Chiral Proline-Based Ligands for Iridium-Catalyzed Asymmetric Hydrogenation

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Denise Rageot

aus Hitzkirch LU, Schweiz

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Meinen Eltern, Silvia & Allain

„If you can't fly then run, if you can't run then walk, if you can't walk then crawl, but whatever you do you have to keep moving forward."

Martin Luther King Jr.

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„Recent Advances in Iridium-Catalyzed Asymmetric Hydrogenation: New Catalysts, Substrates and Applications in Total Synthesis."

Adnan Ganić, Denise Rageot, Lars Tröndlin, Andreas Pfaltz, *Chimia* **2012**, 187-191.

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Ac	acetyl	**conv.**	conversion
abs.	absolute	**C_{Im}**	benzimidazole phosphine/iridium complex
Adm	adamantyl	**C_{Ox}**	benzoxazole phosphine/iridium complex
Ar	aryl	**C_{Th}**	benzothiazole phosphine/iridium complex
Ar_F	3,5-bis(trifluoromethyl)phenyl	**C_{U3}**	trisubstituted ureaphosphine/iridium complex
BSA	*N,O*-bis(trimethylsilyl)acetamide	**C_{U4}**	tetrasubstituted ureaphosphine/iridium complex
***n*Bu**	1-butyl	**Cy**	cyclohexyl
***t*Bu**	*tert*-butyl	**d**	doublet (NMR)
BzOx	benzoxazole	**δ**	chemical shift (NMR)
BzIm	benzimidazole	**Δ**	heated at reflux
BzTh	benzothiazole	**DMAP**	4-*N*,*N*-dimethylaminopyridine
c	concentration	**DMF**	*N*,*N*-dimethyl formamide
C_A	amidophosphine/iridium complex	**DSC**	*N*,*N'*-disuccinimidyl carbonate
calc.	calculated	***de***	diastereoisomeric excess
cat.	catalyst; catalytic	***dr***	diastereoisomeric ratio
C_C	carbamatophosphine/iridium complex	**E**	electrophile
C_H	phosphinohydrazone/iridium complex	***ee***	enantiomeric excess
cod	1,5-cyclooctadiene	***er***	enantiomeric ratio

Et	ethyl	**L_{U4}**	tetrasubstituted ureaphosphine ligand
eq.	equivalent(s)	***m***	*meta* position (phenyl substituents)
ESI-MS	electron spay ionization mass spectroscopy	**M**	molarity ($mol \cdot L^{-1}$)
Fc	ferrocenyl	***m/z***	mass-to-charge ratio
Fl	fluorenyl	**Me**	methyl
Fur	furyl	**Mes**	mesityl, 1,3,5-trimethylphenyl
GC	gas chromatography	**Morph**	morpholine
HPLC	high performance liquid chromatography	**ms**	molecular sieves
i	*ipso* position (phenyl substituents), iso (isopropyl)	**Naph**	naphthyl
J	coupling constant	**NMR**	nuclear magnetic resonance
L	ligand	**Nu**	nucleophile
L_A	amidophosphine ligand	***o***	*ortho* position (phenyl substituents)
L_C	carbamatophosphine ligand	***p***	*para* position (phenyl substituents), pressure
L_H	phosphinohydrazone ligand	**P**	product (of hydrogenation or allylic alkylation)
L_{Im}	benzimidazole phosphine ligand	**Ph**	phenyl
L_{Ox}	benzoxazole phosphine ligand	***i*Pr**	isopropyl
L_{Th}	benzothiazole phosphine ligand	**ppm**	parts per million (10^{-6})
L_{U3}	trisubstituted ureaphosphine ligand	**Pyr**	pyrrolidine

quant.	quantitative	**Ts**	Tosyl, 4-toluenesulfonyl
rac	racemic	**TBAF**	tetrabutylammonium fluoride
R_f	retention factor	**TBDMS**	*tert*-butyldimethylsilyl
rt	room temperature	**THF**	tetrahydrofuran
s	singlet (NMR), strong (IR)	***o*Tol**	*ortho*-tolyl
S	substrate (for hydrogenation or allylic alkylation)	t_R	retention time

Units of measure (except **Å** for Ångström) and their standard unit prefixes were used in accordance with the international system if units (SI), together with the respective prefixes for the type of physical quantity.

For abbreviations related to the analytical data described in the experimental part see section 6.1.2.

CHAPTER 1

IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION AS A TOOL FOR ORGANIC SYNTHESIS

1.1 Introduction

Multiple pharmaceuticals, herbicides, fragrances and flavors manufactured on an industrial scale are known to involve a transition metal-catalyzed reaction in their synthesis.[1] Among these reactions, the most prominent reaction is the asymmetric hydrogenation catalyzed by a transition metal. The relevance of these products can be noticed by the fact that numerous non-specialists are familiar with their names (*e.g.* L-DOPA, ibuprofen and vitamin E). The metal-catalyzed hydrogenation is an attractive reaction for asymmetric synthesis, since it combines highly desirable advantages such as perfect atom economy, high conversions, low catalyst loadings and mild reaction conditions.[2] All these characteristics are well appreciated in modern organic synthesis and explain the various applications of metal-catalyzed asymmetric hydrogenation, not only in academic research but also in industrial synthesis. Although this reaction has been explored for many years and an impressive number of enantioselective catalysts have been developed it is still investigated today. The main goals in this field today are to find solutions to render this reaction more universal, meaning applicable to a wider range of substrates, or to discover more generally applicable, effective, inexpensive and readily available catalysts.[3]

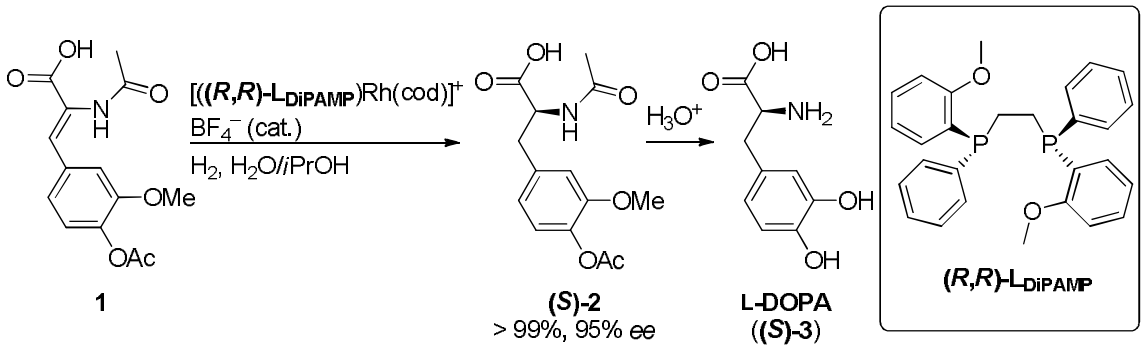
This first chapter of this thesis will show the ongoing need to design novel catalysts for iridium-catalyzed hydrogenation. First, the milestones set to reach today's knowledge in asymmetric hydrogenation reactions catalyzed by a transition metal will be summarized. The subsequent sections will then mainly focus on iridium catalysts for asymmetric hydrogenation, by showing their successful applications in industrial processes (see section 1.3.2) and in natural product synthesis (see section 1.4.2). This perspective will also allow to present many of the designed ligands for iridium-catalyzed asymmetric hydrogenations as well as the broad variety of the substrates they have been applied to (see section 1.4.1). Today's challenges in asymmetric metal-catalyzed hydrogenation,

[1] a) *Asymmetric Catalysis on Industrial Scale: Challenges, Approaches and Solutions* (eds. H.-U. Blaser and H.-J. Federsel), Wiley, Verlag GmbH & Co. KGaA, Weinheim, **2010**; b) J. W. Scott, *Topics in Stereochem.* **1989**, *19*, 209-226; c) H.-U. Blaser, F. Spindler, M. Studer, *Applied Catalysis A: General* **2001**, *221*, 119-143.
[2] G Shang, W. Li, X. Zhang, *Transition Metal-Catalyzed Homogeneous Asymmetric Hydrogenation* in *Catalytic Asymmetric Synthesis* (ed. I. Ojima), Wiley, Hoboken, **2010**, 3rd Ed., pp. 343-436.
[3] a) H.-U. Blaser, B. Pugin, F. Spindler, *Chemistry Today* **2008**, *26*, 37-38; b) J. M. Hawkins, T. J. N. Watson, *Angew. Chem. Int. Ed.* **2004**, *43*, 3224-3228.

will then be discussed in section 1.5; prior to the presentation of the ligand scaffolds that have been investigated as part of the project described in this thesis (see section 1.6).

1.2 Transition Metal-Catalyzed Asymmetric Hydrogenation: a Historical Perspective

The first active catalyst for homogeneous hydrogenation was the rhodium complex discovered by WILKINSON (Nobel Prize 1973, $[(PPh_3)_3Rh]Cl$, Figure 1) and COFFEY.[4] Not much earlier, methods to prepare optically active phosphines were reported by HORNER *et al.* and MISLOW *et al*.[5] The remarkable idea to replace triphenylphosphine by chiral phosphines was obvious to many researchers, but it was first realized by HORNER and KNOWLES, who developed the first asymmetric hydrogenation using a rhodium complex.[6] The enantioselectivities were low, but promising. KNOWLES optimized this catalytic system until it led to the enantioselective synthesis of the rare amino acid L-DOPA (**(*S*)-3**), which was already known at that time to be active in the treatment of Parkinson's disease (Scheme 1).[7] This synthesis and the discovery in 1968 that a chiral rhodium catalyst can be used for catalytic and asymmetric hydrogenation earned KNOWLES the Nobel Prize in Chemistry in 2001 (shared with NOYORI and SHARPLESS).[8]



Scheme 1. Monsanto synthesis of L-DOPA: the process has been in operation since 1978 and was the first transition metal-catalyzed asymmetric synthesis of a commercialized product.[8]

[4] a) J. A. Osborn, F. H. Jardine, Y. F. Young, G. Wilkinson, *J. Chem. Soc. A* **1966**, 1711-1732; b) R. S. Coffey, *Imperial Chemical Industries, Brit. Pat.* **1965**, 1121642.
[5] a) L. Horner, H. Winkler, A. Rapp, A. Mentrup, H. Hoffmann, P. Beck, *Tetrahedron Lett.* **1961**, *2*, 161-166; b) O. Korpiun, K. Mislow, *J. Am. Chem. Soc.* **1967**, *89*, 4784-4786.
[6] a) W. S. Knowles, *Chem. Commun.* **1968**, 1445-1446; b) B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, D. J. Weinkauff, *J. Am. Chem. Soc.* **1977**, *99*, 5946-5952; c) L. Horner, H. Büthe, H. Siegel, *Tetrahedron Lett.* **1968**, *37*, 4023-4026; d) L. Horner, H. Siegel, H. Büthe, *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 942-942.
[7] a) W. S. Knowles, M. J. Sabacky, B. D. Vineyard, *J. Chem. Soc., Chem. Commun.* **1972**, 10-11; b) W. S. Knowles, *Acc. Chem. Res.* **1983**, *16*, 106-112.
[8] W. S. Knowles, *Angew. Chem. Int. Ed.* **2002**, *41*, 1998-2007.

Since the discovery that a metal complex can be used as a homogeneous catalyst for hydrogenations, many important achievements were reported, resulting in today's state-of-the-art in transition metal-catalyzed asymmetric hydrogenations. Figure 1 does not describe the chronological history of progresses accomplished in asymmetric hydrogenation, it is rather thought to give a figurative overview of how a discovery stimulated the next one to reach standards of reactivity. Nowadays countless combinations of ligands and transition metals have been reported to give good to high selectivities in the asymmetric hydrogenation of a myriad of substrates, but Figure 1 is only meant to show the most important compounds that represent landmarks in organometallic chemistry.

Shortly after KNOWLES'and HORNER's discovery, other researchers brought similar contributions and achieved the synthesis of various ligands for transition metals.[9] KAGAN *et al.* introduced C_2-symmetric diphosphines, such as DIOP (2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane, **(*R*,*S*)-L_{DIOP}**, Figure 1) as ligands and showed their synthesis to be practicable.[9a-b]

Another pioneer in this field, awarded with the Nobel Prize together with KNOWLES, is NOYORI.[10] He discovered the C_2-chiral diphosphine ligand BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, **(S_a)-L_{BINAP}**, Figure 1) as a versatile and efficient ligand for various metal-catalyzed transformations, including the asymmetric hydrogenation of α-(acylamino)acrylic acids or esters.[11] BINAP/ruthenium-complexes proved to be more efficient than their rhodium analogues for a broader range of substrates. Besides the C−C double bond reduction of functionalized alkenes, they also allow for the reduction of the C−O double bond in a wide range of ketones.[12] Important industrial syntheses, involving a transformation catalyzed by a BINAP/ruthenium or /rhodium catalyst as key step will be described in more detail in section 1.3.1.

[9] a) T. P. Dang, H. B. Kagan, *J. Chem. Soc. D* **1971**, 481-481; b) H. B. Kagan, T.-P. Dang, *J. Am. Chem. Soc.* **1972**, *94*, 6429-6433; c) J. D. Morrison, R. E. Burnett, A. M. Aguiar, C. J. Morrow, C. Phillips, *J. Am. Chem. Soc.* **1971**, *93*, 1301-1303.
[10] R. Noyori, *Angew. Chem. Int. Ed.* **2002**, *41*, 2008-2022.
[11] A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, *J. Am. Chem. Soc.* **1980**, *102*, 7932-7934.
[12] a) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.* **1988**, *110*, 629-631; b) T. Ohta, H. Takaya, R. Noyori, *Inorg. Chem.* **1988**, *27*, 566-569.

Ligand design for asymmetric hydrogenation catalyzed by a transition metal continued to be the main focus of research for several years and many modifications of the structural environment around the metal center were investigated. BURK *et al.* for instance, designed the bis(phospholane) ligand DuPhos for the rhodium-catalyzed hydrogenation of various olefins (**(*S*,*S*)-L_{DuPhos}**, Figure 1).[13] For a long time C_2-symmetric P,P ligands dominated in asymmetric transition metal catalysis. In the 90s, the planar chiral and non-symmetric ferrocene-based ligands Josiphos were discovered (**(*R*,S_{Fc})-$L_{Josiphos}$**, Figure 1).[14] After the discovery of sterically and electronically non-symmetric P,N ligands by PFALTZ, and independently by HELMCHEN and WILLIAMS, a change in the course of research in chiral ligands could be observed; many ligands that were introduced later on for asymmetric catalysis were non-symmetric.[15] Although the concept of C_2-symmetry has been very successful, the introduction of the non-symmetrical PHOX ligands proved that two electronically and sterically divergent coordinating units can be more effective than C_2-symmetric ligands. PHOX ligands, which were developed originally for palladium-catalyzed allylic substitutions, were also deployed to other transition metal-catalyzed reactions. Excellent enantiomeric excesses and turn over numbers were obtained in the iridium-catalyzed asymmetric hydrogenation of trisubstituted alkenes by the use of these P,N ligands. PHOX/iridium complexes were shown not require a polar coordinating group near to the C−C double bond that is reduced, contrarily to rhodium and ruthenium catalysts.

CRABTREE *et al.* reported already in 1979 that $[Ir(cod)(PCy_3)(Py)]PF_6$ was a highly active catalyst for the hydrogenation of alkenes (CRABTREE's catalyst, Figure 1).[16] This complex hydrogenated alkenes more rapidly than WILKINSON's catalyst. However, deactivation of the catalyst due to the formation of inactive hydride-bridged trinuclear complexes was observed.[16b] Such a trinuclear PHOX/iridium hydride complex was isolated and characterized.[17]

[13] a) M. J. Burk, *J. Am. Chem. Soc.* **1991**, *113*, 8518-8519; b) M. J. Burk, J. E. Feaster, W. A. Nugent, R. L. Harlow, *J. Am. Chem. Soc.* **1993**, *115*, 10125-10138; c) M. J. Burk, *Acc. Chem. Res.* **2000**, *33*, 363-372.
[14] a) A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, *J. Am. Chem. Soc.* **1994**, *116*, 4062-4066; b) H.-U. Blaser, W. Brieden, B. Pugin, F. Spindler, M. Studer, A. Togni, *Top. Catal.* **2002**, *19*, 3-16.
[15] a) A. Pfaltz, W. J. Drury III., *PNAS* **2004**, *101*, 5723-5726; b) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336-345; c) J. M. J. Williams, *Synlett* **1996**, *8*, 705-710.
[16] a) R. H. Crabtree, H. Felkin, G. E. Morris, *J. Organomet. Chem.* **1977**, *141*, 205-215; b) R. Crabtree, *Acc. Chem. Res.* **1979**, *12*, 331-337.
[17] S. P. Smidt, A. Pfaltz, E. Martínez-Vivente, P. S. Pregosin, A. Albinati, *Organometallics* **2003**, *22*, 1000-1009.

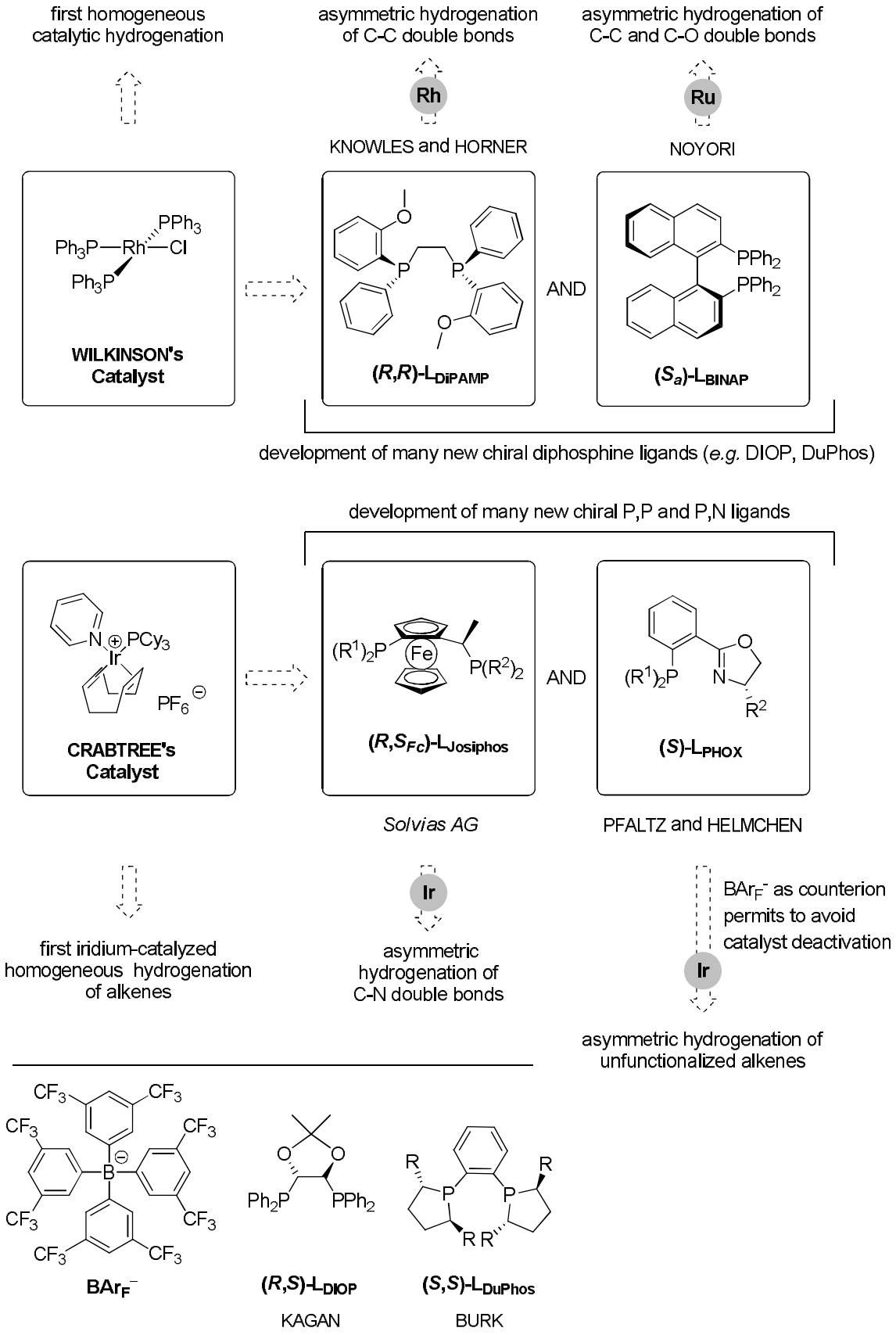


Figure 1. Figurative representation of milestones in metal-catalyzed asymmetric hydrogenation.

The catalyst deactivation was circumvented replacing the PF_6-anion with the weakly coordinating, bulky and apolar BAr_F-couteranion (tetrakis[3,5-bis(trifluoromethyl) phenyl]borate, Figure 1).[18] However, it seems that only this accumulation of different findings (non-symmetric ligands, solvent and counterion effects and the success of the Josiphos ligands in industry) permitted to show that iridium is an interesting alternative to rhodium and ruthenium for the catalytic enantioselective hydrogenation.

The mechanism of the rhodium/phosphine-complex catalyzed asymmetric hydrogenation has been elucidated. Detailed mechanistic studies of the DiPAMP/rhodium-catalyzed asymmetric hydrogenation of acetamidocinnamates were performed by HALPERN and BROWN *et al.*[19] The mechanism of the asymmetric hydrogenation of ketones using a BINAP/ruthenium complex was elucidated by NOYORI *et al.*[20] A definitive rationale of the mechanism of the iridium-catalyzed hydrogenation of C−C double bonds has not been proposed yet.[21] Although several studies have been undertaken, experimental evidence about each step of the catalytic cycle is still lacking and, according to computational studies, it seems that several pathways are possible.[21]

[18] a) A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem. Int. Ed.* **1998**, *37*, 2897-2899; b) S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402-1411; c) I. Krossing, I. Raabe, *Angew. Chem. Int. Ed.* **2004**, *43*, 2066-2090.
[19] a) J. Halpern, *Science* **1982**, *217*, 401-407; b) J. Halpern, *Asymmetric Catalytic Hydrogenation: Mechanism and Origin of Enantioselection*, in *Asymmetric Synthesis* (ed. J. D. Morrison), Academic Press, New York, **1985**, Vol. 5, pp. 41-69; c) J. M. Brown, P. A. Chaloner, *Tetrahedron Lett.* **1978**, *21*, 1877-1880; d) J. M. Brown, P. A. Chaloner, *J. Chem. Soc., Chem. Commun.* **1980**, 344-346; e) J. M. Brown, D. Parker, *Organometallics* **1982**, *1*, 950-956; f) J. M. Brown, L. R. Canning, A. J. Downs, A. M. Forster, *J. Organomet. Chem.* **1983**, *255*, 103-111; g) A. S. C. Chan, J. J. Pluth, J. Halpern, *Inorg. Chim. Acta* **1979**, *37*, 477-479; h) A. S. C. Chan, J. J. Pluth, J. Halpern, *J. Am. Chem. Soc.* **1980**, *102*, 5952-5954; i) A. S. C. Chan, J. Halpern, *J. Am. Chem. Soc.* **1980**, *102*, 838-840; j) C. Landis, J. Halpern, *J. Am. Chem. Soc.* **1987**, *109*, 1746-1754; k) I. D. Gridnev, T. Imamoto, *Acc. Chem. Res.* **2004**, 37, 633-644.
[20] C. A. Sandoval, T. Ohkuma, K. Muñiz, R. Noyori, *J. Am. Chem. Soc.* **2003**, *125*, 13490-13503.
[21] a) R. H. Crabtree, P. C. Demou, D. Eden, J. M. Mihelcic, C. A. Parnell, J. M. Quirk, G. E. Morris, *J. Am. Chem. Soc.* **1982**, *104*, 6994-7001; b) C. Mazet, S. P. Smidt, M. Meuwly, A. Pfaltz, *J. Am. Chem. Soc.* **2004**, *126*, 14176-14181; c) M. J. Burk, M. P. McGrath, R. Wheeler, R. H. Crabtree, J. Am. Chem. Soc. **1988**, *110*, 5034-5039; d) R. Dietiker, P. Chen, *Angew. Chem. Int. Ed.* **2004**, 43, 5513-516; e) X. Cui, K. Burgess, *Chem. Rev.* **2005**, *105*, 3272-3296; f) Y. Zhu, Y. Fan, K. Burgess, *J. Am. Chem. Soc.* **2010**, *132*, 6249-6253; g) Y. Fan, X. Cui, K. Burgess, M. B. Hall, *J. Am. Chem. Soc.* **2004**, *126*, 16688-16689; h) J. Zhou, J. W. Ogle, Y. Fan, V. Banphavichit(Bee), Y. Zhu, K. Burgess, *Chem. Eur. J.* **2007**, *13*, 7162-7170; i) C. Hedberg, K. Källström, P. Brandt, L. K. Hansen, P. G. Andersson, *J. Am. Chem. Soc.* **2006**, *128*, 2995-3001; j) T. L. Church, T. Rasmussen, P. G. Andersson, *Organometallics* **2010**, *29*, 6769-6781; k) P. Brandt, C. Hedberg, P. G. Andersson, *Chem. Eur. J.* **2003**, *9*, 339-347; l) K. H. Hopmann, A. Bayer, *Organometallics* **2011**, *30*, 2483-2497; m) K. Källström, I. Munslow, P. G. Andersson, *Chem. Eur. J.* **2006**, *12*, 3194-3200.

1.3
Metal-Catalyzed Asymmetric Hydrogenation in Industrial Processes

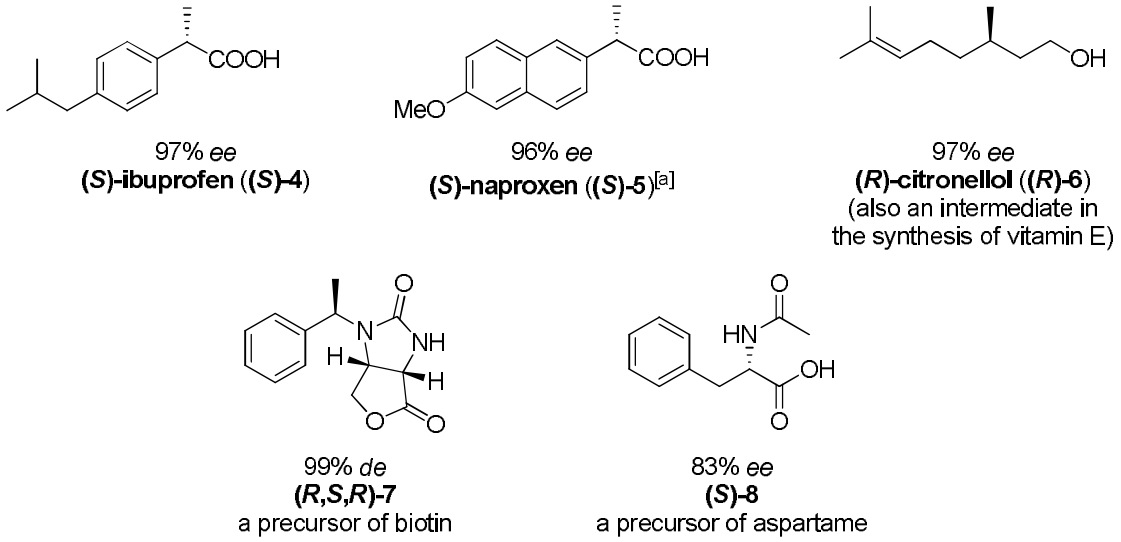
A major concern for chemical processes is efficiency. Catalysis can be highly productive and economical, as it reduces the waste deriving from racemate resolution in enantioselective synthesis. The asymmetric hydrogenation reaction is fundamental for the manufacturing of fine and industrial chemicals and has found application in the industrial synthesis of pharmaceuticals, agrochemicals, flavors and fragrances. Selected examples of transition metal-catalyzed asymmetric hydrogenation for industrial processes will be presented below.

1.3.1
Rhodium and Ruthenium Catalysts for Asymmetric Hydrogenation in Industrial Processes

Most of the asymmetric hydrogenations in industry involve chiral phosphorus ligands and are rhodium- or ruthenium-catalyzed. As described above, the first industrial application of a metal-catalyzed asymmetric hydrogenation was found in the synthesis of L-DOPA (Scheme 1). The catalyst developed by KNOWLES, not only proved to be efficient in the enantioselective synthesis of L-DOPA, but also led to the synthesis of several amino acids, such as phenylalanine, tryptophan and alanine with enantiomeric excess higher than 90%. This application of diphosphine/rhodium catalysts became a standard method for the production of enantiomerically pure amino acids. Although KNOWLES' DiPAMP ligand was efficient, the chiral phospholane DuPhos introduced later on replaced it since this ligand proved to be more convenient hydrogenation of (*E*)/(*Z*)-mixtures of olefins.[13c]

Another significant example of a pharmaceutically important compound that can be synthesized by asymmetric hydrogenation of a C–C double bond using this time a ruthenium-based BINAP catalyst is (*S*)-ibuprofen (**(*S*)-4**, Figure 2). This anti-inflammatory drug was obtained quantitatively from 2-(4-isobutylphenyl)propenoic

acid with 97% *ee*.[22] The synthesis of (*S*)-naproxen (**(*S*)-5**), a chiral anti-inflammatory drug) involves as well an enantioselective hydrogenation that can be catalyzed effectively by the BINAP/ruthenium catalysts developed by NOYORI *et al.*[23] Despite the good results obtained with several catalysts in terms of enantioselectivity, the asymmetric synthesis of (*S*)-naproxen (**(*S*)-5**) by asymmetric hydrogenation is still not valuable for industry. For economical reasons, (*S*)-naproxen is still produced on a large scale by the resolution of a racemate.[1c]



[a] (*S*)-Naproxen is still produced on a large scale by the resolution of a racemate.

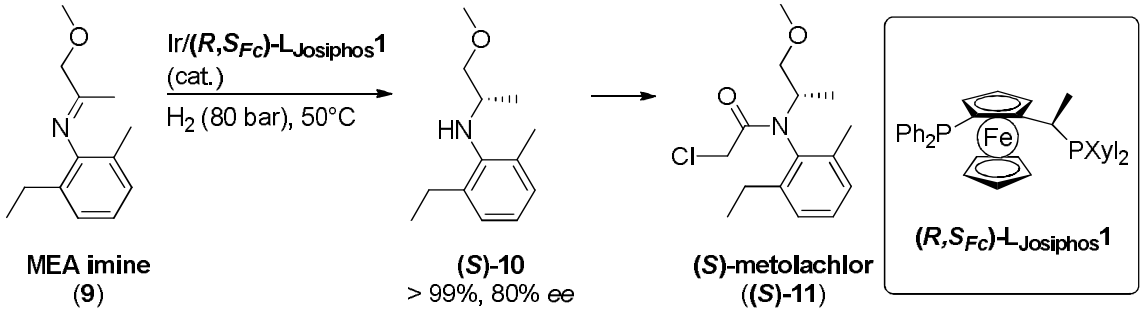
Figure 2. Asymmetric hydrogenation products produced in large scale by the use of chiral ruthenium and rhodium catalysts.[1c,23-26]

Some other compounds synthesized by asymmetric C−C double bond reduction are: citronellol (**(*R*)-6**) by *Takasago*;[1c,24] the intermediate **(*R,S,R*)-7** for biotin by *Lonza*;[1c,25] and the intermediate **(*S*)-8** in the synthesis of aspartame (sweetener) by *Enichem/Anic*[1c,26] (Figure 2). Whereas, the synthesis of citronellol involves as well a BINAP/ruthenium catalyst, the asymmetric hydrogenations affording **(*R,S,R*)-7** and **(*S*)-8** are rhodium-catalyzed.

[22] a) K. Mashima, K. Kusano, N. Sato, Y. Matsumura, K. Nozaki, H. Kumobayashi, N. Sayo, Y. Hori, T. Ishizaki, S. Akutagawa, H. Takaya, *J. Org. Chem.* **1994**, *59*, 3064-3076; b) H. Kumobayashi, T. Miura, N. Sayo, T. Saito, X. Zhang, *Synlett* **2001**, 1055-1064.
[23] a) T. Ohta, H. Takaya, R. Noyori, *Inorg. Chem.* **1988**, *27*, 566-569; b) T. Ohta, H. Takaya, M. Kitamura, K. Nagai, R. Noyori, *J. Org. Chem*. **1987**, *52*, 3174-3176.
[24] S. Akutagawa, *Appl. Catal. A: General* **1995**, *128*, 171-207.
[25] R. Imwinkelried, *Chimia* **1997**, *51*, 300-302.
[26] a) I. Ojima, N. Clos, C. Bastos, *Tetrahedron* **1989**, *45*, 6901-6939; b) M. Fiorini, M. Riocci, M. Giongo, *Eur. Pat. Appl.* **1983**, EP 77099 A2.

1.3.2
Iridium Catalysts for Asymmetric Hydrogenation in Industrial Processes

Among all the production processes known to involve an asymmetric hydrogenation as the key step, only one of them employs an iridium catalyst (Scheme 2).[1c] In fact, iridium catalysts have found so far no commercially important application in the reduction of C−C double bonds, however the Josiphos 1/iridium complex has been applied successfully to the industrial synthesis of the herbicide (*S*)-metolachlor (**(*S*)-11**, Scheme 2). The active ingredient of the grass herbicide, commercialized as Dual®, was first sold as a racemate, until it was found in 1982 that only the (*S*)-enantiomer of metolachlor is bioactive. The iridium/ferrocenyl bisphosphine catalyst found its utility in the asymmetric reduction of the C−N double bond of the imine intermediate: 2-methyl-6-ethylphenyl-1'-methyl-2'-methoxyethylimine (MEA-imine, (**9**)). The Josiphos 1/iridium catalyst showed extremely high activities and high enantioselectivities in the presence of acid and iodine, compared to all the other rhodium/ or iridium/P,P ligand combinations previously tested.[27] *Solvias AG* (formerly *Ciba-Geigy*/*Novartis*) demonstrated that enantioselective hydrogenation can compete against other methods (such as classical resolution, chromatographic separation or biocatalysis) in the production of enantiomerically enriched chiral compounds.

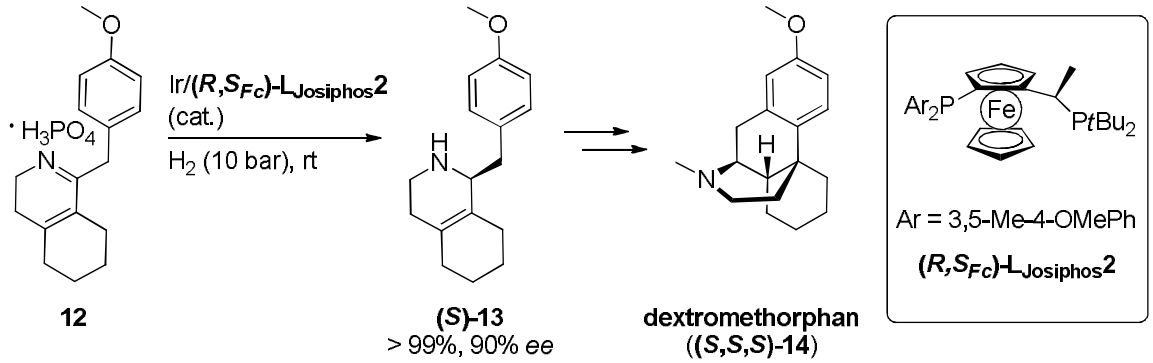


Scheme 2. (*S*)-Metolachlor process.[27]

The *Solvias* Josiphos ligand family is today almost as successful as the BINAP ligand family and has been reported to induce high enantioselectivities in a wide variety of transformations.[28]

[27] H.-U. Blaser, R. Hanreich, H.-D. Schneider, F. Spindler, B. Steinacher,*The Chiral Switch of Metolachlor: The Development of a Large-Scale Enantioselective Catalytic Process*, in *Asymmetric Catalysis on Industrial Scale: Challenges, Approaches and Solutions* (eds. H.-U. Blaser and E. Schmidt), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, FRG, **2004**.
[28] a) H.-U. Blaser, W. Brieden, B. Pugin, F. Spindler, M. Studer, A. Togni, *Top. Catal.* **2002**, *19*, 3-16; b) H.-U. Blaser, B. Pugin, F. Spindler, M. Thommen, *Acc. Chem. Res.* **2007**, *40*, 1240-1250.

However, the enantioselective reduction of C−C double bonds in production is still dominated by rhodium and ruthenium catalysts, most likely due to their high efficiency, extensively reported in the literature. This observation is very surprising, considering the fact that iridium complexes can be more reactive than rhodium and ruthenium catalysts and, in contrast to rhodium and ruthenium complexes do not require an additional coordinating functional group close to the C−C double bond to promote its reduction.[19a,29] Further to these observations and considering the advantageous price of iridium compared to rhodium, efforts are being made to increase the number of industrial processes involving an iridium-catalyzed asymmetric hydrogenation. For instance, in a pilot process at *Lonza*, a Josiphos ligand has been used in combination with iridium in the reduction of the imine intermediate **12** for the preparation of dextromethorphan (**(*S,S,S*)-14**), an antitussive (Scheme 3).[1c,25] Unfortunately though, the catalyst efficiency was reported to be rather low (ton 1 500; compared to 2 000 000 in the hydrogenation of the (*S*)-metolachlor intermediate, Scheme 2).



12 **(*S*)-13** > 99%, 90% *ee* **dextromethorphan** (**(*S,S,S*)-14**)

Scheme 3. Pilot process at *Lonza*: asymmetric hydrogenation of imine **12** to amine **(*S*)-13**, an intermediate in the synthesis of dextromethorphan.

In order to encourage process chemists to consider asymmetric catalysis for the large scale manufacturing of low cost products, the chiral ligands need either to be available in large quantities or at least involve short synthesis. Today's challenges can be seen in two different ways, either researchers seek for the right substrate and catalyst combination using for example high-throughput methods, or go on seeking for more broadly applicable catalysts, that are readily available.

[29] A. Pfaltz, J. Blankenstein, R. Hilgraf, E. Hörmann, S. McIntyre, F. Menges, M. Schönleber, S. P. Smidt, B. Wüstenberg, N. Zimmermann, *Adv. Synth. Catal.* **2003**, *345*, 33-43.

1.4
Iridium-Catalyzed Asymmetric Hydrogenation in Natural Product Synthesis

Many iridium catalysts have been designed and deployed to hydrogenate enantioselectively a broad variety of substrates. As depicted in Figures 3 and 4, a certain type of substrate can often be associated with a type of ligand structure depending on their electronic and steric features. This association can rarely be predicted and a thorough substrate screening is often required to identify the best catalyst for a defined substrate class. Moreover, one should also keep in mind that a substrate class that can be hydrogenated with good enantioselectivities, using already known catalysts is not always tested for each new catalyst system, since researchers try to fill the existing gaps. Therefore, a comparison between all the existing catalysts for each substrate class is not possible. Nevertheless, the iridium-catalyzed asymmetric hydrogenation of C−N and C−C double bonds has proved to be very efficient in academia. In this case, once a catalyst has been found to be active and selective in the hydrogenation of a specific substrate, it becomes an interesting tool for synthesis. Herein, *privileged ligands* for each class of substrate for the iridium-catalyzed asymmetric hydrogenation will first be described (see section 1.4.1). Next, ligands that were applied successfully to natural product syntheses featuring an asymmetric iridium-catalyzed hydrogenation will be presented (see section 1.4.2).

1.4.1
Privileged Chiral Bidentate Ligands for Iridium

Many ligands have been elaborated and the design of new ligand structures is still ongoing. This section describes bidentate ligands that were applied to the asymmetric hydrogenation of C−C, C−N and C−O double bonds. The discussion will be limited to bidentate ligands coordinating to iridium, even though a large number of monodentate ligands was as well developed for iridium-catalyzed asymmetric hydrogenation.[30]

[30] a) N. Mrsic, L. Lefort, J. A. F. J. Boogers, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Adv. Synth. Catal.* **2008**, *350*, 1081-1089; b) G. Erre, K. Junge, S. Enthaler, D. Addis, D. michalik, A. Spannenberg, M. Beller, *Chem. Asian J.* **2008**, *3*, 887-894; c) X.-B. Jiang, M. van den Berg, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Tetrahedron: Asymmetry* **2004**, *15*, 2223-2229; d) X.-B. Jiang, A. J. Minnaard, B. Hessen, B. L. Feringa, A. L. L. Duchateau, J. G. O. Andrien, J. A. F. Boogers, J. G. de Vries, *Org. Lett.* **2003**, *5*, 1503-

1.4.1.1
Bidentate Ligands for Asymmetric Hydrogenation of C−C Double Bonds

Figure 3 shows ligand structures, which allowed to broaden the substrate scope for enantioselective hydrogenation of C−C double bonds employing iridium complexes. This figure offers an overview of the substrates that were efficiently hydrogenated using chiral iridium complexes and shows, at the same time, that the asymmetric hydrogenation reaction is a substrate specific reaction. Each ligand type performs best for a specific substrate class. This does not mean that a specific ligand is not applicable to another substrate class, but that it performs better in the reduction of a particular substrate type it is associated to than others tested previously.

Trisubstituted functionalized and unfunctionalized alkenes can be hydrogenated selectively with a large number of P,N ligands and NHC ligands.[31] In contrast, unfunctionalized tetrasubstituted alkenes could only be hydrogenated successfully using iridium catalysts derived from phosphinooxazolines **(*S*)-L8** with up to 97% *ee* (see Figure 3).[32]

For the hydrogenation of 1,1-disubstituted alkenes, phosphinite–oxazoline ligands derived from threonine (**(*S*,*S*)-$L_{ThrePHOX}$**) were shown to be highly selective (up to 94% *ee*).[33a-b] A broader range of highly functionalized 1,1-disubstituted alkenes were asymmetrically hydrogenated with up to 99% *ee* with chiral phosphite oxazoline ligands **L1***.[33c] A new class of bulky chiral pyranoside phosphite-oxazoline ligands (**L2***) designed by ANDERSSON *et al.* showed as well remarkable enantioselectivities for some 1,1-disubstituted alkenes (up to 99% *ee*).[33d-e]

1506; e) M. T. Reetz, X. Li, *Chem. Commun.* **2006**, 2159-2160; e) A. J. Minnard, B. L. Feringa, L. Lefort, J. G. de Vries, *Acc. Chem. Res.* **2007**, *40*, 1267-1277.
[31] D. H. Woodmansee, A. Pfaltz, *Chem. Commun.* **2011**, *47*, 7912-7916.
[32] M. G. Schrems, E. Neumann, A. Pfaltz, *Angew. Chem. Int. Ed.* **2007**, *46*, 8274-8276.
[33] a) S. McIntyre, E. Hörmann, F. Menges, S. P. Smidt, A. Pfaltz, *Adv. Synth. Catal.* **2005**, *347*, 282-288; b) F. Menges, A. Pfaltz, *Adv. Synth. Catal.* **2002**, *344*, 40-44; c) J. Mazuela, J. J. Verendel, M. Coll, B. Schäffner, A. Börner, P. G. Andersson, O. Pàmies, M. Diéguez, *J. Am. Chem. Soc.* **2009**, *131*, 12344-12353; d) M. Diéguez, J. Mazuela, O. Pàmies, J. J. Verendel, P. G. Andersson, *J. Am. Chem. Soc.* **2008**, *130*, 7208-7209; e) J. Mazuela, P.-O. Norrby, P. G. Andersson, O. Pàmies, M. Diéguez, *J. Am. Chem. Soc.* **2011**, *133*, 13634-13645.

Fewer examples of the successful hydrogenation of C−C double bonds of *α,β*-unsaturated ketones are reported.[34]. Both phosphinooxazolines ligands (**(*S*)-L$_{PHOX}$** and **(*S*)-L3**) allowed for the hydrogenation of *α,β*-disubstituted enones, with enantiomeric excesses of up to 99%.[34a-c] However, for the selective C−C double bond hydrogenation of *β,β*-disubstituted enones, sulfoximine-derived P,N ligands **(*S*)-L4** gave up to 97% *ee* depending on the substituents.[34d] Ferrocenyl-PHOX iridium catalysts (**(*S,S$_{Fc}$*)-L$_{Fc\text{-}PHOX}$** ligands) reduce *α,β*-unsaturated amides with up to 98% *ee*.[35] Only iridium complexes of the spiro ligands, **(*S,S$_a$*)-L$_{SpinPHOX}$** and **(*S,S$_a$*)-L$_{SiPHOX}$**, are reported to reduce enantioselectively *α,β*- and *β,γ*-unsaturated carboxylic acids.[36] Iridium complexes with biphenylphosphine oxazoline ligands (**(*S,S$_a$*)-L5**) are the only ones which were reported to achieve the asymmetric hydrogenation of *α,β*-unsaturated lactones and lactames with high enantioselectivities (up to 98% *ee*).[34e] Moreover, these ligands were also applied to the asymmetric reduction of the to exocyclic C−C double bond of *α,β*-unsaturated ketones.[34e]

Di- and trisubstituted enol phosphinates can be hydrogenated with up to 99% *ee* by iridium complexes bearing P,N ligands **(*S,S,R,R*)-L6**.[37] **(*S,S,R,R*)-L6** ligands, also furnished high enantioselectivities in the iridium-catalyzed reduction of vinyl boronates (up to 98% *ee*).[38] Iridium complexes derived from **(*R*)-L7** proved to be selective in the asymmetric hydrogenation of a few fluorinated alkenes.[39] The same ligand **(*R*)-L7** allowed for high enantioselectivities in the asymmetric hydrogenation of several diphenylvinylphosphine oxides and vinylphosphonates.[40] Very recently (1-chloro-1-alkenyl)boronic esters were hydrogenated with moderate to high enantioselectivities, using Ferrocenyl-PHIM ligands (**(*R,R,S$_{Fc}$*)-L$_{Fc\text{-}PHIM}$**).[41]

[34] a) W.-J. Lu, Y.-W. Chen, X.-L. Hou, *Adv. Synth. Catal.* **2010**, *352*, 103-107; b) S.-M. Lu, C. Bolm, *Angew. Chem. Int. Ed.* **2008**, *47*, 8920-8923; c) W.-J. Lu, Y.-W. Chen, X.-L. Hou, *Angew. Chem. Int. Ed.* **2008**, *47*, 10133-10136; d) S.-M. Lu, C. Bolm, *Chem. Eur. J.* **2008**, *14*, 7513-7516; e) F. Tian, D. Yao, Y. Liu, F. Xie, W. Zhang, *Adv. Synth. Catal.* **2010**, *352*, 1841-1845.
[35] W.-J. Lu, X.-L. Hou, *Adv. Synth. Catal.* **2009**, *351*, 1224-1228.
[36] a) S. Li, S.-F. Zhu, C.-M. Zhang, S. Song, Q.-L. Zhou, *J. Am. Chem. Soc.* **2008**, *130*, 8584-8585; b) Y. Zhang, Z. Han, F. Li, K. Ding, A. Zhang, *Chem. Commun.* **2010**, *46*, 156-158; c) S. Song, S.-F. Zhu, S. Yang, S. Li, Q.-L Zhou, *Angew. Chem. Int. Ed.* **2012**, *51*, 2708-2711.
[37] a) P. Cheruku, S. Gohil, P. G. Andersson, *Org. Lett.* **2007**, *9*, 1659-1661; b) P. Cheruku, J. Diesen, P. G. Andersson, *J. Am. Chem. Soc.* **2008**, *130*, 5595-5599.
[38] A. Paptchikhine, P. Cheruku, M. Engman, P. G. Andersson, *Chem. Commun.* **2009**, 5996-5998.
[39] M. Engman, J. S. Diesen, A. Paptchikhine, P. G. Andersson, *J. Am. Chem. Soc.* **2007**, *129*, 4536-4537.
[40] P. Cheruku, A. Paptchikhine, T. L. Church, P. G. Andersson, *J. Am. Chem. Soc.* **2009**, *131*, 8285-8289.
[41] I. Gazić Smilović, E. Casas-Arcé, S. J. Roseblade, U. Nettekoven, A. Zanotti-Gerosa, M. Kovačevič, Z. Časar, *Angew. Chem. Int. Ed.* **2012**, *51*, 1014-1018.

Protected and unprotected allylic alcohols were reduced with high enantioselectivities using the ligand type **(*R*)-L9** developed by PFALTZ *et al.*, but also using and the carbene oxazoline ligand **(*S*)-L10** designed by BURGESS *et al*.[42] In addition, BURGESS' iridium catalyst (**(*S*)-L10**/iridium complex) permits the asymmetric hydrogenation of vinyl ethers with up to 98% *ee*, a transformation which is so far not achievable with P,N ligands.[43] This same carbene-oxazoline catalyst allows for the asymmetric hydrogenation of dienes.[44]

Bicyclic pyridine phosphinite **(*R*)-L9** are valuable ligands for the iridium-catalyzed asymmetric hydrogenation of a broad range of substrates, but remarkable is their application in the reduction of furane and benzofurane derivatives (up to 99% *ee*), for which no precedent was reported before.[45] These same ligands proved highly efficient in the asymmetric hydrogenation of purely alkyl-substituted alkenes.[46] Chromenes were hydrogenated with excellent enantioselectivities using iridium complexes chelated with phosphinite oxazoline ligands derived from threonine (**(*S*,*S*)-$L_{ThrePHOX}$**).[47]

Screening P,N iridium catalysts developed previously, unfunctionalized enamines were hydrogenated with up to 91% *ee*, using a phosphinooxazoline ligand (**(*S*)-L_{PHOX}**).[48a] The well known PHOX ligands provided the best results for a larger amount of substrates but also other P,N ligands were shown to be effective for the iridium-catalyzed asymmetric hydrogenation of enamines.[48] *N*-Protected indole derivatives were reduced enantioselectively with **(*S*,*S*)-$L_{ThrePHOX}$** and bicyclic pyridine phosphinite **(*R*)-L9** (up to 99% *ee*) but the scope of indoles that underwent selective reduction is very narrow.[49]

[42] a) A. Wang, B. Wüstenberg, A. Pfaltz, *Angew. Chem. Int. Ed.* **2008**, *47*, 2298-2300; b) J. Zhou, K. Burgess, *Angew. Chem. Int. Ed.* **2007**, *46*, 1129-1131; c) J. Zhao, K. Burgess, *J. Am. Chem. Soc.* **2009**, *131*, 13236-13237.
[43] Y. Zhu, K. Burgess, *Adv. Synth. Catal.* **2008**, *350*, 979-983.
[44] X. Cui, K. Burgess, *J. Am. Chem. Soc.* **2003**, *125*, 14212-14213.
[45] S. Kaiser, S. P. Smidt, A. Pfaltz, *Angew. Chem. Int. Ed.* **2006**, *45*, 5194-5197.
[46] S. Bell, B. Wüstenberg, S. Kaiser, F. Menges, T. Netscher, A. Pfaltz, *Science* **2006**, *311*, 642-644.
[47] C. Valla, A. Baeza, F. Menges, A. Pfaltz, *Synlett* **2008**, *20*, 3167-3171.
[48] a) A. Baeza, A. Pfaltz, *Chem. Eur. J.* **2009**, *15*, 2266-2269; b) P. Cheruku, T. L. Church, A. Trifonova, T. Wartmann, P. G. Andersson, *Tetrahedron Lett.* **2008**, *49*, 7290-7293; c) G.-H. Hou, J.-H. Xie, P.-C. Yan, Q.-L. Zhou, *J. Am. Chem. Soc.* **2009**, *131*, 1366-1367.
[49] A. Baeza, A. Pfaltz, *Chem. Eur. J.* **2010**, *16*, 2036-2039.

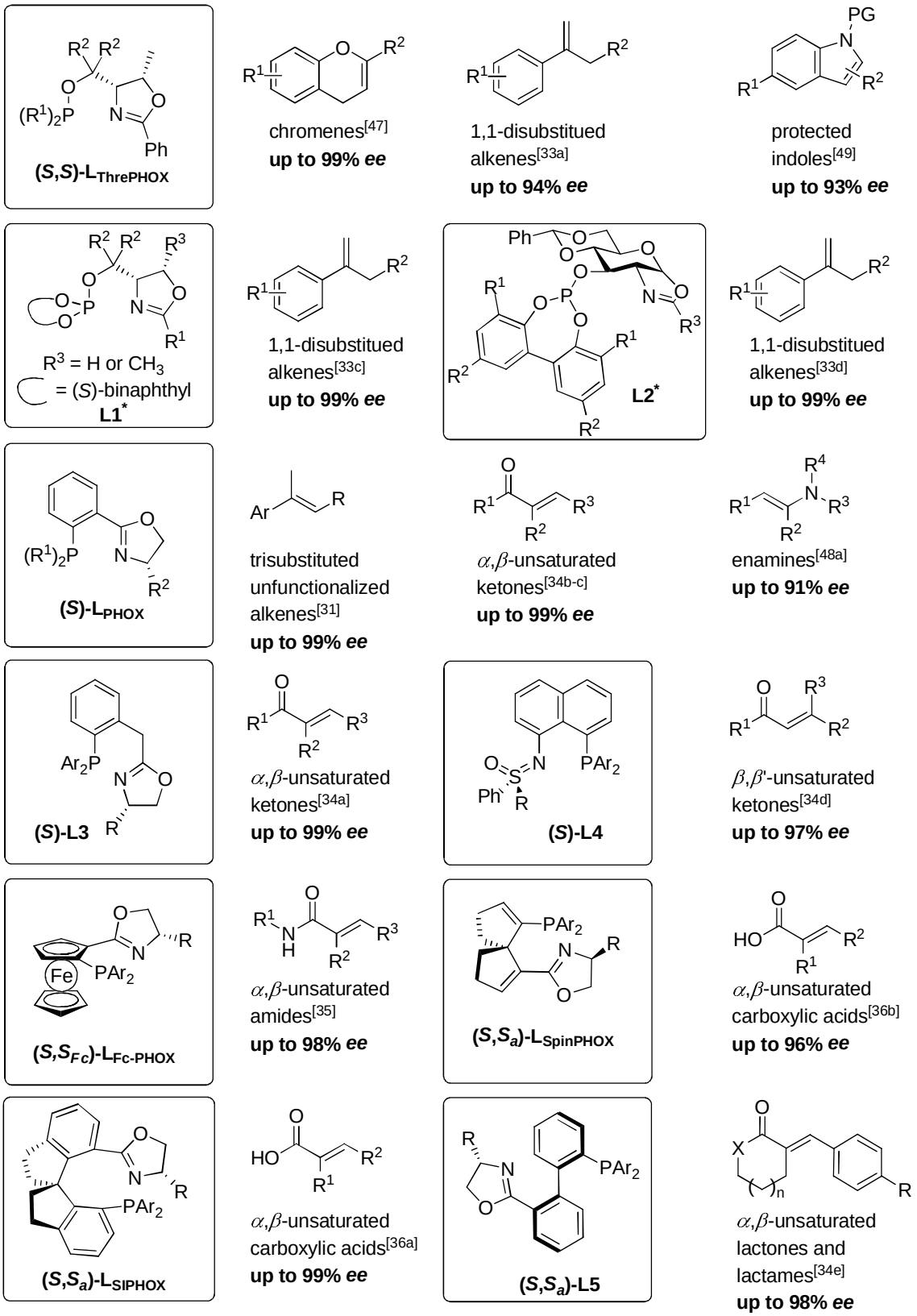


Figure 3. *Privileged ligands* for iridium-catalyzed asymmetric hydrogenation of C−C double bond.

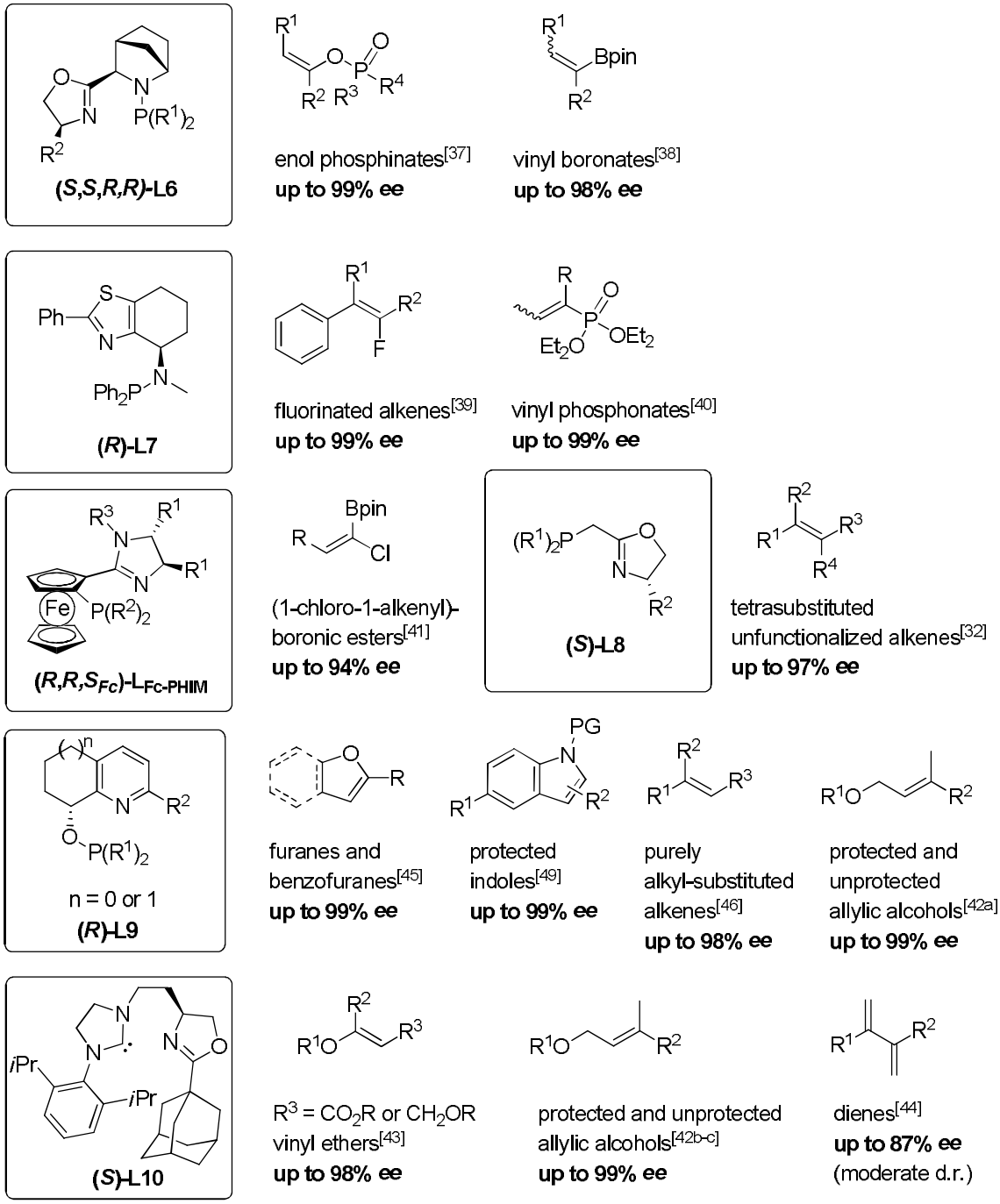


Figure 3. (continued)

Besides P,N ligands constituted from a heterocyclic sp^2-hybridized nitrogen donor in combination with a trisubstituted phosphorus atom, also a C,N ligand (**(*S*)-L10**) having a coordinating *N*-heterocyclic carbene unit was designed and gave astonishingly high selectivities in the iridium-catalyzed asymmetric reduction of several substrates (vinyl ethers, allylic alcohols and dienes, Figure 3).

1.4.1.2

Bidentate Ligands for the Asymmetric Hydrogenation of C−N Double Bonds

In the iridium-catalyzed asymmetric hydrogenations of C−N double bonds not only bidentate P,N ligands proved to be efficient but also P,P ligands. In Figure 4 are depicted selected ligands, which gave high enantioselectivities in the iridium-catalyzed hydrogenation of C−N double bonds.

Besides the Josiphos ligand family presented previously, an impressive amount of various P,N and P,P ligands have been applied to the iridium-catalyzed hydrogenation of various imines.[34a,50] The ligands designed by KNOCHEL *et al.* (**(*S*,*S*$_{Fc}$)-L11**) and those developed by YOSHIDA *et al.* (**(*S*,*S*)-L12**) allow for enantioselectivities up to 99% in the reduction of aromatic *N*-aryl imines, whereas with SpinPHOX ligands (**(*S*,*S*$_a$)-L$_{\text{SpinPHOX}}$**) the hydrogenation of aromatic *N*-benzyl imines can be achieved with up to 98% *ee*.[50g-i] The chiral 1,1-bisphosphanoferrocene ligands **(*S*$_a$,*S*$_a$)-L$_{\text{f-binaphane}}$** led to the hydrogenation of acyclic imines with up to > 99% *ee* and of N−H imines with up to 94% *ee*.[50k]

Quinolines were hydrogenated with the use of sulfoximine-derived P,N ligands (**(*S*)-L4**) for iridium, achieving enantiomeric excesses of up to 92%.[51a] Ferrocenyl-based P,N ligands furnished similar enantioselectivities,[51b] whereas MeO-Biphep ligand, a P,P chelating ligand gave slightly higher enantioselectivities (up to 96%).[51c] Many other P,P ligands were successfully employed for the iridium-catalyzed asymmetric hydrogenation of quinolines.[51d-e]

[50] a) A. Baeza, A. Pfaltz, *Chem. Eur. J.* **2010**, *16*, 4003-4009; b) P. Schnider, G. Koch, R. Prétôt, G. Wang, F. M. Bohnen, C. Krüger, A. Pfaltz, *Chem. Eur. J.* **1997**, *3*, 887-892; c) A. Trifonova, J. S. Diesen, C. J. Chapman, P. G. Andersson, *Org. Lett.* **2004**, *6*, 3825-3827; d) A. Trifonova, J. S. Diesen, P. G. Andersson, *Chem. Eur. J.* **2006**, *12*, 2318-2328., e) C. Moessner, C. Bolm, *Angew. Chem. Int. Ed.* **2005**, *44*, 7564-7567; f) S.-F. Zhu, J.-B. Xie, Y.-Z. Zhang, S. Li, Q.-L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 12886-12891; g) M. N. Cheemala, P. Knochel, *Org. Lett.* **2007**, *9*, 3089-3092; h) Z. Han, Z. Wang, X. Zhang, K. Ding, *Angew. Chem. Int. Ed.* **2009**, *48*, 5345-5349; i) T. Imamoto, N. Iwadate, K. Yoshida, *Org. Lett.* **2006**, *8*, 2289-2292; j) D. Xiao, X. Zhang, *Angew. Chem. Int. Ed.* **2001**, *40*, 3425-3428; k) G. Hou, F. Gosselin, W. Li, J. C. McWilliams, Y. Sun, M. Weisel, P. D. O'Shea, C. Y. Chen, I. W. Davies, X. Zhang, *J. Am. Chem. Soc.* **2009**, *131*, 9882-9883.

[51] a) S.-M. Lu, C. Bolm, *Adv. Synth. Catal.* **2008**, *350*, 1101-1105; b) S.-M. Lu, X.-W. Han, Y.-G. Zhou, *Adv. Synth. Catal.* **2004**, *346*, 909-912; c) W.-B. Wang, S.-M. Lu, P.-Y. Yang, X.-W. Han, Y.-G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536-15037; d) S. H. Chan, K. H. Lam, Y.-M. Li, L. Xu, W. Tang, F. L. Lam, W. H. Lo, W. Y. Yu, Q. Fan, A. S. C. Chan, *Tetrahedron: Asymmetry* **2007**, *18*, 2625-2631; e) F.-R. Gou, W. Li, X. Zhang, Y.-M. Liang, *Adv. Synth. Catal.* **2010**, *352*, 2441-2444.

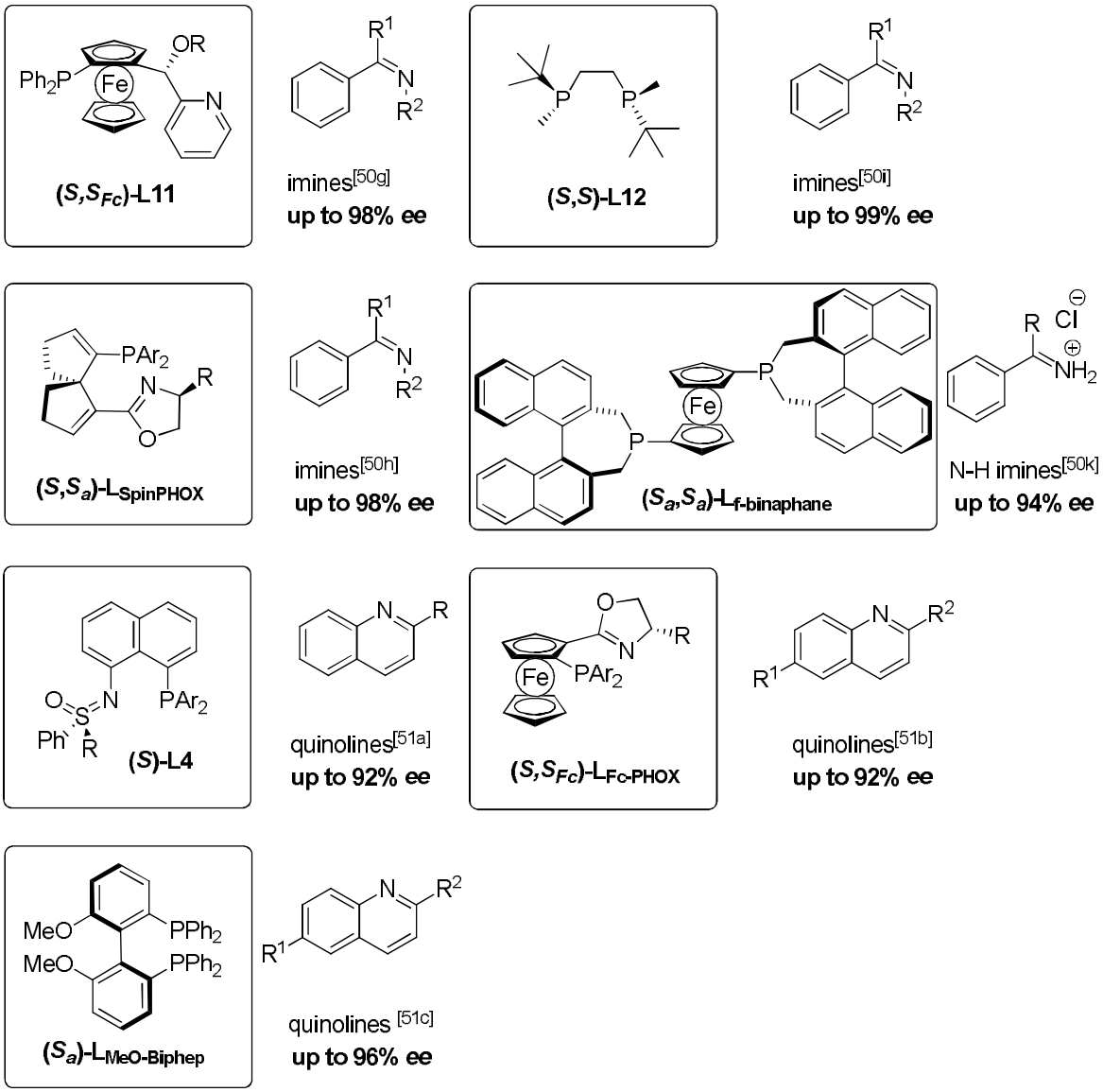


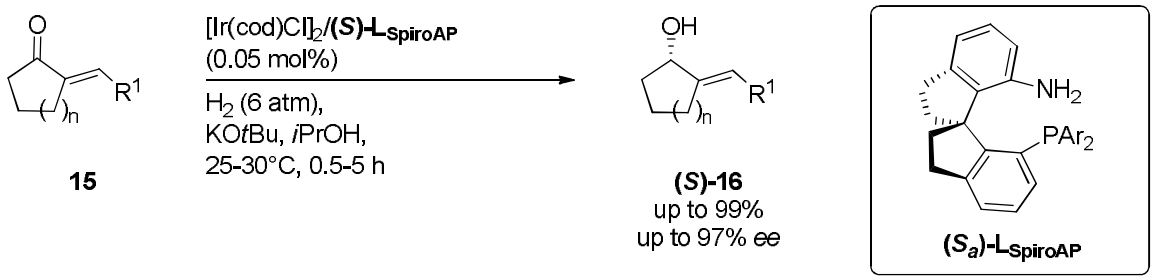
Figure 4. *Privileged ligands* for iridium-catalyzed asymmetric hydrogenation of C−N double bonds.

