). **m.p.**: 245–246 °C (dec.).

2-Phenyl-5*H*-cyclopenta[1]pyridin-7(6*H*)-one oxime (139b)

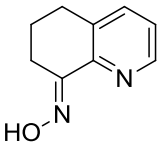


A mixture of ketone **76b** (500 mg, 2.39 mmol, 1.0 eq.), hydoxylamine hydrochloride (332 mg, 4.78 mmol, 2.0 eq.), sodium acetate (686 mg, 8.36 mmol, 3.5 eq.), methanol (6.0 mL) and water (2.0 mL) was

stirred for 20 hours at RT. A precipitate is formed, which was separated by filtration, followed by washing with methanol-water 3:1 mixture (0.6 mL) and with pure *n*-pentane (5 mL) to obtain the title compound (536 mg, 2.39 mmol, quant.) as a pale green solid.

$C_{14}H_{12}N_2O$ (224.26 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 11.20 (s, 1H, N-O*H*), 8.12–8.00 (m, 2H, H_{Ar}), 7.85 (q, *J* = 8.1 Hz, 2H, H_{Ar}), 7.56–7.28 (m, 3H, H_{Ar}), 3.04–2.93 (m, 2H, CH_2), 2.90–2.76 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 159.5 (*C*=N), 155.6 (C_{Ar}), 155.3 (C_{Ar}), 140.8 (C_{Ar}), 138.6 (C_{Ar}), 134.7 (HC_{Ar}), 129.0 (HC_{Ar}), 128.7 (HC_{Ar}), 126.6 (HC_{Ar}), 120.6 (HC_{Ar}), 25.3 (*C*H$_2$), 24.7 (*C*H$_2$) ppm. **MS** (EI, 70 eV, ca. 200°C, *m/z* (%): 224 (100, [M$^+$]), 206 (62), 180 (19), 166 (17), 152 (10), 139 (7), 115 (9), 89 (7), 77 (8). **EA**: calc. (%) C 74.98, H 5.39, N 12.49; found C 71.63, H 5.60, N 11.50. **m.p.**: 235–236 °C

(*E*)-6,7-dihydroquinolin-8(5*H*)-one oxime (139c)



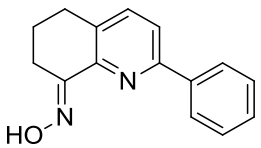
A mixtre of ketone **76b** (1.00 g, 6.79 mmol, 1.0 eq.), of hydroxylamine hydrochloride (0.95 g, 13.6 mmol, 2.0 eq.), sodium acetate (1.85 g, 22.6 mmol, 3.3 eq.), ethanol (6.0 mL) and water (2.0 mL) was stirred at 70 °C for 1 h. The reaction mixtue was cooled down to RT. Filtration, following by washing with water (4 mL) and *n*-heptane (5 mL) gave the title compound **139c** (0.66 g, 4.09 mmol, 60%) as a slightly brown solid.

Procedure directly starting from 5,6,7,8-tetrahydro-quinoline:
A solution of 5,6,7,8-tetrahydro-quinoline (2.13 g, 16.0 mmol, 1.0 eq.) and diisopropylamine (1.62 g, 16.0 mmol, 1.0 eq.) TBME (10 mL) was stirred for 10 min, while dry nitrogen gas was purged through the solution. The solution was then cooled to −20 °C and *n*-BuLi 1.6 M solution (20 mL, 32.0 mmol, 2.0 eq.) was added, while the temperature was kept under −15 °C. The obtained orange / red solution was transfered via cannula to a pre-cooled solution of isopentyl nitrite (6.4 mL, 5.63 g, 48.1 mmol, 3.0 eq.) in TBME (6.0 mL) at −15 °C. The resulting mixture was stirred at −15°C for 1 h, then carefully quentched with water (20 mL). The reaction mixture was allowed to reach RT, and then the phases were separated. The aq. phase re-extracted with TBME (2×15 mL). The aq. fraction was neutralized with HCl 1 M solution. The volume was concentrated in *vacuo* to approximantely ~10 mL. The resulting

slurry was cooled down to 0 °C. The N-oxime precipitates out and was collected by filtration. After washing with *n*-heptane (10 mL) the title compound **139c** was obtained as a brown solid (756 mg, 4.66 mmol, 29%).

$C_9H_{10}N_2O$ (162.19 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 10.2 (br s, 1H, N-O*H*), 8.48 (dd, *J* = 4.7, 1.7 Hz, 1H, H_{Ar}), 7.46 (tdd, *J* = 7.7, 1.6 Hz, 0.6 Hz, 1H, H_{Ar}), 7.17 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 2.91 (t, *J* = 6.7 Hz, 2H, CH_2), 2.80 (t, *J* = 6.1 Hz, 2H, CH_2), 1.90 (quin., *J* = 6.2 Hz, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 152.7 (*C*=N), 148.8 (C_{Ar}), 148.1 (HC_{Ar}), 136.7 (HC_{Ar}), 134.6 (C_{Ar}), 123.5 (HC_{Ar}), 29.4 (*C*H_2), 24.3 (*C*H_2), 21.2 (*C*H_2) ppm. **MS** (EI, 70 eV, ca. 150°C, *m/z* (%): 162 (100, [M^+]). **IR**: $\tilde{\nu}$ = 3125 (m), 3072 (m), 2999 (m), 2936 (m), 2830 (m br), 2084 (m), 1621 (w), 1575 (m), 1475 (s), 1423 (m), 1347 (w), 1311 (w), 1222 (w), 1193 (m), 1185 (m), 1120 (w), 1089 (m), 1039 (w), 969 (s), 903 (m), 877 (s), 843 (m), 792 (s), 730 (s) cm^{-1}. **EA**: calc. (%) C 66.65, H 6.21, N 17.27; found C 66.51, H 6.16, N 17.17. **m.p.**: 171–172 °C (dec.).

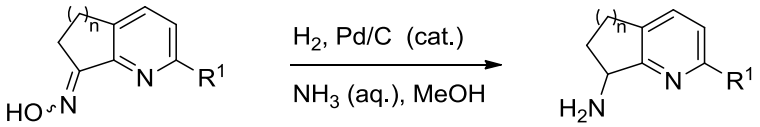
(*E*)-2-phenyl-6,7-dihydroquinolin-8(5*H*)-one oxime (139d)



A mixture of ketone **76d** (800 mg, 3.58 mmol, 1.0 eq.), hydroxylamine hydrochloride (498 mg, 7.16 mmol, 2.0 eq.), sodium acetate (976 mg, 11.9 mmol, 3.3 eq.), ethanol (10 mL) and water (3.0 mL) was stirred at 70 °C for 18 h. After addition of water (5 mL) the reaction mixture was extracted with DCM (3×30 mL). After removal of the volatiles the title compound **139d** was obtained as a slightly yellow solid (829 mg, 3.48 mmol, 97%).

$C_{15}H_{14}N_2O$ (238.28 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 10.24 (br s, 1H, N-O*H*), 8.05 (d, *J* = 8.0 Hz, 2H, H_{Ar}), 7.65 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.55 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.47 (t, *J* = 7.5 Hz, 2H, H_{Ar}), 7.43–7.37 (m, 1H, H_{Ar}), 2.98 (t, *J* = 6.3 Hz, 2H, CH_2), 2.85 (t, *J* = 5.7 Hz, 2H, CH_2), 1.96 (pentet, *J* = 6.2 Hz, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 156.0 (*C*=N), 152.7 (C_{Ar}), 148.6 (C_{Ar}), 130.4 (C_{Ar}), 137.8 (HC_{Ar}), 133.3 (C_{Ar}), 129.0 (HC_{Ar}), 128.8 (HC_{Ar}), 127.2 (HC_{Ar}), 120.8 (HC_{Ar}), 29.0 (Ar*C*H_2), 24.2 (*C*H_2C), 21.1 (CH_2*C*H_2CH_2) ppm. **MS** (EI, 70 eV, ca. 200°C, *m/z* (%): 238 (100, [M^+]), 221 (43), 206 (21), 194 (19), 167 (6), 128 (6), 115 (5). **EA**: calc. (%) C 75.61, H 5.92, N 11.76; found C 73.58, H 5.99, N 11.35. **m.p.**: 82–87 °C.

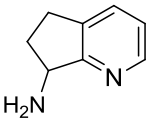
8.6.2 Reduction of N-Oximies



General Procedure I: Pd/C (5% Pd, 1 w% to the oxime) was added to a solution of N-oxime (1.0 eq) in MeOH / ammonia 25 w% aq. solution (5:1, 0.4 M) in a glas vial. The reaction mixture was placed in an autoclave. Hydrogen pressure (5-10 bar) was applied and the mixture was stirred at rt for 12-15 hours. After complete reduction the catalyst was removed by filtration over a *Celite*® pad and washed with DCM (3×50 mL). After drying over $MgSO_4$ and filtration, the solvent was removed under reduced pressure. The crude product was purified by *Kugelrohr* distillation.

Note: The pyridyl amines are not bench-stable. However, they can be stored for months inside a freezer (−18 °C) under innert conditions.

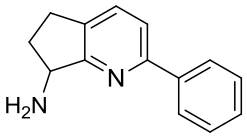
6,7-Dihydro-5*H*-cyclopenta[1]pyridin-7-amine (136a)



The title compound **136a** was obtained following the general procedure **I** for the reduction of oximes using **139a** (200 mg, 1.35 mmol, 1.0 eq.), methanol (2.0 mL), ammonia 25 w% aq. solution (0.5 mL), Pd/C (5%, 57.5 mg. 267.0 µmol, 0.02 eq.) under 5 bar hydrogen gas during 14 hours, and purification by *Kugelrohr* distillation (0.2 mbar, 135–145 °C) as a brown oil (158 mg, 1.18 mmol, 87%).

$C_8H_{10}N_2$ (134.18 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 4.8 Hz, 1H, H_{Ar}), 7.50 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.08 (dd, *J* = 7.5, 4.9 Hz, 1H, H_{Ar}), 4.32 (t, *J* = 7.9 Hz, 1H, C*H*), 2.93 (ddd, *J* = 16.2, 8.9, 3.0 Hz, 1H, CH_2), 2.80 (dt, *J* = 16.4, 8.4 Hz, 1H, CH_2), 2.55 (dtd, *J* = 12.8, 7.9, 3.1 Hz, 1H, CH_2), 2.24 (s, 2H, NH_2), 1.74 (dq, *J* = 12.9, 8.6 Hz, 1H, CH_2) ppm. **b.p.**: 135–145 °C (0.2 mbar).

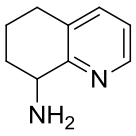
2-Phenyl-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-amine (136b)



The title compound **136b** was obtained following the general procedure **I** for the reduction of oximes using **139b** (520 mg, 2.3 mmol, 1.0 eq.), methanol (5.0 mL), ammonia 25 w% aq. solution (1.0 mL), Pd/C (5%, 98.7 mg. 46.4 µmol, 0.02 eq.) under 9 bar hydrogen gas during 14 hours, and purification by *Kugelrohr* distillation (0.2 mbar, 155–160 °C) as a brown oil (448 mg, 2.13 mmol, 92%).

$C_{14}H_{14}N_2$ (210.28 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.05–7.91 (m, 2H, H_{Ar}), 7.55 (dd, *J* = 19.2, 8.0 Hz, 2H, H_{Ar}), 7.50–7.43 (m, 2H, H_{Ar}), 7.42–7.36 (m, 1H, H_{Ar}), 4.38 (t, *J* = 7.9 Hz, 1H, C*H*), 2.97 (ddd, *J* = 16.3, 8.6, 2.5 Hz, 1H, CH_2), 2.78–2.90 (m, 1H, CH_2), 2.61 (dtd, *J* = 12.8, 7.8, 3.1 Hz, 1H, CH_2), 1.93 (br s, 2H, NH_2), 1.80 (ddd, *J* = 17.1, 12.8, 8.8 Hz, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 166.9 (C_{Ar}), 156.4 (C_{Ar}), 139.9 (C_{Ar}), 134.5 (C_{Ar}), 133.4 (HC_{Ar}), 128.8 (HC_{Ar}), 128.7 (HC_{Ar}), 127.0 (HC_{Ar}), 119.2 (HC_{Ar}), 567.0 (*C*H), 34.4 (*C*H$_2$), 27.6 (*C*H$_2$) ppm. **MS** (EI, 70 eV, ca. 200 °C) *m/z* (%): 210 (100, [M$^+$]), 195 (28), 182 (28), 169 (15), 155 (10), 115 (6), 104 (5), 77 (5). **EA**: calc. (%) C 79.97, H 6.71, N 13.32; found C 78.87, H 6.96, N 12.88. **b.p.**: 155–160 °C (0.2 mbar).

5,6,7,8-Tetrahydroquinolin-8-amine (136c)



The title compound **136c** was obtained following the general procedure **I** for the reduction of oximes using **139c** (660 mg, 4.07 mmol, 1.0 eq.), methanol (10 mL), ammonia 25 w% aq. solution (2 mL), Pd/C (5%, 225 mg. 0.11 mmol, 0.03 eq.) under 5 bar hydrogen gas during 18 hours, and purification by *Kugelrohr* distillation (0.1 mbar, 125–130 °C) as a colorless oil (544 mg, 3.67 mmol, 90%).

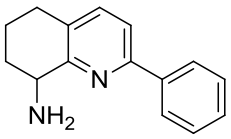
Procedure B:
Zinc dust (18.0 g, 275 mmol, 41 eq.) was added in portions to a mixture of **139c** (1.10 g, 6.78 mmol, 1.0 eq.) in glacial acetic acid (18.0 mL, 18.9 g, 315 mmol, 46 eq.) und ethanol (7.0 mL) under vigorous stirring. The reaction mixture was stirred over night (>14 h) at RT; before the insoluble material was removed by filtration over a *Celite*® pad and washing with ethanol (3×10 mL). After removing the solvent under reduced pressure the residue was extracted with DCM (15 mL) and aqueous NaOH 50% solution (20 mL). The water layer was

washed with DCM (3×20 mL). After drying over $MgSO_4$ the solvent was removed under reduced pressure. The crude product was purified by *Kugelrohr* distillation (0.5 mbar, 150–160 °C) to obtain the title compound **136c** (980 mg, 6.56 mmol, 97%) as a slightly yellow oil.

$C_9H_{12}N_2$ (148.20 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.39 (dd, *J* = 4.7, 0.8 Hz, 1H, H_{Ar}), 7.35 (dd, *J* = 7.7, 0.8 Hz, 1H, H_{Ar}), 7.04 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 3.98 (t, *J* = 5.5 Hz, 1H, C*H*), 2.90–2.65 (m, 2H, CH_2), 2.20–2.13 (m, 1H, CH_2), 2.01 (br s, 2H, NH_2), 1.99–1.89 (m, 1H, CH_2), 1.81–1.64 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 159.6 (C_{Ar}), 147.0 (HC_{Ar}), 136.7 (HC_{Ar}), 131.5 (C_{Ar}), 121.6 (HC_{Ar}), 51.4 (*C*H), 32.0 (*C*H_2), 29.0 (*C*H_2), 19.9 (*C*H_2) ppm. **MS** (EI, 70 eV, RT) *m/z* (%):148 ([M^+], 84), 130 (28), 119 (90), 93 (54), 77 (7), 65 (8), 56 (6), 51 (5), 39 (7). **IR**: $\tilde{\nu}$ = 3364 (w), 2925 (m), 2858 (m), 1746 (m), 1584 (m), 1569 (s), 1426 (s), 1374 (m), 1352 (w), 1215 (w), 1116 (w), 928 (w), 880 (m), 849 (m), 821 (w), 784 (s) cm^{-1}. **EA**: calc. (%) C 72.94, H 8.16, N 18.90; found C 72.21, H 8.19, N 18.49. **b.p.**: 125–130 °C (0.1 mbar).

2-Phenel-5,6,7,8-tetrahydroquinolin-8-amine (136d)

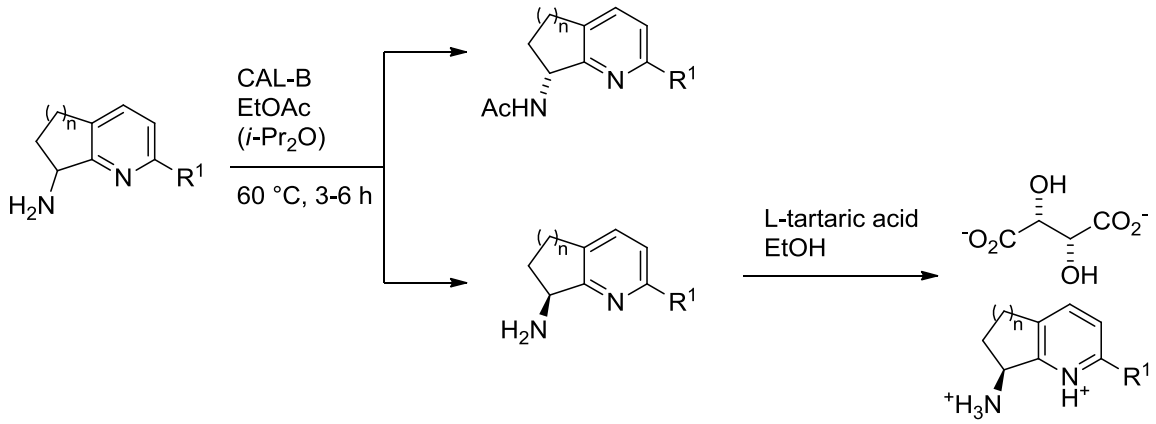


The title compound **136d** was obtained following the general procedure **I** for the reduction of oximes using **139d** (820 mg, 3.44 mmol, 1.0 eq.), methanol (10 mL), ammonia 25 w% aq. solution (2 mL) and Pd/C (5%, 205 mg. 0.01 mmol, 0.03 eq.) under 5 bar hydrogen gas during 18 hours, and purification by *Kugelrohr* distillation (0.3 mbar, 150–155 °C) as a colorless oil (620 mg, 2.77 mmol, 80%).

$C_{15}H_{16}N_2$ (224.30 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.04–7.96 (m, 2H, H_{Ar}), 7.55–7.33 (m, 5H, H_{Ar}), 4.05 (dd, *J* = 8.6, 5.7 Hz, 1H, C*H*), 2.90–2.70 (m, 2H, ArCH_2), 2.31–2.22 (m, 1H, CH_2), 2.14 (br s, 2H, NH_2), 2.06–1.91 (m, 1H, CH_2), 1.88–1.76 (m, 1H, CH_2), 1.76–1.64 (m, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 159.5 (C_{Ar}), 154.7 (C_{Ar}), 139.7 (C_{Ar}), 137.7 (HC_{Ar}), 130.2 (C_{Ar}), 128.8 (HC_{Ar}), 128.7 (HC_{Ar}), 126.9 (HC_{Ar}), 118.6 (HC_{Ar}), 52.0 (*C*HNH_2), 32.3 (*C*H_2CHNH_2), 29.0 (Ar*C*H_2), 20.6 (CH_2*C*H_2CH_2) ppm. **b.p.**: 150–155 °C (0.3 mbar).

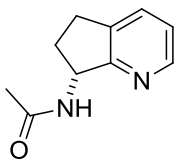
8.6.3 Enzymatic Kinetic Resolution of Primary Amines



General Procedure J: Ethyl acetate (>4 eq.) was added to a mixture of pyridyl amine (1.0 eq.) and CAL-B (40-50 mg/mmol) in diisopropyl ether (0.35 M). The reaction mixture was stirred for a given time at 60 °C. After cooling down to RT, the reaction mixture was filtered over a *Celite*® pad and washed with DCM (3×50 mL). The solvents were removed under reduced pressure. The products were separated by flash chromatography. The formed (*R*)-amide was recrystallized in order to obtain enaniomeric pure material.

The unreacted (*S*)-amine was directly converted to the tartat salt: A boiling solution of L-tartaric acid (>1.3 eq.) in ethanol (0.7 M) was added to a boiling solution of (*S*)-amine (1.0 eq.) in ethanol (0.7 M). The solution was allowed to cool down to RT; while the tartaric salt precipitate. After stirring for 1 h at rt the product was separated by filtration and washed with ethanol (2×0.5 mL).

(*R*)-*N*-(6,7-Dihydro-5*H*-cyclopenta[1]pyridin-7-yl) acetamide ((*R*)-137a)



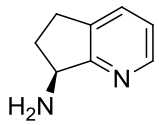
The title compound **(*R*)-137a** was obtained following the general procedure **J** using ethyl acetate (3.0 mL, 2.69 g, 30.5 mmol, 52 eq.), amine **136a** (79.0 mg, 589 µmol, 1.0 eq.), CAL-B (39 mg), after stirring 3.5 h at 60 °C and separation by chromatography (SiO_2, 1.5 cm × 11 cm, DCM / MeOH 9:1) as pale yellow solid (59 mg, 334 µmol, 57%, 79% *ee*).

$C_{10}H_{12}N_2O$ (176.22 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.34 (s, 1H, H_{Ar}), 7.53 (d, *J* = 7.5 Hz, 1H, H_{Ar}), 7.18–7.03 (m, 1H, H_{Ar}), 6.50 (br s, 1H, N*H*), 5.21 (q, *J* = 8.0 Hz, 1H, C*H*), 2.98–2.75 (m, 3H, CH_2), 2.04

(s, 3H, CH_3), 1.85–1.73 (m, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.8 (*C*=O), 162.5 (C_{Ar}), 148.1 (HC_{Ar}), 137.0 (C_{Ar}), 133.1 (HC_{Ar}), 121.8 (HC_{Ar}), 55.4 (*C*H), 33.7 (*C*H_2), 28.0 (*C*H_2), 23.4 (CH_3) ppm. **HPLC** (chiral, Daicel Chiracel AD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 90:10, 0.5 mL/min, 25 °C: t_R = 19.3 min (*R*), 33.8 min (*S*).

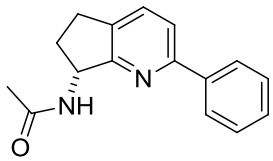
(*S*)-2-Phenyl-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-amine (*S*)-136a



The title compound (*S*)-**136a** was obtained from the enzymatic kinetic resolution after flash chromatography (SiO_2, 1.5 cm × 11 cm, DCM / MeOH 9:2) as brown oil (37 mg, 0.276 µmol, 47%, >99% *ee*).

TLC: (SiO_2, DCM/MeOH 9:2): R_f = 0.33. **HPLC** (chiral, Daicel Chiracel AD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 95:5 + 0.1% *n*-BuNH_2, 0.8 mL/min, 40 °C: t_R = 13.7 min (*S*), 19.8 min (*R*) or Daicel Chiracel OD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 95:5 + 0.1% *n*-BuNH_2, 0.8 mL/min, 40 °C: t_R = 14.8 min (*S*), 17.4 min (*R*). **$[\alpha]_D^{20}$**: −39.8 (*c* = 0.35, $CHCl_3$).

(*R*)-*N*-(2-Phenyl-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-yl) acetamide ((*R*)-137b)

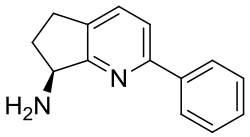


The title compound (*R*)-**137b** was obtained following the general procedure **J** using ethyl acetate (6.0 mL, 5.41 g, 61.4 mmol, 42 eq.), amine **136b** (310 mg, 1.47 mmol, 1.0 eq.), CAL-B (80 mg) after stirring for 3.5 h at 60 °C. Isolation by flash chromatography (SiO_2, 1.5 cm × 10 cm, ethyl acetate) and recrystallization from boiling ethyl acetate (2.5 mL) gave a with solid (186 mg, 0.737 mmol, 50%, 85% *ee*).

$C_{16}H_{16}N_2O$ (252.31 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.96–7.89 (m, 2H, H_{Ar}), 7.62–7.51 (m, 2H, H_{Ar}), 7.50–7.34 (m, 3H, H_{Ar}), 6.68 (br s, 1H, N*H*), 5.23–5.14 (m, 1H, C*H*), 2.95–2.80 (m, 3H, CH_2), 2.10 (s, 3H, CH_3), 1.87–1.72 (m, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.8 (*C*=O), 162.5 (C_{Ar}), 156.5 (C_{Ar}), 139.4 (C_{Ar}), 135.5 (C_{Ar}), 133.6 (HC_{Ar}), 129.0 (HC_{Ar}), 128.9 (HC_{Ar}), 127.1 (HC_{Ar}), 120.0 (HC_{Ar}), 55.7 (*C*H), 33.8 (*C*H_2), 27.8 (*C*H_2), 23.5 (CH_3) ppm. **HPLC**

(chiral, Daicel Chiracel AD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 90:10, 0.5 mL/min, 25 °C: t_R = 19.3 min (*R*), 33.8 min (*S*). **[α]$_D^{20}$**: −86.2 (*c* = 0.70, $CHCl_3$).

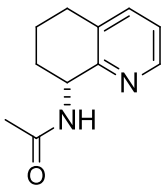
(*S*)-2-Phenyl-6,7-dihydro-5*H*-cyclopenta[1]pyridin-7-amine ((*S*)-136b)



The title compound (*S*)-**136b** was obtained after enzymatic kinetic resolution and separation by flash chromatography (SiO_2, 1.5 cm × 10 cm, DCM / MeOH 9:1) as brown oil (141 mg, 671 µmol, 46%, >99% *ee*).

HPLC (chiral, Daicel Chiracel AD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 95:5 + 0.1% *n*-$BuNH_2$, 0.8 mL/min, 40 °C: t_R = 13.7 min (*S*), 19.8 min (*R*) or Daicel Chiracel OD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 95:5 + 0.1% *n*-$BuNH_2$, 0.8 mL/min, 40 °C: t_R = 14.8 min (*S*), 17.4 min (*R*). **[α]$_D^{20}$**: +56 (*c* = 0.82, $CHCl_3$).

(*R*)-*N*-(5,6,7,8-Tetrahydroquinolin-8-yl)acetamide ((*R*)-137c)

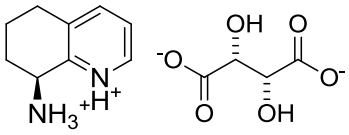


The title compound (*R*)-**137c** was obtained following the general procedure **J** using ethyl acetate (2.0 mL, 1.80 g, 20.5 mmol, 4.1 eq.), amine **136c** (740 mg, 4.99 mmol, 1.0 eq.), CAL-B (230 mg) and diisopropyl ether (15 mL). The reaction mixture was stirred at 60 °C for 6 hours. Isolation by flash chromatography (SiO_2, 3 cm × 15 cm, DCM/MeOH 9:1 → 9:3) gave the amide (459 mg, 2.41 mmol, 48%, 96% *ee*), which was recrystallized from boiling ethyl acetate (9.0 mL) to give enantiopure material (344 mg, 1.81 mmol, 36%, >99% *ee*). The analytical data match the reported values.[124]

$C_{11}H_{14}N_2O$ (190.24 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.38 (d, *J* = 4.6 Hz, 1H, H_{Ar}), 7.41 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.11 (dd, *J* = 7.6, 4.8 Hz, 1H, H_{Ar}), 6.79 (br s, 1H, N*H*) 4.91 (m, 1H, C*H*), 2.80 (t, *J* = 6.6 Hz, 2H, CH_2), 2.60–2.54 (m, 1H, CH_2), 2.06 (s, 3H, CH_3) 1.94–1.84 (m, 2H, CH_2), 1.72–1.55 (m, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.6 (*C*=O), 155.5 (C_{Ar}), 147.0 (HC_{Ar}), 137.3 (HC_{Ar}), 133.2 (C_{Ar}), 122.6 (HC_{Ar}), 51.3 (*C*H), 29.6 (*C*H_2), 28.4 (*C*H_2), 23.9 (*C*H_3), 20.1 (*C*H_2) ppm. **MS** (EI, 70 eV, 100 °C) *m/z* (%): 190 (13, [M^+]), 147 (100). **EA**:

calc. (%) C 69.26; H 7.36; N 14.54; found C 69.36, H 7.36, N 14.73. **TLC**: (SiO_2, DCM/MeOH 9:1): R_f = 0.33. **HPLC** (chiral, Daicel Chiracel AD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 90:10, 1.0 mL/min, 40 °C: t_R = 9.3 min (*R*), 15.1 min (*S*). **$[\alpha]_D^{20}$**: −105 (*c* = 1.10, $CHCl_3$), lit: −90 (*c* = 0.52, $CHCl_3$), for 98% *ee*).[124]

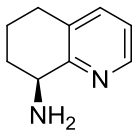
(*S*)-5,6,7,8-Tetrahydro-8-quinolinamine (2*R*,3*R*)-2,3-dihydroxybutanedioate (1:1) ((*SRR*)-140a)



The amine (*S*)-**136c** was obtained from the enzymatic kinetic resolution after the flash chromatography as a slightly yellow oil (323 mg, 2.18 mmol, 44%, *ee* 85%). It was directly converted to the title compound (*S*,*R*,*R*)-**140a** using L-tartaric acid (436 mg, 2.90 mmol, 1.3 eq.) and ethanol (8.0 mL) and recrystallized from boiling methanol (5.0 mL) to give a colorless solid (476 mg, 1.60 mmol, 32%, >99% *ee* determinined as the free amine).

$C_{13}H_{18}N_2O_6$ (298.29 g/mol):
^{1}H-NMR (400 MHz, $(CD_3)_2SO$): δ = 8.45 (dd, *J* = 4.7, 1.5 Hz, 1H, H_{Ar}) 7.61 (dd, *J* = 7.7, 1.4 Hz, 1H, H_{Ar}), 7.32 (dd, *J* = 7.7, 4.7 Hz, 1H, H_{Ar}), 4.35–4.31 (m, 1H, C*H*), 4.10 (br s, 6H, N*H*, O*H*), 3.82 (s, 2H, C*H*OH) 2.78 (t, *J* = 5.8 Hz, 2H, CH_2), 2.27–2.19 (m, 1H, CH_2), 1.96–1.88 (m, 1H, CH_2), 1.82–1.69 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $(CD_3)_2SO$): δ = 174.4 (*C*=O), 152.3 (C_{Ar}), 146.8 (HC_{Ar}), 137.6 (HC_{Ar}), 132.8 (C_{Ar}), 123.4 (HC_{Ar}), 71.4 (*C*HOH), 50.1 (*C*HNH_2), 27.5 (CH_2), 27.4 (CH_2), 19.4 (CH_2) ppm. **MS** (FAB NBA) *m/z* (%): 149 (100, $[M+H]^+$), 132 (25). **EA**: calc. (%) C 52.35; H, 6.08; N, 9.39; found C 52.17, H 6.12, N 9.41. **m.p.**: 165–166 °C (dec.). **$[\alpha]_D^{20}$**: +43.9 (*c* = 0.35, H_2O).

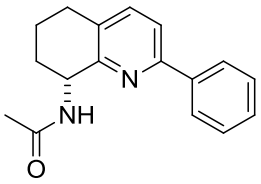
(*S*)-5,6,7,8-Tetrahydroquinolin-8-amine ((*S*)-136c)



A solution of tartaric salt (*S*,*R*,*R*)-**140a** (414 mg, 1.39 mmol) in NaOH 3 M aq. solution (10 mL) was extracted with DCM (5×15 mL). After drying over $MgSO_4$, filtration and removing of the solvent under reduced pressure, the title compound (*S*)-**136c** (190 mg, 1.28 mmol, 92%) was obtained as a colorless oil.

GC (*Brechbühler* β-cyclodextrin DetTButSil (SE54) 25 m × 0.25 mm × 0.25 mm), 120 °C, 15 min, 10 °C/min, 180 °C, 5 min, 100 kPa): t_R = 11.8 min (*S*), 13.7 min (*R*) or **HPLC** (chiral, Daicel Chiracel OD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 95:5 + 0.1% *n*-$BuNH_2$, 0.8 mL/min, 40 °C: t_R = 9.6 min (*S*), 10.7 min (*R*).

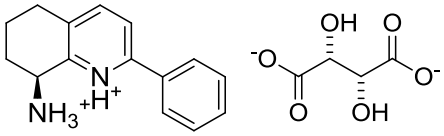
(*R*)-*N*-(2-phenyl-5,6,7,8-tetrahydroquinolin-8-yl)acetamide ((*R*)-137d)



The title compound (*R*)-**137d** was obtained following the general procedure **J** using ethyl acetate (0.90 mL, 812 g, 9.21, 4.0 eq.), amine **136d** (516 mg, 2.30 mmol, 1.0 eq.), CAL-B (106 mg), diisopropyl ether (6 mL), after stirring for 6 h at 60 °C. Isolation by flash chromatography (SiO_2, 3 cm × cm 15 cm, ethylacetate) gave the crude amide (327 mg, 1.23 mmol, 53%, 98% *ee*), which was recrystallized from boiling ethyl acetate (1.5 mL) to give enantiopure material (*R*)-**137d** (190 mg, 0.713 mmol, 30%, >99% *ee*) as a colorless solid.

$C_{17}H_{18}N_2O$ (266.34 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.05–7.97 (m, 2H, H_{Ar}), 7.59 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.51–7.44 (m, 3H, H_{Ar}), 7.43–7.38 (m, 1H, H_{Ar}), 6.76 (br s, 1H, N*H*), 4.88 (dt, *J* = 10.1, 5.1 Hz, 1H, C*H*), 2.84 (t, *J* = 6.6 Hz, 2H, CH_2), 2.76 –2.59 (m, 1H, CH_2CH), 2.12 (s, 3H, CH_3), 1.98–1.87 (m, 2H, CH_2C), 1.70–1.57 (m, 1H, CH_2), ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.8 (*C*=O), 155.2 (C_{Ar}), 154.4 (C_{Ar}), 139.2 (C_{Ar}), 138.1 (HC_{Ar}), 131.5 (C_{Ar}), 129.1 (HC_{Ar}), 129.0 (HC_{Ar}), 126.8 (HC_{Ar}), 119.2 (HC_{Ar}), 51.7 (*C*H), 29.6 (*C*H_2), 28.1 (*C*H_2), 24.0 (CH_3), 20.3 (*C*H_2) ppm. **MS** (EI, 70 eV, 200 °C) *m/z* (%): 266 (37, [M^+]), 223 (100), 207 (24), 195 (8). **EA**: calc. (%) C 76.66; H 6.81; N 10.52; found C 76.37, H 6.96, N 10.49. **TLC**: (SiO_2, ethyl acetate 9:1): R_f = 0.33 **m.p.**: 135–136 °C. **HPLC** (chiral, Daicel Chiracel AD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 80:20, 0.5 mL/min, 25 °C: t_R = 10.8 min (*R*), 14.5 min (*S*). **$[\alpha]_D^{20}$**: −69.0 (*c* = 0.37, $CHCl_3$).