Even though enantioselectivities are excellent, the range of imines and quinolines that undergo highly enantioselective iridium-catalyzed asymmetric hydrogenation remains limited.

1.4.1.3
Bidentate Ligands for the Asymmetric Hydrogenation of C−O Double Bonds

Most of the iridium catalysts developed hitherto display moderate selectivities in the asymmetric hydrogenation of C−O double bonds. The first successful example of a C−O

double bond reduction was reported by DAHLENBURG *et al.*[52] The iridium-catalyzed hydrogenation of ketones with P,N ligands afforded the resulting alcohols with poor enantioselectivities (up to 68% *ee*). For cyclic *α*,*β*-unsaturated ketones, with an exocyclic C−C double bond, ZHOU *et al.* achieved up to 97% *ee* in the selective C−O double bond reduction with iridium complexes derived from chiral spiro aminophosphine ligands (**(S_a)-$L_{SpiroAP}$**, Scheme 4).[53]



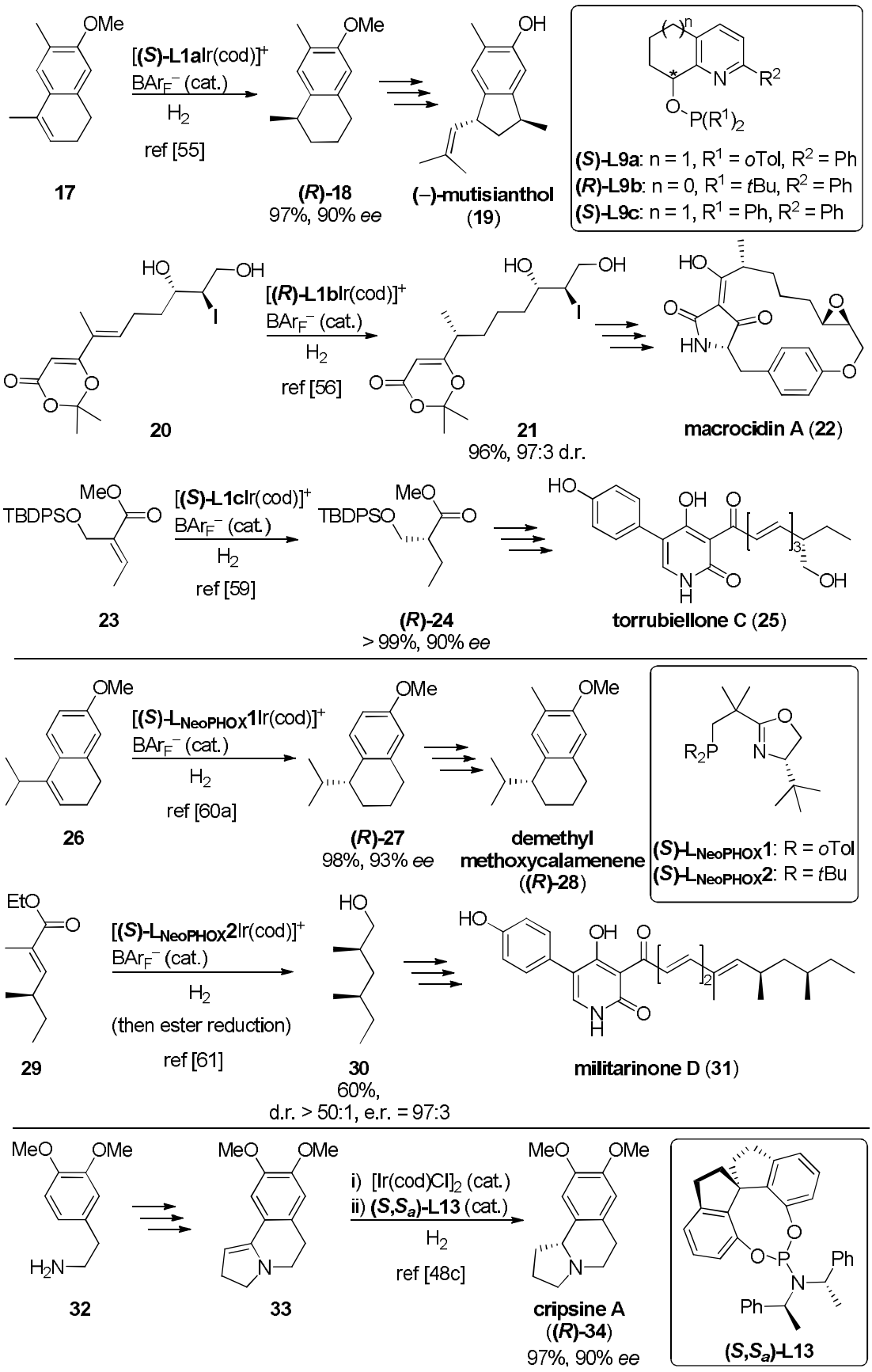
Scheme 4. Asymmetric hydrogenation of *exo*cyclic *α*,*β*-unsaturated ketones.[53]

1.4.2
Natural Product Syntheses Involving an Iridium-Catalyzed Asymmetric Hydrogenation

Several total syntheses of natural products featuring an iridium-catalyzed asymmetric hydrogenation as the key step have been reported and some of them are depicted in Scheme 5.

Shortly after the discovery that pyridylphosphine ligands **(*R*)-L9** allow for the asymmetric hydrogenation of unfunctionalized trialkyl-substituted C−C double bonds, a first example of the enantio- and diastereoselective hydrogenation of farnesol, an important building block for nature but also for organic synthesis was reported.[42a,45-46,54] This type of pyridylphosphine/iridium catalyst could also be applied to the asymmetric hydrogenation of an intermediate in the total synthesis of mutisianthol (**19**)[55] and of macrocidin A (**22**)[57] (Scheme 5).

[52] L. Dahlenburg, R. Götz, *Eur. J. Inorg. Chem.* **2004**, 888-905.
[53] J.-B. Xie, J.-H. Xie, X.-Y. Liu, W.-L. Kong, S. Li, Q.-L. Zhou, *J. Am. Chem. Soc.* **2010**, *132*, 4538-4539.
[54] a) R. Schmid, S. Antoulas, R. Rüttimann, M. Schmid, M. Vecchi, H. Weiser, *Helv. Chim. Acta* **1990**, *73*, 1276-1299; b) N. Cohen, B. Schaer, *J. Org. Chem.* **1992**, *57*, 5783-5785; c) D. R. Threlfall in *Secondary Plant Products* (eds. E. A. Bell, B. V. Charlwood), Springer, Berlin **1980**, pp. 292-298.



Scheme 5. Examples of iridium catalysts used in the total synthesis of natural products (for reaction conditions see the references).

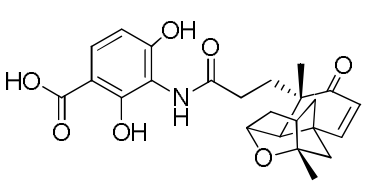
Mutisianthol (**19**) is a sesquiterpene, both its enantiomers were isolated from the roots of *Mutisia homoeantha* and show moderate antitumor activity.[55,56] Macrocidin A (**22**) is a cyclophane tetramic acid that was identified as plant pathogen and represents a potential lead compound for herbicide design.[57,58] The total and enantioselective synthesis of (+)-torrubiellone C (**25**) was also accomplished with a pyridylphosphine/iridium catalyst (Scheme 5).[59]

Subsequent to the identification of NeoPHOX ligands as valuable ligands for the iridium-catalyzed asymmetric hydrogenation of both unfunctionalized and functionalized olefins, they were employed in the total synthesis of the antitumor natural product (*R*)-(+)-7-demethyl-2-methoxycalamenene (**(*R*)-28**).[60] This same ligand class was later used in the stereoselective total synthesis of pyridone alkaloid militarinone D (**31**).[61]

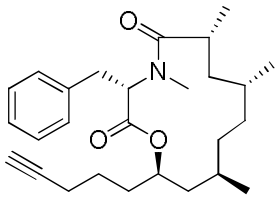
The development of iridium complexes of spiro phosphoramidites as highly enantioselective catalysts for the asymmetric hydrogenation of cyclic enamines led to the synthesis of the biologically active isoquinoline alkaloid crispine A (**(*R*)-34**, Scheme 5).[48c,62] For this transformation the monodentate spiro phosphoramidite ligand **(*S*,*S*$_a$)-L13** showed better enantioselectivities than bidentate ligands.[48c]

The formal total synthesis of platensimycin (**35**), showing potent activity as new type of antibiotic, was achieved by performing two asymmetric hydrogenations catalyzed by P,N iridium complexes in the key steps (Figure 5).[63] BURGESS *et al.* could apply their NHC ligand/iridium complex in the total synthesis of (−)-spongidepsin (**36**), a cytotoxic marine natural product (Figure 5).[64]

[55] G. G. Bianco, H. M. C. Ferraz, A. M. Costa, L. V. Costa-Lotufo, C. Pessoa, M. O. de Moraes, M. G. Schrems, A. Pfaltz, L. F. Silva, Jr. *J. Org. Chem.* **2009**, *74*, 2561-2566.
[56] F. Bohlmann, C. Zdero, N. Le Van, *Phytochemistry* **1979**, *18,* 99-102.
[57] T. Yoshinari, K. Ohmori, M. G. Schrems, A. Pfaltz, K. Suzuki, *Angew. Chem. Int. Ed.* **2010**, *49*, 881-885.
[58] P. R. Graupner, A. Carr, E. Clancy, J. Gilbert, K. L. Bailey, J.-A. Derby, B. Clifford Gerwick, *J. Nat. Prod.* **2003**, *66*, 1558-1561.
[59] H. J. Jessen, A. Schumacher, F. Schmid, A. Pfaltz, K. Gademann, *Org. Lett.* **2011**, *13*, 4368-4370.
[60] a) M. G. Schrems, A. Pfaltz, *Chem. Commun.* **2009**, 6210-6212; b) F. Bohlmann, C. Zdero, H. Robinson, R. King, *Phytochemistry* **1979**, *18*, 1675-1680.
[61] H. J. Jessen, A. Schumacher, T. Shaw, A. Pfaltz, K. Gademann, *Angew. Chem. Int. Ed.* **2011**, *50*, 4222-4226.
[62] Q. Zhang, G. Tu, Y. Zhao, T. Cheng, *Tetrahedron* **2002**, *58*, 6795-6798.
[63] a) K. Tiefenbacher, L. Tröndlin, J. Mulzer, A. Pfaltz, *Tetrahedron* **2010**, *66*, 6508-6513; b) D. Häbich, F. von Nussbaum, *ChemMedChem* **2006**, *1*, 951-954.
[64] a) Y. Zhu, A. Loudet, K. Burgess, *Org. Lett.* **2010**, *12*, 4392-4395; b) A. Grassia, L. Bruno, C. Debitus, S. Marzocco, A. Pino, L. Gomez-Paloma, R. Riccio, *Tetrahedron* **2001**, *57*, 6257-6260.



platensimycin
(35)



(–)-spongidepsin
(36)

Figure 5. Structure of platensimycin and (−)-spongidepsin.

All these reports involving an iridium-catalyzed asymmetric hydrogenation in the total synthesis of natural products are recent. This trend shows the slow establishment of iridium as the metal of choice for certain type of asymmetric hydrogenation and suggest that iridium could also find its place as the metal of choice for industrial applications.

1.5 Challenges for Metal-Catalyzed Asymmetric Hydrogenations

As it was shown by history, for example in the synthesis of chiral (*S*)-metolachlor, the quest for new transition metal-catalysts is still a valuable goal in order to optimize the synthesis of enantiomerically pure active compounds by asymmetric hydrogenation. Between the discovery of the biological activity of metolachlor in 1970 and the start of the production of (*S*)-metolachlor on a ton-scale in 1996, many attempts were made to optimize its enantioselective synthesis. These efforts required first the screening of different metals and then of different ligands, followed by optimization of the reaction conditions.[65] This example, among many other, illustrates well the substrate dependence of metal-catalyzed hydrogenations and the need to discover other active and selective catalysts in order to make asymmetric reduction of double bonds more universal.

Another trend that can be noticed examining more recent reports about asymmetric hydrogenations, is the re-introduction of chiral monodentate phosphorus ligands.[30] Phosphites, phosphonites and phosphoroamidates were reported as interesting and cheap alternative ligands for the iridium-catalyzed asymmetric hydrogenation of alkenes. Their lower cost might compensate for their reduced activity. However, the development of

[65] H.-U. Blaser, *Adv. Synth. Catal.* **2002**, *344*, 17-31.

ligands that are both, efficient and cheap is required. A valuable approach to fulfill these requirements still probably is the design of ligands which are derived from amino acids.

1.6 Objectives of this Work

The main aim of the research project described in this thesis was to develop and optimize easily accessible ligands that can be applied to the iridium-catalyzed asymmetric hydrogenation of various substrates. In the field of asymmetric catalysis, two different approaches can be pursued: (1) a substrate of interest needs to be hydrogenated enantioselectively and the goal of research is to develop a catalyst that fulfills this particular need; or (2) one develops and elaborates new catalyst systems based on today's knowledge and then find an interesting substrate type which could reveal the advantages of this catalyst by comparing its selectivity with previously tested catalysts. This second approach is most used in methodological research and is also how it was proceeded herein. Given the goal to seek for a novel type of catalyst for the asymmetric hydrogenation, three parameters are variable excluding the optimization of the reaction conditions: the metal, the ligand structure and the substrate type. This thesis deals with the ligand structure optimization. The important variations in ligand structure are the following: coordination mode of the ligand (bidentate or monodentate), the atoms that coordinate the metal (P, N, S, C and their substituents influencing the electronic property of the ligand), the size of the metallacycle formed upon coordination (influencing the bite angle in a bidentate coordination manner) and the general steric hindrance generated by the ligand around the active site.

The general scaffold of choice for this project was proline. All ligands that were developed are proline-based (Figure 6).

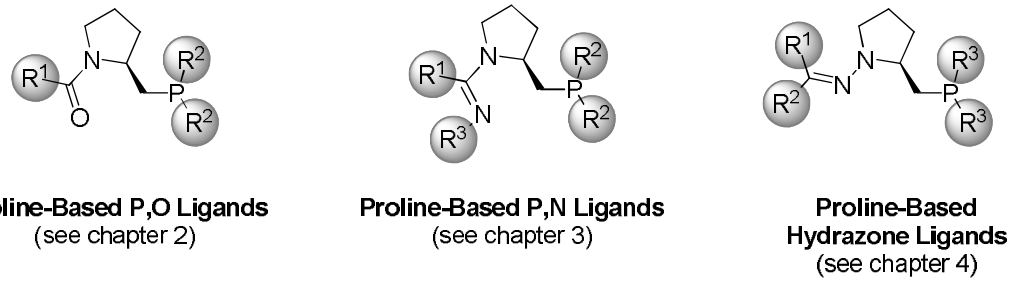
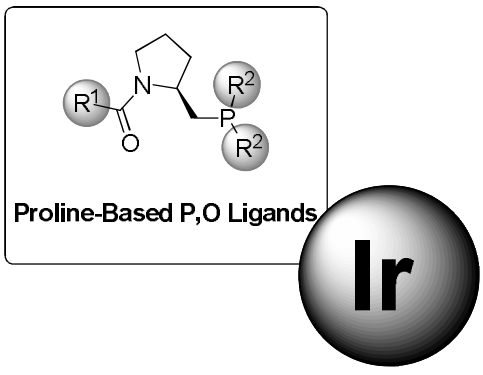


Figure 6. Ligand scaffolds presented herein.

In chapter 2, proline-based P,O ligands will be described in more detail. Amido-, carbamato- as well as ureaphophines were investigated as novel types of ligands. In the following chapters, two different proline-based P,N ligands scaffolds will be presented (chapters 3 and 4). The state-of-the-art ligands for iridium-catalyzed asymmetric hydrogenation are P,N bidentates. The idea to combine the advantages of proline-based ligands with the traditional coordination mode was obvious: proline-based P,N ligands were therefore investigated. Finally, in chapter 5, an attempt to discover further applications of proline-based P,O ligands for transition metal-catalyzed reactions will be described.

CHAPTER 2

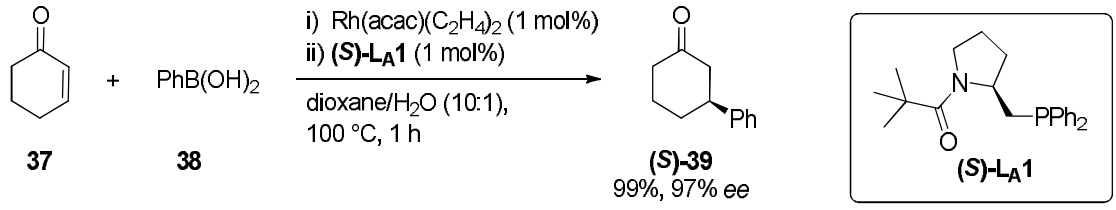
PROLINE-BASED P,O LIGANDS FOR IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION



2.1 Metal-Catalyzed Asymmetric Reactions Involving Bidentate P,O Ligands

As described in chapter 1, a series of ligands was designed and applied successfully to iridium-catalyzed asymmetric hydrogenation of C−C and C−N double bonds. Although an appreciable variety in ligand structure was achieved, most ligands are bidentate P,N ligands. They coordinate to iridium *via* a nitrogen atom and a phosphorus donor. Herein, proline-based ligands will be described which bind to the transition metal *via* a carbonyl oxygen atom and a phosphorus atom. Their synthesis and the analysis of their coordination mode to iridium(I) will be discussed. Furthermore, the results will be shown, which were obtained, when the ligands were applied to the iridium-catalyzed asymmetric hydrogenation of functionalized and unfunctionalized alkenes, as well as a standard imine substrate. Prior to this, previous reports involving P,O ligands in metal-catalyzed reactions will be summarized.

In the field of asymmetric metal catalysis, only a few ligands which are coordinated to the transition metal by a carbonyl oxygen atom have been reported. TOMIOKA *et al.* described amidophosphines as ligands for the asymmetric rhodium-catalyzed 1,4-addition of arylboronic acids to enones with high enantioselectivities (Scheme 6).[66] Amidophosphine **(*S*)-L$_A$1** was reported to behave as a hemilabile ligand for rhodium(I).[67]

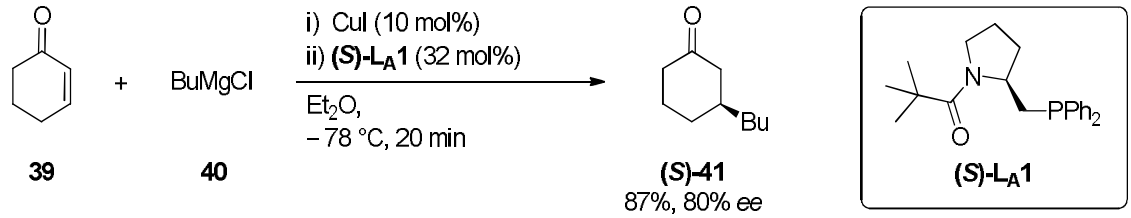


37 **38** **(*S*)-39** 99%, 97% *ee* **(*S*)-L$_A$1**

Scheme 6. Rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to cyclohexenone (**37**) using amidophosphine **(*S*)-L$_A$1** as ligand.[66a]

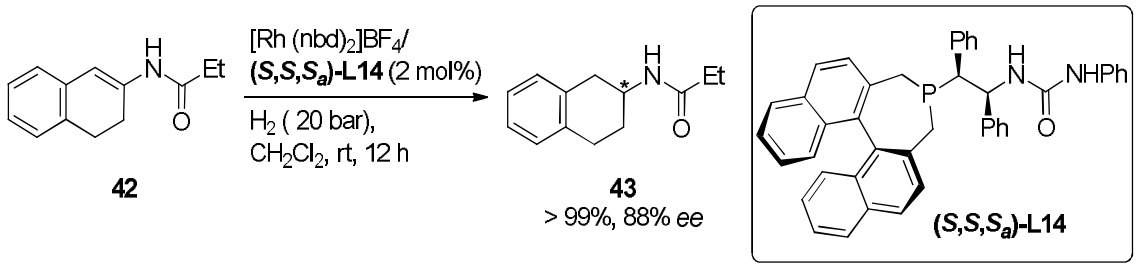
[66] a) M. Kuriyama, K. Nagai, K.-I. Yamada, Y. Miwa, T. Taga, K. Tomioka, *J. Am. Chem. Soc.* **2002**, *124*, 8932-8939; b) Q. Chen, M. Kuriyama, X. Hao, T. Soeta, Y. Yamamoto, K.-I. Yamada, K. Tomioka, *Chem. Pharm. Bull.* **2009**, *57*, 1024-1027.
[67] For reviews on hemilabile ligands see: a) P. Braunstein, F. Naud, *Angew. Chem. Int. Ed.* **2001**, *40*, 680–699; b) P. Braunstein, *J. Organomet. Chem.* **2004**, *689*, 3953-3967; c) A. Bader, E. Lindner, *Coord. Chem. Rev.* **1991**, *108*, 27-110.

These amidophosphines were used as chiral ligands for the enantioselective conjugate addition of various organocopper reagents to cyclic and acyclic *α*,*β*-unsaturated carbonyl compounds, too.[68] Moderate to excellent enantioselectivities were achieved. One example of a catalytic reaction of this type using butylmagnesium chloride and copper iodide in the presence of ligand **(*S*)-L$_A$1** is depicted in Scheme 7.



Scheme 7. Example of the asymmetric conjugate addition of Grignard reagents to cyclic *α*,*β*-unsaturated carbonyl compounds.[68b]

When, alkoxyarylphosphines were investigated as ligands, it was found in the beginning that P,O ligands decrease the reaction rate of the rhodium-catalyzed hydrogenation of 1-hexene.[67c,69] However, REEK *et al.* applied recently a novel type of ureaphosphine P,O ligands that coordinate to rhodium in a bidentate fashion.[70] This system allowed for the asymmetric hydrogenation of cyclic enamides with moderate to good enantioselectivities (Scheme 8).



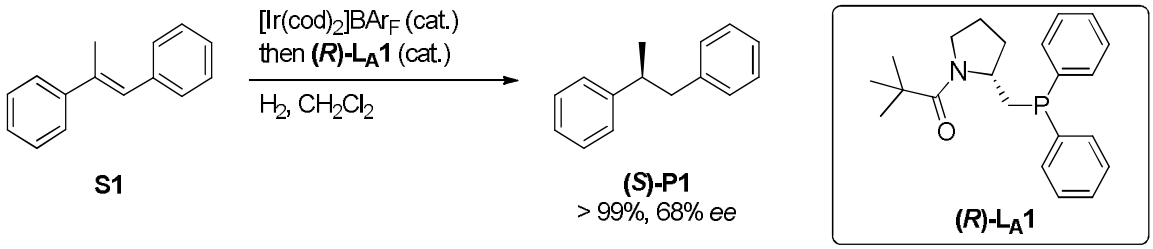
Scheme 8. Rhodium-catalyzed asymmetric hydrogenation of cyclic enamides using a bidentate P,O ligand.[70b]

[68] a) Y. Nakagawa, K. Matsumoto, K. Tomioka, *Tetrahedron* **2000**, *56*, 2857-2863; b) M. Kanai, Y. Nakagawa, K. Tomioka, *Tetrahedron* **1999**, *55*, 3843-3854; c) Y. Nakagawa, M. Kanai, Y. Nagaoka, K. Tomioka, *Tetrahedron* **1998**, *54*, 10295-10307; d) Y. Nakagawa, M. Kanai, Y. Nagaoka, K. Tomioka, *Tetrahedron Lett.* **1996**, *37*, 7805-7808; e) M. Kanai, K. Koga, K. Tomioka, *Tetrahedron Lett.* **1992**, *33*, 7193-7196; f) M. Kanai, Y. Nakagawa, K. Tomioka, *Tetrahedron* **1999**, *55*, 3831-3842; g) K. Nagai, H. Fujihara, M. Kuriyama, K.-i. Yamada, K. Tomioka, *Chem. Lett.* **2002**, 8-9.
[69] L. Horner, G. Simons, *Z. Naturforsch. Teil B* **1984**, *39B*, 497-503.
[70] a) J. Meeuwissen, R. Detz, A. J. Sandee, B. de Bruin, M. A. Siegel, A. L. Spek, J. N. H. Reek, *Eur. J. Inorg. Chem.* **2010**, 2992-2997; b) J. Meeuwissen, R. J. Detz, A. J. Sandee, B. de Bruin, J. N. H. Reek, *Dalton Trans.* **2010**, *39*, 1929-1931.

2.2

An Amidophosphine Representing Proline-Based P,O Ligands for Iridium-Catalyzed Asymmetric Hydrogenation

In a broad automated screening of various combinations of metals and ligands carried out at *Solvias AG* an iridium complex formed *in situ* from bis-(η^4-1,5-cyclooctadiene) iridium(I) tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ([Ir(cod)$_2$]BAr$_F$) and amidophosphine **(*R*)-L$_A$1** was discovered to give promising results.[71] In the asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) this **(*R*)-L$_A$1**/iridium catalyst furnished 68% *ee* (Scheme 9).



Scheme 9. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) using a catalyst formed *in situ* by complexation of [Ir(cod)$_2$]BAr$_F$ with **(*R*)-L$_A$1**.[71,72]

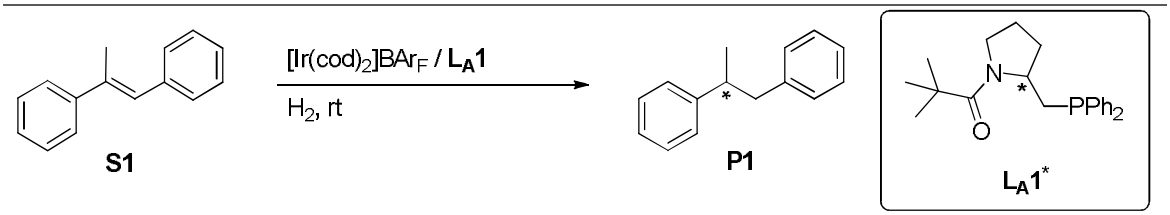
This result triggered the start of the project presented in this chapter in collaboration with *Solvias AG*. The ligand **(*R*)-L$_A$1** was provided by *Solvias AG*. The questions which had primarily to be addressed were: (1) the identification of the coordination mode of this ligand to the transition metal (see section 2.2.2), and (2) the optimization of the selectivities in the asymmetric hydrogenation of alkenes. Therefore, the reaction conditions were studied in detail and afterwards it was investigated, whether this catalytic system can also be applied to the asymmetric hydrogenation of substrates different from the unfunctionalized trisubstituted alkene **S1**.

[71] Unplublished results from *Solvias AG*.
[72] These results were obtained in an automated screening at *Solvias AG*, the detailed reaction conditions are not known.

2.2.1
Initial Results

After the discovery of amidophosphine **(*R*)-L$_A$1** as ligand for iridium of some preliminary screening experiments were carried out. First, the optimization of the reaction conditions for the iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) was pursed. The results from this screening using amidophosphine **(*R*)-L$_A$1** and **(*S*)-L$_A$1** as ligand are summarized in Table 1.

Table 1. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**).[a]



Entry	Ligand	L$_A$1/Ir (ratio)	Solvent	*p* [bar]	*t* [h]	Yield [%][b]	*ee* [%][c]
1	**(*R*)-L$_A$1**	1:2[d]	CH_2Cl_2	50	2	90	58 (*S*)
2	**(*R*)-L$_A$1**	1:1	CH_2Cl_2	50	2	> 99	70 (*S*)
3	**(*R*)-L$_A$1**	2:1[e]	CH_2Cl_2	50	2	79	62 (*S*)
4[f]	**(*R*)-L$_A$1**	1:1	CH_2Cl_2	50	2	**> 99**	**70 (*S*)**
5[f]	**(*S*)-L$_A$1**	1:1	CH_2Cl_2	50	2	> 99	68 (*R*)
6[f]	**(*R*)-L$_A$1**	1:1[g]	CH_2Cl_2	50	2	93	60 (*S*)
7	**(*R*)-L$_A$1**	1:1	CH_2Cl_2	50	1	92	64 (*S*)
8	**(*R*)-L$_A$1**	1:1	CH_2Cl_2	5	2	55	65 (*S*)
9	**(*R*)-L$_A$1**	1:1	CH_2Cl_2	5	1	48	64 (*S*)
10	**(*R*)-L$_A$1**	1:1	$PhCH_3$	50	2	15	53 (*S*)
11	**(*R*)-L$_A$1**	1:1	*t*BuOMe	50	2	79	62 (*S*)
12	**(*R*)-L$_A$1**	1:1	*n*-C_5H_{12}	50	2	15	50 (*S*)
13	**(*R*)-L$_A$1**	1:1	CF_3CH_2OH	50	2	29	*rac*

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), rt; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] **(*R*)-L$_A$1** (1.25 µmol) and $[Ir(cod)_2]BAr_F$ (2.50 µmol); [e] **(*R*)-L$_A$1** (5.00 µmol) and $[Ir(cod)_2]BAr_F$ (2.50 µmol); [f] The reaction was not prepared in a glove box; [g] Results obtained with the isolated precatalyst **(*R*)-C$_A$1** ([(**(*R*)-L$_A$1**)Ir(cod)]BAr_F).

Entries 1 to 3 show the results obtained by variation of the ligand to metal ratio. These experiments were thought to give an initial indication, whether the ligand behaves as a bidentate P,O ligand. Indeed, the best result concerning both activity and selectivity were observed, when a 1:1 ratio of ligand to metal was used (entry 2). If the ligand would behave as monodentate phosphine donor, the active catalyst formed by complexation of two equivalents of **(*R*)-L$_A$1** to one equivalent of the metal, entry 3 should show superior

results compared to entry 2. In addition, the ^{31}P NMR spectra after the *in situ* complexation but prior to the hydrogenation reaction of entry 3 clearly showed a 1:1 mixture of complex **(*R*)-C$_A$1** ([**((*R*)-L$_A$1**)Ir(cod)]BAr$_F$; δ = 9.1 ppm) and free ligand **(*R*)-L$_A$1** (δ = − 25.3 ppm, see also Table 2). The conversion and selectivity were significantly lower, when a 1:2 ratio of ligand to metal was used (entry 1).

By comparing the results in entries 4 and 5 it can be seen that under identical reaction condition the use of the corresponding (*S*)-enantiomer of **L$_A$1*** as ligand causes the almost perfect inversion of selectivity and the (*R*)-configured product is obtained with 68% *ee*. When the precatalyst was isolated prior to the hydrogenation reaction, the enantioselectivity was slightly lower (entry 6). The synthesis and isolation of the precatalyst will be discussed below in section 2.2.2.

The results in entries 7 to 9, show the influence of hydrogen pressure and reaction time on the activity of the catalytic system. After applying 50 bar hydrogen pressure for 1 hour, the reaction yielded 92% of the product with 64% *ee* (entry 7). At 5 bar hydrogen pressure the reaction did not go to completion (entries 8 and 9). The screening of various solvents for this asymmetric hydrogenation reaction did not improve the catalyst efficiency (entries 10 to 13). The use of toluene, *tert*-butylmethylether, *n*-pentane and 2,2,2-trifluoroethanol resulted in reduced yields and enantioselectivities.

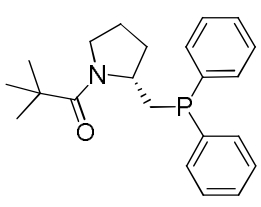
Therefore, the appropriate reaction conditions were determined to be the initial conditions, utilizing: 1 mol% of catalyst at 50 bar hydrogen pressure for 2 hours in dichloromethane at room temperature. These conditions were used for almost all iridium-catalyzed asymmetric hydrogenations presented in this chapter. If parameters are varied, this change will be noted. The product yields obtained in the hydrogenation of any substrate presented herein were determined by GC analysis and the products were not isolated.

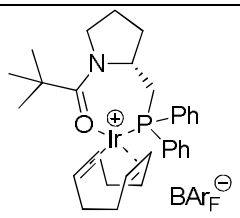
2.2.2
Analysis of the Coordination Mode to Iridium

In order to investigate the coordination mode of the amidophosphine ligand **(*R*)-L_A1** to iridium(I) in the precatalyst structure a series of analytical experiments was carried out. These are described below, involving NMR, IR and X-ray spectroscopy.

Analysis of the coordination mode of amidophosphine **(*R*)-L_A1** to the iridium center in solution was achieved by employing nuclear magnetic resonance (NMR) spectroscopy, measuring the chemical shifts for the free ligand and the *in situ* complexed ligand in deuterated dichloromethane (Table 2). The ^{31}P NMR signals of the phosphorus atom in **(*R*)-C_A1** ([(**(*R*)-L_A1**)Ir(cod)]BAr_F) and in **(*R*)-L_A1** clearly prove its coordination to the metal center (**(*R*)-C_A1**, δ = 9.1 ppm *versus* **(*R*)-L_A1**, δ = − 25.3 ppm). This observation was not surprising, but a similar chemical shift of the ^{13}C NMR signal for the quaternary carbon of the amide functionality was also observed (Table 2). This signal is shifted downfield by 8.8 ppm, when the ligand is complexed to iridium (**(*R*)-C_A1**, δ = 184.7 ppm and **(*R*)-L_A1**, δ = 175.9 ppm). The absence of a second quaternary signal for the carbonyl functionality in the measured sample of **(*R*)-C_A1** indicates the complete binding of the amide carbonyl oxygen to iridium. In the isostructural rhodium(I) complex studied by TOMIOKA *et al.* the ligand was described to behave as a hemilabile ligand.[66a] When complexed to iridium(I), the ligand **(*R*)-L_A1** binds in a bidentate manner, however it is possible that an average chemical shift of two different species is measured, if the rate of exchange is faster than NMR time scale.

Table 2. Comparison of the spectroscopic properties of ligand **(*R*)-L_A1** and complex **(*R*)-C_A1**.





	(*R*)-L_A1	**(*R*)-C_A1**[a]
^{31}P NMR [δ (P)]	− 25.3 ppm	9.1 ppm
^{13}C NMR [δ (C=O)]	175.9 ppm	184.7 ppm
IR [$\tilde{\nu}$ (C=O)]	1615 cm^{-1}	1535 cm^{-1}

[a] The *in situ* complexed ligand was analyzed [Ir(cod)$_2$]BAr_F/**(*R*)-L_A1** (1:1) in CD_2Cl_2.

Stronger evidence for the bidentate chelation of (*R*)-$\mathbf{L_A1}$ to iridium was obtained from infrared (IR) spectroscopy (Table 2). The IR spectrum of the free ligand **(*R*)-$\mathbf{L_A1}$** shows a strong absorption at 1615 cm^{-1}, which was assigned to the C−O bond stretching mode. Lowering of the analogous wavenumber in the IR spectra of **(*R*)-$\mathbf{C_A1}$** to 1535 cm^{-1}, unambiguously confirms the coordination of the carbonyl group to the metal through π* back-donation.

Summarizing the results of the analyses shown above, it is clear that the amidophosphine **(*R*)-$\mathbf{L_A1}$** coordinates in a bidentate fashion to iridium(I). The carbonyl oxygen and the phosphorus atom both coordinate to the metal center *via* σ-donation of electron density. In addition, the carbonyl oxygen is bound by π back-donation from the metal to the π^*-orbital of the carbonyl functionality (Figure 7). Taken together, the interaction between iridium(I) and the carbonyl oxygen of the amidophosphine ligand was shown to be stronger than the analogous rhodium(I) carbonyl ligand interaction.[66a]

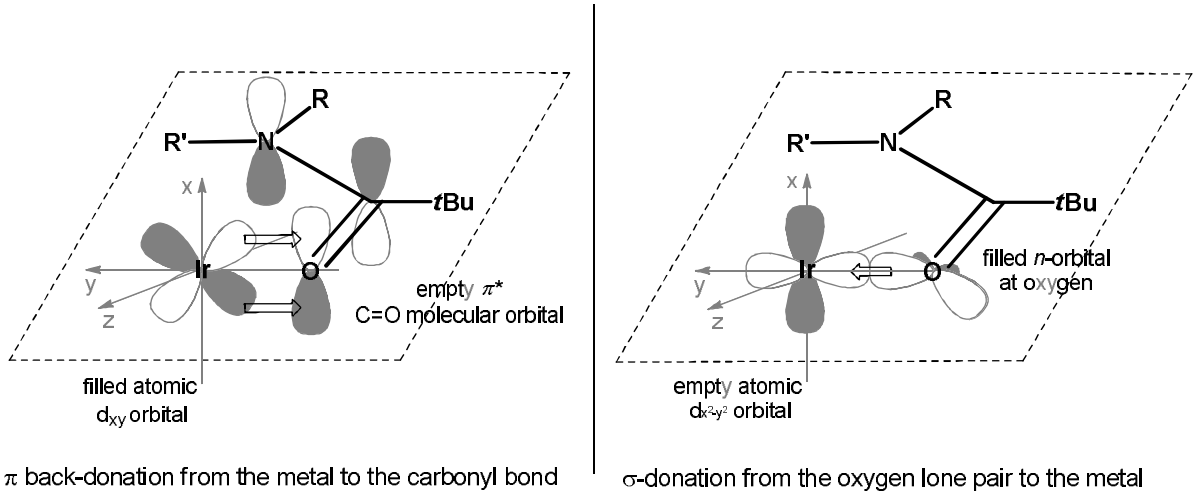
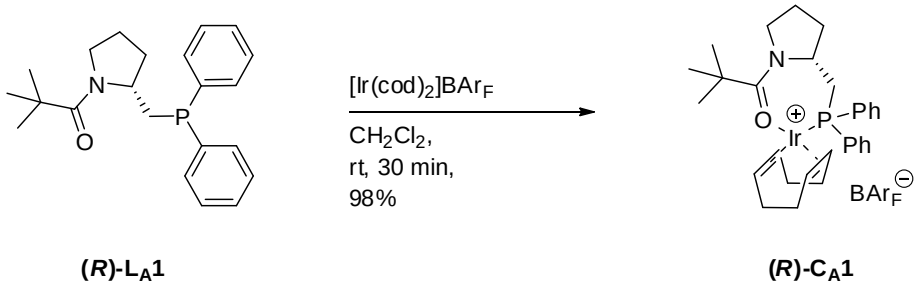


Figure 7. Simplified binding modes of the carbonyl functionality to iridium.

In order to analyze this P,O ligand/iridium complex **(*R*)-$\mathbf{C_A1}$** also in its solid state, the precatalyst **(*R*)-$\mathbf{C_A1}$** was synthesized and isolated. The preparation of complex **(*R*)-$\mathbf{C_A1}$** is depicted in Scheme 10. $[Ir(cod)_2]BAr_F$ was treated with free ligand **(*R*)-$\mathbf{L_A1}$** in dichloromethane and stirred at room temperature for 30 minutes.[73] After evaporation of the solvent the residue was triturated several times with *n*-pentane, whereupon the desired

[73] For the synthesis of $[Ir(cod)_2]BAr_F$ see: V. Semeniuchenko, T E. Exner, V. Khilya, U. Groth, *Appl. Organometal. Chem.* **2011**, *25*, 804-809. The compound is commercially available.

complex **(*R*)-C$_A$1** was obtained (for the detailed procedure see the experimental part). This procedure differed slightly from the standard complexation method described for the isolation of P,N ligand/iridium complexes.[74] For the isolation of precatalyst **(*R*)-C$_A$1**, this standard method did not prove to be suitable, since **(*R*)-C$_A$1** can not be purified by column chromatography. Several attempts were made, but in all cases decomposition of the complex was observed, probably due to the weaker Ir–O bond compared to the Ir–N interaction in the corresponding P,N ligand/iridium complexes.



(*R*)-L$_A$1 **(*R*)-C$_A$1**

Scheme 10. Synthesis of the P,O ligand/iridium complex **(*R*)-C$_A$1**.

Crystals suitable for X-ray diffraction were obtained by recrystallization from dichloromethane solution layered with *n*-pentane in a NMR tube. The solid state structure shows the expected bidentate coordination of the planar amide group and the phosphorus atom to the iridium center.

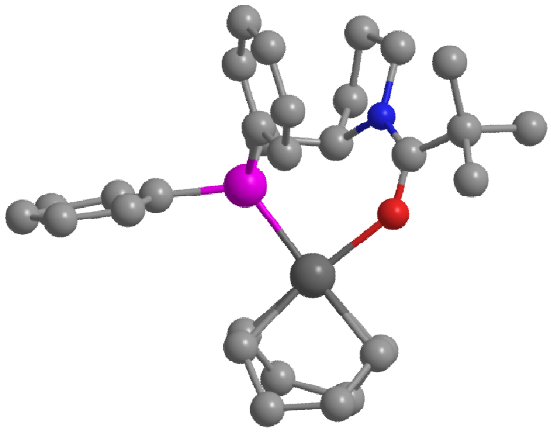


Figure 8. Crystal structure of complex [(**(*R*)-L$_A$1**)Ir(cod)]BAr$_F$. The counterion has been omitted for clarity (red O, blue N, magenta P, dark gray Ir, light gray C).[75]

[74] For a standard method for the complexation of P,N ligands with iridium(I) see: A. Franzke, Dissertation, University of Basel, **2006**, pp. 167-167.
[75] Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Center. The deposition number is 829325.

The conformation of the seven-membered metallacycle formed by chelation of the ligand to iridium(I) can be seen to be boat-like. One of the phenyl substituents of the diphenylphosphino group is oriented in a *pseudo*-axial and the other in a *pseudo*-equatorial fashion (Figure 8). The *pseudo* axial phenyl substituent extends into the same direction as the *tert*-butyl substituent of the amide functionality. The bite angle of the ligand was measured to be 89.31° and the Ir−P and Ir−O distances are 2.295 Å and 2.081 Å respectively.

Amidophosphine **(*R*)-L_A1** clearly represents a stable bidentate P,O ligand, when it is coordinated to iridium(I). Both in solution and in the solid state the amide oxygen atom is bonded to the metal center of the complex. Further analysis of the carbonyl functionality's coordinating behavior during a hydrogenation reaction was carried out by online IR spectroscopy, which allows to measure spectra during the course of the reaction. Strong support was gained that the carbonyl group remains bonded to the transition metal in the active catalyst during the reaction, but the quality of the recorded spectra does not afford a definite proof and therefore, they are not presented here.

After the coordination mode of this first amidophosphine ligand had been clarified and the reaction conditions for the use of this P,O ligand in the iridium-catalyzed hydrogenation of alkenes had been optimized, further derivatives were investigated. This ligand scaffold is highly modular, and therefore various functionalities were introduced. The results of the application of these ligands in the iridium-catalyzed asymmetric hydrogenation of several alkenes as well as in the reduction of an exemplary imine substrate will be described. A separate section will be dedicated to each type of oxygen functionality investigated, starting with carbamatophosphine ligands (**(*S*)-L_C**), followed by amidophosphines (**(*S*)-L_A**) and finally ureaphosphines (**(*S*)-L_{U3}** and **(*S*)-L_{U4}**).

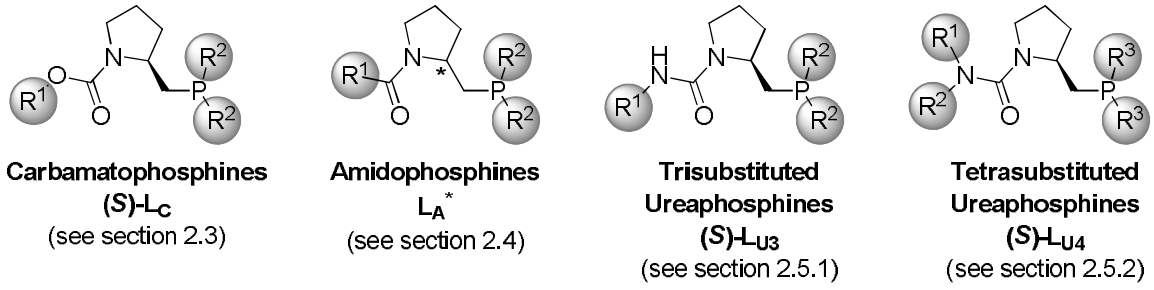


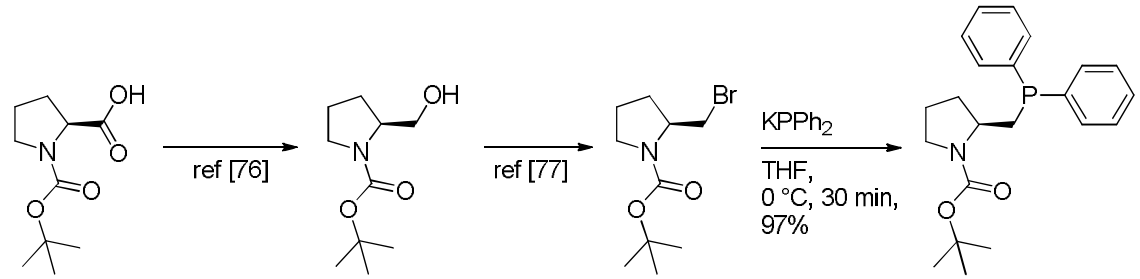
Figure 9. Ligand scaffolds presented herein.

2.3
Proline-Based Carbamatophosphines Ligands

The preparation of the (*S*)-enantiomer of the initially tested chiral ligand $\mathbf{L_A1}^*$ was previously reported by TOMIOKA *et al.*[68b] During the synthesis of amidophosphines substituted with various moieties in the amide and at the phosphorus atom, carbamates became available as well (Scheme 11). These carbamatophosphines were tested in the iridium-catalyzed hydrogenation of unfunctionalized and functionalized alkenes too, as they were thought to have the same potential as the corresponding bidentate amide-based P,O ligands. The results are described below.

2.3.1
Synthesis of Proline-Based Carbamatophosphines

All P,O ligands synthesized and described herein are readily available from the naturally occurring amino acid L-proline. The preparations started from commercially available *N*-(*tert*-butoxycarbonyl)-L-proline (**(*S*)-44**) as depicted in Scheme 11. The reduction of the carboxylic acid using borane as reducing agent *via* a reported procedure led to the desired *N*-(*tert*-butoxycarbonyl)-L-prolinol (**(*S*)-45**) in good yield.[76]

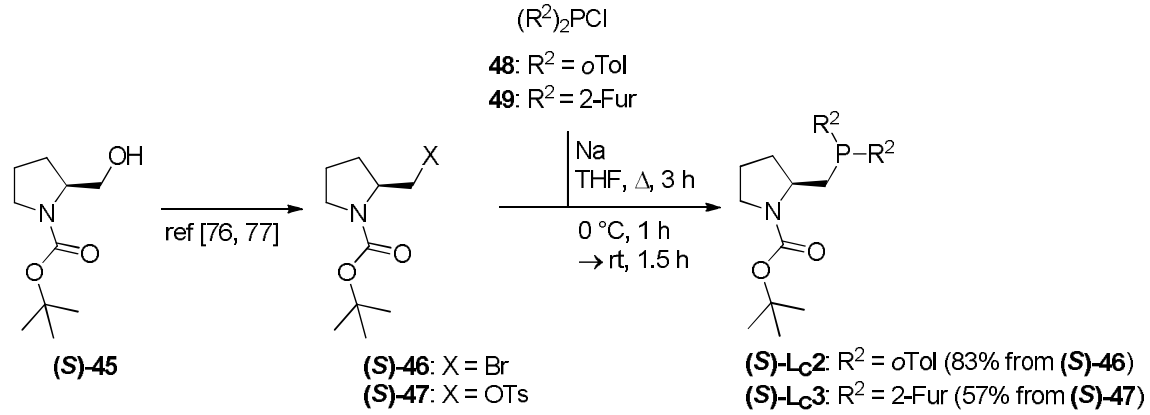


Scheme 11. Synthesis of carbamatophosphine ligand **(*S*)-$\mathbf{L_C1}$**.

Subsequent transformation of the alcohol into a better leaving group was achieved by either an Appel reaction, replacing the alcohol by bromine, or conversion of the alcohol into a tosylate.[76,77] Both reactions were performed and are depicted in Scheme 12.

[76] For the synthesis of *N*-(*tert*-butoxycarbonyl)-L-prolinol (**(*S*)-45**) and (*S*)-*tert*-butyl 2-[(tosyloxy)methyl]pyrrolidine-1-carboxylate (**(*S*)-47**) see: G. Bartoli, M. Bosco, R. Dalpozzo, A. Giuliani, E. Marcantoni, T. Mecozzi, L. Sambri, E. Torregiani, *J. Org. Chem.* **2002**, *67*, 9111-9114.
[77] For the synthesis of (*S*)-*tert*-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate (**(*S*)-46**) see: B. Hinzen, H. Broetz, R. Endermann, K. Henninger, H. Paulsen, S. Raddatz, S. Anlauf, *Ger. Offen.* **2004**, DE 10308107 A1.

Displacement of the bromide in **(*S*)-46** by the diphenylphosphide anion, in analogy to the previously reported procedure of TOMIOKA *et al.* furnished the first carbamatophosphine **(*S*)-L$_C$1** in good overall yield (Scheme 12).[68b]

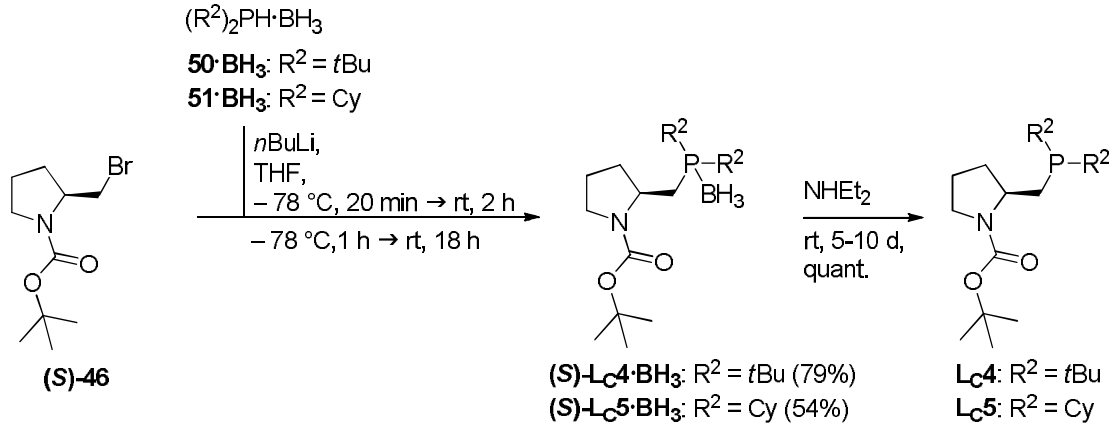


Scheme 12. Synthesis of carbamatophosphines with aryl substituents at the phosphorus atom.

Variation of the phosphorus substituents was carried out using different phosphide anions in the final substitution reaction (Scheme 12). The *ortho*-tolyl-substituted carbamatophosphine **(*S*)-L$_C$2** was obtained from the bromine precursor **(*S*)-46** in 83% yield in the same manner as **(*S*)-L$_C$1**. However, sodium di-*ortho*-tolylphosphide is not commercially available and was obtained *in situ* by the reaction of sodium with chlorodi-*ortho*-tolylphosphine in analogy to the reported *in situ* generation of sodium diphenylphosphide.[68b] In contrast, the di-(2-furyl)-phosphine derivative **(*S*)-L$_C$3** was obtained from tosylate **(*S*)-47** in only moderate yield. The nucleophilic di-(2-furyl)-phosphide anion was generated by the reaction of sodium and chlorodi-(2-furyl)-phosphine. The synthesis of **(*S*)-L$_C$3** starting from **(*S*)-46** was not tried, but the synthesis of di-*ortho*-tolylphosphine **(*S*)-L$_C$3** from tosylate **(*S*)-47** proved to be as well possible in the same range of yield.

In contrast, the synthesis of carbamatophosphines bearing alkyl substituents at the phosphorus atom was not possible from the tosylate precursor **(*S*)-47**. Like **(*S*)-L$_C$1**, dialkylphosphines **(*S*)-L$_C$4** and **(*S*)-L$_C$5** were synthesized from (*S*)-*tert*-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate (**(*S*)-46**, Scheme 13). The protected phosphides for the displacement of the bromide leaving group were generated *in situ* by deprotonation of the respective phosphine borane adducts using *n*-butyllithium. Finally the desired P,O ligands for the generation of iridium complexes were obtained by

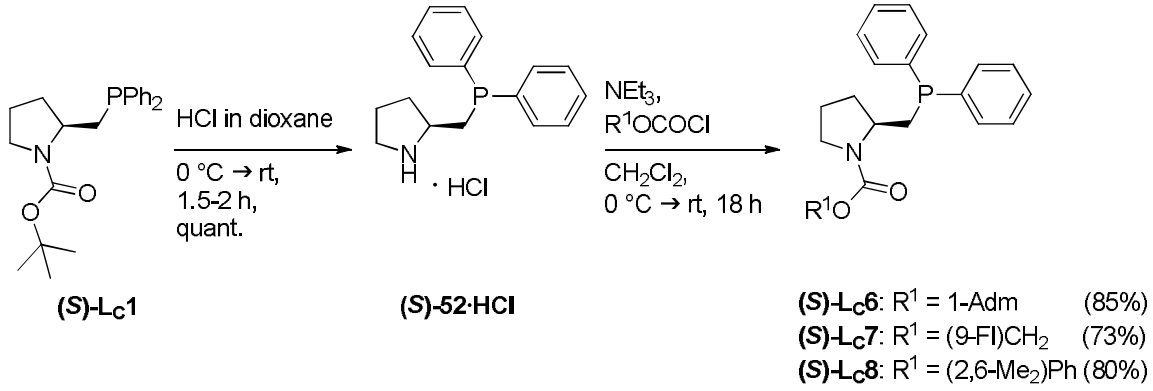
deprotection under standard conditions. This deprotection was carried out by reacting the protected ligands **(*S*)-L$_C$4·BH$_3$** and **(*S*)-L$_C$5·BH$_3$** with diethylamine (Scheme 13). The extended reaction times required for complete deprotection are a serious drawback in the synthesis of these dialkyl-substituted P,O ligands. Heating of the reaction mixture slightly reduced the reaction time. However, compared to other deprotection methods this method can clearly be qualified as cleaner, because simple evaporation of all volatiles under reduced pressure led to the quantitative isolation of the desired P,O ligands (for detailed procedures see the experimental part). Due to this advantage this deprotection method was used as standard protocol even when it was rather slow.



Scheme 13. Synthesis of carbamatophosphines with alkyl substituents at the phosphorus atom.

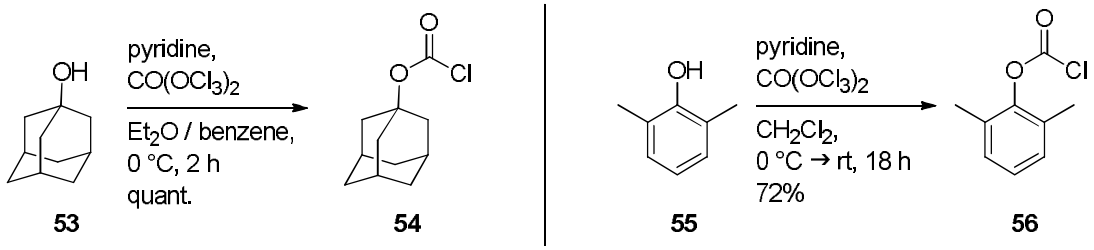
All four carbamatophosphines **(*S*)-L$_C$1** to **(*S*)-L$_C$4**, were used to synthesize amidophosphines (**(*S*)-L$_A$**) and ureaphosphines (**(*S*)-L$_{U3}$** and **(*S*)-L$_{U4}$**). These subsequent synthetic steps will be depicted in the corresponding sections (see sections 2.4.1, 2.5.1.1 and 2.5.2.1).

Derivatives of the carbamatophosphine **(*S*)-L$_C$1** bearing R^1-substituents different from *tert*-butyl were also synthesized (Scheme 14). This was achieved after deprotection of the *tert*-butyl carbamate **(*S*)-L$_C$1** under acidic conditions to obtain **(*S*)-52·HCl** and subsequent reaction of the resulting pyrrolidinium salt with different chloroformates R^{1}OCOCl. For example, **(*S*)-L$_C$7** was isolated after the reaction of **(*S*)-52·HCl** with commercially available 9-fluorenylmethyl chloroformate (FmocCl) in 73% yield.



Scheme 14. Synthesis of carbamatophosphines with different carbamate moieties (abbreviations: 1-Adm for 1- adamantyl, (9-Fl)CH_2 for 9-fluorenylmethyl and (2,6-Me_2)Ph for 2,6-dimethylphenyl).

The other chloroformates **54** and **56** are not commercially available and were synthesized according to literature-known procedures (Scheme 15).[78,79] Both were obtained from their alcohol precursors **53** and **55**, respectively, using triphosgene and pyridine as base. Reacting these chloroformates with pyrrolidinium salt **(*S*)-52·HCl** furnished the carbamatophosphines **(*S*)-L_C6** and **(*S*)-L_C8** in good yields of 85% and 80%, respectively, (see Scheme 14).



Scheme 15. Synthesis of chloroformates **54** and **56**, using triphosgene.[78,79]

[78] For the synthesis of 1-adamantyl chloroformate (**54**) see: R. A. Moos, J. Tian, R. R. Sauers, *Org. Lett.* **2004**, *6*, 4293-4296. This compound was synthesized in analogy to the procedure reported for the synthesis of 3-homoadamantyl chloroformate.

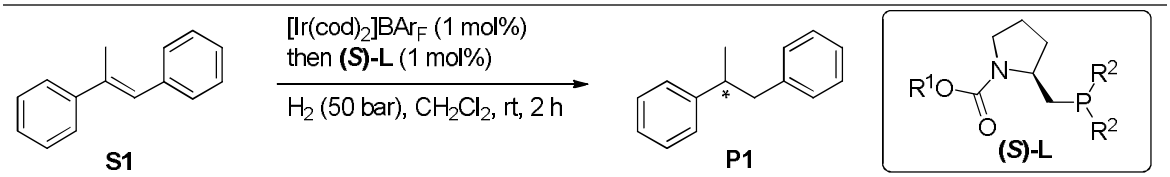
[79] For the synthesis of 2,6-dimethylphenyl chloroformate (**56**) see: M. W. Martin, J. Newcomb, J. J. Nunes, D. C. McGowan, D. M. Armistead, C. Boucher, J. L. Buchanan, W. Buckner, L. Chai, D. Elbaum, L. F. Epstein, T. Faust, S. Flynn, P. Gallant, A. Gore, Y. Gu, F. Hsieh, X. Huang, J. H. Lee, D. Metz, S. Middleton, D. Mohn, K. Morgenstern, M. J. Morrison, P. M. Novak, A. Oliveira-dos-Santos, D. Powers, P. Rose, S. Schneider, S. Sell, Y. Tudor, S. M. Turci, A. A. Welcher, R. D. White, D. Zack, H. Zhao, L. Zhu, X. Zhu, C. Ghiron, P. Amouzegh, M. Ermann, J. Jenkins, D. Johnston, S. Napier, E. Power, *J. Med. Chem.* **2006**, *49*, 4981-4991.

2.3.2
Iridium-Catalyzed Asymmetric Hydrogenations with Carbamatophosphine Ligands

As shown above several carbamatophosphines were easily synthesized. The potential of these compounds as P,O ligands for iridium catalysis was investigated next. The results of the asymmetric hydrogenation of various alkenes are reported in the tables below and will be discussed. The precatalysts were formed by *in situ* complexation prior to the hydrogenation reactions and the hydrogenation reactions were performed under the optimized conditions as described in section 2.2.1.

All eight carbamatophosphines **(*S*)-L$_C$1** to **(*S*)-L$_C$8** were tested in the iridium-catalyzed asymmetric hydrogenation of the unfunctionalized alkene (*E*)-1,2-diphenyl-1-propene (**S1**), first. The results are summarized in Table 3. These ligands did not prove to be very effective in this transformation. Only the use of ligand **(*S*)-L$_C$5** allowed for complete conversion (entry 5). The other catalysts showed only moderate activities (27% to 86% yield). Concerning the use of ligands **(*S*)-L$_C$6** and **(*S*)-L$_C$8**, average yields and enantioselectivities are given, since the reactions were carried out several times (entries 6 and 8).

Table 3. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**).[a]



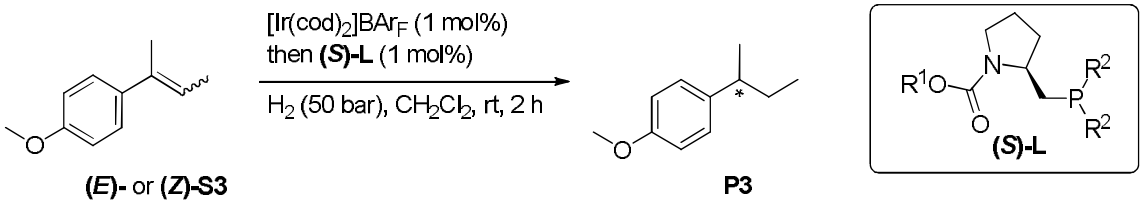
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_C$1**	*t*Bu	Ph	49	66 (*R*)
2	**(*S*)-L$_C$2**	*t*Bu	*o*Tol	86	41 (*R*)
3	**(*S*)-L$_C$3**	*t*Bu	2-Fur	29	45 (*R*)
4	**(*S*)-L$_C$4**	*t*Bu	*t*Bu	**87**	**95 (*R*)**
5	**(*S*)-L$_C$5**	*t*Bu	Cy	**> 99**	**92 (*R*)**
6	**(*S*)-L$_C$6**	1-Adm	Ph	73[d]	76 (*R*)[d]
7	**(*S*)-L$_C$7**	(9-Fl)CH_2	Ph	66	15 (*S*)
8	**(*S*)-L$_C$8**	(2,6-Me_2)Ph	Ph	50[d]	54 (*R*)[d]

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] Average of 2-3 experiments.

The results varied slightly from one experiment to the other. This observation in combination with the low yields obtained with several other **(*S*)-L$_C$** ligands suggest that these carbamatophosphine/iridium complexes partially decompose during the course of the reaction. Moreover, only moderate enantioselectivities were obtained compared to the best P,N ligand complexes. The dialkyl-substituted phosphine derivatives **(*S*)-L$_C$4** and **(*S*)-L$_C$5** furnished the highest enantiomeric excesses of 95% and 92% respectively. As in the case of the initially studied amidophosphine the use of the (*S*)-configured carbamatophosphine ligands afforded the (*R*)-configured product **P1** in excess.

Given the rather disappointing results in terms of activity and selectivity in the hydrogenation of substrate **S1**, these carbamatophosphines were screened only randomly in the iridium-catalyzed hydrogenation of other substrates. In the reduction of other trisubstituted unfunctionalized alkenes, such as 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**), (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)-**and **(*Z*)-S3**), these P,O ligand/iridium catalysts furnished even lower enantiomeric excesses (Scheme 16 and Table 4). The best result was obtained in the hydrogenation of **(*E*)-S3** employing the 1-adamantyl-substituted carbamate **(*S*)-L$_C$6** (76% yield and 30% *ee*, entry 5).

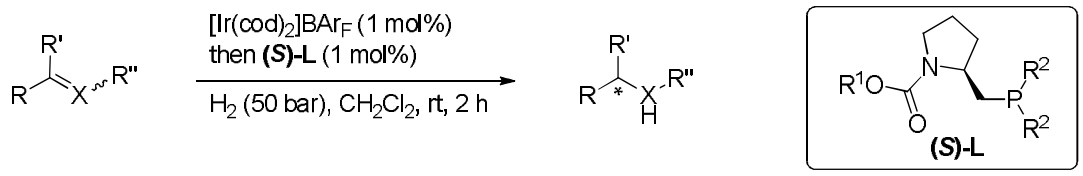
Table 4. Iridium-catalyzed asymmetric hydrogenation of (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)-** and **(*Z*)-S3**).[a]



Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*Z*)-S3**	**(*S*)-L$_C$1**	*t*Bu	Ph	77	9 (*S*)
2	**(*Z*)-S3**	**(*S*)-L$_C$2**	*t*Bu	*o*Tol	82	*rac*
3	**(*E*)-S3**	**(*S*)-L$_C$3**	*t*Bu	2-Fur	95	*rac*
4	**(*Z*)-S3**	**(*S*)-L$_C$3**	*t*Bu	2-Fur	91	*rac*
5	**(*E*)-S3**	**(*S*)-L$_C$6**	1-Adm	Ph	76	30 (*R*)
6	**(*Z*)-S3**	**(*S*)-L$_C$6**	1-Adm	Ph	98	3 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC or GC analysis using a chiral stationary phase (see experimental part).

Several other substrates were hydrogenated in the course of the screening of carbamatophosphines. The best results for each substrate are depicted in Scheme 16.



S2	S5	S11	S12
(*S*)-L_C**6**: 97%, *rac*	(*S*)-L_C**1**: 90%,[d] 63% *ee* (*S*) (*S*)-L_C**6**: 51%, 47% *ee* (*S*)	(*S*)-L_C**1**: 17%, *rac* (*S*)-L_C**2**: 26%, 24% *ee* (*R*) (*S*)-L_C**3**: 22%, 8% *ee* (*R*) (*S*)-L_C**6**: 29%, 2% *ee* (*S*)	(*S*)-L_C**1**:[e] 92%, 9% *ee* (*S*) (*S*)-L_C**2**:[e] 95%, *rac* (*S*)-L_C**3**:[e] 94%, *rac*

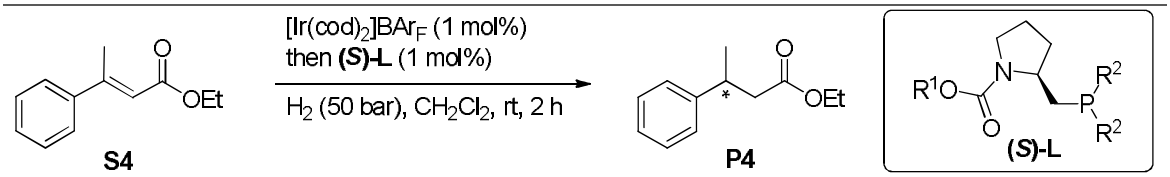
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] Formation of side products was observed (conversion > 99%); [e] The reactions were carried out at 5 bar H_2.

Scheme 16. Iridium-catalyzed asymmetric hydrogenations using carbamatophosphines.[a-c]

No enantioselectivity at all was induced in the reduction of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**). The same results were obtained from the reduction of the 1,1-disubstituted alkene **S12**, where only carbamatophosphine **(*S*)-L_C1** gave a slight enantiomeric excess of 9%. The carbamatophosphine complexes showed only moderate performance in the reduction of C−N double bonds. When imine **S11** was hydrogenated, only low yields of up to 29% were obtained. The highest enantiomeric excess was 24% in this case. At least, 63% *ee* were obtained in the hydrogenation of the allylic alcohol **S5**, when the **(*S*)-L_C1**/iridium complex was used. In this case, complete conversion of the starting material was observed too, but this was accompanied by the formation of side products (> 99% conversion but only 90% yield of the desired hydrogenation product **P5**).

Slightly better yields were achieved, when the trisubstituted functionalized alkene **S4** was reduced (Table 5). An enantiomeric excess of up to 78% of the (*R*)-configured product ethyl 3-phenylbutanoate (**P4**) was obtained using **(*S*)-L_C4** and up to 99% yield were observed using **(*S*)-L_C5** (entries 3 and 4).

Table 5. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**S4**).[a]



S4 **P4** **(*S*)-L**

Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_C1**	*t*Bu	Ph	95	41 (*R*)
2	**(*S*)-L_C2**	*t*Bu	*o*Tol	99	9 (*R*)
3	**(*S*)-L_C4**	*t*Bu	*t*Bu	80	78 (*R*)
4	**(*S*)-L_C5**	*t*Bu	Cy	99	75 (*R*)
5	**(*S*)-L_C6**	1-Adm	Ph	39	53 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

From the results obtained in the iridium-catalyzed asymmetric hydrogenation of C−C and C−N double bonds with carbamatophosphines as P,O ligands it can be seen that these derivatives are not well suited for these applications. Therefore, carbamatophosphines **(*S*)-L_C** were not investigated further and the focus was turned to proline-based amidophosphines **(*S*)-L_A**.

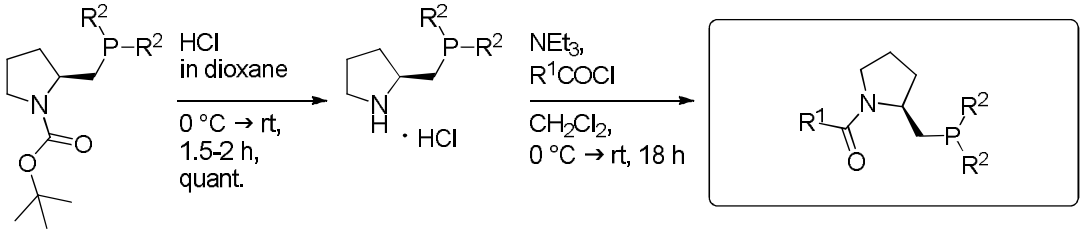
2.4 Proline-Based Amidophosphines Ligands

Several amidophosphines **(*S*)-L_A** bearing various substitution patterns within their carbonyl and phosphine functionalities were synthesized and tested as P,O ligands in the iridium-catalyzed asymmetric hydrogenation of different substrates. The goal was to optimize the ligand structure by introducing different electronic and steric properties, in order to surpass the results obtained with the initial ligand **(*R*)-L_A1** (section 2.2.1). The ligand's scaffold proved highly modular and led to the synthesis of a wide ligand library (see section 2.4.1). The ligands are numbered according to their carbonyl moieties, starting with alkyl groups and followed by aromatic groups, and, within each carbonyl subgroup, according to their phosphorus substituents. This classification allows for a better analysis of the influence of each substituent on the results in the iridium-catalyzed asymmetric hydrogenation reactions. The hydrogenation results varied significantly from substrate to substrate and are described in section 2.4.2. Substrate dependency of the catalyst's selectivity is a well-known phenomenon in asymmetric catalysis and was

already pointed out in chapter 1. This is why many combinations of ligands and substrates were thoroughly screened.

2.4.1
Synthesis of Proline-Based Amidophosphines

The synthesis of amidophosphine ligands **(*S*)-L_A** was carried out following the same strategy used for the synthesis of carbamatophosphines **(*S*)-L_C** described above (see section 2.3.1). Depending on the phosphorus atom substituents the preparation of aryl- and alkyl-substituted amidophosphines will be described separately (see Schemes 17 and 19). Starting from the already described carbamates **(*S*)-L_C1** to **(*S*)-L_C3** (Schemes 11 and 12), the corresponding pyrrolidinium salts **(*S*)-52·HCl**, **(*S*)-57·HCl** and **(*S*)-58·HCl** were obtained in quantitative yields, with different aryl substituents on the phosphorus moiety after removal of the Boc-protecting group (Scheme 17). Reaction of these deprotected amines with acyl chloride derivatives under basic conditions gave rise to a small library of amidophosphines with various substituents R^1 and R^2.



(*S*)-L_C1: R^2 = Ph
(*S*)-L_C2: R^2 = *o*Tol
(*S*)-L_C3: R^2 = 2-Fur

(*S*)-52·HCl: R^2 = Ph
(*S*)-57·HCl: R^2 = *o*Tol
(*S*)-58·HCl: R^2 = 2-Fur

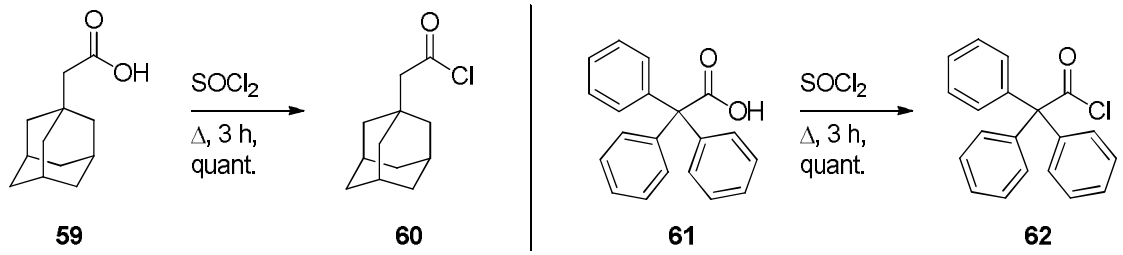
(*S*)-L_A1:	R^1 = *t*Bu,	R^2 = Ph	(98%)
(*S*)-L_A2:	R^1 = *t*Bu,	R^2 = *o*Tol	(90%)
(*S*)-L_A3:	R^1 = *t*Bu,	R^2 = 2-Fur	(86%)
(*S*)-L_A6:	R^1 = (*t*Bu)CH_2,	R^2 = Ph	(26%)
(*S*)-L_A7:	R^1 = 1-Adm,	R^2 = Ph	(96%)
(*S*)-L_A8:	R^1 = 1-Adm,	R^2 = *o*Tol	(83%)
(*S*)-L_A9:	R^1 = 1-Adm,	R^2 = 2-Fur	(61%)
(*S*)-L_A12:	R^1 = (1-Adm)CH_2,	R^2 = Ph	(48%)
(*S*)-L_A13:	R^1 = CPh_3,	R^2 = Ph	(96%)
(*S*)-L_A14:	R^1 = CPh_3,	R^2 = *o*Tol	(67%)
(*S*)-L_A15:	R1 = CPh_3,	R^2 = 2-Fur	(80%)
(*S*)-L_A18:	R^1 = Ph,	R^2 = Ph	(94%)

Scheme 17. Synthesis of amidophosphines with aryl substituents at the phosphorus atom.

This synthetic route is very similar to that used for the synthesis of carbamatophosphines and to the route reported in the literature by TOMIOKA *et al.*[68b] Ligands **(*S*)-L_A1** to

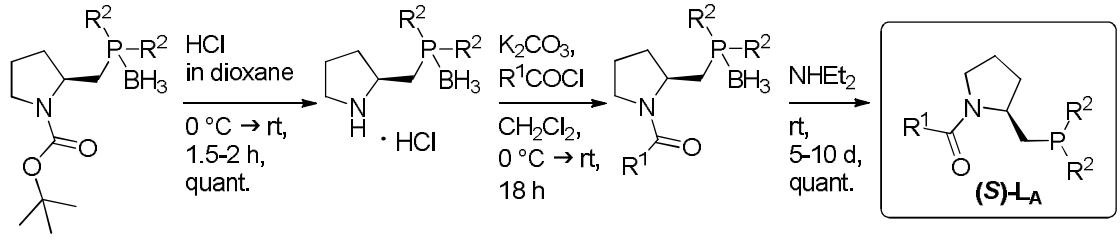
(*S*)-L$_A$3, **(*S*)-L$_A$6** to **(*S*)-L$_A$9**, **(*S*)-L$_A$12** to **(*S*)-L$_A$15** and **(*S*)-L$_A$18** were obtained in moderate to excellent yields (24% to 98%). Both alkyl and aryl substituents were easily introduced in the amide functionality and the steric hindrance was varied by substitution with *t*Bu ≈ 1-Adm < CPh_3.

Most of the acyl chlorides R^1COCl used for amide formation are commercially available. Only the compounds **60** (R^1 = (1-Adm)CH_2) and **62** (R^1 = CPh_3) had to be synthesized prior to their transformation into an amide (Scheme 18). Reacting their carboxylic acid precursors with thionyl chloride at reflux gave the desired acyl chloride derivatives in quantitative yields.



Scheme 18. Synthesis of not commercially available acyl chlorides **60** and **62**.

The synthesis of amidophosphines bearing alkyl substituents at the phosphorus atom is shown in Scheme 19. The carbamatophosphines **(*S*)-L$_C$4·BH$_3$** and **(*S*)-L$_C$5·BH$_3$** were deprotected and the resulting amines treated with the respective acyl chlorides that were already used for the synthesis of the previous diarylphosphine library (see Scheme 17).



(*S*)-L$_C$4·BH$_3$: R^2 = *t*Bu
(*S*)-L$_C$5·BH$_3$: R^2 = Cy

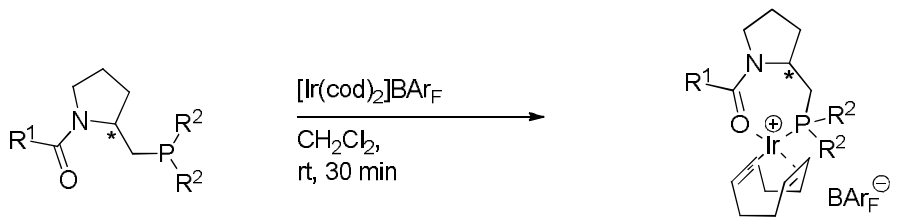
(*S*)-63·HCl: R^2 = *t*Bu
(*S*)-64·HCl: R^2 = Cy

(*S*)-L$_A$4·BH$_3$: R^1 = *t*Bu, R^2 = *t*Bu (24%)
(*S*)-L$_A$5·BH$_3$: R^1 = *t*Bu, R^2 = Cy (67%)
(*S*)-L$_A$10·BH$_3$: R^1 = 1-Adm, R^2 = *t*Bu (43%)
(*S*)-L$_A$11·BH$_3$: R^1 = 1-Adm, R^2 = Cy (83%)
(*S*)-L$_A$16·BH$_3$: R^1 = CPh_3, R^2 = *t*Bu (91%)
(*S*)-L$_A$17·BH$_3$: R^1 = CPh_3, R^2 = Cy (89%)

Scheme 19. Synthesis of amidophosphines with alkyl substituents at the phosphorus atom.

For this substitution reaction potassium carbonate was used as base, since triethylamine promotes the deprotection of the phosphorus atom. In general, the borane adducts of the amidophosphines were obtained in moderate to good yields, although slightly lower efficiencies were observed for fully alkyl-substituted ligands like **(*S*)-L_A4·BH_3** and **(*S*)-L_A10·BH_3** (24% and 43%, respectively, see Scheme 19). Quantitative protecting group removal was carried out with the help of diethylamine, before these amidophosphines were employed as ligands.

In order to obtain the isolated precatalyst **(*S*)-C_A16** and **(*S*)-C_A17**, ligands **(*S*)-L_A16** and **(*S*)-L_A17** were reacted with $[Ir(cod)_2]BAr_F$. These complexations were carried out as in the case of **(*R*)-C_A1** and all three reactions are depicted in Scheme 20. All precatalysts were obtained in excellent yields.



(*R*)-L_A1: R^1 = *t*Bu, R^2 = Ph
(*S*)-L_A16: R^1 = CPh_3, R^2 = *t*Bu
(*S*)-L_A17: R^1 = CPh_3, R^2 = Cy

(*R*)-C_A1: R^1 = *t*Bu, R^2 = Ph (98%)
(*S*)-C_A16: R^1 = CPh_3, R^2 = *t*Bu (99%)
(*S*)-C_A17: R^1 = CPh_3, R^2 = Cy (97%)

Scheme 20. Synthesis of amidophosphine/iridium complexes.

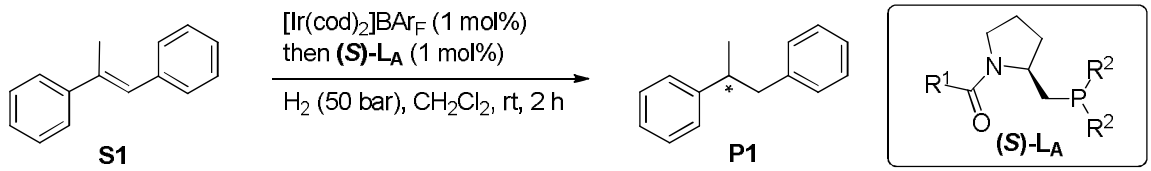
2.4.2 Iridium-Catalyzed Asymmetric Hydrogenations with Amidophosphine Ligands

The amidophosphines were screened systematically in the iridium-catalyzed asymmetric hydrogenation of exemplary unfunctionalized and functionalized trisubstituted alkenes. Since these ligands showed excellent selectivities in the hydrogenation of the standard *α,β*-unsaturated ester **S4**, other *α,β*-unsaturated carbonyl compounds were investigated as substrates, too. These results will be shown below in separate tables for each substrate.

Table 6 summarizes the results obtained in the iridium-catalyzed asymmetric hydrogenation of the initially studied substrate (*E*)-1,2-diphenyl-1-propene (**S1**). Ligand

(*R*)-L$_A$1 from the automated screening at *Solvias AG* is also included for comparison; it gave > 99% conversion and an enantiomeric excess of 70% (entry 1).

Table 6. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*R*)-L$_A$1**	*t*Bu	Ph	> 99	70 (*S*)
2	**(*S*)-L$_A$2**	*t*Bu	*o*Tol	> 99	48 (*R*)
3	**(*S*)-L$_A$3**	*t*Bu	2-Fur	83	45 (*R*)
4	**(*S*)-L$_A$4**	*t*Bu	*t*Bu	99	89 (*R*)
5	**(*S*)-L$_A$5**	*t*Bu	Cy	99	83 (*R*)
6	**(*S*)-L$_A$6**	(*t*Bu)CH$_2$	Ph	> 99	6 (*R*)
7	**(*S*)-L$_A$7**	1-Adm	Ph	73	54 (*R*)
8	**(*S*)-L$_A$8**	1-Adm	*o*Tol	> 99	37 (*R*)
9	**(*S*)-L$_A$9**	1-Adm	2-Fur	95	19 (*R*)
10	**(*S*)-L$_A$10**	1-Adm	*t*Bu	> 99	86 (*R*)
11	**(*S*)-L$_A$11**	1-Adm	Cy	> 99	76 (*R*)
12	**(*S*)-L$_A$12**	(1-Adm)CH$_2$	Ph	97	10 (*R*)
13	**(*S*)-L$_A$13**	CPh$_3$	Ph	71	90 (*R*)
14	**(*S*)-L$_A$14**	CPh$_3$	*o*Tol	80	80 (*R*)
15	**(*S*)-L$_A$15**	CPh$_3$	2-Fur	63	90 (*R*)
16	**(*S*)-L$_A$16**	CPh$_3$	*t*Bu	**> 99**	**98 (*R*)**
17	**(*S*)-L$_A$17**	CPh$_3$	Cy	**> 99**	**96 (*R*)**
18	**(*S*)-L$_A$18**	Ph	Ph	90	2 (*S*)

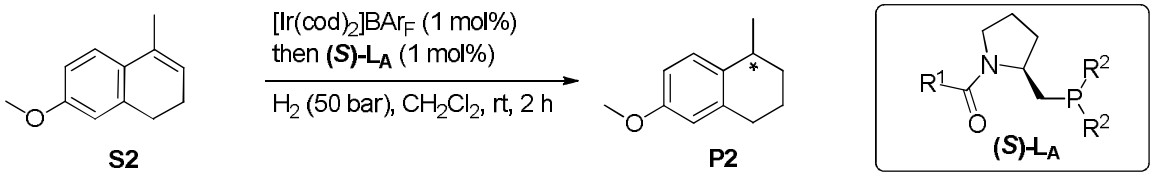
[a] Reaction scale: [Ir(cod)$_2$]BAr$_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Several new ligands, such as **(*S*)-L$_A$10** and **(*S*)-L$_A$13** to **(*S*)-L$_A$17** furnished substantially higher selectivities (entries 10 and 13 to 17). It can be easily seen that ligands with more sterically demanding amides in combination with electron-donating dialkyl phosphines furnished higher enantioselectivities. In addition, the steric demands of the amide groups seem to have a bigger impact on the enantioinduction of the catalysts than the electronic properties of the coordinating phosphorus atom. All trityl (CPh$_3$)-substituted amidophosphines induced enantiomeric excesses of higher than 80% (entries 13 to 17). The lowest selectivities were obtained with ligands **(*S*)-L$_A$6**, **(*S*)-L$_A$12** and **(*S*)-L$_A$18** (entries 6, 12 and 18). Whereas **(*S*)-L$_A$18** comprises a planar phenyl substituent, the other two ligands have a methylene group in α-position to the carbonyl moiety. Both

substitution patterns allow an increased rotational flexibility of the ligand and reduce the steric crowding around the active site of the catalysts, which might explain the lower selectivities. The conversion of the starting material **S1** was not always complete, but overall good yields from 63% to > 99% were obtained in most cases. Dialkylphosphine/iridium catalysts generally exhibited higher activities than their aryl-substituted structural analogs (entries 10, 11, 16 and 17).

Further unfunctionalized trisubstituted alkenes were tested (see Tables 7 and 8). With amidophosphines as P,O ligands only poor to moderate enantioselectivities were achieved. The results for the asymmetric hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**) are shown in Table 7 and the respective data for (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)**-and **(*Z*)-S3**) are summarized in Table 8.

Table 7. Iridium-catalyzed asymmetric hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**).[a]



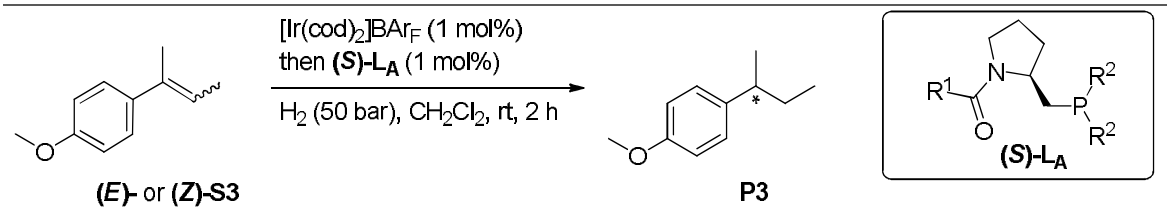
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_A1**	*t*Bu	Ph	97 [> 99]	2 (*S*)
2	**(*S*)-L_A2**	*t*Bu	*o*Tol	77 [83]	*rac*
3	**(*S*)-L_A8**	1-Adm	*o*Tol	82 [88]	*rac*
4	**(*S*)-L_A10**	1-Adm	*t*Bu	97 [> 99]	29 (*S*)
5	**(*S*)-L_A11**	1-Adm	Cy	53 [> 99]	11 (*S*)
6	**(*S*)-L_A13**	CPh_3	Ph	96 [> 99]	2 (*S*)
7	**(*S*)-L_A14**	CPh_3	*o*Tol	56 [73]	4 (*S*)
8	**(*S*)-L_A15**	CPh_3	2-Fur	96 [> 99]	*rac*
9	**(*S*)-L_A16**	CPh_3	*t*Bu	96 [> 99]	16 (*S*)
10	**(*S*)-L_A17**	CPh_3	Cy	95 [> 99]	3 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

In the reduction of **S2** dialkylphosphines again provided complete conversions, albeit these were accompanied by the formation of a small amount of side product. The enantiomeric excesses measured for product **P2** were unsatisfying (*ee*s < 29%). Even the sterically hindered trityl-substituted amides did not achieve enantiomeric excesses higher than 16% (entries 6 to 10).

Taking into account the poor results obtained in the asymmetric reduction of the cyclic substrate **S2** only a few ligands were tested in the hydrogenation of the isomeric substrates **(*E*)-S3** and **(*Z*)-S3** (Table 8). Albeit good yields higher than 83% were measured, only low to moderate selectivities were obtained for both isomers. The best enantioselectivity in the reduction of the (*E*)-isomer was achieved with the trityl-substituted ligand **(*S*)-L$_A$13** (53% *ee*, entry 8). The selectivity in the reduction of the (*E*)-isomer was always higher than in the corresponding reduction of the (*Z*)-isomer.

Table 8. Iridium-catalyzed asymmetric hydrogenation of (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)-** and **(*Z*)-S3**).[a]



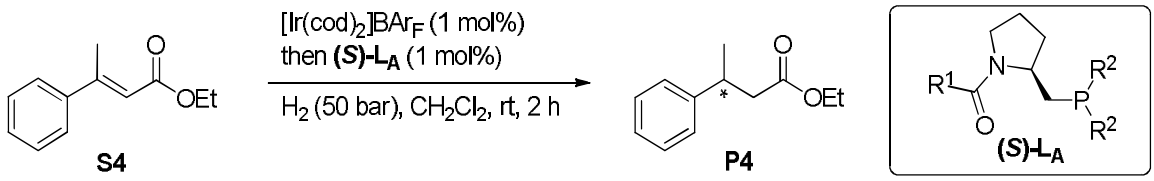
Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*E*)-S3**	**(*R*)-L$_A$1**	*t*Bu	Ph	> 99	44 (*S*)
2	**(*Z*)-S3**	**(*R*)-L$_A$1**	*t*Bu	Ph	> 99	7 (*R*)
3	**(*E*)-S3**	**(*S*)-L$_A$2**	*t*Bu	*o*Tol	> 99	35 (*R*)
4	**(*Z*)-S3**	**(*S*)-L$_A$2**	*t*Bu	*o*Tol	> 99	12 (*S*)
5	**(*E*)-S3**	**(*S*)-L$_A$8**	1-Adm	*o*Tol	88	20 (*R*)
6	**(*Z*)-S3**	**(*S*)-L$_A$8**	1-Adm	*o*Tol	> 99	15 (*S*)
7	**(*Z*)-S3**	**(*S*)-L$_A$9**	1-Adm	2-Fur	> 99	*rac*
8	**(*E*)-S3**	**(*S*)-L$_A$13**	CPh_3	Ph	83	53 (*R*)
9	**(*Z*)-S3**	**(*S*)-L$_A$13**	CPh_3	Ph	99	*rac*
10	**(*E*)-S3**	**(*S*)-L$_A$14**	CPh_3	*o*Tol	88	46 (*R*)
11	**(*Z*)-S3**	**(*S*)-L$_A$14**	CPh_3	*o*Tol	> 99	5 (*R*)
12	**(*E*)-S3**	**(*S*)-L$_A$15**	CPh_3	2-Fur	95	29 (*R*)
13	**(*Z*)-S3**	**(*S*)-L$_A$15**	CPh_3	2-Fur	94	*rac*

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC or GC analysis using a chiral stationary phase (see experimental part).

When functionalized trisubstituted alkenes were tested, amidophosphines proved to be significantly more efficient. The reduction of (*E*)-ethyl 3-phenylbut-2-enoate (**S4**) furnished up to 98% *ee* and complete conversion (entry 14). All amidophosphines **(*S*)-L$_A$** gave good to excellent conversions of **S4**. The selectivities varied depending on the substituents R^1 and R^2. As observed in the asymmetric reduction of **S1**, sterically more demanding R^1-substituents in the ligand gave better enantiomeric excesses (entries 11 to 15) and R^2-alkyl substituents afforded higher selectivities than R^2-aryl substituents. When

amidophosphines bearing a trityl substituent as R^1 were used, enantiomeric excesses of higher than 84% (*R*) were achieved, with di-*ortho*-tolylphosphine ligand **(*S*)-L_A14** being the only exception (57% *ee* (*R*), entry 12). The use of di-*ortho*-tolylphosphine **(*S*)-L_A8** furnished the (*S*)-configured product **P4** with 30% *ee* (entry 7).

Table 9. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**S4**).[a]



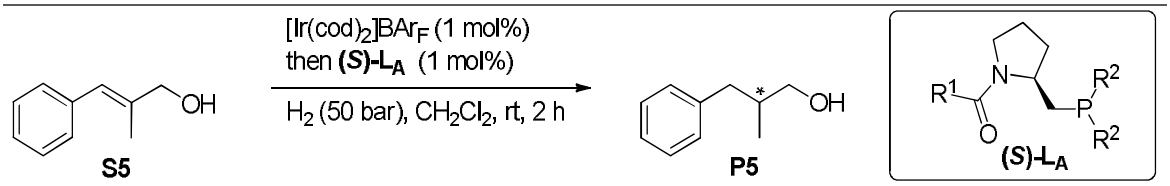
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_A1**	*t*Bu	Ph	65	33 (*R*)
2	**(*S*)-L_A2**	*t*Bu	*o*Tol	99	13 (*R*)
3	**(*S*)-L_A3**	*t*Bu	2-Fur	99	40 (*R*)
4	**(*S*)-L_A4**	*t*Bu	*t*Bu	98	51 (*R*)
5	**(*S*)-L_A5**	*t*Bu	Cy	95	33 (*R*)
6	**(*S*)-L_A7**	1-Adm	Ph	96	15 (*R*)
7	**(*S*)-L_A8**	1-Adm	*o*Tol	97	30 (*S*)
8	**(*S*)-L_A9**	1-Adm	2-Fur	85	14 (*R*)
9	**(*S*)-L_A10**	1-Adm	*t*Bu	> 99	50 (*R*)
10	**(*S*)-L_A11**	1-Adm	Cy	98	26 (*R*)
11	**(*S*)-L_A13**	CPh_3	Ph	88	89 (*R*)
12	**(*S*)-L_A14**	CPh_3	*o*Tol	> 99	57 (*R*)
13	**(*S*)-L_A15**	CPh_3	2-Fur	86	84 (*R*)
14	**(*S*)-L_A16**	CPh_3	*t*Bu	**> 99**	**98 (*R*)**
15	**(*S*)-L_A17**	CPh_3	Cy	**> 99**	**94 (*R*)**
16	**(*S*)-L_A18**	Ph	Ph	99	12 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

Another standard substrate to evaluate the potential of novel catalysts for the asymmetric hydrogenation of alkenes is the allylic alcohol **S5**. The results obtained from the asymmetric reduction of this trisubstituted functionalized alkene by amidophosphine/iridium complexes are presented in Table 10. Conversions were generally higher than 95% throughout the complete ligand set, although the reaction was sometimes accompanied by the formation of decomposition side products (entries 1, 2, 7 and 8). The product **P5** was formed with lower enantioselectivities than observed for **P1** or **P4** (Tables 6 and 9 respectively). The highest enantiomeric excess for the hydrogenation of **S5** was obtained with the di-*ortho*-tolylphosphine **(*S*)-L_A2** (69% *ee*,

entry 2). In contrast to the substrates tested above, the selectivity was superior, when di-*ortho*-tolylphosphines **(*S*)-L$_A$2**, **(*S*)-L$_A$8** and **(*S*)-L$_A$14** were used (entries 2, 3 and 8). This observation indicates that this substrate approaches the active site of the catalyst in different way (for a qualitative model rationalizing the enantioselectivity effected by P,O ligand/iridium complexes see section 2.7).

Table 10. Iridium-catalyzed asymmetric hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**S5**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_A$1**	*t*Bu	Ph	88 [95]	26 (*S*)
2	**(*S*)-L$_A$2**	*t*Bu	*o*Tol	56 [96]	69 (*S*)
3	**(*S*)-L$_A$8**	1-Adm	*o*Tol	> 99	60 (*S*)
4	**(*S*)-L$_A$9**	1-Adm	2-Fur	99	17 (*S*)
5	**(*S*)-L$_A$10**	1-Adm	*t*Bu	> 99	63 (*S*)
6	**(*S*)-L$_A$11**	1-Adm	Cy	> 99	35 (*S*)
7	**(*S*)-L$_A$13**	CPh_3	Ph	97 [> 99]	17 (*S*)
8	**(*S*)-L$_A$14**	CPh_3	*o*Tol	96 [> 99]	37 (*S*)
9	**(*S*)-L$_A$15**	CPh_3	2-Fur	> 99	13 (*S*)
10	**(*S*)-L$_A$16**	CPh_3	*t*Bu	> 99	48 (*S*)
11	**(*S*)-L$_A$17**	CPh_3	Cy	> 99	20 (*R*)

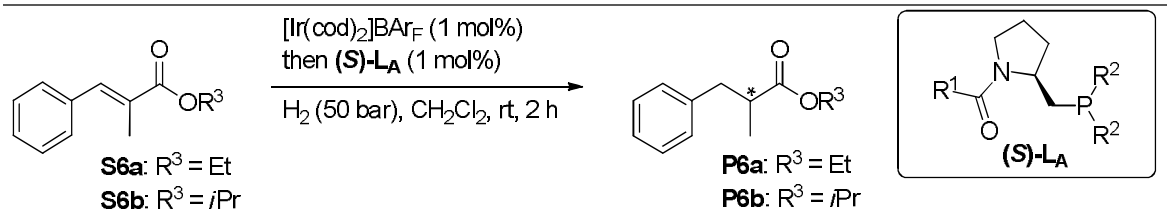
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Considering the higher efficiency of amidophosphines **(*S*)-L$_A$** compared to carbamatophosphines **(*S*)-L$_C$** as P,O ligands for the iridium-catalyzed asymmetric hydrogenation of standard substrates, selected additional substrates were investigated. However, this second screening involved only amidophosphines, which exhibited good selectivities in the asymmetric hydrogenation of the previous substrates, namely the trityl-substituted ligands **(*S*)-L$_A$13**, **(*S*)-L$_A$16** and **(*S*)-L$_A$17**. Since excellent selectivities up to 98% *ee* were obtained for the reduction of **S4**, other trisubstituted *α*,*β*-unsaturated esters were studied next (Tables 11 to 13).

The results obtained in the asymmetric hydrogenation of the more challenging *α*-methyl-substituted esters **S6a** and **S6b** are summarized in Table 11. Pyridyl

phosphonite-based P,N catalysts have previously been reported to reduce these esters with excellent enantioselectivities up to 97% for **S6a** and 99% for **S6b**.[80] Using the trityl-substituted amidophosphines **(*S*)-L$_A$13**, **(*S*)-L$_A$16** and **(*S*)-L$_A$17** showing similar efficiencies for ester **S4** slightly lower enantioselectivities were obtained, but nevertheless **(*S*)-L$_A$17** furnished up to 95% *ee* for **S6b** (entry 6).

Table 11. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl-2-methyl-3-phenylacrylate (**S6a**) and (*E*)-isopropyl 2-methyl-3-phenylacrylate (**S6b**).[a]



Entry	R^3	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	Et	**(*S*)-L$_A$13**	CPh_3	Ph	54	66 (*R*)
2	*i*Pr	**(*S*)-L$_A$13**	CPh_3	Ph	57	77 (*R*)
3	Et	**(*S*)-L$_A$16**	CPh_3	*t*Bu	> 99	90 (*R*)
4	*i*Pr	**(*S*)-L$_A$16**	CPh_3	*t*Bu	> 99	89 (*R*)
5	Et	**(*S*)-L$_A$17**	CPh_3	Cy	> 99	87 (*R*)
6	*i*Pr	**(*S*)-L$_A$17**	CPh_3	Cy	**> 99**	**95 (*R*)**

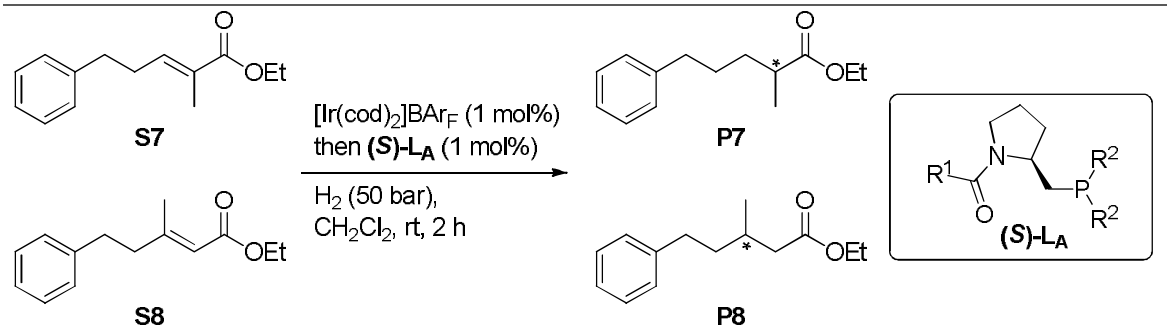
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Generally, the ligands achieved better results for the sterically more demanding isopropyl ester **S6b** compared with the ethyl ester **S6a** (entries 1 and 5 *versus* 2 and 6). The use of **(*S*)-L$_A$16** gave the (*R*)-configured product **P6a** with 90% *ee*, whereas **(*S*)-L$_A$17** permitted to reduce **S6b** to **P6b** with 95% *ee* (*R*).

The reduction of *α*,*β*-unsaturated esters **S7** and **S8**, by the use of amidophosphine ligands proceeded with conversions greater than 96% and moderate enantiomeric excesses of 55% to 85% (Table 12). The *α*-methyl-substituted ester **S7** was reduced with up to 85% *ee*, while the *β*-methyl-substituted ester **S8** was reduced with only 55% *ee* at best. The decreased enantioselectivity of the catalysts in the reduction of these esters may be rationalized by the greater flexibility of substrate **S7** and **S8**, attributed to the longer alkyl chains in *β*-position.

[80] D. H. Woodmansee, M.-A. Müller, M. Neuburger, A. Pfaltz, *Chem. Sci.* **2010**, *1*, 72-78.

Table 12. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2-methyl-5-phenylpent-2-enoate (**S7**) and (*E*)-ethyl 3-methyl-5-phenylpent-2-enoate (**S8**).[a]

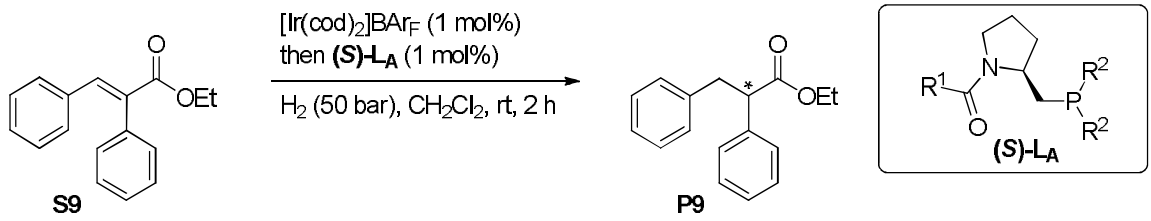


Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**S7**	**(*S*)-L_A13**	CPh_3	Ph	96	74 (−)
2	**S7**	**(*S*)-L_A16**	CPh_3	*t*Bu	> 99	84 (−)
3	**S7**	**(*S*)-L_A17**	CPh_3	Cy	**> 99**	**85 (−)**
4	**S8**	**(*S*)-L_A13**	CPh_3	Ph	> 99	48 (*S*)
5	**S8**	**(*S*)-L_A16**	CPh_3	*t*Bu	> 99	55 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

The very challenging *α*-aryl ester **S9** was reduced in moderate yields and selectivities (Table 13). Although the closely related *α*-methyl-substituted analog **S6a** was obtained in > 99% yield and with 90% *ee* (*R*) using ligand **(*S*)-L_A16** (Table 11), for ester **S9** the ligand **(*S*)-L_A17** furnished the highest selectivity of 84% *ee* albeit with a slightly diminished conversion of 63% (entry 3).

Table 13. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2,3-diphenylacrylate (**S9**).[a]



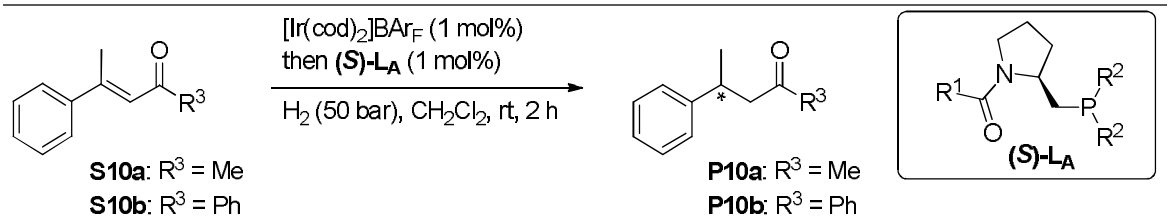
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_A13**	CPh_3	Ph	16	65 (+)
2	**(*S*)-L_A16**	CPh_3	*t*Bu	62	76 (+)
3	**(*S*)-L_A17**	CPh_3	Cy	63	84 (+)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Certainly more impressive is the level of enantioselectivity obtained in the reduction of *α*,*β*-unsaturated ketones **S10a** and **S10b** utilizing several amidophosphine/iridium

catalysts, where the selectivities exceeded the values previously reported for P,N-based systems (Table 14).[81] Sulfoximine-derived P,N ligand/iridium complexes catalyzed the reduction of these substrates with enantiomeric excesses up to 81%. Both di-*tert*-butylphosphine **(*S*)-L$_A$16** and dicyclohexylphosphine **(*S*)-L$_A$17** catalysts yielded **P10a** with 96% *ee* (*R*) (entries 3 and 5). Substrate **S10b** bearing an R^3-phenyl substituent was reduced with up to 95% *ee* (*R*) (entry 6). Conversions in the hydrogenation of **S10b** ranged from 71% to 98%. Even though the enantioselectivities were excellent for this substrate class, the complete conversion of substrate **S10a** using **(*S*)-L$_A$16** and **(*S*)-L$_A$17** was accompanied by minor formation of the saturated alcohol. To overcome this issue the reaction was carried out with isolated, preformed catalysts instead of using the *in situ* complexation method (entries 3 and 5). By using this procedure less overreduction was observed in the case of **(*S*)-L$_A$17** (98% *versus* 95% yield), but the selectivity decreased (98% *versus* 89% *ee* in entry 5).

Table 14. Iridium-catalyzed asymmetric hydrogenation of (*E*)-4-phenylpent-3-en-2-one (**S10a**) and (*E*)-1,3-diphenylbut-2-en-1-one (**S10b**).[a]



Entry	R^3	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**Me**	**(*S*)-L$_A$13**	CPh_3	Ph	85	79 (*R*)
2	**Ph**	**(*S*)-L$_A$13**	CPh_3	Ph	71	87 (*R*)
3	**Me**	**(*S*)-L$_A$16**	CPh_3	*t*Bu	**98**[d] [**98**][e]	**96 (*R*)** [**94 (*R*)**][e]
4	**Ph**	**(*S*)-L$_A$16**	CPh_3	*t*Bu	99	94 (*R*)
5	**Me**	**(*S*)-L$_A$17**	CPh_3	Cy	95[d] [98][e]	96 (*R*) [89 (*R*)][e]
6	**Ph**	**(*S*)-L$_A$17**	CPh_3	Cy	**98**	**95 (*R*)**

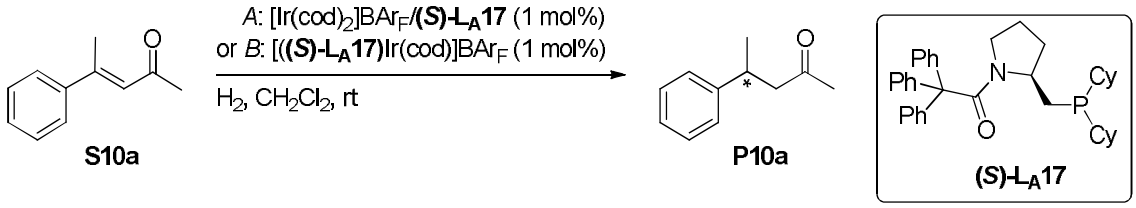
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] Formation of side products was observed (conversions > 99%); [e] Results obtained with the isolated precatalyst.

To address the undesired overreduction of **S10a** different reaction conditions were screened using the **(*S*)-L$_A$17**/iridium catalyst system (Table 15). The influence of the prior isolation of the precatalyst compared to the *in situ* complexation method was investigated, as well as the impact of the reaction time and the hydrogen pressure. At

[81] S.-M. Lu, C. Bolm, *Chem. Eur. J.* **2008**, *14*, 7513-7516.

lower hydrogen pressure both yields and enantioselectivities dropped but no overreduction was observed (entry 5).

Table 15. Optimization of reaction conditions for the iridium-catalyzed asymmetric hydrogenation of (*E*)-4-phenylpent-3-en-2-one (**S10a**) with **(*S*)-L$_A$17**.[a]



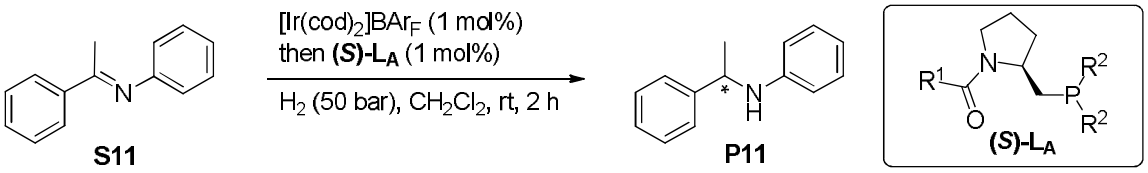
Entry	*p* [bar]	*t* [h]	Complex	Conv. [%][b]	Yield [%][b]	*ee* [%][c]
1	50	2	*A*	> 99	**93**[d]	**96 (*R*)**
2	50	2	*B*	> 99	98	89 (*R*)
3	50	1	*A*	> 99	**97**	**96 (*R*)**
4	50	1	*B*	> 99	98	90 (*R*)
5	5	2	*B*	83	83	86 (*R*)

[a] Reaction scale: catalyst (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Conversions and yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] Average of 2 experiments.

Using the isolated complex **(*S*)-C$_A$17** ([(**(*S*)-L$_A$17**)Ir(cod)]BAr$_F$) as catalyst no influence of the reaction time could by observed and the same results were obtained 1 or 2 hours reaction time (entries 2 and 4). When the *in situ* complexation method was used, no influence of the reaction time on the enantioselectivity of the reaction was observed, either (entries 1 and 3). Comparison of the influence of the catalyst's provenance (isolated **(*S*)-C$_A$17** *versus in situ* complexed **(*S*)-L$_A$17**) shows that the isolation of the precatalyst renders a slight decrease of the amount of overreduced product possible but also impacts the enantiomeric excess (entries 1 and 3 *versus* 2 and 4).

Finally, the imine substrate **S11** was also tested (Table 16), but the amidophosphine/iridium catalysts proved to be not suitable for the reduction of C−N double bonds. Diarylphosphines did not give yields higher than 57% and the selectivities were of 26% *ee* at best. Moreover, the reduction was accompanied by major formation of hydrolysis products. Dialkylphosphines were not tested at all in the hydrogenation of **S11**.

Table 16. Iridium-catalyzed asymmetric hydrogenation of *N*-(1-phenylethylidene)-aniline (**S11**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*R*)-L_A1**	*t*Bu	Ph	12 [56]	14 (*S*)
2	**(*S*)-L_A2**	*t*Bu	*o*Tol	37 [92]	25 (*R*)
3	**(*S*)-L_A8**	1-Adm	*o*Tol	27 [91]	18 (*R*)
4	**(*S*)-L_A9**	1-Adm	2-Fur	15 [66]	7 (*R*)
5	**(*S*)-L_A13**	CPh_3	Ph	9 [64]	11 (*R*)
6	**(*S*)-L_A14**	CPh_3	*o*Tol	57 [95]	13 (*R*)
7	**(*S*)-L_A15**	CPh_3	2-Fur	18 [93]	5 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), CH_2Cl_2 (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Sterically hindered proline-based P,O ligands with alkyl substituents at the phosphorus moiety allowed for the enantioselective hydrogenation of the unfunctionalized trisubstituted alkene **S1** with higher enantiomeric excesses than the initially discovered ligand **(*R*)-L_A1**. In addition, these ligands were applied to the iridium-catalyzed asymmetric hydrogenation of *α,β*-unsaturated ketones and excellent enantiomeric excesses of up to 96% were achieved.

2.5 Proline-Based Ureaphosphines Ligands

Based on the results of the previous section, ureaphosphines were prepared and tested as ligands in the iridium-catalyzed asymmetric hydrogenation of the exemplar substrates presented above. Again, only the best ureaphosphines were applied to the hydrogenation of the more challenging *α,β*-unsaturated esters and ketones. The same phosphorus substituents were introduced in the ureaphosphines, which were already contained in the amidophosphines, namely diphenyl-, di-*ortho*-tolyl-, di-(2-furyl)-, di-*tert*-butyl- and dicyclohexylphosphines were prepared. The incorporation of an urea moiety instead of an amide carbonyl functionality was thought to make an optimization of the electronic as well as steric characteristics of the coordinating oxygen possible, since the adjacent nitrogen atom can be substituted with two groups. The ureaphosphines synthesized and presented below are divided into two classes, namely trisubstituted ureaphosphines

(*S*)-L_{U3} and tetrasubstituted ureaphosphines **(*S*)-L_{U4}** (see Figure 9). First, their synthesis is described and the results of their application as ligand in the asymmetric hydrogenation are summarized, later.

2.5.1
Trisubstituted Ureaphosphines Ligands

A series of trisubstituted ureaphosphine ligands was prepared, which is depicted in Schemes 21 and 23. The urea moiety consists of the pyrrolidine ring (which incorporates the first nitrogen atom) and a second substituent, which is derived from a primary amine (aryl or alkyl substituent as R^1-group).

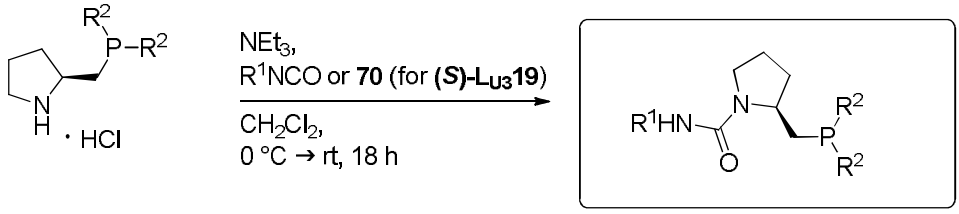
2.5.1.1
Synthesis of Trisubstituted Ureaphosphines

In the following, the synthesis of ureaphosphine ligands is depicted in two schemes: while Scheme 21 shows all diaryl-substituted phosphines that were prepared, the dialkyl-substituted phosphine ligands are presented in Scheme 23.

Ureaphosphine ligands were easily prepared from the previously synthesized carbamates **(*S*)-L_C1**, **(*S*)-L_C2** and **(*S*)-L_C3** with different substituents at the phosphorus atom as starting materials (Schemes 11 and 12). Form the respective deprotected salts **(*S*)-52·HCl**, **(*S*)-57·HCl** and **(*S*)-58·HCl**, several trisubstituted ureaphosphines **(*S*)-L_{U3}** were obtained. The urea functionalities were introduced using isocyanates (R^1NCO) or the succinimidyl carbamate of aniline (**70**) as reagent. Good to excellent yields were achieved for this substitution reaction representing the last step of the ligand synthesis (34% to 92%).

The majority of the isocyanates were commercially available, only triphenylmethyl isocyanate (**66**) and 2,4,6-tri-*tert*-butylmethylphenyl isocyanate (**68**) had to be synthesized (Scheme 22). These were prepared following a literature-known procedures involving the reaction of triphosgene with the respective primary amine.[82,83]

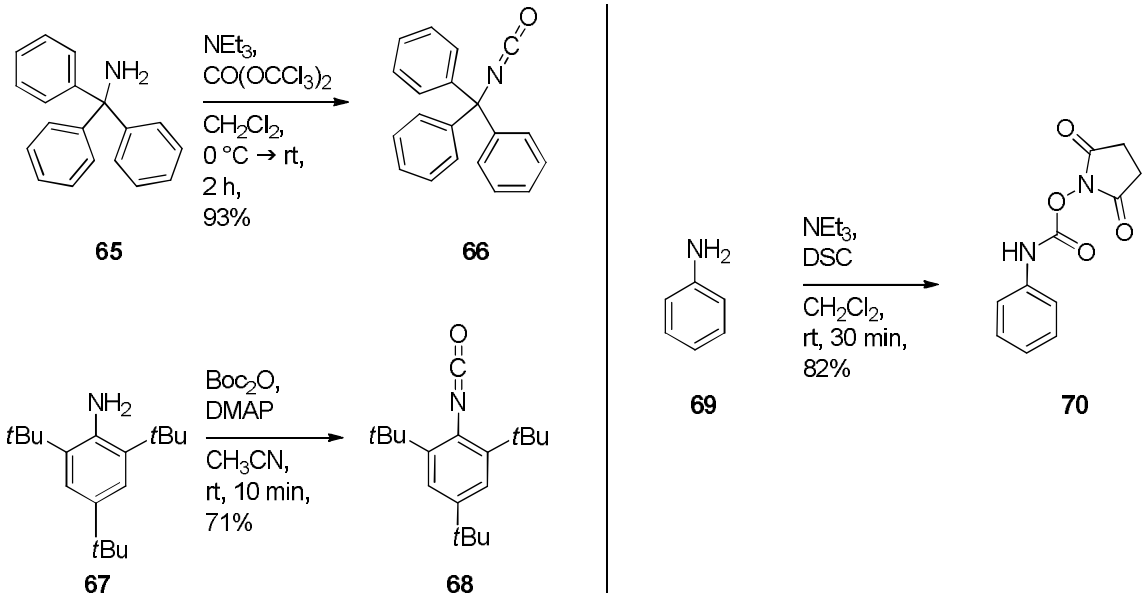
[82] For the synthesis of triphenylmethyl isocyanate (**66**) see: A. G. S. Blommert, J.-H. Weng, A. Dorville, I. McCort, B. Ducos, C. Durieux, B. P. Roques, *J. Med. Chem.* **1993**, *36*, 2868-2877.
[83] For the prodecure followed to prepare 2,4,6-tri-*tert*-butylmethylphenyl isocyanate (**68**) see: H.-J. Knölker, T. Braxmeier, G. Schlechtingen, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2497-2500.



(*S*)-52·HCl: R^2 = Ph
(*S*)-57·HCl: R^2 = *o*Tol
(*S*)-58·HCl: R^2 = 2-Fur

(*S*)-L_{U3}1:	R^1 = *t*Bu,	R^2 = Ph	(78%)
(*S*)-L_{U3}2:	R^1 = *t*Bu,	R^2 = *o*Tol	(56%)
(*S*)-L_{U3}3:	R^1 = *t*Bu,	R^2 = 2-Fur	(65%)
(*S*)-L_{U3}6:	R^1 = *i*Pr,	R^2 = Ph	(71%)
(*S*)-L_{U3}7:	R^1 = Cy,	R^2 = Ph	(76%)
(*S*)-L_{U3}8:	R^1 = Cy,	R^2 = *o*Tol	(52%)
(*S*)-L_{U3}11:	R^1 = 1-Adm,	R^2 = Ph	(94%)
(*S*)-L_{U3}12:	R^1 = 1-Adm,	R^2 = *o*Tol	(79%)
(*S*)-L_{U3}15:	R^1 = CPh_3,	R^2 = Ph	(92%)
(*S*)-L_{U3}16:	R^1 = CPh_3,	R^2 = *o*Tol	(42%)
(*S*)-L_{U3}19:	R1 = Ph,	R^2 = Ph	(49%)
(*S*)-L_{U3}20:	R^1 = Ph,	R^2 = 2-Fur	(61%)
(*S*)-L_{U3}21:	R^1 = Mes,	R^2 = Ph	(82%)
(*S*)-L_{U3}22:	R^1 = Mes,	R^2 = *o*Tol	(67%)
(*S*)-L_{U3}25:	R^1 = (2,4,6-*t*Bu_3)Ph,	R^2 = Ph	(34%)
(*S*)-L_{U3}26:	R^1 = 1-Naph,	R^2 = Ph	(81%)

Scheme 21. Synthesis of trisubstituted ureaphosphines with aryl substituents at the phosphorus atom (abbreviations: Mes for mesityl, (2,4,6-*t*Bu_3)Ph for 2,4,6-tri-*tert*-butylphenyl and 1-Naph for 1-naphthyl).

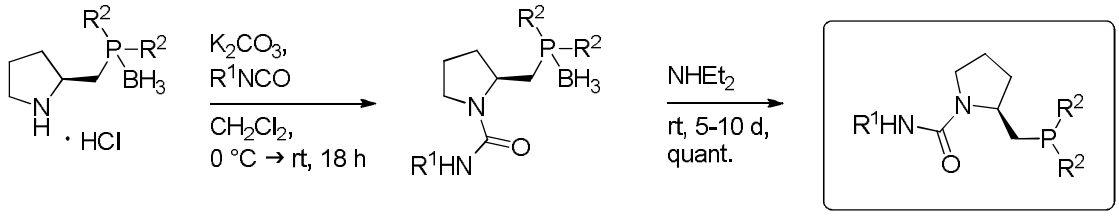


Scheme 22. Synthesis of the isocyanates **66** and **68** and of the succinimidyl carbamate **70**.[82,83]

Additionally, 2,5-dioxopyrrolidin-1-yl phenylcarbamate (**70**) was prepared from aniline (**69**), by reacting it with *N*,*N*'-disuccinimidyl carbonate (DSC) in the presence of

triethylamine (Scheme 22). The desired product was obtained in 82% yield after only 30 minutes. The conditions were not optimized and the reaction was deliberately stopped after 30 minutes to avoid the subsequent formation of 1,3-diphenylurea, that was observed after longer reaction times. The utilization of **70** and phenyl isocyanate proved to be equally effective.

The synthesis of dialkyl-substituted phosphines is depicted in Scheme 23. These ligands comprise the same urea moieties as the derivatives shown in Scheme 21 in combination with either a di-*tert*-butyl- or dicyclohexylphosphine moiety.



(*S*)-63·HCl: R^2 = *t*Bu
(*S*)-64·HCl: R^2 = Cy

(*S*)-L_{U3}4·BH_3:	R^1 = *t*Bu,	R^2 = *t*Bu	(77%)
(*S*)-L_{U3}5·BH_3:	R^1 = *t*Bu,	R^2 = Cy	(64%)
(*S*)-L_{U3}9·BH_3:	R^1 = Cy,	R^2 = *t*Bu	(63%)
(*S*)-L_{U3}10·BH_3:	R^1 = Cy,	R^2 = Cy	(51%)
(*S*)-L_{U3}13·BH_3:	R^1 = 1-Adm,	R^2 = *t*Bu	(72%)
(*S*)-L_{U3}14·BH_3:	R^1 = 1-Adm,	R^2 = Cy	(87%)
(*S*)-L_{U3}17·BH_3:	R^1 = CPh_3,	R^2 = *t*Bu	(88%)
(*S*)-L_{U3}18·BH_3:	R^1 = CPh_3,	R^2 = Cy	(87%)
(*S*)-L_{U3}23·BH_3:	R^1 = Mes,	R^2 = *t*Bu	(90%)
(*S*)-L_{U3}24·BH_3:	R^1 = Mes,	R^2 = Cy	(82%)

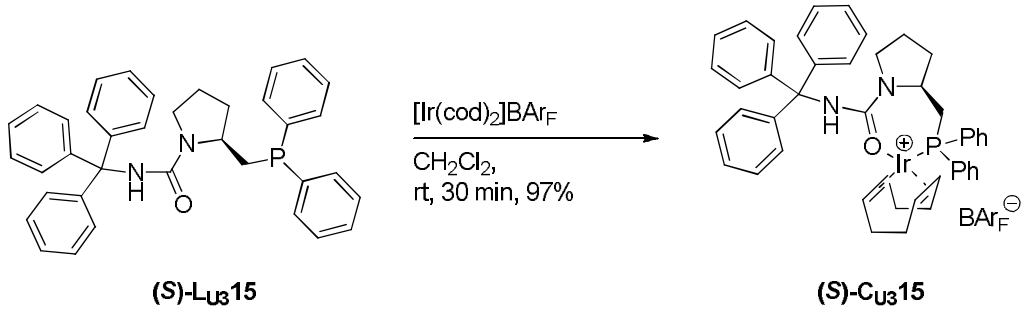
(*S*)-L_{U3}

Scheme 23. Synthesis of trisubstituted ureaphosphines with alkyl substituents at the phosphorus atom.

Ligand precursors **(*S*)-L_{U3}·BH_3** were obtained in good yields by reaction of the pyrrolidinium salts **(*S*)-63·HCl** and **(*S*)-64·HCl** containing the desired borane-protected phosphine moieties with the respective isocyanates (51% to 90% yield, Scheme 23). Potassium carbonate had to be used as base to avoid the premature deprotection of the phosphorus atom. The free ligands were obtained by deprotection with diethylamine as described in the synthesis of dialkyl-substituted amidophosphines, and the ligands were converted to their respective iridium complexes in the same way as shown in Scheme 20.

A representative example for the complexation of ureaphosphines is depicted in Scheme 24. $[Ir(cod)_2]BAr_F$ was stirred with the trisubstituted ureaphosphine **(*S*)-L_{U3}15** in

a 1:1 ratio at room temperature. After evaporation of the solvent and trituration with *n*-pentane the complex **(*S*)-C_{U3}15** was obtained as a yellowish solid in 97% yield.

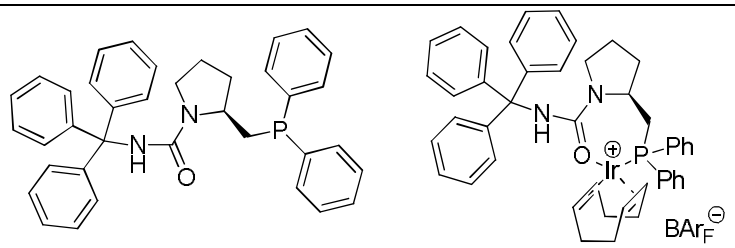


(*S*)-L_{U3}15 **(*S*)-C_{U3}15**

Scheme 24. Synthesis of ureaphosphine/iridium complex **(*S*)-C_{U3}15**.

The coordination mode of **(*S*)-L_{U3}15** to iridium was investigated in order to confirm that similar to amidophosphines, ureaphosphines behave as bidentate P,O ligands. The spectroscopic data in Table 17 confirm a bidentate coordination.

Table 17. Comparison of the spectroscopic properties of ligand **(*S*)-L_{U3}15** and complex **(*S*)-C_{U3}15**.



	(*S*)-L_{U3}15	**(*S*)-C_{U3}15**
^{31}P NMR [δ (P)]	− 21.6 ppm	11.2 ppm
^{13}C NMR [δ (C=O)]	154.5 ppm	163.7 ppm
IR [$\tilde{\nu}$ (C=O)]	1663 cm^{-1}	1569 cm^{-1}

The NMR signals of both the phosphorus and the quaternary carbonyl carbon are shifted downfield, when the ligand is bound to iridium (**(*S*)-C_{U3}15**). Furthermore, the IR spectroscopic data also support that the urea moiety is coordinated to iridium by showing the typical shift of the vibrational wavenumber for the coordinated urea C−O double bond to lower values ($\tilde{\nu}$ = 1663 cm^{-1} for **(*S*)-L_{U3}15** *versus* $\tilde{\nu}$ = 1569 cm^{-1} for **(*S*)-C_{U3}15**). These results are very similar to those obtained in the analysis of amidophosphine coordination to iridium (see Table 2).

The solid state structure of complex **(*S*)-C_{U3}15** is shown in Figure 10. Since the crystallization of the presented BAr_F complexe proved to be difficult, the growth of

suitable single crystals was pursed for the corresponding PF_6 derivative **(*S*)-C_{U3}15**. The procedure for its preparation is basically the same as described in Scheme 24, but instead of $[Ir(cod)_2]BAr_F$, $[Ir(cod)_2]PF_6$ was used. Looking at this structure it can be seen that the trityl group acts like a shield for one side of the metal center. This observation explains the better enantioselectivities obtained with trityl-substituted ureaphosphine ligands in the asymmetric hydrogenation of several substrates described below (Tables 18 and 21). The same is probably true for the good results obtained with trityl-substituted amidophosphines (Tables 6 and 9). In both cases the trityl group might occupy a wider space near the active site of the catalyst and therefore forces the substrates to coordinate in a more defined, less flexible way.

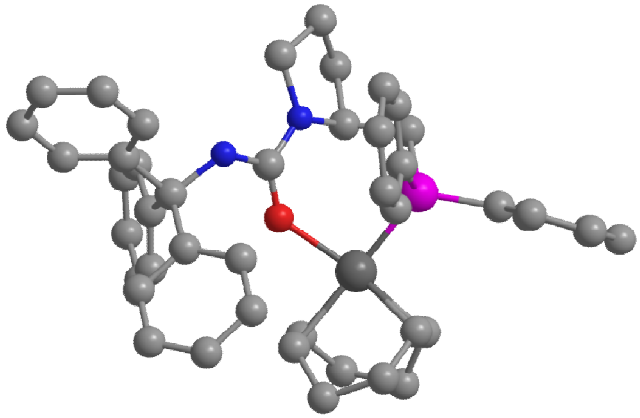


Figure 10. Crystal structure of complex [(**(*S*)-L_{U3}15**)Ir(cod)]PF_6.The counterion has been omitted for clarity (red O, blue N, magenta P, dark gray Ir, light gray C).[84]

No significant differences in the bond lengths can be noticed when the values obtained with the help of the X-ray structures for **(*R*)-C_A1** and **(*S*)-C_{U3}15** are compared (Figures 8 and 10). The Ir−P bond lengths are almost equal in both complexes and the Ir−O bond lengths are just slightly different (Ir−P bonds 2.29 Å for **(*S*)-C_{U3}15** and 2.30 Å for **(*R*)-C_A1**, Ir−O bonds 2.10 Å for **(*S*)-C_{U3}15** and 2.08 Å for **(*R*)-C_A1**). However, more pronounced differences between both precatalysts can be seen concerning their bite angles of 93.3° for **(*S*)-C_{U3}15** and 89.3° for **(*R*)-C_A1**.

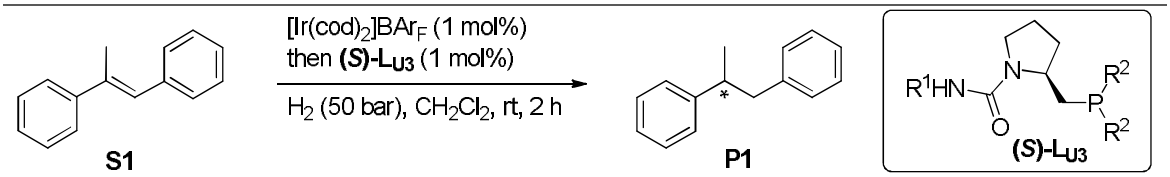
[84] Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Center. The deposition number is 829326.

2.5.5.2
Iridium-Catalyzed Asymmetric Hydrogenations with Trisubstituted Ureaphosphine Ligands

The standard substrate **S1** ((*E*)-1,2-diphenyl-1-propene) was investigated first, once again (Table 18). As it was the case for amidophosphines, (*S*)-configured ureaphosphine/iridium catalysts gave the (*R*)-configured product **P1** in excess. The highest enantiomeric excess obtained with amidophosphines in section 2.4.2 involved ligand **(*S*)-L_A16**, a di-*tert*-butylphosphine with a trityl-substituted amide (98% *ee*). The asymmetric hydrogenation of alkene **S1** using ligands **(*S*)-L_{U3}13**, **(*S*)-L_{U3}15**, **(*S*)-L_{U3}17** and **(*S*)-L_{U3}18** afforded the product **(*R*)-P1** with the same or even better enantiomeric excesses of 98% and more (entries 13, 15, 17 and 18). Overall, several quite efficient ureaphosphine ligands for the iridium-catalyzed asymmetric hydrogenation of **S1** were developed that furnished selectivities of 90% *ee* and more. The same correlations between catalyst structures and selectivities were observed for ureaphosphines and amidophosphines. Interestingly in the case of the urea-based derivatives, also the ligands substituted with a planar R^1-mesityl group **(*S*)-L_{U3}23** and **(*S*)-L_{U3}24** furnished selectivities of 90% *ee* and 92% *ee* (entries 23 and 24). In contrast, the structurally related ligand **(*S*)-L_{U3}25** with a more bulky 2,4,6-tri-*tert*-butyl-phenyl-substituted urea, reduced the alkene **S1** with only 86% conversion and 40% *ee* (entry 25). The steric hindrance of this urea moiety is probably too pronounced and causes overcrowding around the active site of the catalyst making it more difficult for the substrate to bind to the metal center in a defined way.

Comparison of the results obtained for **(*S*)-L_{U3}19**, **(*S*)-L_{U3}21** and **(*S*)-L_{U3}26** with R^1 = phenyl, mesityl and naphtyl, respectively, with **(*S*)-L_{U3}15** with R^1 = trityl indicates that diaryl-substituted ureaphosphines can provide excellent results, when they exhibit increased steric bulk at the carbonyl functionality, while planar substituents are not equally suited as R^1-groups. Taken together, a trityl-substituted urea once again proved to be optimal for obtaining high selectivities, while dialkylphosphines/iridium catalysts gave better results than their structural diaryl analogs in most cases.

Table 18. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**).[a]

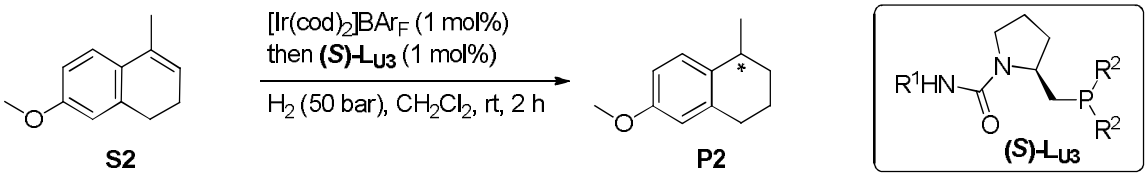


Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U3}1**	*t*Bu	Ph	> 99	73 (*R*)
2	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	50	54 (*R*)
3	**(*S*)-L_{U3}3**	*t*Bu	2-Fur	> 99	62 (*R*)
4	**(*S*)-L_{U3}4**	*t*Bu	*t*Bu	70	93 (*R*)
5	**(*S*)-L_{U3}5**	*t*Bu	Cy	> 99	88 (*R*)
6	**(*S*)-L_{U3}6**	*i*Pr	Ph	> 99	17 (*R*)
7	**(*S*)-L_{U3}7**	Cy	Ph	> 99	36 (*R*)
8	**(*S*)-L_{U3}8**	Cy	*o*Tol	> 99	6 (*R*)
9	**(*S*)-L_{U3}9**	Cy	*t*Bu	96	77 (*R*)
10	**(*S*)-L_{U3}10**	Cy	Cy	> 99	63 (*R*)
11	**(*S*)-L_{U3}11**	1-Adm	Ph	> 99	89 (*R*)
12	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	99	79 (*R*)
13	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	**> 99**	**98 (*R*)**
14	**(*S*)-L_{U3}14**	1-Adm	Cy	**> 99**	**96 (*R*)**
15	**(*S*)-L_{U3}15**	CPh_3	Ph	**> 99**	**99 (*R*)**
16	**(*S*)-L_{U3}16**	CPh_3	*o*Tol	**> 99**	**97 (*R*)**
17	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	**> 99**	**98 (*R*)**
18	**(*S*)-L_{U3}18**	CPh_3	Cy	**> 99**	**99 (*R*)**
19	**(*S*)-L_{U3}19**	Ph	Ph	95	77 (*R*)
20	**(*S*)-L_{U3}20**	Ph	2-Fur	64	70 (*R*)
21	**(*S*)-L_{U3}21**	Mes	Ph	> 99	87 (*R*)
22	**(*S*)-L_{U3}22**	Mes	*o*Tol	> 99	69 (*R*)
23	**(*S*)-L_{U3}23**	Mes	*t*Bu	> 99	92 (*R*)
24	**(*S*)-L_{U3}24**	Mes	Cy	> 99	90 (*R*)
25	**(*S*)-L_{U3}25**	(2,4,6-*t*Bu_3)Ph	Ph	86	40 (*R*)
26	**(*S*)-L_{U3}26**	1-Naph	Ph	> 99	80 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Unfortunately, trisubstituted ureaphosphine/iridium catalysts were not more selective in the asymmetric hydrogenation of the unfunctionalized trisubstituted alkene **S2** compared with the corresponding amidophosphine derivatives (Table 19). Throughout the whole screening of various ureaphosphines involving both dialkyl- and diarylphosphines and various amide R^1-substituents the selectivities in the reduction of cyclic substrate **S2** remained below 23% *ee*. Although the yields in these reactions were good to excellent (75% to 98%), the conversion of **S2** and yields of **P2** were not always identical, since up to 9% of by-products were observed (entry 22).