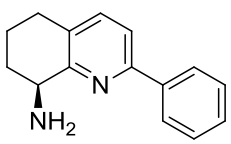
(*S*)-2-Phenyl-5,6,7,8-tetrahydro-8-quinolinamine (2*R*,3*R*)-2,3-dihydroxybutanedioate (1:1) ((*SRR*)-140b)



The amine (*S*)-**137d** was obtained from the enzymatic kinetic resolution after the flash chromatography as a slightly yellow oil (320 mg, 1.43 mmol, 62%, 94% *ee*). It was directly converted to the title compound (*S*,*R*,*R*)-**140b** using L-tartaric acid (236 mg, 1.57 mmol, 1.1 eq.) and ethanol (4.0 mL) and recrystallized from boiling methanol (6.0 mL) to give a colorless solid (215 mg, 0.575 mmol, 25%, >99% *ee*).

$C_{19}H_{22}N_2O_6$ (374.39 g/mol):
^{1}H-NMR (400 MHz, $(CD_3)_2SO$): δ = 8.26–8.22 (m, 2H, H_{Ar}), 7.92 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 7.71 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 7.5–7.40 (m, 3H, H_{Ar}), 4.43 (dd, *J* = 9.0, 6.1 Hz 1H, C*H*NH_2), 3.84 (s, 2H, C*H*OH), 3.74 (br s, 6H), 2.86–2.76 (m, 2H, CH_2), 2.36–2.26 (m, 1H, CH_2), 1.99 (td, *J* = 10.3, 4.7 Hz 1H, CH_2), 1.90–1.73 (m, 2H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $(CD_3)_2SO$): δ = 174.3 (*C*=O), 153.4 (C_{Ar}), 152.0 (C_{Ar}), 138.7 (HC_{Ar}), 137.9 (C_{Ar}), 131.4 (C_{Ar}), 129.2 (HC_{Ar}), 128.7 (HC_{Ar}), 126.7 (HC_{Ar}), 119.5 (HC_{Ar}), 71.3 (*C*HOH), 50.3 (*C*HNH), 27.6 (*C*H_2), 27.2 (*C*H_2), 19.6 (*C*H_2) ppm. **MS** (FAB NBA) *m/z* (%): 225 (100, [M^+]), 208 (26). **IR**: $\tilde{\nu}$ = 3364 (w), 2925 (m), 2858 (m), 1746 (m), 1584 (m), 1569 (s), 1426 (s), 1374 (m), 1352 (w), 1215 (w), 1116 (w), 928 (w), 880 (m), 849 (m), 821 (w), 784 (s) cm^{-1}. **EA**: calc. (%) C 60.95; H, 5.92; N, 7.48; found C 59.42, H 6.17, N 7.41. **m.p.**: 178–179 °C (dec.). **$[\alpha]_D^{20}$**: +70.4 (*c* = 0.35, H_2O).

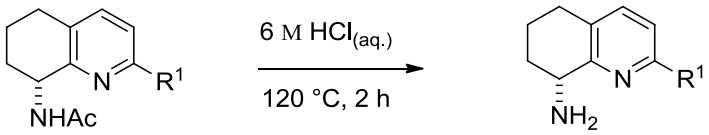
(*S*)-2-phenyl-5,6,7,8-tetrahydroquinolin-8-amine ((*S*)-137d)



A solution of tartaric salt (*S*,*R*,*R*)-**140b** (152 mg, 406 µmol) in aqueous NaOH 3 M aq.solution (10 mL) was extracted with DCM (5×10 mL). After drying over $MgSO_4$, filtration and removing of the solvent under reduced pressure, the title compound (*S*)-**137d** was obtained as a colorless oil (91 mg, 406 µmol, quant.).

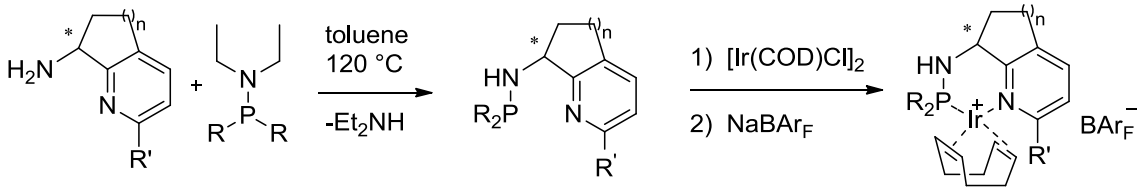
HPLC (chiral, Daicel Chiracel OD-H, (2.6 mm × 250 mm), heptane / *i*-PrOH 95:5 + 0.1% *n*-$BuNH_2$, 0.8 mL/min, 40 °C: t_R = 11.1 min (*S*), 13.1 min (*R*).

8.6.4 Hydrolysis of Amides



A solution of amide in HCl 2 M aq. Solution was stirred for 2 h. After cooling down to RT, the reaction mixture was made basic by adding NaOH 50% aq. solution (1 mL). Extraction with DCM (5×10 mL) gave the free amine, which was purified by *Kugelrohr* distillation (>90% yield).

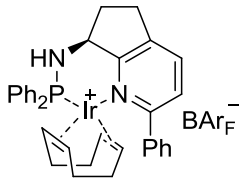
8.6.5 Preparation of Ligands and Complexes



Formation of the Aminophosphine Derived N,P Ligands, General Procedure K: Diethylaminophosphine (1.0 eq.) was added to a solution of pyridyl amine (1.0 eq.) in toluene (0.2-0.3 M). The reaction mixture was stirred at (120-130 °C) under a slightly stream of argon for 12-18 hours. Reaction progress was checked by ^{31}P-NMR analasys. After complete reaction, the solvent was removed in *vacuo* and the crude ligand was converted to the irdium complex using general procedure **G** for the formation of iridium complexes without additional purification.

Diethylaminophosphines: were prepared according to the procedure described by *S. Kaiser*.[57a]

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-*N*-(diphenylphosphino)-(2-phenyl-6,7-dihydro-*5H*-[1]pyrindin)-7-amine-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-142a)



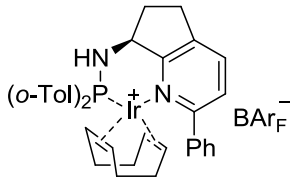
The intermediate ligand (*S*)-**141a** was obtained following general procedure K using diethylaminodiphenyl-phosphine (65 uL, 67.8 mg, 263 µmol), amine (*S*)-**136b** (50 mg, 238 µmol, 1.0 eq.) and toluene (1.0 mL) as a colorless solid (94 mg, 238 µmol, 91%).

The title compound (*S*)-**142a** was obtained following general procedure **G** for the formation of iridium complexes using (*S*)-**141a** (94 mg, 238 µmol, 91%), $[Ir(COD)Cl]_2$ (87.8 mg, 131 µmol, 0.55 eq.), DCM (5.0 mL), $NaBAr_F$ (253 mg, 285 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 20 cm) as a red-brown foam (286 mg, 184 µmol, 70% over two steps).

^{31}P{^{1}H}-NMR of Ph_2PNEt_2 (162 MHz, CD_2Cl_2): δ = 61.4 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (*S*)-**141a** (162 MHz, CD_2Cl_2): δ = 33.9 (s) ppm.

$C_{66}H_{47}BF_{24}IrNOP$ (1558.05 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.87 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.74 (s, 8H, BAr_F-*H*), 7.69–7.63 (m, 3H, H_{Ar}), 7.62–7.45 (m, 17H, BAr_F-*H*, H_{Ar}), 5.54–5.41 (m, 1H, C*H*), 4.41–4.31 (m, 1H, C*H* COD), 4.27 (dd, *J* = 3.6 Hz, 1H, C*H* COD), 3.24–3.04 (m, 3H, CH_2, C*H* COD), 3.04–2.96 (m, 1H, CH_2), 2.93–2.79 (m, 1H, C*H* COD), 2.63 (s, 1H, N*H*), 2.28–2.12 (m, 4H, CH_2 1H, CH_2 COD 3H), 2.02 (dd, *J* = 15.1, 7.8 Hz, 1H, CH_2 COD), 1.87 (m, 1H, CH_2 COD), 1.34–1.19 (m, 2H, CH_2 COD), 1.19–1.10 (m, 1H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 165.0 (s, C_{Ar}), 165.0 (d, *J* = 4 Hz, C_{Ar}), 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.7 (s, C_{Ar}), 139.5 (s, C_{Ar}), 137.8 (s, C_{Ar}), 137.2 (s, HC_{Ar}), 135.9 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.1 (s, HC_{Ar}), 132.0 (s, HC_{Ar}), 131.9 (s, HC_{Ar}), 131.4 (s, HC_{Ar}), 131.3 (s, HC_{Ar}), 131.2 (s, HC_{Ar}), 129.9 (s, HC_{Ar}), 129.8 (d, *J* = 11 Hz, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.4 (d, *J* = 11 Hz, HC_{Ar}), 127.8 (s, HC_{Ar}), 126.7 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 96.5 (d, *J* = 10 Hz, *C*H COD), 88.1 (d, *J* = 16 Hz, *C*H COD), 68.1 (s, *C*H COD), 64.1 (s, *C*H COD), 63.2 (d, *J* = 8 Hz, *C*H), 37.0 (s, *C*H_2 COD), 34.5 (s, *C*H_2 COD), 31.8 (d, *J* = 11 Hz, *C*H_2), 28.8 (s, *C*H_2 COD), 28.7 (s, *C*H_2), 25.3 (s, *C*H_2 COD) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, CD_2Cl_2): δ = 49.7 (s) ppm. **MS** (FAB NBA) *m/z* (%): 695 ($[Ir(L)(COD)]^+$, 100), 585 (18), 507 (22). **EA**: calc. (%) C 50.88, H, 3.04, N, 180; found C 50.77, H 3.13, N 2.06. **m.p.**: 91–92 °C. **$[\alpha]_D^{20}$**: +31.2 (*c* = 1.00, $CHCl_3$).

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-*N*-(di-*ortho*-tolylphosphino)-(2-phenyl-6,7-dihydro-*5H*-[1]pyrindin)-7-amine-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-142b)



The intermediate ligand (*S*)-**141b** was obtained following general procedure **K** using diethylamino-di-*ortho*-tolylphosphine (73.0 mg, 256 µmol, 1.1 eq.), amine (*S*)-**136b** (50 mg, 238 µmol, 1.0 eq.) and toluene (1.0 mL) as a colorless solid (77.6 mg, 184 µmol, 77%).

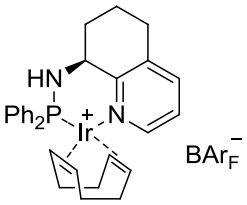
The title compound (*S*)-**142b** was obtained following general procedure **G** for the formation of iridium complexes using ligand (*S*)-**141b** (77.6 mg, 184 µmol, 1.0 eq.). $[Ir(COD)Cl]_2$ (85.9 mg, 128 µmol, 0.55 eq.), DCM (5.0 mL), $NaBAr_F$ (247 mg, 279 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 20 cm) as a red-brown foam (254 mg, 160 µmol, 67% over two steps).

^{31}P{^{1}H}-NMR of $(o\text{-Tol})_2PNEt_2$ (162 MHz, CD_2Cl_2): δ = 49.7 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 18.4 (s) ppm.

$C_{68}H_{50}BF_{24}IrNOP$ (1587.11 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.30–7.79 (m, 2H, *H*$_{Ar}$), 7.75 (s, 8H, BAr_F-*H*), 7.71–7.64 (m, 2H, *H*$_{Ar}$), 7.63–7.50 (m, 8H, BAr_F-*H*, *H*$_{Ar}$), 7.48–7.30 (m, 5H, *H*$_{Ar}$), 7.17–7.09 (m, 1H, *H*$_{Ar}$), 6.77 (br s, 1H, *H*$_{Ar}$), 5.49–5.35 (m, 1H, C*H* COD), 4.66–4.29 (m, 1H, C*H* COD), 4.33 (br s, 1H, C*H*), 3.40–3.16 (m, 1H, CH_2), 3.16–3.06 (m, 1H, CH_2), 3.04–2.88 (m, 5H, C*H* COD, C*H*$_2$ 1H, C*H*$_3$), 2.41 (br s, 3H, C*H*$_3$), 2.35–2.21 (m, 2H, C*H* COD, C*H*$_2$ COD 1H), 2.15–1.82 (m, 5H, C*H*$_2$ 1H, C*H*$_2$ COD 4H), 1.42–1.02 (m, 3H, C*H*$_2$ COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 164.8 (d, *J* = 1 Hz, *C*$_{Ar}$), 162.3 (q, *J*$_{BC}$ = 50 Hz, *C*$_{Ar}$ BAr_F), 161.1 (s, *C*$_{Ar}$), 139.7 (s, *C*$_{Ar}$), 138.0 (s, *C*$_{Ar}$), 137.0 (s, H*C*$_{Ar}$), 135.4 (s, H*C*$_{Ar}$ BAr_F), 133.3 (d, *J* = 15 Hz, *C*$_{Ar}$), 133.0 (s, H*C*$_{Ar}$), 132.6 (d, *J* = 5 Hz, H*C*$_{Ar}$), 132.3 (s, H*C*$_{Ar}$), 131.7 (s, H*C*$_{Ar}$), 129.8 (s, H*C*$_{Ar}$), 129.5 (qq, *J*$_{FC}$ = 31 Hz, *J*$_{BC}$ = 3 Hz, *C*$_{Ar}$ BAr_F), 128.4 (s, *C*$_{Ar}$), 128.1 (s, *C*$_{Ar}$), 127.1 (s, H*C*$_{Ar}$), 126.9 (d, *J* = 10 Hz, H*C*$_{Ar}$), 125.2 (q, *J*$_{FC}$ = 273 Hz, *C*F_3 BAr_F), 118.1 (septett, *J*$_{FC}$ = 4 Hz, H*C*$_{Ar}$ BAr_F), 100.4 (s, *C*H COD), 94.0 (s, *C*H), 68.0 (d, *J* = 16 Hz, *C*H COD), 67.8 (s, *C*H COD), 61.9 (s, *C*H COD), 36.8 (s, *C*H_2 COD), 34.7 (s, *C*H_2 COD), 32.2 (d, *J* = 10 Hz, *C*H_2), 28.7 (s, *C*H_2 COD), 28.4 (s, *C*H_2), 24.9 (s, *C*H_2 COD), 23.7 (br s, C*H*$_3$), 23.3 (s, C*H*$_3$) ppm.**^{31}P{^{1}H}-NMR** (202 MHz, CD_2Cl_2): δ = 59.8 (br s) ppm. **MS** (FAB

NBA) *m/z* (%): 723 ([Ir(L)(COD)]$^+$, 100), 611 (79). **EA**: calc. (%) C 51.49, H, 3.24, N, 1.77; found C 50.70, H 3.06, N 0.78. **m.p.**: 85–86 °C. **$[\alpha]_D^{20}$**: +9.3 (*c* = 1.06, $CHCl_3$).

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-*N*-(diphenylphosphino)-5,6,7,8-tetrahydrochinolin-8-amine-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate ((*S*)-142c)



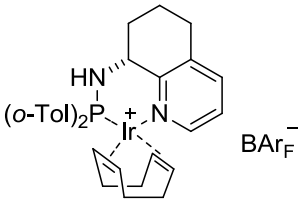
The intermediate ligand (*S*)-**141c** was obtained following general procedure K using diethylaminodiphenyl-phosphine (90 uL, 93.9 mg, 365 µmol, 1.1 eq.), amine (*S*)-**136c** (50 mg, 337 µmol, 1.0 eq.) and toluene (1.0 mL) as a colorless solid (77.6 mg, 234 µmol, 69%). The title compound (*S*)-**142c** was obtained following general procedure **G** using ligand (*S*)-**141c** (77.6 mg, 234 µmol, 1.0 eq.), $[Ir(COD)Cl]_2$ (86.5 mg, 129 µmol, 0.55 eq), DCM (5.0 mL), $NaBAr_F$ (251 mg, 283 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) and recrystallization from diethyl ether (1 mL) and *n*-pentane (25 mL) as a red-brown solid (260 mg, 174 µmol, 48% over two steps).

$^{31}P\{^1H\}$-NMR of Ph_2PNEt_2 (162 MHz, CD_2Cl_2): δ = 61.4 (s) ppm.
$^{31}P\{^1H\}$-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 29.1 (s) ppm.

$C_{61}H_{45}BF_{24}IrN_2P$ (1495.99 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.44 (d, *J* = 5.4 Hz, 1H, H_{Ar}), 7.75 (s, 8H, BAr_F-*H*), 7.59–7.50 (m, 7H, BAr_F-*H*, H_{Ar}), 7.49–7.42 (m, 3H, H_{Ar}), 7.41 (d, *J* = 7.4 Hz, 1H, H_{Ar}), 7.38–7.31 (m, 4H, H_{Ar}), 7.29–7.22 (m, 1H, H_{Ar}), 5.32–5.25 (m, 1H, C*H*), 4.98–4.91 (m, 1H, C*H* COD), 4.58 (p, *J* = 7.2 Hz, 1H, C*H* COD), 3.98–3.87 (m, 1H, C*H* COD), 2.99–2.92 (m, 1H, C*H* COD), 2.84–2.72 (m, 2H, CH_2), 2.71–2.58 (s, 2H, CH_2 COD), 2.53–2.32 (m, 5H, N*H*, CH_2 2H, CH_2 COD 2H), 2.24 (dt, *J* = 15.0, 8.8 Hz, 1H, CH_2 COD), 1.98–1.90 (dt, *J* = 14.3, 8.3 Hz, 2H, CH_2 1H, CH_2 COD 1H), 1.86–1.78 (m, 1H, CH_2 COD), 1.77–1.66 (m, 1H, CH_2), 1.54–1.43 (m, 1H, CH_2 COD) ppm. **$^{13}C\{^1H\}$-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 158.6 (s, C_{Ar}), 149.0 (s, HC_{Ar}), 141.2 (s, HC_{Ar}), 136.4 (s, C_{Ar}), 136.1 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 133.5 (s, HC_{Ar}), 133.4 (s, HC_{Ar}), 132.6 (d, *J* = 2 Hz, HC_{Ar}), 132.1 (d, *J* = 2 Hz, HC_{Ar}), 131.8 (s, HC_{Ar}), 131.6 (s, HC_{Ar}), 130.1 (s, C_{Ar}), 129.7 (s, HC_{Ar}), 129.6 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.2 (s, HC_{Ar}), 129.1 (s, HC_{Ar}), 125.9 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 96.5 (d,

J = 10 Hz, *C*H COD), 88.1 (d, *J* = 16 Hz, *C*H COD), 68.1 (s, *C*H COD), 64.1 (s, *C*H COD), 63.2 (d, *J* = 8 Hz, *C*H), 37.0 (s, *C*H$_2$ COD), 34.5 (s, *C*H$_2$ COD), 31.8 (d, *J* = 11 Hz, *C*H$_2$), 28.8 (s, *C*H$_2$ COD), 28.7 (s, *C*H$_2$), 25.3 (s, *C*H$_2$ COD), 18.5 (s, *C*H$_2$) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 51.1 ppm. **MS**: (FAB NBA) *m/z* (%): 633 ([Ir(L)(COD)]$^+$, 100), 445 (21). **IR**: $\tilde{\nu}$ = 2951 (w), 2887 (w), 1609 (w), 1453 (w), 1436 (w), 1353 (s), 1271 (s), 1160 (s), 1119 (s), 996 (w), 885 (m), 838 (m), 790 (w), 724 (w), 713 (m), 698 (w), 679 (m), 669 (m), 620 (w) cm^{-1}. **EA**: calc. (%) C 48.98, H, 3.03, N, 1.87; found C 48.98, H 3.14, N 2.03. **[α]$_D^{20}$**: +46.2 (*c* = 1.09, $CHCl_3$). **m.p.**: 159–161 °C.

(*R*)-(−)-[η^4-1,5-Cyclooctadiene-*N*-(di-*ortho*-tolylphosphino)-5,6,7,8-tetrahydrochinolin-8-amine-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate ((*R*)-142d)



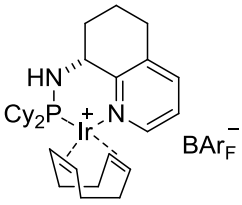
The intermediate ligand (*R*)-**141d** was obtained following a modifaction of general procedure **C** using amine (*R*)-**136c** (21 mg, 142 µmol, 1.0 eq.), DMAP (20.8 mg, 170 µmol, 1.2 eq.), chloro-di-*ortho*-tolyl-phosphine (42.3 mg, 170 µmol, 1.2 eq.), and DCM (0.5 mL) after purification by filtration over aluminum oxide (d×h, 2 cm × 3 cm, cyclohexane / TBME 1:1, degassed) as a colorless solid (33.0 mg, 91.6 µmol, 65%). The title compound (*R*)-**142d** was obtained following general procedure **G** using (*R*)-**141d** (33.0 mg, 91.6 µmol, 1.0 eq.), $[Ir(COD)Cl]_2$ (30.9 mg, 46.0 µmol, 0.5 eq.), DCM (2.0 mL), $NaBAr_F$ (98.0 mg, 111 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1 cm × 12 cm) and recrystallization from diethyl ether (1 mL) and *n*-pentane (25 mL) as a red-brown solid (45.0 mg, 29.5 µmol, 21% over two steps).

^{31}P{^{1}H}-NMR of (*o*-Tol)$_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 13.5 (s) ppm.

$C_{63}H_{49}BF_{24}IrN_2P$ (1524.04 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.64–8.43 (m, 1H, *H*$_{Ar}$), 8.24 (br s, 1H, *H*$_{Ar}$), 7.73 (s, 8H, BAr_F-*H*), 7.56 (m, 4H, BAr_F-*H*), 7.52 (d, *J* = 7.8 Hz, 1H *H*$_{Ar}$), 7.42–7.30 (m, 3H, *H*$_{Ar}$), 7.28–7.08 (m, 4H, *H*$_{Ar}$), 6.68 (br s, 1H, *H*$_{Ar}$), 5.20–5.10 (m, 1H, C*H* COD), 5.10–4.88 (m, 1H, C*H*), 4.46–4.26 (m, 1H, C*H* COD), 3.88–3.76 (m, 1H, C*H* COD), 2.94–2.44 (m, 9H, C*H* COD 1H, C*H*$_2$ 2H, C*H*$_2$ COD 2H, C*H*$_3$ 3H, N*H*), 2.44–2.30 (m, 3H, C*H*$_3$), 2.27–2.12 (m, 2H, C*H*$_2$ COD), 2.09–1.87 (m, 5H, C*H*$_2$ 3H, C*H*$_2$ COD 2H), 1.86–1.71 (m, 1H, C*H*$_2$ COD), 1.72–1.59

(m, 1H, CH_2), 1.58–1.40 (m, 1H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 158.7 (s, C_{Ar}), 149.3 (s, HC_{Ar}), 141.2 (s, HC_{Ar}), 136.3 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.9 (d, J = 6.8 Hz, HC_{Ar}), 132.3 (d, J = 1 Hz, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 126.7 (d, J = 11 Hz, HC_{Ar}), 126.5 (d, J = 7.9 Hz, C_{Ar}), 125.7 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 95.8 (s, *C*H COD), 92.7 (s, *C*H COD), 66.7 (s, *C*H COD), 66.2 (s, *C*H COD), 57.2 (s, *C*H), 37.4 (s, *C*H_2 COD), 34.4 (d, J = 6 Hz, *C*H_2 COD), 30.7 (d, J = 11 Hz, *C*H_2), 29.3 (s, *C*H_3), 28.8 (s, *C*H_2 COD), 28.8 (s, *C*H_2), 22.5 (s, *C*H_3), 25.3 (s, *C*H_2 COD), 18.7 (s, *C*H_2) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 54.7 ppm. **MS**: (FAB NBA) *m/z* (%): 661 ([Ir(L)(COD)]$^+$, 100), 549 (27), 443 (11), 371 (12). **EA**: calc. (%) C 49.65, H, 3.24, N, 1.84; found C 48.85, H 3.06, N 1.58.

(*R*)-(+)-[η^4-1,5-Cyclooctadiene-*N*-(dicyclohexylphosphino)-5,6,7,8-tetrahydrochinolin-8-amine-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate ((*R*)-142e)



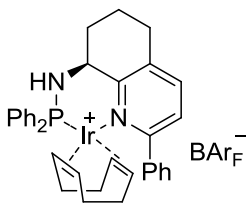
The intermediate ligand was obtained following general procedure **H** using amine (*R*)-**136c** (43.6 mg, 294 µmol, 1.0 eq.), chloro-dicyclohexylphosphine (70.0 µL, 73.8 mg, 317 µmol, 1.1 eq.), NaH (17.7 mg, 736 µmol, 2.5 eq.), THF (1 mL), DMF (0.1 mL) and filtration over aluminum oxide (d×h, 2 cm × 3 cm, cyclohexane / TBME 9:1, degassed) as a colorless solid (23.4 mg, 67.9 µmol, 23%). The title compound (*R*)-**142e** was obtained following general procedure **G** using (*R*)-**136c** (23.4 mg, 67.9 µmol, 23%), $[Ir(COD)Cl]_2$ (22.8 mg, 34.0 µmol, 0.5 eq.), DCM (1.0 mL), $NaBAr_F$ (70.9 mg, 80.0 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) and recrystallization from diethyl ether (1 mL) and *n*-pentane (25 mL) as a red-brown solid (49.0 mg, 32.5 µmol, 11% over two steps).

^{31}P{^{1}H}-NMR of Cy_2PCl (162 MHz, CD_2Cl_2): δ = 126.1 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 45.8 (s) ppm.

$C_{61}H_{57}BF_{24}IrN_2P$ (1508.08 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 8.50 (d, J = 5.4 Hz, 1H, H_{Ar}), 7.73 (s, 8H, BAr_F-*H*), 7.63 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.56 (s 4H, BAr_F-*H*), 7.34–7.26 (m, 1H, H_{Ar}), 4.95–4.85 (m, 1H, C*H* COD), 4.62–4.52 (m, 1H, C*H*), 4.50–4.40 (m, 1H, C*H* COD), 4.09 (p, J = 7.1 Hz, 1H, C*H*

COD), 3.57–3.48 (m, 1H, C*H* COD), 2.90–2.81 (m, 1H, CH_2), 2.79–2.66 (m, 2H, CH_2 1H, CH_2 COD 1H), 2.66–2.54 (m, 1H, CH_2 COD), 2.44–2.33 (m, 1H, CH_2), 2.32–2.19 (m, 2H, C*H*P, CH_2 COD 1H), 2.19–1.97 (m, 5H, C*H*P, CH_2 COD 2H, *C*H$_2$ Cy 3H), 1.94–1.85 (m, 2H, CH_2), 1.84–1.75 (m, 2H, CH_2 COD 1H, N*H*), 1.75–1.62 (m, 5H, *C*H$_2$ Cy 3H, CH_2 COD 1H, CH_2 1H), 1.62–1.45 (m, 4H, CH_2 COD 1H, *C*H$_2$ Cy 3H), 1.43–1.08 (m, 8H, *C*H$_2$ Cy), 1.05 – 0.93 (m, 1H, *C*H$_2$ Cy), 0.74–0.60 (m, 2H, *C*H$_2$ Cy) ppm.**^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 159.1 (s, C_{Ar}), 150.0 (s, HC_{Ar}), 141.2 (s, HC_{Ar}), 135.7 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 129.4 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 125.3 (s, HC_{Ar}), 125.2 (q, J_{FC} = 272 Hz, *C*F$_3$ BAr_F), 118.0 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 94.3 (d, *J* = 14 Hz, *C*H COD), 94.2 (d, *J* = 10 Hz, *C*H COD), 66.4 (s, *C*H COD), 62.9 (s, *C*H COD), 58.3 (d, *J* = 7 Hz, *C*H), 38.8 (d, *J* = 32 Hz, *C*HP), 38.3 (d, *J* = 3 Hz, *C*H$_2$ COD), 34.2 (d, *J* = 34 Hz, *C*HP), 34.1 (s, *C*H$_2$), 30.7 (d, *J* = 9 Hz, *C*H$_2$ COD), 29.4 (s, *C*H$_2$), 29.3 (d, *J* = 5.5 Hz, *C*H$_2$ Cy), 29.0 (s, *C*H$_2$ Cy), 28.8 (s, *C*H$_2$ COD), 28.5 (s, *C*H$_2$ Cy), 27.2 (d, *J* = 9 Hz, *C*H$_2$ Cy), 27.0 (d, *J* = 6 Hz, *C*H$_2$ Cy), 26.91 (s, *C*H$_2$ Cy), 26.89 (d, *J* = 20 Hz, *C*H$_2$ Cy), 26.8 (s, *C*H$_2$ Cy), 26.4 (s, *C*H$_2$ Cy), 26.0 (d, *J* = 7 Hz, *C*H$_2$ Cy), 25.8 (s, *C*H$_2$ COD), 18.7 (s, *C*H$_2$) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 61.5 ppm. **MS**: (FAB NBA) *m/z* (%): 645 ([M]$^+$, 100), 533 (13), 443 (11), 371 (12). **EA**: calc. (%) C 48.58, H, 3.81, N, 1.86; found C 48.01, H 3.66, N 1.59. **[α]$_D^{20}$**: +56 (*c* = 1.01, $CHCl_3$). **m.p.**: 102–103 °C.

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-*N*-(diphenylphosphino)-2-phenyl-5,6,7,8-tetrahydrochinolin-8-amine-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate ((*S*)-142f)



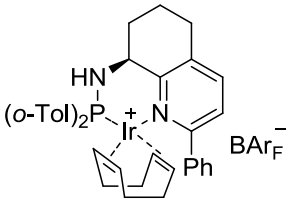
The intermediate ligand (*S*)-**141f** was obtained following general procedure K using diethylaminodiphenyl-phosphine (40 uL, 41.7 mg, 162 µmol, 1.1 eq.), amine (*S*)-**137d** (33.0 mg, 141 µmol, 1.0 eq.) and toluene (1.0 mL) as a colorless solid (49.0 mg, 120 µmol, 85%).

The title compound (*S*)-**142f** was obtained following general procedure **G** using ligand (*S*)-**141f** (49.0 mg, 120 µmol, 1.0 eq.), $[Ir(COD)Cl]_2$ (40.3 mg, 60.0 µmol, 0.5 eq.), DCM (3.0 mL), $NaBAr_F$ (127 mg, 143 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 3 cm × 15 cm) and recrystallization from diethyl ether (1 mL) and *n*-pentane (25 mL) as a red-brown foam (94.0 mg, 59.8 µmol, 50% over two steps).

^{31}P{^{1}H}-NMR of Ph_2PNEt_2 (162 MHz, CD_2Cl_2): δ = 61.4 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 30.6 (s) ppm.

$C_{67}H_{49}BF_{24}IrN_2P$ (1572.08 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.74 (s, 8H, BAr_F-*H*), 7.68 (t, *J* = 7.3 Hz, 1H, H_{Ar}), 7.63–7.54 (m, 9H, BAr_F-*H*, H_{Ar}), 7.54–7.46 (m, 8H, H_{Ar}), 7.44–7.41 (m, 1H, H_{Ar}), 7.39–7.33 (m, 2H, H_{Ar}), 5.52 (p, *J* = 6.5 Hz, 1H, C*H*), 4.45–4.38 (m, 1H, C*H* COD), 4.35–4.28 (m, 1H, C*H* COD), 3.15 (p, *J* = 7.1 Hz, 1H, C*H* COD), 3.00 (dt, *J* = 16.7, 5.8 Hz, 1H, CH_2), 2.91 (dt, *J* = 17.0, 6.0 Hz, 1H, CH_2), 2.74–2.62 (m, 2H, C*H* COD, CH_2 COD 1H), 2.34–2.18 (m, 2H, CH_2 1H, CH_2 COD 1H), 2.08–1.82 (m, 5H, N*H*, CH_2 2H, CH_2 COD 2H), 1.81–1.70 (m, 1H, CH_2 COD 1H), 1.35–1.19 (m, 2H, CH_2 COD), 1.19–1.10 (m, 1H, CH_2), 1.10–1.00 (m, 1H, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.5 (s, C_{Ar}), 159.2 (s, C_{Ar}), 141.4 (s, HC_{Ar}), 139.6 (s, C_{Ar}), 135.8 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 132.3 (d, *J* = 58 Hz, C_{Ar}), 132.0 (s, HC_{Ar}), 131.94 (d, *J* = 3 Hz, HC_{Ar}), 131.88 (d, *J* = 2 Hz, HC_{Ar}), 130.92 (s, HC_{Ar}), 130.85 (s, HC_{Ar}), 130.77 (s, HC_{Ar}), 130.67 (s, HC_{Ar}), 130.4 (s, HC_{Ar}), 129.9 (s, HC_{Ar}), 129.8 (s, HC_{Ar}), 129.7 (s, HC_{Ar}), 129.6 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 128.4 (s, C_{Ar}), 126.1 (s, HC_{Ar}), 125.8 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 96.3 (d, *J* = 8 Hz, *C*H COD), 82.4 (d, *J* = 17 Hz, *C*H COD), 69.7 (s, *C*H COD), 65.9 (s, *C*H COD), 57.2 (d, *J* = 9 Hz, *C*H), 36.4 (d, *J* = 4 Hz, *C*H_2 COD), 35.4 (s, *C*H_2), 32.0 (d, *J* = 11 Hz, *C*H_2 COD), 29.7 (s, *C*H_2), 28.8 (s, *C*H_2 COD), 24.4 (s, *C*H_2 COD), 20.2 (s, *C*H_2) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 40.8 ppm. **MS**: (FAB NBA) *m/z* (%): 709 ([Ir(L)(COD)]$^+$, 100), 599 (23), 521 (15). **IR**: $\tilde{\nu}$ = 2951 (w), 2887 (w), 1609 (w), 1453 (w), 1434 (w), 1437 (w), 1353 (s), 1274 (s), 1158 (m), 1118 (s), 1000 (w), 933 (w), 885 (m), 839 (m), 761 (w), 744 (w), 713 (m), 697 (w), 680 (s), 669 (m), 636 (w), 621 (w) cm^{-1}. **[α]$_D^{20}$**: +36.3 (*c* = 1.02, $CHCl_3$). **m.p.**: 76–77 °C.

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-*N*-(di-*ortho*-tolylphosphino)-2-phenyl-5,6,7,8-tetrahydrochinolin-8-amine-iridium(I)]-tetrakis-[3,5-bis(trifluormethyl)phenyl]borate ((*S*)-142g)



The intermediate ligand (*S*)-**141g** was obtained following general procedure K using diethylamino-di-*ortho*-tolylphosphine (63 mg, 221 µmol, 1.0 eq.), amine (*S*)-**137d** (49. 0 mg, 218 µmol, 1.0 eq.) and toluene (1.0 mL) as a colorless solid (83.0 mg, 190 µmol, 87%).

The title compound (*S*)-**142g** was obtained following general procedure **G** using ligand (*S*)-**141g** (83.0 mg, 190 µmol, 1.0 eq.), $[Ir(COD)Cl]_2$ (63.8 mg, 95.0 µmol, 0.5 eq.), DCM (3.0 mL), $NaBAr_F$ (186 mg, 210 µmol, 1.2 eq.), after purification by flash chromatography (SiO_2, 3 cm × 14 cm) and recrystallization from diethyl ether (1 mL) and *n*-pentane (25 mL) as a red-brown foam (162 mg, 101 µmol, 46% over two steps).