Table 19. Iridium-catalyzed asymmetric hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**).[a]



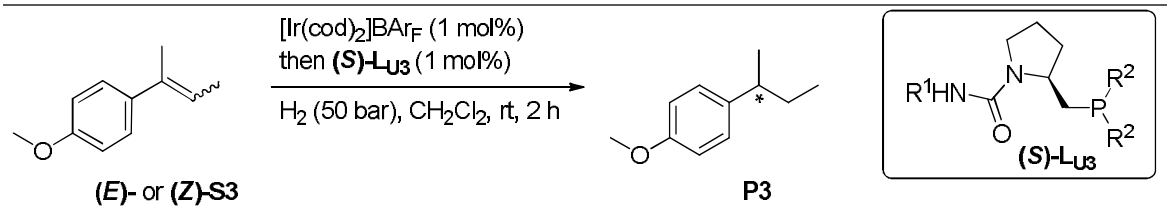
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U3}1**	*t*Bu	Ph	88 [91]	*rac*
2	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	93	23 (*S*)
3	**(*S*)-L_{U3}4**	*t*Bu	*t*Bu	96 [98]	20 (*S*)
4	**(*S*)-L_{U3}5**	*t*Bu	Cy	92 [> 99]	10 (*S*)
5	**(*S*)-L_{U3}6**	*i*Pr	Ph	93 [96]	2 (*R*)
6	**(*S*)-L_{U3}7**	Cy	Ph	87 [90]	2 (*R*)
7	**(*S*)-L_{U3}8**	Cy	*o*Tol	98	*rac*
8	**(*S*)-L_{U3}9**	Cy	*t*Bu	75 [78]	4 (*S*)
9	**(*S*)-L_{U3}10**	Cy	Cy	89 [> 99]	*rac*
10	**(*S*)-L_{U3}11**	1-Adm	Ph	99	4 (*S*)
11	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	99	23 (*S*)
12	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	98	6 (*R*)
13	**(*S*)-L_{U3}14**	1-Adm	Cy	91 [98]	3 (*S*)
14	**(*S*)-L_{U3}15**	CPh_3	Ph	87	*rac*
15	**(*S*)-L_{U3}16**	CPh_3	*o*Tol	86	2 (*R*)
16	**(*S*)-L_{U3}18**	CPh_3	Cy	93 [> 99]	5 (*R*)
17	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	95 [> 99]	17 (*S*)
18	**(*S*)-L_{U3}19**	Ph	Ph	97 [> 99]	2 (*S*)
19	**(*S*)-L_{U3}21**	Mes	Ph	> 99	14 (*S*)
20	**(*S*)-L_{U3}22**	Mes	*o*Tol	98	9 (*S*)
21	**(*S*)-L_{U3}23**	Mes	*t*Bu	96 [> 99]	10 (*S*)
22	**(*S*)-L_{U3}24**	Mes	Cy	91 [> 99]	4 (*S*)
23	**(*S*)-L_{U3}25**	(2,4,6-*t*Bu_3)Ph	Ph	79 [81]	4 (*S*)
24	**(*S*)-L_{U3}26**	1-Naph	Ph	93	14 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Although the results of the screening shown, above, in Table 19 were not very encouraging to pursue the iridium-catalyzed asymmetric hydrogenation of more demanding unfunctionalized alkenes, the reduction of **(*E*)-S3** and **(*Z*)-S3** was attempted with several trisubstituted ureaphosphine ligands (**(*S*)-L_{U3}**) (Table 20). The screening was rather unsystematic, since no clear trends concerning the preferred electronic and steric properties of the catalysts in order to achieve high enantioinduction was obtained from the previous screening, using **S2**. The reduction of **(*E*)-S3** with **(*S*)-L_{U3}19** as ligand led to **(*R*)-P3** in > 99% yield and 41% *ee* (entry 12). **(*S*)-L_{U3}2** permitted to obtain **(*S*)-P3** in

99% yield and 55% *ee* from **(*Z*)-S3** (entry 3). In these reductions involving the (*Z*)-isomer of **S3**, di-*ortho*-tolylphosphines ligands generally induced higher enantiomeric excesses than the respective diphenylphosphine ligands (entries 1, 3, 8 and 10).

Table 20. Iridium-catalyzed asymmetric hydrogenation of (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)-**and **(*Z*)-S3**).[a]

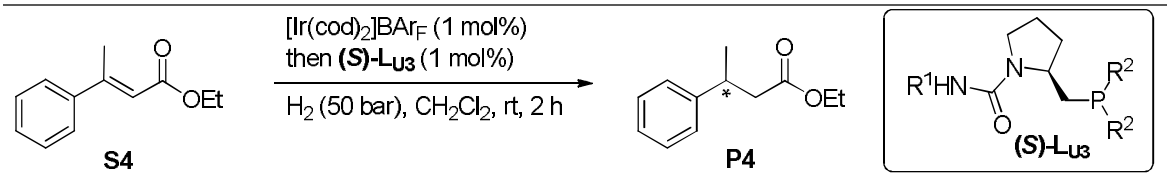


Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*Z*)-S3**	**(*S*)-L_{U3}1**	*t*Bu	Ph	> 99	16 (*S*)
2	**(*E*)-S3**	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	51	3 (*R*)
3	**(*Z*)-S3**	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	99	55 (*S*)
4	**(*E*)-S3**	**(*S*)-L_{U3}6**	*i*Pr	Ph	> 99	7 (*R*)
5	**(*Z*)-S3**	**(*S*)-L_{U3}6**	*i*Pr	Ph	> 99	14 (*S*)
6	**(*E*)-S3**	**(*S*)-L_{U3}7**	Cy	Ph	> 99	17 (*R*)
7	**(*Z*)-S3**	**(*S*)-L_{U3}7**	Cy	Ph	> 99	17 (*S*)
8	**(*Z*)-S3**	**(*S*)-L_{U3}11**	1-Adm	Ph	> 99	21 (*S*)
9	**(*E*)-S3**	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	65	*rac*
10	**(*Z*)-S3**	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	> 99	35 (*S*)
11	**(*Z*)-S3**	**(*S*)-L_{U3}15**	CPh_3	Ph	> 99	18 (*S*)
12	**(*E*)-S3**	**(*S*)-L_{U3}19**	Ph	Ph	> 99	41 (*R*)
13	**(*Z*)-S3**	**(*S*)-L_{U3}19**	Ph	Ph	> 99	8 (*R*)
14	**(*E*)-S3**	**(*S*)-L_{U3}21**	Mes	Ph	90	19 (*R*)
15	**(*Z*)-S3**	**(*S*)-L_{U3}21**	Mes	Ph	> 99	15 (*S*)
16	**(*Z*)-S3**	**(*S*)-L_{U3}25**	(2,4,6-*t*Bu_3)Ph	Ph	> 99	6 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC or GC analysis using a chiral stationary phase (see experimental part).

All the synthesized trisubstituted ureaphosphines were tested in the asymmetric hydrogenation of the functionalized alkenes **S4** and **S5**. The results obtained in the ligand screening for the *α,β*-unsaturated ester (*E*)-ethyl 3-phenylbut-2-enoate (**S4**) are shown in Table 21. Unlike in the asymmetric reduction of the unfunctionalized alkene **S1** only one ligand furnished an excellent enantiomeric excess, namely the dicyclohexylphosphine **(*S*)-L_{U3}18** with a trityl-substituted urea functionality. The (*R*)-configured product **P4** was obtained with > 99% yield and 98% *ee* (entry 18).

Table 21. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**S4**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U3}1**	*t*Bu	Ph	> 99	83 (*R*)
2	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	52	19 (*R*)
3	**(*S*)-L_{U3}3**	*t*Bu	2-Fur	60	50 (*R*)
4	**(*S*)-L_{U3}4**	*t*Bu	*t*Bu	58	53 (*R*)
5	**(*S*)-L_{U3}5**	*t*Bu	Cy	> 99	78 (*R*)
6	**(*S*)-L_{U3}6**	*i*Pr	Ph	> 99	7 (*R*)
7	**(*S*)-L_{U3}7**	Cy	Ph	> 99	40 (*R*)
8	**(*S*)-L_{U3}8**	Cy	*o*Tol	99	8 (*R*)
9	**(*S*)-L_{U3}9**	Cy	*t*Bu	69	40 (*R*)
10	**(*S*)-L_{U3}10**	Cy	Cy	> 99	48 (*R*)
11	**(*S*)-L_{U3}11**	1-Adm	Ph	> 99	83 (*R*)
12	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	99	71 (*R*)
13	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	92 (*R*)
14	**(*S*)-L_{U3}14**	1-Adm	Cy	> 99	93 (*R*)
15	**(*S*)-L_{U3}15**	CPh_3	Ph	99	92 (*R*)
16	**(*S*)-L_{U3}16**	CPh_3	*o*Tol	99	85 (*R*)
17	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	99	93 (*R*)
18	**(*S*)-L_{U3}18**	CPh_3	Cy	**> 99**	**98 (*R*)**
19	**(*S*)-L_{U3}19**	Ph	Ph	> 99	74 (*R*)
20	**(*S*)-L_{U3}20**	Ph	2-Fur	48	41 (*R*)
21	**(*S*)-L_{U3}21**	Mes	Ph	99	87 (*R*)
22	**(*S*)-L_{U3}22**	Mes	*o*Tol	99	49 (*R*)
23	**(*S*)-L_{U3}23**	Mes	*t*Bu	> 99	88 (*R*)
24	**(*S*)-L_{U3}24**	Mes	Cy	> 99	90 (*R*)
25	**(*S*)-L_{U3}25**	(2,4,6-*t*Bu_3)Ph	Ph	> 99	57 (*R*)
26	**(*S*)-L_{U3}26**	1-Naph	Ph	99	77 (*R*)

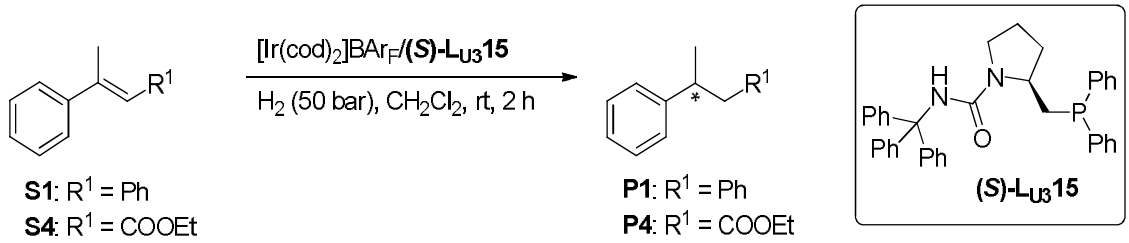
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

Several other ligands furnished selectivities of more than 90% (entries 13 to 15, 17, 18 and 24), though these derivatives incorporate bulky adamantyl, trityl or mesityl groups as R^1-substituent. Isopropyl or cyclohexyl substituents at this position proved not to be suitable and only 7% to 48% *ee* were achieved in these cases (entries 6 to 10). For a given R^1-group the combination with R^2-alkyl substituents proved to be more efficient concerning enantioselectivities than the respective combination with R^2-aryl substituents (entries 13 and 14 *versus* 11 and 12, as well as 17 and 18 *versus* 15 and 16). The ligand with *tert*-butyl substituents as R^1-groups represents the only exception to this observation:

while 83% *ee* was achieved for the diphenylphosphine all other ureaphosphines in this subgroup showed lower selectivities (entries 1 to 5). In general, conversions were excellent except for di-*ortho*-tolylphosphine **(*S*)-L$_{U3}$2**, for di-(2-furyl)-phosphines **(*S*)-L$_{U3}$3** and **(*S*)-L$_{U3}$20** and di-*tert*-butylphosphines **(*S*)-L$_{U3}$4** and **(*S*)-L$_{U3}$9** (entries 2 to 4, 9 and 20).

At this stage the influence of the catalyst loading on the activity and selectivity of the complexes was investigated (Table 22). For this purpose **(*S*)-L$_{U3}$15** was chosen as ligand for these test reactions, since it gave complete conversions and good selectivities in the asymmetric reduction of both the unfunctionalized alkene **S1** and the ester substrate **S4**. With 1 mol% of catalyst loading 99% *ee* was obtained in the hydrogenation of **S1** and 92% *ee* in the reduction of **S4** (entries 1 and 4).

Table 22. Influence of the catalyst loading using **(*S*)-L$_{U3}$15**.[a]

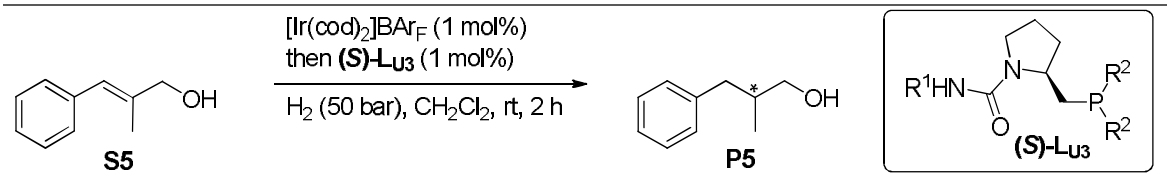


Entry	Substrate	Loading	Yield [%][b]	*ee* [%][c]
1	**S1**	1 mol%	**> 99**	**99 (*R*)**
2	**S1**	0.5 mol%	97	95 (*R*)
3	**S1**	0.1 mol%	65	82 (*R*)
4	**S4**	1 mol%	**99**	**92 (*R*)**
5	**S4**	0.5 mol%	99	90 (*R*)
6	**S4**	0.1 mol%	21	86 (*R*)

[a] Reaction scale: substrate (125 µmol), solvent (0.25 mL); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC or GC analysis using a chiral stationary phase (see experimental part).

Reduction of the catalyst loading to 0.5 mol% resulted in a slight decrease of the selectivities for both products **P1** and **P4** (entries 2 and 5). An additional reduction of the catalyst loading to 0.1 mol% impaired the enantioselectivities even more and also caused a drastic decrease of the conversions of starting materials **S1** and **S4** (entries 3 and 6). Since the observed trends were consistent for both investigated substrates, no further investigations concerning the lowering of catalyst loadings were carried out, and in all following hydrogenation reactions 1 mol% of catalyst was used.

Table 23. Iridium-catalyzed asymmetric hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**S5**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U3}1**	*t*Bu	Ph	91 [> 99]	54 (*S*)
2	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	> 99	57 (*S*)
3	**(*S*)-L_{U3}4**	*t*Bu	*t*Bu	> 99	47 (*S*)
4	**(*S*)-L_{U3}5**	*t*Bu	Cy	> 99	32 (*S*)
5	**(*S*)-L_{U3}6**	*i*Pr	Ph	95 [> 99]	32 (*S*)
6	**(*S*)-L_{U3}7**	Cy	Ph	87 [> 99]	32 (*S*)
7	**(*S*)-L_{U3}8**	Cy	*o*Tol	> 99	40 (*S*)
8	**(*S*)-L_{U3}9**	Cy	*t*Bu	> 99	59 (*S*)
9	**(*S*)-L_{U3}10**	Cy	Cy	> 99	44 (*S*)
10	**(*S*)-L_{U3}11**	1-Adm	Ph	20 [25]	73 (*S*)
11	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	89 [95]	72 (*S*)
12	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	61 (*S*)
13	**(*S*)-L_{U3}14**	1-Adm	Cy	> 99	39 (*S*)
14	**(*S*)-L_{U3}15**	CPh_3	Ph	> 99	71 (*S*)
15	**(*S*)-L_{U3}16**	CPh_3	*o*Tol	> 99	71 (*S*)
16	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	> 99	20 (*S*)
17	**(*S*)-L_{U3}18**	CPh_3	Cy	> 99	38 (*S*)
18	**(*S*)-L_{U3}19**	Ph	Ph	83 [> 99]	11 (*S*)
19	**(*S*)-L_{U3}21**	Mes	Ph	> 99	9 (*S*)
20	**(*S*)-L_{U3}22**	Mes	*o*Tol	> 99	34 (*S*)
21	**(*S*)-L_{U3}23**	Mes	*t*Bu	> 99	7(*S*)
22	**(*S*)-L_{U3}24**	Mes	Cy	> 99	10 (*R*)
23	**(*S*)-L_{U3}25**	(2,4,6-*t*Bu_3)Ph	Ph	> 99	26 (*R*)
24	**(*S*)-L_{U3}26**	1-Naph	Ph	> 99	14 (*R*)

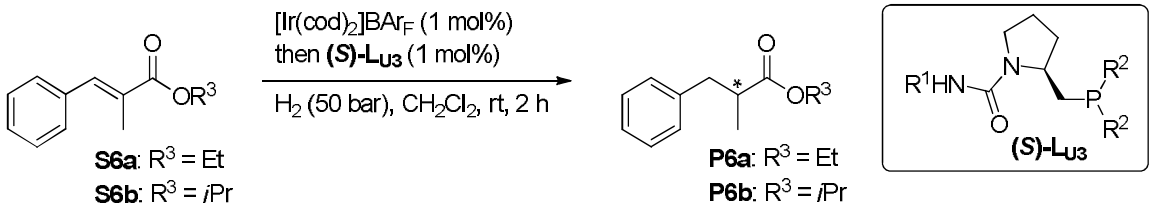
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Most ureaphosphine/iridium catalysts gave more or less quantitative conversions for allylic alcohol **S5** (see Table 23). Although the activities were excellent, these complexes showed rather moderate selectivities. The best enantiomeric excess measured for the reduction of allylic alcohol **S5** was 73% *ee* (*S*), but unfortunately the lowest conversion of the whole series was obtained in this case (entry 10). Some other ligands also showed selectivities of more than 70% *ee*, namely **(*S*)-L_{U3}12**, **(*S*)-L_{U3}15** and **(*S*)-L_{U3}16** (entries 11, 14 and 15). These ligands once again bear bulky urea substituents, like adamantyl or trityl moieties, but interestingly resemble diarylphosphine derivatives.

Therefore, this substrate is reduced with higher selectivities when aryl-substituted rather than alkyl-substituted phosphines are used. This observation was already made, when amidophosphines were used as P,O ligands in this transformation (see Table 10).

Because of the excellent results for ester substrate **S4** (Table 21), selected trisubstituted ureaphosphines were as well screened in the asymmetric hydrogenation of other trisubstituted *α,β*-unsaturated esters **S6a**, **S6b**, **S7**, **S8** and **S9** as well as the *α,β*-unsaturated ketones **S10a** and **S10b**. The results for these investigations are shown below. High enantioselectivities were obtained for the iridium-catalyzed asymmetric hydrogenation of the *α*-methyl-substituted *α,β*-unsaturated esters **S6a** and **S6b** (Table 24).

Table 24. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2-methyl-3-phenylacrylate (**S6a**) and (*E*)-isopropyl 2-methyl-3-phenylacrylate (**S6b**).[a]



Entry	R^3	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	Et	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	90 (*R*)
2	*i*Pr	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	92 (*R*)
3	Et	**(*S*)-L_{U3}15**	CPh_3	Ph	> 99	86 (*R*)
4	*i*Pr	**(*S*)-L_{U3}15**	CPh_3	Ph	**> 99**	**95 (*R*)**
5	Et	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	79	84 (*R*)
6	*i*Pr	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	87	87 (*R*)
7	Et	**(*S*)-L_{U3}18**	CPh_3	Cy	98	68 (*R*)
8	*i*Pr	**(*S*)-L_{U3}18**	CPh_3	Cy	> 99	71 (*R*)

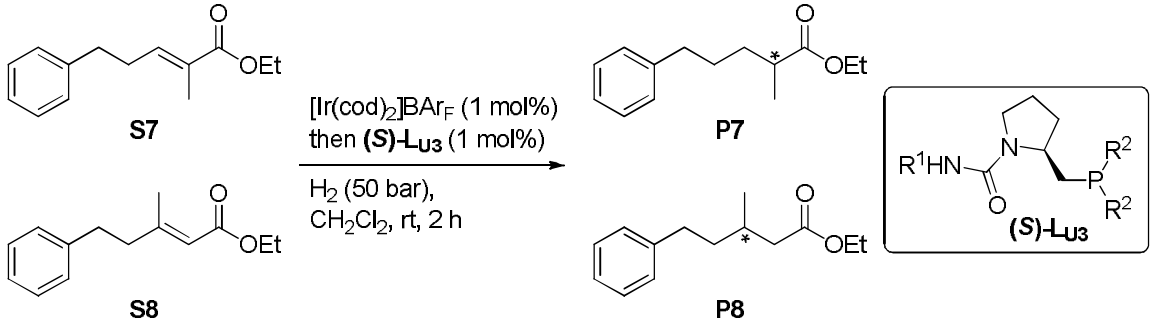
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Interestingly, the trisubstituted ureaphosphine **(*S*)-L_{U3}18**, which afforded the highest enantiomeric excess in the reduction of the *β*-methyl-substituted *α,β*-unsaturated ester **S4** (see Table 21) afforded, compared with the other ligands, the lowest selectivities in this case (entries 7 and 8). The isopropyl ester **S6b** was always hydrogenated with higher enantiomeric excesses to **P6b** than **S6a** to the corresponding product **P6a** probably as a consequence of the increased steric bulk of the ester functionality. The asymmetric reduction of both substrates afforded the respective (*R*)-configured products in excesses. Noteworthy is the observation that, the R^1-adamantyl-substituted ligand **(*S*)-L_{U3}13**

furnished the highest enantiomeric excess in the reduction of **S6a** (92% *ee*, entry 2) and not one of the R^1-trityl-substituted derivatives (90% *ee*, entry 1). Substrate **S6b** was reduced with 95% *ee* by using the trityl-substituted ligand **(*S*)-L_{U3}15** (entry 4).

α,*β*-Unsaturated esters **S7** and **S8**, with an additional ethylene bridge in the *β*-position were both hydrogenated with complete conversions within 2 hours with all tested trisubstituted ureaphosphines (Table 25).

Table 25. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2-methyl-5-phenylpent-2-enoate (**S7**) and (*E*)-ethyl 3-methyl-5-phenylpent-2-enoate (**S8**).[a]



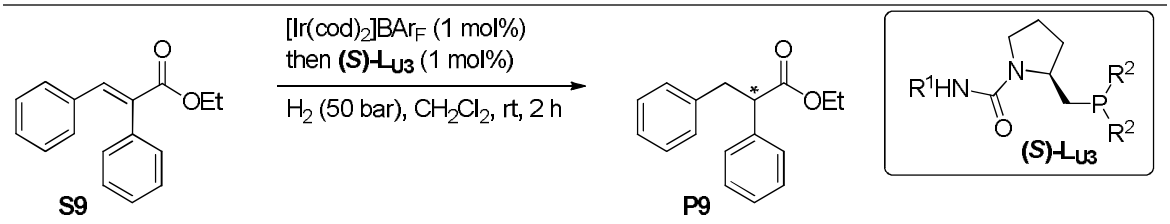
Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**S7**	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	87 (−)
2	**S7**	**(*S*)-L_{U3}15**	CPh_3	Ph	> 99	89 (−)
3	**S7**	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	> 99	86 (−)
4	**S7**	**(*S*)-L_{U3}18**	CPh_3	Cy	> 99	78 (−)
5	**S8**	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	70 (*S*)
6	**S8**	**(*S*)-L_{U3}15**	CPh_3	Ph	> 99	77 (*S*)
7	**S8**	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	> 99	68 (*S*)
8	**S8**	**(*S*)-L_{U3}18**	CPh_3	Cy	> 99	68 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

The *α*-methyl-substituted substrate **S7** was reduced with slightly better selectivities (78% to 89% *ee*) than the *β*-methyl-substituted substrate **S8** (68% to 77% *ee*). In both cases, the highest enantioselectivities were induced by the R^1-trityl-substituted diphenylphosphine ligand **(*S*)-L_{U3}15**, with 89% *ee* for the reduction of **S7** and 77% *ee* for **P8** (entries 2 and 6). Compared with the results obtained with amidophosphines in section 2.4.2 the selectivities were better for both substrates, when trisubstituted ureaphosphines were used (Table 12 *versus* 25).

Comparing the results obtained in the asymmetric hydrogenation of the α-phenyl-substituted ester **S9** utilizing amidophosphine/iridium catalysts and trisubstituted ureaphosphines the later yielded lower selectivities (Table 13 *versus* 26).

Table 26. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2,3-diphenylacrylate (**S9**).[a]



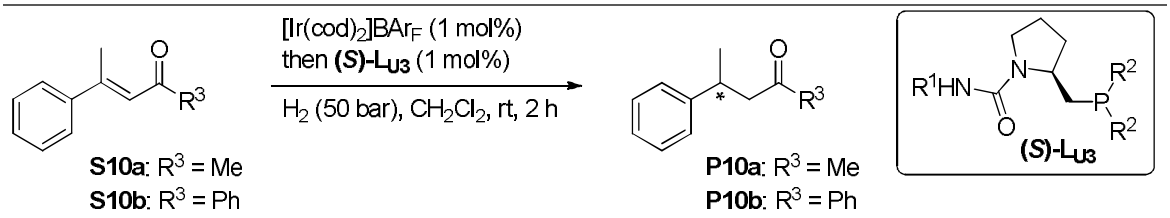
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	> 99	55 (+)
2	**(*S*)-L_{U3}15**	CPh_3	Ph	66	79 (+)
3	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	6	11 (+)
4	**(*S*)-L_{U3}18**	CPh_3	Cy	83	10 (−)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Only ligand **(*S*)-L_{U3}15** furnished **(+)-P9**, with an enantiomeric excess of 79% (entry 2). **(*S*)-L_{U3}13** and **(*S*)-L_{U3}18**, both being substituted with R^2-alkyl groups, showed higher conversions albeit with only moderate enantiomeric excesses (entries 1 and 4). In contrast, the iridium complex chelated by di-*tert*-butylphosphine **(*S*)-L_{U3}17** converted only 6% of **S9** into the respective product (entry 3). Interestingly, the use of the two trityl derivatives, di-*tert*-butylphosphine **(*S*)-L_{U3}17** and dicyclohexylphosphine **(*S*)-L_{U3}18** gave excesses of the opposite product enantiomers, although the absolute values were very low (11% *ee* (+) for **(*S*)-L_{U3}17** and 10% *ee* (−) for **(*S*)-L_{U3}18**, entries 3 and 4).

However, in the iridium-catalyzed asymmetric hydrogenation of α,β-unsaturated ketones trisubstituted ureaphosphines/iridium complexes furnished excellent enantioselectivities (Table 27). The most selective catalyst was found to be the **(*S*)-L_{U3}15**/iridium complex (entries 3 and 4). It performed the reduction of **S10a** with 93% *ee* and of the phenyl-substituted compound **S10b** with 95% *ee*.

Table 27. Iridium-catalyzed asymmetric hydrogenation of (*E*)-4-phenylpent-3-en-2-one (**S10a**) and (*E*)-1,3-diphenylbut-2-en-1-one (**S10b**).[a]

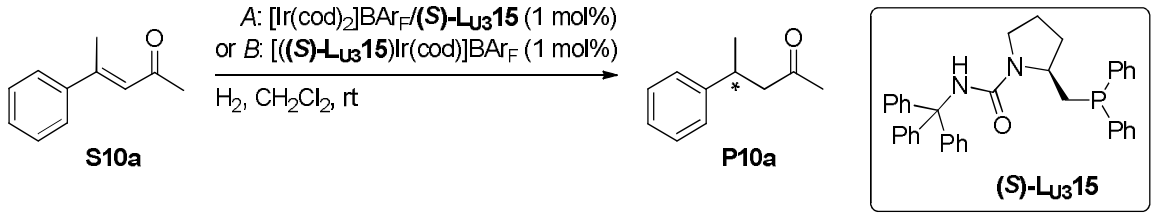


Entry	R^3	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**Me**	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	87[d]	86 (*R*)
2	**Ph**	**(*S*)-L_{U3}13**	1-Adm	*t*Bu	98	82 (*R*)
3	**Me**	**(*S*)-L_{U3}15**	CPh_3	Ph	98[d] [99][e]	93 (*R*) [91 (*R*)][e]
4	**Ph**	**(*S*)-L_{U3}15**	CPh_3	Ph	**> 99**	**95 (*R*)**
5	**Me**	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	86[f]	79 (*R*)[f]
6	**Ph**	**(*S*)-L_{U3}17**	CPh_3	*t*Bu	86	80 (*R*)
7	**Me**	**(*S*)-L_{U3}18**	CPh_3	Cy	95[d]	82 (*R*)
8	**Ph**	**(*S*)-L_{U3}18**	CPh_3	Cy	98	90 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] Formation of the saturated alcohol was observed (conversions > 99%); [e] Results obtained with the isolated precatalyst; [f] Average of 2 experiments.

As shown in Table 27, the conversions of **S10a** were complete (except for the use of **(*S*)-L_{U3}17**), but the reactions were accompanied by the reduction to the saturated alcohol in variable and uncontrolled amounts (entries 1, 3 and 7). To address this issue a screening of reaction conditions was carried out using the trisubstituted ureaphosphines **(*S*)-L_{U3}15** as chiral ligand (Table 28).

Table 28. Optimization of reaction conditions for the iridium-catalyzed asymmetric hydrogenation of (*E*)-4-phenylpent-3-en-2-one (**S10a**) with **(*S*)-L_{U3}15**.[a]



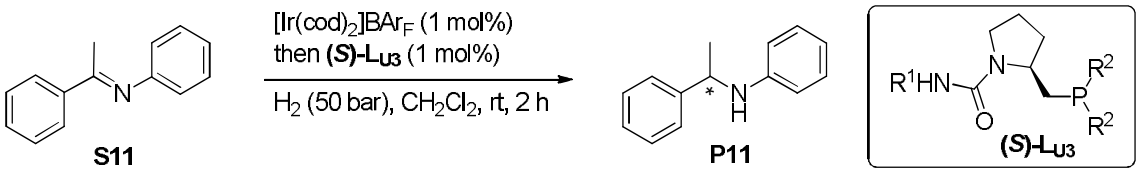
Entry	*p* [bar]	*t* [h]	Complex	Conv. [%][b]	Yield [%][b]	*ee* [%][c]
1	50	2	*A*	> 99	**98**	**93 (*R*)**
2	50	2	*B*	> 99	99	91 (*R*)
3	50	1	*B*	> 99	> 99	90 (*R*)
4	5	2	*A*	46	45	76 (*R*)
5	5	2	*B*	80	80	86 (*R*)

[a] Reaction scale: catalyst (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Conversions and yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Appling the isolated **(*S*)-L_{U3}15**/iridium complex as catalyst in the reduction of **S10a** did not give any overreduction after one hour reaction time (> 99% conversion and > 99% yield, entry 3), but the enantioselectivity decreased slightly compared to the value obtained, when the complex was formed *in situ* (entry 1). Lowering the hydrogen pressure resulted in reduced enantioselectivities and conversions, independent of the precatalyst's provenance (entries 4 and 5). Therefore, for this particular reaction, the conditions described in entry 1 are best suited; the amount of overreduction product is minimal and the enantioselectivity is excellent (2% of the respective saturated alcohol and 93% *ee* of **(*R*)-P10a**).

In the asymmetric reduction of C–N double bonds ureaphosphines showed similar unsatisfying results as their amidophosphines congeners. The results of the ligand screening in the hydrogenation of imine **S11** are shown in Table 29. In general good conversions of the starting material **S11** were measured, but the yields of **P11** were low, mostly hydrolysis products were obtained. Nevertheless, the usage of di-*ortho*-tolylphosphine **(*S*)-L_{U3}12** furnished **P11** with 59% *ee* of the (*R*)-configured product (entry 6).

Table 29. Iridium-catalyzed asymmetric hydrogenation of *N*-(1-phenylethylidene)-aniline (**S11**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U3}1**	*t*Bu	Ph	15 [90]	24 (*R*)
2	**(*S*)-L_{U3}2**	*t*Bu	*o*Tol	46 [97]	37 (*R*)
3	**(*S*)-L_{U3}6**	*i*Pr	Ph	8 [90]	7 (*R*)
4	**(*S*)-L_{U3}7**	Cy	Ph	5 [85]	19 (*R*)
5	**(*S*)-L_{U3}11**	1-Adm	Ph	24 [93]	2 (*S*)
6	**(*S*)-L_{U3}12**	1-Adm	*o*Tol	30 [95]	59 (*R*)
7	**(*S*)-L_{U3}15**	CPh_3	Ph	5 [62]	2 (*R*)
8	**(*S*)-L_{U3}19**	Ph	Ph	23 [90]	2 (*R*)
9	**(*S*)-L_{U3}21**	Mes	Ph	22 [95]	4 (*R*)
10	**(*S*)-L_{U3}25**	(2,4,6-*t*Bu_3)Ph	Ph	5 [48]	19 (*S*)
11	**(*S*)-L_{U3}26**	1-Naph	Ph	18 [90]	4 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part): conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

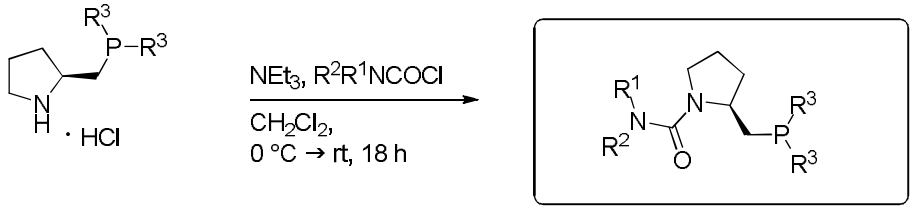
Trisubstituted dialkylphosphines with sterically hindered urea substituents were successfully used as ligands for the iridium-catalyzed asymmetric hydrogenation of several trisubstituted alkenes. In particular, excellent enantiomeric excesses were achieved in the asymmetric reduction of α,β-unsaturated esters and ketones.

2.5.2
Tetrasubstituted Ureaphosphines Ligands

In this section proline-based ligands with tetrasubstituted urea moieties will be described. These differ from trisubstituted ligands described in section 2.5.1 only in bearing an additional substituent at the second urea nitrogen atom.

2.5.2.1
Synthesis of Tetrasubstituted Ureaphosphines

The synthesis of tetrasubstituted proline-based ureaphosphines is described below. These compounds were prepared following similar procedures as in the synthesis of trisubstituted ureaphosphines (Scheme 21), but carbamoyl chlorides (R^2R^1NCOCl) instead of isocyanates were used for urea formation. These ligands were isolated in variable yields ranging from 39 to 93%, depending on the carbamoyl chlorides used.

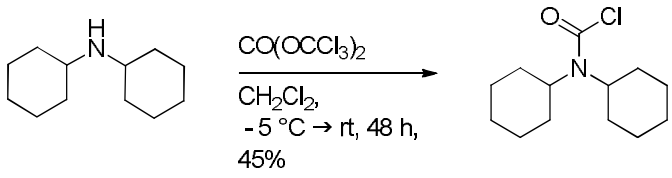


(*S*)-52·HCl: R^3 = Ph
(*S*)-57·HCl: R^3 = *o*Tol
(*S*)-58·HCl: R^3 = 2-Fur

(*S*)-L_{U4}1: R^1 = *i*Pr, R^2 = *i*Pr, R^3 = Ph (75%)
(*S*)-L_{U4}2: R^1 = *i*Pr, R^2 = *i*Pr, R^3 = *o*Tol (93%)
(*S*)-L_{U4}5: R^1 = Cy, R^2 = Cy, R^3 = Ph (83%)
(*S*)-L_{U4}6: R^1 = Cy, R^2 = Cy, R^3 = *o*Tol (81%)
(*S*)-L_{U4}9: R^1 = Ph, R^2 = Ph, R^3 = Ph (77%)
(*S*)-L_{U4}10: R^1 = Ph, R^2 = Ph, R^3 = *o*Tol (61%)
(*S*)-L_{U4}13: R^1R^2N = Morpholine R^3 = Ph (60%)
(*S*)-L_{U4}14: R^1 = Me, R^2 = Ph, R^3 = Ph (39%)

Scheme 25. Synthesis of tetrasubstituted ureaphosphines with aryl substituents at the phosphorus atom.

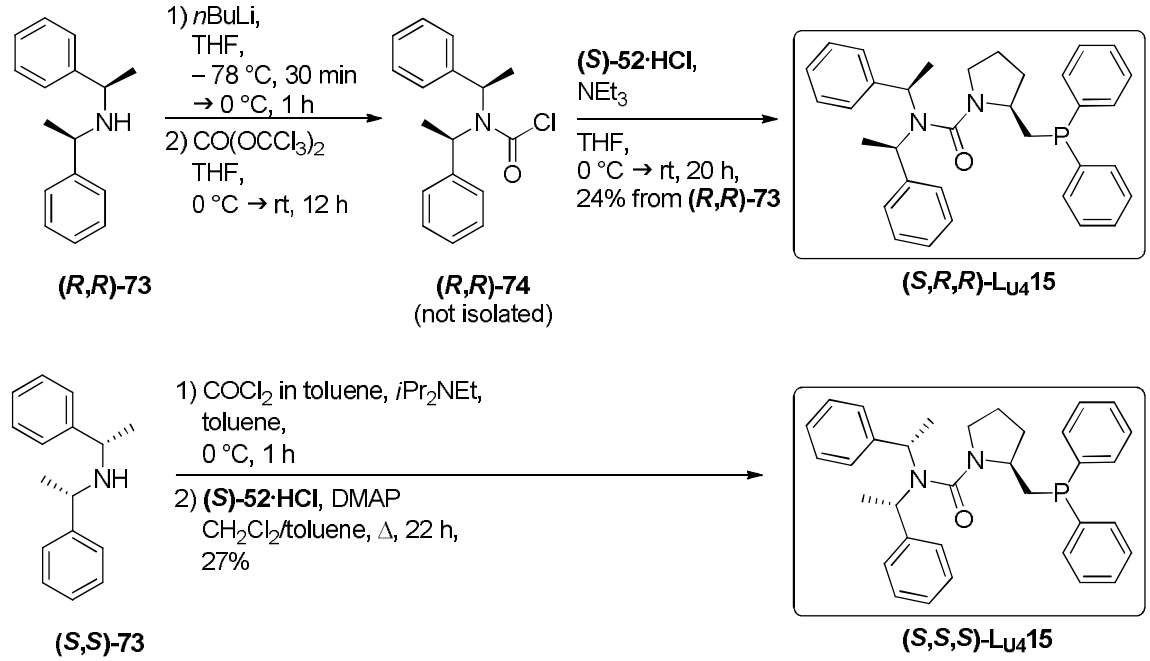
Many carbamoyl chlorides shown above are commercially available, but carbamoyl chloride **72** was synthesized from dicyclohexyl amine (**71**) and triphosgene. *N*,*N*-Dicyclohexylcarbamoyl chloride (**72**) was obtained in 45% yield in analogy to a literature-known procedure.[85]



71 **72**

Scheme 26. Synthesis of *N*,*N*-Dicyclohexylcarbamoyl chloride (**72**).[85]

For the preparation of the diastereoisomeric derivatives **(*S*,*R*,*R*)-L$_{U4}$15** and **(*S*,*S*,*S*)-L$_{U4}$15** a different procedure was developed (Scheme 27).



Scheme 27. Synthesis of diastereoisomeric ureaphosphines **(*S*,*R*,*R*)-L$_{U4}$15** and **(*S*,*S*,*S*)-L$_{U4}$15**.

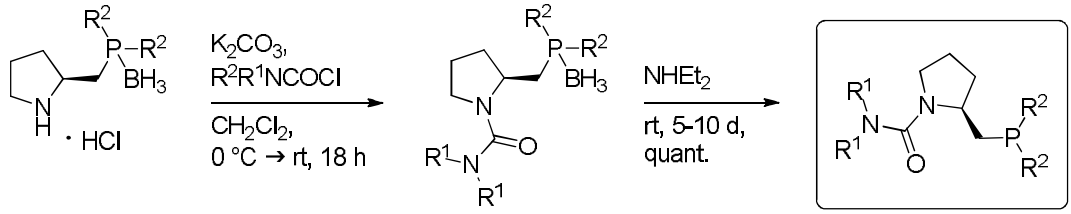
Bis[(*R*)-1-phenylethyl]amine (**(*R*,*R*)-73**) could not be converted into the respective carbamoyl chloride **(*R*,*R*)-74** in the same way than the secondary amine **71** into carbamoyl chloride **72** (Scheme 26). Therefore, the amine **(*R*,*R*)-73** was first

[85] *N*,*N*-Dicyclohexylcarbamoyl chloride (**72**) was prepared in analogy to the procedure reported for the synthesis of *N*,*N*-di-isopropylcarbamoyl chloride: D. Hoppe, R. Hanko, A. Brönneke, F. Lichtenberg, E. van Hülsen, *Chem. Ber.* **1985**, *118*, 2822-2851.

deprotonated by *n*-butyllithium to increase its nucleophilicity and then reacted with triphosgene. The resulting carbamoyl chloride **(*R*,*R*)-74** was not isolated and subsequently reacted with the pyrrolidinium chloride **(*S*)-52·HCl** under basic conditions. The desired ligand **(*S*,*R*,*R*)-L_{U4}15** was obtained in 24% yield *via* this sequence (Scheme 27). These reaction conditions were not optimized and a different procedure was used for the synthesis of the diastereomeric ligand **(*S*,*S*,*S*)-L_{U4}15**.

It was thought that better yields might be achieved by using directly phosgene instead of triphosgene, which generates only a small amount of phosgene *in situ*. For that reason amine **(*S*,*S*)-73** was treated with a solution of phosgene in toluene. To the crude reaction mixture pyrrolidinium salt **(*S*)-52·HCl** was added, and then the reaction was heated at reflux overnight. The yield of **(*S*,*S*,*S*)-L_{U4}15** (27%) was not significantly improved by the use of this method, though, and does not justify the application of the highly toxic phosgene as reagent in this case.

Tetrasubstituted ureaphosphines bearing alkyl substituents at the phosphorus atom were synthesized from the borane-protected dialkylphosphines **(*S*)-63·HCl** and **(*S*)-64·HCl** (Scheme 28).



(*S*)-63·HCl: R^2 = *t*Bu
(*S*)-64·HCl: R^2 = Cy

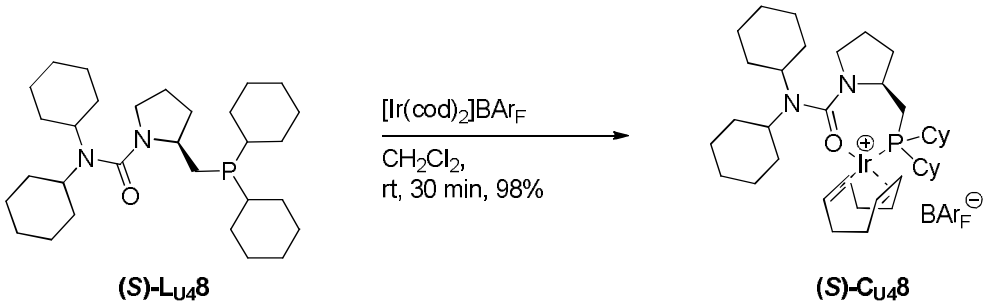
(*S*)-L_{U4}3·BH_3: R^1 = *i*Pr, R^2 = *t*Bu (47%)
(*S*)-L_{U4}4·BH_3: R^1 = *i*Pr, R^2 = Cy (86%)
(*S*)-L_{U4}7·BH_3: R^1 = Cy, R^2 = *t*Bu (69%)
(*S*)-L_{U4}8·BH_3: R^1 = Cy, R^2 = Cy (61%)
(*S*)-L_{U4}11·BH_3: R^1 = Ph, R^2 = *t*Bu (43%)
(*S*)-L_{U4}12·BH_3: R^1 = Ph, R^2 = Cy (92%)

(*S*)-L_{U4}

Scheme 28. Synthesis of tetrasubstituted ureaphosphines with alkyl substituents at the phosphorus atom.

Only urea functionalities with two identical substituents at the second nitrogen atom introduced (R^1 = isopropyl, cyclohexyl or phenyl) and the desired protected ligands were isolated in moderate to excellent yields (43% to 92%).

Again an exemplary complexation reaction using one of these tetrasubstituted ligands was carried out (Scheme 29). With the same procedure as in the syntheses of **(*R*)-C$_A$1** and **(*S*)-C$_{U3}$15** depicted in Schemes 10 and 24, the corresponding complex **(*S*)-C$_{U4}$8** was isolated as yellowish solid in 98% yield.



(*S*)-L$_{U4}$8 **(*S*)-C$_{U4}$8**

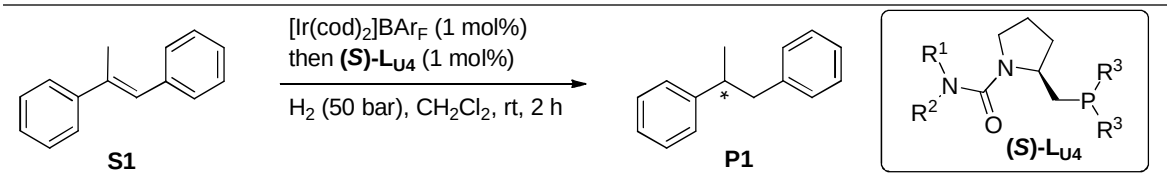
Scheme 29. Synthesis of ureaphosphine/iridium complex **(*S*)-C$_{U4}$8**.

2.5.2.2 Iridium-Catalyzed Asymmetric Hydrogenations with Tetrasubstituted Ureaphosphine Ligands

All tetrasubstituted ureaphosphine ligands were applied to the iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**, Table 30).

Overall, moderate to excellent enantioselectivities and conversions were achieved. Remarkably, identical results were obtained, when the structurally di-*tert*-butylphosphines **(*S*)-L$_{U4}$3** and **(*S*)-L$_{U4}$7** were used, both gave > 99% yield and enantiomeric excesses of 99% for the (*R*)-configured alkane **P1** (entries 3 and 7). The use of related di-*ortho*-tolylphosphines **(*S*)-L$_{U4}$2** and **(*S*)-L$_{U4}$6** furnished identical selectivities (79% (*R*)) and similar conversions, too (94% *versus* 92%, entries 2 and 6). Dialkylphosphines performed better than the structurally related diarylphosphines in all cases. Ureaphosphine **(*S*)-L$_{U4}$14** with different substituents at the second nitrogen atom provided only 94% yield and 42% *ee* the iridium-catalyzed asymmetric hydrogenation of **S1** (entry 14).

Table 30. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**).[a]



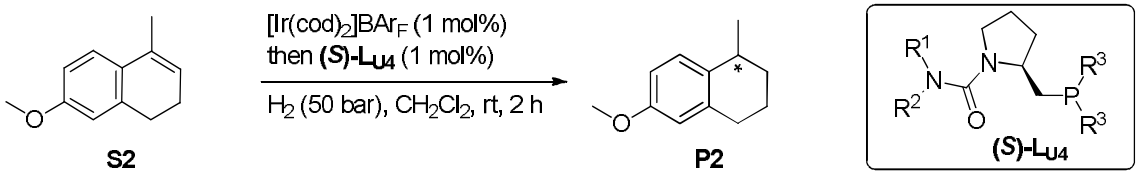
Entry	Ligand	R^1	R^2	R^3	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U4}1**	*i*Pr	*i*Pr	Ph	67	90 (*R*)
2	**(*S*)-L_{U4}2**	*i*Pr	*i*Pr	*o*Tol	94	79 (*R*)
3	**(*S*)-L_{U4}3**	*i*Pr	*i*Pr	*t*Bu	**> 99**	**99 (*R*)**
4	**(*S*)-L_{U4}4**	*i*Pr	*i*Pr	Cy	> 99	94 (*R*)
5	**(*S*)-L_{U4}5**	Cy	Cy	Ph	64	81 (*R*)
6	**(*S*)-L_{U4}6**	Cy	Cy	*o*Tol	92	79 (*R*)
7	**(*S*)-L_{U4}7**	Cy	Cy	*t*Bu	**> 99**	**99 (*R*)**
8	**(*S*)-L_{U4}8**	Cy	Cy	Cy	**> 99**	**97 (*R*)**
9	**(*S*)-L_{U4}9**	Ph	Ph	Ph	97	63 (*R*)
10	**(*S*)-L_{U4}10**	Ph	Ph	*o*Tol	99	43 (*R*)
11	**(*S*)-L_{U4}11**	Ph	Ph	*t*Bu	> 99	90 (*R*)
12	**(*S*)-L_{U4}12**	Ph	Ph	Cy	> 99	78 (*R*)
13	**(*S*)-L_{U4}13**	**R^1R^2N** = Morpholine		Ph	69	29 (*R*)
14	**(*S*)-L_{U4}14**	Ph	Me	Ph	94	42 (*R*)
15	**(*S,R,R*)-L_{U4}15**	(*R*)-CHMePh	(*R*)-CHMePh	Ph	70	64 (*R*)
16	**(*S,S,S*)-L_{U4}15**	(*S*)-CHMePh	(*S*)-CHMePh	Ph	32	37 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

The hydrogenations with the diastereoisomeric derivatives **(*S,R,R*)-L_{U4}15** and **(*S,S,S*)-L_{U4}15** as ligands showed a moderate match/mismatch effect. Although both catalysts yielded an excess of the (*R*)-configured product, very different catalyst activities were observed (70% yield for **(*S,R,R*)-L_{U4}15** and 32% yield for **(*S,S,S*)-L_{U4}15**, entries 15 and 16).

Investigating 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**) in the iridium-catalyzed hydrogenation involving tetrasubstituted ureaphosphines ligands resulted in low enantioinductions throughout (Table 31). 28% *ee* (*S*) were achieved with the di-*ortho*-tolylphosphine **(*S*)-L_{U4}2**, representing the best value (entry 2). In general the use of diarylphosphines resulted in moderate yields, whereas dialkyl-substituted phosphines led to excellent conversions (entries 3, 4, 7, 8, 11 and 12).

Table 31. Iridium-catalyzed asymmetric hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**).[a]

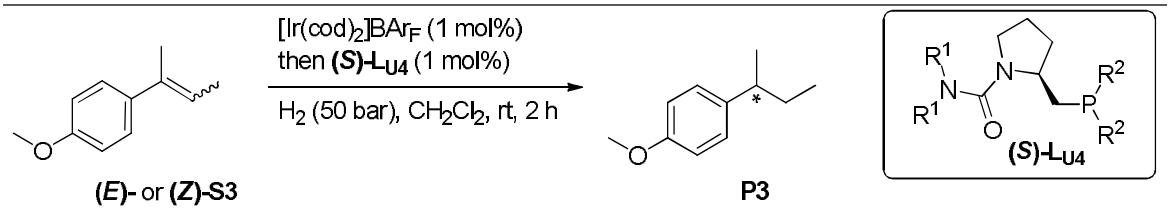


Entry	Ligand	R^1	R^2	R^3	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U4}1**	*i*Pr	*i*Pr	Ph	79 [85]	6 (*S*)
2	**(*S*)-L_{U4}2**	*i*Pr	*i*Pr	*o*Tol	58 [62]	28 (*S*)
3	**(*S*)-L_{U4}3**	*i*Pr	*i*Pr	*t*Bu	98	6 (*S*)
4	**(*S*)-L_{U4}4**	*i*Pr	*i*Pr	Cy	97 [> 99]	4(*R*)
5	**(*S*)-L_{U4}5**	Cy	Cy	Ph	36 [39]	8 (*S*)
6	**(*S*)-L_{U4}6**	Cy	Cy	*o*Tol	64 [70]	19 (*S*)
7	**(*S*)-L_{U4}7**	Cy	Cy	*t*Bu	97 [> 99]	5 (*R*)
8	**(*S*)-L_{U4}8**	Cy	Cy	Cy	97 [> 99]	13 (*R*)
9	**(*S*)-L_{U4}9**	Ph	Ph	Ph	98	*rac*
10	**(*S*)-L_{U4}10**	Ph	Ph	*o*Tol	74 [84]	3 (*S*)
11	**(*S*)-L_{U4}11**	Ph	Ph	*t*Bu	94 [> 99]	19 (*S*)
12	**(*S*)-L_{U4}12**	Ph	Ph	Cy	98 [> 99]	5 (*S*)
13	**(*S*)-L_{U4}14**	Ph	Me	Ph	85 [93]	*rac*

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

The results for the reduction of both isomers of **S3**, namely **(*E*)**- and **(*Z*)-S3**, are shown in Table 32. Slightly higher enantiomeric excesses were observed than in the reduction of **S2**, although these were still disappointingly low. Selectivities of more than 40% *ee* (*R*) were achieved by the ligands **(*S*)-L_{U4}1**, **(*S*)-L_{U4}2**, **(*S*)-L_{U4}5** and **(*S*)-L_{U4}10** in the asymmetric hydrogenation of the (*E*)-isomer (entries 1, 3, 5 and 10). The reduction of the (*Z*)-isomer generally resulted in the formation of an excess of the (*S*)-enantiomeric product, although the absolute values were even lower. The highest value with 25% *ee* was accomplished by the **(*S*)-L_{U4}6**/iridium catalyst (entry 8). None of the proline-based P,O ligand/iridium catalyst presented above gave satisfactory selectivities in the asymmetric hydrogenation of the trisubstituted unfunctionalized alkenes **S2**, **(*E*)-S3** and **(*Z*)-S3**. This fact indicates that all these P,O ligand/iridium catalysts can be applied efficiently only in the hydrogenation of sterically more encumbered substrates.

Table 32. Iridium-catalyzed asymmetric hydrogenation of ((*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)-** and **(*Z*)-S3**).[a]



(*E*)- or (*Z*)-S3 → **P3**

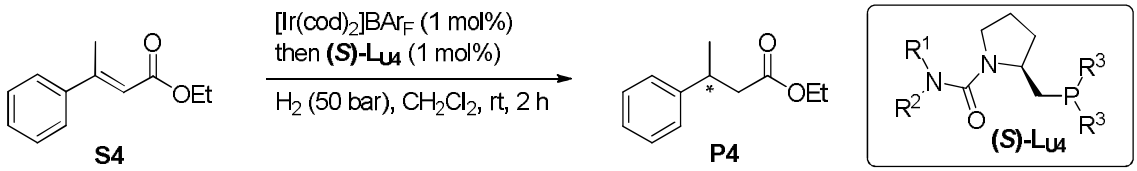
Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*E*)-S3**	**(*S*)-L_{U4}1**	*i*Pr	Ph	48	45 (*R*)
2	**(*Z*)-S3**	**(*S*)-L_{U4}1**	*i*Pr	Ph	90	19 (*S*)
3	**(*E*)-S3**	**(*S*)-L_{U4}2**	*i*Pr	*o*Tol	87	42 (*R*)
4	**(*Z*)-S3**	**(*S*)-L_{U4}2**	*i*Pr	*o*Tol	93	24 (*S*)
5	**(*E*)-S3**	**(*S*)-L_{U4}5**	Cy	Ph	79	43 (*R*)
6	**(*Z*)-S3**	**(*S*)-L_{U4}5**	Cy	Ph	84	23 (*S*)
7	**(*E*)-S3**	**(*S*)-L_{U4}6**	Cy	*o*Tol	55	37 (*R*)
8	**(*Z*)-S3**	**(*S*)-L_{U4}6**	Cy	*o*Tol	93	25 (*S*)
9	**(*Z*)-S3**	**(*S*)-L_{U4}9**	Ph	Ph	99	5 (*S*)
10	**(*E*)-S3**	**(*S*)-L_{U4}10**	Ph	*o*Tol	92	42 (*R*)
11	**(*Z*)-S3**	**(*S*)-L_{U4}10**	Ph	*o*Tol	> 99	4 (*S*)
12	**(*E*)-S3**	**(*S*,*R*,*R*)-L_{U4}15**	(*R*)-CHMePh	Ph	99	25 (*R*)
13	**(*E*)-S3**	**(*S*,*S*,*S*)-L_{U4}15**	(*S*)-CHMePh	Ph	99	21 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC or GC analysis using a chiral stationary phase (see experimental part).

In contrast, the suitability of these catalysts for the enantioselective hydrogenation of trisubstituted *α,β*-unsaturated esters was also observed, when tetrasubstituted ureaphosphines were used as ligands for the reduction of **S4** (Table 33). As it was the case in the asymmetric hydrogenation of **S1**, the di-*tert*-butylphosphines with isopropyl and cyclohexyl substituents at the nitrogen atom (**(*S*)-L_{U4}3** and **(*S*)-L_{U4}7**) achieved complete conversions and the highest enantiomeric excesses (entries 3 and 7). A similar enantiomeric excess was measured for the electronically and sterically closely related ligand **(*S*)-L_{U4}8** with four cyclohexyl substituents in total (entry 8). Interesting is the comparison of the results obtained with the two pairs of diphenylphosphine ligands **(*S*)-L_{U3}19** (R^1 = phenyl and R^2 = H)/**(*S*)-L_{U4}9** (R^1 = R^2 = phenyl) and **(*S*)-L_{U3}7** (R^1 = cyclohexyl and R^2 = H)/**(*S*)-L_{U4}5** (R^1 = R^2 = cyclohexyl) (Tables 21 and 33). While the presence of the second R^2-phenyl moiety in the urea functionality did not give any increase of selectivity, the introduction of a second R^2-cyclohexyl substituent did. The use of **(*S*)-L_{U4}5** afforded an enantiomeric excess of 69% for the (*R*)-configured product **P4**, while **(*S*)-L_{U3}7** gave only 40% *ee* (*R*) (see Table 33, entry 5 and see Table 21, entry 7). In

contrast, no improvement was observed going from ligand **(*S*)-L_{U4}9** to **(*S*)-L_{U3}19** (70% *ee* for **(*S*)-L_{U4}9**, see Table 33, entry 9 *versus* 74% *ee* for **(*S*)-L_{U3}19**, see Table 21, entry 9).

Table 33. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**S4**).[a]

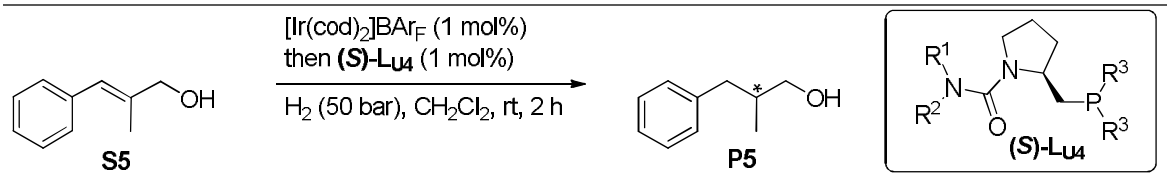


Entry	Ligand	R^1	R^2	R^3	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U4}1**	*i*Pr	*i*Pr	Ph	26	66 (*R*)
2	**(*S*)-L_{U4}2**	*i*Pr	*i*Pr	*o*Tol	> 99	44 (*R*)
3	**(*S*)-L_{U4}3**	*i*Pr	*i*Pr	*t*Bu	**> 99**	**97 (*R*)**
4	**(*S*)-L_{U4}4**	*i*Pr	*i*Pr	Cy	> 99	90 (*R*)
5	**(*S*)-L_{U4}5**	Cy	Cy	Ph	53	69 (*R*)
6	**(*S*)-L_{U4}6**	Cy	Cy	*o*Tol	99	50 (*R*)
7	**(*S*)-L_{U4}7**	Cy	Cy	*t*Bu	**> 99**	**99 (*R*)**
8	**(*S*)-L_{U4}8**	Cy	Cy	Cy	**> 99**	**97 (*R*)**
9	**(*S*)-L_{U4}9**	Ph	Ph	Ph	99	70 (*R*)
10	**(*S*)-L_{U4}10**	Ph	Ph	*o*Tol	98	45 (*R*)
11	**(*S*)-L_{U4}11**	Ph	Ph	*t*Bu	> 99	86 (*R*)
12	**(*S*)-L_{U4}12**	Ph	Ph	Cy	> 99	80 (*R*)
13	**(*S*)-L_{U4}13**	**R^1R^2N** = Morpholine		Ph	68	43 (*R*)
14	**(*S*)-L_{U4}14**	Ph	Me	Ph	99	29 (*R*)
15	**(*S*,*R*,*R*)-L_{U4}15**	(*R*)-CHMePh	(*R*)-CHMePh	Ph	69	59 (*R*)
16	**(*S*,*S*,*S*)-L_{U4}15**	(*S*)-CHMePh	(*S*)-CHMePh	Ph	27	51 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

The C−C double bond of the allylic alcohol **S5** was reduced with slightly better enantioselectivities, when tetrasubstituted ureaphosphines were used compared with the results of the P,O ligands presented in the previous sections (Table 34 *versus* Tables 10 and 23). While trisubstituted ureaphosphines **(*S*)-L_{U3}15** and **(*S*)-L_{U3}16**, both bearing diarylphosphine and trityl-substituted urea units allowed for 71% *ee* (*S*) and > 99% yield of **P5** as the best results (see Table 23, entries 14 and 15), tetrasubstituted ureaphosphines furnished up to 83% *ee* (Table 34, entry 6). In addition, the use of other diarylphosphines yielded selectivities of 80%, containing for example di-isopropyl-substituted ureas (entries 1 and 2). Rather surprising were the high enantiomeric excesses measured for di-*tert*-butylphosphines **(*S*)-L_{U4}3** and **(*S*)-L_{U4}7** (78% *ee* (*S*) and 81% *ee* (*S*), respectively, entries 3 and 7). Finally, the complete conversion of **S5** without formation of any side products for almost all catalysts has to be pointed out.

Table 34. Iridium-catalyzed asymmetric hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**S5**).[a]

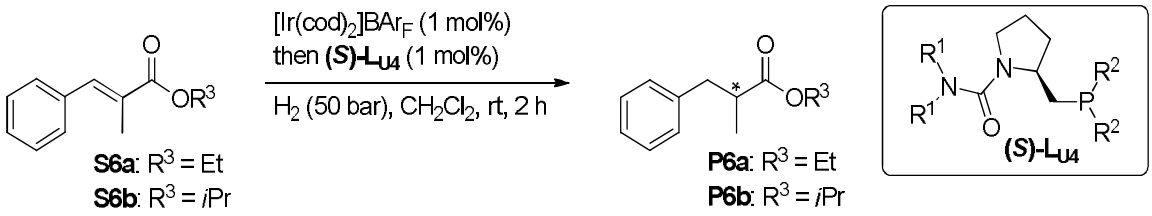


Entry	Ligand	R^1	R^2	R^3	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U4}1**	*i*Pr	*i*Pr	Ph	> 99	80 (*S*)
2	**(*S*)-L_{U4}2**	*i*Pr	*i*Pr	*o*Tol	> 99	80 (*S*)
3	**(*S*)-L_{U4}3**	*i*Pr	*i*Pr	*t*Bu	> 99	78 (*S*)
4	**(*S*)-L_{U4}4**	*i*Pr	*i*Pr	Cy	> 99	51 (*S*)
5	**(*S*)-L_{U4}5**	Cy	Cy	Ph	> 99	74 (*S*)
6	**(*S*)-L_{U4}6**	Cy	Cy	*o*Tol	**> 99**	**83 (*S*)**
7	**(*S*)-L_{U4}7**	Cy	Cy	*t*Bu	> 99	81 (*S*)
8	**(*S*)-L_{U4}8**	Cy	Cy	Cy	> 99	49 (*S*)
9	**(*S*)-L_{U4}9**	Ph	Ph	Ph	> 99	18 (*S*)
10	**(*S*)-L_{U4}10**	Ph	Ph	*o*Tol	> 99	29 (*S*)
11	**(*S*)-L_{U4}11**	Ph	Ph	*t*Bu	> 99	15 (*S*)
12	**(*S*)-L_{U4}12**	Ph	Ph	Cy	> 99	8 (*S*)
13	**(*S*)-L_{U4}13**	**R^1R^2N** = Morpholine		Ph	99	34 (*S*)
14	**(*S*)-L_{U4}14**	Ph	Me	Ph	> 99	33 (*S*)
15	**(*S*,*R*,*R*)-L_{U4}15**	(*R*)-CHMePh	(*R*)-CHMePh	Ph	96	55 (*S*)
16	**(*S*,*S*,*S*)-L_{U4}15**	(*S*)-CHMePh	(*S*)-CHMePh	Ph	> 99	46 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Because of the fact that tetrasubstituted ureaphosphines/iridium catalysts furnish enantiomeric excesses up to 99% in the asymmetric hydrogenation of the C−C double bond of *α*,*β*-unsaturated esters (see Table 33), other *α*,*β*-unsaturated esters were investigated as substrates. The results for the reduction of (*E*)-ethyl 2-methyl-3-phenylacrylate (**S6a**) and (*E*)-isopropyl 2-methyl-3-phenylacrylate (**S6b**) are summarized in Table 35. Good to excellent selectivities were obtained in the iridium-catalyzed hydrogenation of these *α*-methyl-substituted esters using the new P,O ligands. Conversions were complete for all the tested tetrasubstituted ureaphosphines and the ethyl ester **S6a** was hydrogenated with up to 91% *ee* (entry 3). The same catalyst which achieved this result gave the highest enantiomeric excess of 90% in the hydrogenation of the isopropyl ester **S6b**, too. The trisubstituted ureaphosphine **(*S*)-L_{U3}15** with a trityl moiety performed even better, though, and 95% *ee* was obtained in the reduction of **S6b** for this ligand (see Table 24, entry 4).

Table 35. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2-methyl-3-phenlacrylate (**S6a**) and (*E*)-isopropyl 2-methyl-3-phenylacrylate (**S6b**).[a]

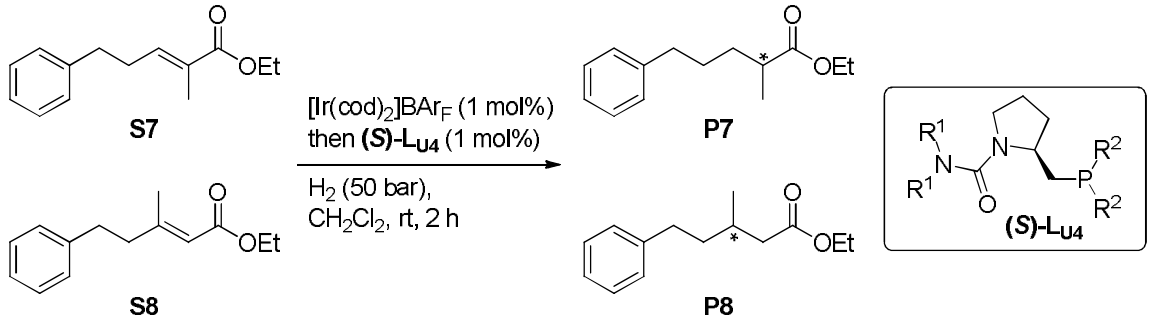


Entry	R^3	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	Et	**(*S*)-L_{U4}3**	*i*Pr	*t*Bu	> 99	81 (*R*)
2	*i*Pr	**(*S*)-L_{U4}3**	*i*Pr	*t*Bu	> 99	88 (*R*)
3	Et	**(*S*)-L_{U4}7**	Cy	*t*Bu	**> 99**	**91 (*R*)**
4	*i*Pr	**(*S*)-L_{U4}7**	Cy	*t*Bu	**> 99**	**90 (*R*)**
5	Et	**(*S*)-L_{U4}8**	Cy	Cy	> 99	83 (*R*)
6	*i*Pr	**(*S*)-L_{U4}8**	Cy	Cy	> 99	87 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Table 36 summarizes the results obtained from the iridium-catalyzed asymmetric hydrogenation of substrates **S7** an **S8**.

Table 36. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2-methyl-5-phenylpent-2-enoate (**S7**) and (*E*)-ethyl 3-methyl-5-phenylpent-2-enoate (**S8**).[a]



Entry	Substrate	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**S7**	**(*S*)-L_{U4}3**	*i*Pr	*t*Bu	> 99	73 (−)
2	**S7**	**(*S*)-L_{U4}7**	Cy	*t*Bu	**> 99**	**91 (−)**
3	**S7**	**(*S*)-L_{U4}8**	Cy	Cy	> 99	86 (−)
4	**S8**	**(*S*)-L_{U4}7**	Cy	*t*Bu	> 99	76 (*S*)
5	**S8**	**(*S*)-L_{U4}8**	Cy	Cy	> 99	66 (*S*)

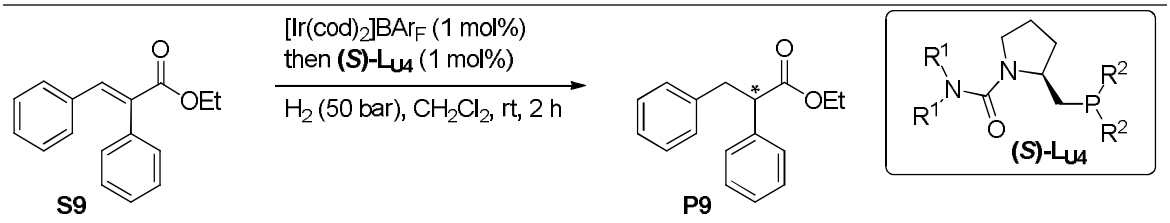
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

The α-methyl-substituted ester **S7** and the β-methyl-substituted ester **S8**, bearing an alkyl-chain as β-substituent, were as well reduced with excellent conversions with the help of

tetrasubstituted ureaphosphines as P,O ligands for iridium (Table 36). The highest enantiomeric excess for the iridium-catalyzed reduction of **S7** was obtained with **(*S*)-L$_{U4}$7** (entry 2). This di-*tert*-butylphosphine/iridium catalyst gave 91% *ee* of **(−)-P7**. In the reduction of **S8** up to 76% *ee* was achieved. This result compares favorably with the best selectivities, which were obtained with trisubstituted ureaphosphines (see Table 25, entry 6).

In the asymmetric reduction the bulky *β*-phenyl-substituted *α*,*β*-unsaturated ester **S9** dialkylphosphines gave only good to moderate enantioselectivities (34% to 75% *ee*, Table 37). The conversions of **S9** were never complete and, curiously the **(*S*)-L$_{U4}$3**/iridium catalyst yielded only 30% of **P9**. This result is remarkable, since in the previous screenings the closely related **(*S*)-L$_{U4}$3**/ and **(*S*)-L$_{U4}$7**/iridium catalysts showed similar activities and selectivities in most cases.

Table 37. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 2,3-diphenylacrylate (**S9**).[a]



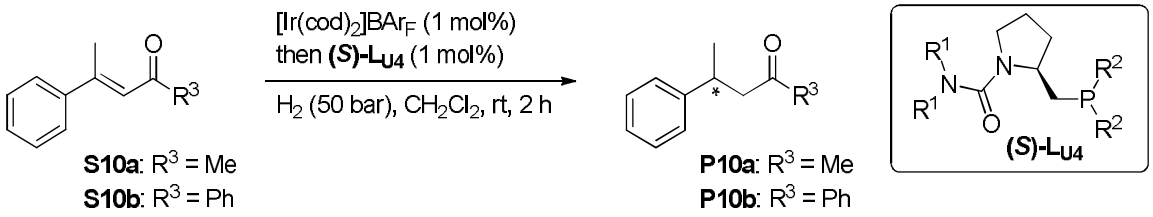
Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_{U4}$3**	*i*Pr	*t*Bu	30	34 (+)
2	**(*S*)-L$_{U4}$7**	Cy	*t*Bu	88	75 (+)
3	**(*S*)-L$_{U4}$8**	Cy	Cy	94	41 (+)

[a] Reaction scale: [Ir(cod)$_2$]BAr$_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

Finally, enones **S10a** and **S10b** were also investigated as substrates for the asymmetric hydrogenation using tetrasubstituted ureaphosphine/iridium catalysts (Table 38). Conversions of the *α*,*β*-unsaturated ester **S10a** were complete for all the tested ligands, but once again overreduction was observed (entries 1, 2 and 4). Especially the reduction utilizing ligand **(*S*)-L$_{U4}$7** was prone to this unwanted side reaction. The amount of saturated alcohol obtained varied between individual repetitions of this reaction. Therefore, the average result is presented (entry 2). **S10a** was reduced with an enantiomeric excess of up to 94% with **(*S*)-L$_{U4}$3** (entry 1). In the reduction of the

phenyl-substituted substrate **S10b** no overreduction was observed. **S10b** was transformed with 94% yield into **P10b** and 84% *ee* using **(*S*)-L$_{U4}$7** (entry 3).

Table 38. Iridium-catalyzed asymmetric hydrogenation of (*E*)-4-phenylpent-3-en-2-one (**S10a**) and (*E*)-1,3-diphenylbut-2-en-1-one (**S10b**).[a]

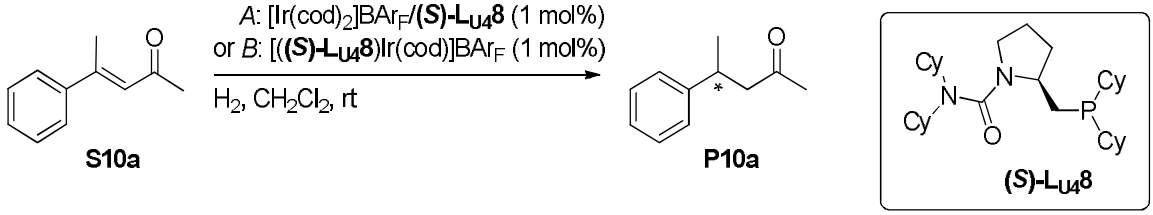


Entry	R^3	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**Me**	**(*S*)-L$_{U4}$3**	*i*Pr	*t*Bu	88[d]	94 (*R*)
2	**Me**	**(*S*)-L$_{U4}$7**	Cy	*t*Bu	68[d,f] [94][e]	92 (*R*)[f] [94 (*R*)][e]
3	**Ph**	**(*S*)-L$_{U4}$7**	Cy	*t*Bu	94	84 (*R*)
4	**Me**	**(*S*)-L$_{U4}$8**	Cy	Cy	88[d] [94][e]	87 (*R*) [87 (*R*)][e]
5	**Ph**	**(*S*)-L$_{U4}$8**	Cy	Cy	96	82 (*R*)

[a] Reaction scale: [Ir(cod)$_2$]BAr$_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] Formation of the saturated alcohol was observed (conversions > 99%); [e] Results obtained with the isolated precatalyst; [f] Average of 3 experiments.

Since the results above indicated that completely alkyl-substituted ureaphosphines promote the overreduction of **S10a**, different reaction conditions were tested (Table 39).

Table 39. Iridium-catalyzed asymmetric hydrogenation of (*E*)-4-phenylpent-3-en-2-one (**S10a**): reaction condition optimisation with **(*S*)-L$_{U4}$8**.[a]



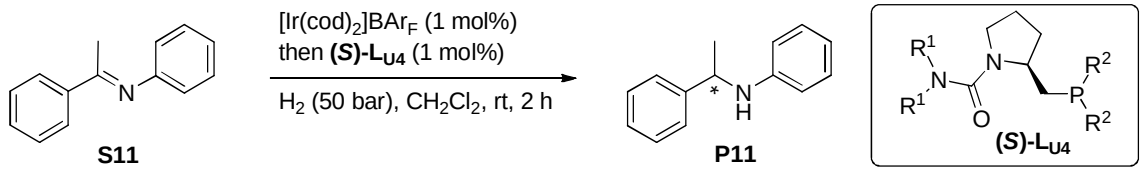
Entry	*p* [bar]	*t* [h]	Complex	Conv. [%][b]	Yield [%][b]	*ee* [%][c]
1	50	2	*A*	> 99	88	87 (*R*)
2	50	2	*B*	> 99	94	87 (*R*)
3	50	1	*B*	> 99	95	87 (*R*)
4	5	2	*A*	65	64	20 (*R*)
5	5	2	*B*	> 99	97	56 (*R*)

[a] Reaction scale: catalyst (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Conversions and yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

The exemplary ligand **(*S*)-L_{U4}8** bearing four cyclohexyl substituents was used for this purpose. By applying the previously isolated, preformed precatalyst **(*S*)-C_{U4}8** ([(**(*S*)-L_{U4}8**)Ir(cod)]BAr_F, Scheme 29) the yield of the desired product **P10a** was increased from 88% to 94%, without detectable decrease in the selectivity (entries 1 and 2). The yield was still 95%, when the reaction was run for half of the time and the enantiomeric excess did not change (entry 3). These results prove that longer reaction times are not responsible for increased amounts of overreduction. When lower hydrogen pressure was utilized the hydrogenation was also complete after 2 hours as long the isolated precatalyst was used, but conversion was lower, when the *in situ* generated precatalyst was used (entries 4 and 5).

In addition, the standard imine **S11** was again tested using several tetrasubstituted ureaphosphines (Table 40). Interestingly, the use of di-*ortho*-tolylphosphine **(*S*)-L_{U4}2** resulted in 98% yield (entry 2). This same ligand achieved the best enantiomeric excess of 38% for product **P11**, too. This value is certainly not impressive, but compared to the previous results in the reduction of **S11** (see Tables 16 and 29, as well as Scheme 16) for the other classes of P,O ligands, it is quite remarkable (entry 2). Although the measured selectivities in Table 40 are small, it can be seen that *ortho*-tolyl-substituted ligands favor the formation of the opposite product enantiomers compared with their relatives, with phenyl moieties.

Table 40. Iridium-catalyzed asymmetric hydrogenation of *N*-(1-phenylethylidene)-aniline (**S11**).[a]



Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{U4}1**	*i*Pr	Ph	36 [89]	11 (*S*)
2	**(*S*)-L_{U4}2**	*i*Pr	*o*Tol	98 [98]	39 (*R*)
3	**(*S*)-L_{U4}5**	Cy	Ph	40 [90]	15 (*S*)
4	**(*S*)-L_{U4}6**	Cy	*o*Tol	64 [92]	24 (*R*)
5	**(*S*)-L_{U4}9**	Ph	Ph	18 [91]	4 (*S*)
6	**(*S*)-L_{U4}10**	Ph	*o*Tol	34 [92]	6 (*S*)

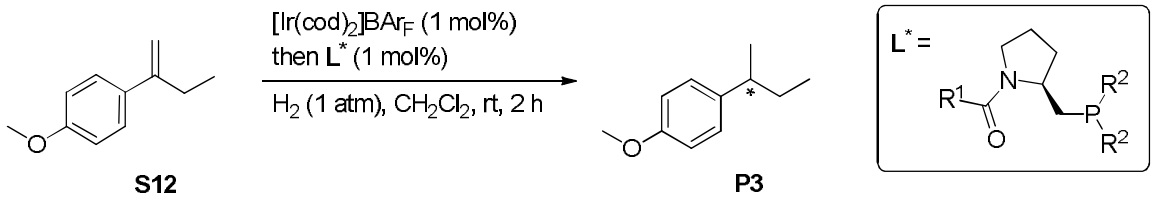
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are give in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

In summary, slightly lower enantiomeric excesses were achieved with tetrasubstituted ureaphosphines than with trisubstituted ureaphosphines. Nevertheless all developed ligands could be applied to the iridium-catalyzed asymmetric hydrogenation of various trisubstituted functionalized alkenes and enantiomeric excesses up to 99% could be achieved.

2.6 Iridium-Catalyzed Asymmetric Hydrogenation of Other Substrates, Using Proline-Based P,O Ligands

In the course of this project several other alkenes were as well tested as substrates for the iridium-catalyzed asymmetric hydrogenation with proline-based P,O ligands. These additional reactions involving the use of amidophosphines, trisubstituted and tetrasubstituted ureaphosphines as ligands are summarized below.

Table 41. Iridium-catalyzed asymmetric hydrogenation of 2-(4-methoxyphenyl)-1-butene (**S12**).[a]



S12 **P3**

Entry	Ligand	R^1	R^2	Yield [%][b]	*ee* [%][c]
1	(*R*)-L_A**1**	*t*Bu	Ph	> 99	31 (*R*)
2[d]	(*R*)-L_A**1**	*t*Bu	Ph	> 99	19 (*R*)
3[e]	(*R*)-L_A**1**	*t*Bu	Ph	> 99	19 (*R*)
4	(*S*)-L_A**2**	*t*Bu	*o*Tol	> 99	27 (*S*)
5[e]	(*S*)-L_A**7**	1-Adm	Ph	> 99	6 (*S*)
6	(*S*)-L_A**8**	1-Adm	*o*Tol	> 99	14 (*S*)
7[e]	(*S*)-L_A**9**	1-Adm	2-Fur	> 99	*rac*
8	(*S*)-L_A**13**	CPh_3	Ph	> 99	65 (*S*)
9	(*S*)-L_{U3}**1**	*t*BuNH	Ph	> 99	3 (*R*)
10	(*S*)-L_{U3}**6**	*i*PrNH	Ph	> 99	7 (*R*)
11	(*S*)-L_{U3}**11**	1-AdmNH	Ph	> 99	3 (*S*)
12	(*S*)-L_{U4}**5**	Cy_2N	Ph	> 99	23 (*S*)
13	(*S*)-L_{U4}**9**	Ph_2N	Ph	> 99	10 (*S*)

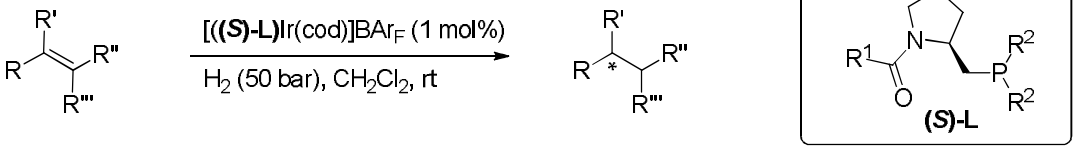
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [d] The reaction was carried out at 5 bar H_2; [e] The reactions were stirred for 1 hour under 5 bar hydrogen pressure.

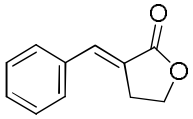
In Table 41 shows the results obtained in the asymmetric hydrogenation of the terminal double bond of 2-(4-methoxyphenyl)-1-butene (**S12**). This substrate is known to be hydrogenated with higher selectivities at lower hydrogen pressures. Therefore, the reductions were carried out either at atmospheric pressure or at 5 bar. **S12** was fully converted into **P3** independently of the iridium catalyst, which was used. The obtained enantiomeric excesses were rather low. The highest value was obtained with ligand **(*S*)-L$_A$13** and 65% *ee* (*R*) was achieved (entry 8). As expected, the enantioselectivity decreased with increasing hydrogen pressure (entries 1 to 3).

Furthermore, lactones and chromenes were tested as substrates for the iridium-catalyzed asymmetric hydrogenation using several proline-based P,O ligands (Scheme 30). Although these P,O ligand-based iridium catalysts showed higher activities in the reduction of several substrates than previously reported P,N ligand/iridium catalysts, no conversion of the chromenes **S14** and **S15** was observed with these derivatives. Nevertheless, in the hydrogenation of lactone **S13** bearing an exocyclic C−C double bond 61% conversion and 61% *ee* (*R*) were achieved with the trisubstituted ureaphosphine **(*S*)-L$_{U3}$15**. These results are not competitive with the selectivities that were obtained with other iridium catalysts.[34e,47] Tetrasubstituted alkenes, which were previously hydrogenated with excellent enantioselectivities using phosphinooxazoline/iridium complexes, are not suitable substrates for this novel type of catalysts.[32] No conversion of 1-methoxy-4-(3-methylbut-2-en-2-yl)-benzene (**S16**) was achieved with any of the tested catalysts.

Amidophosphine/ and trisubstituted ureaphosphine/iridium catalysts were applied to the asymmetric hydrogenation of boronic esters derivatives within the PFALTZ group by ADNAN GANIĆ, too. Complete conversions were observed in the reduction of **S17** (Scheme 30). Only low to moderate enantiomeric excesses were determined, though. The reduction of **S17** was accomplished with 55% *ee* using the amidophosphine ligand **(*S*)-L$_A$7**. In contrast, excellent enantioselectivities were achieved by the use of other iridium catalysts bearing P,N ligands.[86]

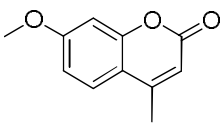
[86] A. Ganić, A. Pfaltz, *Chem. Eur. J.* **2012**, *18*, 6724-6728.





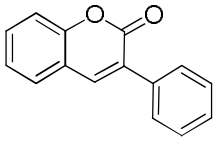
S13[a]

(*S*)-L_{U3}**15**: 61%, 61% *ee* (–)



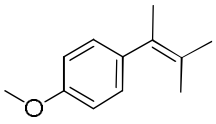
S14[a]

(*S*)-L_{U3}**15**: no conversion



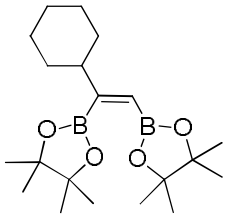
S15[a]

(*S*)-L_{U3}**15**: no conversion



S16[a]

(*S*)-L_A**1**: no conversion



S17[b]

(*S*)-L_A**7**: > 99% conv., 55% *ee* (+)
(*S*)-L_A**13**: > 99% conv., 23% *ee* (–)
(*S*)-L_{U3}**15**: > 99% conv., 43% *ee* (–)

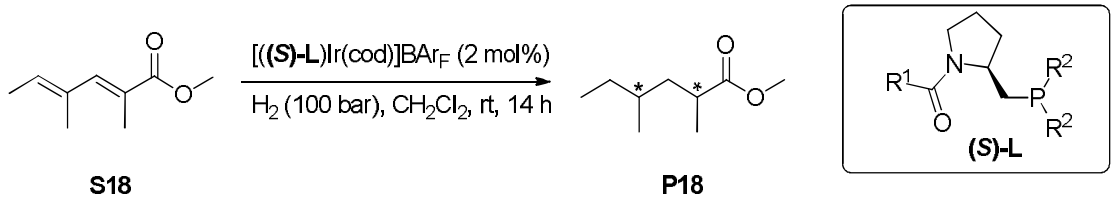
[a] Reaction conditions: 0.5 M in substrate, 2 h; [b] Reaction conditions: 0.5 M in substrate, > 12 h; [c] Yields were determined by GC analysis; [d] Enantioselectivities were determined by GC or HPLC analysis using a chiral stationary phase (see experimental part for **S13** and **S16**; and reference [86] for **S17**).

Scheme 30. Iridium-catalyzed asymmetric hydrogenations of various substrates with proline-based P,O ligands.[c-d]

Finally, proline-based/iridium complexes were screened among other catalysts in the asymmetric hydrogenation of dienes within the PFALTZ group by DR. ANDREAS SCHUMACHER (Table 42). The reduction of (2*E*,4*E*)-methyl 2,4-dimethylhexa-2,4-dienoate (**S18**) was achieved with excellent conversions using these catalysts. No reduction of only one C−C double bond was observed and both bonds were efficiently hydrogenated. Moderate diastereo- and enantioselectivities were achieved. The use of the tetrasubstituted ureaphosphine **(*S*)-L_{U4}5** induced a diastereoisomeric ratio of 60:40, in combination with 89% *ee* for the *syn*-product and 41% *ee* for the *anti*-product (entry 3). Other P,O ligand/iridium catalysts were also tested but did not provide efficient reductions of diene **S18** to **P18**. Better results were obtained with C,N ligand/iridium catalysts.[87]

[87] A. Schumacher, Dissertation, University of Basel, **2012**.

Table 42. Iridium-catalyzed asymmetric hydrogenation of (2*E*, 4*E*)-methyl-2,4-dimethylhexa-2,4-dienoate (**S18**).[87]



S18 **P18**

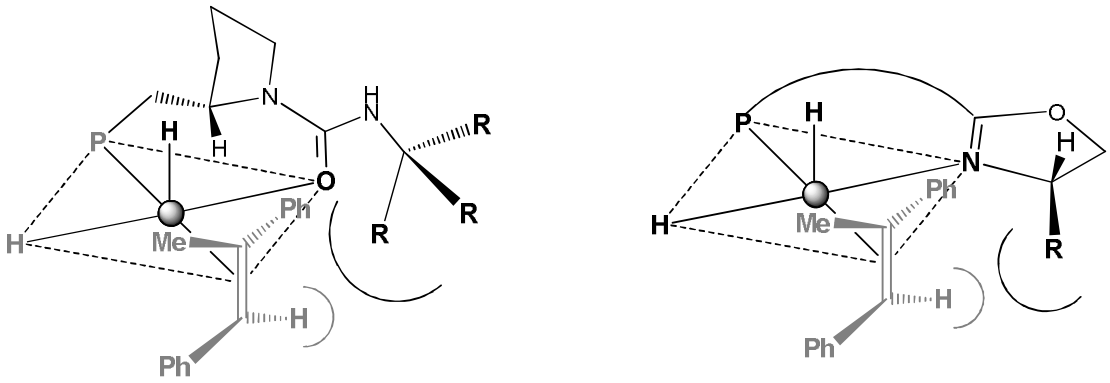
Entry	Ligand	R^1	R^2	Yield [%][a]	*ee* [%][b] *syn*/*anti*	*dr* [%][b] *syn*:*anti*
1	**(*S*)-L_A7**	1-Adm	Ph	> 99	28/20	43:57
2	**(*S*)-L_A13**	CPh_3	Ph	> 99	84/26	60:40
3	**(*S*)-L_{U4}5**	Cy_2N	Ph	> 99	89/41	60:40

[a] Yields were determined by GC analysis; [b] Diastereo- and enantioselectivities were determined by GC analysis using a chiral stationary phase.

2.7 Model Rationalizing the Enantioselectivity

A potential short explanation for the excellent enantioselectivities furnished by these catalysts for certain substrate classes will be given below. Although experimental structural information concerning the intermediates in the catalytic cycle is still scarce, computational studies of P,N ligand/iridium and C,N ligand/iridium catalysts suggest that the enantiodiscrimination takes place during the migratory insertion step.[21b,21e-l] In a PHOX/iridium complex as well as in a P,O ligand-based catalyst, the olefin is proposed to coordinate *trans* to the phosphorus atom as shown in Figure 11.

Generally, proline-based iridium catalysts bearing bulky amido or urea functionalities furnished higher enantioselectivities. In Figure 11 a model is presented, which compares a PHOX/iridium complex with an ureaphosphine/iridium catalyst, for which a crystal structure of the precatalyst was obtained (see Figure 10). Assuming an analogous coordination mode for P,O ligands as for PHOX ligands, a steric repulsion between the substrates and the bulky urea moiety of the ligand is expected as drawn in Figure 11. The large substituent of the urea group (or amide group in other P,O ligands) occupies a similar region in space like the substituent at the oxazoline ring of a PHOX ligand, namely the lower right quadrant. This is the reason, why the smallest substituent of the coordinated alkene substrate, which in most cases is a hydrogen atom, is oriented towards this crowded area in both complexes.



P,O catalyst **P,N catalyst**

Figure 11. Qualitative model rationalizing the enantioselectivity of P,O ligand/iridium and P,N ligand/iridium catalysts.

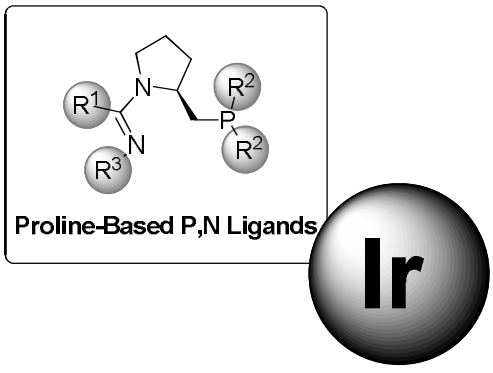
This qualitative model explains, why rather bulky amide or urea groups are necessary for an efficient discrimination of transition states and therefore high enantioselectivities, and rationalizes the sense of asymmetric induction. In accordance with the crystal structures obtained for the precatalyst **(*R*)-C_A1** and **(*S*)-L_{U3}15** the rather big pocket at the active metal center might be the reason, why only sterically quite demanding substrates can be oriented efficiently for selective reduction by coordinating to iridium.

2.8 Conclusion

In conclusion, a new ligand system for the iridium-catalyzed asymmetric hydrogenation of trisubstituted functionalized and unfunctionalized alkenes was developed. Starting from a known amidophosphine, discovered by high-throughput screening and based on a highly modular and readily available proline scaffold, a wide range of structurally related ligands were synthesized. The flexibility of the synthetic approach enabled the extensive structural tuning by variation of the coordinating phosphorus and oxygen donors. It was shown that proline-derived phosphines bearing bulky amide or urea groups at the pyrrolidine nitrogen form efficient catalysts for the asymmetric reduction of various alkenes. Most notably are the results achieved for α,β-unsaturated carboxylic esters and ketones, where these novel catalysts compare favorably with or even surpass the enantioselectivities reported for the best P,N and C,N ligands.

CHAPTER 3

PROLINE-BASED P,N LIGANDS FOR IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION



3.1
P,N Ligands for Iridium-Catalyzed Asymmetric Hydrogenation

All bidentate P,N ligands applied to iridium-catalyzed asymmetric hydrogenation were designed to bind to the metal through a heterocyclic sp^2-hybridized nitrogen donor in combination with a trisubstituted phosphorus atom. Unfortunately, no single P,N ligand/iridium catalyst performs efficiently in the asymmetric hydrogenation of all type of substrates. However, modifications of the P,N ligand scaffolds led to highly selective catalysts for specific targets.[88] This trend was already described in chapter 1, and explains the large number of P,N ligands that were designed. In this chapter, some P,N ligands will be described in more detail. Particular attention will be given to the size of the metallacycles that are formed upon coordination of the P,N ligands to iridium (see sections 3.1.1 and 3.1.2). This analysis, will permit to rationalize the choice of the proline-based scaffold that was investigated in this work for the development of novel P,N ligands forming a seven-membered metallacycle with iridium. Finally, the use of several proline-based P,N ligands for the iridium-catalyzed asymmetric hydrogenation of alkenes will be discussed (see section 3.2.2).

3.1.1
P,N Ligands Forming a Six-Membered Metallacycle with Iridium

In order to create a well-defined chiral environment in close proximity to the iridium center of a catalyst, several characteristics of the ligand structure were shown to be important: (1) the substituents of both coordinating atoms (nitrogen and phosphorus), which influence the electronic properties of the catalyst; (2) the steric hindrance generated by the ligand around the metal, which favors the approach of one of the enantiotopic faces of the substrate towards the active site of the catalyst; and (3) the size of the metallacycle formed by coordination of the ligand, which influences the bite angle and the general shape of the catalyst. Moreover, chirality was incorporated in all the regions of the metallacycle backbone. Many of the P,N ligands that were reported to afford high enantioselectivities in the iridium-catalyzed hydrogenation form a six-membered metallacycle when bound to the transition metal (Figure 12).

[88] a) D. H. Woodmansee, A. Pfaltz, *Top. Organomet. Chem.* **2011**, *34*, 71-76; b) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029-3069; see also references [18b, 21e, 21m, 31].

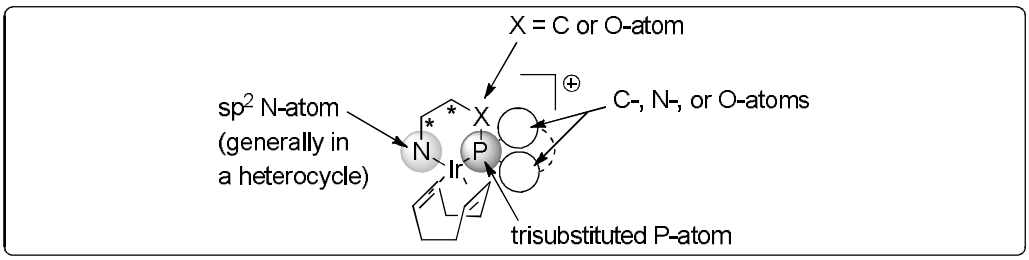


Figure 12. Figurative representation of efficient P,N ligand/iridium complexes used in iridium-catalyzed asymmetric hydrogenation and forming a six-membered metallacycle.

Several P,N ligands forming a six-membered metallacycle with iridium such as, phosphinooxazolines (**(*S*)-L$_{PHOX}$**[89] and **(*S*,*S*$_{Fc}$)-L$_{Fc\text{-}PHOX}$**[90]) or pyridylphosphine ligands **(*R*)-L9**,[91] were already shown in chapter 1 (see Figures 3 and 4, and Scheme 5). Figure 13 shows further P,N ligands, which were designed for enantioselective iridium-catalyzed hydrogenation.

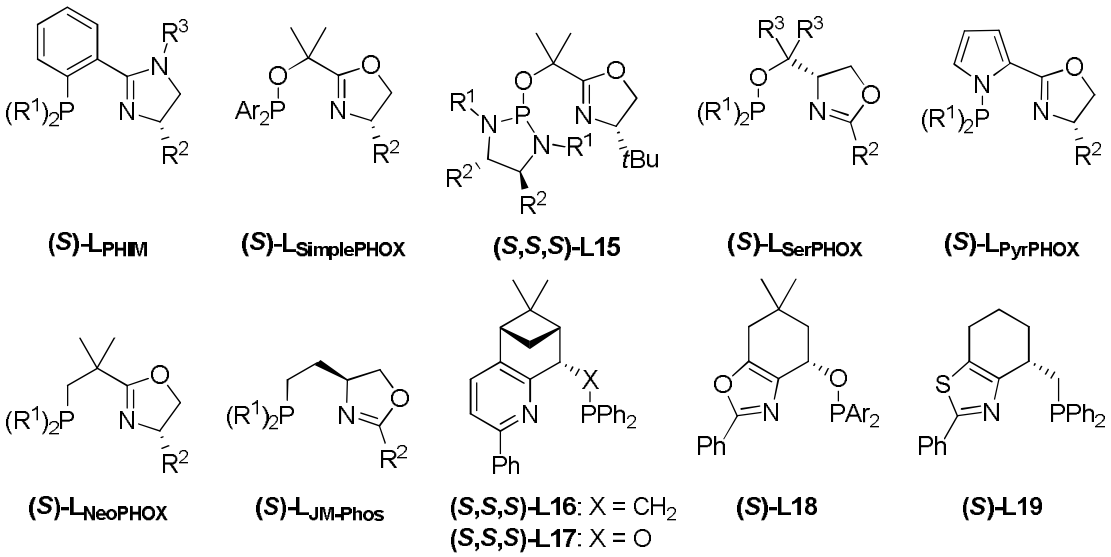


Figure 13. Further P,N ligands forming a six-membered metallacycle with iridium, and used in iridium-catalyzed asymmetric hydrogenation.

All of them coordinate to iridium through a nitrogen atom, which is part of a heterocycle and a phosphorus atom, but display different electronic properties and introduce unequal

[89] a) D. G. Blackmond, A. Lightfoot, A. Pfaltz, T. Rosner, P. Schnider, N. Zimmermann, *Chirality* **2000**, *12*, 442-449; b) S. P. Smidt, N. Zimmermann, M. Studer, A. Pfaltz, *Chem. Eur. J.* **2004**, *10*, 4685-4693; c) C. Valla, A. Pfaltz, *Chemistry Today* **2004**, 4-7; d) S. P. Smidt, F. Menges, A. Pfaltz, *Org. Lett.* **2004**, *6*, 2023-2026; e) A. Franzke, F. Voss, A. Pfaltz, *Tetrahedron* **2011**, *67*, 4358-4363; see also references [15b, 18a, 31, 33a, 34b-c, 35, 48a, 49, 50a-b].

[90] X. Li, Q. Li, X. Wu, Y. Gao, D. Xu, L. Kong, *Tetrahedron: Asymmetry* **2007**, *18*, 629-634; see also references [35, 51b].

[91] Q. B. Liu, C. B. Yu, Y.-G. Zhou, *Tetrahedron Lett.* **2006**, *47*, 4733-4736; see also references [42a, 45, 46, 48a, 49].

levels of steric hindrance around the transition metal. Another important feature of these ligands is the rigidity of the backbone, which influences the enantioinduction in the hydrogenation reaction.

All of these P,N ligands achieved high enantioselectivities in the iridium-catalyzed hydrogenation, but most of them were not employed so broadly as the structures shown in chapter 1. For example, PHIM ligands (**(*S*)-L_{PHIM}**) were mostly applied to unfunctionalized alkenes and in several cases better enantioselectivities were obtained than with analogous PHOX ligands.[92] Zwitterionic iridium complexes with PHOX and PHIM ligands have also been investigated.[93] SimplePHOX ligands induced good enantioselectivities in the reduction of a broad range of standard substrates (*e.g.* terminal alkenes, trisubstituted functionalized and unfunctionalized alkenes, imines and enamines).[94] Chiral bis(*N*-sulfonylamino)- and bis(*N*-arylamino)-phosphine-oxazolines **(*S*,*S*,*S*)-L15** were also designed as bidentate P,N ligands for iridium.[95] In particular bis(*N*-arylamino)phosphine oxazolines showed good enantioselectivities in the reduction of unfunctionalized olefins and α,β-unsaturated carboxylic esters.[95a] SerPHOX ligands are closely related to ThrePHOX ligands and allowed for excellent enantiomeric excesses in the asymmetric reduction of trisubstituted and terminal alkenes (Figures 3 and 13).[96] Similar results, were obtained when PyrPHOX ligands were employed in the reduction of standard trisubstituted olefins, but they found no other application so far.[97] NeoPHOX ligands were also used in the asymmetric reduction of trisubstituted alkenes and imines, but found more fruitful application in the synthesis of natural products (Scheme 5).[50a,60a,61] JM-Phos were employed as P,N ligand for iridium for the enantioselective hydrogenation of trisubstituted alkenes and for some arylakene substrates high enantioselectivities were obtained.[98] Pinene-derived ligands **(*S*,*S*,*S*)-L16** and **(*S*,*S*,*S*)-L17**[99] and phosphinite ligands **L18**[100] were applied to the iridium-catalyzed

[92] F. Menges, M. Neuburger, A. Pfaltz, *Org. Lett*. **2002**, *4*, 4713-4716; see also reference [50a].
[93] A. Franzke, A. Pfaltz, *Chem. Eur. J.* **2011**, *17*, 4131-4144.
[94] M. Harmata, X. Hong, *Org. Lett.* **2005**, *7*, 3581-3581; see also references [31, 33a, 48a, 50a, 89c, 89d].
[95] a) M. Schönleber, R. Hilgraf, A. Pfaltz, *Adv. Synth. Catal.* **2008**, *350*, 2033-2038; b) R. Hilgraf, A. Pfaltz, *Synlett* **1999**, *11*, 1814-1816.
[96] J. Blankenstein, A. Pfaltz, *Angew. Chem. Int. Ed.* **2001**, *40*, 4445-4447; see also references [33a, 89c]
[97] P. G. Cozzi, N. Zimmermann, R. Hilgraf, S. Schaffner, A. Pfaltz, *Adv. Synth. Catal.* **2001**, *343*, 450-454; see also reference [31].
[98] D.-R. Hou, J. Reibenspies, T. J. Colacot, K. Burgess, *Chem. Eur. J.* **2001**, *7*, 5391-5400.
[99] a) J. J. Verendel, P. G. Andersson, *Dalton Trans.* **2007**, *47*, 5603-5610; b) X. Meng, X. Li, D. Xu, *Tetrahedron: Asymmetry* **2009**, *20*, 1402-1406.
[100] K. Kallström, C. Hedberg, P. Brandt, A. Bayer, P. G. Andersson, *J. Am. Chem. Soc.* **2004**, *126*, 14308-14309; see also reference [39].

asymmetric hydrogenation of a wide range of trisubstituted functionalized and unfunctionalized alkenes, and furnished good to excellent enantioselectivities depending on the substrate. Thiazole derived P,N ligands **(*S*)-L19** [101] and **(*R*)-L7**[39,40] are closely related (Figures 3 and 13). However, whilst **(*R*)-L7** permitted the asymmetric reduction of fluorinated alkenes,[39] **(*S*)-L19** gave high enantioselectivities in the reduction of trifluoromethyl alkenes.[101]

3.1.2
P,N Ligands Forming a Non-Six-Membered Metallacycle with Iridium

Even though, Figures 3 and 13 show that most of the P,N ligands applied successfully to the iridium-catalyzed asymmetric hydrogenation bind to the metal center by forming a six-membered metallacycle with iridium, other P,N ligands forming either smaller or larger metallacycles have been investigated (Figure 14.).

An impressive example showing the influence of the metallacycle size was the development and application of phosphinooxazolines **(*S*)-L8**.[32] These P,N ligands allowed for the reduction of tetrasubstituted alkenes with excellent enantioselectivities, whereas for example PHOX ligands (**(*S*)-L$_{PHOX}$**) performed poorly. In contrast, these phophanyl oxazolines **(*S*)-L8**, forming a five-membered metallacycle with iridium delivered poor selectivities with trisubstituted alkenes.[32]

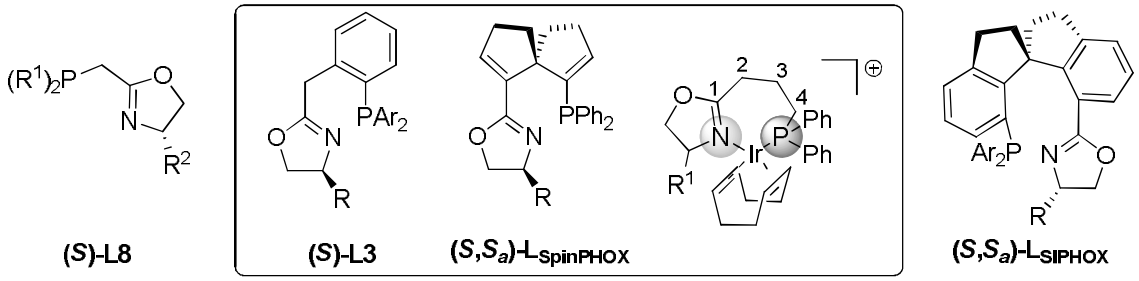


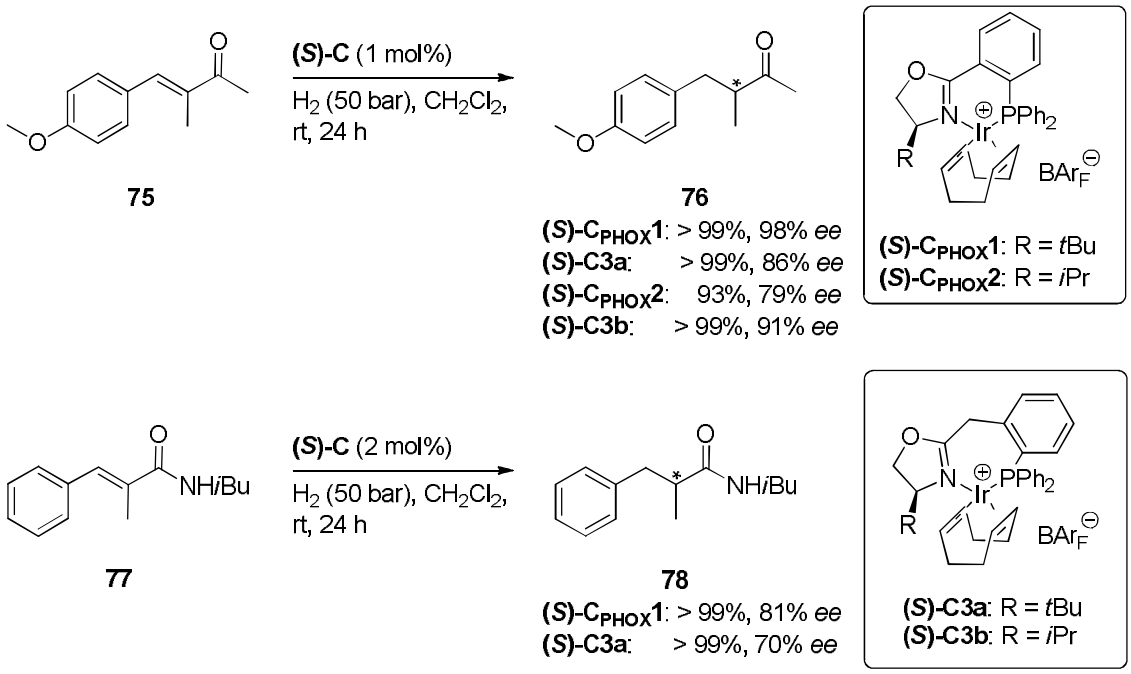
Figure 14. Efficient P,N ligands forming a non-six-membered metallacycle with iridium, and exploited for iridium-catalyzed asymmetric hydrogenation.

Chiral substituted P,N ligands **(*S*)-L3**, derived from the well-known PHOX ligands, permit the highly enantioselective iridium-catalyzed hydrogenation of trisubstituted

[101] M. Engman, P. Cheruku, P. Tolstoy, J. Berquist, S. F. Völker, P. G. Andersson, *Adv. Synth. Catal.* **2009**, *351*, 375-378; see also references [21i, 39].

functionalized and unfunctionalized alkenes, *α,β*-unsaturated ketones and amides, as well as imines.[34a,34c,35] This ligand system allows to analyze the influence of the ring-size of the iridacycle formed by chelation of the bidentate ligand. By comparing the results obtained in the iridium-catalyzed asymmetric hydrogenation of *α,β*-unsaturated ketones with **(*S*)-L$_{PHOX}$** and **(*S*)-L3** ligands, bearing the same R-substituent, no general trend in the influence of the chelating ring size was found (Scheme 31).

The *α,β*-unsaturated ketone **75**, was reduced with 98% *ee* by the **(*S*)-C$_{PHOX}$1** complex, whilst lower enantioselectivity was achieved employing the analogous complex **(*S*)-C3a**. In contrast, when the corresponding isopropyl-substituted ligands were used, **(*S*)-C3b** induced higher enantiomeric excess than **(*S*)-C$_{PHOX}$2** (91% *ee versus* 79 *ee*). In the iridium-catalyzed asymmetric hydrogenation of the *α,β*-unsaturated amide shown below, the PHOX/iridium complex **(*S*)-C$_{PHOX}$1** gave higher enantiomeric excess than **(*S*)-C3a** (81% *ee* for **(*S*)-C$_{PHOX}$1** and 70% *ee* for **(*S*)-C3a**).



Scheme 31. Comparison of the asymmetric hydrogenation results obtained using PHOX ligands and their phosphinooxazoline analogs **(*S*)-L3**.[34c,35]

The spirocycles SpinPHOX (**(*S*,*S$_a$*)-L$_{SpinPHOX}$**) and the spiroindanes SIPHOX (**(*S*,*S$_a$*)-L$_{SIPHOX}$**), both of them bearing a rather rigid backbone, from a seven- and a nine-membered metallacycle, respectively, when bound to iridium (see Figure 14). SpinPHOX

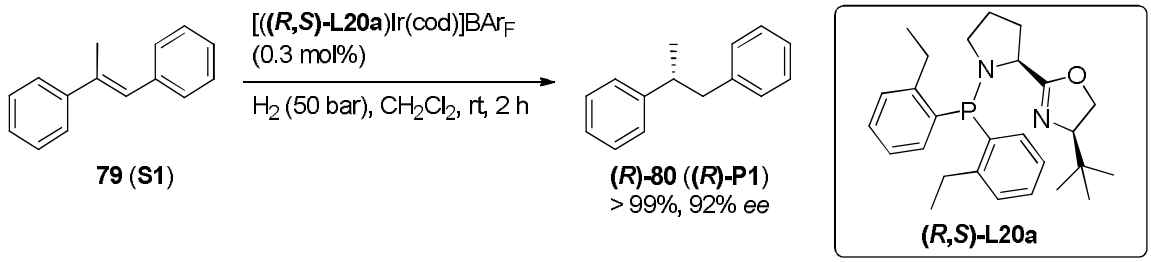
and SIPHOX ligands were employed for the iridium-catalyzed hydrogenation of *α,β*-unsaturated carboxylic esters and imines.[36a-b,50f,50h] SpinPHOX ligands induced up to 99% *ee* in the iridium-catalyzed hydrogenation of cinnamic and tiglic acid derivatives,[36a] and SIPHOX ligands for the reduction of acrylic acid derivatives with up to 96% *ee*.[36b] PHOX/iridium catalysts reduced *α,β*-unsaturated carboxylic acids with moderate enantioselectivity (81% *ee*).[102] Although this is the only report of the reduction of *α,β*-unsaturated acids by a PHOX/iridium complex to take for comparison, SIPHOX and SpinPHOX furnished excellent enantioselectivities in this reduction. Both SIPHOX/ and SpinPHOX/iridium catalysts were also used successfully in the asymmetric hydrogenation of imines, affording excellent enantioselectivities of up to 97%.[50f,50h] However, the asymmetric imine reduction can also be achieved with high enantioselectivities, using for example PHOX, SimplePHOX and NeoPHOX ligands (Figures 3 and 13).[50a]

In summary, it can be seen that the size of the iridacycle has an impact on the selectivity of the catalyst, but a rationale accounting for such an effect has not yet been proposed, and the level of enantioinduction of catalysts with different iridacycles can not be anticipated *a priori*.

3.2 Proline-Based P,N Ligands

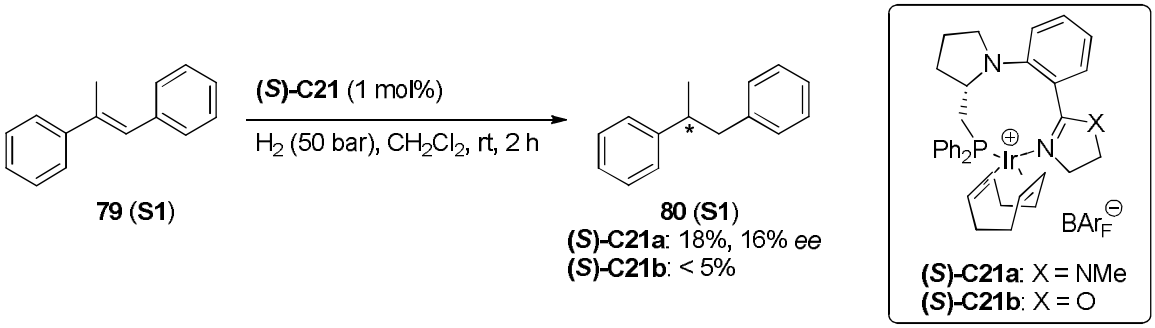
Many P,N ligands applied to the iridium-catalyzed asymmetric hydrogenation are derived from naturally occurring amino acids (*e.g.* PHOX, ThrePHOX, SerPHOX and SimplePHOX). Nevertheless, only a few P,N ligands derived from proline have been investigated for this asymmetric transformation. One example is the ligand **(*R*,*S*)-L20a** designed by GILBERTSON, forming a six-membered metallacycle with iridium (Scheme 32).[103] The iridium complexes of such proline-derived phosphinooxazoline ligands were applied to the asymmetric hydrogenation various functionalized and unfunctionalized aromatic alkenes and gave good enantioselectivities, although overall they were less effective than analogous PHOX ligands.[31,103]

[102] A. Scrivanti, S. Bovo, A. Ciappa, U. Matteoli, *Tetrahedron Lett.* **2006**, *47*, 9261-9265.
[103] G. Xu, S. R Gilbertson, *Tetrahedron Lett.* **2003**, *44*, 953-955.



Scheme 32. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) with GILBERTSON's ligand (**(*R*,*S*)-L20a**).[103]

Other proline-based P,N ligands have been investigated, by SARAH WEHLE, within the PFALTZ group.[104] These ligands were designed to form a nine-membered metallacycle with iridium. However, low selectivities and activities were observed in the iridium-catalyzed hydrogenation of alkenes (Scheme 33). Higher catalyst's activities were observed in the reduction of imines.[104]



Scheme 33. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) with proline-based ligands forming a nine-membered metallacycle.[104]

Figure 15 presents the proline-based P,N ligands investigated herein. Since proline-based P,O ligands were shown to be efficient in the enantioselective iridium-catalyzed hydrogenation of several substrate classes (chapter 2), it became obvious to develop related P,N versions of these. In fact, P,N ligands/iridium complexes represent the most reliable class of catalysts for asymmetric hydrogenation of C−C double bonds. Therefore, it was thought to combine both, the well-known chelation of bidentate P,N ligands and the advantage of the high modularity of proline-based scaffolds (Figure 15). It is interesting to note that, even if a series of P,N ligands has already been designed, only a

[104] S. Wehle, Masterarbeit, University of Basel **2011**.

few of them form a seven-membered metallacycle with iridium. Moreover, as shown above, a bigger ring-size of the metallacycle can be advantageous.

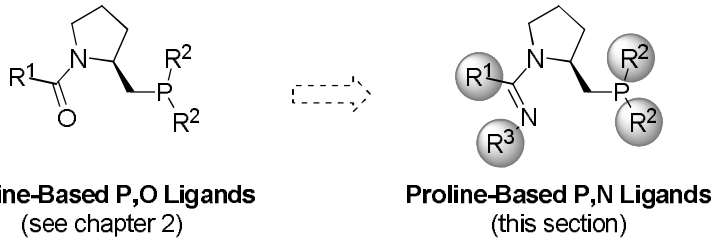
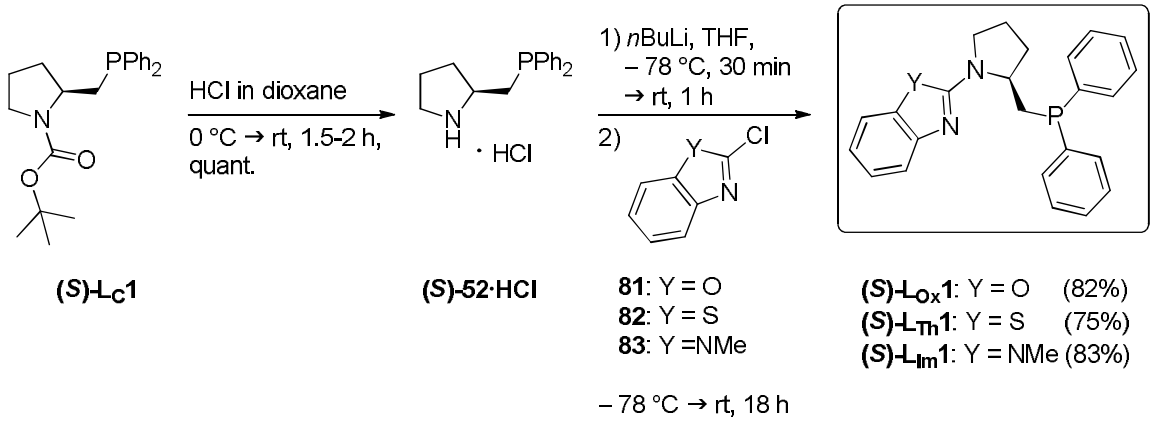


Figure 15. Ligand scaffolds presented herein.

First the synthesis of P,N proline-based ligands will be presented (see section 3.2.1) and then the results obtained in the iridium-catalyzed asymmetric hydrogenation of various alkenes will be discussed (see section 3.2.2). The ligands are named depending on their heterocyclic moiety in order to allow for a better comparison of the results achieved when these ligands were employed for the iridium-catalyzed asymmetric hydrogenation (see section 3.2.2).

3.2.1
Synthesis of Proline-Based P,N Ligands

The synthesis of proline-based P,N ligands was thought to be straightforward starting from the carbamatophosphines **(*S*)-L$_C$** presented in chapter 1. Carbamatophosphines, bearing aryl substituents at the phosphorus atom were obtained from L-proline (Schemes 11 and 12). Diphenylphosphines **(*S*)-L$_{Ox}$1**, **(*S*)-L$_{Th}$1** and **(*S*)-L$_{Im}$1** were obtained from compound **(*S*)-L$_C$1** after Boc-deprotection under acidic conditions (Scheme 34). The resulting pyrrolidinium salt **(*S*)-52·HCl** was deprotonated, by means of *n*-butyllithium and then reacted with the respective heterocyclic moiety: 2-chlorobenzoxazole, 2-chlorobenzothiazole and 2-chloro-1-methyl-1*H*-benzo[*d*] imidazole (**83**). The reactions led to the isolation of benzoxazole **(*S*)-L$_{Ox}$1**, benzothiazole **(*S*)-L$_{Th}$1** and benzimidazole **(*S*)-L$_{Im}$1** in good yields (75% to 83%, Scheme 34).

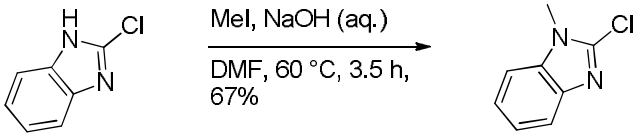


(*S*)-L$_C$1 **(*S*)-52·HCl** **81**: Y = O; **82**: Y = S; **83**: Y =NMe

(*S*)-L$_{Ox}$1: Y = O (82%)
(*S*)-L$_{Th}$1: Y = S (75%)
(*S*)-L$_{Im}$1: Y = NMe (83%)

Scheme 34. Synthesis of proline-based P,N ligands, varying the heterocyclic moiety.

2-Chlorobenzoxazole and 2-chlorobenzothiazole are commercially available, whilst the related 2-chloro-1-methyl-1*H*-benzo[*d*]imidazole (**83**) was prepared according to a known procedure.[105] 2-Chlorobenzimidazol (**85**) was methylated using iodomethane in the presence of sodium hydroxide, the product **83** was obtained in 67% yield (Scheme 35).

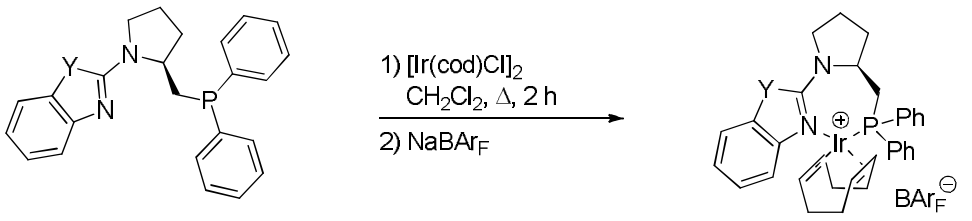


85 **83**

Scheme 35. Synthesis of 2-chloro-1-methyl-1*H*-benzo[*d*]imidazole (**83**).[105]

The respective iridium complexes **(*S*)-C$_{Ox}$1**, **(*S*)-C$_{Th}$1** and **(*S*)-C$_{Im}$1** were obtained in excellent yields (81% to 92%) according to the standard method reported for the complexation of P,N ligands to iridium (Scheme 36).[74] The ligands were transformed into their respective iridium complexes by reacting them with $[Ir(cod)Cl]_2$ (bis(1,5-cyclooctadiene)diiridium(I) dichloride). After the exchange of the chloride counterion, for BAr_F, the complexes were purified by column chromatography on silica gel. This purification method was possible for P,N ligand/iridium complexes, in contrast to proline-based P,O ligand/iridium complexes (see section 2.2.2).

[105] R. Lemura, T. Kawashima, T. Fukuda, K. Ito, G. Tsukamoto, *J. Med. Chem.* **1986**, *29*, 1178-1183.

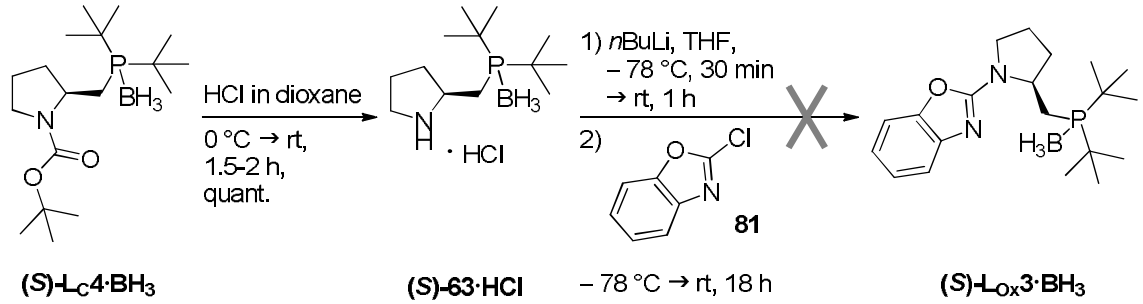


(*S*)-L$_{Ox}$1: Y = O
(*S*)-L$_{Th}$1: Y = S
(*S*)-L$_{Im}$1: Y = NMe

(*S*)-C$_{Ox}$1: Y = O (89%)
(*S*)-C$_{Th}$1: Y = S (81%)
(*S*)-C$_{Im}$1: Y = NMe (92%)

Scheme 36. Synthesis of diphenylphosphine P,N ligand/iridium complexes: **(*S*)-C$_{Ox}$1**, **(*S*)-C$_{Th}$1**, and **(*S*)-C$_{Im}$1**.

Since the synthesis of diphenyphosphine-substituted ligands (**(*S*)-L$_{Ox}$1**, **(*S*)-L$_{Th}$1**, and **(*S*)-L$_{Im}$1**) was straightforward, the synthesis of proline-based P,N ligands bearing different substituents at the phosphorus atom was attempted using the same procedure (Scheme 37). However, when the borane-protected aminophosphine **(*S*)-63·HCl** was tried to be substituted with 2-chlorobenzoxazole, the desired compound **(*S*)-L$_{OX}$3·BH$_3$** could not be obtained.



(*S*)-L$_C$4·BH$_3$ **(*S*)-63·HCl** **(*S*)-L$_{Ox}$3·BH$_3$**

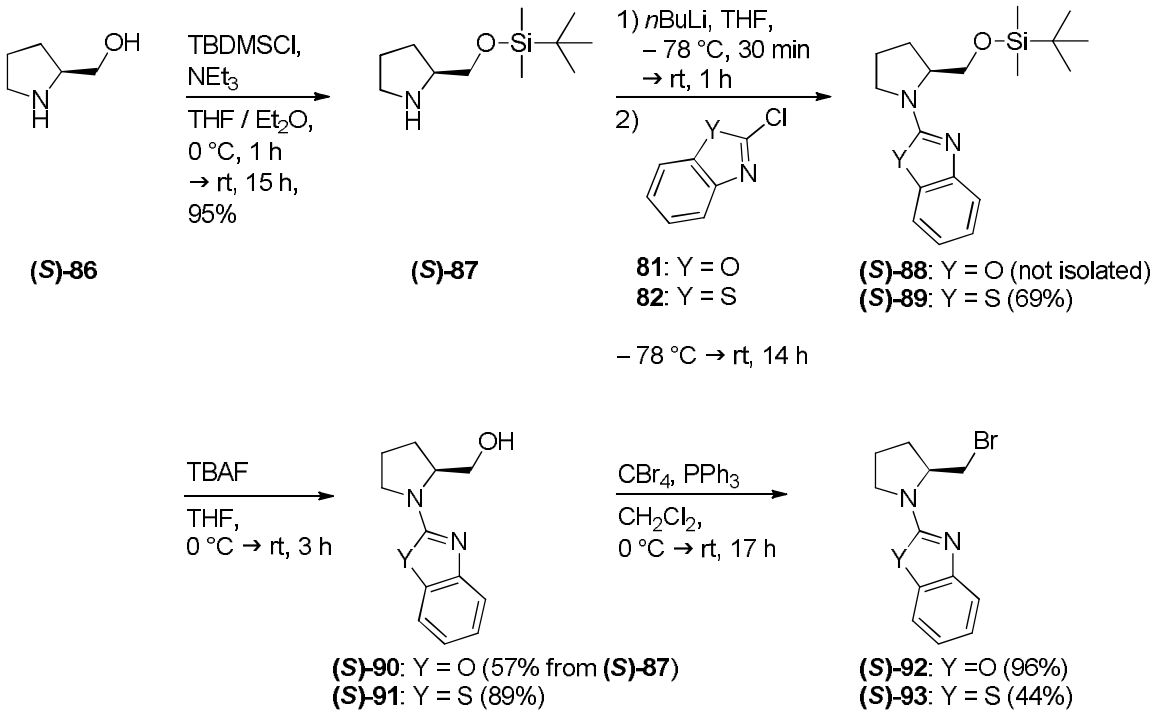
Scheme 37. Attempted synthesis of the benzoxazoline ligand **(*S*)-L$_{Ox}$3·BH$_3$**.

No consumption of 2-chlorobenzoxazole was observed under the reaction conditions shown above. Longer reaction times did not promote the reaction, and when heated at reflux, decomposition of the pyrrolidine **(*S*)-63·HCl** was observed. Since *n*-butyllithium is known to be compatible with borane-protected phosphines, it is likely that the steric bulk of the phosphorus substituents inhibits the reaction.

Consequently, a second synthetic approach to the desired proline-based P,N ligands was attempted. The synthesis of all the ligands prepared so far herein, involved the substitution at the pyrrolidine nitrogen atom in the last synthetic step. An obvious

alternative approach would introduce the pyrrolidine nitrogen substituents prior to the phosphine group in order to avoid the issues described above.

This second synthetic route to proline-based P,N ligands is depicted in Scheme 38. Starting from commercially available L-prolinol these ligands were obtained in five or six steps depending on the phosphorus moiety (Schemes 38, 39 and 40).



(*S*)-**86** (*S*)-**87** **81**: Y = O; **82**: Y = S (*S*)-**88**: Y = O (not isolated); (*S*)-**89**: Y = S (69%)

(*S*)-**90**: Y = O (57% from (*S*)-**87**); (*S*)-**91**: Y = S (89%) (*S*)-**92**: Y =O (96%); (*S*)-**93**: Y = S (44%)

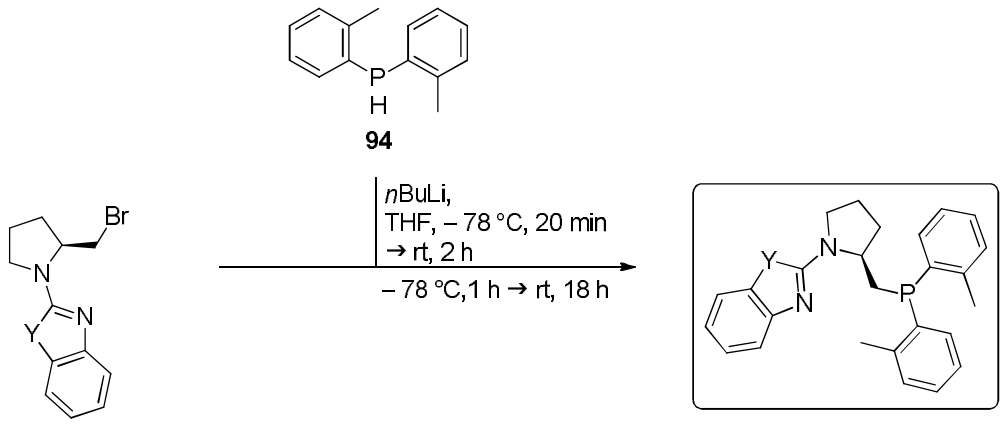
Scheme 38. First steps of the second synthetic route to proline-based P,N ligands.

The oxygen atom of L-prolinol was first protected with *tert*-butyldimethylsilyl (TBDMS).[106] The pyrrolidine **(*S*)-87** was then deprotonated and reacted with the corresponding 2-chloro-substituted heterocycle (benzoxazole and benzothiazole) under the same conditions described for the synthesis of **(*S*)-L$_{Ox}$1** and **(*S*)-L$_{Th}$1** (Scheme 38). Benzothiazole **(*S*)-89** was obtained in 69% yield by this route. The next synthetic step involved the removal of the TBDMS protecting group. Standard procedure using tetrabutylammonium fluoride (TBAF) was followed for deprotection and permitted the isolation of compounds **(*S*)-90** and **(*S*)-91**. The benzoxazole **(*S*)-88** was not isolated, prior to its deprotection. In fact, several attempts to purify **(*S*)-88** by column chromatography on silica gel resulted in cleavage of the TBDMS ether and thus in a loss in yield.

[106] For the synthesis of (*S*)-2-{[(*tert*-butyldimethylsilyl)oxy]methyl}pyrrolidine (**(*S*)-87**) see: J. Mařík, B. Bennettová, R. Tykva, M. Buděšínsky, J. Hlaváček, *J. Peptide Res.* **2001**, *57*, 401-408.

Therefore, the crude compound **(*S*)-88** was directly subjected to deprotection conditions and the resulting benzoxazole **(*S*)-90** was isolated in 57% yield over three steps. Surprisingly, purification of the benzothiazole **(*S*)-89** was not problematic and the TBDMS protecting group was removed after purification. Compounds **(*S*)-90** and **(*S*)-91** were both transformed into their respective bromides **(*S*)-92** and **(*S*)-93**, through an Appel reaction, under the same conditions described for the synthesis of proline-based P,O ligands (Schemes 11 and 12).

Bromides **(*S*)-92** and **(*S*)-93** were subsequently displaced by phosphides (Scheme 39 and 40). Di-*ortho*-tolylphosphine substituents were introduced by substitution of bromides **(*S*)-92** and **(*S*)-93** with di-*ortho*–tolylphosphide, generated *in situ* by deprotonation of di-*ortho*-tolylphosphine (**94**) by *n*-butyllithium. In this way, di-*ortho*-tolylphosphines **(*S*)-L_{Ox}2** and **(*S*)-L_{Th}2** were isolated in 83% and 59% yield respectively.

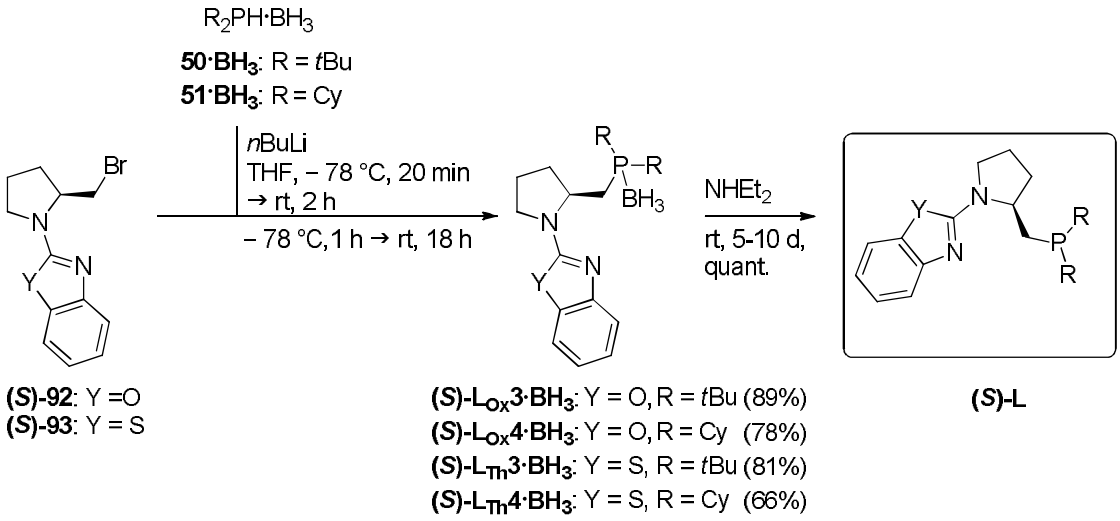


Scheme 39. Synthesis of di-*ortho*-tolylphosphine P,N ligands: **(*S*)-L_{Ox}2**, and **(*S*)-L_{Th}2**.

The synthesis of these compounds in the way depicted in Scheme 34 for the synthesis of diphenylphosphines was not attempted, but it seems likely that it would also be appropriate for ligands **(*S*)-L_{Ox}2** and **(*S*)-L_{Th}2**.