^{31}P{^{1}H}-NMR of $(o\text{-Tol})_2PNEt_2$ (162 MHz, CD_2Cl_2): δ = 49.7 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 19.3 (s) ppm.

$C_{69}H_{53}BF_{24}IrN_2P$ (1600.14 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.75 (s, 8H, BAr_F-*H*), 7.70 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.66 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 7.57 (s, 4H, BAr_F-*H*), 7.52–7.40 (m, 6H, H_{Ar}), 7.39–7.29 (m, 4H, H_{Ar}), 7.26–7.15 (m, 2H, H_{Ar}), 7.04–6.96 (m, 1H, H_{Ar}), 5.30–5.23 (m, 1H, C*H*), 4.58 (t, *J* = 6.4 Hz, 1H, C*H* COD), 4.43–4.34 (m, 1H, C*H* COD), 3.36 (br s, 1H, C*H* COD), 3.08 (s, 3H, CH_3), 3.01 (dt, *J* = 16.9, 5.5 Hz, 1H, CH_2), 2.89 (dt, *J* = 17.0, 6.1 Hz, 1H, CH_2), 2.68–2.54 (m, 2H, C*H* COD, CH_2 COD 1H), 2.47 (s, 3H, CH_3), 2.44–2.32 (m, 2H, CH_2 1H, CH_2 COD 1H), 2.21–2.07 (m, 2H, CH_2), 2.06–1.93 (m, 2H, CH_2 COD), 1.72 (ddd, *J* = 25.9, 15.1, 8.0 Hz, 2H, CH_2 COD), 1.60–1.48 (m, 1H, CH_2 COD 1H), 1.35–1.22 (m, 2H, CH_2 COD), 1.16–0.99 (m, 2H, CH_2, CH_2 COD) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 160.7 (s, C_{Ar}), 158.5 (s, C_{Ar}), 142.6 (d, *J* = 11 Hz, C_{Ar}), 141.2 (s, HC_{Ar}), 140.6 (d, *J* = 12 Hz, C_{Ar}), 139.7 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 135.1 (s, C_{Ar}), 134.7 (s, C_{Ar}), 134.6 (s, C_{Ar}), 133.1 (d, *J* = 9 Hz, HC_{Ar}), 132.8 (d, *J* = 10 Hz, HC_{Ar}), 132.7 (d, *J* = 8 Hz, HC_{Ar}), 132.3 (d, *J* = 2 Hz, HC_{Ar}), 133.1 (s, HC_{Ar}), 131.7 (s, HC_{Ar}), 130.2 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 127.3 (d, *J* = 10 Hz, HC_{Ar}), 126.9 (d, *J* = 10 Hz, HC_{Ar}), 126.7 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, CF_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 89.8 (br s, *C*H COD), 77.7 (br s, *C*H COD), 72.3 (br s, *C*H COD), 67.8 (s, *C*H COD), 55.8 (d, *J* = 8 Hz, *C*H), 36.2

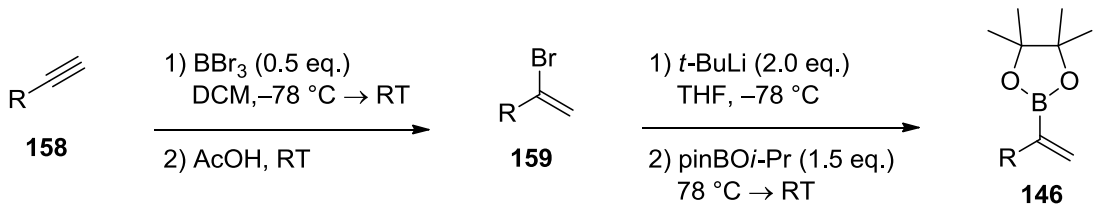
(d, J = 4 Hz, CH_2 COD), 35.2 (s, CH_2), 32.0 (d, J = 10 Hz, CH_2 COD), 29.7 (s, CH_2), 29.2 (s, CH_2 COD), 24.2 (d, J = 3 Hz, CH_2 COD), 24.0 (d, J = 7 Hz, CH_3), 22.7 (d, J = 7 Hz, CH_3), 20.1 (s, CH_2) ppm. **$^{31}P\{^1H\}$-NMR** (162 MHz, CD_2Cl_2): δ = 43.4 (br s) ppm. **MS**: (FAB NBA) *m/z* (%): 737 ($[Ir(L)(COD)]^+$, 100), 625 (50), 533 (11). **IR**: $\tilde{\nu}$ = 2952 (w), 2882 (w), 1609 (w), 1464 (w), 1433 (w), 1352 (s), 1271 (s), 1159 (m), 1117 (s), 1096 (s), 999 (w), 929 (w), 885 (m), 838 (m), 806 (w), 758 (m), 744 (w), 713 (m), 698 (w), 681 (m), 669 (m), 622 (w) cm^{-1}. **EA**: calc. (%) C 51.79, H, 3.34, N, 1.75; found C 51.71, H 3.46, N 1.93. **$[\alpha]_D^{20}$**: +15.9 (c = 1.06, $CHCl_3$). **m.p.**: 140–141 °C.

8.7 Iridium-Catalyzed Enantioselective Hydrogenation of Alkenylboronic Esters

8.7.1 Substrate Synthesis

Substrates **146g** (Aldrich 659193), **149d** (Alfa-Aesar L19651) and **146h** (Alfa-Aesar L19576) are commercially available and were used as received.

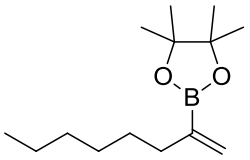
8.7.2 Terminal Vinylboronates *via* Vinylbromides



General Procedure L: Alkyne (10 mmol) was added drop wise to a 1 M solution of boron tribromide (5.0 mmol) at –78 °C. The resulting solution was allowed to warm to room temperature over 3 h. Glacial acetic acid (mL) was added to the mixture and stirred for 1 h. This mixture was quenched with water (10 mL), extracted with pentane (3×20 mL). Combined organic layers were washed with sat. $NaHCO_3$ solution (4×15 mL) until the pH of the water phase stays basic, than with water (15 mL) and brine (15 mL). After drying over $MgSO_4$, the solvent was removed under reduced pressure. The crude product was diluted with pentane (1 mL) and purified over a plug of silica gel (SiO_2, 3 cm × 4 cm), followed by elution with *n*-pentane (300 mL). The solvent was removed under reduced pressure (>300 mbar,

40 °C) to obtain the intermediate vinyl bromide which was subsequently dissolved in THF (0.6 M) and cooled to −78 °C. *t*-BuLi 1.6 M solution in pentane (2 eq.) was added drop wise, and the resulting mixture (dark brown solution) was stirred for 45 minutes at –78 °C. A solution of 2-Isopropoxy-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (1.5 eq.) in THF (1.5 M) was added drop wise and the mixture was allowed to warm to rt over 2.5 h (1 h stirred without cooling). 1 M aq. HCl (10 mL) was added under ice bath control and the mixture was stirred for 30 min. Extraction with DCM (3×50 mL), followed by drying over $MgSO_4$, filtration and concentration in *vacuo* provided the crude product. Purification was performed by flash chromatography, *Kugelrohr* distillation or using both methods if necessary.

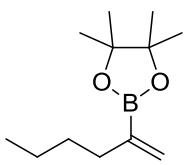
2-(Oct-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (146a):



Following the general procedure **L** using 1-octyne (1.3 mL, 970 mg, 8.80 mmol, 1 eq.), 1 M solution of boron tribromide (4.5 mL, 4.5 mmol, 0.5 eq.) and glacial acetic acid (2 mL), vinyl bromide (913 mg, 4.78 mmol, 54%) was isolated, which was subsequently converted to the vinylboronate **146a** using 1.6 M solution of *t*-BuLi in pentane (6 mL, 9.6 mmol, 2 eq.) and 2-isopropoxy-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (1.56 mL, 1.43 g, 7.66 mmol, 1.6 eq.). After purification by flash chromatography (1.5 cm × 20 cm, *n*-pentane / TBME 1:0 → 50:1 → 20:1) the title compound **146a** (660 mg, 2.77 mmol, 31% over two steps) was obtained as a colorless liquid. The analytical data are in agreement with reported values.[141]

$C_{14}H_{27}BO_2$ (238.17 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.74 (d, *J* = 3.4 Hz, 1H, C=CH_2), 5.38 (br s, 1H, C=CH_2), 2.13 (t, *J* = 7.5 Hz, 2H, CH_2C=C), 1.46–1.35 (m, 2H, CH_2), 1.32–1.16 (m, 18H, 6×CH_2, CH_3-pin), 0.87 (t, *J* = 6.8 Hz, 3H CH_3CH$_2$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 128.9 (C=*C*H$_2$), 83.5 (*C*CH$_3$-pin), 35.6 (*C*H$_2$), 32.0 (*C*H$_2$), 29.4 (*C*H$_2$), 29.2 (*C*H$_2$), 25.0 (*C*H$_3$-pin), 22.9 (*C*H$_2$), 14.3 (*C*H$_3$) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 5 min): t_R = 13.2 min. **TLC** (SiO_2, *n*-pentane / TBME 20:1): R_f = 0.50 (visualization with $KMnO_4$).

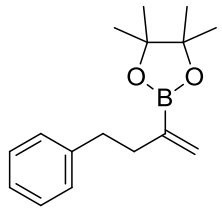
2-(Hex-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (146b)



Following the general procedure **L** using 1-hexyne (2.1 mL, 1.49 g, 18.1 mmol, 1 eq.), 1 M solution of boron tribromide (9.0 mL, 9.0 mmol, 0.49 eq.) and glacial acetic acid (2 mL), vinyl bromide (2.60 g, 15.9 mmol, 88%) was isolated, which was subsequently converted to the vinylboronates **146b** using 1.6 M solution of *t*-BuLi in pentane (20 mL, 32.0 mmol, 2.0 eq.) and 2-isopropoxy-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (5.0 mL, 4.56 g, 24.5 mmol, 1.5 eq.). After purification by flash chromatography (3.5 cm × 13 cm, *n*-pentane / Et_2O 20:1) and distillation over a short *Vigreux* (3 cm, 65−68 °C / 12 mbar) the title compound **146b** (1.09 g, 5.17 mmol, 29% over two steps) was obtained as a colorless liquid.

$C_{12}H_{23}BO_2$ (210.12 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.75 (d, *J* = 3.3 Hz, 1H, C=CH_2), 5.58 (br s, 1H, C=CH_2), 2.14 (t, *J* = 7.4 Hz, 2H, CH_2C), 1.47–1.34 (m, 2H, CH_2), 1.33–1.24 (m, 14H, CH_2, CH_3-pin), 0.89 (t, *J* = 7.2 Hz, 3H CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 128.8 (C=*C*H_2), 83.4 (*C*CH_3-pin), 35.2 (*C*H_2), 31.5 (*C*H_2), 24.9 (*C*H_3-pin), 22.5 (*C*H_2), 14.2 (*C*H_3) ppm. **MS** (EI) *m/z* (%): 210 ([M]$^+$, 58), 194 (43), 167 (26), 152 (100), 139 (5), 125 (15), 110 (32), 101 (18), 95 (17), 82 (43), 69 (42), 59 (23), 41 (47). **EA**: calc. (%) for $C_{12}H_{23}BO_2$ C 68.50, H 11.03; found C 68.45, H 11.13. **IR**: $\tilde{\nu}$ = 2974 (m), 2959 (m), 2956 (w), 2926 (s), 2361 (w), 1740 (w), 1616 (w), 1427 (m), 1369 (s), 1346 (m), 1308 (s), 1144 (s), 968 (w), 939 (w), 862 (w), 677 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 5 min): t_R = 9.3 min. **TLC** (SiO_2, *n*-pentane / TBME 20:1): R_f = 0.55 (visualization with $KMnO_4$).

2-(4-Phenylbut-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (146e)

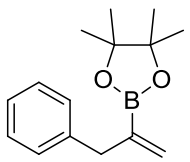


Following the general procedure **L** using 4-phenyl-1-butyne (1.2 mL, 1.11 g, 8.54 mmol, 1 eq.), 1 M solution of boron tribromide (5.0 mL, 5.0 mmol, 0.58 eq.) and glacial acetic acid (1 mL), vinyl bromide (981 mg, 4.65 mmol, 54%) was isolated, which was subsequently converted to the vinylboronate **146e** using 1.6 M solution of *t*-BuLi in pentane (6.0 mL, 9.60 mmol, 2.06 eq.) and 2-isopropoxy-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (1.70 mL, 1.55 g, 8.31 mmol,

1.5 eq.). After purification by *Kugelrohr* distillation (125−130 °C / 0.2 mbar) the title compound **146e** (799 mg, 3.03 mmol, 36% over two steps) was obtained as a colorless oil.

$C_{16}H_{23}BO_2$ (258.16 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.33–7.26 (m, 2H, H_{Ar}), 7.23–7.11 (m, 3H, H_{Ar}), 5.80 (d, J = 3.3 Hz, 1H, C=CH_2), 5.62 (br s, 1H, C=CH_2), 2.76 (dd, J = 9.3, 6.7 Hz, 2H, Ar-CH_2), 2.51–2.36 (m, 2H, CH_2C), 1.27 (s, 12H, CH_3-pin) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 142.6 (C_{Ar}), 129.6 (C=CH$_2$), 128.7 (HC_{Ar}), 128.3 (HC_{Ar}), 125.7 (HC_{Ar}), 83.5 (CCH$_3$-pin), 37.4 (CH$_2$), 35.8 (CH$_2$), 24.9 (CH$_3$-pin) ppm. **MS** (EI) *m/z* (%): 258 ([M]$^+$, 7), 243 (5), 201 (7), 158 (33), 130 (75), 117 (12), 105 (9), 101 (24), 91 (100), 84 (47), 77 (6), 69 (11), 65(17), 57 (12), 43 (32). **HRMS**: calc. (%) 258.1786; found 258.1788. **IR**: $\tilde{\nu}$ = 2977 (m), 2927 (m), 2858 (w), 1615 (w), 1604 (w), 1496 (w), 1452 (m), 1439 (m), 1425 (m), 1408 (w), 1367 (s), 1344 (m), 1307 (s), 1271 (w), 1213 (m), 1195 (m), 1165 (m), 1140 (s), 1110 (w), 1074 (w), 969 (m), 941 (m), 836 (w), 749 (w), 699 (s), 672 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 5 min): t_R = 20.1 min.

2-(3-Phenylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (146f)

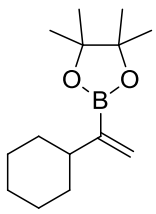


Following the general procedure **L** using 3-phenyl-1-propyne (0.6 mL, 560 g, 4.82 mmol, 1 eq.), 1 M solution of boron tribromide (2.9 mL, 2.90 mmol, 0.6 eq.) and glacial acetic acid (1 mL) the intermediate vinyl bromide (450 mg, 2.28 mmol, 47%) was isolated, which was subsequently converted to the vinylboronate **146f** using 1.6 M solution of *t*-BuLi in pentane (3.0 mL, 9.60 mmol, 2.1 eq.) and 2-isopropoxy-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (0.70 mL, 1.55 g, 8.31 mmol, 1.5 eq.). After purification by flash chromatography (1.5 cm × 18 cm, cyclohexane / TMBE 1:0→100:1→50:1→20:1) and by *Kugelrohr* distillation (100-110 °C / 0.2 mbar) the title compound **146f** (162 mg, 0.664 mmol, 14% over two steps) was obtained as a colorless oil. The analytical data are in agreement with reported values.[141]

$C_{15}H_{21}BO_2$ (244.14 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.31–7.23 (m, 2H, H_{Ar}), 7.22–7.12 (m, 3H, H_{Ar}), 5.83 (d, J = 3.2 Hz, 1H, C=CH_2), 5.52 (br s, 1H, C=CH_2), 3.48 (s, 2H, Ar-CH_2), 1.21 (s, 12H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 140.8 (C_{Ar}), 130.0 (C=CH$_2$), 129.3 (HC_{Ar}), 128.2 (HC_{Ar}), 125.8 (HC_{Ar}), 83.6 (CCH$_3$-pin), 41.5 (Ar-CH$_2$), 24.8 (CH$_3$-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 5 min): t_R = 14.9 min. **TLC** (SiO_2, cyclohexane / TBME 20:1): R_f = 0.35.

2-(1-Cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (146h)

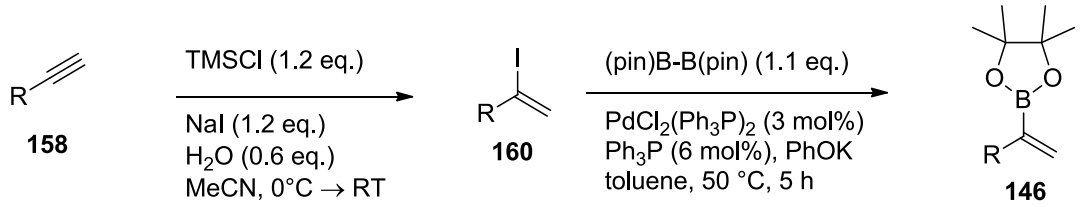


Following the general procedure **L** using cyclohexylacetylene (1.31 mL, 1.08 g, 10.0 mmol, 1 eq.), 1 M solution of boron tribromide (5.0 mL, 5.0 mmol, 0.5 eq.) and glacial acetic acid (1 mL), the intermediate vinyl bromide (1.10 g, 5.82 mmol, 58%) was isolated, which was subsequently converted to the vinylboronate **146h** using 1.6 M solution of *t*-BuLi in pentane (7.5 mL, 12 mmol, 2.1 eq.) and 2-isopropoxy-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (3.1 mL, 2.83 g, 15.2 mmol, 1.5 eq.). After purification by *Kugelrohr* distillation (75−80 °C / 0.2 mbar) the title compound **146h** (560 mg, 2.37 mmol, 24% over two steps) was obtained as a colorless oil. The analytical data are in agreement with reported values.[141]

$C_{14}H_{25}BO_2$ (236.19 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.70 (d, J = 3.0 Hz, 1H, C=CH_2), 5.58 (br s, 1H, C=CH_2), 2.20–2.03 (m, 1H, CHC), 1.82–1.63 (m, 5H, CH_2), 1.36–1.24 (m, 14H, CH_2, pin-CH_3), 1.21–1.08 (m, 3H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 126.0 (C=CH$_2$), 83.3 (CCH$_3$-pin), 42.9 (CH), 32.6 (CH$_2$), 26.9 (CH$_2$), 26.5 (CH$_2$), 24.8 (CH$_3$-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 5 min): t_R = 13.2 min.

8.7.3 Terminal Vinylboronates *via* Vinyliodides

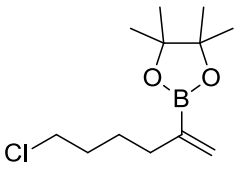


Preparation of the vinyliodides: To a solution of sodium iodide (1.2 eq.) in acetonitrile (0.25 M) was added TMSCl (1.2 eq.) at 0 °C, followed 15 min later by H_2O (0.6 eq.) and alkyne (1.0 eq.). The reaction mixture was slowly allowed to reach rt and stirring was continued for 2 h. The reaction mixture was diluted with ether (50 mL) and washed with ½-sat. $NaHCO_3$ solution (50 mL, pH 8), water (25 mL) and with aq. $Na_2S_2O_3$ 5% solution (25 mL) to obtain a clear solution. The organic phase was dried over $MgSO_4$, filtrated and the solvent was removed under reduced pressure (40 °C / 500 mbar).

Important Note: The TBS protecting group was not stable under these reaction conditions and thus had to be introduced after the reaction.

Miyaura-Borylation: Free alcohols were protected using TBSCl (1.1 eq.) and DMAP (1.1 eq.) in DCM (0.1 M). A mixture of $PdCl_2(PPh_3)_2$ (3 mol-%), Ph_3P (6 mol-%), bis(pinacolato)dibron (1.1 eq.), and potassium phenoxide (1.5 eq.) was treated with vinyl iodine (1.0 eq.) and toluene (0.6 M). The red brown reaction mixture was stirred for 5 hours at 50 °C. After cooling down to rt the reaction mixture was extracted with water (10 mL). The aquous phase was washed with DCM (5 mL) and combined organic layers were washed with brine (10 mL). Drying over $MgSO_4$ and concentration in *vacuo* gave a red crude oil. Purification by *Kugelrohr* distillation or by flash chromatography (SiO_2) gave the desired vinylboronate.

2-(6-Chlorohex-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1c)

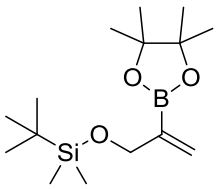


Following the general procedure **L** (1st part) using 6-chloro-1-hexyne (1.1 mL, 972 mg, 8.33 mmol, 1 eq.), 1 M solution of boron tribromide (5.0 mL, 5.0 mmol, 0.55 eq.) and glacial acetic acid (1 mL), the intermediate vinyl bromide (1.43 g, 5.47 mmol, 80%) was isolated. A partial amount (395 mg, 2.00 mmol, 1.0 eq.) was subsequently converted to the vinylboronate

146c following the procedure for *Miyaura* Borylation) using $PdCl_2(PPh_3)_2$ (43.0 mg, 61.3 µmol, 3 mol-%), Ph_3P (32.5 mg, 123 µmol 6 mol-%), bis(pinacolato)dibron (559 mg, 2.20 mmol, 1.1 eq.) and 1 M potassium phenoxide suspension in toluene (3 mL, 3.00 mmol, 1.5 eq.). After purification by *Kugelrohr* distillation and by flash chromatography (SiO_2, 3 cm × 18 cm, cyclohexane / ethyl acetate 50:1) the title compound **146c** (160 mg, 654 µmol, 32% for the second step) was obtained as a colorless liquid.

$C_{12}H_{22}BClO_2$ (244.57 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.79 (d, *J* = 3.4 Hz, 1H, C=CH_2), 5. (d, *J* = 1.3 Hz, 1H, C=CH_2), 3.54 (t, *J* = 6.8 Hz, 2H, ClCH_2), 2.23–2.11 (m, 2H, CH_2), 1.86–1.70 (m, 2H, CH_2), 1.62–1.49 (m, 2H, CH_2), 1.26 (s, 12H, CH_3-pin) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 129.6 (C=*C*H_2), 83.5 (*C*CH_3-pin), 45.3 (Cl*C*H_2), 34.6 (*C*H_2C), 32.3 (*C*H_2), 26.5 (*C*H_2), 24.9 (*C*H_3-pin) ppm. **MS** (EI) *m/z* (%): 244 ([M]$^+$, 1), 229 (13), 187 (14), 167 (15), 153 (33), 123 (12), 111 (15), 101 (10), 95 (10), 84 (44), 67 (39), 59 (33), 44 (47), 41 (100). **EA**: calc. (%) for $C_{12}H_{22}BClO_2$ C 58.93, H 9.07; found C 58.86, H 9.03. **IR**: $\tilde{\nu}$ = 2978 (m), 2961 (w), 2933 (m), 1864 (w), 1615 (w), 1443 (w), 1427 (m), 1368 (s), 1309 (s), 1273 (w), 1261 (w), 1214 (w), 1143 (s), 1110 (w), 968 (w), 942 (w), 860 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 5 min): t_R = 13.7 min. **TLC** (SiO_2, cyclohexane / ethyl acetate 50:1): R_f = 0.11 (visualization with $KMnO_4$).

***tert*-Butyldimethyl((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)oxy)silane (146d)**

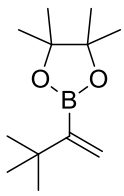


The vinyl iodine was obtained using sodium iodide (3.04 g, 20.3 mmol, 1.2 eq.), TMSCl (2.6 mL, 2.23 g, 20.5 mmol, 1.1 eq.), water (183 µL, 183 mg 10.2 mmol, 0.6 eq.) and propargyl alcohol (1.0 mL, 949 mg, 16.9 mmol, 1 eq.) as purple luquide (1.75 g, 9.51 mmol, 56%). A partial amount (500 mg, 2.72 mmol, 1.0 eq.) was protected using TBSCl (451 mg, 2.99 mmol, 1.1 eq.), DMAP (365 mg, 2.99 mmol, 1.1 eq.) and DCM (20 mL). The isolated TBS-protected alcohol (650 mg, 2.18 mmol, 80%) was applied for the *Miyaura* Borylation using $PdCl_2(PPh_3)_2$ (48.4 mg, 69.0 µmol, 3 mol-%), Ph_3P (36.6 mg, 138 µmol, 6 mol-%), bis(pinacolato)dibron (601 mg, 2.37 mmol, 1.1 eq.) and potassium phenoxide (427 mg, 3.23 mmol, 1.5 eq.) in toluene (6.0 mL). After work-up and purification by flash

chromatography (2 cm × 13 cm, *n*-pentane / Et_2O 20:1) the title compound **146d** (370 mg, 1.24 mmol, 58%) was obtained as a colorless liquid. The analytical data are in agreement with reported values.[154]

$C_{15}H_{31}BO_3Si$ (298.30 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.96 (br s, 1H, C=CH_2), 5.92–5.81 (m, 1H, C=CH_2), 4.28 (t, *J* = 2.0 Hz, 2H, OCH_2C), 1.26 (s, 12H, CH_3-pin), 0.92 (s, 9H, CCH_3), 0.06 (s, 6H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 127.3 (C=*C*H_2), 83.5 (*C*CH_3-pin), 64.7 (O*C*H_2), 26.1 (C(*C*H_3)$_3$), 18.6 (*C*(CH_3)$_3$), −5.2 (Si*C*H_3) ppm. **MS** (EI) *m/z* (%): 283 ([M-CH_3]$^+$, 3), 241 (79), 167 (11), 157 (34), 141 (26), 125 (30), 119 (41), 99 (28), 83 (100), 75 (18), 55 (16). **IR**: $\tilde{\nu}$ = 2956 (m), 2929 (s), 2897 (w), 2886 (w), 2856 (m), 1597 (w), 1494 (w), 1471 (m), 1448 (m), 1441 (m), 1303 (w), 1258 (s), 1086 (s), 1036 (s), 1005 (w), 858 (w), 835 (s), 797 (s), 679 (w), 631 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 18.0 min. **TLC** (SiO_2, *n*-pentane / Et_2O 20:1): R_f = 0.36 (visualization with $KMnO_4$).

2-(3,3-Dimethylbut-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (146i)

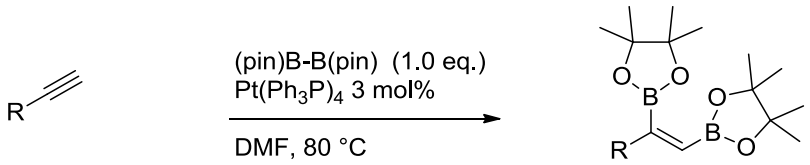


The intermediate vinyl iodide was obtained using 3,3-dimethyl-1-butyne (1.2 mL, 792 mg, 9.64 mmol, 1.0 eq.) sodium iodide (3.66 g, 11.6 mmol, 1.2 eq.), TMSCl (1.5 mL, 1.28 g, 11.8 1.23 eq.) and water (110 µL, 110 mg, 6.11 mmol, 0.63 eq.) in acetonitrile (10 mL) after purification by flash chromatography (SiO_2, *n*-pentane, 3 cm × 15 cm) as a purple liquid (1.63 mg, 7.76 mmol, 81%). A partial amount of the vinyl iodide (420 mg, 2.00 mmol, 1.0 eq.) was applied in the *Miyaura* Borylation using $PdCl_2(PPh_3)_2$ (45.0 mg, 64.1 µmol, 3.2 mol-%), Ph_3P (34 mg, 128 µmol, 6.4 mol-%), bis(pinacolato)dibron (559 mg, 2.20 mmol, 1.1 eq.) and potassium phenoxide (197 mg, 3.00 mmol, 1.5 eq.) in toluene (12 mL). After work-up and purification by flash chromatography (3 cm × 8 cm, *n*-pentane / Et_2O 100:1) the title compound **146i** (153 mg, 728 µmol, 36%) was obtained as a colorless liquid. The analytical data are in agreement with reported values.[154]

$C_{12}H_{23}BO_2$ (210.18 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.66 (d, *J* = 2.7 Hz, 1H, C=CH_2), 5.56 (br s, 1H, C=CH_2), 1.27 (s, 12H, pin-CH_3), 1.09 (s, 9H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 124.2 (*C*H_2), 83.2 (*C*CH_3-pin), 35.5 (*C*CH_3), 29.6 (*C*H_3), 24.9 (*C*H_3-pin) ppm. **GC-MS** (*Restek* Rtx®-5MS, 100 °C, 2 min, 10 °C/min, 270 °C, 10 min): 13.9 min. **MS** (EI) *m/z* (%): 210 (M^+, 16), 195 (18), 153 (78), 137 (10), 109 (56), 101 (80), 95 (52), 84 (100), 69 (67), 67 (28), 59 (11), 57 (18), 55 (29), 43 (32), 41 (47). **HRMS**: calc. (%) 210.1786; found 210.1786. **IR**: $\tilde{\nu}$ = 2978 (m), 2954 (m), 2930 (w), 2870 (w), 1603 (w), 1481 (w), 1468 (w), 1410 (w), 1354 (s), 1300 (s), 1246 (m), 1146 (s), 1124 (s), 968 (m), 943 (w), 883 (w), 862 (m), 835 (w), 741 (w), 702 (m), 699 (w) cm^{-1}.

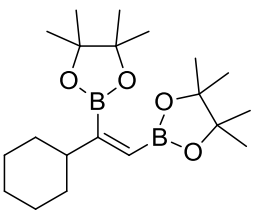
8.7.4 Preparation of 1,2-Bis-Boronates



158 **149a-d**

General Procedure M: To a solution of bis(pinacolato)diboron (1.0 eq.) and tetrakis(triphenylphosphine)platinum (0) (3 mol%) in dimethylformamide (0.2 M) the corresponding alkyne (1.1 eq.) was added. The obtained bright yellow solution was stirred at 80 °C for 20 hours. After cooling down to RT; the reaction mixture was diluted with TBME (100 mL) and extracted with ½-sat. NaCl solution (5×150 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Purification was performed by flash chromatography, *Kugelrohr* distillation or using both methods if necessary.

(*E*)-2,2'-(1-Cyclohexylethene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (149a)



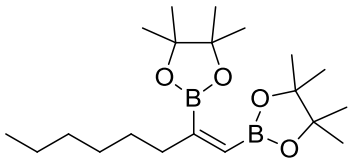
Following the general procedure **M** using bis(pinacolato)diboron (883 mg, 3.48 mmol, 1.0 eq.), tetrakis(triphenylphosphine)platinum (0) (130 mg, 104 µmol, 3 mol-%), and cyclohexylacetylene (0.5 mL, 414 mg, 3.83 mmol, 1 eq.) in DMF (20 mL), after purification by

Kugelrohr distillation (200−210 °C / 0.4 mbar) and flash chromatography (SiO_2, 4 cm × 10 cm, cyclohexane/TBME 20:1) the title compound **149a** (1.02 g, 2.82 mmol, 83%) was obtained as a colorless solid. The analytical data are in agreement with reported values.[155]

$C_{20}H_{36}B_2O_4$ (362.12 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.79 (s, 1H, C=C*H*), 2.09 (t, *J* = 11.1 Hz, 1H, C*H*), 1.78–1.69 (m, 4H, CH_2), 1.64 (t, *J* = 12.4 Hz, 1H, CH_2), 1.33 (s, 12H, pin-CH_3), 1.25 (s, 12H, pin-CH_3), 1.30–1.07 (m, 5H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 83.8 (*C*CH_3-pin), 83.4 (*C*CH_3-pin), 47.8 (*C*H), 32.4 (*C*H_2), 26.8 (*C*H_2), 26.4 (*C*H_2), 25.2 (*C*H_3-pin), 25.0 (*C*H_3-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 27.7 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.12 (visualization with $KMnO_4$). **m.p.**: 63−64 °C.

(*E*)-2,2‘-(Oct-1-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (149b)

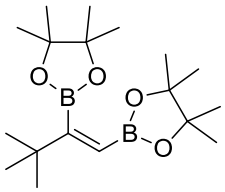


Following the general procedure **M** using bis(pinacolato)diboron (1.25 g, 4.92 mmol, 1.0 eq.) tetrakis(triphenylphosphine)-platinum (0) (184 mg, 148 µmol, 3 mol-%), and 1-octyne (0.8 mL, 597 mg, 5.42 mmol, 1.1 eq.) in DMF (30 mL) and after purification by *Kugelrohr* distillation (200−210 °C / 0.4 mbar) and flash chromatography (SiO_2, 4 cm × 12 cm, cyclohexane/TBME 20:1) the title compound **149b** (1.32 g, 3.62 mmol, 74%) was obtained as a colorless liquid. The analytical data are in agreement with reported values.[155]

$C_{20}H_{38}B_2O_4$ (364.14 g/mol):

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 5.83 (s, 1H, C=C*H*), 2.21 (t, *J* = 7.7 Hz, 2H, CH_2), 1.47–1.36 (m, 2H, CH_2), 1.31 (s, 12H, pin-CH_3), 1.26 (s, 12H, pin-CH_3), 1.29–1.10 (m, 6H, CH_2), 0.86 (t, *J* = 6.8 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 83.7 (*C*CH_3-pin), 83.4 (*C*CH_3-pin), 40.0 (*C*H_2), 31.9 (*C*H_2), 29.2 (*C*H_2), 28.7 (*C*H_2), 25.04 (*C*H_3-pin), 25.01 (*C*H_3-pin), 22.7 (*C*H_2), 14.2 (*C*H_3) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 25.5 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.15 (visualization with $KMnO_4$). **m.p.**: 100−101 °C.

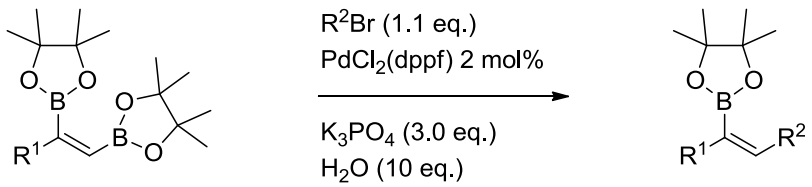
(*E*)-2,2'-(3,3-Dimethylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (149c)



Following the general procedure **M** using bis(pinacolato)diboron (1.30 g, 5.11 mmol, 1.0 eq.) tetrakis(triphenylphosphine)-platinum (0) (191 mg, 153 µmol, 3 mol-%), and 3,3-dimethyl-1-butyne (0.7 mL, 462 mg, 5.62 mmol, 1.1 eq.) in DMF (30 mL) and after purification by *Kugelrohr* distillation (180−190 °C / 0.2 mbar) the title compound **149c** (1.43 g, 4.25 mmol, 83%) was obtained as a white solid.