Dialkylphosphines were used as borane adducts (**50·BH_3** and **51·BH_3**) in order to prevent undesired oxidation of the phosphorus atom. Di-*tert*-butyl- and dicyclohexylphosphines were deprotonated *in situ* and then reacted with the respective bromides in order to get **(*S*)-L_{Ox}3** and **(*S*)-L_{Ox}4**, as well as **(*S*)-L_{Th}3** and **(*S*)-L_{Th}4** as borane adducts. The products

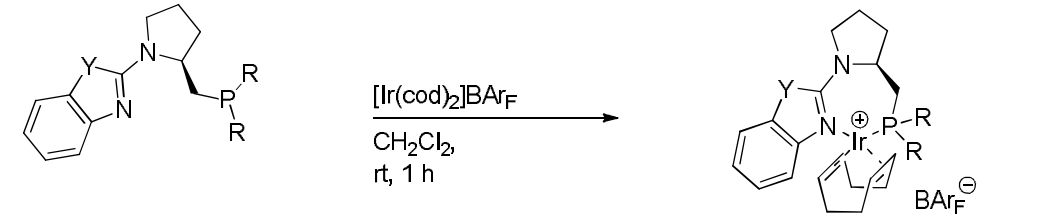
were isolated in moderate to good yields (66% to 89%, Scheme 40). Removal of the borane protecting group with diethylamine was carried out in analogy to the procedure described above (Schemes 19, 23 and 28, for the detailed procedure see the experimental part).



Scheme 40. Synthesis of proline-based P,N ligands with alkyl-substituted phosphine moieties.

Further derivatives of the benzimidazole ligand **(*S*)-L_{Im}1** were not prepared. This ligand induced lower selectivities compared to benzoxazole and benzimidazole derivatives, when tested in the iridium-catalyzed asymmetric hydrogenation (see section 3.2.2.2).

These proline-based P,N ligands were transformed into their corresponding iridium complexes (Scheme 41). The complexes **(*S*)-C_{Ox}2** to **(*S*)-C_{Ox}4** and **(*S*)-C_{Th}2** to **(*S*)-C_{Th}4** were obtained by complexation with $[Ir(cod)_2]BAr_F$ in generally excellent yields (> 84%).



(*S*)-L_{Ox}2: Y = O, R = *o*Tol
(*S*)-L_{Ox}3: Y = O, R = *t*Bu
(*S*)-L_{Ox}4: Y = O, R = Cy
(*S*)-L_{Th}2: Y = S, R = *o*Tol
(*S*)-L_{Th}3: Y = S, R = *t*Bu
(*S*)-L_{Th}4: Y = S, R = Cy

(*S*)-C_{Ox}2: Y = O, R = *o*Tol (55%)
(*S*)-C_{Ox}3: Y = O, R = *t*Bu (95%)
(*S*)-C_{Ox}4: Y = O, R = Cy (84%)
(*S*)-C_{Th}2: Y = S, R = *o*Tol (97%)
(*S*)-C_{Th}3: Y = S, R = *t*Bu (94%)
(*S*)-C_{Th}4: Y = S, R = Cy (98%)

Scheme 41. Synthesis of proline-based P,N ligand/iridium complexes.

3.2.2 Iridium-Catalyzed Asymmetric Hydrogenations with Proline-Based P,N Ligands

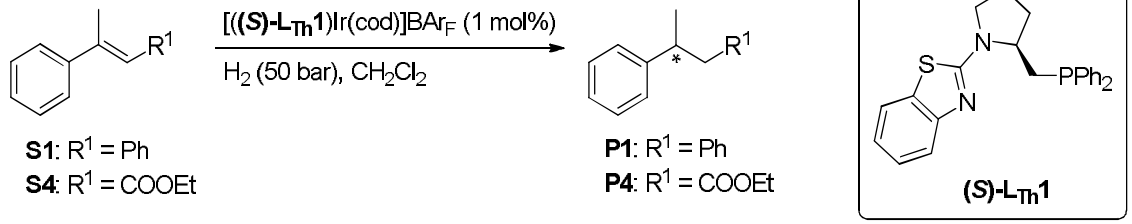
In order to determine the efficiency of these novel ligands, all the precatalysts obtained above were tested in the asymmetric hydrogenation of various substrates. The results are shown below. In contrast, to when proline-based P,O ligands were tested, all the hydrogenation reactions using P,N ligands were set up outside of a glove box, as all the precatalysts that were isolated proved to be stable for storage (Schemes 36 and 41). As in the previous chapter, if not otherwise noted in the corresponding table, the conversion of starting material is identical to the yield of product. Both yield and conversion were determined by GC analysis, and the products were not isolated.

3.2.2.1 Initial Results

Initially, the optimization of the reaction conditions was investigated. Different reaction conditions were tested for two catalysts in the asymmetric hydrogenation of the trisubstituted substrates (*E*)-1,2-diphenyl-1-propene (**S1**) and (*E*)-ethyl 3-phenylbut-2-enoate, using (**S4**) (see Tables 43 and 44). The reaction conditions optimized for the iridium-catalyzed asymmetric hydrogenation involving P,O ligands, were also found to be optimal, when **(*S*)-L_{Th}1** was used as P,N ligand (see Table 44, entries 1 and 5). The reaction was complete within 2 hours at room temperature. When the reactions were carried out at 50 °C, the enantiomeric excesses obtained in the reduction of **S1** and **S4** were identical (entries 1 and 5 *versus* 4 and 6). No considerable impact of the reaction temperature on the selectivity of this catalyst could be observed.

Interestingly, the concentration of both the substrate and catalyst had a dramatic effect on the conversion of the starting material **S1** and on the enantiomeric excess of the product **P1** (entry 1 *versus* 2). At a substrate concentration of 200 μmol·mL^{-1}, also longer reaction time did not improve the conversion of alkene **S1** (entry 3).

Table 43. Optimization of the reaction conditions for the iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) and (*E*)-ethyl 3-phenylbut-2-enoate (**S4**) with **(*S*)-L_{Th}1**.[a]

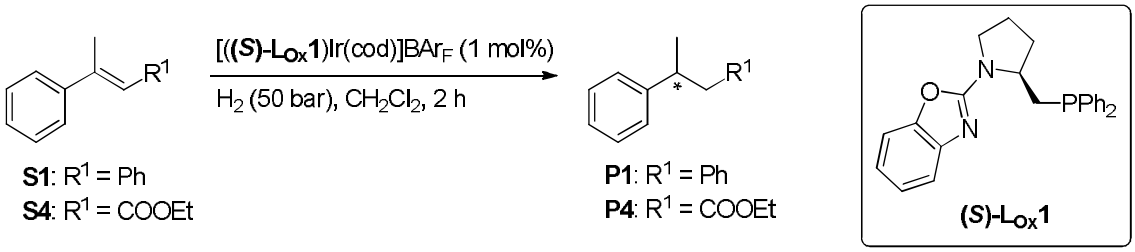


Entry	Substrate	*T* [°C]	*t* [h]	$c_{Substrate}$ [µmol·mL^{-1}]	Yield [%][b]	*ee* [%][c]
1	**S1**	rt	2	500	> 99	80 (*R*)
2	**S1**	rt	2	200	49	77 (*R*)
3	**S1**	rt	18	200	50	68 (*R*)
4	**S1**	50	2	500	> 99	80 (*R*)
5	**S4**	rt	2	500	> 99	76 (*R*)
6	**S4**	50	2	500	> 99	75 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

The same trend was observed, when **(*S*)-L_{Ox}1** was used as ligand (see Table 44). Both substrates **S1** and **S4**, were reduced with the same selectivity regardless of the reaction temperature. Nevertheless, in the reduction the *α*,*β*-unsaturated ester **S4**, the use of ligand **(*S*)-L_{Ox}1** did not result in full conversion of the substrate (87% and 96% yield).

Table 44. Optimization of the reaction conditions for the iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) and (*E*)-ethyl 3-phenylbut-2-enoate (**S4**) with **(*S*)-L_{Ox}1**.[a]



Entry	Substrate	*T* [° C]	Yield [%][b]	*ee* [%][c]
1	**S1**	rt	> 99	81 (*R*)
2	**S1**	50	> 99	81 (*R*)
3	**S4**	rt	87	81 (*R*)
4	**S4**	50	96	80 (*R*)

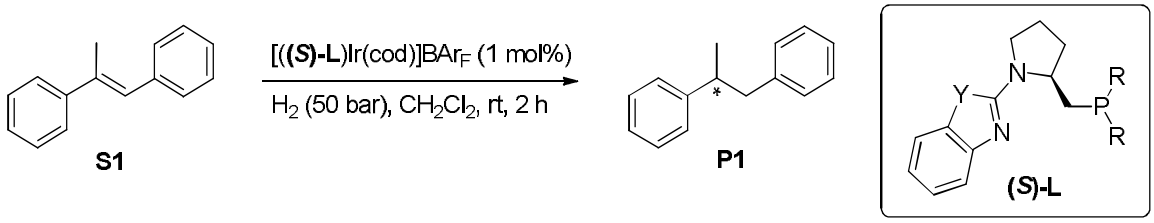
[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

Since the reaction temperature was shown not to impact on the enantioselectivity of the reaction and changes in the concentration of the reagents had a negative impact on the selectivity of the catalyst, the initially tested reaction conditions were chosen for further screening reactions. No other parameters were varied since most of the reactions above showed full conversion. All the reactions below were carried out with 1 mol% of catalyst at 50 bar hydrogen pressure for 2 hours in dichloromethane at room temperature.

3.2.2.2
Screening of Various Hydrogenation Substrates

Table 45 summarizes the results obtained in the iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**). The results obtained under the optimized conditions for the use of ligands **(*S*)-L$_{Ox}$1** and **(*S*)-L$_{Th}$1** are reported again for comparison (entries 1 and 5). The starting material **S1** was converted completely with all the tested complexes, with the exception of **(*S*)-L$_{Im}$1**/iridium complex (entry 9). The iridium catalyst chelated by **(*S*)-L$_{Im}$1** gave 82% conversion and only 52% *ee*. All other catalysts furnished higher enantioselectivities (≥ 80%). When ligand **(*S*)-L$_{Ox}$3** was used, 99% *ee* (*R*) was recorded.

Table 45. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**).[a]



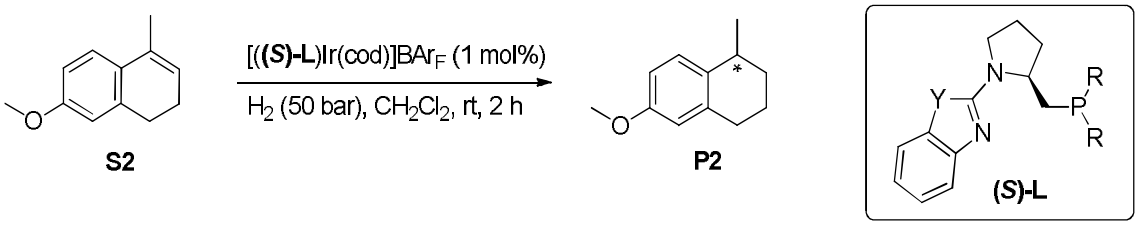
Entry	Ligand	Y	R	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_{Ox}$1**	O	Ph	> 99	81 (*R*)
2	**(*S*)-L$_{Ox}$2**	O	*o*Tol	**> 99**	**97 (*R*)**
3	**(*S*)-L$_{Ox}$3**	O	*t*Bu	**> 99**	**99 (*R*)**
4	**(*S*)-L$_{Ox}$4**	O	Cy	**> 99**	**97 (*R*)**
5	**(*S*)-L$_{Th}$1**	S	Ph	> 99	80 (*R*)
6	**(*S*)-L$_{Th}$2**	S	*o*Tol	90	88 (*R*)
7	**(*S*)-L$_{Th}$3**	S	*t*Bu	**> 99**	**95 (*R*)**
8	**(*S*)-L$_{Th}$4**	S	Cy	> 99	80 (*R*)
9	**(*S*)-L$_{Im}$1**	NMe	Ph	82	52 (*R*)

[a] Reaction scale: [Ir(cod)$_2$]BAr$_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

In general, comparing ligands substituted with the same phosphine substituents, benzoxazoline ligands (**(*S*)-L$_{Ox}$1** to **(*S*)-L$_{Ox}$4**) gave better enantioselectivities than benzothiazole ligands (**(*S*)-L$_{Th}$1** to **(*S*)-L$_{Th}$4**, entries 1 to 4 *versus* 5 to 8). Di-*tert*-butylphosphines achieved the highest enantiomeric excesses compared to analogous ligands, bearing the same heterocyclic moiety (entries 3 and 7). But also **(*S*)-L$_{Ox}$2** and **(*S*)-L$_{Ox}$4** induced high enantioselectivities (97% *ee*, entries 2 and 4).

Diphenylphosphine ligands were tested in the iridium-catalyzed asymmetric hydrogenation of the cyclic unfunctionalized alkene **S2** (Table 46). Moderate to good yields were obtained by the use of these ligands (71 to 90%). However, the enantioselectivities achieved were low (2% to 23% *ee*). As proline-based P,O ligands, these P,N ligands seem not to be suited for the asymmetric reduction of this substrate type. Therefore, substrate **S2** was not further investigated.

Table 46. Iridium-catalyzed asymmetric hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**S2**).[a]



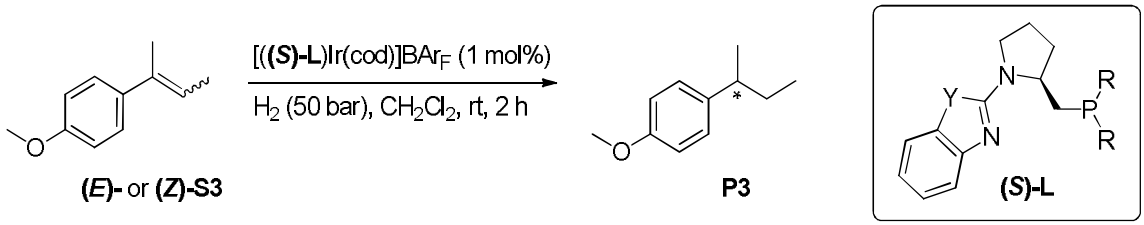
Entry	Ligand	Y	R	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_{Ox}$1**	O	Ph	90 [> 99]	23 (*S*)
2	**(*S*)-L$_{Th}$1**	S	Ph	89	27 (*S*)
3	**(*S*)-L$_{Im}$1**	NMe	Ph	71	2 (*S*)

[a] Reaction scale: [Ir(cod)$_2$]BAr$_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol); [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

In the iridium-catalyzed asymmetric hydrogenation of the unfunctionalized alkenes **(*E*)-** and **(*Z*)-S3**, proline-based P,N ligands showed to be better suited than their related proline-based P,O ligands. The P,O ligands presented in chapter 2, induced only low to moderate enantiomeric excesses in this transformation (see Tables 4, 8, 20, and 32). When proline-based P,N ligands were tested, moderate to good enantioselectivities were measured (40% to 86% *ee*, Table 47). Enantiomeric excesses up to 86% were obtained in the asymmetric hydrogenation of the (*E*)-isomer of **S3** and up to 76% were achieved in the enantioselective reduction of the (*Z*)-isomer (entries 3 and 8). In general, the

(*E*)-isomer was reduced with higher enantioselectivities than the (*Z*)-isomer, except for the reaction with the catalyst derived from **(*S*)-L$_{Th}$1** (entry 8). Conversions of 99% and more were obtained with all the catalysts and for both substrates, (*E*)-**S3** and (*Z*)-**S3**.

Table 47. Iridium-catalyzed asymmetric hydrogenation of (*E*)- and (*Z*)-2-(4-methoxyphenyl)-2-butene (**(*E*)-** and **(*Z*)-S3**).[a]

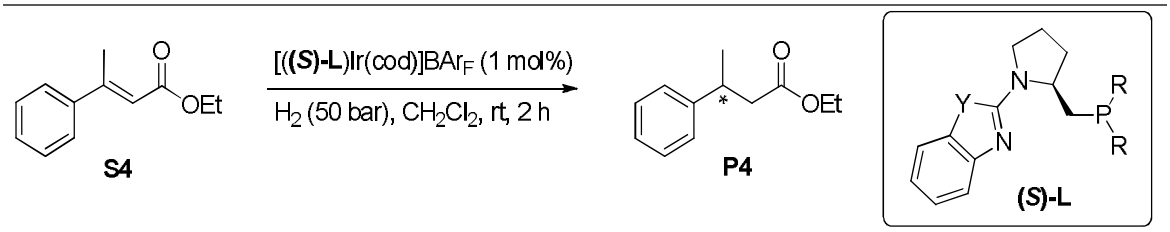


Entry	Substrate	Ligand	Y	R	Yield [%][b]	*ee* [%][c]
1	**(*E*)-S3**	**(*S*)-L$_{Ox}$1**	O	Ph	99	72 (*R*)
2	**(*Z*)-S3**	**(*S*)-L$_{Ox}$1**	O	Ph	> 99	50 (*S*)
3	**(*E*)-S3**	**(*S*)-L$_{Ox}$2**	O	*o*Tol	**99**	**86 (*R*)**
4	**(*Z*)-S3**	**(*S*)-L$_{Ox}$2**	O	*o*Tol	> 99	67 (*S*)
5	**(*Z*)-S3**	**(*S*)-L$_{Ox}$3**	O	*t*Bu	> 99	42 (*S*)
6	**(*Z*)-S3**	**(*S*)-L$_{Ox}$4**	O	Cy	> 99	40 (*S*)
7	**(*E*)-S3**	**(*S*)-L$_{Th}$1**	S	Ph	99	56 (*R*)
8	**(*Z*)-S3**	**(*S*)-L$_{Th}$1**	S	Ph	**> 99**	**76 (*S*)**
9	**(*E*)-S3**	**(*S*)-L$_{Th}$2**	S	*o*Tol	98	64 (*R*)
10	**(*Z*)-S3**	**(*S*)-L$_{Th}$2**	S	*o*Tol	> 99	55 (*S*)
11	**(*Z*)-S3**	**(*S*)-L$_{Th}$3**	S	*t*Bu	> 99	51 (*S*)
12	**(*Z*)-S3**	**(*S*)-L$_{Th}$4**	S	Cy	> 99	55 (*S*)
13	**(*Z*)-S3**	**(*S*)-L$_{Im}$1**	NMe	Ph	99	49 (*S*)

[a] Reaction scale: [Ir(cod)$_2$]BAr$_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by HPLC or GC analysis using a chiral stationary phase (see experimental part).

The reduction of the trisubstituted functionalized alkene **S4** proceeded with excellent conversions and good selectivities (Table 48). Only the iridium catalyst derived from the imidazole ligand **(*S*)-L$_{Im}$1**, afforded low *ee*-values (29%, entry 9). Several ligands furnished *ee* ≥ 90% (entries 1, 3, 4, 7, and 8). The highest enantioselectivities were provided by di-*tert*-butylphosphine ligands: **(*S*)-L$_{Ox}$3** and **(*S*)-L$_{Th}$3** (entries 3 and 7). As for the reduction of the unfunctionalized alkene **S1**, substrate **S4** was also reduced preferentially to the (*R*)-configured alkane by the use of these (*S*)-configured P,N ligands.

Table 48. Iridium-catalyzed asymmetric hydrogenation of (*E*)-ethyl 3-phenylbut-2-enoate (**S4**).[a]

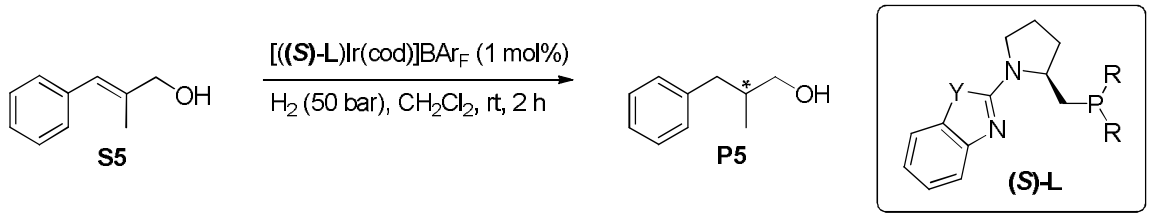


Entry	Ligand	Y	R	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_{Ox}$1**	O	Ph	87	81 (*R*)
2	**(*S*)-L$_{Ox}$2**	O	*o*Tol	> 99	92 (*R*)
3	**(*S*)-L$_{Ox}$3**	O	*t*Bu	**> 99**	**98 (*R*)**
4	**(*S*)-L$_{Ox}$4**	O	Cy	> 99	95 (*R*)
5	**(*S*)-L$_{Th}$1**	S	Ph	> 99	76 (*R*)
6	**(*S*)-L$_{Th}$2**	S	*o*Tol	> 99	85 (*R*)
7	**(*S*)-L$_{Th}$3**	S	*t*Bu	**> 99**	**96 (*R*)**
8	**(*S*)-L$_{Th}$4**	S	Cy	> 99	90 (*R*)
9	**(*S*)-L$_{Im}$1**	NMe	Ph	> 99	29 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

The results obtained from the asymmetric reduction of the allylic alcohol **S5** are shown in Table 49. The conversion of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**S5**) was mostly complete with all the catalysts tested.

Table 49. Iridium-catalyzed asymmetric hydrogenation of (*E*)-2-methyl-3-phenylprop-2-en-1-ol (**S5**).[a]



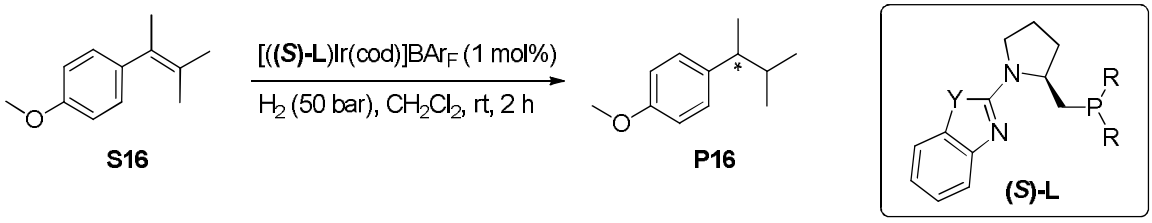
Entry	Ligand	Y	R^1	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L$_{Ox}$1**	O	Ph	42 [55]	47 (*S*)
2	**(*S*)-L$_{Ox}$2**	O	*o*Tol	> 99	72 (*S*)
3	**(*S*)-L$_{Ox}$4**	O	Cy	85 [> 99]	40 (*S*)
4	**(*S*)-L$_{Th}$1**	S	Ph	96 [> 99]	87 (*S*)
5	**(*S*)-L$_{Th}$2**	S	*o*Tol	**> 99**	**89 (*S*)**
6	**(*S*)-L$_{Th}$4**	S	Cy	92 [> 99]	63 (*S*)
7	**(*S*)-L$_{Im}$1**	NMe	Ph	94 [> 99]	25 (*S*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part), conversions are given in parenthesis; [c] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part).

However, reduction to the saturated alcohol was often accompanied by the formation of side products (entries 3, 4, 6 and 7). Ligands bearing di-*ortho*-tolylphosphines gave higher enantioselectivities, compared to their analogues substituted with other phosphines (72% *ee* for **(*S*)-L_{Ox}2** and 89% *ee* for **(*S*)-L_{Th}2**, entries 2 and 5). Nevertheless, also the use of **(*S*)-L_{Th}1** as ligand permitted to hydrogenate substrate **S5** with 87% *ee* (*S*) (entry 4). The (*S*)-configured product **P5** was formed preferentially with the tested (*S*)-configured catalysts. However, benzothiazole/iridium catalysts gave better enantiomeric excesses than their analogous benzoxazoles, whereas in the previous examples generally slightly better selectivities were achieved by benzoxazole/iridium catalysts (see Tables 45 and 48).

The iridium-catalyzed hydrogenation of 1-methoxy-4-(3-methylbut-2-en-2-yl)benzene (**S16**) was as well attempted with proline-based P,N ligands (Table 50). Unfortunately, these catalysts did not prove to be more suitable for the asymmetric reduction of tetrasubstituted alkenes, than proline-based P,O ligands (Table 50 *versus* Schemes 16 and 30). Low conversions (13% to 30%) and enantioselectivities (up to 12% *ee*) were obtained. No other P,N ligand-based catalyst of this type was tested for the iridium-catalyzed hydrogenation of **S16**.

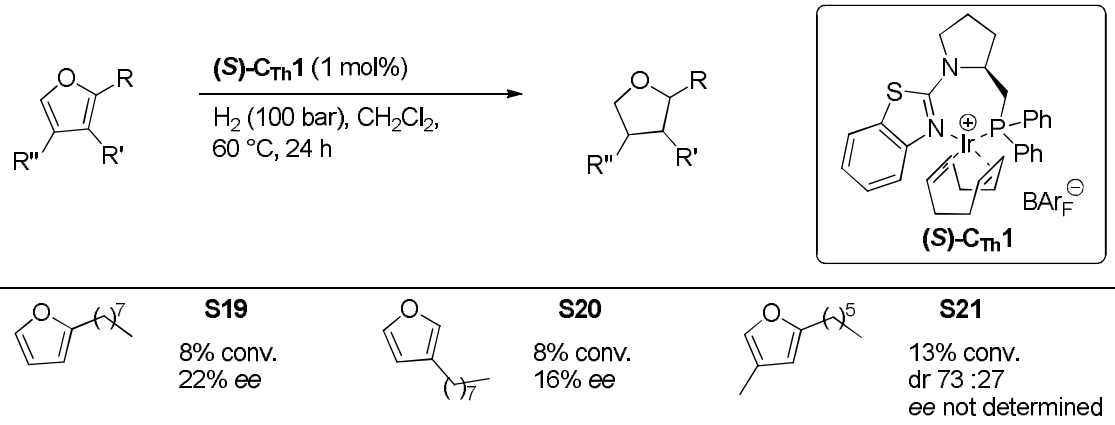
Table 50. Iridium-catalyzed asymmetric hydrogenation of 1-methoxy-4-(3-methylbut-2-en-2-yl)benzene (**S16**).[a]



Entry	Ligand	Y	R	Yield [%][b]	*ee* [%][c]
1	**(*S*)-L_{Ox}1**	O	Ph	36	*rac*
2	**(*S*)-L_{Th}1**	S	Ph	13	12 (−)
3	**(*S*)-L_{Im}1**	NMe	Ph	20	4 (−)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (2.50 µmol), ligand (2.50 µmol), solvent (0.5 mL), substrate (250 µmol), the reactions were prepared outside of a glove box; [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part).

Proline-based P,N ligands were also applied to the iridium-catalyzed asymmetric hydrogenation of furanes within the PFALTZ group by LARISSA PAULI (Scheme 42).[107]



[a] Conversions were determined by GC analysis; [b] Enantioselectivities were determined by GC or HPLC analysis using a chiral stationary phase.

Scheme 42. Iridium-catalyzed asymmetric hydrogenations of furanes with proline-based P,N ligands.[a-b]

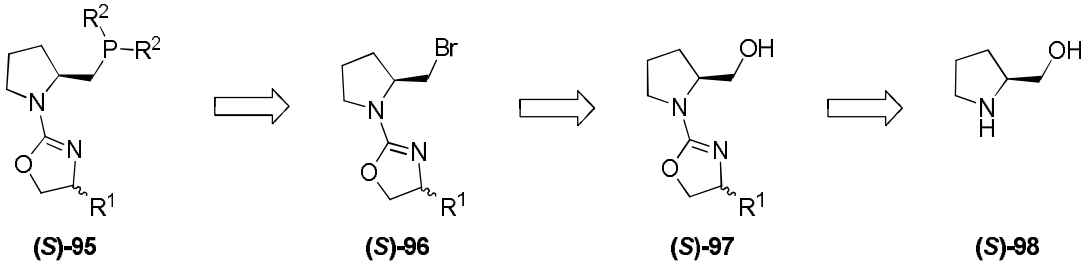
All tested furanes **S19** to **S21** gave the corresponding tetrahydrofuranes in very poor yields and unsatisfying selectivities (8% to 13% conversion and 16% to 22% *ee*), even though the chosen reaction conditions were harsher than those used for the reduction of alkenes. Furanes and benzofuranes were hydrogenated previously with enantiomeric excesses of up to 99% and more using pyridylphosphine (**(*R*)-L9**)/iridium catalyst (Figure 3).[45]

3.3 Conclusions and Outlook

In conclusion, a novel type of P,N ligands was developed for the iridium-catalyzed asymmetric hydrogenation of trisubstituted unfunctionalized and functionalized alkenes. These chiral P,N ligands were readily prepared in enantiomerically pure form starting from the amino acid L-prolinol. As the proline-based P,O ligands presented in chapter 2, these ligands are highly modular and their structures can be easily tuned by variation of the coordinating nitrogen and phosphorus units. Moreover, these scaffolds represent further examples of ligands forming a seven-membered metallacycle with iridium.

[107] L. Pauli, unpublished results.

The ligands prepared involved different heterocylic moieties, such as benzoxazoline, benzothiazole and benzimidazole. However, other heterocyclic moieties could be introduced as substituents at the pyrrolidine nitrogen. An example of further ligands which could be synthesized, is depicted in Scheme 43.



(*S*)-95 **(*S*)-96** **(*S*)-97** **(*S*)-98**

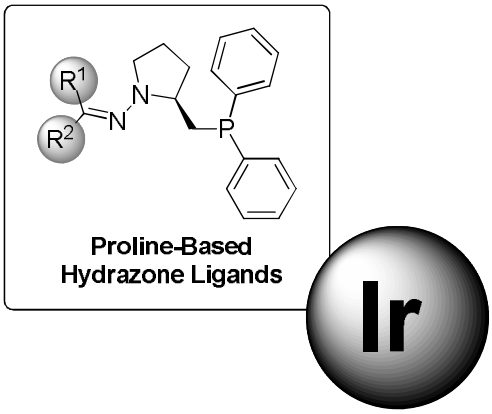
Scheme 43. Outlook: further proline-based P,N ligands derived from amino alcohol **(*S*)-98**.

This substitution of the pyrrolidine nitrogen would allow to generate a greater variety in the structure of proline-based P,N ligands. Moreover, these derivatives would be derived from readily available amino acids with a wide variety of R^1-groups.

In addition, a broader substrate screening with the prepared proline-based P,N ligands should be carried out in order to determine both their further potential but also their limitations. So far, these ligands were shown to be efficient in the asymmetric reduction of certain trisubstituted functionalized and unfunctionalized alkenes and inefficient in the iridium-catalyzed reduction of tetrasubstituted alkenes and furanes. Although other P,N ligands gave as good or even better results in the iridium-catalyzed asymmetric hydrogenation of the same substrates, it is possible that these ligands perform better in the reduction of substrates not tested so far.

CHAPTER 4

PHOSPHINOHYDRAZONE LIGANDS FOR IRIDIUM-CATALYZED ASYMMETRIC HYDROGENATION



4.1
SAMP/RAMP Hydrazones in Asymmetric Synthesis

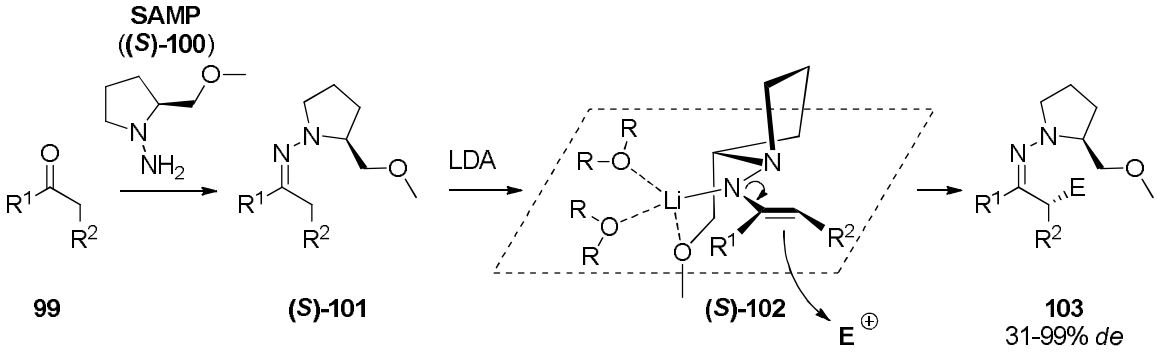
(*S*)-(−)-1-Amino-2-(methoxymethyl)pyrrolidine (SAMP) and its (*R*)-stereoisomer (RAMP) have been widely used as chiral auxiliaries in the enantioselective synthesis of many compounds. First, a brief summary of diastereoselective methodologies based on these auxiliaries will be given and examples of applications will be shown. Moreover, proline-based phosphinohydrazones and other phosphinohydrazones were also used as ligands for transition metal-catalysis. Only a few palladium-catalyzed reactions involving phosphinohydrazones ligands are known and will be described below. These reports inspired the development of proline-based phosphinohydrazones, which were investigated. Their synthesis and attempts to obtain their respective iridium complexes will be discussed in more details in section 4.2.1. Furthermore, initial results of the application of these phosphinohydrazones as chiral ligands for the iridium-catalyzed asymmetric hydrogenation of alkenes will be shown (see section 4.2.2).

4.1.1
The SAMP/RAMP Hydrazone Methodology

The SAMP/RAMP hydrazone methodology has found many applications and is commonly used in asymmetric synthesis. ENDERS *et al.* discovered SAMP and RAMP as chiral auxiliaries for the α-alkylation of ketones and aldehydes in 1976 (see Scheme 44).[108] The chiral hydrazones **(*S*)-101** are obtained by mixing the chiral auxiliary (SAMP, **(*S*)-100**) with a carbonyl compound **99**. While aldehydes react without difficulty, ketones need to be refluxed with catalytic amounts of acid in benzene or cyclohexane under water separation conditions. The hydrazone intermediates **(*S*)-101** are then deprotonated (mostly by means of LDA (lithium di-isopropylamide)) to obtain azaenolates **(*S*)-102**. Mechanistic investigations showed that only one geometrical isomer is formed upon deprotonation (Scheme 44).[109] Electrophilic attack proceeds with high

[108] a) D. Enders, H. Eichenauer, *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 549-551; b) D. Enders, H. Eichenauer, *Tetrahedron Lett.* **1977**, *2*, 191-194; c) D. Enders, P. Fey, H. Kipphardt, *Org. Synth.* **1987**, *65*, 173-182; d) D. Enders, H. Kipphardt, P. Fey, *Org. Synth.* **1987**, *65*, 183-202.
[109] a) K. G. Davenport, H. Eichenauer, D. Enders, M. Newcomb, D. E. Bergbreiter, *J. Am. Chem. Soc.* **1979**, *101*, 5654-5659; b) D. Enders, G. Bachstädter, K. A M. Kremer, M. Marsch, K. Harms, G. Boche, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1522-1524; c) W. Bauer, D. Seebach, *Helv. Chim. Acta* **1984**, *67*, 1972-1988.

diastereofacial differentiation, as shown in Scheme 44. The stereochemical outcome of the reaction can therefore be controlled by the use of either SAMP or RAMP as auxiliary.

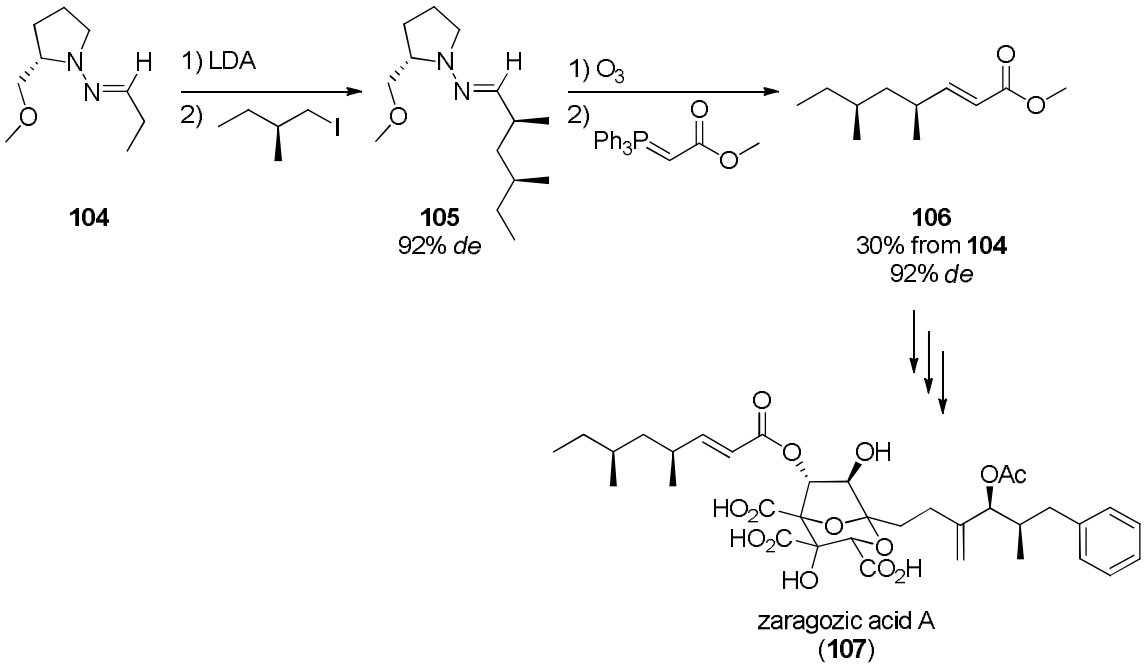


Scheme 44. *α*-Alkylation of ketones and aldehydes, using SAMP (**(*S*)-100**) as a chiral auxiliary.

Both enantiomers of this chiral auxiliary are readily available from the amino acid proline.[108c] Many electrophiles, such as alkyl halides, but also Michael acceptors, carbonyl compounds, halide-substituted esters, oxiranes and aziridines are tolerated and illustrate the broad applicability of this methodology.[110] Subsequent hydrolysis permits to obtain the original carbonyl functionality, but other cleavage reactions can as well introduce further functionalities, such as amino groups.[110]

Since the discovery of this methodology, many alkylations of this type were achieved with excellent enantioselectivities and allowed for the asymmetric synthesis of numerous natural products. An example is shown in Scheme 45.[111] ENDERS' hydrazines were deployed in the alkylation of propionaldehyde to obtain the 1,3-dimethyl-substituted hydrazone **105** with 92% *de* in the synthesis of the C6 side chain of zaragozic acid A (**107**). Subsequent ozonolysis of the crude hydrazone **105** and Wittig olefination gave the desired ester **106** in 30% overall yield and 92% *de*. This synthetic sequence was achieved by NICOLAOU *et al.* and applied to the total synthesis to zaragozic acid A (**107**).

[110] A. Job, C. F. Janeck, W. Bettray, R. Peters, D. Enders, *Tetrahedron* **2002**, *58*, 2253-2329.
[111] a) K. C. Nicolaou, E. W. Yue, S. L. Greca, A. Nadin, Z. Yang, J. E. Leresche, T. Tsuri, Y. Naniwa, F. De Riccardis, *Chem. Eur. J.* **1995**, *1*, 467-494; b) A. Nadin, K. C. Nicolaou, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1622-1656.



Scheme 45. Application of the SAMP hydrazone methodology to the total synthesis of zaragozic acid A (**107**).[111]

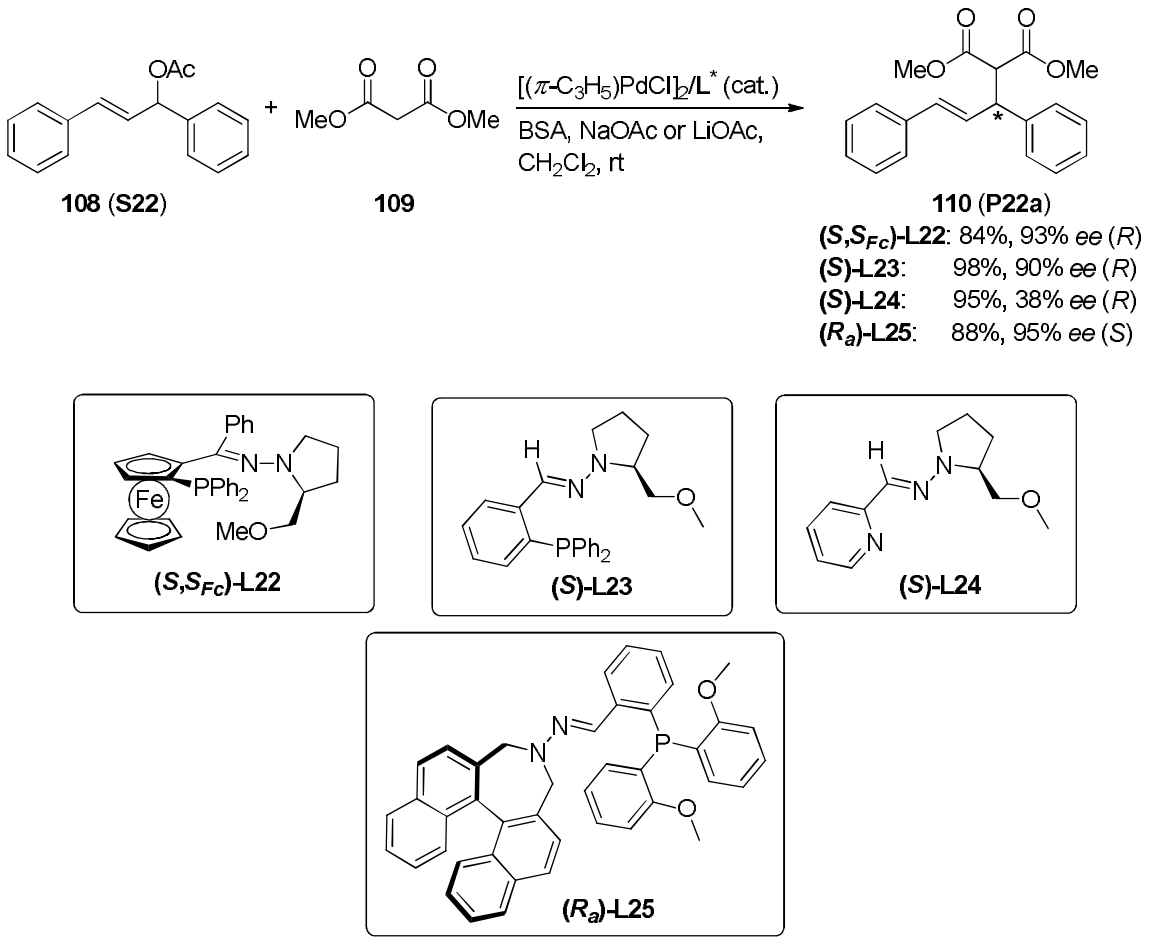
When introduced these chiral hydrazone intermediates were mostly subjected to alkylation reactions, but since then many alternative transformations were accomplished such as aldol reactions, Michael reactions, rearrangements and Diels−Alder reactions.[110]

4.1.2
SAMP Hydrazones as Ligands in Organometallic Chemistry

Whilst SAMP hydrazines were used successfully as chiral auxiliaries for asymmetric syntheses, only a few publications report the use of SAMP hydrazones as chiral ligands for asymmetric catalysis.[108,112] Nevertheless, hydrazones **(*S*,*S*$_{Fc}$)-L22**, **(*S*)-L23**, **(*S*)-L24** and **(*R*$_a$)-L25** were all used as ligands in the palladium-catalyzed allylic alkylation reaction (Scheme 46). In the palladium-catalyzed allylic alkylation of (*E*)-1,3-diphenylallyl-acetate (**108**) with dimethyl malonate (**109**) enantiomeric excesses up to 93% were obtained using ferrocene phosphinohydrazone (**(*S*,*S*$_{Fc}$)-L22**). SAMP hydrazone **(*S*)-L23** was as well used as P,N ligand for this reaction; the alkylation product

[112] a) T. Mino, W. Imiya, M. Yamashita, *Synlett* **1997**, 583-584; b) T. Mino, M. Shiotsuki, N. Yamamoto, T. Suenaga, M. Sakamoto, T. Fujita, M. Yamashita, *J. Org. Chem.* **2001**, *66*, 1795-1797; c) D. Enders, R. Peters, R. Lochtman, J. Runsink, *Eur. J. Org. Chem.* **2000**, 2839-2850; d) D. Enders, R. Peters, R. Lochtman, J. Runsink, *Synlett* **1997**, 1462-1464.

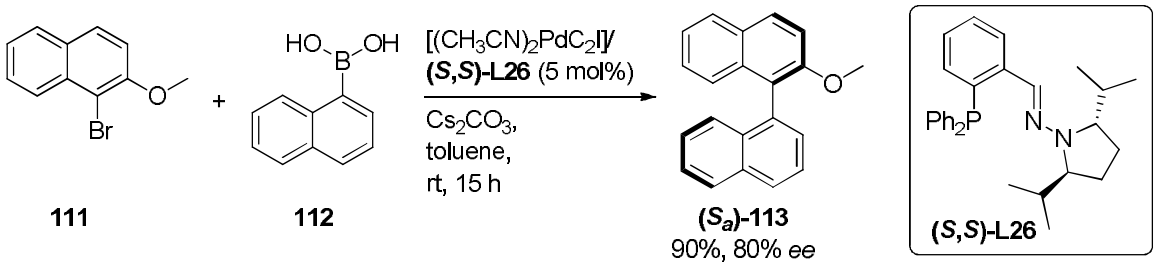
was obtained with excellent yield and an enantiomeric excess of 90%. The closely related SAMP hydrazone **(*S*)-L24**, was employed as N,N ligand in the same catalytic transformation. Although the product was obtained in nearly quantitative yield, only an enantiomeric excess of 38% was achieved. WIDHALM *et al.* reported binaphthyl-based azepine derivatives, such as **(R_a)-L25** and their use as ligands in the same reaction, achieving an enantiomeric excess of 95%.[113]



Scheme 46. Hydrazones ligands for the palladium-catalyzed allylic alkylation reaction.[108b,112,113]

Very recently, phosphinohydrazones were reported as suitable ligands for the asymmetric Suzuki−Miyaura cross-coupling reaction.[114] Excellent to good yields and enantioselectivities were obtained in the asymmetric cross-coupling of functionalized aryl bromides and triflates to afford axially chiral biaryls. An example is shown in Scheme 47.

[113] M. Widhalm, M. Abraham, V. B. Arion, S. Saarsalu, U. Maeorg, *Tetrahedron: Asymmetry* **2010**, *21*, 1971-1982.
[114] A. Ros, B. Estepa, A. Bermejo, E. Álvarez, R. Fernández, J. M. Lassaletta, *J. Org. Chem.* **2012**, *77*, 4740-4750.



Scheme 47. SAMP Hydrazones as ligands for the palladium-catalyzed cross-coupling reaction.[114]

4.2 Phosphinohydrazones Ligands

Inspired by both, the structure of SAMP hydrazones (see section 4.1) and the proline-based ligands presented earlier herein (see chapters 2 and 3), proline-based phosphinohydrazones **(*S*)-L_H** were investigated as ligands for iridium (Figure 16). These phosphinohydrazone ligands **(*S*)-L_H** were thought to form a six-membered metallacycle with iridium, like many other P,N ligands reported in literature (see section 3.1.1). The synthesis of these ligands and their respective iridium complexes are described below (see section 4.2.1). Initial results obtained when these phosphinohydrazones were used as ligands in the iridium-catalyzed asymmetric hydrogenation will be shown in section 4.2.2.

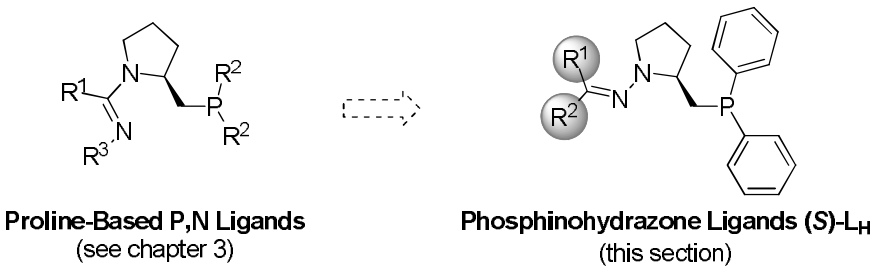
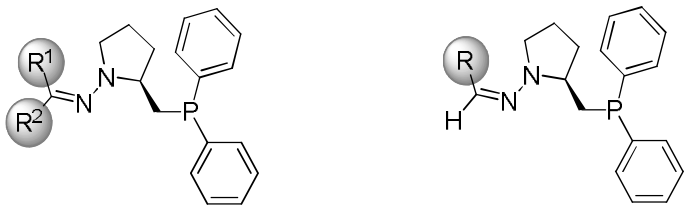


Figure 16. Ligand scaffolds presented herein.

4.2.1 Synthesis of Phosphinohydrazones Ligands and Iridium Complexes

Different synthetic strategies were attempted for the synthesis of phosphinohydrazones **(*S*)-L_H**. The syntheses of ketohydrazones and aldhydrazones will be described separately (Figure 17). The complexation of the prepared ligands to iridium will be discussed directly after the description of the synthetic methods attempted.



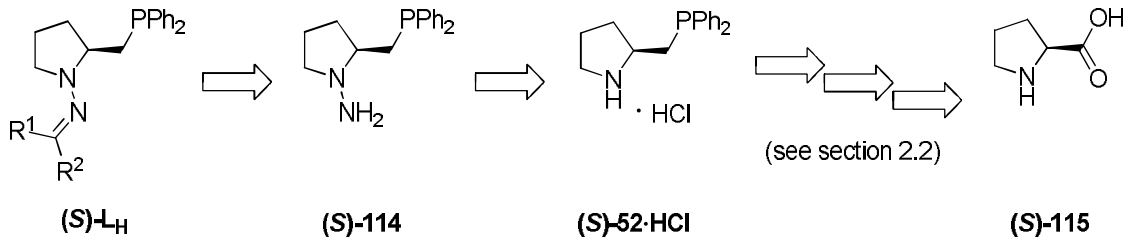
Ketohydrazones
(see section 4.2.1.1)

Aldhydrazones
(see section 4.2.1.2)

Figure 17. Phosphinohydrazone ligand structures.

4.2.1.1
Ketohydrazone Ligands

The retrosynthetic approach depicted in Scheme 48 was first considered to synthesize these phosphinohydrazones **(*S*)-L_H**. This strategy would allow to use all the intermediates, which were involved in the synthesis of proline-based P,O ligands (see section 2.3.1).



(*S*)-L_H **(*S*)-114** **(*S*)-52·HCl** **(*S*)-115**

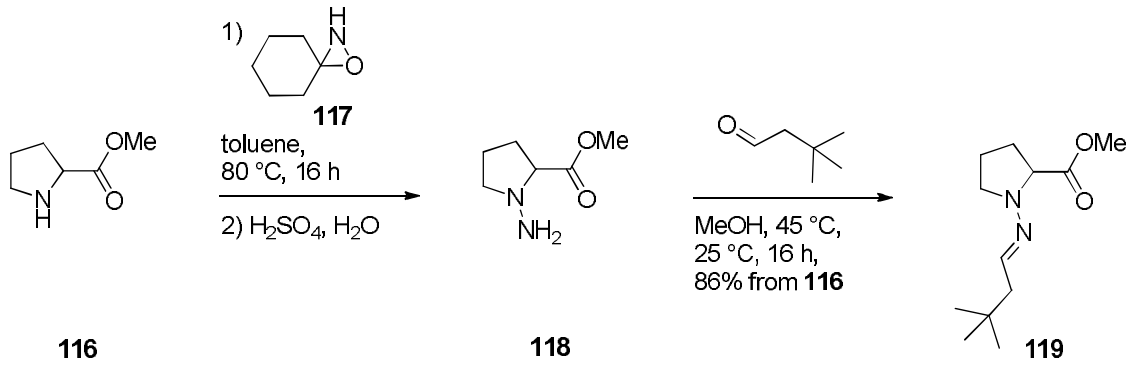
Scheme 48. 1st Retrosynthetic analysis to phosphinohydrazones **(*S*)-L_H**.

In addition, it permits to introduce the hydrazone functionality in the last synthetic step so that various R^1- and R^2-substituents can be easily installed on a common intermediate and the synthesis of a small library of **(*S*)-L_H** ligands could be rapidly achieved. Hydrazones **(*S*)-L_H** were thought to be accessible from the hydrazine **(*S*)-114**, *via* condensation with a variety of ketones. Hydrazine **(*S*)-114** would be obtained from pyrrolidinium salt **(*S*)-52·HCl**.

N-substituted oxaziridines were used as source of electrophilic nitrogen in the synthesis of hydrazines and alkoxyl amines.[115] In fact, one method to introduce the hydrazine moiety on a proline-derived compound using 1-oxa-2-azaspiro[2.5]octane (**117**) was reported

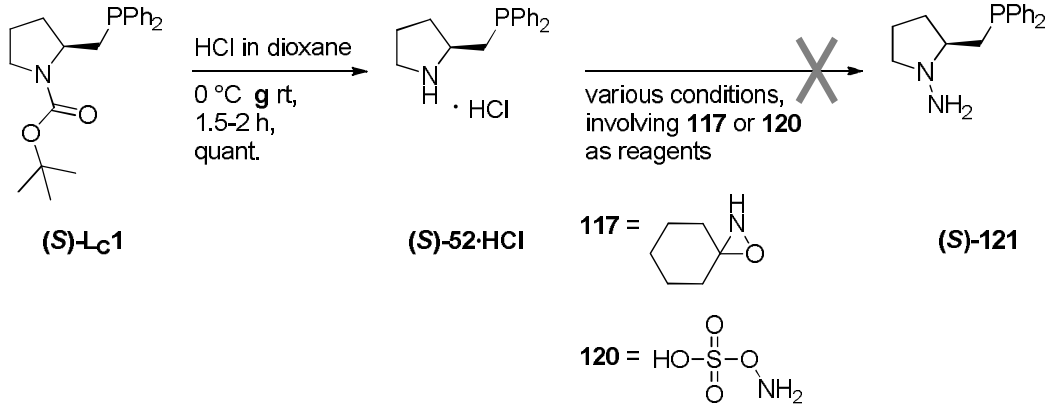
[115] S. Andreae, E. Schmitz, *Synthesis* **1991**, 327-341.

previously (Scheme 49).[116] Hydroxylamine-*O*-sulfonic acid (**120**) as well has been widely used as reagent for the *N*-amination of various heterocycles, like for example pyrroles and aziridines.[117] Therefore, the *N*-substitution of **(*S*)-52** was attempted using both reagents, **117** and **120** as sources of electrophilic nitrogen (Scheme 50).



Scheme 49. Synthesis of 1-(3,3-dimethyl-butylamino)-pyrrolidine-2-carboxylic acid methyl ester (**119**), involving **117** as electrophilic nitrogen source.

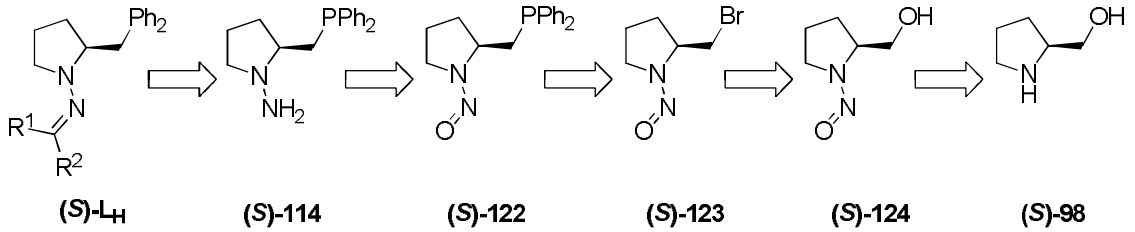
However, when used for the *N*-amination of pyrrolidine **(*S*)-52**, none of these reagents prooved to be effective. Various reaction conditions were tested, involving the screening of solvents, temperatures and bases, but hydrazine **(*S*)-121** was never obtained (Scheme 50). The compatibility of these reagents (**117** and **120**) with the phosphine moiety is therefore doubted.



Scheme 50. Attempted synthesis of hydrazine **(*S*)-121** from pyrrolidinium salt **(*S*)-52·HCl**.

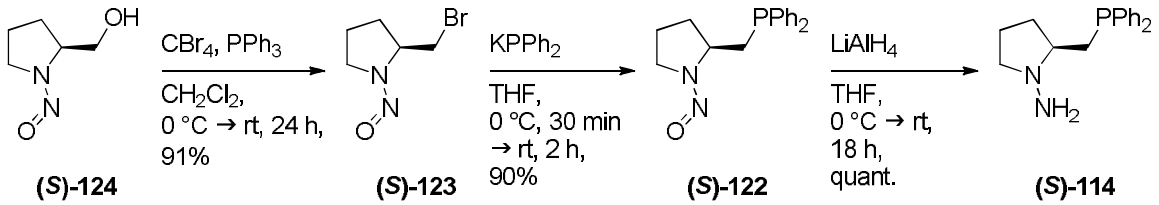
[116] F. Ruebsam, Z. Sun, B. Ayida, Y. Zhou, A. X. Xiang, *PCT Int. Appl.* 2008073987, **2008**.
[117] a) J. T. Hunt, T. Mitt, R. Borzilleri, J. Gullo-Brown, J. Fargnoli, B. Fink, W.-C. Han, S. Mortillo, G. Vite, B. Wautlet, T. Wong, C. Yu, X. Zheng, R. Bhide, *J. Med. Chem.* **2004**, *47*, 4054-4059; b) S. J. Brois, *Tetrahedron Lett.* **1968**, *57*, 5997-6000.

Instead of screening further reaction conditions or additional *N*-amination reagents different from **117** and **120**, an alternative retrosynthetic approach was proposed (Scheme 51). In order to avoid, possible issues concerning the stability of the phosphine moiety, this second retrosynthesis suggests the formation of the N–N bond prior to the introduction of the phosphine functionality.



Scheme 51. 2nd Retrosynthetic analysis to phosphinohydrazones **(*S*)-L_H**, starting from L-prolinol (**(*S*)-98**).

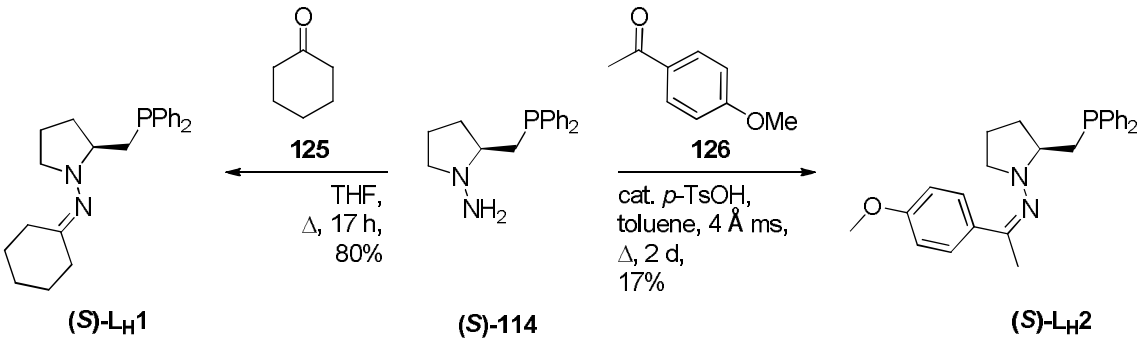
Nitrosamine **(*S*)-124** was obtained in quantitative yield, starting from L-prolinol (**(*S*)-98**) that was reacted with *tert*-butylnitrite, as described in the literature.[118] This nitrosamine was then converted into compound **(*S*)-122**, under reaction conditions similar to those described previously (see section 2.3.1). The desired nitrosamine **(*S*)-122** was obtained in excellent yields *via* an Appel reaction, followed by displacement of the bromine of **(*S*)-123** by diphenylphosphide (Scheme 52). Nitrosamine **(*S*)-122** was then reduced to the desired hydrazine **(*S*)-114** in quantitative yield with lithium aluminum hydride as reducing agent.



Scheme 52. Synthesis of hydrazine **(*S*)-114**.

Hydrazine **(*S*)-114** was finally condensated with cyclohexanone (**125**) and 1-(4-methoxyphenyl)ethanone (**126**) (Scheme 53). The reaction of **(*S*)-114** with the ketone **125** proceeded smoothly affording phosphinohydrazone **(*S*)-L_H1** in 80% yield, whereas the condensation with **126** proceeded poorly (17% yield for **(*S*)-L_H2**).

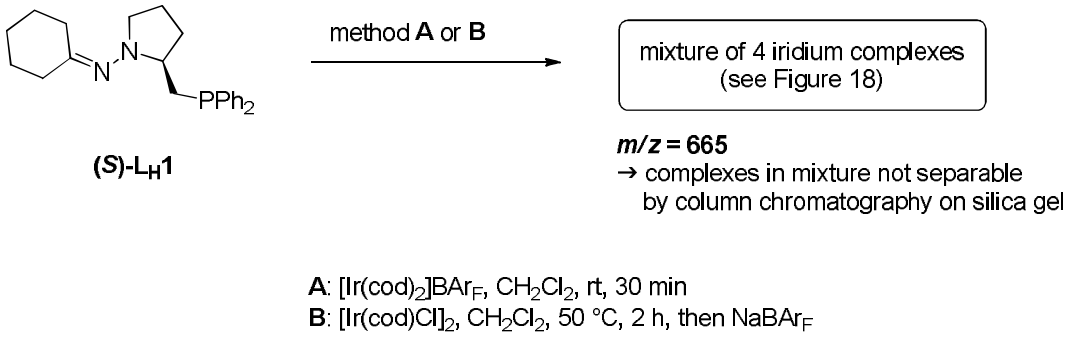
[118] R. Lazny, A. Nodzewska, B. Zabicka, *J. Comb. Chem.* **2008**, *10*, 986-991.



Scheme 53. Synthesis of phosphinohydrazones **(*S*)-L_H1** and **(*S*)-L_H2**.

Both phosphinohydrazones **(*S*)-L_H1** and **(*S*)-L_H2** were complexed to iridium, but the isolation of the desired phosphinohydrazone/iridium precatalyst proved not possible (Schemes 54 and 55). Two different issues arised and will be described separately below.

Both the complexation methods (**A** and **B**) used for the complexation of **(*S*)-L_H1** afforded a mixture of iridium complexes (Scheme 54).



Scheme 54. Complexation of phosphinohydrazone **(*S*)-L_H1** with iridium.

The mixture of complexes obtained was identical in both cases and the products could not be separated by column chromatography on silica gel (Figure 18, NMR spectra in red). Although only the expected mass was measured for the mixture by ESI-MS, the analytical data were not conclusive about the structure of these iridium species. The ^{31}P NMR spectrum is shown in Figure 18.

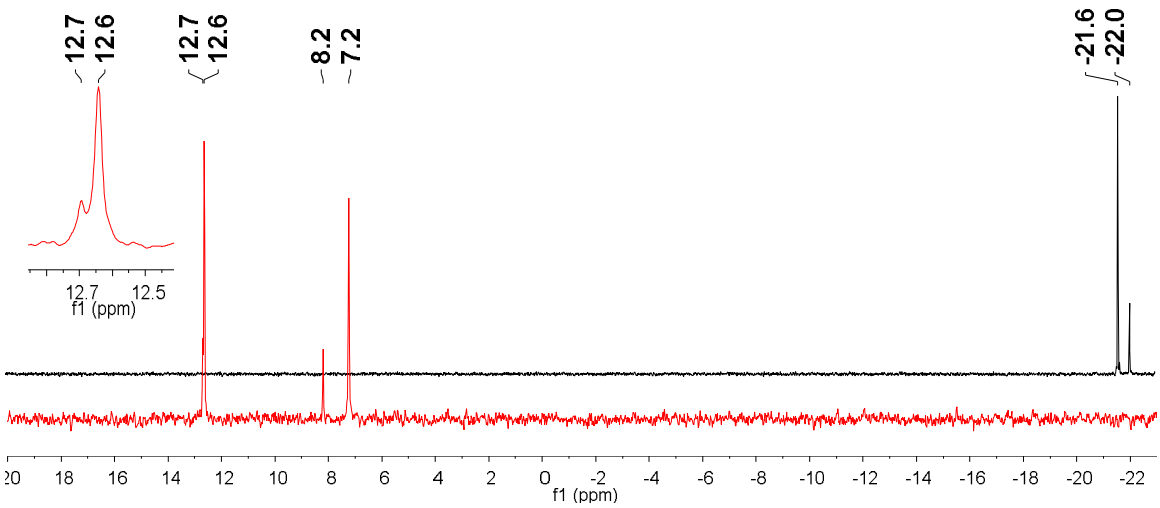
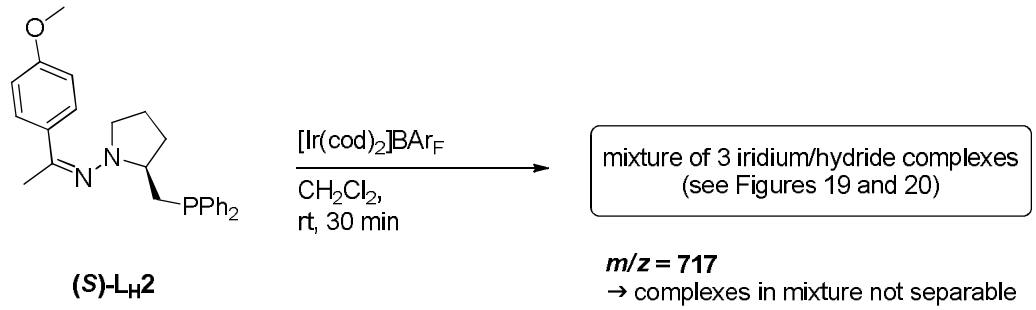


Figure 18. ^{31}P NMR Analysis of the iridium complexes formed by coordination of **(*S*)-L_H1**.
In black: free ligand ***(S)-L_H1*** *in CD_2Cl_2; and in red:* ***(S)-L_H1****/Ir complex in CD_2Cl_2.*

In the ^{31}P NMR spectrum of the free ligand **(*S*)-L_H1**, two rotamers were observed ($\delta = -21.6$ and -22.0 ppm). These rotamers were thought to be able to interconvert under the complexation conditions or, if they can not convert into each other, that one conformer would be favored for complexation. However, the fact that both complexation methods, involving different iridium precursors and also different reaction temperatures, afforded an identical mixture of iridium complexes suggests that these conformers do not interconvert or that in both cases a thermodynamic product mixture is formed. Further analyses were not carried out, as the separation of a single iridium complex for asymmetric hydrogenation seems not possible. Phosphinohydrazone **(*S*)-L_H1** was not further investigated.

When phosphinohydrazone **(*S*)-L_H2** was complexed to iridium another issue arised: a mixture of three iridium/hydride species was obtained, resulting from C−H insertion of iridium into the *ortho*-position of the phenyl-ring of the hydrazone and again these complexes could not be separated (Scheme 55). At least, this characteristic is not unexpected as it has already been observed in the iridium-catalyzed asymmetric hydrogenation of imines within the PFALTZ group.[119]

[119] Unpublished results.



Scheme 55. Complexation of phosphinohydrazone **(*S*)-L_H2** with iridium.

The presence of more than one phosphine species in the ^{31}P NMR spectra was assigned to the formation of several diastereomeric C−H insertion complexes **127** (see Figure 22). Both, the ^{31}P and the ^{1}H NMR spectra show the presence of three iridium/hydride complexes (see Figures 19 and 20). Although, the corresponding *m/z* was not observed by ESI-MS, the unusual signal at δ = 27.5 ppm may also originate from the iridium complex of the phosphine oxide of **(*S*)-L_H2**.