$C_{18}H_{34}B_2O_4$ (336.08 g/mol):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 5.83 (s, 1H, C=C*H*), 1.35 (s, 12H, pin-CH_3), 1.25 (s, 12H, pin-CH_3), 1.08 (s, 9H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 83.9 (*C*CH_3-pin), 83.4 (*C*CH_3-pin), 37.8 (*C*$(CH_3)_3$), 29.9 (C(*C*$H_3)_3$), 25.5 (*C*H_3-pin), 25.0 (*C*H_3-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 21.7 min. **MS** (EI) *m/z* (%): 321 ([M-CH_3]$^+$, 1), 278 (10), 236 (8), 221 (5), 195 (72), 166 (37), 154 (19), 139 (10), 123 (6), 109 (12), 96 (21), 83 (100), 69 (22), 55 (19), 41 (15). **EA**: calc. (%) for $C_{18}H_{34}B_2O_4$ C 64.33, H 10.20; found C 64.18, H 9.94. **IR**: $\tilde{\nu}$ = 2976 (m), 2964 (w), 1606 (m), 1380 (m), 1371 (m), 1336 (s), 1305 (s), 1269 (w), 1244 (w), 1221 (m), 1212 (w), 1166 (w), 1138 (s), 1110 (w), 983 (w), 969 (m), 900 (w), 874 (w), 858 (m), 851 (m), 835 (w), 825 (w) cm^{-1}. **m.p.**: 101−102 °C.

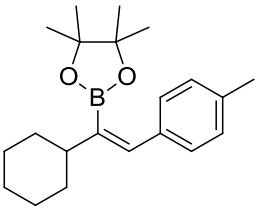
8.7.5 Suzuki-Miyaura Coupling



General Procedure N: To a mixture of aryl bromide (1.1 eq.), $PdCl_2$(dppf)-DCM complex (2 mol%), bis boronate **149a-d** (1.0 eq.) and K_3PO_4 (3.0 eq.) were added THF (0.15 M) and degassed water (10.0 eq.). The obtained brown suspension was stirred at 80 °C for 16 hours. After cooling down to RT; the reaction mixture was diluted with water (5 mL) and extracted

with TBME (3×5 mL). Combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Purification was performed by flash chromatography, *Kugelrohr* distillation or even using both methods if necessary.

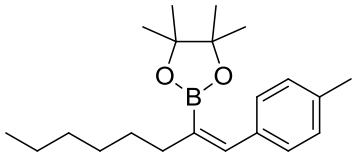
(*E*)-2-(1-Cyclohexyl-2-(*p*-tolyl)vinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149e)



Following the general procedure **N** using 4-bromotoluene (88 mg, 513 µmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (7.62 mg, 9.33 µmol, 2 mol%), **149a** (169 mg, 467 µmol, 1.0 eq.), K_3PO_4 (306 mg, 1.40 mmol, 3.0 eq.), THF (2.80 mL) and H_2O (85 µL, 85 mg, 4.72 mmol, 10 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 20 cm, cyclohexane/TBME 1:0 → 500:1 → 250:1 → 100:1 → 50:1) the title compound **149e** (92 mg, 282 µmol, 60%) was obtained as a white solid.

$C_{21}H_{31}BO_2$ (326.28 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.0 Hz, 2H, H_{Ar}), 7.05 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 6.80 (s, 1H, C=C*H*), 2.31 (s, 3H, CH_3), 2.26–2.10 (m, 1H, C*H*), 1.87–1.74 (m, 4H, C_6H_{11}), 1.73–1.61 (m, 1H, C_6H_{11}), 1.30–1.24 (m, 4H, C_6H_{11}), 1.27 (s, 12H, pin-CH_3), 1.22–1.07 (m, 1H, C_6H_{11}) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 136.8 (C=*C*H), 136.7 (C_{Ar}), 136.5 (C_{Ar}), 128.7 (HC_{Ar}), 128.1 (HC_{Ar}), 83.6 (*C*CH_3-pin), 46.6 (*C*H), 33.3 (*C*H_2), 26.9 (*C*H_2), 26.4 (*C*H_2), 25.1 (*C*H_3-pin), 21.3 (*C*H_3) ppm. **MS** (EI) *m/z* (%): 326 ([M]$^+$, 74), 311 (7), 283 (6), 269 (13), 244 (29), 231 (18), 226 (24), 211 (8), 198 (100), 187 (5), 183 (32), 169 (16), 158 (35), 155 (27), 143 (41), 131 (25), 128 (35), 117 (22), 115 (21), 105 (35), 101 (35), 95 (6), 91 (18), 84 (52), 79 (14), 77 (11), 69 (18), 59 (15), 57 (17), 55 (46), 43 (45), 41 (68). **HRMS**: calc. (%) 326.2412; found 326.2409. **IR**: $\tilde{\nu}$ = 2990 (w), 2978 (w), 2918 (s), 2847 (m), 1615 (w), 1569 (w), 1510 (m), 1227 (w), 1420 (w), 1392 (m), 1339 (w), 1301 (s), 1291 (s), 1253 (s), 1207 (w), 1167 (w), 1134 (s), 1104 (m), 981 (w), 960 (m), 945 (w), 906 (w), 883 (m), 854 (s), 827 (m), 804 (m), 761 (w), 724 (m), 710 (w), 670 (w), 620 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 29.1 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.24. **m.p.**: 54−55 °C.

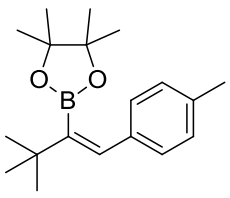
(*E*)-2-(1-(*p*-Tolyl))oct-1-en-2-yl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149f)



Following the general procedure **N** using 4-bromotoluene (150 µL, 209 mg, 1.22 mmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (14.4 mg, 22 µmol, 2 mol%), **149b** (404 mg, 1.11 mmol, 1.0 eq.), K_3PO_4 (721 mg, 3.30 mmol, 3.0 eq.), THF (7 mL) and H_2O (200 µL, 200 mg, 11.1 mmol, 10 eq.), after purification by flash chromatography (SiO_2, 3 cm × 15 cm, cyclohexane/TBME 1:0 → 20:1) and *Kugelrohr* distillation (150–160 °C / 0.15 mbar) the title compound **149f** (230 mg, 701 µmol, 62%) was obtained as a colorless oil.

$C_{21}H_{33}BO_2$ (328.30 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 8.0 Hz, 2H, H_{Ar}), 7.06 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 6.84 (s, 1H, C=C*H*), 2.32 (s, 3H, Ar-CH_3), 2.31–2.26 (m, 2H, C_6H_{10}), 1.53–1.43 (m, 2H, C_6H_{10}), 1.40–1.26 (m, 6H, C_6H_{10}), 1.26 (s, 12H, pin-CH_3), 0.89 (t, *J* = 6.8 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 139.8 (C=*C*H), 136.6 (C_{Ar}), 136.3 (C_{Ar}), 128.7 (HC_{Ar}), 128.1 (HC_{Ar}), 83.5 (*C*CH_3-pin), 38.4 (*C*H_2), 31.9 (*C*H_2), 29.9 (*C*H_2), 29.2 (*C*H_2), 24.9 (*C*H_3-pin), 22.8 (*C*H_2), 21.3 (Ar-*C*H_3), 14.3 (*C*H_3) ppm. **MS** (EI) *m/z* (%): 328 ([M]$^+$, 99), 271 (14), 244 (42), 228 (38), 213 (44), 200 (51), 171 43), 157 (80), 143 (61), 139 (12), 131 (47), 129 (67), 118 (68), 115 (30), 105 (44), 101 (100), 91 (22), 83 (78), 55 (61), 43 (80), 41 (79). **HRMS**: calc. (%) 328.2574; found 328.2572. **IR**: $\tilde{\nu}$ = 2977 (m), 2955 (m), 2924 (s), 2853 (m), 1615 (w), 1510 (w), 1463 (w), 1391 (m), 1370 (w), 1339 (w), 1302 (s), 1253 (s), 1212 (w), 1164 (w), 1143 (s), 1111 (w), 964 (w), 863 (w), 803 (w), 713 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 26.9 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.24.

(*E*)-2-(3,3-Dimethyl-1-(*p*-tolyl)but-1-en-2-yl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149g)

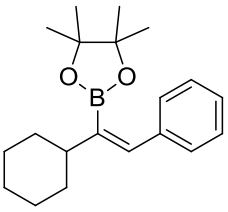


Following the general procedure **N** using 4-bromotoluene (112 mg, 655 µmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (10.0 mg, 12.2 µmol, 2 mol%), **149c** (200 mg, 595 µmol, 1.0 eq.), K_3PO_4 (721 mg, 3.30 mmol, 3.0 eq.), THF (4 mL) and H_2O (110 µL, 110 mg, 6.11 mmol, 10 eq.), after

purification by flash chromatography (SiO_2, 3 cm × 12 cm, cyclohexane/TBME 1:0 → 100:1) and *Kugelrohr* distillation (150–160 °C / 0.15 mbar) the title compound **149g** (118 mg, 393 µmol, 66%) was obtained as a colorless oil.

$C_{19}H_{29}BO_2$ (300.24 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 8.0 Hz, 2H, H_{Ar}), 7.06 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 6.84 (s, 1H, C=C*H*), 2.31 (s, 3H, Ar-CH_3), 1.24 (s, 12H, pin-CH_3), 1.19 (s, 9H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 137.1 (C_{Ar}), 136.3 (C_{Ar}), 133.9 (C=*C*H), 128.7 (HC_{Ar}), 128.1 (HC_{Ar}), 83.6 (*C*CH_3-pin), 36.2 (*C*CH_3), 30.4 (C*C*H_3), 25.3 (*C*H_3-pin), 21.3 (Ar-*C*H_3) ppm. **MS** (EI) *m/z* (%): 300 ([M]$^+$, 67), 285 (31), 200 (41), 185 (100), 172 (56), 169 (11), 157 (78), 143 (35), 131 (20), 128 (28), 119 (15), 115 (21), 105 (13), 101 (47), 91 (17), 83 (54), 77 (9), 69 (13), 67 (13), 59 (12), 55 (41), 43 (50), 41 (79). **EA**: calc. (%) for $C_{19}H_{29}BO_2$ C 76.01, H 9.74; found C 76.22, H 9.71. **IR**: $\tilde{\nu}$ = 2961 (m), 2951 (w), 2903 (w), 2366 (w), 1516 (w), 1511 (m), 1479 (w), 1462 (w), 1412 (w), 1384 (s), 1336 (w), 1298 (s), 1251 (s), 1210 (w), 1142 (s), 1110 (w), 1037 (w), 1006 (w), 960 (w), 860 (m), 832 (w), 808 (w), 686 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 22.2 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.23.

(*E*)-2-(1-Cyclohexyl-2-phenylvinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4i)

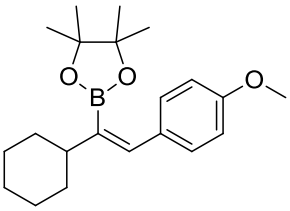


Following the general procedure **N** using bromobeneze (70 µL, 104 mg, 664 µmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (9.9 mg, 12.1 µmol, 2 mol%), **149a** (219 mg, 604 µmol, 1.0 eq.), K_3PO_4 (397 mg, 1.81 mmol, 3.0 eq.), THF (4.0 mL) and H_2O (109 µL, 109 mg, 6.05 mmol, 10 eq.), after purification by flash chromatography (SiO_2, 3 cm × 12 cm, cyclohexane/TBME 1:0 → 500:1 → 250:1 → 100:1) the title compound **149i** (137 mg, 439 µmol, 73%) was obtained as a white solid.

$C_{20}H_{29}BO_2$ (312.25 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 7.5 Hz, 2H, H_{Ar}), 7.28–7.22 (m, 2H, H_{Ar}), 7.21–7.14 (m, 1H, H_{Ar}), 6.85 (s, 1H, C=C*H*), 2.26–2.14 (m, 1H, C_6H_{11}), 1.88–1.74 (m, 4H, C_6H_{11}), 1.70 (d, *J* = 12.5 Hz, 1H, C_6H_{11}), 1.39–1.25 (m, 4H, C_6H_{11}), 1.26 (s, 12H, pin-CH_3), 1.23–

1.09 (m, 1H, C_6H_{11}) ppm. **$^{13}C\{^1H\}$-NMR** (101 MHz, $CDCl_3$): δ = 139.5 (C_{Ar}), 136.7 (C=CH), 128.0 (HC_{Ar}), 127.8 (HC_{Ar}), 126.7 (HC_{Ar}), 83.5 (CCH_3-pin), 46.5 (CH), 33.1 (CH_2), 26.7 (CH_2), 26.2 (CH_2), 24.9 (CH_3-pin) ppm. **MS** (EI) *m/z* (%): 312 ($[M]^+$, 43), 297 (3), 255 (13), 230 (16), 212 (19), 199 (4), 184 (100), 169 (13), 155 (26), 144 (51), 129 (48), 117 (31), 115 (31), 105 (23), 101 (37), 95 (11), 91 (35), 84 (81), 79 (14), 77 (18), 69 (25), 67 (21), 59 (14), 57 (16), 55 (46), 43 (48), 41 (76). **EA**: calc. (%) for $C_{20}H_{29}BO_2$ C 76.93; H 9.36; found C 76.72; H 9.19;. **IR**: $\tilde{\nu}$ = 2981 (m), 2925 (s), 2848 (s), 1617 (w), 1598 (w), 1574 (w), 1486 (w), 1427 (m), 1410 (m), 1370 (m), 1344 (w), 1305 (s), 1293 (s), 1256 (s), 1207 (m), 1166 (w), 1135 (s), 1113 (s), 1028 (w), 962 (m), 936 (w), 914 (w), 882 (m), 863 (m), 852 (s), 823 (w), 783 (m) 749 (s), 731 (s), 690 (s), 668 (m), 635 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 27.2 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.22. **m.p.**: 53−54 °C.

(*E*)-2-(1-Cyclohexyl-2-(4-methoxyphenyl)vinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149j)

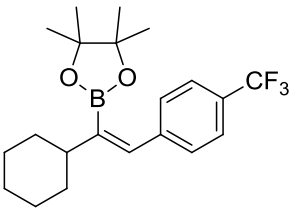


Following the general procedure **N** using 4-bromoanisole (80 µL, 119 mg, 637 µmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (10.2 mg, 12.5 µmol, 2 mol%), **149a** (210 mg, 579 µmol, 1.0 eq.), K_3PO_4 (380 mg, 1.74 mmol, 3.0 eq.), THF (4.0 mL) and H_2O (104 µL, 104 mg, 5.79 mmol, 10 eq.), after purification by flash chromatography (SiO_2, 1.5 cm × 27 cm, cyclohexane / TBME 100:1 → 50:1) the title compound **149j** (126 mg, 368 µmol, 64%) was obtained as a white solid.

$C_{21}H_{31}BO_3$ (342.28 g/mol):
^1H-NMR (500 MHz, $CDCl_3$): δ = 7.28–7.23 (m, 2H, H_{Ar}), 6.81–6.76 (m, 3H, H_{Ar}, C=CH), 3.79 (s, 3H, OCH_3), 2.24–2.09 (m, 1H, C_6H_{11}), 1.83–1.74 (m, 4H, C_6H_{11}), 1.72–1.65 (m, 1H, C_6H_{11}), 1.36–1.28 (m, 4H, C_6H_{11}), 1.27 (s, 12H, pin-CH_3), 1.21–1.13 (m, 1H, C_6H_{11}) ppm. **$^{13}C\{^1H\}$-NMR** (126 MHz, $CDCl_3$): δ = 158.8 (C_{Ar}), 136.5 (C=CH), 132.4 (C_{Ar}), 129.4 (HC_{Ar}), 113.4 (HC_{Ar}), 83.6 (CCH_3-pin), 55.4 (CH_3), 46.6 (CH), 33.3 (CH_2), 26.9 (CH_2), 26.4 (CH_2), 25.1 (CH_3-pin) ppm. **MS** (EI) *m/z* (%): 342 ($[M]^+$, 98), 327 (57), 299 (6), 285 (9), 270 (8), 260 (39), 247 (21), 242 (18), 234 (8), 227 (8), 214 (51), 199 (19), 184 (19), 171 (22), 159 (37), 155 (14), 147 (21), 144 (31), 134 (23), 128 (26), 121 (79), 115 (36), 108 (11), 101 (42),

91 (19), 83 (100), 77 (19), 69 (18), 59 (20), 57 (21), 55 (63), 43 (57), 41 (85). **HRMS**: calc. (%) 342.2361; found 342.2367. **IR**: $\tilde{\nu}$ = 2976 (w), 2921 (m), 2849 (m), 1607 (m), 1572 (w), 1508 (s), 1443 (w), 1391 (w), 1368 (w), 1338 (w), 1309 (m), 1290 (s), 1258 (m), 1241 (s), 1215 (m), 1176 (m), 1147 (w), 1136 (s), 1121 (w), 1106 (m), 1205 (s), 983 (w), 960 (w), 906 (w), 881 (m), 861 (m), 832 (s), 808 (m), 758 (w), 731 (w), 716 (m), 672 (w), 653 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 20 min): t_R = 34.7 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.22. **m.p.**: 66−67 °C.

(*E*)-2-(1-Cyclohexyl-2-(4-(trifluoromethyl)phenyl)vinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149k)

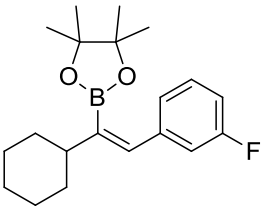


Following the general procedure **N** using 4-bromo-trifluorotoluene (90 µL, 144 mg, 640 µmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (10.2 mg, 12.5 µmol, 2 mol%), **149a** (211 mg, 582 µmol, 1.0 eq.), K_3PO_4 (382 mg, 1.75 mmol, 3.0 eq.), THF (4.0 mL) and H_2O (105 µL, 105 mg, 5.81 mmol, 10 eq.), after purification by flash chromatography (SiO_2, 2 cm × 13 cm, cyclohexane/TBME 100:1 → 50:1) the title compound **149k** (142 mg, 374 µmol, 64%) was obtained as a white solid.

$C_{21}H_{28}BF_3O_2$ (380.25 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.2 Hz, 2H, H_{Ar}), 7.41 (d, *J* = 8.5 Hz, 2H, H_{Ar}), 6.84 (s, 1H, C=C*H*), 2.26–2.14 (m, 1H, C_6H_{11}), 1.88–1.75 (m, 4H, C_6H_{11}), 1.74–1.64 (m, 1H, C_6H_{11}), 1.38–1.28 (m, 4H, C_6H_{11}), 1.25 (s, 12H, pin-CH_3), 1.19–1.12 (m, 1H, C_6H_{11}) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 143.2 (C_{Ar}), 135.5 (C=*C*H), 128.8 (q, J_{CF} = 32.3 Hz, C_{Ar}), 128.4 (HC_{Ar}), 124.9 (q, J_{CF} = 3.8 Hz, HC_{Ar}CCF_3), 124.5 (q, J_{CF} = 272 Hz, *C*F_3), 83.9 (*C*CH_3-pin), 46.6 (*C*H), 33.0 (*C*H_2), 27.8 (*C*H_2), 26.3 (*C*H_2), 25.0 (*C*H_3-pin) ppm. **^{19}F{^{1}H}-NMR** (376 MHz, $CDCl_3$): −62.3 (s) ppm. **MS** (EI) *m/z* (%): 380 ([M]$^+$, 30), 365 (5), 361 (8), 323 (19), 298 (12), 279 (12), 252 (47), 212 (26), 197 (9), 183 (17), 177 (9), 265 (8), 159 (9), 143 (5), 128 (6), 101 (40), 95 (18), 84 (100), 69 (20), 67 (18), 59 (12), 57 (13), 55 (31), 43 (35), 41 (50). **HRMS**: calc. (%) 380.2129; found 380.2137. **IR**: $\tilde{\nu}$ = 2981 (w), 2925 (m), 2851 (w), 1612 (m), 1573 (w), 1447 (w), 1423 (w), 1391 (m), 1370 (w), 1320 (s), 1302 (s), 1250 (s), 1210 (w), 1161 (s), 1138 (m), 1107 (s), 1064 (s), 1014 (m), 987 (w), 960 (m),

906 (w), 888 (w), 867 (w), 853 (m), 832 (s), 819 (m), 790 (w), 763 (w), 718 (w), 679 (m), 658 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 25.9 min. **TLC** (SiO_2, cyclohexane/TBME 20:1): R_f = 0.22. **m.p.**: 63−64 °C.

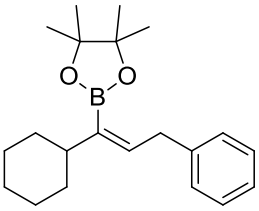
(*E*)-2-(1-Cyclohexyl-2-(3-fluorophenyl)vinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149l)



Following the general procedure **N** using 1-bromo-3-fluorobenzene (80 µL, 125 mg, 716 µmol, 1.1 eq.), $PdCl_2$(dppf)-DCM complex (11.5 mg, 14.0 µmol, 2 mol%), **149a** (236 mg, 651 µmol, 1.0 eq.), K_3PO_4 (428 mg, 1.95 mmol, 3.0 eq.), THF (5.0 mL) and H_2O (120 µL, 120 mg, 6.66 mmol, 10 eq.), after purification by flash chromatography (SiO_2, 2 cm × 15 cm, cyclohexane/ethyl acetate 50:1) the title compound **149l** (161 mg, 488 µmol, 75%) was obtained as a white solid.

$C_{20}H_{28}BFO_2$ (330.24 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.23–7.14 (m, 1H, H_{Ar}), 7.10–7.02 (m, 2H, H_{Ar}), 6.87 (ddd, *J* = 8.5, 2.5, 1.2 Hz, 1H, H_{Ar}), 6.79 (s, 1H, C=C*H*), 2.26–2.13 (m, 1H, C_6H_{11}), 1.88–1.73 (m, 4H, C_6H_{11}), 1.69 (dd, *J* = 12.6, 1.3 Hz, 1H, C_6H_{11}), 1.37–1.28 (m, 4H, C_6H_{11}), 1.26 (s, 12H, pin-CH_3), 1.21–1.08 (m, 1H, C_6H_{11}) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 162.8 (d, J_{CF} = 245 Hz, FC_{Ar}), 142.0 (d, J_{CF} = 7.6 Hz, $C_{Ar\text{-}m\text{-}F}$), 135.6 (d, J_{CF} = 2.3 Hz, C=*C*H), 129.4 (d, J_{CF} = 8.5 Hz, H$C_{Ar\text{-}m\text{-}F}$), 124.0 (d, J_{CF} = 1.7 Hz, H$C_{Ar\text{-}p\text{-}F}$), 114.7 (d, J_{CF} = 21.4 Hz, H$C_{Ar\text{-}o\text{-}F}$), 113.6 (d, J_{CF} = 21.2 Hz, H$C_{Ar\text{-}o\text{-}F}$), 83.9 (*C*CH_3-pin), 46.6 (*C*H), 33.1 (*C*H_2), 26.8 (*C*H_2), 26.4 (*C*H_2), 25.0 (*C*H_3-pin) ppm. **^{19}F{^{1}H}-NMR** (376 MHz, $CDCl_3$): −114.6 (s) ppm. **MS** (EI) *m/z* (%): 330 ($[M]^+$, 47), 273 (15), 248 (12), 230 (19), 205 (10), 202 (80), 187 (7), 174 (8), 162 (36), 147 (28), 141 (10), 135 (15), 128 (10), 123 (9), 115 (10), 109 (17), 101 (49), 95 (20), 84 (100), 81 (10), 69 (21), 55 (22), 43 (16), 41 (24). **EA**: calc. (%) for $C_{20}H_{28}BFO_2$ C 72.74; H 8.55; found C 72.64, H 8.57. **IR**: $\tilde{\nu}$ = 2979 (m), 2927 (s), 2849 (m), 1609 (w), 1580 (m), 1482 (w), 1445 (m), 1416 (w), 1390 (m), 1369 (w), 1338 (w), 1301 (s), 1291 (s), 1256 (m), 1240 (m), 1209 (w), 1165 (w), 1133 (s), 1115 (s), 986 (m), 960 (m), 901 (w), 882 (w), 863 (w), 848 (m), 830 (w), 800 (w), 776 (s), 752 (w), 728 (w), 688 (s), 667 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701, 100 °C, 2 min, 7 °C/min, 270 °C, 10 min): 27.0 min. **TLC** (SiO_2, cyclohexane/ethyl acetate 50:1): R_f = 0.11. **m.p.**: 33−34 °C.

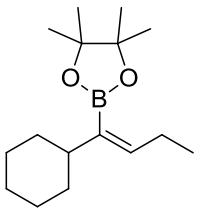
(*E*)-2-(1-Cyclohexyl-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149m)



This compound was obtained according to the procedure published by Shimizu and coworkers:[156] To a mixture of $Pd(PPh_3)_4$ (28.9 mg, 25.0 µmol, 5 mol%), Cs_2CO_3 (977 mg, 3.00 mmol, 6.0 eq.), and **149a** (217 mg, 600 µmol) 1.3 eq.) were added subsequently benzyl bromide (60 µL, 85.8 mg, 502 µmol, 1.0 eq.), THF (10 mL) and water (450 µL, 450 mg, 25.0 mmol, 50 eq.). The obtained suspension was stirred at 60 °C for 3 h. After cooling down to rt the reaction mixture was treated with water (10 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by flash chromatography (SiO_2, 2 cm × 16 cm, cyclohexane/TBME 100:1 → 50:1) the title compound **149m** (127 mg, 389 µmol, 78%) was obtained as a white solid.

$C_{21}H_{31}BO_2$ (326.28 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.31–7.24 (m, 2H, H_{Ar}), 7.24–7.13 (m, 3H, H_{Ar}), 6.03 (t, *J* = 7.5 Hz, 1H, C=C*H*), 3.61 (d, *J* = 7.6 Hz, 2H, Ar-CH_2), 2.07 (t, *J* = 11.2 Hz, 1H, C_6H_{11}), 1.76–1.58 (m, 4H, C_6H_{11}), 1.30 (s, 12H, pin-CH_3), 1.28–1.05 (m, 6H, C_6H_{11}) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 141.8 (C_{Ar}), 139.6 (C=*C*H), 128.8 (HC_{Ar}), 128.4 (HC_{Ar}), 125.8 (HC_{Ar}), 83.2 (*C*CH_3-pin), 44.6 (*C*H), 38.0 (Ar-*C*H_2), 33.3 (*C*H_2), 27.0 (*C*H_2), 26.5 (*C*H_2), 25.0 (*C*H_3-pin) ppm. **MS** (EI) *m/z* (%): 326 ($[M]^+$, 23), 241 (32), 235 (13), 230 (5), 226 (17), 199 (6), 197 (9), 191 (5), 165 (8), 155 (5), 144 (89), 135 (44), 129 (16), 121 (5), 117 (20), 107 (23), 101 (100), 91 (33), 85 (2), 83 (54), 81 (11), 79 (12), 69 (10), 67 (17), 57 (15), 55 (31), 43 (12), 41 (19). **EA**: calc. (%) for $C_{21}H_{31}BO_2$ C 77.30, H 9.58; found C 77.21, H 9.44. **IR**: $\tilde{\nu}$ = 2977 (m), 2919 (s), 2851 (m), 1628 (m), 1601 (w), 1494 (w), 1449 (w), 1421 (w), 1402 (s), 1368 (m), 1356 (m), 1345 (w), 1313 (m), 1298 (w), 1285 (m), 1251 (s), 1210 (m), 1163 (w), 1136 (s), 1068 (w), 1030 (w), 983 (m), 962 (m), 932 (m), 890 (w), 873 (m), 849 (m), 832 (m), 746 (s), 732 (w), 715 (m), 699 (s), 681 (m), 661 (w), 620 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 28.7 min. **TLC** (SiO_2, cyclohexane/ethyl acetate 50:1): R_f = 0.30. **m.p.**: 48−49 °C.

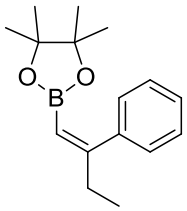
(*E*)-2-(1-Cyclohexylbut-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (149n)



This compound was obtained according to the procedure published by Shimizu and coworkers:[157] To a mixture of $Pd(OAc)_2$ (6.2 mg, 27.9 µmol, 5 mol%), [*t*-Bu_2MePH]BF_4 (13.8 mg, 55.8 µmol, 10 mol%), NaOH (67.0 mg, 1.67 mmol, 3.0 eq.), and **149a** (202 mg, 558 µmol, 1.0 eq.) were added ethyl bromide (50 µL, 73.0 mg, 670 µmol, 1.2 eq.) and dry dioxane (1.5 mL). The obtained suspension was stirred at 60 °C for 20 h. After cooling down to rt the reaction mixture was diluted with ethyl acetate (5 mL), filtered over a plug of silica gel (2 cm × 2 cm) and washed with ethyl acetate (3×5 mL). Combined filtrates were concentrated in *vacuo*. After purification by flash chromatography (SiO_2, 2 cm × 20 cm, cyclohexane/ethyl acetate 500:1) the title compound **149n** (28 mg, 106 µmol, 19%) was obtained as a colorless oil.

$C_{16}H_{29}BO_2$ (264.21 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.87 (t, *J* = 7.4 Hz, 1H, C=C*H*), 2.22 (pent., *J* = 7.5 Hz, 2H, CH_2CH$_3$), 1.98 (dq, *J* = 11.6, 4.0, 3.2 Hz, 1H, C_6H_{11}), 1.77–1.55 (m, 5H, C_6H_{11}), 1.28 (s, 12H, pin-CH_3), 1.33–1.06 (m, 5H, C_6H_{11}), 0.95 (p, *J* = 7.5 Hz, 3H, CH_2CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 142.9 (C=*C*H), 83.0 (*C*CH_3-pin), 44.6 (*C*H), 33.4 (*C*H_2), 27.0 (*C*H_2), 26.5 (*C*H_2), 25.0 (*C*H_3-pin), 24.9 (CH_2*C*H_2CH_3), 14.9 (CH_2*C*H_3) ppm. **MS** (EI) *m/z* (%): 264 ([M]$^+$, 15), 207 (23), 179 (12), 164 (17), 149 (5), 136 (100), 121 (9), 107 (21), 101 (50), 95 (14), 84 (81), 81 (18), 79 (12), 69 (15), 67 (20), 57 (10), 55 (22), 43 (12), 41 (18). **HRMS**: calc. (%) 264.2256; found 264.2256. **IR**: $\tilde{\nu}$ = 2975 (m), 2923 (s), 2852 (s), 2360 (w), 1702 (w), 1626 (w), 1473 (w), 1448 (m), 1405 (w), 1370 (m), 1325 (m), 1298 (m), 1285 (s), 1251 (s), 1214 (w), 1143 (s), 1105 (m), 1023 (w), 983 (w), 864 (w), 803 (w), 714 (m), 676 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 17.7 min. **TLC** (SiO_2, cyclohexane/ethyl acetate 500:1): R_f = 0.10 (visualization with $KMnO_4$).

(*Z*)-4,4,5,5-Tetramethyl-2-(2-phenylbut-1-en-1-yl)-1,3,2-dioxaborolane (149o):



To a solution of zirconocene dichloride (351 mg, 1.20 mmol, 1.2 eq.) in THF (6.0 mL) *n*-BuLi (1.6 M, 1.5 mL, 2.40 mmol, 2.4 mmol, 2.4 eq.) was added drop wise at −78 °C. The reaction mixture was stirred for 1 h at −78 °C. Ethylene gas was passed into the reaction mixture using a Teflon® cannula during 5 min, than a ballon filled with ethylene gas was placed on the reaction flask for 1 h. The cooling bath was removed and the reaction mixture was stirred for additional 1 h. 2-Phenyl-1-ethynylboronic acid pinacol ester (228 mg, 1.00 mmol, 1.0 eq.) was added and the reaction mixture was stirred for 1 h at RT. The reaction mixture was quenched by adding HCl 1M solution (5 mL) and extracted with diethyl ether (3×10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by *Kugelrohr* distillation (115–120 °C/ 0.4 mbar) gave the title compound **149o** (96 mg, 372 µmol, 37%) as a colorless oil. The analytical data are in agreement with reported values.[148]

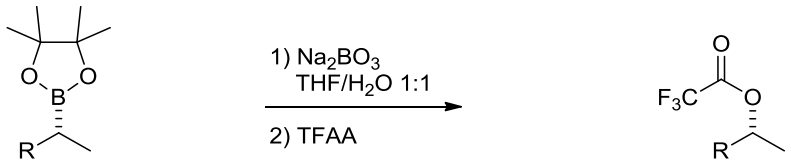
$C_{16}H_{23}BO_2$ (258.16 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.30–7.22 (m, 5H, H_{Ar}), 5.44 (d, *J* = 1.3 Hz, 1H, C=C*H*), 2.48 (qd, *J* = 7.2, 1.3 Hz, 2H, CH_2CH_3), 1.12 (s, 12H, pin-CH_3), 1.04 (t, *J* = 7.4 Hz, 3H, CH_2CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 163.8 (*C*=CH), 143.2 (C_{Ar}), 128.0 (HC_{Ar}), 127.7 (HC_{Ar}), 127.3 (HC_{Ar}), 83.1 (CCH_3-pin), 33.5 (CH_2CH_3), 24.7 (CH_3-pin), 12.7 (CH_2CH_3) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 18.7 min.

8.7.6 Hydrogenation at Low Pressure and Low Temperature, General Procedure O

A 2 mL-glass vial was charged with a stirring bar, iridium catalyst (0.5 mol-%) and substrate (50-100 µmol). The mixture was dissolved in DCM (0.2 M) and placed in an autoclave. The equipment was pressurized with nitrogen (1 bar) and cooled down to −20 °C for 1 hour. The autoclave was then five times pressurized up to 10 bar with hydrogen and the pressure released. The reaction was performed under 2 bar H_2 atmosphere during 4 hours at −20 °C. After releasing the hydrogen pressure the reaction mixture was allowed to reach rt and the solvent was removed under reduced pressure. The crude product was taken up in *n*-heptane (1 mL) and purified over a plug of silica gel (SiO_2, 0.5 cm × 1 cm *n*-heptane/TBME 10:1) to obtain analytically pure hydrogenation product.

General Procedure P for the Oxidation of the Analytical Samples:

In a 2 mL-glass vial hydrogenation product (50-100 µmol) was dissolved in THF/water 1:1 (0.2 M) and oxidized using potassium perborate monohydrate (1.5 eq.). After stirring for 1 h at RT, the reaction mixture was extracted with DCM (3×1 mL). The combined organic layers were dried over $MgSO_4$ and filtrated. To the filtrate trifluoroacetic anhydride TFAA (5-10 eq.) was added and the mixture was stirred for 30 min at RT. The volatiles were removed by purging with nitrogen (carefully, some samples are volatile). The residue was dissolved in *n*-heptane (1 mL) and analyzed by GC.



147 **177**

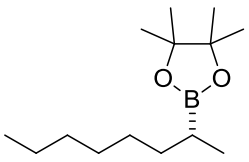
Assignment of the Absolute Configuration:

The absolute configuration of **147a** was assigned by comparison of the chiral GC spectra obtained after oxidation and trifluoroacetylation with an authentic GC spectra of trifluoroacetylated (*S*)-octan-2-ol obtained via enzymatic kinetic resolution of racemic secondary alcohols.[95] All other products were assigned in analogy with this.

8.7.7 Analytical Data for the Hydrogenation Products Derived from Terminal Alkenylboronic Esters

For known compounds only $[\alpha]_D^{20}$, ^1H, ^{13}C-NMR and conditions for *ee* determination (t_r of main enantiomer highlighted in bold in all cases) are listed.

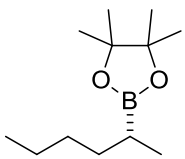
(*R*)-2-(Octan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147a)[141]



$C_{14}H_{29}BO_2$ (240.19 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.49–1.40 (m, 1H, C*H*), 1.39–1.12 (br m, 9H, CH_2), 1.23 (s, 12H, CH_3-pin), 1.09–0.92 (m, 4H, CH_3, CH_2), 0.87 (t, *J* = 6.8 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 82.9 (*C*CH_3-pin), 33.4 (*C*H_2), 32.0 (*C*H_2), 29.7 (*C*H_2), 29.1 (*C*H_2), 24.89 (*C*H_3-pin), 24.86

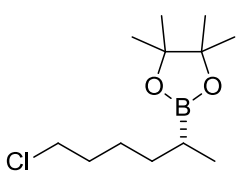
(*C*H$_3$-pin), 22.8 (*C*H$_2$), 15.7 (CH*C*H$_3$), 14.3 (*C*H$_3$) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 270 °C, 5 min): t_R = 13.1 min. **[α]$_D^{20}$**: −1.5 (*c* = 1.00, CH_2Cl_2). **GC** (chiral, (30 m × 0.25 mm × 0.12 µm), 60 kPa H_2, 50 °C, 1 °C/min, 65 °C, 10 °C/min, 160 °C, 10 min): 96% *ee*, t_R = **13.0 min** (*R*), 14.3 min (*S*) as oxidation / trifluoroacetylation product.

(*R*)-2-(Hexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147b)



$C_{12}H_{25}BO_2$ (212.14 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 1.45–1.35 (m, 1H, C*H*), 1.34–1.22 (m, 6H, C*H*$_2$), 1.20 (s, 12H, C*H*$_3$-pin), 1.00–0.78 (m, 6H, C*H*$_3$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 83.2 (*C*CH$_3$-pin), 33.5 (*C*H$_2$), 31.7 (*C*H$_2$), 25.10 (*C*H$_3$-pin), 25.07 (*C*H$_3$-pin), 23.5 (*C*H$_2$), 15.9 (CH*C*H$_3$), 14.6 (*C*H$_3$) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 270 °C, 5 min): t_R = 9.0 min. **MS** (EI) *m/z* (%): 212 ([M]$^+$, 0.9), 197 (33), 170 (6), 154 (5), 141 (5), 129 (23), 126 (34), 112 (34), 101 (14), 85 (67), 71 (64), 55 (42), 43 (100). **HRMS**: calc. (%) for [M-CH$_3$] 197.1708; found 197.1700. **IR**: $\tilde{\nu}$ = 2976 (m), 2956 (s), 2924 (s), 2871 (m), 2855 (m), 2361 (w), 2324 (w), 1463 (m), 1407 (w), 1381 (s), 1373 (s), 1313 (s), 1275 (m), 1249 (w), 1229 (w), 1144 (s), 1111 (w), 967 (w), 859 (w), 786 (w), 670 (w), 631 (w) cm^{-1}. **[α]$_D^{20}$**: −4.4 (*c* = 0.55, $CHCl_3$). **GC** (chiral, *Chiraldex G-TA*, γ–cyclodextrin TFA (30 m × 0.25 mm × 0.12 µm), 60 kPa H_2, 40 °C, 10 min, 10 °C/min, 160 °C, 10 min): 95% *ee*, t_R = **8.0 min** (*R*), 11.7 min (*S*) as oxidation / trifluoroacetylation product.

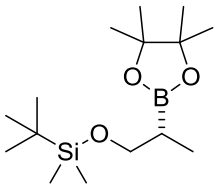
(*R*)-2-(6-Chlorohexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147c)



$C_{12}H_{24}BClO_2$ (246.58 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 3.54 (t, *J* = 6.8 Hz, 2H, ClC*H*$_2$), 1.75 (dt, *J* = 13.7, 6.8 Hz, 2H, ClCH$_2$C*H*$_2$), 1.50–1.37 (m, 3H, C*H*$_2$, C*H*), 1.32–1.24 (m, 2H, C*H*$_2$), 1.21 (s, 12H, C*H*$_3$-pin), 0.95–0.77 (m, 3H, C*H*$_3$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 83.4 (*C*CH$_3$-pin), 45.9 (Cl*C*H$_2$), 33.5 (*C*H$_2$), 33.0 (*C*H$_2$), 26.7 (*C*H$_2$), 25.12 (*C*H$_3$-pin), 25.08 (*C*H$_3$-pin), 15.8 (CH*C*H$_3$) ppm. **MS** (EI) *m/z* (%): 246 ([M]$^+$, 0.6), 233 (10), 231 (32), 162 (15), 160 (39), 146 (18), 131 (11), 118 (15), 105

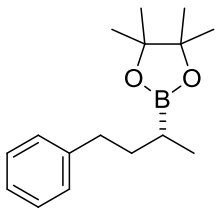
(16), 101 (13), 83 (66), 69 (47), 55 (72), 43 (100). **EA**: calc. (%) for $C_{12}H_{24}BClO_2$ C 58.45, H 9.81; found C 58.70, H 9.98. **IR**: $\tilde{\nu}$ = 2977 (s), 2930 (s), 2868 (m), 2361 (w), 2330 (w), 1463 (m), 1379 (s), 1314 (s), 1256 (w), 1217 (m), 1145 (s), 1110 (w), 967 (w), 858 (w), 688 (w), 649 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 16.0 min. **$[\alpha]_D^{20}$**: −5.2 (*c* = 1.20, CH_2Cl_2). **GC** (chiral, *Chiraldex G-TA*, γ–cyclodextrin TFA (30 m × 0.25 mm × 0.12 µm), 60 kPa H_2, 40 °C, 40 min, 10 °C/min, 160 °C, 10 min): 94% *ee*, t_R = 31.8 min (*R*), 34.3 min (*S*) as oxidation / trifluoroacetylation product.

(*R*)-*tert*-Butyldimethyl((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propoxy)silane (147d)



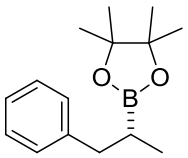
$C_{15}H_{33}BO_3Si$ (300.32 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.67 (dd, *J* = 9.5, 6.1 Hz, 1H, OC*H*$_2$), 3.60 (dd, *J* = 9.4, 7.4 Hz, 1H, OC*H*$_2$), 1.28–1.25 (m, 1H, C*H*), 1.23 (s, 12H, C*H*$_3$-pin), 0.97 (d, *J* = 7.4 Hz, 3H, CHC*H*$_3$), 0.88 (s, 9H, C C*H*$_3$), 0.06 (s, 6H, SiC*H*$_3$) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 83.1 (*C*CH$_3$-pin), 66.3 (O*C*H$_2$), 26.1 (C*C*H$_3$), 24.94 (*C*H$_3$-pin), 24.92 (*C*H$_3$-pin), 12.3 (CH*C*H$_3$), –5.2 (s, Si*C*H$_3$) ppm. **MS** (EI) *m/z* (%): 285 ([M-CH_3]$^+$, 2), 243 (54), 185 (10), 143 (23), 119 (29), 101 (35), 83 (100), 75 (18), 55 (10). **HRMS**: calc. (%) for [M-CH_3] 285.2052; found 285.2055. **IR**: $\tilde{\nu}$ = 2959 (m), 2928 (m), 2360 (w), 2328 (w), 1469 (w), 1460 (w), 1375 (w), 1318 (w), 1259 (s), 1217 (m), 1145 (w), 1090 (s), 1024 (s), 803 (m), 757 (s), 667 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 15.3 min. **GC** (chiral, *Macherey-Nagel* Hydrodex-ß-3P (25 m × 0.25 mm × 0.25 µm), 60 kPa H_2, 90 °C, 90 min, 10 °C/min, 180 °C, 10 min): 88% *ee*, t_R = 74.1 min (*S*), **78.7 min** (*R*). **$[\alpha]_D^{20}$**: −0.6 (*c* = 0.70, $CHCl_3$).

(*R*)-2-(4-Phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147e)



$C_{16}H_{25}BO_2$ (260.18 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.29–7.23 (m, 2H, H_{Ar}), 7.22–7.11 (m, 3H, H_{Ar}), 2.61 (t, J = 8.1 Hz, 2H, Ar-CH_2), 1.80–1.66 (m, 1H, CH_2), 1.62–1.49 (m, 1H, CH_2), 1.31–1.19 (m, 13H, CH, CH_3-pin), 1.06–0.94 (m, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 143.7 (C_{Ar}), 128.8 (HC_{Ar}), 128.5 (HC_{Ar}), 125.8 (HC_{Ar}), 83.2 (CCH$_3$-pin), 35.5 (CH$_2$), 35.4 (CH$_2$), 25.95 (CH$_3$-pin), 25.90 (CH$_3$-pin), 15.6 (CH$_3$) ppm. **MS** (EI) *m/z* (%): 260 ([M]$^+$, 12), 245 (5), 187 (7), 160 (5), 145 (5), 132 (100), 117 (14), 105 (11), 101 (30), 99 (22), 91 (45), 85 (69), 69 (15), 57 (18), 55 (13), 43 (12), 41 (11). **HRMS**: calc. (%) 260.1943; found 260.1948. **IR**: $\tilde{\nu}$ = 3025 (w), 2976 (m), 2925 (m), 2870 (w), 2854 (w), 1603 (w), 1496 (w), 1457 (m), 1382 (m), 1368 (s), 1314 (s), 1273 (w), 1213 (w), 1165 (m), 1143 (s), 1111 (w), 1010 (w), 967 (w), 861 (m), 847 (w), 746 (w), 699 (s), 670 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 20.0 min. **[α]$_D^{20}$**: −8.7 (c = 1.20, CH_2Cl_2). **GC** (chiral, *Chiraldex G-TA*, γ–cyclodextrin TFA (30 m × 0.25 mm × 0.12 µm), 60 kPa H_2, 75 °C, 0 min, 1 °C/min, 100 °C, 0 min, 10 °C/min, 160 °C, 10 min): 94% *ee*, t_R = **22.0 min** (*R*), 22.7 min (*S*) as oxidation / trifluoroacetylation product.

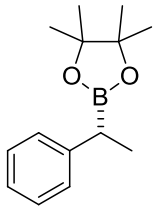
(*R*)-2-(1-Phenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147f)[141]



$C_{15}H_{23}BO_2$ (246.15 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.28–7.18 (m, 4H, H_{Ar}), 7.17–7.11 (m, 1H, H_{Ar}), 2.81 (dd, J = 13.6, 7.5 Hz, 1H, Ar-CH_2), 2.54 (dd, J = 13.6, 8.4 Hz, 1H, Ar-CH_2), 1.42–1.31 (m, 1H, CH), 1.19 (s, 6H, CH_3-pin), 1.18 (s, 6H, CH_3-pin), 0.97 (d, J = 7.4 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 142.5 (C_{Ar}), 129.0 (HC_{Ar}), 128.1 (HC_{Ar}), 125.7 (HC_{Ar}), 83.1 (CCH$_3$-pin), 39.1 (Ar-CH$_2$), 24.86 (s, CH$_3$-pin), 24.84 (s, CH$_3$-pin), 15.3 (CH$_3$) ppm. **MS** (EI) *m/z* (%): 246 ([M]$^+$, 5), 231 (8), 189 (16), 145 (29), 131 (15), 118 (34), 105 (21), 91 (67), 84 (100), 69 (11), 65 (11), 59 (11), 55 (14), 43 (30). **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 17.9 min. **HPLC** (chiral, Daicel Chiracel OD-H,

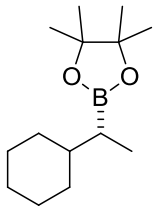
0.46 cm×25 cm, *n*-heptane, 0.5 mL/min, 25 °C): 94% *ee*, t_R = **22.8 min** (*R*), 26.2 min (*S*). $[\alpha]_D^{20}$: −2.1 (*c* = 0.71, $CHCl_3$).

(*R*)-2-(1-Phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147g)[158]



$C_{14}H_{21}BO_2$ (232.13 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.21–7.12 (m, 4H, H_{Ar}), 7.10–6.99 (m, 1H, H_{Ar}), 2.36 (q, *J* = 7.5 Hz, 1H, Ar-C*H*), 1.26 (d, *J* = 7.5 Hz, 3H, CH_3), 1.14 (s, 6H, CH_3-pin), 1.12 (s, 6H, CH_3-pin) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 145.1 (C_{Ar}), 128.4 (HC_{Ar}), 127.9 (HC_{Ar}), 125.2 (HC_{Ar}), 83.4 (*C*CH_3-pin), 24.76 (s, *C*H_3-pin), 24.72 (s, *C*H_3-pin), 17.2 (*C*H_3) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 16.1 min. **HPLC** (chiral, Daicel Chiracel OJ-H, 4.6 mm × 250 mm, *n*-heptane / *i*-propanol 99:1, 0.5 mL/min, 20 °C): 4% *ee*, t_R = 9.4 min (*R*), 11.0 min (*S*).

(*R*)-2-(1-Cyclohexylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (147h)[141]



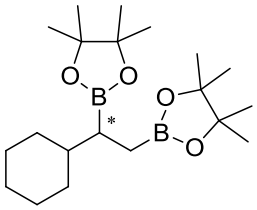
$C_{14}H_{27}BO_2$ (238.17 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.77–1.56 (m, 5H, C*H*B, C*H,* CH_2), 1.37–0.83 (m, 10H, CH_2, CH_3), 1.23 (m, 12H, CH_3-pin) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 82.9 (*C*CH_3-pin), 40.6 (*C*H), 32.9 (*C*H_2), 32.0 (*C*H_2), 26.92 (*C*H_2), 26.86 (2×*C*H_2), 24.97 (*C*H_3-pin), 24.88 (*C*H_3-pin), 12.7 (*C*H_3) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 5 min): t_R = 13.1 min. $[\alpha]_D^{20}$: −0.3 (*c* = 0.70, $CHCl_3$). **GC** (chiral, *Brechbühler SE54* ß-cyclodextrin DEtTButSil, (25 m × 0.25 mm × 0.25 µm) 100 kPa H_2, 50 °C, 0 min, 1 °C/min, 70 °C, 10 °C/min, 160 °C, 10 min): 33% *ee*, t_R = 15.3 min (*S*), 16.0 min (*R*) as oxidation / trifluoroacetylation product.

8.7.8 General Procedure R for Hydrogenation at Elevated Pressure

A 2 mL-glass vial was charged with a stirring bar, iridium catalyst (1.0 mol%) and substrate (25-200 µmol). The mixture was dissolved in DCM (0.2 M) and placed in an autoclave. The autoclave was then three times pressurized up to 50 bar with hydrogen and the pressure released. The reaction was performed under 50 bar H_2 atmosphere for a given time at RT. After releasing the hydrogen pressure the solvent was removed under reduced pressure or under a stream of nitrogen. The crude product was taken up in *n*-heptane (1 mL) and purified over a plug of silica (SiO_2, 0.5 cm × 1 cm, *n*-heptane/TBME 10:1) to obtain the hydrogenation product suitable for analysis.

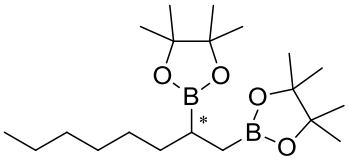
8.7.9 Analytical Data for the Hydrogenation Products Derived from Trisubstituted Boronic Esters

(+)-2,2'-(1-Cyclohexylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (150a)[159]



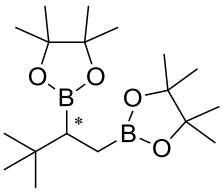
$C_{20}H_{38}B_2O_4$ (364.14 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.68–1.53 (m, 5H, C_6H_{11},), 1.37–1.27 (m, 1H, C*H*), 1.23 (s, 12H, pin-CH_3), 1.22 (s, 12H, pin-CH_3), 1.18–0.96 (m, 6H, C_6H_{11}), 0.86 (dd, *J* = 15.7, 11.1 Hz, 1H, CH_2B), 0.76 (dd, *J* = 15.7, 5.0 Hz, 1H, CH_2B) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 82.90 (*C*CH_3-pin), 82.87 (*C*CH_3-pin), 41.6 (*C*H), 32.3 (*C*H_2), 32.1 (*C*H_2), 27.03 (*C*H_2), 27.00 (*C*H_2), 26.88 (*C*H_2), 25.10 (*C*H_3-pin), 25.09 (*C*H_3-pin), 24.9 (*C*H_3-pin), 24.8 (*C*H_3-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 5 min): t_R = 25.9 min. **$[\alpha]_D^{20}$**: +3.0 (*c* = 0.90, $CHCl_3$). **GC** (chiral, *Varian* CP-Chiralsil-dex CB (25 m × 0.25 mm × 0.25 µm), 60 kPa H_2, 120 °C, 0 min, 0.1 °C/min, 142 °C, 0 min, 10 °C/min, 160 °C, 10 min): 95% *ee* , t_R = 204 min (+), 206 min (−) or *Chiraldex G-TA* γ–cyclodextrin TFA (30 m × 0.25 mm × 0.12 µm), 60 kPa H_2, 100 °C, 10 min, 10 °C/min, 160 °C, 10 min): t_R = **9.8 min** (+), 10.4 (−) as oxidation / trifluoroacetylation product.

(+)-2,2'-(Octane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (150b)



$C_{20}H_{40}B_2O_4$ (366.15 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.51–1.36 (m, 1H, C*H*), 1.35–1.04 (m, 10H, C_6H_{13}), 1.23 (s, 12H, pin-CH_3), 1.22 (s, 12H, pin-CH_3), 0.93–0.83 (m, 4H, CH_3, CH_2B), 0.76 (dd, *J* = 15.8, 5.9 Hz, 1H, CH_2B) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 82.94 (*C*CH_3-pin), 82.87 (*C*CH_3-pin), 34.0 (*C*H_2), 32.0 (*C*H_2), 29.7 (*C*H_2), 29.0 (*C*H_2), 25.06 (*C*H_3-pin), 24.99 (*C*H_3-pin), 24.92 (*C*H_3-pin), 24.89 (*C*H_3-pin), 22.8 (*C*H_2), 14.3 (*C*H_3) ppm. **MS** (EI) *m/z* (%): 351 ([M-CH_3]$^+$, 2), 307 (7), 225 (33), 183 (9), 127 (9), 113 (14), 101 (6), 84 (100), 69 (18), 55 (13), 41 (9). **EA**: calc. (%) for $C_{20}H_{40}B_2O_4$ C 65.61, H 11.01; found C 65.41; H, 10.78. **IR**: $\tilde{\nu}$ = 2977 (m), 2959 (w), 2923 (s), 2853 (w), 1466 (w), 1368 (m), 1334 (s), 1311 (s), 1267 (w), 1214 (w), 1163 (w), 1140 (s), 968 (m), 885 (w), 845 (w), 671 (w), 631 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 24.2 min. **[α]$_D^{20}$**: +0.9 (*c* = 0.93, $CHCl_3$). **GC** (chiral, *Chiraldex* γ–cyclodextrin TFA G-TA (30 m × 0.25 mm × 0.12 µm), 60 kPa H_2, 100 °C, 10 min, 10 °C/min, 160 °C, 10 min): t_R = **8.3 min** (+), 8.8 (−) as oxidation / trifluoroacetylation product.

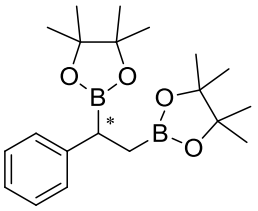
(+)-2,2'-(3,3-Dimethlybutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (150c)



$C_{18}H_{36}B_2O_4$ (338.10 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.25 (s, 12H, pin-CH_3), 1.22 (s, 6H, pin-CH_3), 1.21 (s, 6H, pin-CH_3), 0.96 (dd, *J* = 11.8, 4.5 Hz, 1H, C*H*B), 0.91 (s, 9H, CH_3), 0.86–0.74 (m, 2H, CH_2B) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 83.0 (*C*CH_3-pin), 82.8 (*C*CH_3-pin), 32.5 (*C*$(CH_3)_3$), 29.2 (C(*C*H_3)$_3$), 25.35 (*C*H_3-pin), 25.24 (*C*H_3-pin), 24.99 (*C*H_3-pin), 24.76 (*C*H_3-pin) ppm. **MS** (EI) *m/z* (%): 323 ([M-CH_3]$^+$, 4), 280 (11), 223 (15), 197 (75), 182 (78), 167 (16), 140 (16), 127 (6), 101 (10), 97 (8), 83 (100), 69 (29), 57 (19), 55 (27), 43 (13), 41 (20). **EA**: calc. (%) for $C_{18}H_{36}B_2O_4$ C 63.94, H 10.73; found C 63.94; H 10.60. **IR**: $\tilde{\nu}$ = 2976 (m), 2932 (w), 2886 (w), 1609 (w), 1267 (w), 1389 (m), 1368 (s), 1353 (s), 1305 (s), 1274 (w), 1237 (m), 1214 (w), 1191 (w), 1163 (m), 1139 (s), 1110 (m), 1095 (w), 1051 (w), 1007 (w), 967 (s), 919 (w), 879 (m), 846 (m), 835 (w), 815 (w), 769 (w), 691 (w), 673 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 20.5 min. **[α]$_D^{20}$**: +0.5 (*c* = 0.77, $CHCl_3$). **GC** (chiral, *Brechbühler SE54* ß-cyclodextrin

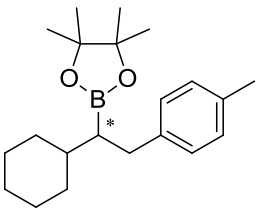
DEtTButSil (25 m × 0.25 mm × 0.25 µm), 100 kPa H_2, 50 °C, 0 min, 1 °C/min, 60 °C, 0 min, 10 °C/min, 180 °C, 10 min): 86% *ee*, t_R = 5.3 min (–), **7.0 min** (+) as oxidation / trifluoroacetylation product.

(+)-2,2'-(1-Phenylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (150d)[159]



$C_{20}H_{32}B_2O_4$ (358.09 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 4.4 Hz, 4H, H_{Ar}), 7.09 (h, *J* = 4.1 Hz, 1H, H_{Ar}), 2.52 (dd, *J* = 11.0, 5.7 Hz, 1H, Ar-C*H*), 1.38 (dd, *J* = 16.0, 11.0 Hz, 1H, CH_2), 1.20 (s, 12H, pin-CH_3), 1.19 (s, 6H, pin-CH_3), 1.17 (s, 6H, pin-CH_3), 1.11 (dd, *J* = 16.0, 5.7 Hz, 1H, CH_2) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 145.5 (C_{Ar}), 128.3 (HC_{Ar}), 128.0 (HC_{Ar}), 125.0 (HC_{Ar}), 83.3 (*C*CH_3-pin), 83.2 (*C*CH_3-pin), 25.1 (*C*H_3-pin), 24.84 (*C*H_3-pin), 24.81 (*C*H_3-pin), 24.6 (*C*H_3-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 26.9 min. **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane, 0.5 mL/min, 20 °C): 98% *ee*, t_R = 26.4 min (–), **32.4 min** (+). **$[\alpha]_D^{20}$**: +31.0 (*c* = 0.80, $CHCl_3$).

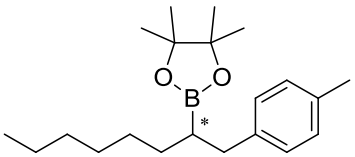
(–)-2-(1-Cyclohexyl-2-(*p*-tolyl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150e)



$C_{21}H_{33}BO_2$ (328.30 g/mol):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.11–7.08 (m, 2H, H_{Ar}), 7.03 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 2.74 (dd, *J* = 13.5, 6.2 Hz, 1H, Ar-CH_2), 2.61 (dd, *J* = 13.5, 10.7 Hz, 1H, Ar-CH_2), 2.29 (s, 3H, Ar-CH_3), 1.85–1.66 (m, 4H, C_6H_{11},), 1.64 (dddd, *J* = 12.4, 5.0, 3.1, 1.6 Hz, 1H, C*H*), 1.47–1.35 (m, 1H, C_6H_{11}), 1.32–1.10 (m, 4H, C_6H_{11}), 1.13 (s, 6H, pin-CH_3), 1.08 (s, 6H, pin-CH_3), 1.09–0.93 (m, 2H, C_6H_{11}) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$): δ = 139.7 (C_{Ar}), 134.9 (C_{Ar}), 128.9 (HC_{Ar}), 128.8 (HC_{Ar}), 83.0 (*C*CH_3-pin), 40.0 (*C*H), 34.7 (*C*H_2), 33.3 (*C*H_2), 32.4 (*C*H_2), 26.92 (*C*H_2), 26.91 (*C*H_2), 26.87 (*C*H_2), 24.99 (*C*H_3-pin), 24.96 (*C*H_3-pin), 21.1 (*C*H_3) ppm. **MS** (EI) *m/z* (%): 328 ([M]$^+$, 12), 271 (2), 223 (3), 200 (100), 179 (2), 167 (8), 165 (10), 145 (7), 143 (5), 131 (7), 118 (22), 105 (72), 101 (34), 91 (12), 84 (60), 79 (12), 69 (10), 57 (16), 55 (37), 41 (34). **HRMS**: calc. (%) 328.2569 found 328.2571. **IR**: $\tilde{\nu}$ = 3382 (br m), 3026

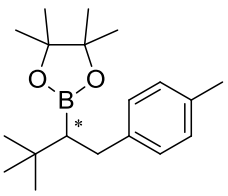
(w), 2977 (m), 2928 (w), 2862 (w), 2362 (w), 2335 (w), 1600 (w), 1497 (m), 1449 (m), 1236 (m), 1364 (s), 1326 (s), 1248 (w), 1213 (w), 1142 (s), 1105 (w), 1071 (w), 1028 (w), 971 (m), 910 (w), 852 (m), 789 (w), 734 (m), 700 (s), 671 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 28.2 min. **HPLC** (chiral, Daicel Chiracel OD-H, 4.6 mm × 250 mm, *n*-heptane, 0.5 mL/min, 20 °C): 97% *ee*, t_R = **11.0 min** (−), 13.9 min (+). **$[\alpha]_D^{20}$**: –8.8 (*c* = 0.76, $CHCl_3$).

(+)-2-(1-(*p*-Tolyl)octan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150f)



$C_{21}H_{35}BO_2$ (330.31 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.09 (d, *J* = 8.1 Hz, 2H, H_{Ar}), 7.04 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 2.68 (dd, *J* = 13.6, 8.3 Hz, 1H, Ar-CH_2), 2.60 (dd, *J* = 15.7, 7.2 Hz, 1H, Ar-CH_2), 2.29 (s, 3H, Ar-CH_3), 1.42–1.20 (m, 11H, C_5H_{10}, C*H*), 1.17 (s, 6H, pin-CH_3), 1.14 (s, 6H, pin-CH_3), 0.87 (t, *J* = 6.9 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 139.4 (C_{Ar}), 135.0 (C_{Ar}), 128.9 (HC_{Ar}), 128.8 (HC_{Ar}), 83.0 (*C*CH_3-pin), 37.0 (*C*H_2), 32.0 (*C*H_2), 31.2 (*C*H_2), 29.7 (*C*H_2), 29.3 (*C*H_2), 24.92 (*C*H_3-pin), 24.87 (*C*H_3-pin), 22.8 (*C*H_2), 14.2 (*C*H_3) ppm. **MS** (EI) *m/z* (%): 330 ($[M]^+$, 12), 315 (3), 273 (4), 229 (3), 202 (100), 159 (7), 145 (7), 131 (21), 118 (22), 105 (94), 101 (17), 91 (11), 84 (78), 79 (9), 69 (12), 57 (12), 55 (23), 43 (31), 41 (32). **EA**: calc. (%) for C 76.36, H 10.68; found C 76.08; H, 10.55. **IR**: $\tilde{\nu}$ = 2974 (m), 2951 (s), 2866 (m), 2362 (w), 2328 (w), 1514 (s), 1473 (w), 1370 (s), 1319 (s), 1239 (m), 1213 (w), 1142 (s), 1104 (w), 975 (w), 864 (w), 839 (w), 805 (w), 667 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 25.9 min. **HPLC** (chiral, Daicel Chiracel OD-H, 4.6 mm × 250 mm, *n*-heptane, 1.0 mL/min, 20 °C): 95% *ee*, t_R = 6.1 min (−), **9.2 min** (+). **$[\alpha]_D^{20}$**: +3.3 (*c* = 0.81, $CHCl_3$).

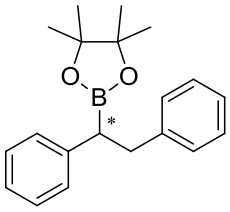
(–)-2-(3,3-Dimethyl-1-(*p*-tolyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150g)



$C_{19}H_{31}BO_2$ (302.26 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 8.0 Hz, 2H, H_{Ar}), 7.06 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 2.78 (dd, *J* = 13.1, 4.2 Hz, 1H, Ar-CH_2), 2.56 (t, *J* = 12.9 Hz, 1H, Ar-CH_2), 2.27 (s, 3H, Ar-CH_3), 1.29–1.22 (m, 1H, C*H*),

1.04 (d, J = 33.8 Hz, 12H, pin-CH_3), 1.02 (s, 9H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 137.1 (C_{Ar}), 134.9 (C_{Ar}), 129.1 (HC_{Ar}), 128.8 (HC_{Ar}), 82.9 (CCH$_3$-pin), 32.7 (CCH$_3$), 32.3 (ArCH$_2$), 29.8 (CCH$_3$), 25.2 (CH$_3$-pin), 24.7 (CH$_3$-pin), 21.3 (Ar-CH$_3$) ppm. **MS** (EI) *m/z* (%): 302 ([M]$^+$, 14), 287 (3), 245 (9), 231 (2), 201 (3), 189 (12), 174 (100), 159 (22), 145 (16), 131 (7), 128 (4), 118 (9), 105 (80), 101 (21), 97 (9), 84 (95), 77 (8), 69 (13), 57 (40), 55 (21), 43 (30), 41 (40). **EA**: calc. (%) for $C_{19}H_{31}BO_2$ 302.2417; found submitted. **IR**: $\tilde{\nu}$ = 2974 (m), 2951 (s), 2886 (m), 2361 (w), 2329 (w), 1514 (m), 1473 (w), 1370 (s), 1319 (s), 1239 (m), 1213 (w), 1142 (s), 1104 (w), 975 (w), 864 (w), 839 (w), 805 (m), 776 (w), 667 (w), 631 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 5 min): t_R = 21.8 min. **HPLC** (chiral, Daicel Chiracel OD-H, 4.6 mm × 250 mm, *n*-heptane, 1.0 mL/min, 20 °C): 96% *ee*, t_R = 4.3 min (+), **4.7 min** (−). **[α]$_D^{20}$**: – 26.8 (c = 0.80, $CHCl_3$).

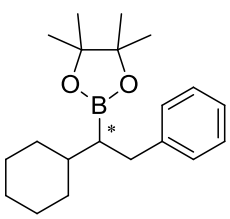
(−)-2-(1,2-Diphenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150h)[160]



$C_{20}H_{25}BO_2$ (308.22 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41–7.10 (m, 10H, H_{Ar}), 3.17 (dd, J = 13.5, 9.8 Hz, 1H, Ar-CH_2), 2.98 (dd, J = 13.6, 7.0 Hz, 1H, Ar-CH_2), 2.70 (dd, J = 9.8, 6.9 Hz, 1H, Ar-CH), 1.13 (s, 6H, pin-CH_3), 1.12 (s, 6H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 142.7 (C_{Ar}), 141.9 (C_{Ar}), 129.0 (HC_{Ar}), 128.5 (HC_{Ar}), 128.4 (HC_{Ar}), 128.2 (HC_{Ar}), 125.9 (HC_{Ar}), 125.5 (HC_{Ar}), 83.5 (CCH$_3$-pin), 39.0 (CH$_2$), 24.7 (s, CH$_3$-pin), 24.6 (s, CH$_3$-pin) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 27.2 min. **HPLC** (chiral, Daicel Chiracel OJ-H, 4.6 mm × 250 mm, *n*-heptane / *i*-propanol 99:1, 0.5 mL/min, 20 °C): 96% *ee*, t_R = 10.6 min (−), 15.0 min (+). **[α]$_D^{20}$**: −42.2 (c = 0.78, $CHCl_3$).

(−)-2-(1-Cyclohexyl-2-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (150i)

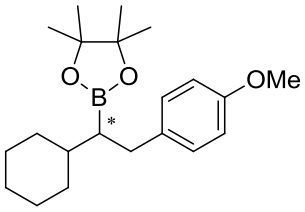


$C_{20}H_{31}BO_2$ (314.27 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.25–7.18 (m, 4H, H_{Ar}), 7.16–7.08 (m, 1H H_{Ar}), 2.80 (dd, J = 13.4, 6.1 Hz, 1H, Ar-CH_2), 2.63 (dd, J = 13.4,

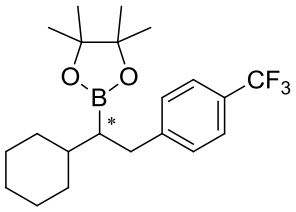
11.0 Hz, 1H, Ar-CH_2), 1.88–1.60 (m, 5H, C_6H_{11}), 1.48–1.37 (m, 1H, C*H*), 1.34–1.04 (m, 6H, C_6H_{11}), 1.11 (s, 6H, pin-CH_3), 1.06 (s, 6H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 142.9 (C_{Ar}), 129.1 (HC_{Ar}), 128.1 (HC_{Ar}), 125.6 (HC_{Ar}), 83.0 (CCH$_3$-pin), 40.1 (*C*H), 35.1 (*C*H$_2$), 33.3 (*C*H$_2$), 32.5 (*C*H$_2$), 26.92 (*C*H$_2$), 26.90 (*C*H$_2$), 26.87 (*C*H$_2$), 25.0 (*C*H$_3$-pin), 24.9 (*C*H$_3$-pin) ppm. **MS** (EI) *m/z* (%): 314 ([M]$^+$, 4), 299 (5), 257 (7), 223 (13), 186 (100), 179 (3), 167 (12), 145 (4), 131 (9), 129 (6), 123 (5), 117 (6), 109 (3), 104 (16), 101 (44), 95 (9), 91 (45), 84 (63), 81 (6), 69 (8), 67 (7), 65 (6), 57 (12), 55 (29), 43 (17), 41 (26). **EA**: calc. (%) for $C_{20}H_{31}BO_2$ C 76.44, H 9.94; found C 76.23, H 9.83. **IR**: $\tilde{\nu}$ = 2977 (m), 2920 (s), 2850 (m), 1602 (w), 1495 (w), 1447 (m), 1205 (w), 1379 (s), 1360 (m), 1315 (m), 1239 (m), 1213 (w), 1143 (s), 1107 (w), 1030 (w), 975 (w), 961 (w), 863 (w), 699 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 20 min): t_R = 26.7 min. **HPLC** (chiral, Daicel Chiracel IC, 4.6 mm × 250 mm, *n*-heptane, 0.75 mL/min, 20 °C): 99% *ee*, t_R = 10.0 min (+), **10.5 min** (−). **[α]$_D^{20}$**: −8.1 (*c* = 0.78, $CHCl_3$).