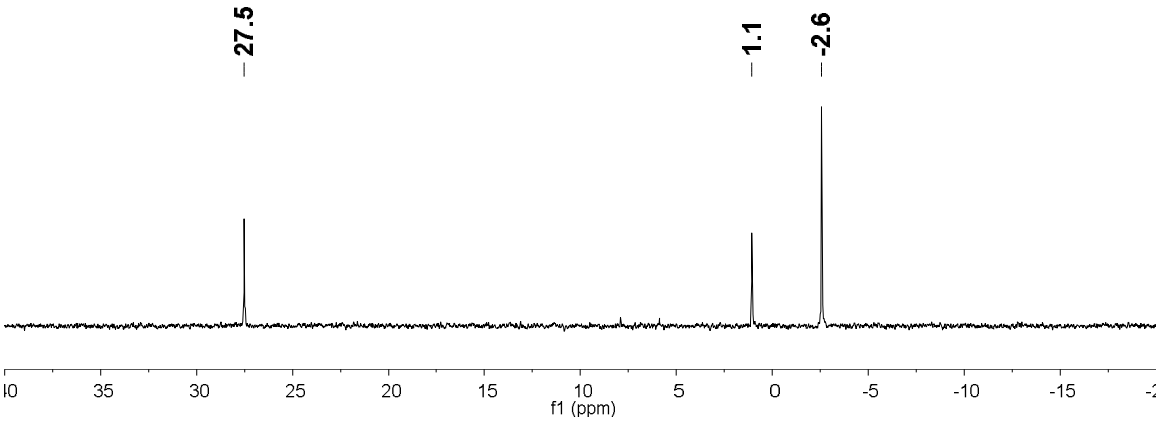


Figure 19. ^{31}P NMR Analysis of the iridium complexes formed by coordination of **(*S*)-L_H2**.

Three hydride signals can be observed in the ^{1}H NMR spectrum: one singlet and two doublets (Figure 20). This observation suggests that only two of the three iridium complexes obtained have the phosphorus atom and the inserted hydrogen atoms in close enough proximity to allow for coupling. The coupling constants for the doublets at δ = − 14.9 and – 15.7 ppm in the ^{1}H NMR spectrum (J = 7.7 and 8.6 Hz respectively), suggest that the corresponding two complexes have both their phosphorus and hydride atoms *cis* to each other. Typical coupling values are: $^{2}J_{H,P}$(*cis*) = 10-30 Hz, and $^{2}J_{H,P}$(*trans*) = 90-160 Hz.

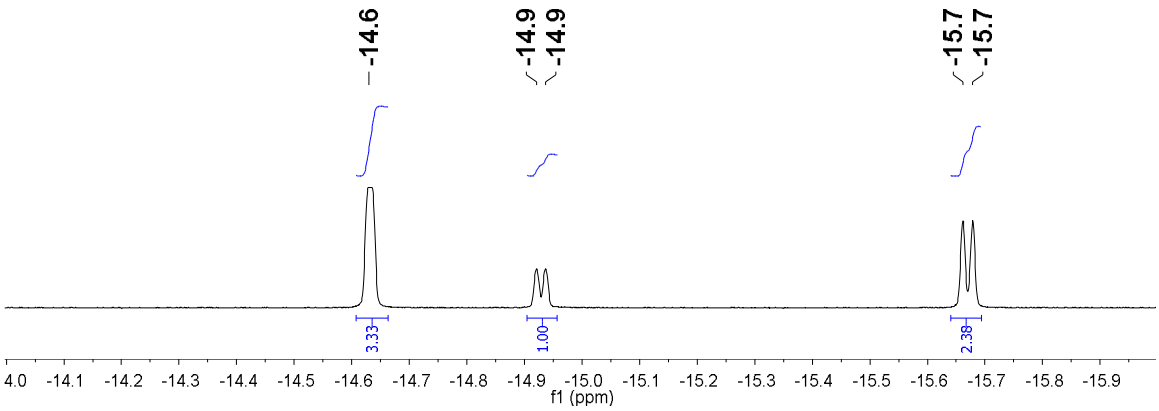


Figure 20. ^{1}H NMR Analysis of the iridium complex formed by coordination of **(*S*)-L_H2**.
Three hydride signals are observed: δ = − 14.6 (s), − 14.9 (d, J = 7.7 Hz), − 15.7 (d, J = 8.6 Hz) ppm.

However, the 2D-NMR experiment allowing for the correlation of ^{1}H and ^{31}P NMR spectra, does not support the assumption that the third signal in the ^{31}P NMR spectrum (δ = 27.5 ppm) is due to an impurity (Figure 21).

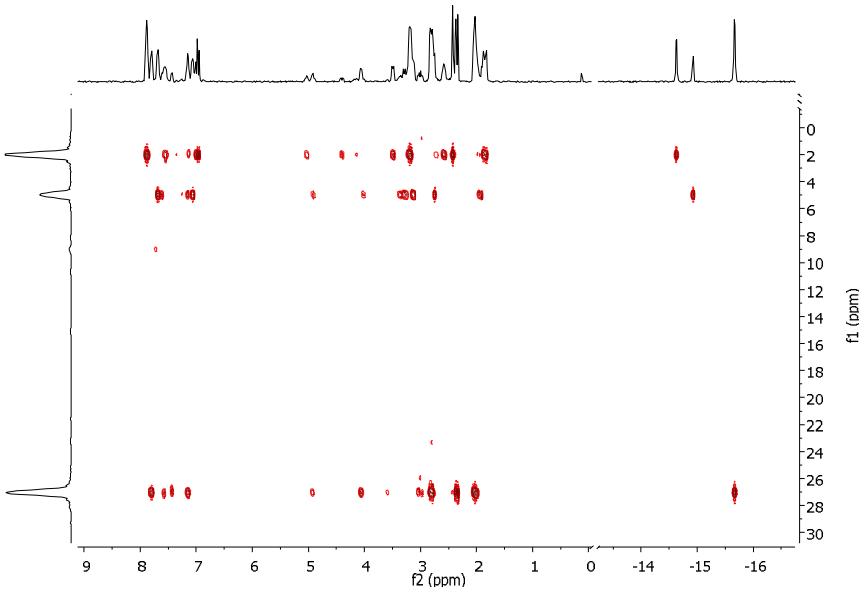


Figure 21. 2D NMR Analysis of the iridium complex formed by coordination of **(*S*)-L_H2**: correlation of ^{1}H and ^{31}P NMR spectra.

In fact, although the chemical shift of this signal is shifted atypically in the ^{31}P NMR spectrum, it is clearly correlated to a hydride signal on the basis of the ^{1}H NMR shift.

All the iridium/hydride species, which can possibly be formed by the complexation and insertion of **(*S*)-L_H2** to iridium are depicted in Figure 22. First of all, the two coordination

sites occupied by 1,5-cyclooctadiene need to be *cis* to each other. Structures **127a** and **127b** can most likely be assigned to the two doublets observed in the ^{1}H NMR spectrum (Figure 20). However, the structure of the complex showing a singlet in this same spectrum remains unclear. While, structures **127c** and **127d** are unlikely, due to the absence of the typical *trans* coupling constant between the hydride and phosphorus atoms, structures **127e** and **127f** are also unlikely due to the distorted and planar bidentate chelation mode of ligand **(*S*)-L$_H$2**. In addition, complexes **127e** and **127f** should display a doublet as signal with a similar *cis* coupling constant in the ^{1}H NMR spectrum.

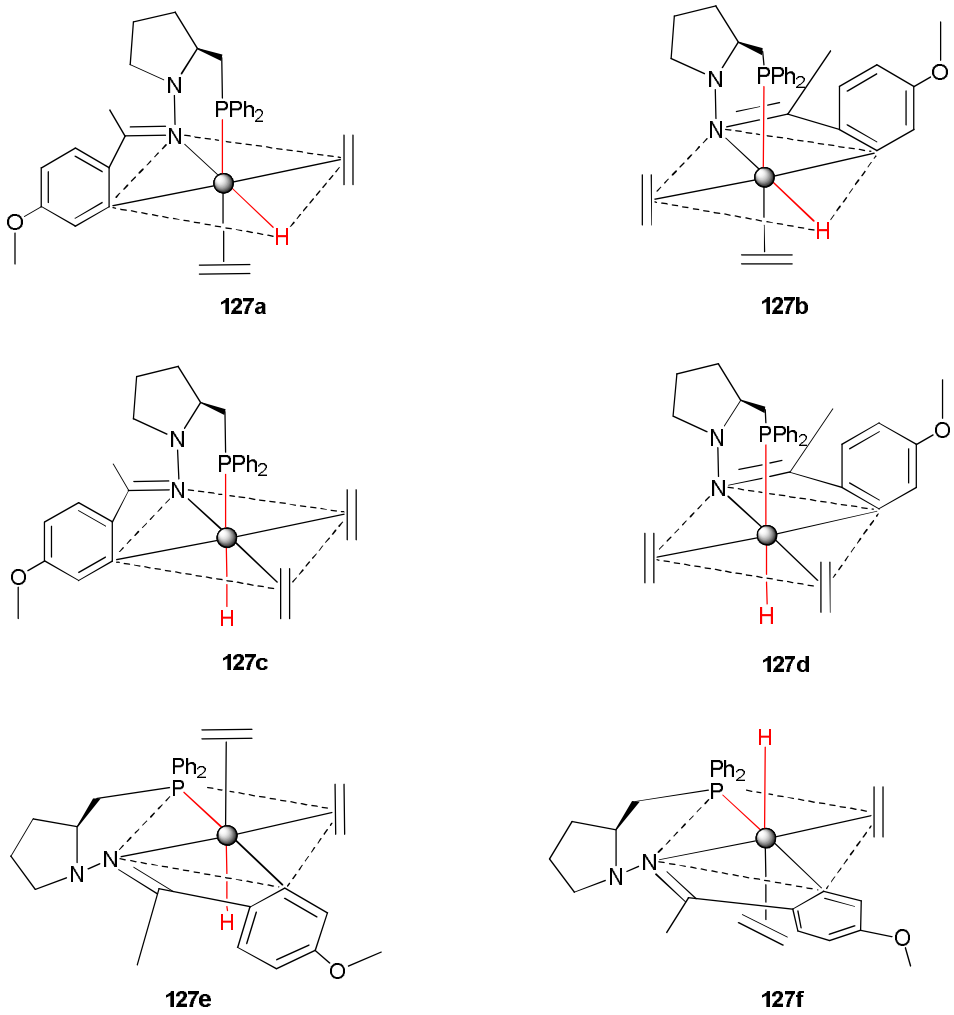
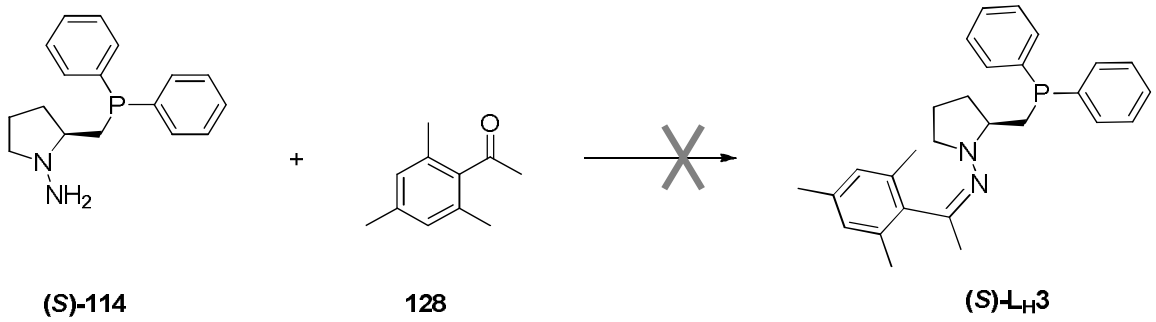


Figure 22. Possible iridium/hydride species formed by the complexation of **(*S*)-L$_H$2**.

Another possibility could be that the ligand coordination does not occur as assumed, which would mean: (1) the pyrrolidine nitrogen atom could coordinate as nitrogen donor, or (2) the ligand chelates only through the phosphorus atom and the inserted C−H bond

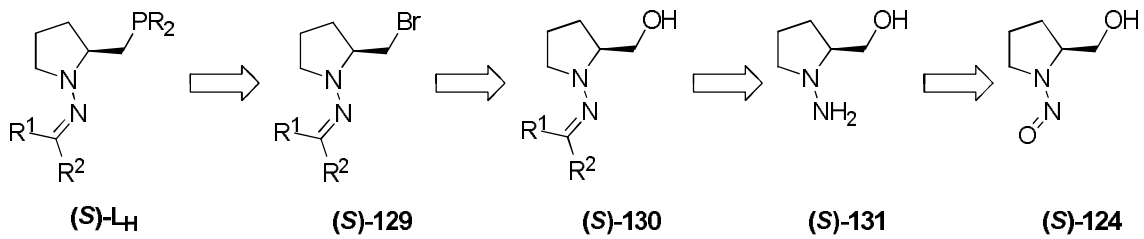
and a solvent molecule occupies the last coordination site. These coordination modes could explain the highly different chemical shifts of the hydride and phosphorus signals.

No further analyses were carried out. Based on these results phosphinohydrazone ligands with *ortho*-substituted phenyl substituents were investigated in order to avoid C−H insertion. Therefore the synthesis of phosphinohydrazone **(*S*)-L_H3** was attempted (Scheme 56). This ligand was thought to be accessible from the condensation of the pyrrolidine **(*S*)-114** with 1-mesitylethanone (**128**), in the same way as **(*S*)-L_H1** and **(*S*)-L_H2** (see Scheme 53). However, none of the tested reaction conditions led to the formation of the desired phosphinohydrazone **(*S*)-L_H3**.



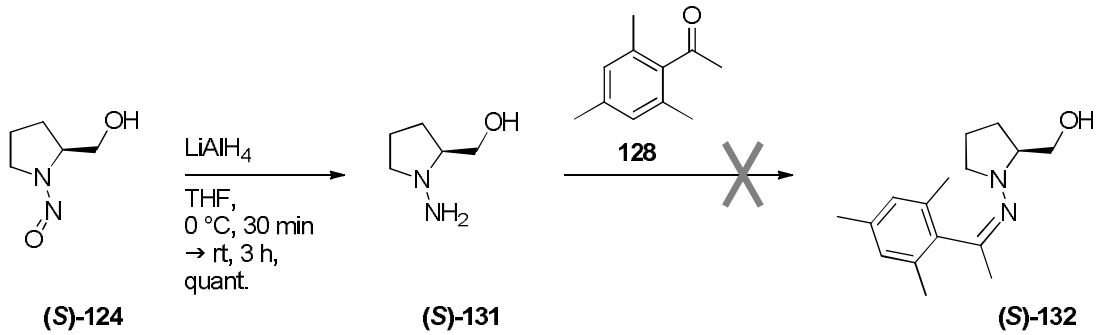
Scheme 56. Attempted synthesis of the ketohydrazone ligand **(*S*)-L_H3**.

A third synthetic pathway was developed: the retrosynthetic strategy is depicted in Scheme 57. This synthesis involves again the formation of the N−N bond prior to the introduction of the phosphine moiety, but also the condensation reaction prior to the introduction of the phosphine. The synthesis of the nitrosamine **(*S*)-124** was already described above.



Scheme 57. 3rd Retrosynthetic analysis to phosphinohydrazones **(*S*)-L_H**, starting from nitrosamine **(*S*)-124**.

The reduction of nitrosamine **(*S*)-124** was carried out by the use of lithium aluminum hydride, in the same way than in the reduction of **(*S*)-122** (see Schemes 52 and 58). However, the condensation of hydrazine **(*S*)-131** with the desired ketone **128** was not achieved. Probably, the steric hindrance around the electrophilic carbonyl group in **128** does not allow for the nucleophilic attack of the hydrazine **(*S*)-131**.

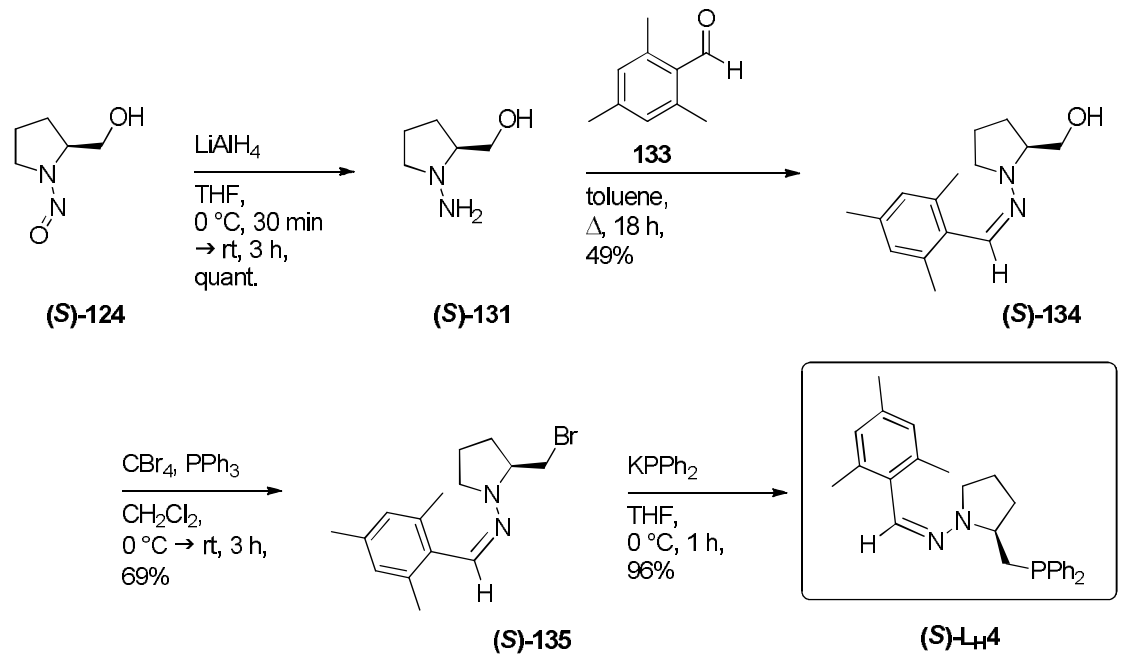


Scheme 58. Attempted synthesis of proline-based hydrazone ligands from ketones.

Ketohydrazones were abandoned as targets for the development of phosphinohydrazone ligands. Not only their synthesis proved difficult, but also the problems encountered during their complexation to iridium made this approach unattractive. Therefore, the synthesis of aldhydrazones was investigated.

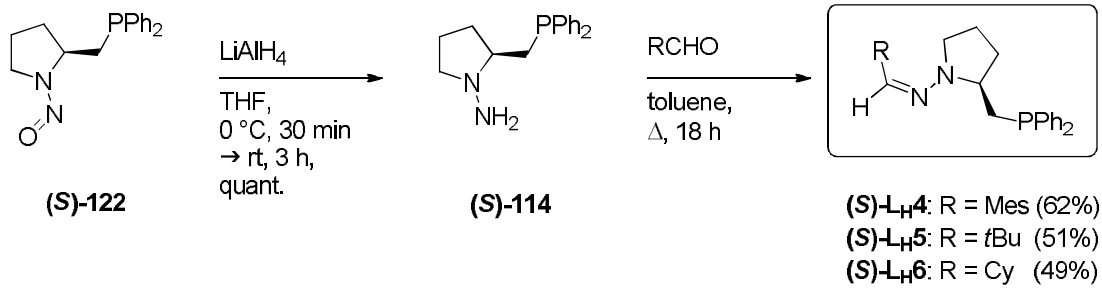
4.2.1.2
Aldhydrazone Ligands

For the synthesis of aldhydrazones the synthetic route depicted in Scheme 59 was followed. Nitrosamine **(*S*)-124** was reduced to hydrazine **(*S*)-131** as described above. Compound **(*S*)-131** was condensated with 2,4,6-trimethylbenzaldehyde (**133**) under refluxing conditions in toluene and the aldhydrazone **(*S*)-134** was isolated in 49% yield (Scheme 59). Subsequently, the alcohol **(*S*)-134** was converted to its bromine derivative **(*S*)-135** through an Appel reaction (69% yield). Finally, the phosphinohydrazone ligand **(*S*)-L_H4** was isolated, after displacement of the bromine by diphenylphosphide in 96% yield. In contrast to the synthesis of ketohydrazones, the synthesis of aldhydrazone **(*S*)-L_H4** proceeded smoothly in good overall yield.



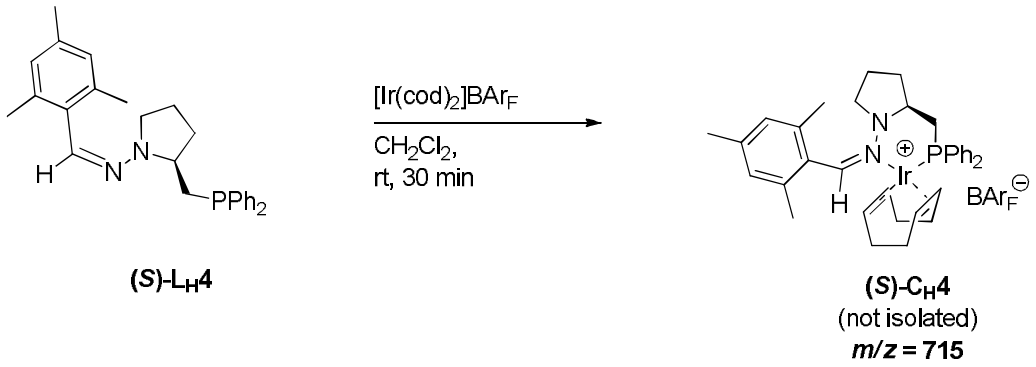
Scheme 59. Synthesis of proline-based hydrazone ligand **(*S*)-L_H4** from aldehydes.

Since the condensation of the hydrazine **(*S*)-131** with aldehyde (**133**) was straightforward (Scheme 59), other aldhydrazones were prepared (Scheme 61). The synthesis of aldhydrazones was carried out from hydrazine **(*S*)-114**, following the retrosynthetic analysis depicted in Scheme 51. Aldhydrazones **(*S*)-L_H4**, **(*S*)-L_H5** and **(*S*)-L_H6** were prepared by this method. The yields for the condensation reactions were moderate and ranged from 49% to 62% (Scheme 61).



Scheme 61. Synthesis of proline-based aldhydrazones **(*S*)-L_H4**, **(*S*)-L_H5** and **(*S*)-L_H6**.

Complexation of **(*S*)-L_H4** to iridium was carried out *in situ* (Scheme 60). In contrast to phosphinohydrazones **(*S*)-L_H1** and **(*S*)-L_H2**, ligand **(*S*)-L_H4** formed only one iridium species upon complexation (see Figure 23). ESI-MS measurements supported the formation of the desired compound **(*S*)-C_H4** (*m/z* = 715).



(*S*)-L_H4 **(*S*)-C_H4** (not isolated) ***m/z* = 715**

Scheme 60. Complexation of phosphinohydrazone **(*S*)-L_H4** with iridium.

Figure 23 shows the ^{31}P NMR spectra of the free phosphinohydrazone ligand **(*S*)-L_H4** (black trace) and that of the corresponding **(*S*)-L_H4**/iridium complex (red trace). While the free ligand showed a chemical shift of $\delta = -22.6$ ppm, the signal was shifted downfield upon addition of the iridium source. Only one peak was observed when the ligand was complexed *in situ* with $[Ir(cod)_2]BAr_F$ in CD_2Cl_2: $\delta = -13.4$ ppm (red trace).

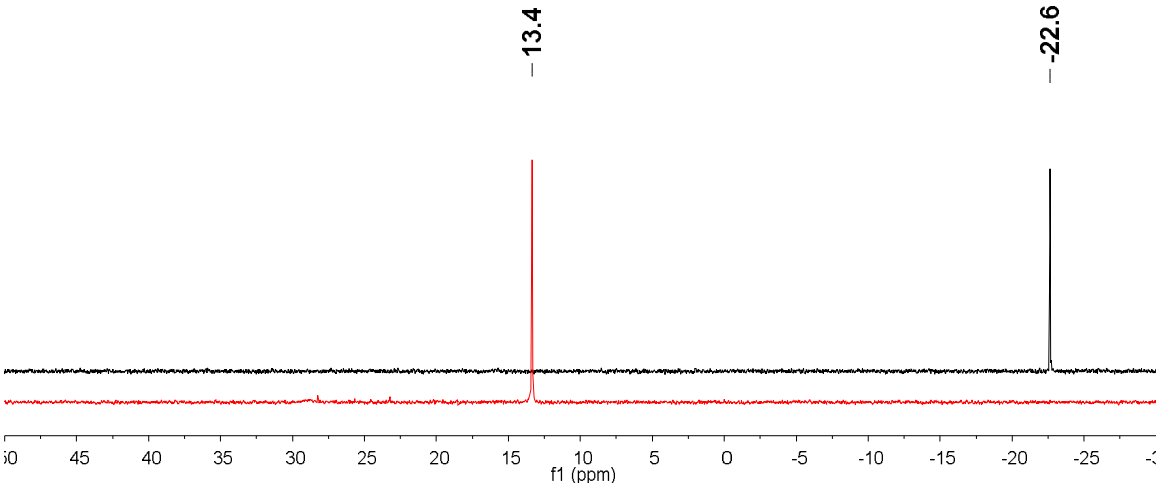


Figure 23. ^{31}P NMR Analysis of the iridium complex formed by coordination of **(*S*)-L_H4**.
In black: free ligand ***(S)-L_H4*** *in CD_2Cl_2; and in red:* ***(S)-L_H4****/Ir complex in CD_2Cl_2.*

However, complex **(*S*)-C_H4** proved very sensitive to moisture and could not be isolated. All attempts to purify the compound by: (1) column chromatography; (2) recrystalization or (3) washing of the crude product with *n*-pentane in order to remove the free cyclooctadiene, resulted in partial decomposition of **(*S*)-C_H4**.

In addition, the complex **(*S*)-C_H4** formed by *in situ* complexation with $[Ir(cod)_2]BAr_F$ in absolute CD_2Cl_2 was shown to form a different species over time (Figure 24). Even

tough, the solvent was treated with basic aluminum oxide prior to use. Upon decomposition of **(*S*)-C_H4**, the formation of a broad signal (δ = 28.8 ppm) was observed (blue trace). The same signal was observed, when the purification and isolation of the complex was attempted. Further investigations to identify this second species were not conclusive.

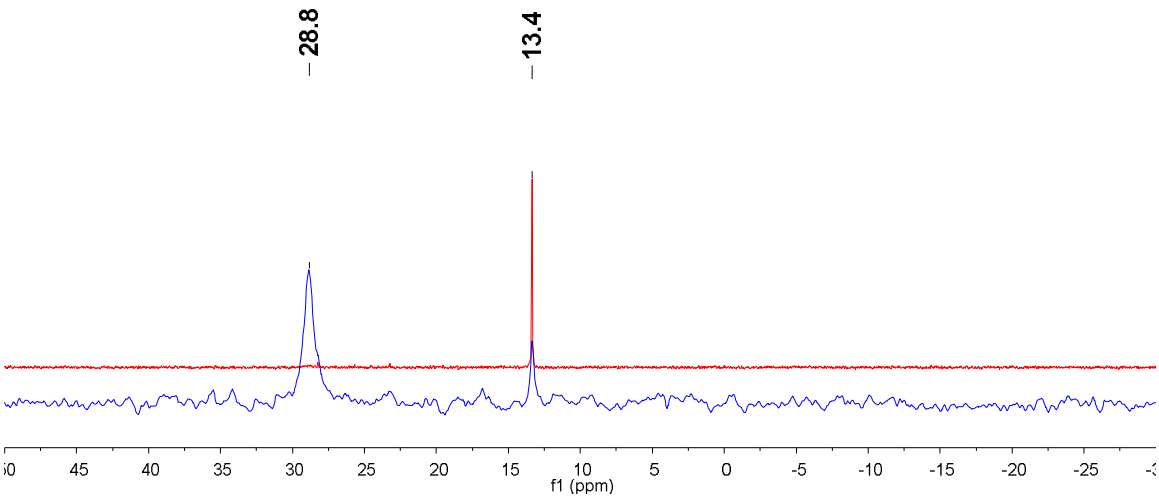


Figure 24. ^{31}P NMR Analysis revealing the decomposition of the iridium complex **(*S*)-C_H4**.
In red: freshly prepared complex in CD_2Cl_2; and in blue: the same complex approximately 2 hours after preparation.

The complexation of **(*S*)-L_H5** and **(*S*)-L_H6** showed similar characteristics to the complexation of ligand **(*S*)-L_H4**. Therefore, these complexes were not isolated and prepared *in situ* for an initial screening as catalysts for the iridium-catalyzed asymmetric hydrogenation.

The complex **(*S*)-C_H6** formed by *in situ* complexation with [Ir(cod)$_2$]BAr_F in absolute CD_2Cl_2 showed as well two signals in the ^{31}P NMR spectra: δ = 10.7 ppm and δ = 38.8 ppm in a ratio close to 4:1. Nevertheless, crystals suitable for X-ray analysis were obtained by crystallization from the stock solution of precatalyst prepared by *in situ* complexation and layered with *n*-pentane (see Figure 25). The solid state structure shows the expected bidentate coordination. The ligand forms a six-membered metallacycle upon coordination through the second hydrazone nitrogen and the phosphorus atom to the iridium center.

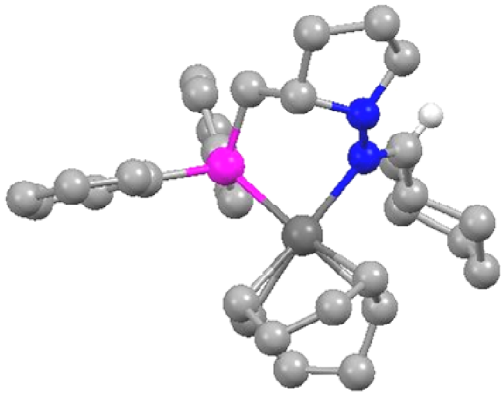


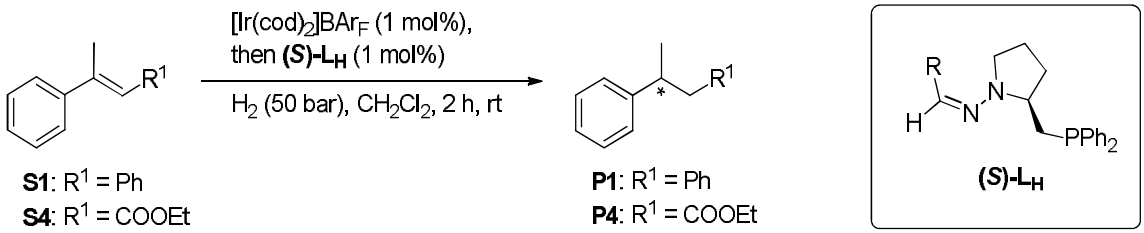
Figure 25. Crystal structure of complex [(**(*S*)-L_H6**)Ir(cod)]BAr_F. The counterion has been omitted for clarity (blue N, magenta P, dark gray Ir, light gray C; Ir−P bond (2.27 Å), Ir−N bond (2.13 Å), N−N bond (1.40 Å), and P−Ir−N angle (84.7°)).

4.2.2 Iridium-Catalyzed Asymmetric Hydrogenations with Proline-Based Phosphinohydrazones Ligands

As described above, three aldhydrazones (**(*S*)-L_H4**, **(*S*)-L_H5** and **(*S*)-L_H6**) were prepared and complexed *in situ* to iridium. Next, the potential of these chiral phosphinohydrazones as ligands for iridium catalysis was investigated. The catalysts were formed *in situ* by complexation prior to the hydrogenation reaction, but were used directly after preparation, in order to minimize the formation of the unknown second species (see Figure 24).

The results of the iridium-catalyzed asymmetric hydrogenation of alkenes **S1** and **S4** are reported in Table 51. Excellent conversions were obtained by the use of these phosphinohydrazones **(*S*)-L_H4** to **(*S*)-L_H6** as chiral ligands for iridium; conversions of 99% and more were measured in all cases after only 2 hours. However, the enantioselectivities achieved in this catalytic transformation were fluctuating. In fact, for a same test reaction, the values were not reproducible and varied over a large range of values. For example in the asymmetric reduction of **S1,** the use of ligand **(*S*)-L_H4** afforded up to 91% *ee* of the (*R*)-configured alkane **P1** (entry 1). When the same reaction was repeated several times, the values were never consistent, ranging from 23% *ee* (*R*) to 91% *ee* (*R*).

Table 51. Iridium-catalyzed asymmetric hydrogenation of (*E*)-1,2-diphenyl-1-propene (**S1**) and (*E*)-ethyl 3-phenylbut-2-enoate (**S4**), using proline-based hydrazone ligands **(*S*)-L_H**.[a]



S1: R^1 = Ph
S4: R^1 = COOEt

P1: R^1 = Ph
P4: R^1 = COOEt

(*S*)-L_H

Entry	Substrate	Ligand	R	Yield [%][b]	*ee* [%][c]
1	**S1**	**(*S*)-L_H4**	Mes	> 99	61 (*R*)[d] [91 (*R*)][e]
2	**S4**	**(*S*)-L_H4**	Mes	> 99	54 (*R*)[d] [84 (*R*)][e]
3	**S1**	**(*S*)-L_H5**	*t*Bu	> 99	24 (*S*)[d] [29 (*S*)][e]
4	**S4**	**(*S*)-L_H5**	*t*Bu	> 99	12 (*S*)
5	**S1**	**(*S*)-L_H5**	Cy	> 99	23 (*R*)[d] [34 (*R*)][e]
6	**S4**	**(*S*)-L_H6**	Cy	> 99	21 (*R*)

[a] Reaction scale: $[Ir(cod)_2]BAr_F$ (1.25 µmol), ligand (1.25 µmol), solvent (0.25 mL), substrate (125 µmol); [b] Yields were determined by GC analysis (see experimental part); [c] Enantioselectivities were determined by GC analysis using a chiral stationary phase (see experimental part); [d] Average of 2-4 experiments; [e] Best enantiomeric excess obtained.

Irreproducibility of the results was also observed with the other catalysts in the asymmetric hydrogenation of **S1** and **S4**. Therefore, the average *ee*-value obtained is given and in brackets the best enantiomeric excess obtained for each test reaction is shown. Although, the enantiomeric excesses showed large fluctuations, it seems that the mesityl-substituted ligand **(*S*)-L_H4** furnishes higher enantioinduction than its *tert*-butyl- and cyclohexyl-substituted analogues (**(*S*)-L_H5** and **(*S*)-L_H6**).

These results indicate that decomposition of the complex occurs faster than the hydrogenation reaction with **(*S*)-C_H4**. In addition, the unidentified species might as well be an active reducing agent, which would explain the complete conversions and fluctuating selectivities.

4.3 Conclusion

Only a few proline-based phosphinohydrazones derived from aldehydes were synthesized. The synthesis of phosphinohydrazones from ketones proved to be difficult. Both types of compounds, ketohydrazones and aldhydrazones, were complexed to iridium but different issues arised. Whereas the *in situ* complexation of aldhydrazones was

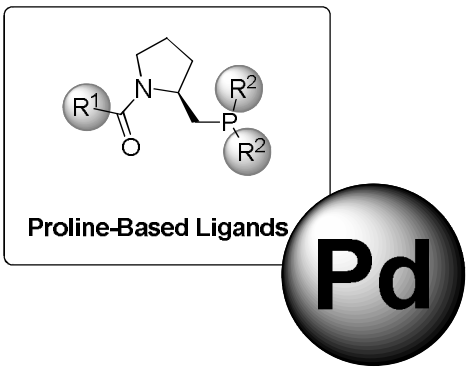
successful, ketohydrazones formed only mixtures of several iridium species, which could not be separated and clearly identified.

Aldhydrazone iridium complexes, were not stable and decomposed. Nevertheless, they were tested in the iridium-catalyzed asymmetric hydrogenation of alkenes. Full conversions to the desired reduction product were obtained. The enantioselectivities are fluctuating and it is likely that the decomposition process is fast and interferes with the desired asymmetric reduction of the substrate. The decomposition process was not investigated. These initial results suggest that these ligands are too sensitive to be practical.

However, an X-ray structure of a phosphinohydrazone/iridium complex was obtained and confirms the expected bidentate coordination mode of aldhydrazones to iridium.

CHAPTER 5

PROLINE-BASED LIGANDS FOR PALLADIUM-CATALYZED ALLYLIC ALKYLATION REACTION



5.1 Privileged Chiral Ligands for Asymmetric Catalysis

So called, *privileged ligands*, are chiral ligands, which can be applied to various asymmetric catalytic reactions.[120] As described in chapter 2, proline-based amidophosphines and ureaphosphines were applied successfully in the iridium-catalyzed asymmetric hydrogenation of trisubstituted alkenes and furnished high enantioselectivities for certain classes of substrates. Because palladium complexes with P,N ligands have proved to be efficient catalysts for allylic substitution, it was explored whether these proline-based ligands can also be applied to these reactions. First in this chapter, will be given an overview of *privileged ligands* for metal catalysis which are known today (see section 5.1) and then the results obtained when these proline-based ligands were applied to palladium catalysis will be presented (see section 5.3.2). Moreover, attempts to elucidate the coordination mode of these ligands to palladium will be discussed.

Several ligand classes have been shown to have a general scope and were applied to more than one transition metal-catalyzed reaction. To these chiral ligands was given the status of *privileged ligands*. Figure 26 shows some of these *privileged chiral ligands* and gives an overview of the reactions they were used in. Only the most common enantioselective transition metal-catalyzed transformations are depicted.

The non-symmetrical and modular phosphinooxazolines **(*S*)-L$_{PHOX}$** for example were applied as P,N ligands in various metal-catalyzed reactions.[121] They were not only applied to iridium-catalyzed enantioselective hydrogenation of imines and trisubstituted alkenes, but also in the palladium-catalyzed allylic alkylation and Heck reaction and in the iridium-catalyzed intramolecular Pauson−Khand reaction.[121]

[120] a) T. P. Yoon, E. N. Jacobsen, *Science* **2003**, *299*, 1691-1693; b) *Privileged Chiral Ligands and Catalysts* (ed. Q.-L. Zhou), Wiley-VCH, Weinheim, **2011**.
[121] For catalytic asymmetric reactions involving PHOX ligands see: a) P. Von Matt, A. Pfaltz, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 566-568; b) J. Sprinz, G. Helmchen, *Tetrahedron Lett.* **1993**, *34*, 1769-1772; c) G. J. Dawson, C. G. Frost, J. M. Williams, S. J. Coote, *Tetrahedron Lett.* **1993**, *34*, 3149-3150; d) O. Loiseleur, P. Meier, A. Pfaltz, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 200-202; e) O. Loiseleur, M. Hayashi, N. Schmees, A. Pfaltz, *Synthesis* **1997**, 1338-1345; f) Z.-L. Lu, E. Neumann, A. Pfaltz, *Eur. J. Org. Chem.* **2007**, 4189-4192.

Other ligands, which have been presented previously herein as important ligands for transition metal-catalyzed asymmetric hydrogenations are: BINAP or SEGPHOS, and DuPhos or BPE phospholanes. BINAP and SEGPHOS ligands form two large families of related ligands. Both are based on a biphenyl architecture with a C_2 axial chirality; BINAP is based on a bisnaphthalene backbone and SEGPHOS on a bis(1,3-benzodioxole) backbone. Nevertheless, SEGPHOS ligands lead often to higher enantioselectivities and therefore SEGPHOS (**(*R*$_a$)-L$_{\mathbf{SEGPHOS}}$**) is depicted in Figure 26. SEGPHOS not only proved to be efficient in the enantioselective hydrogenation of amino ketones,[122a] but also in 1,4-additions of arylboronic acids to coumarins (rhodium-catalyzed);[122b] hydrosilylations of ketones (copper-catalyzed);[122c-d] and in reductive aminations (ruthenium-catalyzed).[122e] C_2-Symmetric bis(phospholanes), **(*R*,*R*)-L$_{\mathbf{DuPhos}}$** and **(*R*,*R*)-L$_{\mathbf{BPE}}$** form as well an extensive ligand library. They have proven to be efficient in the rhodium-catalyzed asymmetric hydrogenation of enamides, enol esters, ketoesters, imines and other substrates,[123a-d] as well as in the copper-catalyzed allylboration of ketones.[123f]

Chiral bisoxazolines (**(*S*,*S*)-L$_{\mathbf{BOX}}$**) promote a great number of asymmetric reactions, involving various transition metals.[124] BOX ligand and their derivatives were used mostly in copper-catalyzed reactions, as: cyclopropanation of alkenes,[124d-f] and aziridination of styrenes.[124g] BOX ligands were also applied to Diels−Alder reactions.[124i-j]

[122] For catalytic asymmetric reactions involving SEGPHOS ligands see: a) T. Ohkuma, D. Ishii, H. Takeno, R. Noyori, *J. Am. Chem. Soc.* **2000**, *122*, 6510-6511; b) G. Chen, N. Tokunaga, T. Hayashi, *Org. Lett.* **2005**, *7*, 2285-2288; c) D. Tomita, R. Wada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2005**, *127*, 4138-4139; d) B. H. Lipshutz, A. Lower, R. J. Kucejko, K. Noson, *Org.Lett.* **2006**, *8*, 2969-2972; e) H. Shimizu, I. Nagasaki, K. Matsumura, N. Sayo, T. Saito, *Acc. Chem. Res.* **2007**, *40*, 1385-1393.

[123] For catalytic asymmetric reactions involving DuPhos and BPE phospholane ligands see: a) M. J. Burk, J. E. Feaster, *J. Am. Chem. Soc.* **1992**, *114*, 6266-6267; b) M. J. Burk, J G. Allen, W. F. Kiesman, *J. Am. Chem. Soc.* **1998**, *120*, 657-663; c) M. J. Burk, T. G. P. Harper, C. S. Kalberg, *J. Am. Chem. Soc.* **1995**, *117*, 4423-4424; d) M. J. Burk, F. Bienewald, S. Challenger, A. Derrick, J. A. Ramsden, *J. Org. Chem.* **1999**, *64*, 3290-3298; e) C. González-Arellano, A. Corma, M. Iglesias, F. Sánchez, *Chem. Commun.* **2005**, 3451-3451; f) R. Wada, K. Oisaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2004**, *126*, 8910-8911; g) A. Côté, V. N. G. Lindsay, A. B. Charrette, *Org. Lett.* **2007**, *9*, 85-87.

[124] For catalytic asymmetric reactions involving BOX ligands see: a) G. Desimoni, G. Faita, K. A. Jørgensen, *Chem. Rev.* **2006**, *106*, 3561-3651; b) A. K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron: Asymmetry* **1998**, *9*, 1-45; c) J. S. Johnson, D. A. Evans, *Acc. Chem. Res.* **2000**, *33*, 325-335; d) D. A. Evans, K. A. Woerpel, M. M. Hinman, M. M. Faul, *J. Am. Chem. Soc.* **1991**, *113*, 726-728; e) E. Jezek, A. Schall, P. Kreitmeier, O. Reiser, *Synlett* **2005**, 915-918; f) R. B. Chor, B. Nosse, S. Sörgel, C. Böhm, M. Seitz, O. Reiser, *Chem. Eur. J.* **2003**, *9*, 260-270; g) D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson, D. M. Barnes, *J. Am. Chem. Soc.* **1993**, *115*, 5328-5329; h) Z. Sun, S. Yu, Z. Ding, D. Ma, *J. Am. Chem. Soc.* **2007**, *129*, 9300-9301; i) D. A. Evans, S. J. Miller, T. Lecta, *J. Am. Chem. Soc.* **1993**, *115*, 6460-6461; j) E. J. Corey; N. Imai, H.-Y. Zhang, *J. Am. Chem. Soc.* **1991**, *113*, 728-729; k) K. Juhl, N. Gathergood, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2001**, *40*, 2995-2997.

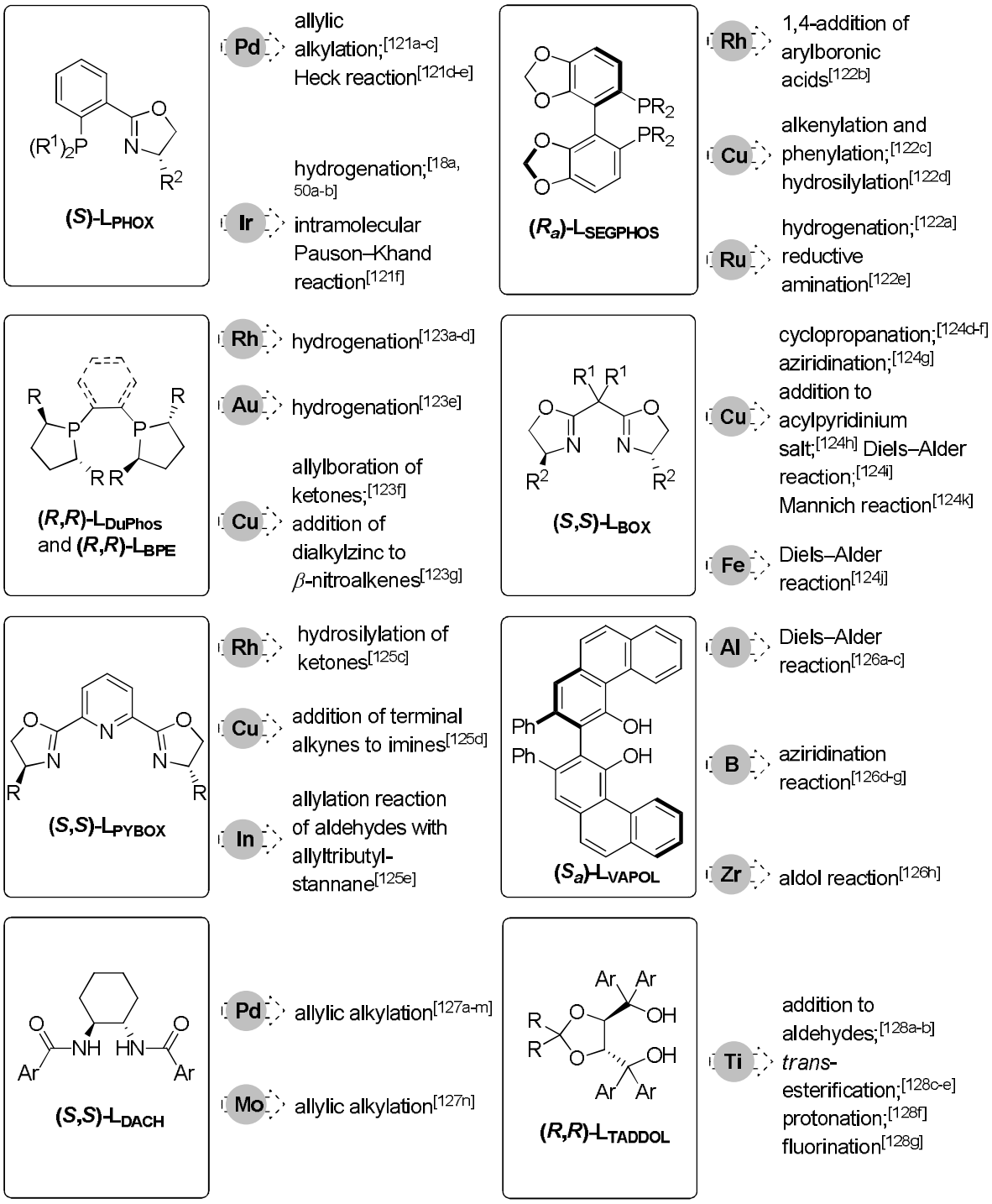


Figure 26. *Privileged ligands* for asymmetric catalysis.[120]

PYBOX ligands (**(*S*,*S*)-L$_{PYBOX}$**), which are constituted of a pyridine-ring flanked by two oxazoline groups are related to BOX ligands.[125a-b] They were applied to the rhodium-

[125] For catalytic asymmetric reactions involving PYBOX ligands see: a) G. Desimoni, G. Faita, P. Quadrelli, *Chem. Rev.* **2003**, *103*, 3119-3154; b) H. Nishiyama, H. Sakaguchi, T. Nakamura, M. Horihata, M. Kondo, K. Itoh, *Organometallics* **1989**, *8*, 846-848; c) H. Nishiyama, S.-B. Park, K. Itoh, *Tetrahedron:*

catalyzed hydrosilylation of ketones,[125c] and to the copper-catalyzed addition of terminal alkynes to imines.[125d]

BINOL and its related axially chiral biaryl ligands form a widely used class of ligands in asymmetric synthesis and were applied to many reactions, such as Diels−Alder reaction, carbonyl additions and reductions and Michael addition. Herein, VAPOL (3-3'-biphenantrol) is depicted as a representative axially chiral biaryl ligand. This ligand has proven to be highly efficient in catalytic asymmetric Diels−Alder, aldol and aziridination reactions.[126]

C_2-symmetric diaminocyclohexyl ligands (**(*S*,*S*)-L_{DACH}**), were designed for asymmetric allylic alkylation reactions.[127] Many nucleophiles can be employed to form multiple types of bonds (carbon, oxygen and nitrogen nucleophiles). DACH ligands were used efficiently for this reaction, both palladium and molybdenum catalysts can be employed.

Many other ligands have been used in many asymmetric reactions.[120] Although, TADDOLs (*α*,*α*,*α*,*α*-tetraaryl-1,3-dioxolane-4,5-dimethanols, **(*R*,*R*)-L_{TADDOL}**) have found numerous applications in asymmetric synthesis, generally their titanium complexes were used.[128]

Asymmetry **1992**, *3*, 1029-1034; d) C. Wei, C.-J. Li, *J. Am. Chem. Soc.* **2002**, *124*, 5638-5639; e) J. Lu, M.-L. Hong, S.-J. Ji, T.-P. Loh, *Chem. Commun.* **2005**, 1010-1012.

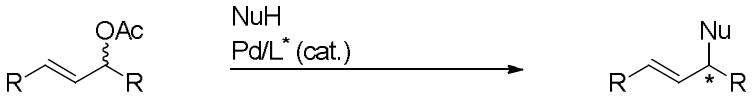
[126] For catalytic asymmetric reactions involving VAPOL ligands see: a) J. Bao, W. D. Wulff, A. L. Rheingold, *J. Am. Chem. Soc.* **1993**, *115*, 3814-3815; b) J. Bao, W. D. Wulff, *Tetrahedron Lett.* **1995**, 36, 3321-3324; c) D. P. Heller, D. R. Goldberg, W. D. Wulff *J. Am. Chem. Soc.* **1997**, *119*, 10551-10552; d) J. C. Antilla, W. D. Wulff, *Angew. Chem. Int. Ed.* **2000**, *39*, 4518-4521; e) C. Loncaric, W. D. Wulff, *Org. Lett.* **2001**, *3*, 3675-3678; f) A. P. Patwardhan, V. R. Pulgam, Y. Zhang, W. D. Wulff, *Angew. Chem. Int. Ed.* **2005**, *44*, 6169-6172; g) A. P. Patwardhan, Z. Lu, V. R. Pulgam, W. D. Wulff, *Org. Lett.* **2005**, *7*, 2201-2204; h) S. Xue, S. Yu, Y. Deng, W. D. Wulff, *Angew. Chem. Int. Ed.* **2001**, *40*, 2271-2274.

[127] For catalytic asymmetric reactions involving DACH ligands see: a) B. M. Trost, D. L. Van Vranken, *Chem. Rev.* **1996**, *96*, 395-422; b) B. M. Trost, M. R. Machacek, A. Aponick, *Acc. Chem. Res.* **2006**, *39*, 747-760; c) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921-2943; d) B. M. Trost, *Acc. Chem. Res.* **1996**, *29*, 355-364; e) B. M. Trost, R. C. Bunt, *J. Am. Chem. Soc.* **1994**, *116*, 4089-4090; f) M. Ernst, G. Helmchen, *Angew. Chem. Int. Ed.* **2002**, *41*, 4054-4056; g) B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1999**, *121*, 3543-3544; h) B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **2003**, *125*, 3090-3100; i) B. M. Trost, M. L. Crawley, *J. Am. Chem. Soc.* **2002**, *124*, 9328-9329; j) B. M. Trost, M. J. Krische, R. Radinov, G. Zanoni, *J. Am. Chem. Soc.* **1996**, *118*, 6297-6298; k) B. M. Trost, S. R. Pulley, *J. Am. Chem. Soc.* **1995**, *117*, 10143-10144; l) B. M. Trost, D. L. Van Vranken, *J. Am. Chem. Soc.* **1993**, *115*, 444-458; m) B. M. Trost, D. L. Van Vranken, C. Bingel, *J. Am. Chem. Soc.* **1992**, *114*, 9327-9343; n) B. M. Trost, K. Dogra, *Org. Lett.* **2007**, *9*, 861-863.

[128] For catalytic asymmetric reactions involving TADDOL ligands see: a) D. Seebach, A. K. Beck, A. Heckel, *Angew. Chem., Int. Ed.* **2001**, *40*, 92-138; b) R. O. Duthaler, A. Hafner, *Chem. Rev*. **1992**, *92*, 807-832; c) D. Seebach, G. Jaeschke, Y. M. Wang, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2395-2396; d) G. Jaeschke, D. Seebach, *J. Org. Chem.* **1998**, *63*, 1190-1197; e) D. Seebach, R. Dahinden, R. E. Marti, A. K. Beck, D. A. Plattner, F. N. M. Kühnle, *J. Org. Chem.* **1995**, *60*, 1788-1799; f) A. Cuenca, M. Medio-Simón, G. Asensio Aguilar, D. Weibel, A. K. Beck, D. Seebach, *Helv. Chim. Acta* **2000**, *83*, 3153-3162; g) L. Hintermann, A Togni, *Angew. Chem. Int. Ed.* **2000**, *39*, 4359-4362.

5.2 Palladium-Catalyzed Allylic Alkylation Reaction

The palladium-catalyzed asymmetric allylic alkylation has proven to be an exceptionally powerful method for the construction of stereogenic centers (Scheme 62). This method permits to form multiple types of bond (C−C, C−O, C−S and C−N bonds). The allylic alkylation methodology has been intensively studied and can be catalyzed by various transition metals, such as palladium, iridium, nickel, molybdenum or platinum.[129] In addition, a large number of ligands have been developed and optimized for this asymmetric transformation. Nevertheless, the most import examples have been shown in Figure 26 above to be PHOX and DACH ligands derivatives.[126a,129]

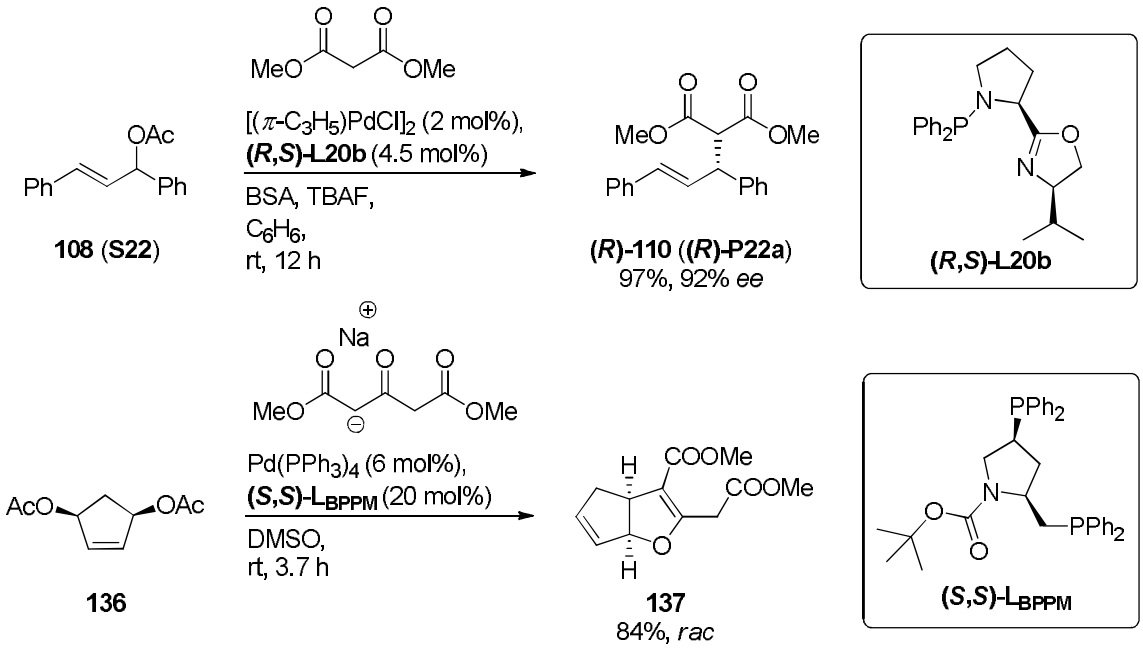


Scheme 62. Palladium-catalyzed allylic alkylation reaction.

5.3 Palladium-Catalyzed Allylic Alkylation Reaction with Proline-Based Ligands

Although, chiral proline-based ligands have been applied as ligands in asymmetric palladium-catalyzed allylic alkylation reactions, the selectivities were lower than with state-of-the-art ligands. GILBERTSON *et al.* studied the proline-based phosphinooxazoline **(*R*,*S*)-L20b**, as a ligand for the palladium-catalyzed alkylation of dimethyl malonate (Scheme 63).[130] SHIBASAKI *et al.* tested the well known BPPM ligand (**(*S*,*S*)-L_{BPPM}**) in the palladium-catalyzed alkylation of cyclopentene diol derivatives to form cyclopentanoids.[131] High yields of the cyclized product were obtained, but no selectivity was observed (Scheme 63).

[129] a) A. Pfaltz, M. Lautens, *Allylic Substitution Reactions* in *Comprehensive Asymmetric Catalysis* (ed. E. N. Jacobsen, A. Pfaltz, and H. Yamamoto), Springer, Berlin, **1999**, 1st Ed., Vol. 2, pp. 833-884; b) B. M. Trost, *Asymmetric Allylic Alkylation Reactions* in *Catalytic Asymmetric Synthesis* (ed. I. Ojima), Wiley-VCH, New York, **2000**, 2nd Ed., pp. 593-649.
[130] G. Xu, R. Gilbertson, *Tetrahedron Lett.* **2002**, *43*, 2811-2814.
[131] M. Mori, S. Nukui, M. Shibasaki, *Chem. Lett*. **1991**, 1797-1800.



Scheme 63. Palladium-catalyzed allylic alkylation reaction with proline-based chiral ligands.

As shown by TOMIOKA *et al.* amidophosphine **(*S*)-L$_A$1** can be applied to rhodium-catalyzed 1,4-addition of boronic esters to enones, but also in the copper-catalyzed 1,4-addition of Grignard reagents to cyclic *α,β*-unsaturated carbonyl compounds (Figure 27).[66a,68a]. Derivatives of **(*S*)-L$_A$1**, were found to be efficient P,O ligands for the iridium-catalyzed asymmetric hydrogenation of various trisubstituted alkenes (see chapter 2).

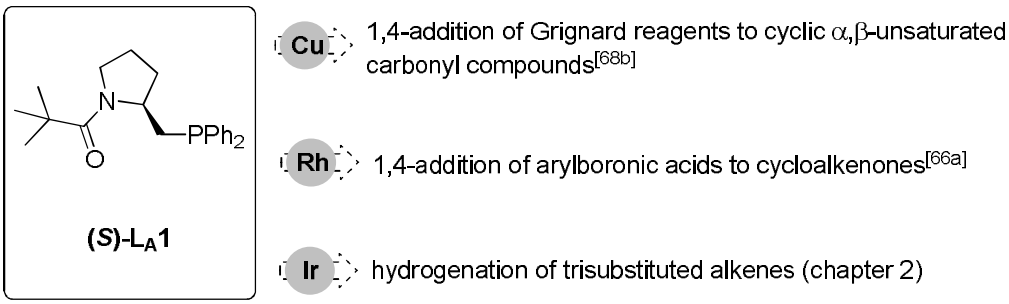


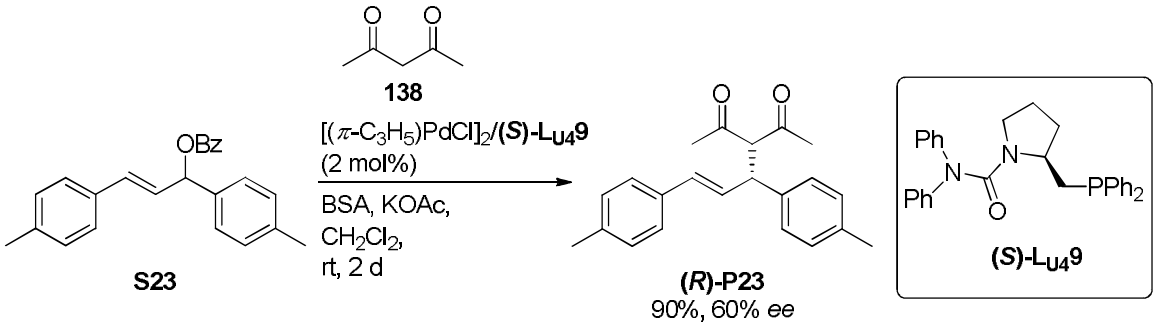
Figure 27. Applications of proline-based amidophosphine **(*S*)-L$_A$1** in asymmetric catalysis.

Therefore, these same proline-based P,O ligands, described in chapter 2, were applied to the palladium-catalyzed allylic alkylation. This reaction was chosen to evaluate the potential of these ligands, since the privileged PHOX ligand was highly efficient in both, the iridium-catalyzed asymmetric hydrogenation and the palladium-catalyzed allylic alkylation reaction. In addition, it was thought to be more interesting to investigate a

transition metal, different from those that were already investigated for this ligand type, namely rhodium, copper and iridium. This project was carried out in collaboration with DR. CHRISTIAN EBNER within the PFALTZ group.

5.3.1
Initial Results

In an initial experiment the tetrasubstituted ureaphosphine ligand **(*S*)-L_{U4}9** was tested in the palladium-catalyzed allylic alkylation of (*E*)-1,3-di-*para*-tolylallyl-benzoate (**S23**) (Scheme 64). The tested tetrasubstituted ureaphosphine **(*S*)-L_{U4}9** gave product **P23** in 90% yield with an enantiomeric excess of 60%. This result was encouraging for further investigations. As this reaction is known to proceed with high enantioselectivity using for example PHOX ligands, it was chosen as test reaction for the screening of further proline-based ligands. All the screening reactions were carried out by DR. CHRISTIAN EBNER.

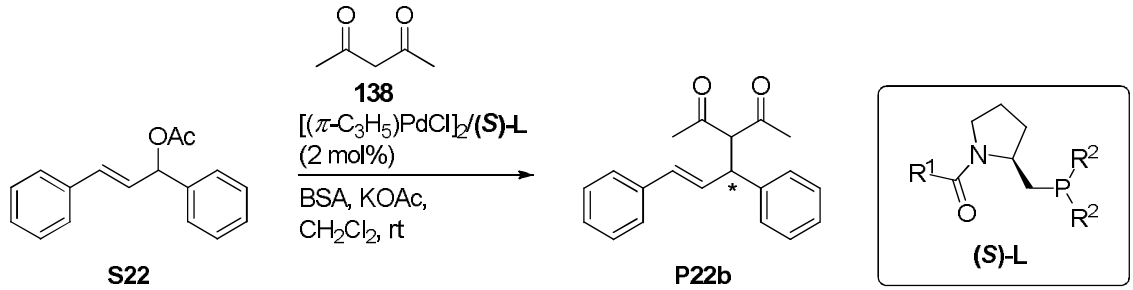


Scheme 64. Initial testing of proline-based ligands in the palladium-catalyzed allylic alkylation.

5.3.2
Palladium-Catalyzed Allylic Alkylation with Amido- and Ureaphosphine Ligands

Several other proline-based ligands were tested in the palladium-catalyzed allylic substitution of (*E*)-1,3-di-*para*-tolylallyl-acetate (**S22**) with dimethyl malonate as carbon nucleophile (Table 52). At least one representative of the different proline-based ligands described in chapter 2 was tested, namely, tetrasubstituted ureaphosphines (**(*S*)-L_{U4}9** and **(*S*)-L_{U4}10**), trisubstituted ureaphosphines (**(*S*)-L_{U3}19**) and amidophosphines (**(*S*)-L_A13** and **(*S*)-L_A14**).

Table 52. Palladium-catalyzed allylic alkylation of (*E*)-1,3-diphenylallyl-acetate (**S22**), using proline-based ligands.



S22 **P22b**

Entry	Ligand	R^1	R^2	*t* [h]	Yield [%][a]	*ee* [%][b]
1	**(*S*)-L_{U3}19**	NHPh	Ph	24	92	47 (*R*)
2	**(*S*)-L_{U4}9**	NPh_2	Ph	17	94	54 (*R*)
3[c]	**(*S*)-L_{U4}9**	NPh_2	Ph	17	56	52 (*R*)
4[d]	**(*S*)-L_{U4}9**	NPh_2	Ph	89	70	62 (*R*)
5	**(*S*)-L_{U4}10**	NPh_2	*o*Tol	42	28	62 (*S*)
6	**(*S*)-L_A13**	CPh_3	Ph	16	92	49 (*R*)
7	**(*S*)-L_A14**	CPh_3	*o*Tol	39	26	50 (*S*)

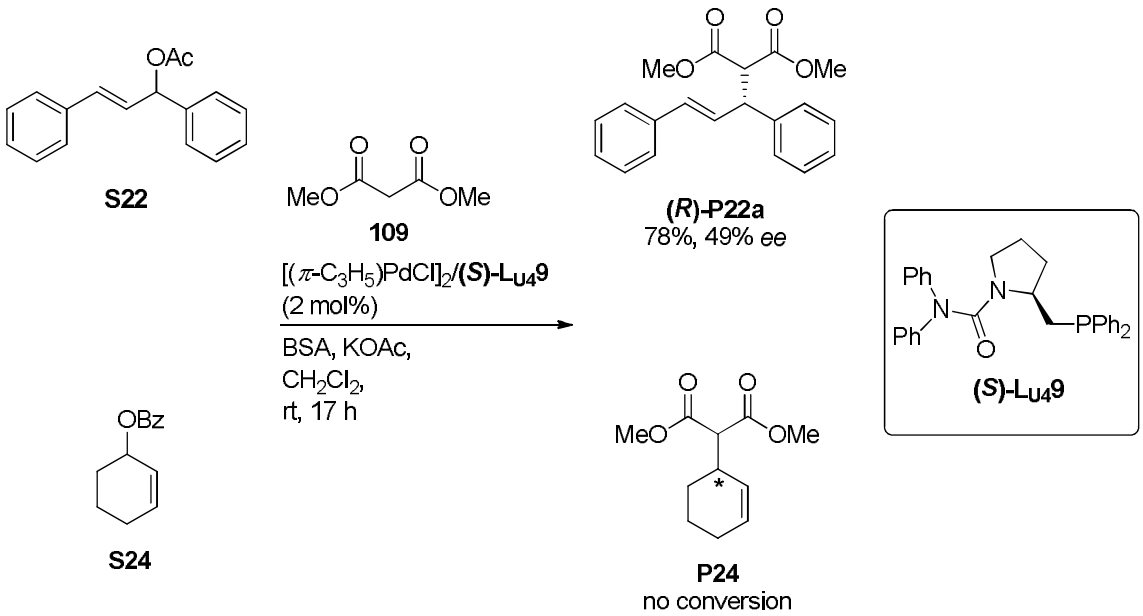
[a] Yields were isolated; [b] Enantioselectivities were determined by HPLC analysis using a chiral stationary phase (see experimental part); [c] 5 mol% $NaBAr_F$ was used as an additive; [d] The reaction was carried out in toluene.

In all cases conversion to the desired compound was found. Furthermore all catalysts led to enantioenriched product in the range of 50 to 60% *ee*. Diphenylphosphines as ligands allowed for higher activity of the catalyst compared to di-*ortho*-tolylphosphines (entries 1, 2, 6 *versus* 5, 7). Interestingly, whenever the di-*ortho*-tolylphosphine derivatives were used the reaction resulted in the formation of the other product enantiomer compared to the reactions using the diphenylphosphine derivatives although the configuration of the stereogenic center of the ligand was the same for all ligands.