(−)-2-(1-Cyclohexyl-2-(4-methoxyphenyl)ethyl)--4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150j)



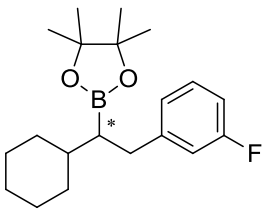
$C_{21}H_{33}BO_3$ (344.39 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.15–7.09 (m, 2H, H_{Ar}), 6.80–6.75 (m, 2H H_{Ar}), 3.76 (s, 3H, OCH_3), 2.73 (dd, *J* = 13.5, 6.1 Hz, 1H, Ar-CH_2), 2.58 (dd, *J* = 13.5, 10.9 Hz, 1H, Ar-CH_2), 1.85–1.59 (m, 5H, C_6H_{11}), 1.49–1.36 (m, 1H, C*H*), 1.29–0.99 (m, 6H, C_6H_{11}), 1.12 (s, 6H, pin-CH_3), 1.07 (s, 6H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 157.7 (C_{Ar}), 135.0 (C_{Ar}), 130.0 (HC_{Ar}), 113.6 (HC_{Ar}), 83.0 (CCH$_3$-pin), 55.4 (CH$_3$), 40.0 (*C*H), 34.2 (*C*H$_2$), 33.3 (*C*H$_2$), 32.4 (*C*H$_2$), 26.93 (*C*H$_2$), 26.92 (*C*H$_2$), 26.88 (*C*H$_2$), 25.01 (*C*H$_3$-pin), 24.97 (*C*H$_3$-pin) ppm. **MS** (EI) *m/z* (%): 344 ([M]$^+$, 12), 215 (17), 121 (100), 84 (6), 77 (5), 55 (11), 43 (7), 41 (12). **EA**: calc. (%) for $C_{21}H_{33}BO_3$ C 73.26; H 9.66; found C 73.32; H 9.56. **IR**: $\tilde{\nu}$ = 2974 (m), 2920 (s), 2849 (m), 1717 (w), 1609 (w), 1582 (w), 1510 (s), 1463 (w), 1447 (m), 1379 (m), 1259 (w), 1240 (s), 1215 (m), 1176 (m), 1165 (m), 1142 (s), 1101 (w), 1034 (m), 976 (w), 961 (w), 889 (w), 864 (w), 839 (m), 807 (w), 720 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 20 min): t_R = 33.2 min. **HPLC** (chiral, Daicel Chiracel OD-H, 4.6 mm × 250 mm, *n*-heptane, 0.5 mL/min, 20 °C): 97% *ee*, t_R = 23.0 min (+), **26.4 min** (−). **[α]$_D^{20}$**: −12.0 (*c* = 0.85, $CHCl_3$).

(−)-2-(1-Cyclohexyl-2-(4-(trifluoromethyl)phenyl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150k)



$C_{21}H_{30}BF_3O_2$ (382.27 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, J = 8.1 Hz, 2H, H_{Ar}), 7.31 (d, J = 8.0 Hz, 2H, H_{Ar}), 2.82 (dd, J = 13.5, 6.0 Hz, 1H, Ar-CH_2), 2.70 (dd, J = 13.4, 11.0 Hz, 1H, Ar-CH_2), 1.85–1.61 (m, 5H, C_6H_{11}), 1.48–1.36 (m, 1H, C*H*), 1.35–0.98 (m, 6H, C_6H_{11}), 1.11 (s, 6H, pin-CH_3), 1.06 (s, 6H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 147.3 (C_{Ar}), 129.4 (HC_{Ar}), 125.0 (q, J_{CF} = 3.7 Hz, HC_{Ar}), 83.2 (CCH$_3$-pin), 40.1 (*C*H), 35.0 (*C*H$_2$), 33.2 (*C*H$_2$), 32.4 (*C*H$_2$), 26.9 (*C*H$_2$), 26.8 (*C*H$_2$), 24.9 (s, *C*H$_3$-pin) ppm. **^{19}F{^{1}H}-NMR** (382 MHz, $CDCl_3$): −62.3 (s) ppm. **MS** (EI) *m/z* (%): 382 ([M]$^+$, 0.5), 367 ([M-CH$_3$]$^+$,9), 363 (7), 325 (29), 299 (4), 282 (3), 263 (8), 254 (5), 243 (5), 234 (14), 223 (7), 213 (7), 199 (5), 179 (6), 167 (14), 159 (31), 153 (6), 140 (11), 128 (15), 123 (7), 109 (8), 101 (44), 95 (10), 91 (4), 84 (100), 81 (7), 69 (11), 59 (12), 57 (16), 55 (41), 43 (25), 41 (34). **EA**: calc. (%) for $C_{21}H_{30}BF_3O_2$ C 65.98, H 7.91; found C 65.78; H 7.92. **IR**: $\tilde{\nu}$ = 2979 (w), 2923 (s), 2852 (m), 2361 (w), 2338 (w), 1617 (w), 1450 (w), 1415 (w), 1376 (m), 1323 (s), 1267 (w), 1240 (w), 1163 (m), 1142 (s), 1123 (s), 1068 (m), 1018 (w), 976 (w), 961 (w), 844 (w), 815 (w), 634 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 25.7 min. **$[\alpha]_D^{20}$**: −8.3 (c = 0.93, $CHCl_3$). **HPLC** (chiral, Daicel Chiracel AD-H, 4.6 mm × 250 mm, *n*-heptane / *i*-propanol 99:1, 0.5 mL/min, 20 °C): 98% *ee*, t_R = 19.8 min (+), 32.2 min (−) as oxidation product.

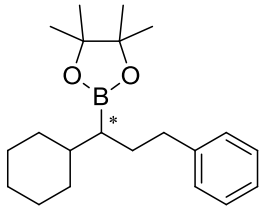
(−)-2-(1-Cyclohexyl-2-(3-fluorophenyl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150l)



$C_{20}H_{30}BFO_2$ (332.26 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.17 (td, J = 7.9, 6.2 Hz, 1H, H_{Ar}), 6.97 (d, J = 7.7 Hz, 1H, H_{Ar}), 6.94–6.88 (m, 1H, H_{Ar}), 6.81 (td, J = 8.3, 2.0 Hz, 1H, H_{Ar}), 2.77 (dd, J = 13.5, 6.0 Hz, 1H, Ar-CH_2), 2.64 (dd, J = 13.4, 11.0 Hz, 1H, Ar-CH_2), 1.84–1.60 (m, 5H, C_6H_{11}), 1.42 (dddd, J = 14.7, 11.5, 6.4, 3.2 Hz, 1H, C*H*), 1.33–1.00 (m, 6H, C_6H_{11}), 1.12 (s, 6H, pin-CH_3), 1.08 (s, 6H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 162.9 (d, J_{CF} = 245 Hz, FC_{Ar}),

145.7 (d, J_{CF} = 7.2 Hz, $C_{Ar\text{-}m\text{-}F}$), 129.5 (d, J_{CF} = 8.3 Hz, $HC_{Ar\text{-}m\text{-}F}$), 124.7 (d, J_{CF} = 2.7 Hz, $HC_{Ar\text{-}p\text{-}F}$), 115.9 (d, J_{CF} = 20.7 Hz, $HC_{Ar\text{-}o\text{-}F}$), 112.4 (d, J_{CF} = 21.1 Hz, $HC_{Ar\text{-}o\text{-}F}$), 83.2 ($CCH_3$-pin), 40.1 (*C*H), 35.0 (d, J_{CF} = 1.1 Hz, Ar-CH_2), 33.2 (CH_2), 32.4 (CH_2), 26.90 (CH_2), 26.85 (CH_2), 24.99 (s, CH_3-pin), 24.95 (s, CH_3-pin) ppm. **^{19}F{^{1}H}-NMR** (382 MHz, $CDCl_3$): −114.6 (s) ppm. **MS** (EI) *m/z* (%): 332 ($[M]^+$, 3), 317 (10), 275 (39), 179 (12), 167 (18), 149 (7), 141 (6), 137 (5), 135 (5), 128 (14), 123 (16), 110 (72), 101 (79), 95 (15), 84 (100), 69 (13), 57 (19), 55 (32), 43 (13), 41 (19). **EA**: calc. (%) for $C_{20}H_{30}BFO_2$ C 72.30, H 9.10; found C 72.11, H 9.08. **IR**: $\tilde{\nu}$ = 2978 (m), 2922 (s), 2851 (m), 2360 (w), 2335 (w), 1615 (w), 1588 (m), 1487 (m), 1447 (m), 1404 (w), 1376 (s), 1360 (m), 1315 (m), 1285 (w), 1268 (w), 1239 (m), 1215 (m), 1165 (w), 1142 (s), 1106 (w), 1070 (w), 977 (w), 960 (w), 945 (w), 887 (w), 858 (m), 779 (w), 756 (s), 688 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 26.6 min. **HPLC** (chiral, Daicel Chiracel OD-H, 4.6 mm × 250 mm, *n*-heptane / *i*-propanol 95:5, 0.5 mL/min, 20 °C): 98% *ee*, t_R = 10.4 min (+), **12.2 min** (−) as oxidation product. **$[\alpha]_D^{20}$**: −6.5 (*c* = 0.79, $CHCl_3$).

(−)-2-(1-Cyclohexyl-3-phenylpropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150m)

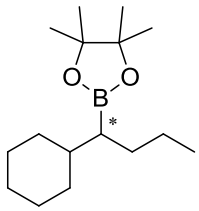


$C_{21}H_{33}BO_2$ (328.30 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.30–7.23 (m, 2H, H_{Ar}), 7.21–7.12 (m, 3H, H_{Ar}), 2.63 (ddd, *J* = 13.5, 10.8, 5.3 Hz, 1H, Ar-CH_2), 2.60 (ddd, *J* = 13.5, 10.5, 6.3 Hz, 1H, Ar-CH_2), 1.81–1.59 (m, 7H, C_6H_{11}), 1.46–1.37 (m, 1H, CH_2), 1.33–1.00 (m, 6H, C_6H_{11}), 1.28 (s, 12H, pin-CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 143.4 (C_{Ar}), 128.5 (HC_{Ar}), 128.3 (HC_{Ar}), 125.7 (HC_{Ar}), 83.0 (CCH_3-pin), 39.8 (*C*H), 36.2 (CH_2), 33.0 (CH_2), 32.6 (CH_2), 31.2 (CH_2), 26.95 (CH_2), 26.93 (CH_2), 26.90 (CH_2), 25.3 (CH_3-pin), 25.0 (CH_3-pin) ppm. **MS** (EI) *m/z* (%): 328 ($[M]^+$, 8), 237 (4), 200 (100), 153 (4), 145 (6), 140 (6), 137 (8), 131 (6), 129 (7), 117 (23), 109 (29), 104 (56), 101 (46), 95 (9), 91 (39), 85 (98), 81 (9), 79 (5), 69 (14), 67 (13), 57 (8), 55 (30), 43 (12), 41 (16). **EA**: calc. (%) for $C_{21}H_{33}BO_2$ C 76.83, H 10.13; found C 76.67, H 10.21. **IR**: $\tilde{\nu}$ = 2976 (w), 2922 (s), 2850 (m), 1495 (w), 1448 (m), 1386 (m), 1370 (w), 1355 (m), 1310 (s), 1268 (w), 1273 (w), 1223 (s), 1213 (m), 1167 (w), 1139 (s), 1105 (w), 1029 (w), 967 (m), 960 (m), 906 (w), 888 (w), 864 (s), 843 (m), 770 (m), 732 (s), 724 (s), 697 (s), 671 (m) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He,

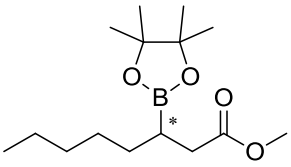
100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 29.2 min. **HPLC** (chiral, Daicel Chiracel OD-H, 4.6 mm × 250 mm, *n*-heptane, 0.2 mL/min, 20 °C): 96% *ee*, t_R = **29.6 min** (−), 32.3 min (+). **[α]$_D^{20}$**: −1.1 (*c* = 0.80, $CHCl_3$).

(+)-2-(1-Cyclohexylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (150n)



$C_{16}H_{31}BO_2$ (266.23 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.83–1.52 (m, 5H, C_6H_{11}), 1.48–1.08 (m, 8H, C_6H_{11}, C_3H_7), 1.25 (s, 12H, pin-CH_3), 1.08–0.92 (m, 2H, C_4H_8), 0.91–0.80 (m, 4H, C_4H_8) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 82.9 (CCH$_3$-pin), 39.9 (*C*H), 33.1 (CH_2), 32.7 (CH_2), 31.3 (CH_2), 29.7 (CH_2), 26.99 (CH_2), 26.96 (CH_2), 25.1 (CH_3-pin), 25.0 (CH_3-pin), 23.0 (CH_2), 14.7 (CH_3) ppm. **MS** (EI) *m/z* (%): 266 ([M]$^+$, 2), 251 (13), 209 (11), 181 (5), 165 (8), 155 (7), 138 (24), 129 (65), 123 (8), 110 (8), 101 (43), 97 (36), 84 (100), 69 (19), 67 (16), 57 (9), 55 (36), 43 (17), 41 (20). **HRMS**: calc. (%) 266.2412; found 266.2412. **IR**: $\tilde{\nu}$ = 2967 (m), 2921 (s), 2952 (s), 2359 (w), 2332 (w), 1454 (w), 1377 (s), 1312 (m), 1243 (w), 1146 (s), 968 (w), 891 (w), 860 (w), 627 (w) cm^{-1}. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 18.0 min. **[α]$_D^{20}$**: +0.5, (*c* = 0.60, $CHCl_3$). **GC** (chiral, *Brechbühler SE54* ß-cyclodextrin DEtTButSil (25 m × 0.25 mm × 0.25 µm), 100 kPa H_2, 80 °C, 0 min, 0.25 °C/min, 100 °C, 10 °C/min, 180 °C, 10 min): 97% *ee*, t_R = 107 min (−), **110 min** (+).

(*R*)-Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octanoate (150p) [64]

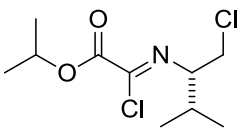


$C_{15}H_{29}BO_4$ (284.20 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.64 (m, 3H, OCH_3), 2.48–2.33 (m, 2H, CH_2CO), 1.49–1.38 (m, 1H, C*H*), 1.36–1.26 (m, 8H, CH_2), 1.24 (s, 6H, pin-CH_3), 1.23 (s, 6H, pin-CH_3), 0.86 (t, *J* = 6.8 Hz, 3H, CH_3) ppm. **GC** (*Restek* Rtx®-1701 (30 m × 0.25 mm × 0.25 µm), 60 kPa He, 100 °C, 2 min, 10 °C/min, 250 °C, 10 min): t_R = 16.3 min, 17.2 min (**146p**). **GC** (chiral, Varian CP-Sil 88 (25 m × 0.25 mm × 0.25 µm), 60 kPa H_2, 110 °C, 80 min, 10 °C/min, 160 °C, 5 min):, 90% *ee*, t_R = 75.2 min (*R*), 77.5 min (*S*).

8.8 P-Alkyl SimplePHIM Derived Ir-Complexes and Modification of SimplePHOX Derived Ir- Complexes for Asymmetric Hydrogenation

8.8.1 Formation of Ligand Precursorsors

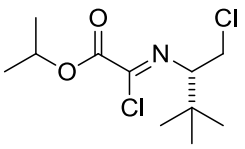
(*S*,*Z*)-*iso*-Propyl 2-chloro-2-((1-chloro-3-methylbutan-2-yl)imino)acetate ((*S*)-169a)



DMF (12 µL, 11.3 mg, 155 µmol, 0.025 eq.) was added to a solution of (*S*)-isopropyl 2-((1-hydroxy-3-methylbutan-2-yl)amino)-2-oxoacetate (1.33 g, 6.12 mmol, 1.0 eq.) in thionyl chloride (3.6 mL, 5.90 g, 49.6 mmol, 8.1 eq.). The reaction mixture was stirred at 85 °C for 6 hours. After removing the excess of thionyl chlorid in *vacuo*, the crude product was purified by *Kugelrohr* distillation (140–150 °C, 0.3mbar) to obtain the title compound (*S*)-**169a** as a colorless oil (1.17 g, 4.60 mmol, 75%). The analytical data match the reported values.[147a]

$C_{10}H_{17}ClNO_2$ (254.15 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.17 (p, *J* = 6.3 Hz, 1H, OC*H*), 3.94 (ddd, *J* = 8.3, 6.1, 4.0 Hz, 1H, CH_2Cl), 3.81–3.59 (m, 2H CC*H*N, CH_2Cl), 2.07 (dq, *J* = 13.8, 6.8 Hz, 1H, C*H*(CH_3)$_2$), 1.37 (dd, *J* = 6.3, 0.8 Hz, 6H, OCH(CH_3)$_2$), 0.95 (dd, *J* = 10.4, 6.8 Hz, 6H, (CH(CH_3)$_2$) ppm. **MS** (EI) *m/z* (%): 218 ([M-Cl]$^+$, 3), 211 (13), 176 (35), 168 (32), 134 (22), 105 (26), 91 (11), 69 (99), 54 (10), 43 (100). **b.p.**: 140–150 °C (0.3 mbar), lit. 100 °C (0.15 mbar).[147a]

(*S*,*Z*)-*iso*-Propyl 2-chloro-2-((1-chloro-3,3-dimethylbutan-2-yl)imino)acetate ((*S*)-169b)

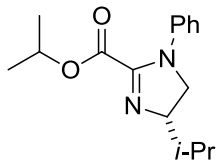


DMF (8 µL, 7.58 mg, 104 µmol, 0.025 eq.) was added to a solution of (*S*)-isopropyl 2-((1-hydroxy-3,3-dimethylbutan-2-yl)amino)-2-oxo-acetate (960 mg, 4.15 mmol, 1.0 eq.) in thionyl chloride (2.4 mL, 3.95 g, 33.2 mmol, 8.0 eq.). The reaction mixture was stirred at 85 °C for 16 hours. After removing the excess of thionyl chlorid in *vacuo*, the crude product was purified by *Kugelrohr* distillation (100–105 °C, 0.15 mbar) to obtain the title compound (*S*)-**169b** as a slightly yellow oil (1.03 g, 3.84 mmol, 93%). The analytical data match the reported values.[147a]

$C_{11}H_{19}ClNO_2$ (268.18 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 5.27–5.09 (m, 1H, OC*H*), 3.88 (ddd, *J* = 19.1, 10.5, 2.1 Hz, 2H, CH_2Cl), 3.73–3.59 (m, 1H CC*H*N), 1.37 (dd, *J* = 6.2, 3.1 Hz, 6H, CH(CH_3)$_2$), 0.97 (s, 9H, (CH_3)$_3$C) ppm. **GC** (Me_2Si, 100 °C, 2 min, 10 °C/min, 270 °C, 10 min): 9.92 min. **MS** (EI) *m/z* (%): 267 ([M]$^+$, 0.3), 225 (10), 169 (78), 134 (87), 88 (12), 83 (36), 69 (14), 57 (84), 43 (100). **b.p.**: 100–105 °C (0.15 mbar), lit. 100 °C (0.15 mbar).[147a]

(*S*)-*iso*-Propyl 4-(*iso*-propyl)-1-phenyl-4,5-dihydro-1*H*-imidazole-2-carboxylate ((*S*)-170a)

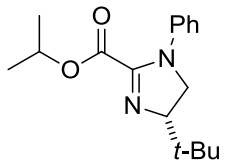


A solution of aniline (0.6 mL, 0.613 g, 6.58 mmol, 1.4 eq.) in toluene (3.0 mL) was added to solution of (*S*)-**169a** (1.17 g, 4.62 mmol, 1.0 eq.) and triethylamine (4.2 mL, 3.04 g, 30.0 mmol, 6.5 eq.) in toluene (12 mL). The clear reaction mixture was stirred at 120 °C for 15 hours. After cooling down to rt the reaction mixture was extracted with 1M aq. KOH solution (2×10 mL) and combined aqueous layers were washed with toluene (2×20 mL). After drying over $MgSO_4$, the solvent was removed under reduced pressure. The crude product was purified by *Kugelrohr* distillation (140–145 °C / 0.3 mbar) to obtain the title compound (*S*)-**170a** as a slightly yellow oil (833 mg, 3.04 mmol, 66%). The analytical data match the reported values.[147a]

$C_{16}H_{22}N_2O_2$ (274.36 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.30–7.21 (m, 2H, H_{Ar}), 7.07 (t, *J* = 7.4 Hz, 1H, H_{Ar}), 6.93 (d, *J* = 7.6 Hz, 2H, H_{Ar}), 5.08 (hept, *J* = 6.3 Hz, 1H, OC*H*), 4.03 (ddd, *J* = 10.5, 9.2, 6.4 Hz, 1H, CH_2N), 3.90 (dd, *J* = 10.6, 9.2 Hz, 1H, CH_2N), 3.57 (t, *J* = 9.1 Hz, 1H, C*H*N), 1.96–1.83 (m, 1H, C*H*(CH_3)$_2$), 1.15 (dd, *J* = 12.9, 6.3 Hz, 6H, OCH(CH_3)$_2$), 1.02 (d, *J* = 6.7 Hz, 3H, CH_3), 0.91 (d, *J* = 6.8 Hz, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 161.0 (*C*=O), 154.3 (*C*=N), 141.5 (C_{Ar}), 129.2 (HC_{Ar}), 124.5 (HC_{Ar}), 121.1 (HC_{Ar}), 71.7 (N*C*H), 70.5 (O*C*H), 55.0 (*C*H$_2$), 33.0 (*C*H(CH$_3$)$_2$), 21.5 (OCH(*C*H$_3$)$_2$), 21.4 (OCH(*C*H$_3$)$_2$), 19.2 (*C*H$_3$), 18.2 (*C*H$_3$) ppm. **MS** (EI) *m/z* (%): 274 ([M]$^+$, 15), 231 (68), 189 (46), 171 (100), 145 (13), 118 (14), 77 (17), 43 (13). **b.p.**: 140–145 °C (0.2 mbar).

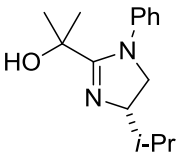
(*S*)-*iso*-Propyl 4-(*tert*-butyl)-1-phenyl-4,5-dihydro-1*H*-imidazole-2-carboxylate ((*S*)-170b)



A solution of aniline (0.45 mL, 0.46 g, 4.93 mmol, 1.3 eq.) in toluene (2.0 mL) was added to solution of (*S*)-**169b** (1.03 g, 3.84 mmol, 1.0 eq.) and triethylamine (3.5 mL, 2.53 g, 25.0 mmol, 6.5 eq.) in toluene (10 mL). The clear reaction mixture was stirred at 110 °C for 14 hours. After cooling down to rt the reaction mixture was extracted with KOH 1 M aq. solution (2×6 mL) and combined aqueous layers were washed with toluene (2×20 mL). After drying over $MgSO_4$, the solvent was removed under reduced pressure. The crude product was purified by *Kugelrohr* distillation (140–145 °C / 0.2 mbar) to obtain the title compound (*S*)-**170b** as a slightly yellow oil (345 mg, 1.20 mmol, 31%). The analytical data match the reported values.[147a]

$C_{17}H_{24}N_2O_2$ (288.38 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 2H, H_{Ar}), 7.12–7.06 (m, 1H, H_{Ar}), 6.99–6.94 (m, 2H, H_{Ar}), 5.10 (hept, *J* = 6.3 Hz, 1H, OC*H*), 4.01 (dd, *J* = 11.0, 9.0 Hz, 1H, CH_2N), 3.89 (dd, *J* = 11.0, 9.3 Hz, 1H, CH_2N), 3.66 (t, *J* = 9.2 Hz, 1H, CC*H*N), 1.16 (dd, *J* = 18.7, 6.3 Hz, 6H, CH(CH_3)$_2$), 0.97 (s, 9H, (CH_3)$_3$C) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 161.2 (*C*=O), 154.3 (*C*=N), 141.6 (C_{Ar}), 129.2 (HC_{Ar}), 124.4 (HC_{Ar}), 121.0 (HC_{Ar}), 75.2 (N*C*H), 70.4 (O*C*H), 53.5 (*C*H_2), 34.3 (*C*(CH$_3$)$_3$), 26.1 (C(*C*H$_3$)$_3$), 21.5 (OCH(*C*H$_3$)$_2$), 21.4 (OCH(*C*H$_3$)$_2$) ppm. **MS** (EI) *m/z* (%): 267 ([M]$^+$, 0.3), 225 (10), 169 (78), 134 (87), 88 (12), 83 (36), 69 (14), 57 (84), 43 (100). **b.p.**: 130–135 °C (0.2 mbar).

(*S*)-2-4-(*iso*-Propyl)-1-phenyl-4,5-dihydro-1*H*-imidazol-2-yl)propan-2-ol ((*S*)-171b)



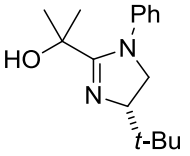
A methylmagnesium bromide 3 M solution in diethyl ether (1.0 mL, 3.00 mmol, 2.8 eq.) was slowly added to a solution of (*S*)-**171a** (295 mg, 1.08 mmol, 1.0 eq.) in diethyl ether (12 mL) at −78 °C. The reaction mixture was slowly allowed to reach rt and stirred for additional 15 hours. NH_4Cl-aq. sat. solution (10 mL) was added under ice bath control. After warming to RT; the layers were separated and the aqueous phase was washed with TBME (2×10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure

to obtain the title compound (*S*)-**171b** without further purification (257 mg, 1.04 mmol, 97%). The analytical data match the reported values.[147a]

$C_{15}H_{22}N_2O$ (246.35 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41–7.35 (m, 2H, H_{Ar}), 7.34–7.27 (m, 1H, H_{Ar}), 7.28–7.20 (m, 2H, H_{Ar}), 4.88 (br s, 1H, O*H*), 3.95–3.79 (m, 2H, CH_2N), 3.59 (t, *J* = 8.0 Hz, 1H, C*H*), 1.89–1.70 (m, 1H, C*H*$(CH_3)_2$), 1.20 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.02 (d, *J* = 6.7 Hz, 3H, CHCH_3), 0.91 (d, *J* = 6.8 Hz, 3H, CHCH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.4 (*C*=N), 142.9 (C_{Ar}), 129.5 (HC_{Ar}), 129.2 (HC_{Ar}), 127.8 (HC_{Ar}), 69.5 (*C*OH), 68.5 (N*C*H), 61.4 (*C*H_2N), 33.4 (*C*H$(CH_3)_2$), 29.3 (C(*C*$H_3)_2$), 28.9 (C(*C*$H_3)_2$), 18.8 (*C*H_3), 18.2 (*C*H_3) ppm.

(*S*)-2-4-(*tert*-Butyl)-1-phenyl-4,5-dihydro-1*H*-imidazol-2-yl)propan-2-ol (171a)

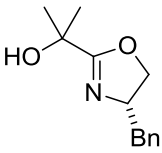


A methylmagnesium bromide 3 M solution in diethyl ether (1.3 mL, 3.90 mmol, 3.40 eq.) was slowly added to a solution of (*S*)-**171b** (335 mg, 1.16 mmol, 1.0 eq.) in diethyl ether (13 mL) at −78 °C. The reaction mixture was slowly allowed to reach rt and stirred for additional 15 hours. NH_4Cl-aq. sat. solution (10 mL) was added under ice bath control. After warming to rt, the layers were separated and the aqueous phase was washed with TBME (2×10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to obtain the title compound (*S*)-**171a** without further purification (303 mg, 1.16 mmol, quant.). The analytical data match the reported values.[147a]

$C_{16}H_{24}N_2O$ (260.37 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41–7.35 (m, 2H, H_{Ar}), 7.33–7.28 (m, 1H, H_{Ar}), 7.25–7.21 (m, 2H, H_{Ar}), 5.08 (br s, 1H, O*H*), 3.88 (dd, *J* = 10.6, 8.7 Hz, 1H, CH_2N), 3.78 (dd, *J* = 8.6, 7.8 Hz, 1H, CH_2N), 3.68 (dd, *J* = 10.6, 8.7 Hz, 1H, CC*H*N), 1.20 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 0.95 (s, 9H, (C$H_3)_3$C) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 170.3 (*C*=N), 142.8 (C_{Ar}), 129.5 (HC_{Ar}), 129.3 (HC_{Ar}), 127.9 (HC_{Ar}), 71.5 (N*C*H), 69.4 (*C*OH), 60.1 (*C*H_2N), 34.4 (*C*$(CH_3)_3$), 29.5 (C(*C*$H_3)_2$), 28.7 (C(*C*$H_3)_2$), 25.9 (C(*C*$H_3)_3$), 22.3 (*C*H_3) ppm. **MS** (FAB NBA) *m/z* (%): 261 ([M+H]$^+$, 100), 203 (20), 145 (7), 106 (6).

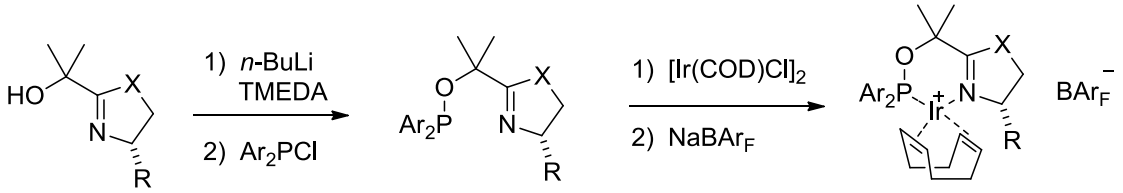
(*S*)-2-4-(Benzyl)-4,5-dihydrooxazol-2-yl)propan-2-ol ((*S*)-173d)



A mixture of 2-hydroxyisobutyric acid (2.60 g, 25.0 mmol, 1.0 eq.) and (*S*)-phenylalaninol (3.97 g, 26.3 mmol, 1.05 eq.) in mesytelene (50 mL) was stirred using a Dean-Stark at 170 °C for 16 h. After cooling down to RT, the reaction mixture was washed with NH_4Cl aq. sat. solution (100 mL) and brine (100 mL). After drying over $MgSO_4$, and filtration, the solvent was removed under reduce pressure. Purification by flash chromatography (SiO_2, 3 cm × 15 cm, ethyl acetate / cyclohexane 1:1) gave the title compound (*S*)-**173d** as a colorless oil (1.53 g, 6.98 mmol, 28%).

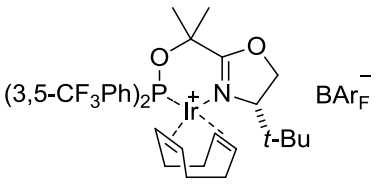
$C_{13}H_{17}NO_2$ (219.28 g/mol):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.33–7.27 (m, 2H, H_{Ar}), 7.25–7.17 (m, 3H, H_{Ar}), 4.48–4.36 (m, 1H, NC*H*), 4.30 (dd, *J* = 9.3, 8.5 Hz, 1H, CH_2O), 4.10 (dd, *J* = 8.4, 7.9 Hz, 1H, CH_2O), 3.28 (br s, 1H, O*H*), 3.06 (dd, *J* = 13.8, 5.1 Hz, 2H, CH_2), 2.71 (dd, *J* = 13.8, 7.9 Hz, 2H, CH_2), 1.42 (s, 3H, CH_3), 1.39 (s, 3H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$): δ = 173.0 (*C*=N), 137.6 (C_{Ar}), 129.6 (HC_{Ar}), 128.7 (HC_{Ar}), 126.7 (HC_{Ar}), 72.4 (N*C*H), 69.0 (*C*OH), 66.8 (*C*H_2O), 41.6 (*C*H_2), 28.0 (*C*H_3), 27.8 (*C*H_3) ppm. **MS** (FAB NBA) *m/z* (%): 220 ([M-H]$^+$, 100), 191 (11). **EA**: calc. (%) C 71.21; H 7.81; N 6.39; found C 70.32, H 8.20, N 6.74. **[α]$_D^{20}$**: −20.8 (*c* = 1.00, $CHCl_3$). **TLC** (SiO_2, cyclohexane / ethyl acetate 1:1): R_f = 0.23.

8.8.2 Formation of the *P*-Aryl Ligands and Their Complexes



General Procedure Q (Formation of P-Aryl Ligands): A 1.6 M solution of *n*-BuLi (1.3 eq.) and TMEDA (1.3 eq.) were added to a solution of the tertiary alcohol (1.0 eq.) in *n*-pentane (0.1 M) at −78 °C. After removing the cooling bath, the reaction mixture was stirred for 1 h at rt. Afterwards arylchlorophosphine (1.3 eq.) was added at 0 °C. The reaction mixture was stirred at rt, while the reaction progress was analyzed by ^{31}P-NMR. After reaching full conversion the solvent was removed in *vacuo*. The obtained crude product was purified by flash chromatography under inert conditions (degassed solvents). The obtained N,P ligand was converted to the corresponding iridium complex following general procedure **G**.

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-{2-(4-*tert*-butyl)-4,5-dihydro-oxazole-2-yl)-2-bis(3,5(trifluoromethyl)phenyl)phosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-26d)

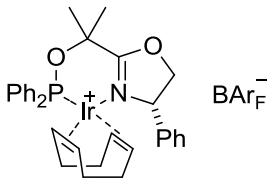


The intermediate ligand (*S*)-**174d** was obtained following general procedure **Q** for using (*S*)-2-(4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)propan-2-ol (79.4 mg, 428 µmol, 1.0 eq.), *n*-pentane (5 mL), TMEDA (85 µL, 65.5 mg, 563 µmol, 1.3 eq.), *n*-BuLi (0.35 mL, 560 µmol, 1.3 eq.), and bis(3,5-di(trifluoromethyl)phenyl)-chlorophosphine (276 mg, 560 µmol, 1.3 eq.). After stirring for 16 hours at rt and purification by flash chromatography (SiO_2, 1.5 cm × 15 cm, *n*-pentane / TBME 20:1) the N,P ligand (*S*)-**174d** was obtained as a colorless oil (107 mg, 167 µmol, 39%). Subsequent complexation following general procedure **G** using $[Ir(COD)Cl]_2$ (56.0 mg, 83.4 µmol, 0.5 eq.), DCM (5.0 mL) and $NaBAr_F$ (177 mg, 200 µmol, 1.2 eq.) gave the title compound (*S*)-**26d** after purification by flash chromatography (SiO_2, 1.5 cm × 18 cm) and recrystallization from dethyl ether (1.0 mL) and *n*-pentane (25 mL) as an orange solid (202 mg, 112 µmol, 26% over two steps).

$^{31}P\{^{1}H\}$-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.
$^{31}P\{^{1}H\}$-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 83.3 (p, J_{FP} = 6.0 Hz) ppm.

$C_{66}H_{48}BF_{36}IrNO_2P$ (1805.04 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 8.30 (d, *J* = 11.5 Hz, 2H, H_{Ar}), 8.15 (d, *J* = 43.1 Hz, 2H, H_{Ar}), 7.76 ((s, 8H, BAr_F-*H*), 7.64 (d, *J* = 11.1 Hz, 2H, H_{Ar}), 7.59 (s, 4H, BAr_F-*H*), 5.59–5.51 (m, 1H, C*H* COD), 5.35–5.26 (m, 1H, C*H* COD), 4.71 (dd, *J* = 10.2, 3.7 Hz, 1H, CH_2), 4.48 (t, *J* = 9.9 Hz, 1H, C*H*), 3.90 (dd, *J* = 9.5, 3.7 Hz, 1H, CH_2), 3.85–3.74 (m, 1H, C*H* COD), 2.78 (dd, J = 15.9, 7.9 Hz, 1H, CH_2 COD), 2.72–2.50 (m, 3H, C*H* COD, CH_2 COD), 2.43 (s, 3H, CH_3), 2.40–2.31 (m, 1H, CH_2 COD), 2.28–2.15 (m, 1H, CH_2 COD), 2.10–1.89 (m, 2H, CH_2 COD), 1.85 (d, *J* = 1.4 Hz, 3H, CH_3), 1.78–1.64 (m, 1H, CH_2 COD), 0.66 (s, 9H, (CH_3)$_3$C) ppm. **$^{31}P\{^{1}H\}$-NMR** (162 MHz, CD_2Cl_2): δ = 96.6 (s) ppm. **$^{19}F\{^{1}H\}$-NMR** (377 MHz, CD_2Cl_2): −63.2 (s, CF_3 BAr_F), −64.0 (d, J_{FP} = 32.5 Hz, CF_3) ppm. **MS**: (FAB NBA) *m/z* (%): 942 ([Ir(L)(COD)]$^+$, 100), 466 (10), 168 (66). **m.p.**: 160–161 °C. **$[\alpha]_D^{20}$**: –24.3 (*c* = 1.03, $CHCl_3$).

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-{2-(4-phenyl)-4,5-dihydro-oxazole-2-yl)-2-diphenylphosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-26h)

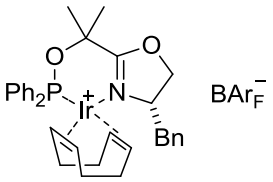


The intermediate ligand (*S*)-**174h** was obtained following general procedure **Q** using (*S*)-2-(4-phenyl-4,5-dihydrooxazol-2-yl)propan-2-ol (87.9 mg, 428 µmol, 1.0 eq.), *n*-pentane (5 mL), TMEDA (84 µL, 64.7 mg, 557 µmol, 1.3 eq.), *n*-BuLi (0.35 mL, 560 µmol, 1.3 eq.), and diphenylchlorophosphine (100 µL, 123 mg, 557 µmol, 1.3 eq.). After stirring for 5 hours at rt and purification by flash chromatography (SiO_2, 1.5 cm × 15 cm, *n*-pentane / TBME 10:1) the N,P ligand (*S*)-**174h** (14 mg, 35.9 µmol, 8%) was obtained as a colorless oil. Subsequent complexation following general procedure **G** using $[Ir(COD)Cl]_2$ (13.2 mg, 19.7 µmol, 0.5 eq.), DCM (1.0 mL) and $NaBAr_F$ (38.2 mg, 43.1 µmol, 1.2 eq.) gave the title compound (*S*)-**26h** after purification by flash chromatography (SiO_2, 1.5 cm × 12 cm) as an orange-red solid (25 mg, 16.1 µmol, 4% over two steps).

$^{31}P\{^{1}H\}$-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.
$^{31}P\{^{1}H\}$-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 95.5 (s) ppm.

$C_{64}H_{48}BF_{24}IrNO_2P$ (1805.04 g/mol):
^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 7.75 (s, 8H, BAr_F-*H*), 7.66 (dd, *J* = 14.4, 5.3 Hz, 3H, H_{Ar}), 7.57 (s, 4H, BAr_F-*H*), 7.54–7.40 (m, 5H, H_{Ar}), 7.39–7.32 (m, 1H, H_{Ar}), 7.28–7.12 (m, 4H, H_{Ar}), 6.76 (d, *J* = 7.9 Hz, 2H, H_{Ar}), 5.23 (dd, *J* = 10.4, 6.9 Hz, 1H, CH_2), 5.15–5.03 (m, 1H, C*H* COD), 4.89 (t, *J* = 10.0 Hz, 1H, C*H*), 4.44 (dd, J = 9.5, 6.8 Hz, 1H, CH_2), 3.47–3.33 (m, 1H, C*H* COD), 2.90–2.70 (m, 1H, C*H* COD), 2.51–2.31 (m, 6H, C*H* COD, CH_3, CH_2 COD), 2.29–2.16 (m, 2H, CH_2 COD), 2.08–1.99 (m, 1H, CH_2 COD), 1.97–1.84 (m, 4H, CH_3, CH_2 COD), 1.81–1.72 (m, 1H, CH_2 COD), 1.68–1.61 (m, 1H, CH_2 COD) ppm. **$^{31}P\{^{1}H\}$-NMR** (162 MHz, CD_2Cl_2): δ = 101.8 (s) ppm. **MS**: (FAB NBA) *m/z* (%): 690 ($[Ir(L)(COD)]^+$, 100), 620 (24), 580 (10), 602 (11), 484 (15), 168 (66). **EA**: calc. (%) C 49.50, H 3.12, N 0.90; found C 48.87, H 3.13, N 1.17. **m.p.**: 87–88 °C. **$[\alpha]_D^{20}$**: +5.0 (*c* = 0.90, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-{2-(4-benzyl)-4,5-dihydro-oxazole-2-yl)-2-diphenylphosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate (26i)



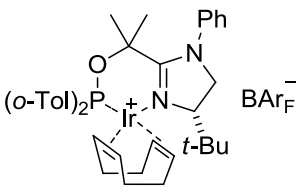
The intermediate ligand (*S*)-**174i** was obtained following the general procedure **H** using alcohol (*S*)-**173d** (61.1 mg, 279 µmol, 1.0 eq.), KH (22.3 mg, 557 µmol, 2.0 eq.), diphenylchlorophosphine (50 µL, 61.5 mg, 279 µmol, 1.0 eq.), and THF (0.5 mL). After stirring for 40 hours at rt and flash chromatography (SiO_2, 1.5 cm × 13 cm, *n*-pentane / TBME 20:1) the N,P ligand (*S*)-**174i** (102 mg, 253 µmol, 91%) was obtained as a colorless oil. Subsequent complexation following general procedure **G** using $[Ir(COD)Cl]_2$ (93.4 mg, 139 µmol, 0.5 eq.), DCM (5.0 mL) and $NaBAr_F$ (269 mg, 304 µmol, 1.2 eq.) gave the title compound (*S*)-**26i** after purification by flash chromatography (SiO_2, 3 cm × 11 cm) as an orange foam (43 mg, 27.4 µmol, 10% over two steps).

$^{31}P\{^{1}H\}$-NMR of Ph_2PCl (162 MHz, CD_2Cl_2): δ = 79.1 (s) ppm.
$^{31}P\{^{1}H\}$-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 94.8 (s) ppm.

$C_{65}H_{50}BF_{24}IrNO_2P$ (1567.06 g/mol):

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 7.97–7.86 (m, 2H, H_{Ar}), 7.74 (s, 8H, BAr_F-*H*), 7.69–7.57 (m, 3H, H_{Ar}), 7.56 (s, 4H, BAr_F-*H*), 7.55–7.43 (m, 3H, H_{Ar}), 7.32–7.18 (m, 5H, H_{Ar}), 6.95 (dd, *J* = 6.4, 2.9 Hz, 2H, H_{Ar}), 5.38–5.32 (m, 1H, C*H* COD), 5.19 (p, *J* = 7.4 Hz, 1H, C*H* COD), 4.47–4.33 (m, 3H, CH_2, C*H*), 3.70–3.61 (m, 1H, C*H* COD), 3.27–3.18 (m, 1H, CH_2), 2.92 – 2.79 (m, 1H, C*H* COD), 2.65–2.32 (m, 4H, CH_2 1H, CH_2 COD 3H), 2.29 (s, 4H, CH_2 COD 1H, CH_3), 2.18–2.00 (m, 2H, CH_2 COD), 1.99–1.85 (m, 1H, CH_2 COD), 1.78–1.62 (m, 4H, CH_2 COD 1H, CH_3) ppm. **^{13}C{^{1}H}-NMR** (101 MHz, CD_2Cl_2): δ = 176.0 (d, *J* = 7.2, *C*=N), 162.3 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 135.4 (s, HC_{Ar} BAr_F), 134.8 (s, C_{Ar}), 134.5 (s, C_{Ar}), 133.7 (s, HC_{Ar}), 133.6 (d, *J* = 3 Hz, HC_{Ar}), 133.5 (s, HC_{Ar}), 132.7 (d, *J* = 2 Hz, HC_{Ar}), 131.2 (s, HC_{Ar}), 131.0 (s, HC_{Ar}), 130.4 (s, C_{Ar}), 130.0 (s, HC_{Ar}), 129.9 (s, HC_{Ar}), 129.8 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 129.4 (s, HC_{Ar}), 129.42 (s, HC_{Ar}), 129.35 (s, HC_{Ar}), 129.31 (s, HC_{Ar}), 128.5 (s, HC_{Ar}), 125.2 (q, J_{FC} = 273 Hz, *C*F_3 BAr_F), 118.1 (septett, J_{FC} = 4 Hz, HC_{Ar} BAr_F), 98.9 (d, *J* = 12 Hz, *C*H COD), 97.9 (d, J = 12 Hz, *C*H COD), 79.9 (d, *J* = 4 Hz, *C*(CH_3)$_2$), 74.8 (s, *C*H_2), 67.0 (s, *C*H), 66.0 (s, *C*H COD), 62.8 (s, *C*H COD), 42.9 (s, *C*H_2), 36.0 (d, *J* = 4 Hz, *C*H_2 COD), 33.3 (d, J = 3 Hz, *C*H_2 COD), 32.4 (d, *J* = 2.0 Hz, C(*C*H_3)$_2$), 30.0 (d, *J* = 2 Hz, C(*C*H_3)$_2$), 27.3 (s, *C*H_2 COD), 26.0 (d, *J* = 6 Hz, *C*H_2 COD) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 102.0 (s) ppm. **MS**: (FAB NBA) *m/z* (%): 704 ([Ir(L)(COD)]$^+$, 100), 596 (12), 500 (19), 393 (14). **m.p.**: 89–90 °C. **[α]$_D^{20}$**: –16.1 (*c* = 0.97, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-{2-(4-*tert*-butyl)-4,5-dihydro-1*H*-imidazol-2-yl)-2-di-*ortho*-tolylphosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-162g)



The intermediate ligand was obtained following general procedure **Q** using alcohol (*S*)-**171b** (96.1 mg, 369 µmol, 1.0 eq.), *n*-pentane (5 mL), TMEDA (73 µL, 56.2 mg, 484 µmol, 1.3 eq.), *n*-BuLi (0.30 mL, 480 µmol, 1.3 eq.) and di-*ortho*-tolylchlorophosphine (119 mg, 480 µmol, 1.3 eq.). After stirring for 16 hours at rt and purification by flash chromatography (SiO_2, 1.5 cm × 12 cm, *n*-pentane / diethylether / triethylamine 8:1:1) the N,P ligand (21 mg, 44.4 µmol, 12%) was obtained as a colorless oil. Subsequent complexation following general procedure **G** using $[Ir(COD)Cl]_2$ (14.9 mg, 22.2 µmol, 0.5 eq.), DCM (1.0 mL) and $NaBAr_F$

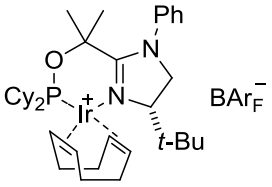
(47.2 mg, 53.3 µmol, 1.2 eq.) gave the title compound (*S*)-**162g** after purification by flash chromatography (SiO_2, 1.5 cm × 12 cm) as an orange foam (65 mg, 39.7 µmol, 11% over two steps).

$^{31}P\{^1H\}$-NMR of (*o*-Tol)$_2$PCl (162 MHz, CD_2Cl_2): δ = 75.3 (s) ppm.
$^{31}P\{^1H\}$-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 75.2 (s) ppm.

$C_{70}H_{61}BF_{24}IrN_2OP$ (1636.21 g/mol):
^1H-NMR (500 MHz, CD_2Cl_2): δ = 8.36 (br s, 1H, *H*$_{Ar}$), 7.75 (s, 8H, BAr_F-*H*), 7.57 (s, 4H, BAr_F-*H*), 7.52–7.03 (m, 12H, *H*$_{Ar}$), 5.46–5.38 (m, 1H, C*H* COD), 5.04–4.90 (m, 1H, C*H* COD), 3.96–3.87 (m, 2H, C*H*$_2$), 3.85–3.73 (m, 2H, C*H*, C*H* COD, 2.73–2.54 (m, 2H, C*H*$_2$ COD 1H, C*H* COD 1H), 2.54–2.32 (m, 7H, C*H*$_2$ COD, C*H* COD, C(C*H*$_3$)$_2$),2.19–1.89 (m, 7H, C*H*$_2$ COD 1H, 2×Ar-C*H*$_3$), 1.81–1.65 (m, 1H, C*H*$_2$ COD), 1.62–1.48 (m, 1H, C*H*$_2$ COD), 1.25 (s, 3H, C(C*H*$_3$)$_2$), 0.92 (s, 9H, (C*H*$_3$)$_3$C) ppm.**$^{13}C\{^1H\}$-NMR** (126 MHz, CD_2Cl_2): δ = 169.4 (d, J_{CP} = 4 Hz, *C*=N), 162.4 (q, J_{BC} =50 Hz, *C*$_{Ar}$ BAr_F), 140.6 (s, *C*$_{Ar}$), 135.4 (s, H*C*$_{Ar}$ BAr_F), 133.2 (d, J_{PC} = 3 Hz, H*C*$_{Ar}$), 132.9 (d, J_{CP} = 4 Hz, H*C*$_{Ar}$), 132.8 (d, J_{PC} = 6 Hz, H*C*$_{Ar}$), 132.2 (d, J_{PC} = 2 Hz, H*C*$_{Ar}$),131.2 (s, H*C*$_{Ar}$),130.5 (s, H*C*$_{Ar}$), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, *C*$_{Ar}$ BAr_F), 126.9 (d, J = 11 Hz, H*C*$_{Ar}$), 126.1 (d, J = 13 Hz, *C*$_{Ar}$), 125.2 (q, J_{CF} = 272 Hz, *C*F_3 BAr_F), 118.1 (septet, J_{CF} = 4 Hz, H*C*$_{Ar}$ BAr_F), 98.4 (br s, *C*H COD), 95.5 (d, J_{PC} = 13 Hz, *C*H COD), 82.2 (d, J_{PC} = 5 Hz, *C*(CH$_3$)$_2$), 72.1 (s, C*H*), 63.6 (s, *C*H COD), 59.7 (s, C*H*$_2$), 37.6 (br s, *C*(CH$_3$)$_3$, 35.0 (s, *C*H COD), 34.5 (s, *C*H$_2$ COD), 33.4 (s, C(*C*H$_3$)$_2$), 29.6 (d, *J* = 6 Hz, *C*H$_2$ COD), 29.3 (s, C(*C*H$_3$)$_2$), 26.2 C(*C*H$_3$)$_3$, 25.6 (s, 2×*C*H$_2$ COD), 23.3 (s, *C*H$_3$), 21.8 (br s, *C*H$_3$) ppm. **$^{31}P\{^1H\}$-NMR** (162 MHz, CD_2Cl_2): δ = 105.2 (br s) ppm. **$[\alpha]_D^{20}$**: –16.1 (*c* = 0.97, $CHCl_3$).

8.8.3 Formation of the P-Alkyl Ligands and Their Complexes

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-{2-(4-*tert*-butyl)-4,5-dihydro-1*H*-imidazol-2-yl)-2-dicyclohexyl-phosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-162h)



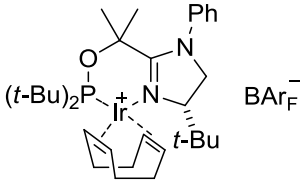
The intermediate ligand was obtained following general procedure **H** using alcohol (*S*)-**171a** (59.0 mg, 226 µmol, 1.0 eq.), chloro-dicyclohexylphosphine (50 µL, 52.7 mg, 226 µmol, 1.0 eq.), KH (15.5 mg, 386 µmol, 1.7 eq.), and THF (0.5 mL), after stirring for 12 hours at rt and filtration over a plug of er a plug of *Celite*® using a *Schlenk* fritt (d × h, 2 cm × 1 cm). The N,P ligand was subsequently converted to the Ir-complex following general procedure **G** using [Ir(COD)Cl]$_2$ (76.0 mg, 113 µmol, 0.5 eq.), DCM (5.0 mL) and NaBAr$_F$ (221 mg, 249 µmol, 1.1 eq.) to obtain the title compound (*S*)-**162h** after purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) as an orange-yellow foam (90 mg, 55.5 µmol, 25% over two steps).

^{31}P{^{1}H}-NMR of Cy_2PCl (162 MHz, CD_2Cl_2): δ = 126.1 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 129.8 (s) ppm.

$C_{68}H_{69}BF_{24}IrN_2OP$ (1636.21 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.76 (s, 8H, BAr$_F$-*H*), 7.59 (s, 4H, BAr$_F$-*H*), 7.52–7.43 (m, 3H, H_{Ar}), 7.21 (br s, 2H, H_{Ar}), 5.19–5.12 (m, 1H, C*H* COD), 4.84 (p, *J* = 7.7 Hz, 1H, C*H* COD), 4.12–4.05 (m, 1H, C*H* COD), 4.02 (dd, *J* = 11.4, 3.2 Hz, 1H, CH_2), 3.86 (t, *J* = 11.2 Hz, 1H, NC*H*), 3.71 (dd, *J* = 11.0, 3.3 Hz, 1H, CH_2N), 3.54–3.46 (m, 1H, C*H* COD), 2.58 (dd, *J* = 15.3, 7.8 Hz, 1H, CH_2 COD), 2.53–2.37 (m, 3H, CH_2 COD, CH_2 Cy 2H), 2.37–2.28 (m, 1H, CH_2 COD), 2.28–2.14 (m, 5H, C(CH_3)$_2$ 3H, C*H*P 1H, CH_2 COD 1H), 2.14–2.05 (m, 2H, C*H*P, CH_2 COD), 2.03–1.97 (m, 1H, CH_2 COD), 1.96–1.79 (m, 5H, CH_2 Cy), 1.77–1.69 (m, 2H, CH_2 Cy), 1.65–1.47 (m, 5H, CH_2 COD 2H, CH_2 Cy), 1.46–1.31 (m, 2H, CH_2 Cy), 1.31–1.18 (m, 6H, CH_2 Cy), 1.12 (s, 9H, (CH_3)$_3$C), 1.06 (d, *J* = 1.5 Hz, 3H, C(CH_3)$_2$) ppm.
^{13}C{^{1}H}-NMR (126 MHz, CD_2Cl_2): δ = 171.8 (s, *C*=N),162.4 (q, J_{BC} = 50 Hz, C_{Ar} BAr$_F$), 140.6 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr$_F$), 131.2 (s, HC_{Ar}), 130.5 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr$_F$), 125.2 (q, J_{CF} = 272 Hz, *C*F$_3$ BAr$_F$), 118.1 (septet, J_{CF} = 4 Hz, HC_{Ar} BAr$_F$), 96.2 (d, J_{PC} = 11 Hz *C*H COD), 95.7 (d, J_{PC} = 12 Hz, *C*H COD), 80.0 (d, J_{PC} = 5Hz, *C*(CH$_3$)$_2$), 70.8 (s, C*H*), 59.7 (s, CH_2), 57.8 (s, *C*H COD), 57.4 (s, *C*H COD), 47.2 (d, *J* = 33

Hz, C*H*P), 43.4 (d, *J* = 28 Hz, C*H*P), 37.9 (d, *J* = 3 Hz, *C*H$_2$ COD), 35.3 (s, *C*(CH$_3$)$_3$, 33.5 (d, *J* = 6 Hz, *C*H$_2$ COD), 32.7 (s, C(*C*H$_3$)$_2$), 29.8 (s, *C*H$_2$ COD), 29.3 (d, *J* = 6 Hz, *C*H$_2$ Cy), 29.1 (d, *J* = 3 Hz, *C*H$_2$ Cy), 28.7 (d, *J* = 4 Hz, *C*H$_2$ Cy), 28.3 (d, *J* = 4 Hz, *C*H$_2$ Cy), 28.2 (s, C(*C*H$_3$)$_2$), 28.0 (d, *J* = 9 Hz, *C*H$_2$ Cy), 27.9 (d, *J* = 5 Hz, *C*H$_2$ Cy), 27.7 (d, *J* = 10 Hz, *C*H$_2$ Cy), 27.5 (d, *J* = 13 Hz, *C*H$_2$ Cy), 26.8 (s, *C*H$_2$ Cy), 26.6 (s, *C*H$_2$ Cy), 25.8 C(*C*H$_3$)$_3$, 25.1 (s, *C*H$_2$ COD) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 109.2 (s) ppm. **[α]$_D^{20}$**: +6.7 (*c* = 0.53, $CHCl_3$).

(*S*)-(+)-[η^4-1,5-Cyclooctadiene-{2-(4-*tert*-butyl)-4,5-dihydro-1*H*-imidazol-2-yl)-2-di-*tert*-butyl-phosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-162i)



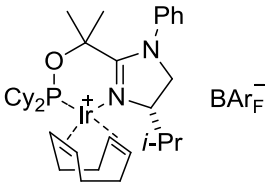
The intermediate ligand was obtained following general procedure **H** using alcohol (*S*)-**171a** (34.0 mg, 131 µmol, 1.0 eq.), di-*tert*-butyl-chlorophosphine (25 µL, 23.8 mg, 131 µmol, 1.0 eq.), KH (9.0 mg, 224 µmol, 1.7 eq.), and THF (0.5 mL), after stirring for 13 hours at rt and filtration over a plug of er a plug of *Celite*® using a *Schlenk* fritt (d × h, 2 cm × 1 cm). The N,P ligand was subsequently converted to the Ir-complex following general procedure **G** using [Ir(COD)Cl]$_2$ (43.9 mg, 65.3 µmol, 0.5 eq.), DCM (3.0 mL) and NaBAr$_F$ (127 mg, 144 µmol, 1.1 eq.) and purification by flash chromatography (SiO_2, 1.5 cm × 15 cm) to provide the title compound (*S*)-**162i** as a orange-yellow foam (112 mg, 71.4 µmol, 55% over two steps).

^{31}P{^{1}H}-NMR of (*t*-Bu)$_2$PCl (162 MHz, CD_2Cl_2): δ = 146.4 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 144.2 (s) ppm.

$C_{64}H_{65}BF_{24}IrN_2OP$ (1568.18 g/mol):
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 7.76 (s, 8H, BAr$_F$-*H*), 7.58 (s, 4H, BAr$_F$-*H*), 7.51–7.42 (m, 3H, *H*$_{Ar}$), 7.21 (br d, *J* = 5.7 Hz, 2H, *H*$_{Ar}$), 5.37–5.32 (m, 1H, C*H* COD), 4.74 (p, *J* = 7.8 Hz, 1H, C*H* COD), 4.44–4.37 (m, 1H, C*H* COD), 3.97 (t, *J* = 11.2 Hz, 1H, NC*H*), 3.91 (dd, *J* = 11.0, 3.3 Hz, 1H, C*H*$_2$), 3.86 (dd, *J* = 11.1, 3.0 Hz, 1H, C*H*$_2$N), 3.73–3.65 (m, 1H, C*H* COD), 2.53 (dd, *J* = 15.6, 7.7 Hz, 1H, C*H*$_2$ COD), 2.49–2.38 (m, 2H, C*H*$_2$ COD), 2.30 (dd, *J* = 15.5, 8.0 Hz, 1H, C*H*$_2$ COD), 2.19–2.08 (m, C*H*$_2$ COD 1H), 1.96–1.87 (m, 4H, C(C*H*$_3$)$_2$, C*H*$_2$ COD 1H), 1.63–1.52 (m, 2H, C*H*$_2$ COD), 1.42–1.31 (br m, 18H, (C*H*$_3$)$_3$C)$_2$P), 1.19 (s, (C*H*$_3$)$_3$C),

1.15 (s, 3H, C(CH_3)$_2$) ppm. **^{13}C{^{1}H}-NMR** (126 MHz, CD_2Cl_2): δ = 170.6 (d, J_{PC} = 2 Hz, *C*=N), 162.4 (q, J_{BC} = 50 Hz, C_{Ar} BAr_F), 140.5 (s, C_{Ar}), 135.4 (s, HC_{Ar} BAr_F), 131.1 (s, HC_{Ar}), 130.5 (s, HC_{Ar}), 129.5 (qq, J_{FC} = 31 Hz, J_{BC} = 3 Hz, C_{Ar} BAr_F), 125.2 (q, J_{CF} = 272 Hz, *C*F_3 BAr_F), 118.1 (septet, J_{CF} = 4 Hz, HC_{Ar} BAr_F), 95.3 (d, J_{PC} = 10 Hz *C*H COD), 92.7 (d, J_{PC} = 14 Hz, *C*H COD), 80.0 (d, J_{PC} = 8Hz, *C*(CH_3)$_2$), 69.8 (s, NC*H*), 61.7 (s, CH_2N), 61.7 (s, *C*H COD), 57.3 (s, *C*H COD), 43.1 (d, *J* = 26 Hz, (CH$_3$)$_3$*C*)$_2$P), 39.9 (d, *J* = 24 Hz, (CH$_3$)$_3$*C*)$_2$P), 38.2 (d, *J* = 4 Hz, *C*H$_2$ COD), 35.5 (s, *C*(CH$_3$)$_3$, 34.9 (d, *J* = 2 Hz, *C*H$_2$ COD), 33.7 (s, C(*C*H$_3$)$_2$), 30.6 (d, *J* = 5 Hz, (*C*H$_3$)$_3$C)$_2$P), 28.5 (s, C(*C*H$_3$)$_2$), 27.3 (s, *C*H$_2$ COD), 26.4 (br s, (*C*H$_3$)$_3$C)$_2$P), 23.8 (s, *C*H$_2$ COD) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 138.7 (s) ppm. **[α]$_D^{20}$**: +60.8 (*c* = 0.56, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-{2-(4-*iso*-propyl)-4,5-dihydro-1*H*-imidazol-2-yl)-2-dicyclohexyl-phosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-162j)



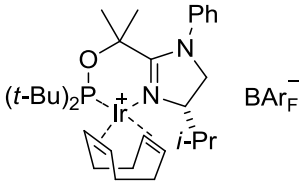
The intermediate ligand was obtained following general procedure **H** using alcohol (*S*)-**171b** (67 mg, 272 μmol, 1.0 eq.), chlorodicyclohexylphosphine (60 μL, 63.2 mg, 272 μmol, 1.0 eq.), KH (22.0 mg, 548 μmol, 2.0 eq.), and THF (0.5 mL), after stirring for 12 hours at rt and filtration over a plug of er a plug of *Celite*® using a *Schlenk* (d × h, 2 cm × 1 cm). The N,P ligand was subsequently converted to the Ir-complex following general procedure **G** using $[Ir(COD)Cl]_2$ (62.0 mg, 92.3 μmol, 0.5 eq.), DCM (5.0 mL) and $NaBAr_F$ (178 mg, 201 μmol, 1.1 eq.) and after purification by flash chromatography (SiO_2, 1 cm × 10 cm) to give the title compound (*S*)-**162j** as an orange-yellow foam (70.0 mg, 43.6 μmol, 24%). This compound contains the corresponding cyclometalled complex **175a** (ca. 20%; ^{1}H-NMR of the Ir-H: −16.40 (d, *J* = 18.4 Hz)).

^{31}P{^{1}H}-NMR of Cy_2PCl (162 MHz, CD_2Cl_2): δ = 126.1 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 122.3 (s) ppm.
^{31}P{^{1}H}-NMR of the Ir$^{(III)}$-complex **175a** (162 MHz, CD_2Cl_2): δ = 145.8 (s) ppm.

$C_{67}H_{67}BF_{24}IrN_2OP$ (1606.25 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.72 (s, 8H, BAr_F-*H*), 7.53 (s, 4H, BAr_F-*H*), 7.45–7.37 (m, 3H, H_{Ar}), 7.21–7.06 (m, 2H, H_{Ar}), 5.15–5.07 (m, 1H, C*H* COD), 4.77 (dd, *J* = 12.2, 6.6 Hz, 1H, C*H* COD), 4.20–4.05 (m, 1H, C*H* COD), 4.02–3.91 (m, 1H), 3.91–3.72 (m, 3H), 3.50–3.42 (m, 1H), 2.60–2.37 (m, 4H), 2.20–1.95 (m, 1H), 1.93–1.79 (m, 6H), 1.78–1.78 (m, 2H, CH_2), 1.68–1.55 (m, 4H), 1.51–1.15 (m, 16H), 1.03 (s, 3H), 0.99 (dd, *J* = 12.5, 6.8 Hz, 6H) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 112.9 (s) ppm. **MS**: (FAB NBA) *m/z* (%): 743 ([Ir(L)(COD)]$^+$, 100), 691 (21), 529 (28), 229 (73. **EA**: calc. (%) C 50.10; H 4.20; N 1.74; found C 48.83, H 4.31, N 1.87. **m.p.**: 65–66 °C. **$[\alpha]_D^{20}$**: −3.0 (*c* = 0.56, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-{2-(4-*iso*-propyl)-4,5-dihydro-1*H*-imidazol-2-yl)-2-di-*tert*-butyl-phosphinite-propane}-iridium(I)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-162k)



The intermediate ligand was obtained following general procedure **H** using alcohol (*S*)-**171b** (65.0 mg, 263 µmol, 1.0 eq), di-*tert*-butyl-chlorophosphine (50 µL, 47.5 mg, 263 µmol, 1.0 eq.), KH (22.0 mg, 548 µmol, 2.1 eq.), and THF (0.5 mL), after stirring for 15 hours at rt and filtration over a plug of er a plug of *Celite*® using a *Schlenk* fritt. (d × h, 2 cm × 1 cm). The intermediate N,P was subsequently converted to the Ir-complex following general procedure **G** using $[Ir(COD)Cl]_2$ (65.0 mg, 96.8 µmol, 0.5 eq.), DCM (5.0 mL) and $NaBAr_F$ (221 mg, 249 µmol, 1.1 eq.) and purification by flash chromatography (SiO_2, 2 cm × 13 cm) to give the title compound (*S*)-**162k** as an orange-yellow foam (254 mg, 163 µmol, 62%). This compound consist predominatly in the corresponding cyclometalled form (**175b**).

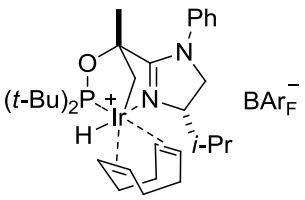
^{31}P{^{1}H}-NMR of (*t*-Bu)$_2$PCl (162 MHz, CD_2Cl_2): δ = 146.4 (s) ppm.
^{31}P{^{1}H}-NMR of the ligand (162 MHz, CD_2Cl_2): δ = 143.8 (s) ppm.

$C_{63}H_{63}BF_{24}IrN_2OP$ (1554.15 g/mol):

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.76 (s, 8H, BAr_F-*H*), 7.56 (s, 4H, BAr_F-*H*), 7.48–7.36 (m, 3H, H_{Ar}), 7.22–7.04 (m, 2H, H_{Ar}), 4.97 (t, *J* = 6.8 Hz, 1H, 1H), 4.81–4.73 (m, 1H), 4.73–4.66 (m, 1H), 4.21–4.13 (m, 1H), 4.13–4.06 (m, 1H), 4.02–3.98 (m, 1H), 3.97–3.90 (m, 1H), 3.31–

3.25 (m, 1H), 3.16–3.07 (m, 1H), 2.65–2.45 (m, 1H), 2.40–2.24 (m, 3H), 2.20–2.00 (m, 1H), 1.81–1.63 (m, 2H), 1.37 (d, *J* = 14.7 Hz, 9H), 1.30 (dd, *J* = 13.9, 7.2 Hz, 6H), 1.24 (d, *J* = 14.7 Hz, 9H), 1.15 (s, 3H), 1.01 (d, *J* = 6.9 Hz, 3H) ppm. **^{31}P{^{1}H}-NMR** (162 MHz, CD_2Cl_2): δ = 133.2 (s) ppm.**MS**: (FAB NBA) *m/z* (%): 691 ($[Ir(L)(COD)]^+$, 100), 529 (29), 465 (14), 229 (81). **EA**: calc. (%) C 48.69; H 4.09; N 1.80; found C 47.37, H 4.96, N 1.92. **m.p.**: 119–120 °C (dec.). **$[\alpha]_D^{20}$**: −8.7 (*c* = 0.59, $CHCl_3$).

(*S*)-(−)-[η^4-1,5-Cyclooctadiene-{2-(4-*iso*-propyl)-4,5-dihydro-1*H*-imidazol-2-yl)-2-di-*tert*-butyl-phosphinite-propane}-hydrido-iridium(III)]-tetrakis-(3,5-bis-(trifluoromethyl)-phenyl)-borate ((*S*)-175b)



The cyclometallated complex was obtained by slowly bubbling (1 bubble / second) hydrogen gas in to a solution of (*S*)-**162k** in THF (1 mL) at −30 °C during 12 h. The complex (*S*)-**175b** is not stable at rt and it was directly analyzed by NMR at −30 °C

$C_{63}H_{63}BF_{24}IrN_2OP$ (1554.15 g/mol):

^{1}H{^{31}P}--NMR (500 MHz, THF-d_8, 248 K): δ = 7.83 (s, 8H, BAr_F-*H*), 7.62 (s, 4H, BAr_F-*H*), 7.56–7.35 (m, 5H, H_{Ar}), 5.12–5.03 (m, 1H, C*H* COD), 4.90–4.80 (m, 2H, C*H* COD), 4.41 (d, *J* = 10.6 Hz, 1H, NC*H*), 4.27–4.20 (m, 1H, CH_2N), 4.15 (q, *J* = 7.5 Hz, 1H, C*H* COD), 4.02 (t, *J* = 11.0 Hz, 1H, CH_2N), 3.32 (dd, *J* = 15.5, 8.0 Hz, 1H, CH_2 COD), 3.26–3.16 (m, CH_2 COD), 2.80–2.67 (m, 1H, CH_2 COD), 2.67–2.55 (m, 1H, CH_2 COD), 2.47–2.32 (m, 3H, CH_2 COD 2H, C*H*(CH_3)$_2$)), 1.97–1.78 (m, 2H, CH_2 COD), 1.54 (m, 3H, CCH_3), 1.43 (s, 9H, C(CH_3)$_3$), 1.31 (s, 9H, C(CH_3)$_3$), 1.07 (d, *J* = 6.6 Hz, 6H, CH(CH_3)$_2$), 0.99 (d, *J* = 11.1 Hz, 2H, Ir-CH_2), −16.2 (s, 1H, Ir-H) ppm. **^{31}P{^{1}H}-NMR** (202 MHz, THF-d_8, 248 K): δ = 146.03 (d, *J* = 4.9 Hz) ppm.

8.9 Asymmetric Hydrogenations of Model Olefins

8.9.1 Hydrogenation at Elevated Pressure

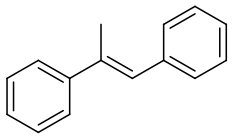
A 2 mL-glass vial was charged with a stirring bar, iridium catalyst (1.0 mol%) and substrate (25-200 μmol). The mixture was dissolved in DCM (0.2 M) and placed in an autoclave. The autoclave was then three times pressurized up to 50 bar with hydrogen and the pressure released. The reaction was performed under 50 bar H_2 atmosphere for a given time at RT. After releasing the hydrogen pressure the solvent was removed under reduced pressure or under a stream of nitrogen. Heptane (1 mL) was added to the crude product, which was purified over a plug of silica gel (SiO_2, 0.5 cm × 1 cm, *n*-heptane / TBME 10:1) to obtain the hydrogenation product suitable for analysis.

8.9.2 Hydrogenation at Ambient Pressure

A 2 mL-glass vial was charged with a stirring bar, iridium catalyst (1.0 mol%) and substrate (25-200 μmol). The mixture was dissolved in DCM (0.2 M) and placed in a glas flask, which was closed with a rubber septum. A H_2-filled ballon equipped with a needle was put on the septum and the flask was flushed with hydrogen for 5 min. The reaction was performed under H_2-filled ballon for a given time at RT. Afterwards the solvent was removed under reduced pressure or under a stream of nitrogen. Th crude product was taken up in *n*-heptane (1 mL) and purified over a plug of silica gel (SiO_2, 0.5 cm × 1 cm, *n*-heptane / TBME 10:1) to obtain the hydrogenation product suitable for analysis.

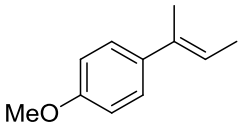
8.9.3 Analytical Data for the Model Olefins

(*E*)-Prop-1-ene-1,2-diyldibenzene (7)



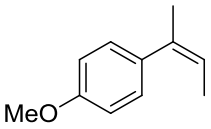
GC (Restek Rtx-1701 (30 m × 0.25 mm × 0.25 μm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 18.3 min (**7**), 21.4 min (**8**). **HPLC** (chiral, Daicel Chiracel OJ, 0.46 cm × 25 cm, *n*-heptane / *i*-PrOH = 99:1, 0.5 mL/min, 25 °C): t_R = 15.6 min ((*R*)-**8**), 23.8 min ((*S*)-**8**).

(*E*)-2-(4-Methoxyphenyl)-2-butene (90)



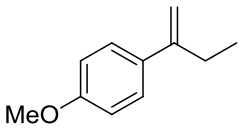
GC (*Chiraldex* γ-cyclodextrin TFA G-TA, (30 m × 0.25 mm × 0.12 μm), 60 kPa H_2, (60 °C, 30 min, 5 °C/min, 100 °C, 20 °C/min, 160 °C, 10 min): t_R = 38.4 min ((*S*)-**89**), 38.6 min ((*R*)- **89**), 41.2 min (**90**).

(*Z*)-2-(4-Methoxyphenyl)-2-butene (91)



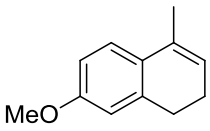
GC (*Chiraldex* γ-cyclodextrin TFA G-TA (30 m × 0.25 mm × 0.12 μm), 60 kPa H_2, 60 °C, 30 min, 5 °C/min, 100 °C, 20 °C/min, 160 °C, 10 min): t_R = 38.4 min ((*S*)-**89**), 38.6 min ((*R*)- **89**), 39.3 min (**91**).

2-(4-Methoxyphenyl)-1-butene (88)



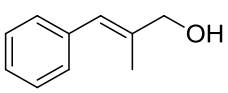
GC (*Chiraldex* γ-cyclodextrin TFA G-TA (30 m × 0.25 mm × 0.12 μm), 60 kPa H_2, 60 °C, 30 min, 5 °C/min, 100 °C, 20 °C/min, 160 °C, 10 min): t_R = 38.4 min ((*S*)-**89**), 38.6 min ((*R*)- **89**), 40.3 min (**88**).

7-Methoxy-1,2-dihydro-naphthalene (72)



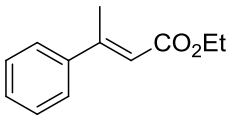
GC (Restek Rtx-1701 (30 m × 0.25 mm × 0.25 μm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 15.0 min (**72**), 17.6 min (**73**), 19.8 min (**115**). **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane, 0.75 mL/min, 25 °C): t_R = 20.4 min ((*R*)-**73**), 27.0 min ((*S*)-**73**).

(*E*)-2-Methyl-3-phenylprop-2-en-1-ol (24)



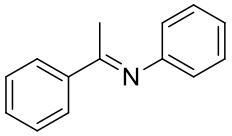
GC (Restek Rtx-1701 (30 m × 0.25 mm × 0.25 μm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 14.6 min (**25**), 16.5 min (**24**). **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane / *i*-PrOH = 95.5, 0.5 mL/min, 40 °C): t_R = 15.3 min ((*R*)-**25**), 17.5 min ((*S*)-**25**).

(*E*)-Ethyl 3-phenylbut-2-enoate (98)



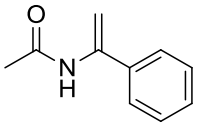
GC (*Chiraldex* γ-cyclodextrin TFA G-TA (30 m × 0.25 mm × 0.12 μm), 60 kPa H_2, 85 °C, 50 min, 10 °C/min, 160 °C, 5 min): t_R = 42.9 min ((*R*)-**99**), 44.9 min ((*S*)-**99**), 57.0 min (**98**).

(*E*)-N-(1-phenylethylidene)aniline (13)



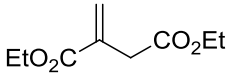
GC (Macherey-Nagel Optima 5-Amin (30 m × 0.25 mm × 0.5 μm), 60 kPa He, 150 °C, 7 °C/min, 250 °C, 10 min): t_R = 12.6 min (**14**), 12.9 min (**13**), 4.9 min (**48**), 5.4 (**116**). **HPLC** (chiral, Daicel Chiracel OD-H, 0.46 cm × 25 cm, *n*-heptane / *i*-PrOH = 99.1, 0.5 mL/min, 25 °C): t_R = 24.6 min ((*S*)-**14**), 33.0 min ((*R*)-**14**).

***N*-(1-phenylvinyl)acetamide (92)**



GC (Macherey-Nagel Optima 5-Amin (30 m × 0.25 mm × 0.5 μm), 60 kPa He, 150 °C, 15 min, 10 °C/min, 250 °C, 15 min): t_R = 19.2 min (H_2-**92**), 19.8 min (**92**). **GC** (Macherey-Nagel Hydroxyβ 3P (30 m × 0.25 mm × 0.25 μm), 60 kPa H_2, (150 °C, 20 min, 10 °C/min, 180 °C, 10 min)): t_R = 14.6 min ((−)-H_2-**92**), 15.2 min ((+)-H_2-**92**).

Dimethyl 2-methylenesuccinate (93)



GC (Restek Rtx-1701 (30 m × 0.25 mm × 0.25 μm), 60 kPa He, 100 °C, 2 min, 7 °C/min, 250 °C, 10 min): t_R = 8.9 min (H_2-**93**), 9.8 min (**93**). **GC** (*Chiraldex* γ-cyclodextrin TFA G-TA (30 m × 0.25 mm × 0.12 μm), 60 kPa H_2, 85 °C, 50 min, 10 °C/min, 160 °C, 5 min): t_R = 19.2 min ((*S*)-H_2-**93**), 20.2 min ((*R*)-H_2-**99**).

Chapter 9

Appendix

9.1 Crystallographic Data

	(*S*)-**36a**	(*S*)-**36b**
molecular formula	$C_{66}H_{46}BF_{24}IrNOP$	$C_{68}H_{50}BF_{24}IrNOP$
molecular weight [g mol^{-1}]	1559.06	1587.11
shape	plate	plate
color	red	red
temperature [K]	123	123
crystal system	triclinic	triclinic
space group	P −1	P 1
crystal size [mm^3]	0.06 · 0.14 · 0.21	0.05 · 0.12 · 0.18
α [Å]	14.0804(5)	13.0655(3)
β [Å]	15.0274(5)	13.5579(3)
γ [Å]	16.3297(6)	18.9456(5)
α [°]	95.216(2)	89.6510(10)
β [°]	106.248(2)	73.6170(10)
γ [°]	103.438(2)	89.2350(10)
V [Å^3]	3181.1	3219.48
Z	4	2
F(000)	1540	1572
θ-range for data collection [°]	1.704–27.960	1.625–34.971
$\rho_{calc.}$ [g cm^{-3}]	1.628	1.637
absorption coeff. μ [mm^{-1}]	2.238	2.213
measured reflections	60034	177675
independent reflections	15146 (merging r = 0.027)	55681 (merging r = 0.030)
used refelctions[a]	13416	46871
parameters refined	991	1937
R[c]	0.0292	0.0289
R_w[d]	0.0397	0.0372
goodness of fit	1.2551	1.1422

[a] Observation criterion: $I>2\sigma(I)$; [c] $R = \Sigma||F_0| - |F_C|| / \Sigma |F_0|$; [d] $R_w = \{\Sigma[w(F_0 - F_C)^2] / \Sigma [w(F_0)2]\}^{1/2}$.

	(*S*)-**36e**	*rac.*-**81**
molecular formula	$C_{69}H_{52}BF_{24}IrNOP$	$C_{62}H_{45}BF_{24}IrNOP$
molecular weight [g mol^{-1}]	1601.13	1510.00
shape	plate	
color	orange	
temperature [K]	123	293
crystal system	orthorhombic	monoclinic
space group	P 2_1 2_1 2_1	P 1 2_1/c 1
crystal size [mm^3]	0.06 · 0.24 · 0.34	
α [Å]	12.9995(3)	12.7350(6)
β [Å]	13.2409(3)	22.6817(11)
γ [Å]	37.3728(10)	21.3144(10)
α [°]	90	90
β [°]	90	102.276(2)
γ [°]	90	90
V [Å^3]	6432.8(3)	6015.9(5
Z	4	4
F(000)	3176	2980
θ-range for data collection [°]	1.632–36.328	2.045–34.167
$\rho_{calc.}$ [g cm^{-3}]	1.653	1.667
absorption coeff. *μ* [mm^{-1}]	2.216	2.363
measured reflections	156484	117359
independent reflections[a]	30871 (merging r = 0.030)	24169 (merging r = 0.042)
used refelctions	28673 (I>2.0σ(I))	13936 (I>3.0σ(I))
parameters refined	911	964
R[c]	0.0332	0.0676
R_w[d]	0.0275	0.1368
goodness of fit	1.1068	1.0037

[a] Observation criterion: $I>2\sigma(I)$; [c] $R = \Sigma||F_0| - |F_C|| / \Sigma |F_0|$; [d] $R_w = \{\Sigma[w(F_0 - F_C)^2] / \Sigma [w(F_0)2]\}^{1/2}$.

	rac.-**87b**	(*S*)-**142c**
molecular formula	$C_{65}H_{54}BF_{24}IrNOPSi$	$C_{61}H_{45}BF_{24}IrN_2P$
molecular weight [g mol^{-1}]	1583.19	1496.00
shape	plate	block
color	red	red
temperature [K]	223	123
crystal system	monoclinic	monoclinic
space group	P 2_1/c	C 2/c
crystal size [mm^3]	0.06 · 0.17 · 0.31	0.12 · 0.21 · 0.39
α [Å]	12.7903(4)	18.5427(4)
β [Å]	26.6398(8)	17.9275(4)
γ [Å]	19.6578(6)	36.1256(8)
α [°]	90	90
β [°]	97.2480(10)	94.1250(10)
γ [°]	90	90
V [Å^3]	6644.5(4)	11977.9(5)
Z	4	9
F(000)	3144	5904
θ-range for data collection [°]	2.089–33.772	1.582–37.833
$\rho_{calc.}$ [g cm^{-3}]	1.583	1.659
absorption coeff. *μ* [mm^{-1}]	2.161	2.372
measured reflections	229385	194372
independent reflections[a]	24168 (merging r = 0.030)	32197 (merging r = 0.028)
used refelctions	13324 (I>3.0σ(I))	21977 (I>2.0σ(I))
parameters refined	1081	892
R[c]	0.0508	0.0455
R_w[d]	0.0838	0.0643
goodness of fit	1.0244	1.0954

[a] Observation criterion: $I>2\sigma(I)$; [c] $R = \Sigma||F_0| - |F_C|| / \Sigma |F_0|$; [d] $R_w = \{\Sigma[w(F_0 - F_C)^2] / \Sigma [w(F_0)2]\}^{1/2}$.

	(*S*)-**142c**	(S)-**162k**
molecular formula	$C_{66}H_{47}BF_{24}IrN_2P$	$C_{63}H_{62}BF_{24}IrN_2OP$
molecular weight [g mol^{-1}]	1558.07	1553.16
shape	block	block
color	orange	orange
temperature [K]	123	123
crystal system	monoclinic	monoclinic
space group	P 2_1	P 2_1
crystal size [mm^3]	0.04 · 0.09 · 0.23	0.040 · 0.110 · 0.180
α [Å]	13.0936(4)	18.2207(4)
β [Å]	35.2531(10)	17.5477(5)
γ [Å]	13.4599(4)	20.3871(5)
α [°]	90	90
β [°]	90.7950(10)	97.4150(10)
γ [°]	90	90
V [Å^3]	6212.4(3)	6463.9(3
Z	4	4
F(000)	3080	3100
θ-range for data collection [°]	1.938–29.995	1.606-32.576
$\rho_{calc.}$ [g cm^{-3}]	1.666	1.596
absorption coeff. *μ* [mm^{-1}]	2.291	2.202
measured reflections	55185	89879
independent reflections[a]	32967 (merging r = 0.019)	44797 (merging r = 0.048)
used refelctions	28450 (I>2.0σ(I))	28065 (I>2.0σ(I))
parameters refined	1712	1898
R[c]	0.0228	0.0450
R_w[d]	0.0269	0.0549
goodness of fit	1.1195	0.0549

[a] Observation criterion: $I>2\sigma(I)$; [c] $R = \Sigma||F_0| - |F_C|| / \Sigma |F_0|$; [d] $R_w = \{\Sigma[w(F_0 - F_C)^2] / \Sigma [w(F_0)2]\}^{1/2}$.

9.2 List of Abbraviations

Å	Ångström
Ac	acetyl
AcOAC	acetic anhydride
AcOH	acetic acid
Alk	alkyl
anth	anthracenyl
aq.	aqueous
Ar	aryl
BAr_F	tetrakis[3,5-bis(trifluoro-methyl)phenyl]borate
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
br	broad
Bu	butyl
c	concentration
CAL-B	*Candida Antartica* Lipase B
calc.	calculated
cat.	catalytic or catalyst
COD	cycloocta-1,5-diene
conv.	conversion
COSY	correlation spectroscopy
Cy	cyclohexyl
D	sodim D line
d	day(s) or doublet (NMR)
δ	chemical shift
DCE	1,2-dichloroethane
DCM	dichloromethane
dec.	decomposition
DIPAMP	1,2-bis((*R*)-(2-methoxyphenyl)(phenyl)phosphino)ethane
DIPEA	*N*,*N*-diisopropylethylamine
DMAP	N,N-4-(dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
dppf	1,1’-bis(diphenyl-phosphino)ferrocene
E	opposite
EA	elemental analysis
ee	enantiomeric excess
EI	electron-impact ionization
eq.	equivalent(s)
ESI	electrospray ionization
Et	ethyl
EtOH	ethanol
FAB	fast atom bomardement
GC	gas chromatography
h	hour(s)
HPLC	high performance liquid chromatography

Hz	Hertz
i-Pr	2-propyl
Im	imidazoline
i-PrOH or IPA	2-propanol
J	coupling constant
M	molar [mol / L]
m	multiplet (NMR) or medium (IR)
m.p.	melting point
m/z	mass-to-charge ratio
MALDI	matrix assisted laser desorption ionization
MCPBA	3-chloroperoxybenzoic acid
Me	methyl
MeOH	methanol
min	minute(s)
mL	milliliter
MS	mass spectrometry or mole-sieves
n.d.	not determined
n.o.	not observed
NBA	3-nitrobenzyl aclohol
n-BuLi	1-butyl lithium
NfF	nonafluorobutanesulfonyl fluoride
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser enhancement spectroscopy
n-Pr	1-propyl
o	ortho
o-Tol	*ortho*-tolyl
p	para
Ph	phenyl
PHIM	phosphino-imidazoline
PHOX	phosphino-oxazoline
ppm	parts per million
q	quartet
quint	quintet
rac.	racemic
R_F	retention factor
rt	room temperature
s	singlet (NMR) or strong (IR)
SAMP	(*S*)-(–)-1-amino-2-methoxy-methylpyrrolidine
sat.	saturated
sec	second(s)
T	temperature
t	triplet (NMR) or time
t or *tert.*	tertiary
TBAF	tetrabutylammonium fluoride
TBME	*tert*-butyl methyl ether
TBS	*tert*-butyldimethylsilyl
t-Bu	*tert*-butyl

t-BuLi	*t*-butyl lithium
TEA	triethylamine
tert	tertiary
Tf	trifluoromethanesulfonyl
TFAA	trifluoroacetic anhydride
THF	tetrahydrofurane
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl
Tol	tolyl
tR	retention time
Ts	tosyl
w	weak (IR)
Z	together

Chapter 10

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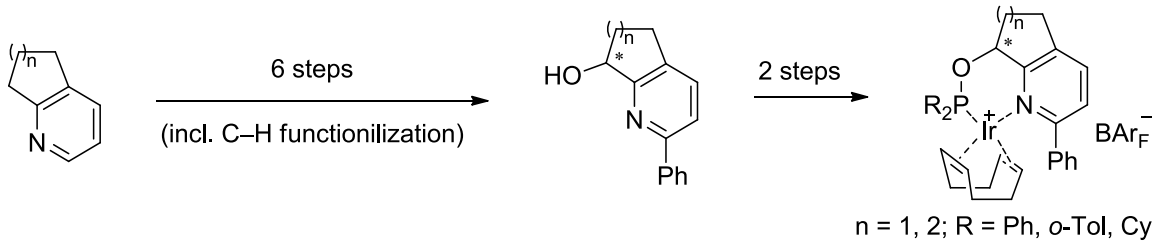
Chapter 11

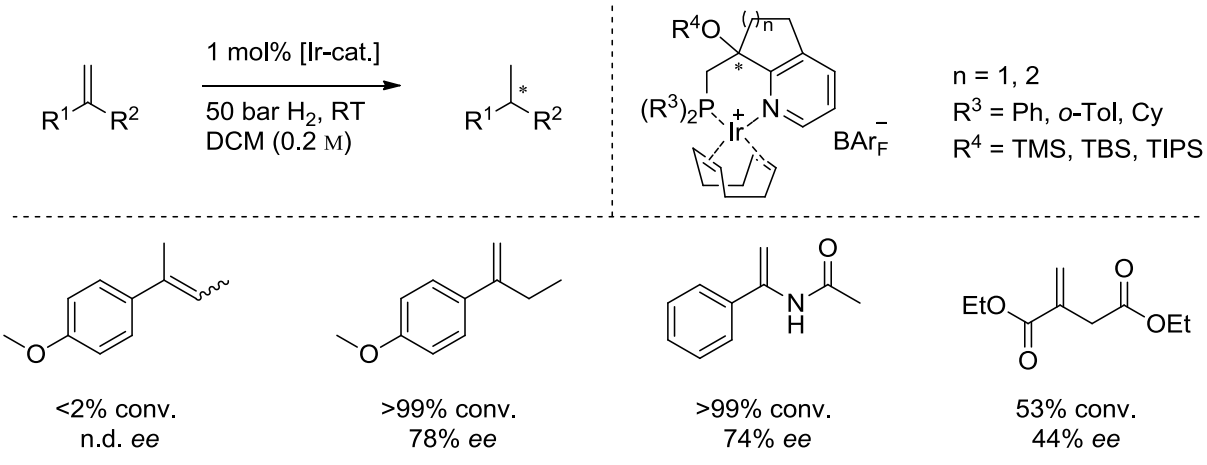
Summary

The aim of this thesis was the development of new N,P ligands for iridium-catalyzed asymmetric hydrogenations and evaluation of alkenyl boronic esters as substrates for this transformation. Initially, a concise synthetic route towards bicyclic pyridine-phosphinite ligand complexes was implemented. The characteristic features of the new synthesis are a regioselective C−H functionalization, which allows fast preparation of pyridyl alcohols and the operationally simple synthesis of phosphinite ligand complexes (scheme 11.1).



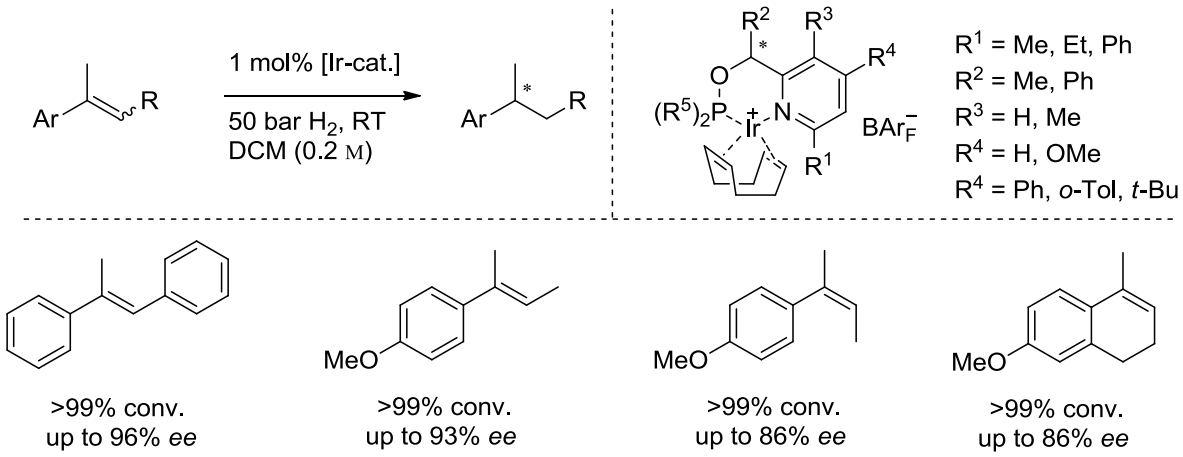
Scheme 11.1: Fast preparation of pyridyl alcohols and formation of pyridine-phosphinite ligand complexes.

The middle section is mainly dedicated to structural modifications of the N,P ligand scaffold, in order to tune the activity and the selectivity. First the development of pyridine derived N,P ligands containing a quaternary stereogenic center is described. While a phosphinite based N,P ligand was found to undergo an irreversible cyclometallation reaction to produce stable, but catalytically inactive $Ir^{(III)}$-complexes, five novel pyridine-phosphine derived $Ir^{(I)}$-complexes were synthesized and applied in the asymmetric hydrogenation of olefins. A remarkably high selectivity towards the reduction of terminal versus trisubstituted C=C bonds was found. These are the first examples of Ir-complexes being able to chemoselectively reduce a terminal C=C bond in the presence of a trisubstitued C=C bond even at elevated pressure. However, for several variably substituted terminal olefins only moderate enatioselectivities were obtained (up to 78% *ee*; scheme 11.2).



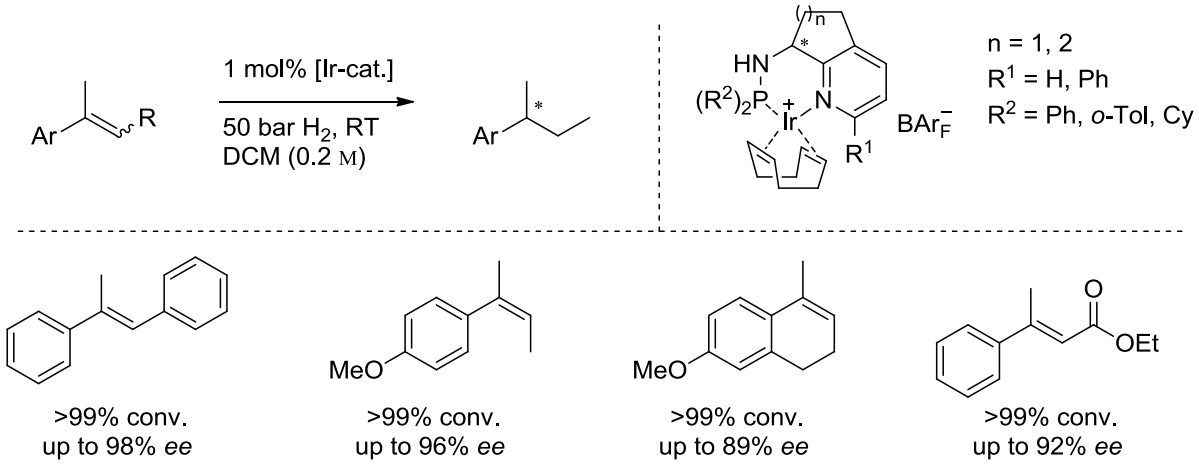
Scheme 11.2: New Ir-complexes derived from N,P ligands bearing quaternary stereogenic center for the selective hydrogenation of terminal olefins.

Furthermore, pyridine-phosphinite ligands lacking the fused bicyclic motif were investigated during this work. Six new iridium complexes, with different electronic and steric properties were obtained and applied in the iridium-catalyzed asymmetric hydrogenation. They provided high enantioselectivities (86-96% *ee*) in the hydrogenation of several unfunctionalized olefins (scheme 11.3).



Scheme 11.3: Application of new Ir-complexes lacking the rigid bicyclic motif in the hydrogenation of unfunctionalized olefins.

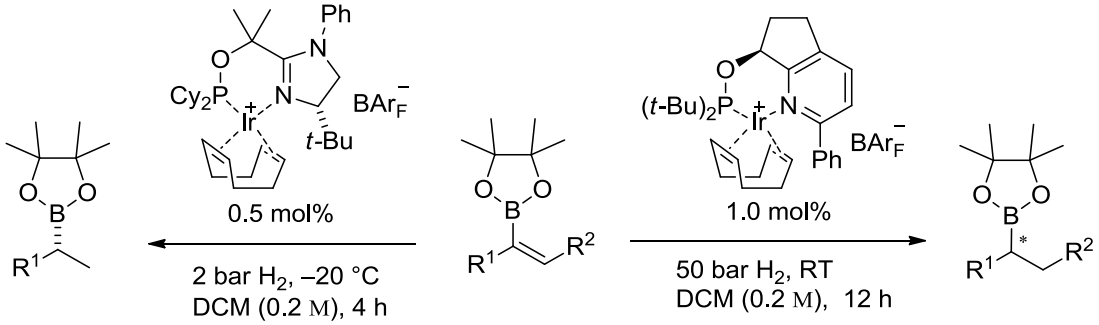
Amino-phosphine derived N,P ligands were investigated as well. The corresponding iridium complexes were successfully applied in the asymmetric hydrogenation of unfunctionalized and partially functionalized olefins, furnishing excellent enantioselectivities (up to 98% *ee*; scheme 11.4).



Scheme 11.4: Application of new Ir-complexes lacking the rigid bicyclic motif in the hydrogenation of unfunctionalized olefins.

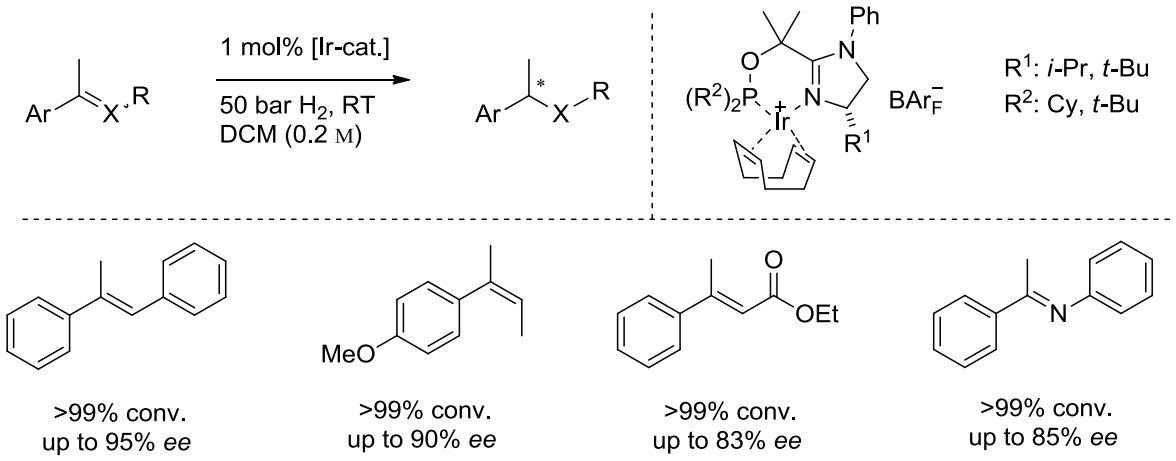
Chiral alkyl boronic esters are useful building blocks in organic chemistry, since the C−B bond can be readily converted into C−O, C−N and C−C bonds in a stereospecific manner. In this work two different iridium complexes are reported, which provide efficient access to this

valuable class of compounds. While an Ir-complex derived from an phosphine-imidazoline ligand was identified as a highly efficient catalyst for the enantioselective hydrogenation of terminal vinyl boronic esters, trisubstituted boronates were reduced with high activity and excellent enantioselectivity employing a pyridine-phosphinite derived Ir-complex (scheme 11.5).



Scheme 11.5: Ir-catalyzed symmetric hydrogenation of alkenyl boronic esters.

Finally the synthesis of the phosphinitoimidazoline ligand complexes, which were identified as the best catalysts for the hydrogenation of terminal vinyl boronic esters, is described. Besides boron-based substrates, these complexes showed also high activity and enantioselecitvity in the asymmetric hydrogenation of unfunctionalized olefins and imines (scheme 11.6). In this context an unusual cyclometallation was observed for Ir-complexes with an isopropyl residue on the imidazoline scaffold. The cyclometallation arises from the insertion of the metal into one of the geminal methyl groups and was found to be reversible and temperature dependent.



Scheme 11.6: Ir-catalyzed symmetric hydrogenation C=C and C=N bonds using phosphine-imidazoline derived Ir-compelxes.

Curriculum Vitae **Adnan GANIĆ**

Date of birth:	October 12, 1980
Place of birth:	Travnik, Bosnia and Herzegovina
Nationality:	Swiss / Bosnian and Herzegovinian

Education:

03/2008-08/2012	PhD studies under the supervision of Prof. Dr. Andreas Pfaltz at the University of Basel. "*Iridium-Catalyzed Asymmetric Hydrogenation:Development of New N,P Ligands andEnantioselective Hydrogenation of Alkenyl Boronic Esters*".
10/2006-01/2008	Master of Science in Chemistry, University of Basel. Grade 5.6 Master thesis under the supervision of Prof. Dr. Andreas Pfaltz. "*Synthese von neuen modularen P,N-Liganden für die Iridium-katalysierte asymmetrische Hydrierung* ".
10/2002-02/2006	Diploma in Chemistry, Fachhochschule Nordwestschweiz, Muttenz. Grade 5.1 Diploma thesis under the supervision of Prof. Dr. Daniel Gygax. "*Entwicklung neuartiger fluoreszenzmarkierten 8-Oxo-Guonosin-Derivaten zur Qualifizierung von DNA Schäden*".
08/2001-06/2002	Professional Maturity, Basel. Grade 5.2
08/1998-08/2001	Chemistry Laboratory Assistant Apprenticeship, F. Hoffmann-La Roche AG, Basel. Grade 5.4

Employment:

07/2011-09/2012	"Swiss Sciences Concentrates a *Chimia* Column". Preparation of short abstracts of interesting recent publications of Swiss origin, under the supervision of Prof. Dr. Thomas Ward at the University of Basel.
04/2006-09/2006	Chemistry Laboratory Assistant, F. Hoffmann-La Roche AG, Basel. Process Research on GMP small scale production plant.

Awards:

09/09/2011	SCS-Metrohm Award for best oral presentation, Fall Meeting of the Swiss Chemical Society, EFPL Lausanne (CH).

Teaching Experience:

02/2011-08/2011	Direct supervision of advanced student Nicola Polimene, during his master thesis in chemistry in the research group of Prof. Dr. Andreas Pfaltz.
05/2008-05/2010	Direct supervision of undergraduate students in chemistry, during three and six weeks laboratory practical courses in the research group of Prof. Dr. Andreas Pfaltz.
09/2008-06/2010	Laboratory teaching assistant of bachelor students in biology and pharmacy during two weeks laboratory practical courses in basic organic chemistry, Department of Chemistry, University of Basel.

Presentations and Workshops:

11/09/2011	Oral communication: "*Iridium-catalyzed Asymmetric Hydrogenation of Boronic Esters*", Fall Meeting of the Swiss Chemical Society, EFPL Lausanne (CH).
22/07/2011	Poster presentation: "*Iridium-catalyzed Asymmetric Hydrogenation of Boronic Esters*", Heidelberg Forum of Molecular Catalysis, Heidelberg (D).
17-27/08/2010	Poster presentation: "*Design of New P,N-Ligands for Iridium-catalyzed Asymmetric Hydrogenation*", 120th BASF Summer Course, Ludwigshafen (D).
23-25/09/2009	Poster presentation: "*Design of New P,N-Ligands for Iridium-catalyzed Asymmetric Hydrogenation*", 29th Regio Symposium of the Cross-Border University Study Programs of the Universities of Basel (CH), Freiburg i.Br. (D) and Mulhouse (F), Schloss Beuggen, Rheinfelden (D).
12-16/07/2009	Poster presentation: "*Synthesis of New P,N-Ligands for Iridium-Catalyzed Asymmetric Hydrogenation*", 16th European Symposium on Organic Chemistry, Prag (CZ).
06-09/07/2008	Poster presentation: "*Synthesis of New Modular P,N-Ligands for the Iridium-catalyzed Asymmetric Hydrogenation*", 20th International Symposium on Chirality, Geneva (CH).

During my education at the University of Basel and the "Fachhochschule Nordwestschweiz" (Univeristy of Applied Sciences, Northwest Switzerland) I attented lectures given by:

E. C. Constable, B. Giese, P. C. Hauser, J.P. Maier, W. P. Maier, M. Mayor, M. Meuwly, A. Pfaltz, H. Wegner, H. Wennemers, M. Barblan, D. Gygax, E. Hungerbühler, M. Hürzeler, U. Pieles, H.-R. Schmutz and B. Zehnder.