When it was tried to optimize the reaction conditions in order to increase the selectivity of the catalysts, both, a change in solvent and the addition of an additive did not lead to the desired effect. The use of toluene as solvent, instead of dichloromethane resulted in a slight increase in selectivity (62% *ee versus* 54% *ee*), but reduced the activity of the catalyst (70% *versus* 94% yield, entries 2 and 4). The addition of $NaBAr_F$ as additive, which is known to accelerate the reaction *via* anion exchange as reported by LLOYD-JONES *et al.* had a negative impact on both, activity and selectivity of the catalyst (entry 3).[132]

[132] L. A. Evans, N. Fey, J. N. Harvey, D. Hose, G. C. Lloyd-Jones, P. Murray, A. G. Orpen, R. Osborne, G. J. J. Owen-Smith, M. Purdie, *J. Am. Chem. Soc.* **2008**, *130*, 14471-14473.

In order to test a different nucleophile, (*E*)-1,3-diphenylallyl acetate (**S22**) was reacted with dimethyl malonate (**109**) using the tetrasubstituted ureaphosphine **(*S*)-L$_{U4}$9** as ligand (Scheme 65). The desired reaction product **P22a** was formed and isolated in 78% yield with an enantiomeric excess of 49%.



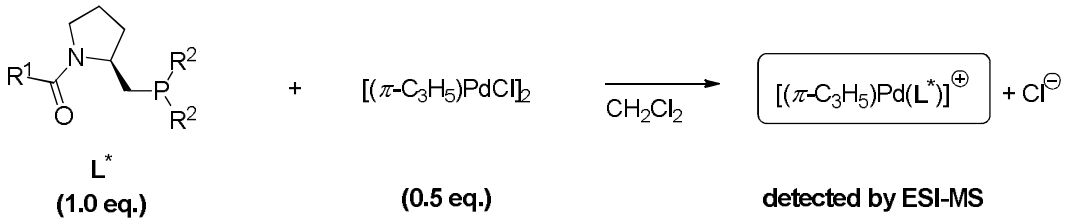
Scheme 65. Palladium-catalyzed allylic alkylation of (*E*)-1,3-diphenylallyl-acetate (**S22**) and cyclohex-2-en-1-yl-benzoate (**S24**), using the proline-based ligand **(*S*)-L$_{U4}$9**.

Further, cyclohex-2-en-1-yl benzoate (**S24**) was tested as substrate (Scheme 65). Again dimethyl malonate was used as nucleophile. Unfortunately, using **(*S*)-L$_{U4}$9**, no conversion to the desired product was observed even after 3 days reaction time.

5.3.3
Analysis of the Coordination Mode to Palladium

In order to determine, the coordination mode of these proline-based ligands to palladium, ESI-MS and NMR analyses were carried out for three ligands (**(*S*)-L$_{U3}$19**, **(*S*)-L$_{U4}$10** and **(*S*)-L$_{A}$14**). The main intention was to find out whether these ligands bind to palladium in a bidentate fashion, as it was shown to be the case with iridium or in a hemilabile manner, as it was shown to be the case for rhodium.[66,67]

First, ESI-MS analyses of the *in situ* prepared precatalysts performed (Scheme 66). When the ligands **(*S*)-L_{U3}19**, **(*S*)-L_{U4}10** and **(*S*)-L_A14** were reacted with $[(\pi\text{-}C_3H_5)PdCl]_2$ in dichloromethane and the resulting mixtures were analyzed by ESI-MS, a signal corresponding to the mass of the respective $[(\pi\text{-}C_3H_5)Pd(\mathbf{L}^*)]^+$ complex was observed.



(*S*)-L_{U3}19: R^1 = NHPh, R^2 = Ph
(*S*)-L_{U4}10: R^1 = NPh_2, R^2 = *o*Tol
(*S*)-L_A14: R^1 = CPh_3, R^2 = *o*Tol

Scheme 66. ESI-MS Analysis of *in situ* formed precatalysts.

However, further signals with a lower mass were found, which could not be assigned. This finding does not prove that these ligands bind in a bidentate fashion palladium, but suggests that it is likely in order to occupy all coordination sites.

In order to gain further information about the coordination mode of these ligands, NMR studies were carried out. First, it was tested whether the phosphorus atom is coordinated to the metal center in the palladium complex. For this purpose ^{31}P NMR-spectra of the free ligands and the complexes were recorded to compare the corresponding chemical shifts.

Figure 28 shows such spectra for the tetrasubstituted ureaphosphine ligand **(*S*)-L_{U3}19**. While the free ligand showed a chemical shift at $\delta = -22.3$ ppm (red trace), the signal was shifted downfield upon addition of the palladium source. In CD_2Cl_2 (blue trace) two signals were found due to restricted rotation of the allyl moiety in the complex. When the NMR spectra was measured in DMSO-*d*6 (the complexation was carried out in dichloromethane as before) only one signal was observed. This observation confirms that the two signals seen, when measured in dichloromethane, origin from the presence of rotamers. Comparable observations were made for the *in situ* complexation of ligands **(*S*)-L_{U4}9** and **(*S*)-L_{U4}10**. Again a downfield shift of the signal of the phosphorus atom was observed upon coordination of the ligands to palladium. In CD_2Cl_2, rotamers were as

well observed and in DMSO-*d*6 only one signal was found for both complexes. These findings suggest that for all the tested ligands, coordination through the phosphorus atom takes place.

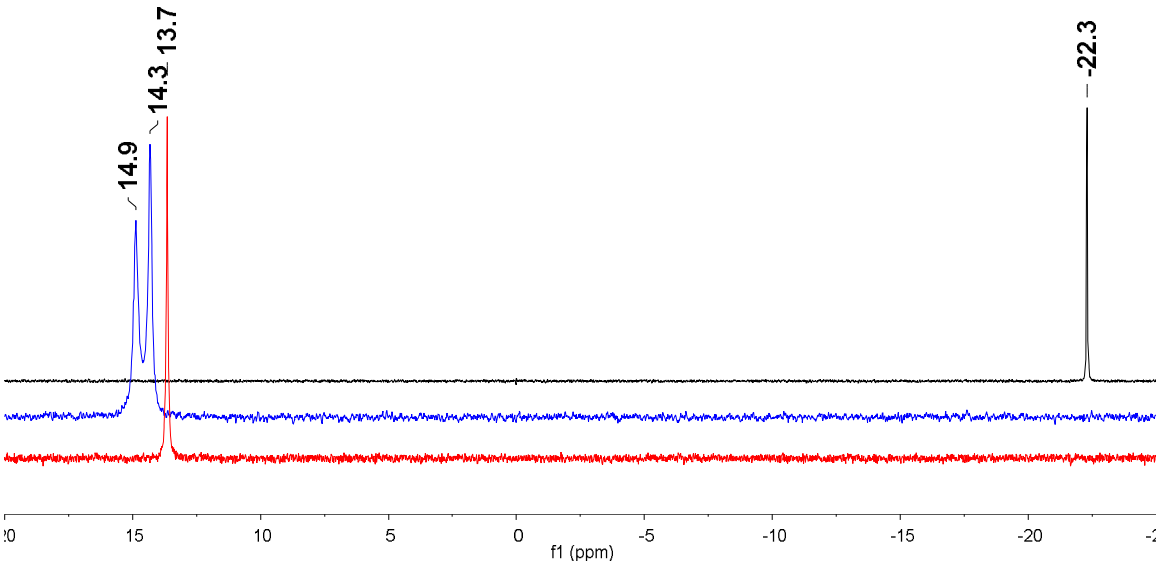


Figure 28. ^{31}P NMR Analysis of the palladium-precatalyst formed by coordination of **(*S*)-L$_{U3}$19** (in black: free ligand **(*S*)-L$_{U3}$19** in CD_2Cl_2; in blue: **(*S*)-L$_{U3}$19**/Pd complex in CD_2Cl_2; and in red: **(*S*)-L$_{U3}$19**/Pd complex in $(CD_3)_2SO$).

Next it was examined whether the carbonyl oxygen atom is as well coordinating to the palladium center. If this would be the case a significant change of the signal of the quaternary carbonyl carbon atom should be observed in the ^{13}C NMR spectra of the complexes. When, ureaphosphines and amidophosphines were found to coordinate to iridium as bidentate P,O ligands to iridium, the signal of the quaternary carbon atom was shifted by 9.2 ppm and 7.8 ppm downfield, respectively in the ^{13}C NMR spectra (see Tables 17 and 2 in chapter 2).

However, such a change in the chemical shift was not found, when the tested ligands were complexed to palladium (Table 53). In particular, the carbonyl function of the free ligands **(*S*)-L$_{U4}$10** showed the same chemical shift as in its respective palladium complex (δ = 158.7 ppm). The same signals were found for the analysis of the coordination of ligand **(*S*)-L$_{U4}$9** with the same chemical shift. For the trisubstituted ureaphosphine **(*S*)-L$_{U3}$19** a slight highfield shift was observed for the corresponding palladium complex (δ = 153.8 ppm for the free ligand and δ = 151.0 ppm). However, this does not prove that

the chemical shift is originating from complete coordination of the oxygen atom towards the palladium center.

Table 53. Comparison of the spectroscopic properties of the free ligands and their respective palladium precatalysts.

Compound[a-b]	**^{13}C NMR** [δ (C=O)]
(S)-L_{U3}19	153.8 ppm
(S)-L_{U3}19/Pd complex	151.0 ppm
(S)-L_{U4}9	158.7 ppm
(S)-L_{U4}9/Pd complex	158.8 ppm
(S)-L_{U4}10	158.7 ppm
(S)-L_{U4}10/Pd complex	158.7 ppm

[a] The *in situ* complexed ligands were analyzed: $[(\pi\text{-}C_3H_5)PdCl]_2$/ligand (0.5:1) in CD_2Cl_2; [b] The free ligands were analyzed in $CDCl_3$.

The small differences in the chemical shifts of the quaternary carbonyl atom suggest that these proline-based ligands coordinate in a monodentate fashion and that one coordination site is occupied by the chloride anion. However this does not exclude a reactive cationic P,O ligand/iridium complex as the catalytic intermediate. Attempts to isolate, the precatalyst in its solid state failed.

5.4 Conclusions and Outlook

In conclusion, the investigated proline-based ligands were shown to be applicable in the palladium-catalyzed allylic alkylation reaction. These palladium catalysts showed good activities but low selectivities. Considering, the high levels of enantioselectivities, which have been reported for these transformations, the catalyst tested herein are not competitive. Therefore, no further screening of ligands of this type and substrates were carried out. The analysis of the coordination manner, of these proline-based ligands to palladium was not conclusive. It was only confirmed that this ligands bind through their phosphorus atom to palladium.

From the results obtained herein, these ligands are most likely not well-suited for asymmetric palladium catalysis. Nevertheless, they could be tested in many other transition metal-catalyzed reactions, in order to define their potential. In addition, it would be interesting to test them as well in the iridium- or copper-catalyzed allylic

alkylation reaction, since they are known to coordinate to both of them. Currently, these same P,O ligands are investigated as ligands for the iridium-catalyzed Heck-reaction.

CHAPTER 6

EXPERIMENTAL PART

6.1
General Information

6.1.1
Working Techniques and Reagents

Commercially available reagents were purchased from *Acros*, *Aldrich* or *Fluka* and used as received. Diethylamine was distilled from calcium hydride.

All preparative reactions, involving a phosphine compound were carried out in flame-dried glassware under inert atmosphere using Schlenk techniques, except for the compounds synthesized according to **general procedure 2** (see section 6.1.2). All reactions were carried out in abs. solvents.

The solvents were collected from a purification column system (PureSolv, Innovative Technology Inc.) or purchased from *Aldrich* or *Fluka* in sure/sealed^{TM} bottles over molecular sieves.

Column chromatographic purifications were performed on *Fluka* silica gel 60 (Buchs, particle size 40-63 nm). The eluents were of technical grade and distilled prior to use.

The hydrogenation experiments were prepared under purified nitrogen in a glove box (MBraun Labmaster 130) and dichloromethane was purchased from Aldrich (≥ 99.5%, over molecular sieves).

6.1.2
Analytical Methods

Melting Points (m.p.): Melting points were determined on a Büchi 535 apparatus and are uncorrected.

Thin Layer Chromatography (TLC): TLC plates were obtained from Machrey-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): NMR spectra were measured either on a Bruker Avance 400 (400 MHz) or a Bruker Avance 500 (500 MHz) spectrometer. The chemical shifts (δ) are given in ppm. The chemical shift δ values were corrected to the signal of the deuterated solvents: 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR) for $CDCl_3$; 5.32 ppm (^{1}H NMR) and 53.5 ppm (^{13}C NMR) for CD_2Cl_2; and 2.50 ppm (^{1}H NMR) and 39.52 ppm (^{13}C NMR) for $(CD_3)_2SO$. ^{31}P NMR spectra are calibrated relative to 85% phosphoric acid (δ = 0 ppm) and ^{19}F NMR spectra relative to $CFCl_3$ (δ = 0 ppm) as external standards. ^{13}C and ^{31}P NMR spectra were recorded ^{1}H-decoupled. The assignment of ^{1}H and ^{13}C signals was accomplished, when needed by two-dimensional correlation experiments (COSY (correlation spectroscopy), HSQC (heteronuclear multiple quantum coherence) and HMBC (heteronuclear multiple quantum coherence)). Multiplets are assigned as: s (singlet), d (doublet), t (triplet), q (quartet), sept (septet) and m (multiplet). Broad signals are assigned with: br (broad).

Infrared Spectroscopy (IR): Infrared spectra were collected on a Shimadzu FTIR-8400S spectrometer. The compounds were measured as pure substance *via* Specac ATR attachment. When, the solid samples were measured as potassium bromide discs, the spectra were collected on a Perkin Elmer 1600 series FTIR spectrometer. The absorption bands are given in wave numbers ($\tilde{\nu}$ [cm^{-1}]). The peak intensity is described by: s (strong), m (medium), w (weak).

Mass Spectroscopy (MS): Mass spectra were measured by DR. HEINZ NADIG (Department of Chemistry, University of Basel) on a VG70-250 spectrometer (electron ionization (EI)) or on a MAR 312 spectrometer (fast atom bombardment (FAB)). FAB

was performed with 3-nitrobenzyl alcohol (NBA)) as matrix. ESI MS spectra were measured by DR. CHISTIAN EBNER and FLORIAN BÄCHLE (Department of Chemistry, University of Basel) on a Finnigan MAT LCQ. The signals are given in mass-to-charge ratios (*m/z*). The fragments and relative intensities are given in brackets.

Optical Rotations ($[\alpha]_D^{20}$): Optical rotations were measured on a Perkin Elmer Polarimeter 341 (in a cuvette (l = 1 dm)) at 20 °C at 589 nm. The concentration (c) is given in g/100 mL.

Elemental Analysis (EA): Elemental analyses were measured by WERNER KIRSCH and SYLVIE MITTELHEISSER (Department of Chemistry, University of Basel) on a Leco CHN-900 (C-, H-, N-detection). The data are indicated in mass percent.

High Resolution Mass Spectrometry (HRMS): High resolution mass spectra were recorded in the group of DR. STEFAN SCHÜRCH (Department for Chemistry and Biochemistry, University of Bern) on a Thermo Fisher Scientific LTQ Orbitrap XL (ESI-MS) spectrometer.

High Performance Liquid Chromatography (HPLC): HPLC analyses were performed on Shimadzu systems with SLC-10A system controller, CTO-10AC column oven, LC10-AD pump system, DGU-14A degasser and SPD-M10A diode array- or UV/VIS detector. Chiral columns Chiracel AD-H, AS-H, OB-H, OD-H, OJ or OJ-H (4.6 x 250 mm) from Daicel Chemical Industries were used.

Gas Chromatography (GC): Gas chromatograms were recorded on Carlo Erba HRGC Mega2 Series 800 (HRGS Mega2) instruments. Separations on achiral phases were performed on a Restek Rtx-1701 (30 m x 0.25 mm x 0.25 µmol) or a Macherey-Nagel Optima 5-Amin (0.25 mm x 0.25 µm x 30 m) column. Separations of enantiomers were achieved on a *Chiraldex* γ-cyclodextrin TFA G-TA (30 m x 0.25 mm x 0.12 µm) or a *Brechbühler* β-cyclodextrin DEtTButSil (SE54), (0.25 mm x 0.25 µm x 25 m) column.

6.2 General Synthetic Procedures

General procedure 1: synthesis of arylated phosphines[68c]

Hydrogen chloride (4.0 M in 1,4-dioxane, > 3.0 eq.) was added drop wise at 0 °C to a solution of the (*S*)-*Boc*-(2-phosphino)pyrrolidine precursor (**(*S*)-L_C1**, **(*S*)-L_C2**, **(*S*)-L_C3**, **(*S*)-L_C4·BH_3** or **(*S*)-L_C5·BH_3**, 300-500µmol, 1.0 eq., 7.0 M) in 1,4-dioxane. The mixture was stirred at room temperature for 1.5-2 hours and then reduced to dryness. The resulting crude was treated three times with benzene (2 x 2 mL) and then concentrated under high vacuum to afford a colorless foam. A solution of NEt_3 (> 3.0 eq.), the respective carbonyl compound (> 1.2 eq.) and the deprotected amine (2 M) in dichloromethane was stirred at 0 °C for 2 hours. The conversion was monitored by TLC analysis and in some cases the reaction mixture was allowed to warm to room temperature overnight. After addition of aqueous 10% Na_2CO_3, the mixture was extracted with dichloromethane (3 x). The combined extracts were washed successively with aqueous 10% HCl, aqueous saturated $NaHCO_3$, H_2O, brine, and then dried over $MgSO_4$. The solvent was evaporated and the crude product purified by column chromatography on silica gel. Unless otherwise noted all the synthesized compounds, were isolated as colorless solid foam after freezing the compounds in liquid N_2 and letting warm up under high vacuum for several hours.

General procedure 2: synthesis of alkylated phosphine borane adducts

The procedure is identical to **general procedure 1** but involves the use of K_2CO_3 (> 10 eq.) instead of NEt_3.

General procedure 3: deprotection of alkylated phosphine borane adducts

Borane-protected phosphine (100 µmol) was dissolved in $HNEt_2$ (3.0 mL) under argon and stirred at room temperature for 5-10 days. The conversion was monitored by ^{31}P NMR analysis. After completion of the reaction all volatiles were removed under high vacuum at 60 °C.

General procedure 4: synthesis of acyl chlorides from carboxylic acids

Carboxylic acid (400-500 μmol) was mixed with thionyl chloride (1 mL) and heated at reflux for 3 hours under inert atmosphere. The reaction mixture was allowed to cool to room temperature, before the excess thionyl chloride was removed *in vacuo* to afford the desired acyl chloride in quantitative yield. The product was used in the next synthetic step without further purification.

General procedure 5: synthesis of iridium complexes from $[Ir(cod)_2]BAr_F$

Ligand (50.0-100 mg, 1.0 eq.) and $[Ir(cod)_2]BAr_F$ (1.0 eq.)[73] were mixed in abs. CH_2Cl_2 (3-5 mL) and stirred for 30 minutes at room temperature. The solvent was evaporated and the residue was triturated with *n*-pentane (3 x 5 mL) before it was dried *in vacuo* for several hours. The desired complex was isolated as yellowish or orange solid.

General procedure 6: synthesis of phosphines (*S*)-L_{Ox}1, (*S*)-L_{Th}1, and (*S*)-L_{Im}1

Carbamatophosphine **(*S*)-L_C** was Boc-deprotected as described in **general procedure 1**, to afford the respective salt **(*S*)-52·HCl**, **(*S*)-57·HCl**, or **(*S*)-58·HCl** as a colorless foam. This salt (300-500 μmol, 1.0 eq.) was then dissolved in tetrahydrofuran (6 mL) and a 1.6 M solution of *n*-butyllithium (1.5 eq.) in hexanes was slowly added at – 78 °C in a acetone/dry ice bath. The resulting solution was then stirred for 30 minutes at – 78 °C and for 1 hour at room temperature, where it turned yellow. After cooling the solution again to – 78 °C, the desired heteroaromatic compound (**81**, **82** or **83**, 1.5 eq.) was added and the reaction mixture was allowed to warm to room temperature overnight. At 0 °C in an ice bath, aqueous saturated $NaHCO_3$ (5 mL) was added drop wise. Ethyl acetate (10 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and then reduced to dryness under reduced pressure. The crude was purified by column chromatography on silica gel.

General procedure 7: synthesis of proline-based P,N ligands

Phosphine (**94**, **50·BH_3** or **51·BH_3**) was dissolved in tetrahydrofuran (10 M) and a 1.6 M solution of *n*-butyllithium (1.1-1.2 eq.) in hexanes was slowly added at – 78 °C in an acetone/dry ice bath. The resulting solution was stirred for 20 minutes at – 78 °C and then for 2 hours at room temperature. A solution of the desired bromide (**(*S*)-92** or **(*S*)-93**,

1.0 eq.) in tetrahydrofuran (10 M) was added, after cooling the solution again to – 78 °C. The reaction mixture was allowed to warm to room temperature overnight. At 0 °C in an ice bath, aqueous saturated $NaHCO_3$ was added drop wise to quench the reaction. Ethyl acetate was then added and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x). The combined organic layers were washed with brine, dried over $MgSO_4$ and then reduced to dryness under reduced pressure. The crude was purified by column chromatography on silica gel.

General procedure 8: synthesis of iridium complexes from $[Ir(cod)Cl]_2$

Ligand **(*S*)-L_{Ox1}**, **(*S*)-L_{Th1}** or **(S)-L_{Im}1** (200-300 µmol, 1.0 eq.) and bis(1,5-cyclooctadiene)diiridium(I) dichloride (0.50 eq.) were dissolved in dichloromethane (5 mL). The resulting solution was heated at reflux for 2 hours, before it was allowed to cool to room temperature. At room temperature, $NaBAr_F$ (1.3 eq.) was added and the resulting mixture was allowed to stir for 5 minutes. H_2O (5 mL) was then added and the resulting biphasic mixture was vigorously stirred for 30 minutes. The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic extracts were dried over MgSO4 and the solvent was evaporated under reduced pressure. The product was purified by column chromatography on silica gel. Elution of the side products with cyclohexane/dichloromethane (100:0 → 1:1) and then of the product (1:1 → 0:100), afforded the desired complex **(*S*)-C_{Ox}1**, **(*S*)-C_{Th}1** or **(*S*)-C_{Im}1** as an orange solid.

General procedure 9: synthesis of iridium complexes from $[Ir(cod)_2]BAr_F$

Ligand (10.0-20.0 mg, 1.0 eq.) and $[Ir(cod)_2]BAr_F$ (1.0 eq.)[73] were mixed in abs. CH_2Cl_2 (1-2 mL) and stirred for 1 hour at room temperature. The solvent was evaporated and the residue was purified by column chromatography on silica gel. Elution of the side products with cyclohexane/dichloromethane (100:0 → 1:1) and then of the product (1:1 → 0:100), afforded the desired complexes **(*S*)-C_{Ox}** or **(*S*)-C_{Th}**, as an orange solid.

General procedure 10: synthesis of aldhydrazone (*S*)-L_H4, (*S*)-L_H5 and (*S*)-L_H6

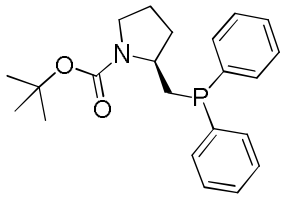
(*S*)-2-[(Diphenylphosphino)methyl]pyrrolidin-1-amine (**(*S*)-114**, 100 mg, 352 µmol, 1.0 eq.) and the respective aldehyde (2.5 eq.) were mixed in abs. tetrahydrofuran (2 mL)

in a flame-dried Young tube. The resulting mixture was then heated at reflux for 18 hours, before the solvent was removed *in vacuo*. The crude was purified by column chromatography on silica gel.

6.3
Proline-Based P,O Ligands: Preparation and Analytical Data

6.3.1
Carbamatophosphines (*S*)-L_C and Precursors

(*S*)-*tert*-Butyl 2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L_C1)

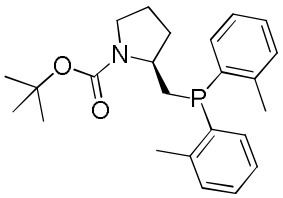


To a solution of (*S*)-*tert*-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate (**(*S*)-46**, 2.00 g, 5.63 mmol, 1.0 eq.)[77] in abs. tetrahydrofuran (10 mL) was added drop wise under argon atmosphere a 0.5 M solution of potassium diphenylphosphide in tetrahydrofuran (17.0 mL, 8.50 mmol, 1.5 eq.) at 0 °C in an ice bath. The reaction mixture was then allowed to stir at 0 °C for 30 minutes before it was filtered through celite. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel (5 x 19 cm), eluting with hexanes/ethyl acetate (9:1). The title compound **(*S*)-L_C1** was obtained as a colorless semisolid (2.01 g, 5.44 mmol, 97%).

$C_{22}H_{28}NO_2P$ (369.44 g·mol^{-1}):
R_f = 0.24 (SiO_2, hexanes/ethyl acetate 9:1).**^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.64-7.22 (m, 10 H, Ph/Ph'-*H*), 4.10-3.77 (m, 1 H, Pyr-2-*H*), 3.50-3.19 (m, 2 H, Pyr-5-*H*), 2.96-2.62 (m, 1 H, C*H*H'P), 2.15-1.69 (m, 5 H, CH*H'*P and Pyr-*H*), 1.41 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 154.4 (s, *C*=O), 139.8-138.8 (br m, Ph-*i*-*C*), 138.1-137.4 (br m, Ph'-*i*-*C*), 133.1 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.6 (d, $^2J_{C,P}$ = 20 Hz, Ph'-*o*-*C*H), 128.9-128.4 (br m, Ph-*C*H), 79.5/78.9* (br s, *t*Bu-*C*), 55.4 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 46.9/46.3* (br s, Pyr-5-*C*H_2), 34.1/33.2* (br, *C*H_2P), 31.5/31.0* (br s, Pyr-3-*C*H_2), 28.7/28.6* (s, *t*Bu-*C*H_3), 24.0/23.1* (br s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.0/– 21.6* (s) ppm. In the ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:1 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (KBr): $\tilde{\nu}$ = 2975m, 2874m, 1687s, 1478m, 1391s, 1247m, 1172s, 1107s, 952w, 917w, 857w cm^{-1}. **MS** (+ EI): *m/z* (%) = 369 (1, M^+), 313 (16), 312 (59), 296 (20), 285 (44),

284 (22), 216 (14), 215 (19), 203 (23), 202 (60), 201 (84), 200 (24), 199 (57), 186 (14), 185 (29), 184 (10), 183 (54), 128 (16), 121 (48), 114 (38), 108 (18), 91 (15), 84 (100), 83 (92), 77 (11), 70 (72), 57 (98), 41 (22). $[\alpha]_D^{20} = -40.2$ (c = 1.51, $CHCl_3$). **Elemental analysis**: calc. C 71.52%, H 7.64%, N 3.79%; found: C 71.52%, H 7.70%, N 3.67%.

(*S*)-*tert*-Butyl 2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L_C2)

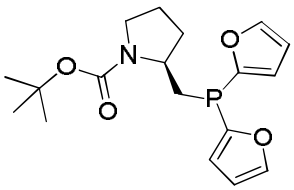


To a suspension of sodium (370 mg, 16.1 mmol, 4.0 eq.) in abs. tetrahydrofuran (25 mL) was added chlorodi-(*o*-tolyl)phosphine (**48**, 1.50 g, 6.03 mmol, 1.5 eq.) under argon atmosphere and the mixture was heated at reflux for 3 hours. The resulting mixture was cooled to 0 °C and a solution of (*S*)-*tert*-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate (**(*S*)-46**)[77] (1.06 g, 4.01 mmol, 1.0 eq.) in abs. tetrahydrofuran (15 mL) was added drop wise. After stirring for 1 hour at 0 °C, the reaction mixture was filtered through celite before the solvent was removed *in vacuo*. Column chromatography on silica gel (5 x 17 cm), eluting with hexanes/ethyl acetate (4:1) afforded **(*S*)-L_C2** (1.32 g, 3.32 mmol, 83%) as a colorless semisolid.

$C_{24}H_{32}NO_2P$ (397.49 g·mol^{-1}):
R_f = 0.48 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.84-6.95 (m, 8 H, *o*Tol/*o*Tol'-*H*), 4.22-3.82 (m, 1 H, Pyr-2-*H*), 3.44-3.19 (m, 2 H, Pyr-5-*H*), 2.65-2.10 (m, 8 H, CH_2P and *o*Tol-CH_3), 2.04-1.70 (m, 4 H, Pyr-*H*), 1.42 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 154.4 (s, *C*=O), 141.8-141.4 (m, *o*Tol/*o*Tol'-2-*C*), 137.4-137.1 (br m, *o*Tol-1-*C*), 136.1-135.5 (br m, *o*Tol'-1-*C*), 132.0-131.4 (br m, *o*Tol/*o*Tol'-6-*C*H), 130.2-129.9 (br m, *o*Tol/*o*Tol'-3-*C*H), 128.6-128.4 (br m, *o*Tol/*o*Tol'-4-*C*H), 126.3-125.6 (br m, *o*Tol/*o*Tol'-5-*C*H), 79.6/79.2* (br s, *t*Bu-*C*), 55.1/53.4* (br d, $^2J_{C,P}$ = 19/24 Hz, Pyr-2-*C*H), 46.6/46.2* (s, Pyr-5-*C*H_2), 33.1-32.3 (m, *C*H_2P), 31.4/30.9* (br s, Pyr-3-*C*H_2), 28.7 (s, *t*Bu-*C*H_3), 23.8/23.1* (br s, Pyr-4-*C*H_2), 21.6-21.0 (br m, *o*Tol/*o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 41.5/ – 41.9* (s) ppm. In the ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:1 and therefore nuclei, which are detected twice

are marked with an asterisk. **IR** (KBr): $\tilde{\nu}$ = 2972m, 2875m, 1691s, 1590w, 1454m, 1393s, 1250w, 1169s, 1108s, 1034w, 952w, 917w, 876w, 749m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 397 (12, M^+), 314 (17), 340 (62), 324 (20), 313 (24), 230 (23), 229 (56), 228 (20), 227 (62), 215 (18), 214 (50), 213 (76), 211 (13), 197 (12), 196 (11), 165 (13), 135 (11), 133 (15), 128 (15), 122 (18), 114 (46), 105 (14), 91 (13, $C_7H_7^+$), 84 (100), 83 (18), 70 (62), 57 (50), 41 (10). $[\alpha]_D^{20}$ = – 46.3 (*c* = 1.19, $CHCl_3$). **Elemental analysis**: calc. C 72.52%, H 8.11%, N 3.52%; found: C 72.36%, H 8.52%, N 3.57%.

(*S*)-*tert*-Butyl 2-{[di(furan-2-yl)phosphino]methyl}pyrrolidine-1-carboxylate ((*S*)-L_C3)



The synthesis was carried out in analogy to the preparation of **(*S*)-L_C3** using sodium (1.00 g, 43.5 mmol, 16 eq.), chlorodi(furan-2-yl)phosphine (**49**, 900 mg, 4.49 mmol, 1.6 eq.), and (*S*)-*tert*-butyl-2-[(tosyloxy)methyl]pyrrolidine-1-carboxylate (**(*S*)-47**, 836 mg, 2.81 mmol, 1.0 eq.). Column chromatography on silica gel (4 x 19 cm), eluting with dichloromethane (100%) yielded the title compound **(*S*)-L_C3** (561 mg, 1.61 mmol, 57%), as a colorless solid.

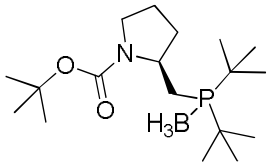
(*S*)-*tert*-butyl 2-[(tosyloxy)methyl]pyrrolidine-1-carboxylate (**(*S*)-47**),[76] was prepared according to the literature procedure and purified by column chromatography on silica gel, eluting with hexanes/ethyl acetate (7:3), $\mathbf{R_f}$ = 0.24).

$C_{18}H_{24}NO_4P$ (349.36 $g \cdot mol^{-1}$):

m.p. 111-113 °C. $\mathbf{R_f}$ = 0.43 (SiO_2, CH_2Cl_2 100%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.61 (br s, 2 H, Fur/Fur'-5-*H*), 6.72 (m, 2 H, Fur/Fur'-3-*H*), 6.36 (m, 2 H, Fur/Fur'-4-*H*), 3.95-3.80 (br s, 1 H, Pyr-2-*H*), 3.40-3.22 (m, 2H, Pyr-5-*H*), 2.76 ("dt", *J* = 13, 3.4 Hz, 1 H, C*H*H'P), 2.18 ("t", *J* = 11 Hz, 1 H, CH*H*'P), 1.93-1.61 (m, 4 H, Pyr-*H*), 1.43 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 154.4 (s, *C*=O), 151.4 ("t", $^1J_{C,P}$ = 16 Hz, Fur/Fur'-2-*C*), 147.1 (s, Fur/Fur'-5-*C*H), 120.2 (d, $^2J_{C,P}$ = 26 Hz, Fur/Fur'-3-*C*H), 110.8 ("t", $^3J_{C,P}$ = 6.1 Hz, Fur/Fur'-4-*C*H), 79.3 (s, *t*Bu-*C*), 55.3 (d, $^2J_{C,P}$ = 22 Hz, Pyr-2-*C*H), 46.4 (s, Pyr-5-*C*H_2), 31.0 (br s, Pyr-3-*C*H_2), 28.7 (s, *t*Bu-*C*H_3), 23.5 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 66.8 (s) ppm.

IR (KBr): $\tilde{\nu}$ = 2927m, 2876m, 1676s, 1551w, 1455m, 1397s, 1365m, 1247w, 1175m, 1119m, 1066w, 1002m, 953w, 904w, 876w cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 349 (6, M^+), 293 (21), 292 (56), 276 (23), 265 (35), 264 (14), 182 (14), 181 (46), 180 (28), 165 (66), 150 (27), 136 (11), 128 (14), 114 (71), 109 (15), 84 (18), 83 (74), 81 (30), 70 (91), 57 (100), 41 (23). $[\alpha]_D^{20}$ = – 31.6 (*c* = 1.00, $CHCl_3$). **Elemental analysis**: calc. C 61.53%, H 7.46%, N 3.99%; found: C 61.79%, H 7.07%, N 3.74%.

(*S*)-*tert*-Butyl 2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxylate borane adduct ((*S*)-$L_C4 \cdot BH_3$)



Di-*tert*-butylphosphine borane adduct (**50·BH_3**, 755 mg, 4.72 mmol, 1.1 eq.)[133] was dissolved in abs. tetrahydrofuran (15 mL) and cooled to – 78 °C, before a 1.6 M solution of *n*-butyllithium (2.95 mL, 4.72 mmol, 1.1 eq.) in hexanes was slowly added. The reaction mixture was then stirred for 20 minutes at – 78 °C and for 2 hours at room temperature. After cooling the solution again to – 78 °C, a solution of (*S*)-*tert*-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate (**(*S*)-46**, 1.13 g, 4.28 mmol, 1.0 eq.)[77] in abs. tetrahydrofuran (10 mL) was added *via* cannula. The reaction was monitored by ^{31}P NMR analysis (the R_f-values of starting material and product are highly similar). The mixture was then stirred at – 78 °C for 1 hour before it was allowed to warm up to room temperature overnight. After completion of the reaction, the mixture was poured into aqueous saturated $NaHCO_3$ (100 mL) and extracted with diethyl ether (3 x 200 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated. Column chromatography on silica gel (4 x 18 cm), eluting with hexanes/ethyl acetate (19:1) afforded **(*S*)-$L_C4 \cdot BH_3$** (1.16 g, 3.38 mmol, 79%) as a colorless solid.

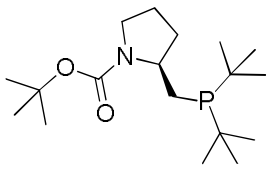
$C_{18}H_{39}BNO_2P$ (343.29 $g \cdot mol^{-1}$):

m.p. 140-142 °C. **R_f** = 0.17 (SiO_2, hexanes/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.13-4.05 (m, 1 H, Pyr-2-*H*), 3.42-3.26 (m, 2 H, Pyr-5-H_2), 2.51-1.96 (m, 3 H, C*H*H'P, Pyr-3-H_2), 1.86-1.72 (m, 2 H, Pyr-4-H_2), 1.54-1.40 (m, 1 H, CH*H*'P),

[133] For the synthesis of di-*tert*-butylphosphine borane adduct (**50·BH_3**) see: E. Neumann, Dissertation, University of Basel, **2006** pp.138-138; available from http://pages.unibas.ch/diss/2006/DissB_7467.htm.

1.45 (s, 9 H, O*t*Bu-*H*), 1.35 (br d, $^{3}J_{H,P}$ = 12 Hz, 9 H, P*t*Bu-*H*), 1.22 (d, $^{3}J_{H,P}$ = 13 Hz, 9 H, P*t*Bu'-*H*), 0.89-0.05 (br m, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 154.4 (s, *C*=O), 79.6 (br s, O*t*Bu-*C*), 55.4 (d, $^{2}J_{C,P}$ = 5.6 Hz, Pyr-2-*C*H), 46.7 (s, Pyr-5-*C*H_2), 33.2 (d, $^{1}J_{C,P}$ = 27 Hz, P*t*Bu-*C*), 32.1 (d, $^{1}J_{C,P}$ = 27 Hz, P*t*Bu'-*C*), 31.9 (s, Pyr-3-*C*H_2), 28.8 (s, O*t*Bu-*C*H_3), 28.3 (d, $^{2}J_{C,P}$ = 1.0 Hz, P*t*Bu-*C*H_3), 27.9 (d, $^{2}J_{C,P}$ = 1.1 Hz, P*t*Bu'-*C*H_3), 23.1 (br s, Pyr-4-*C*H_2), 22.1 (d, $^{1}J_{C,P}$ = 23 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.6 (br d, $^{1}J_{P,B}$ = 67 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2966m, 2953m, 2873w, 2388w, 1682s, 1678m, 1645m, 1470m, 1386s, 1364m, 1287w, 1161m, 1096s, 998s, 955m, 813s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 344 (10, $[M + H]^+$), 342 (15), 330 (13), 287 (15), 286 (100), 285 (25), 240 (28), 216 (21), 57 (39). $[\alpha]_D^{20}$ = – 54.7 (*c* = 1.02, $CHCl_3$). **Elemental analysis**: calc. C 62.98%, H 11.45%, N 4.08%; found: C 63.02%, H 11.19%, N 4.19%.

(*S*)-*tert*-Butyl 2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L$_C$4)

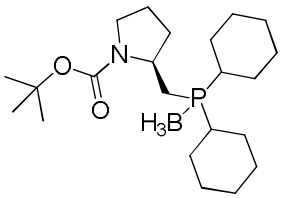


Product **(*S*)-L$_C$4** was prepared according to **general procedure 3** from **(*S*)-L$_C$4·BH$_3$**.

$C_{18}H_{36}NO_2P$ (329.46 g·mol^{-1}):

^{31}P{^{1}H} NMR (162 MHz, CD_2Cl_2): δ = 20.8/20.1 (s) ppm. In the ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ration close to 1:1.

(*S*)-*tert*-Butyl 2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxylate borane adduct ((*S*)-L_C5·BH_3)

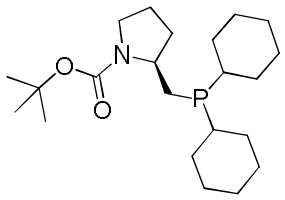


The synthesis in analogy to the preparation of **(*S*)-L_C4·BH_3** using dicyclohexylphosphine borane adduct (**51·BH_3**, 1.59 g, 7.50 mmol, 1.1 eq.),[134] a 1.6 M solution of *n*-butyllithium (4.70 mL, 7.50 mmol, 1.1 eq.) in hexanes, and a solution of (*S*)-*tert*-butyl 2-(bromomethyl)pyrrolidine-1-carboxylate (**(*S*)-46**, 1.80 g, 6.81 mmol, 1.0 eq.)[77] in abs. tetrahydrofuran allowed for the isolation of compound **(*S*)-L_C5·BH_3** (1.46 g, 3.69 mmol, 54%) as a colorless solid.

$C_{22}H_{43}BNO_2P$ (395.37 g·mol^{-1}):
m.p. 89-91 °C. **R_f** = 0.20 (SiO_2, hexanes/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.04 (br s, 1 H, Pyr-2-*H*), 3.32 (br s, 2 H, Pyr-5-H_2), 2.40-1.17 (m, 37 H, CH_2P, Cy-*H*, Pyr-*H* and *t*Bu-*H*), 0.90-0.10 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 154.3 (s, *C*=O), 79.3 (s, *t*Bu-*C*), 53.8 (br d, $^2J_{C,P}$ = 2.8 Hz, Pyr-2-*C*H), 46.4 (br s, Pyr-5-*C*H_2), 34.5-33.5 (br m, Cy/Cy'-*C*H), 32.0 (br s, Pyr-3-*C*H_2), 28.7 (s, *t*Bu-*C*H_3), 28.4-26.0 (m, Cy/Cy'-*C*H_2), 24.2-22.3 (m, Pyr-4-*C*H_2 and *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 21.2 (br d, $^1J_{P,B}$ = 68 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2927m, 2853m, 2389w, 2352w, 2333w, 1684s, 1680s, 1474w,1448m, 1388s, 1363m, 1355m, 1164m, 1105s, 1070m, 1082m, 1000m, 813m cm^{-1}. **MS** (FAB, NBA + KCl): *m/z* (%) = 434 (24, $[M + K]^+$), 394 (23, $[M - H]^+$), 382 (19, $[M - BH_2]^+$), 339 (20), 338 (100), 292 (42), 291 (11), 242 (21), 192 (11), 160 (13), 136 (12), 57 (22), 55 (14), 41 (12). $[\alpha]_D^{20}$ = – 33.5 (*c* = 1.04, $CHCl_3$). **Elemental analysis**: calc. C 66.83%, H 10.96%, N 3.54%; found: C 66.82%, H 10.82%, N 3.66%.

[134] For the synthesis of dicyclohexylphosphine borane adduct (**51·BH_3**) see: C. A. Busacca, J. C. Lorenz, N. Grinberg, N. Haddad, H. Lee, Z. Li, M. Liang, D. Reeves, A. Saha, R. Varsolona, C. H. Senanayake, *Org. Lett.* **2008**, *10*, 341-344.

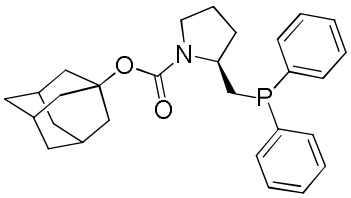
(*S*)-*tert*-Butyl 2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L_C5)



Product **(*S*)-L_C5** was prepared according to **general procedure 3** from **(*S*)-L_C5·BH_3**.

$C_{22}H_{40}NO_2P$ (381.53 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = − 11.4/ −11.6 (s) ppm. In the ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ration close to 1:1.

(*S*)-Adamantan-1-yl-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L_C6)

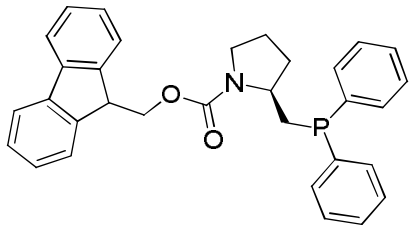


Product **(*S*)-L_C6** (85%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 1-adamantyl chloroformate (**54**)[78] and isolated as a colorless semisolid.

$C_{28}H_{34}NO_2P$ (447.55 g·mol^{-1}):
R_f = 0.27 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.04-7.75 (m, 1 H, Ph-*o*-*H*), 7.75-7.19 (m, 9 H, Ph/Ph'-*H*), 4.10-3.79 (m, 1 H, Pyr-2-*H*), 3.46-3.15 (m, 2 H, Pyr-5-H_2), 2.96-2.64 (m, 1 H, C*H*H'P), 2.42-1.15 (m, 20 H, CH*H*'P, Pyr-*H* and Adm-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 154.1 (s, *C*=O), 139.2-138.9 (m, Ph-*i*-*C*), 138.2-137.3 (m, Ph'-*i*-*C*), 133.4-132.3 (m, Ph/Ph'-*C*H), 131.9-130.3 (m, Ph/Ph'-*C*H), 129.1-128.3 (m, Ph/Ph'-*C*H), 78.9-78.6 (m, Adm-1-*C*), 55.4/53.2* (br d, Pyr-2-*C*H), 46.8/46.2* (br s, Pyr-5-*C*H_2), 42.0 (s, Adm-2/8/9-*C*H_2), 36.3 (s, Adm-4/6/10-*C*H_2), 34.1/33.1* (br d, $^1J_{C,P}$ = 17 Hz, *C*H_2P), 31.4/29.8* (br s, Pyr-3-*C*H_2), 31.0 (s, Adm-3/5/7-*C*H), 23.9/23.1* (br s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.4/– 22.2* (s) ppm. In the ^{1}H, ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:2 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (neat): $\tilde{\nu}$ = 2918m,

2852m, 1727w, 1675s,1436m, 1393s, 1352m, 1298m, 1208m, 1187m, 1116s, 1056m, 917w, 871w, 742m, 696m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 447 (1, M^+), 350 (11), 312 (41), 285 (11), 284 (62), 211 (18), 201 (21), 183 (11), 136 (10), 135 (100), 93 (11). $[\alpha]_D^{20} = -37.9$ (c = 1.00, $CHCl_3$). **HRMS** (ESI): calc. for $C_{28}H_{35}NO_2P$ ($[M+H]^+$): 448.2400; found: 448.2391.

(*S*)-(9*H*-Fluoren-9-yl)methyl-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L_C7)



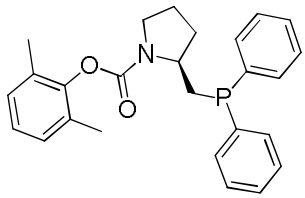
Product **(*S*)-L_C7** (73%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 9-fluorenylmethyl chloroformate.

$C_{32}H_{30}NO_2P$ (491.56 $g \cdot mol^{-1}$):

m.p. 138-140 °C. **R_f** = 0.35 (SiO_2, hexanes/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.84-7.16 (m, 18 H, Ph/Ph'-*H* and Fl-*H*), 4.37-4.16 (m, 3 H, Fl-9-*H* and CH_2O), 4.06-3.93 (m, 1 H, Pyr-2-*H*), 3.49-3.32 (m, 2 H, Pyr-5-H_2), 2.95-2.82/2.65-2.54* (m, 1 H, C*H*H'P), 2.22-1.73 (m, 5 H, CH*H*'P and Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 154.5 (s, *C*=O), 144.4 (br s, Fl-8a/9a-*C*), 141.3 (br s, Fl-4a/4b-*C*), 139.7-139.0 (m, Ph-*i*-*C*), 137.9 (d, $^1J_{C,P}$ = 14 Hz, Ph'-*i*-*C*), 132.9 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.8-128.2 (m, Ph/Ph'-*C*H), 127.6 (s, Fl-3/6-*C*H), 127.0 (br s, Fl-4/5-*C*H), 125.2 (br s, Fl-2/7-*C*H), 119.9 (s, Fl-1/8-*C*H), 67.0/66.8* (s, *C*H_2O), 56.0/55.4* (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 47.4 (s, Fl-9-*C*H), 46.9/46.5* (s, Pyr-5-*C*H_2), 33.9/32.9* (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.6/30.8* (d, $^3J_{C,P}$ = 8.1 Hz, Pyr-3-*C*H_2), 24.0/23.2* (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 22.6/– 22.9* (s) ppm. In the ^{1}H, ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 2:3 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (neat): $\tilde{\nu}$ = 3049w, 2960w, 2918w, 2903w, 2843w, 1674s, 1474m, 1417s, 1353m, 1332s, 1308m, 1218w, 1191m, 1120s, 1101m, 1046w, 1025w, 996w, 970w, 916m, 822m, 746s, 699s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 491 (2, M^+), 201 (17), 200 (88), 199 (29),

185 (14), 183 (20), 179 (32), 178 (100), 176 (14), 84 (13), 83 (15), 70 (66). $[\alpha]_D^{20}$ = – 75.5 (c = 1.11, $CHCl_3$). **HRMS** (ESI): calc. for $C_{32}H_{31}NO_2P$ ($[M+H]^+$): 492.2087; found: 492.2077.

(*S*)-2,6-Dimethylphenyl-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxylate ((*S*)-L_C8)

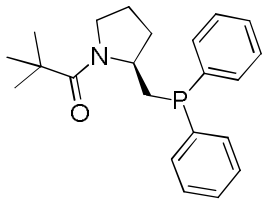


Product **(*S*)-L_C8** (80%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 2,6-dimethylphenyl chloroformate (**56**)[79] and isolated as a colorless semisolid.

$C_{26}H_{28}NO_2P$ (417.48 g·mol^{-1}):
R_f = 0.40 (SiO_2, hexanes/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.63 ("t", $^3J_{H,H}$ = 7.3 Hz, 1 H, Ph-*o*-*H*), 7.52 ("t", $^3J_{H,H}$ = 7.4 Hz, 1 H, Ph'-*o*-*H*), 7.43-7.26 (m, 7 H, Ph/Ph'-*H*), 7.26-7.21 (m, 1 H, Ph/Ph'-*H*), 7.08-6.95 (m, 3 H, Ar-*H*), 4.12-4.02 (m, 1 H, Pyr-2-*H*), 3.70-3.64 (m, 1 H, Pyr-5-*H*H'), 3.58-3.49 (m, 1 H, Pyr-5-H*H'*), 3.16-2.98 (m, 1 H, C*H*H'P), 2.25-1.86 (m, 11 H, CH*H'*P, Pyr-*H* and Ar-CH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 152.4/152.3* (s, *C*=O), 148.6/148.3* (s, Ar-*i*-*C*), 139.5-138.8 (m, Ph-*i*-*C*), 137.0-136.6 (m, Ph'-*i*-*C*), 133.4-132.2 (m, Ph-*o*-*C*H), 130.8 (br s, Ar-*o*-*C*), 129.0-128.1 (m, Ph/Ph'-*C*H and Ar-*m*-*C*H), 125.4 (s, Ar-*p*-*C*H), 56.5-55.8 (m, Pyr-2-*C*H), 47.0* (s, Pyr-5-*C*H_2), 34.5/32.8* (d, $^1J_{C,P}$ = 14 Hz, *C*H_2P), 31.8/30.9* (d, $^3J_{C,P}$ = 7.8 Hz, Pyr-3-*C*H_2), 24.1/23.3* (s, Pyr-4-*C*H_2), 16.5 (br s, Ar-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.9/– 22.4* (s) ppm. In the ^{1}H, ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:1 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (neat): $\tilde{\nu}$ = 3050m, 2971m, 2952m, 2874m, 1708s, 1695s, 1480m, 1432m, 1380s, 1336m, 1266m, 1165s, 1095m, 1063m, 1026m, 918w, 869w, 848w, 767m, 739m, 697s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 417 (23, M^+), 297 (16), 296 (84), 218 (23), 200 (15), 199 (14), 187 (13), 186 (18), 185 (100), 183 (57), 174 (20), 105 (13), 84 (14). $[\alpha]_D^{20}$ = − 113.8 (c = 1.01, $CHCl_3$). **HRMS** (ESI): calc. for $C_{26}H_{29}NO_2P$ ($[M+H]^+$): 418.1930; found: 418.1923.

6.3.2
Amidophosphines (*S*)-L_A and Precursors

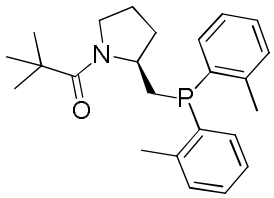
(*S*)-1-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one ((*S*)-L_A1)



Product **(*S*)-L_A1** (98%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and pivaloyl chloride.

$C_{22}H_{28}NOP$ (353.44 g·mol^{-1}):
m.p. 92-93 °C. **R_f** = 0.35 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, CD_2Cl_2): δ = 7.64 ("t", *J* = 7.1 Hz, 2 H, Ph/Ph'-*o*-*H*), 7.41-7.26 (m, 8 H, Ph/Ph'-*H*), 4.22-4.15 (m, 1 H, Pyr-2-*H*), 3.72-3.67 (m, 1 H, Pyr-5-*H*H'), 3.54-3.49 (m, 1 H, Pyr-5-H*H'*), 2.90 ("br d", *J* = 12 Hz, 1 H, C*H*H'P), 2.02-1.89 (m, 4 H, CH*H'*P, Pyr-4-*H*H' and Pyr-3-*H*$_2$), 1.83-1.74 (m, 1 H, Pyr-4-H*H'*), 1.18 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ = 175.9 (s, *C*=O), 139.8 (d, $^1J_{C,P}$ = 15 Hz, Ph-*i*-*C*), 138.0 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 133.1 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.6 (s, Ph-*p*-*C*H), 128.5-128.3 (m, Ph/Ph'-*C*H), 57.1 (d, $^2J_{C,P}$ = 18 Hz, Pyr-2-*C*H), 48.0 (s, Pyr-5-*C*H$_2$), 39.0 (s, *t*Bu-*C*), 32.5 (d, $^1J_{C,P}$ = 13 Hz, *C*H$_2$P), 29.6 (d, $^3J_{C,P}$ = 9.2 Hz, Pyr-3-*C*H$_2$), 27.4 (s, *t*Bu-*C*H$_3$), 25.5 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 25.3 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3054m, 2957s, 2876s, 1615s, 1476m, 1408s, 1372s, 1211m, 1160m, 1091m, 1026w, 995w, 921m, 836w, 785w, 747s, 698s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 353 (2, M^+), 296 (13), 201 (28), 183 (23), 152 (100), 121 (11), 84 (11), 69 (20), 57 (29). $[\alpha]_D^{20}$ = – 88.1 (*c* = 1.10, $CHCl_3$). **Elemental analysis**: calc. C 74.76%, H 7.98%, N 3.96%; found: C 74.77%, H 7.85%, N 3.87%.

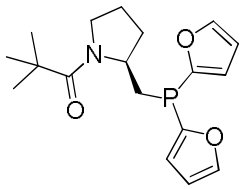
(*S*)-1-{2-[(Di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one ((*S*)-L_A2)



Product **(*S*)-L_A2** (90%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and pivaloyl chloride.

$C_{24}H_{32}NOP$ (381.49 g·mol^{-1}):
m.p. 110-112 °C. **R_f** = 0.48 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.93-7.82 (br s, 1 H, *o*Tol-6-*H*), 7.33-7.23 (m, 2 H, *o*Tol-4-*H* and *o*Tol-5-*H*), 7.20-7.13 (m, 3 H, *o*Tol/*o*Tol'-3-*H* and *o*Tol'-4-*H*), 7.09-7.00 (m, 2 H, *o*Tol'-5-*H* and *o*Tol'-6-*H*), 4.25-4.17 (m, 1 H, Pyr-2-*H*), 3.72-3.66 (m, 1 H, Pyr-5-*H*H'), 3.57-3.50 (m, 1 H, Pyr-5-H*H'*), 2.88-2.77 (m, 1 H, C*H*H'P), 2.50 (s, 3 H, *o*Tol-CH_3), 2.31 (s, 3 H, *o*Tol'-CH_3), 2.04-1.94 (m, 3 H, Pyr-3-H_2 and Pyr-4-*H*H'), 1.87-1.77 (m, 1 H, Pyr-4-H*H'*), 1.66 ("t", *J* = 12 Hz, 1 H, CH*H'*P), 1.20 (s, 9 H, *t*Bu-CH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 176.0 (s, *C*=O), 142.2 (d, $^2J_{C,P}$ = 25 Hz, *o*Tol-2-*C*), 141.7 (d, $^2J_{C,P}$ = 27 Hz, *o*Tol'-2-*C*), 137.6 (d, $^1J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 136.1 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 131.9 (s, *o*Tol-6-*C*H), 131.8 (s, *o*Tol'-6-*C*H), 130.0 (d, $^3J_{C,P}$ = 4.6 Hz, *o*Tol-3-*C*H), 129.9 (d, $^3J_{C,P}$ = 5.0 Hz, *o*Tol'-3-*C*H), 128.5 (s, *o*Tol-4-*C*H), 128.4 (s, *o*Tol'-4-*C*H), 126.2 (s, *o*Tol-5-*C*H), 126.1 (s, Tol'-5-*C*H), 57.1 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 47.9 (s, Pyr-5-*C*H_2), 39.0 (s, *t*Bu-*C*), 31.4 (d, $^1J_{C,P}$ = 14 Hz, *C*H_2P), 29.6 (d, $^3J_{C,P}$ = 10 Hz, Pyr-3-*C*H_2), 27.4 (s, *t*Bu-*C*H_3), 25.5 (d, $^4J_{C,P}$ = 4.2 Hz, Pyr-4-*C*H_2), 21.1 (d, $^3J_{C,P}$ = 8.4 Hz, *o*Tol-CH_3), 20.8 (d, $^3J_{C,P}$ = 6.9 Hz, *o*Tol'-CH_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 41.5 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3046w, 2965s, 1613s, 1472m, 1460m, 1406s, 1373m, 1265w, 1225m, 1170m, 923w, 877w, 833w, 757s, 724m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 381 (5, M^+), 229 (18), 213 (12), 153 (11), 152 (100), 70 (14), 69 (16), 57 (30). $[\alpha]_D^{20}$ = – 106 (*c* = 0.980, $CHCl_3$). **Elemental analysis**: calc. C 75.56%, H 8.45%, N 3.67%; found: C 75.41%, H 8.40%, N 3.55%.

(*S*)-1-(2-{[Di(furan-2-yl)phosphino]methyl}pyrrolidin-1-yl)-2,2-dimethylpropan-1-one ((*S*)-L_A3)

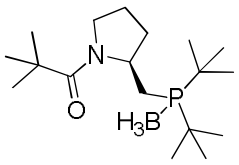


Product **(*S*)-L_A3** (86%) was prepared according to **general procedure 1** from **(*S*)-L_C3** and pivaloyl chloride.

$C_{18}H_{24}NO_3P$ (333.36 g·mol^{-1}):

m.p. 108-110 °C. **R_f** = 0.53 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.62-7.58 (m, 2 H, Fur/Fur'-5-*H*), 6.85-6.82 (m, 1 H, Fur-3-*H*), 6.73-6.70 (m, 1 H, Fur'-3-*H*), 6.38-6.34 (m, 2 H, Fur/Fur'-4-*H*), 4.35-4.25 (m, 1 H, Pyr-2-*H*), 3.72-3.64 (m, 1 H, Pyr-5-*H*H'), 3.53-3.43 (m, 1 H, Pyr-5-H*H'*), 2.82 (br d, *J* = 12 Hz, 1 H, C*H*H'P), 2.26 (dd, $^2J_{H,P}$ = 13 Hz, $^2J_{H,H}$ = 9.8 Hz, 1 H, CH*H'*P), 1.97-1.70 (m, 3 H, Pyr-*H*), 1.65-1.52 (m, 1 H, Pyr-*H*), 1.21 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 1765 (s, *C*=O), 148.6 (d, $^1J_{C,P}$ = 7.8 Hz, Fur-2-*C*), 148.0 (d, $^1J_{C,P}$ = 7.7 Hz, Fur'-2-*C*), 147.0 (s, Fur-5-*C*H), 146.9 (s, Fur'-5-*C*H), 120.2 (d, $^2J_{C,P}$ = 24 Hz, Fur-3-*C*H), 119.7 (d, $^2J_{C,P}$ = 18 Hz, Fur'-3-*C*H), 110.8 (d, $^3J_{C,P}$ = 2.7 Hz, Fur-4-*C*H), 110.7 (d, $^3J_{C,P}$ = 3.6 Hz, Fur'-4-*C*H), 57.0 (d, $^2J_{C,P}$ = 25 Hz, Pyr-2-*C*H), 47.9 (s, Pyr-5-*C*H_2), 39.3 (s, *t*Bu-*C*), 30.0 (s, Pyr-3-*C*H_2), 29.4 (d, $^1J_{C,P}$ = 7.1 Hz, *C*H_2P), 27.7 (s, *t*Bu-*C*H_3), 25.6 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 70.5 (br) ppm. **IR** (KBr): $\tilde{\nu}$ = 3114m, 2963s, 2924s, 2217w, 1735w, 1604s, 1460m, 1407s, 1367m, 1258w, 1215w, 1156m, 1112w, 1066w, 1013m, 903w, 831w cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 333 (4, M^+), 276 (29), 181 (18), 153 (11), 152 (100), 96 (10), 84 (17), 70 (19), 69 (27), 57 (48), 41 (15). $[\alpha]_D^{20}$ = – 38.3 (*c* = 0.989, $CHCl_3$). **Elemental analysis**: calc. C 64.85%, H 7.26%, N 4.20%; found: C 64.61%, H 7.34%, N 3.92%.

(*S*)-1-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one borane adduct ((*S*)-L_A4·BH_3)

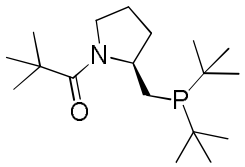


Product **(*S*)-L_A4·BH_3** (24%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and pivaloyl chloride.

$C_{18}H_{39}BNOP$ (327.29 g·mol^{-1}):

m.p. 99-103 °C. **R_f** = 0.21 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.40-4.32 (m, 1 H, Pyr-2-*H*), 3.70-3.64 (m, 1 H, Pyr-5-*H*H'), 3.58-3.52 (m, 1 H, Pyr-5-H*H'*), 2.55 ("td", J = 15, 2.5 Hz, 1 H, C*H*H'P), 2.20-2.09 (m, 1 H, Pyr-3-*H*H'), 2.05-1.96 (m, 1 H, Pyr-3-H*H'*), 1.96-1.87 (m, 1 H, Pyr-4-*H*H'), 1.87-1.77 (m, 1 H, Pyr-4-H*H'*), 1.40 (d, $^3J_{H,P}$ = 13 Hz, 9 H, P*t*Bu-*H*), 1.36-1.28 (m, 1 H, CH*H'*P), 1.26 (s, 9 H, C*t*Bu-*H*), 1.24 (d, $^3J_{H,P}$ = 12 Hz, 9 H, P*t*Bu'-*H*), 0.94-0.05 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 176.7 (s, *C*=O), 57.7 (d, $^2J_{C,P}$ = 5.0 Hz, Pyr-2-*C*H), 48.0 (s, Pyr-5-*C*H_2), 39.3 (s, C*t*Bu-*C*), 33.2 (d, $^1J_{C,P}$ = 27 Hz, P*t*Bu-*C*), 32.1 (d, $^1J_{C,P}$ = 28 Hz, P*t*Bu'-*C*), 30.6 (s, Pyr-3-*C*H_2), 28.3 (d, $^2J_{C,P}$ = 1.5 Hz, P*t*Bu-*C*H_3), 28.0 (d, $^1J_{C,P}$ = 1.2 Hz, P*t*Bu'-*C*H_3), 27.8 (s, C*t*Bu-*C*H_3), 25.3 (s, Pyr-4-*C*H_2), 21.7 (d, $^1J_{C,P}$ = 24 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 40.3 (br d) ppm. **IR** (neat): $\tilde{\nu}$ = 2967m, 2922m, 2874m, 2378m, 1611s, 1471m, 1404m, 1371s, 1341w, 1208w, 1182w, 1149m, 1069m, 1021m, 929w, 885m, 816m cm^{-1}. **MS** (FAB, NBA + KCl): *m/z* (%) = 366 (18, [M + K]$^+$), 327 (11), 326 (42, [M –H]$^+$), 314 (16, [M − BH_2]$^+$), 299 (15), 298 (70), 256 (35), 242 (24), 240 (37), 200 (16), 184 (14), 128 (11), 57 (100), 41 (23). $[\alpha]_D^{20}$ = – 89.2 (c = 1.05, $CHCl_3$).

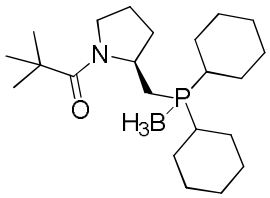
(*S*)-1-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one ((*S*)-L_A4)



Product **(*S*)-L_C4** was prepared according to **general procedure 3** from **(*S*)-L_C4·BH_3**.

$C_{18}H_{36}NOP$ (313.46 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 22.2 (s) ppm.

(*S*)-1-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one borane adduct ((*S*)-L_A5·BH_3)

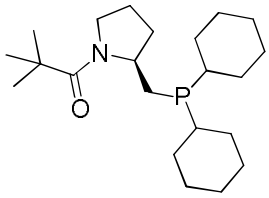


Product **(*S*)-L_A5·BH_3** (67%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and pivaloyl chloride.

$C_{22}H_{43}BNOP$ (379.37 g·mol^{-1}):
R_f = 0.16 (SiO_2, hexanes/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.35-4.27 (m, 1 H, Pyr-2-*H*), 3.69-3.63 (m, 1 H, Pyr-5-*H*H'), 3.56-3.51 (m, 1 H, Pyr-5-H*H'*), 2.39 ("t", *J* = 14 Hz, 1 H, C*H*H'P), 2.09-1.90 (m, 5 H, Pyr-3-H_2, Pyr-4-*H*H' and Cy/Cy'-1-*H*), 1.89-1.78 (m, 7 H, Pyr-4-H*H'* and Cy/Cy'-*H*), 1.75-1.66 (m, 4 H, Cy/Cy'-*H*), 1.53-1.19 (m, 20 H, CH*H'*P, *t*Bu-*H* and Cy/Cy'-*H*), 0.83-0.05 (br m, 3 H, BH_3) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 176.5 (s, *C*=O), 56.3 (d, $^2J_{C,P}$ = 4.6 Hz, Pyr-2-*C*H), 47.9 (s, Pyr-5-*C*H_2), 39.3 (s, *t*Bu-*C*), 32.7 (d, $^1J_{C,P}$ = 32 Hz, Cy-1-*C*H), 32.4 (d, $^1J_{C,P}$ = 35 Hz, Cy'-1-*C*H), 30.4 (s, Pyr-3-*C*H_2), 27.7 (s, *t*Bu-*C*H_3), 27.3 (d, $^2J_{C,P}$ = 5.5 Hz, Cy/Cy'-*C*H_2), 27.2 (d, $^2J_{C,P}$ = 5.5 Hz, Cy/Cy'-*C*H_2), 27.0 (s, Cy/Cy'-*C*H_2), 26.9-26.8 (m, 2 Cy/Cy'-*C*H_2), 26.7 (s, Cy/Cy'-*C*H_2), 26.6 (br s, Cy/Cy'-*C*H_2), 26.4 (br s, Cy/Cy'-*C*H_2), 26.2 (br s, Cy/Cy'-*C*H_2), 26.1 (br s, Cy/Cy'-*C*H_2), 25.4 (s, Pyr-4-*C*H_2), 24.0 (d, $^1J_{C,P}$ = 27 Hz, *C*H_2P) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 21.5 (br d) ppm. **IR** (neat): $\tilde{\nu}$ = 2928s, 2852s, 1716m, 1616s, 1581m, 1477m, 1448m, 1402s,

1361s, 1205w, 1159m, 1142m, 1064m, 1004m, 923w, 854m cm^{-1}. **MS** (FAB, NBA + KCl): *m/z* (%) = 418 (24, $[M + K]^+$), 379 (16), 378 (61, $[M - H]^+$), 366 (28, $[M - BH_2]^+$), 351 (24), 350 (100), 294 (14), 282 (34), 200 (11), 115 (13), 83 (11), 57 (53), 55 (20), 41 (19). $[\alpha]_D^{20}$ = – 51.5 (*c* = 0.862, $CHCl_3$).

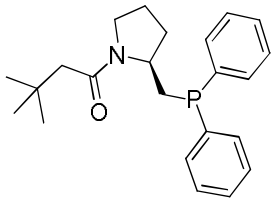
(*S*)-1-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one ((*S*)-L_A5)



Product **(*S*)-L_C5** was prepared according to **general procedure 3** from **(*S*)-L_C5·BH_3**.

$C_{22}H_{40}NOP$ (365.53 $g \cdot mol^{-1}$):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = −10.4 (s) ppm.

(*S*)-1-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}-3,3-dimethylbutan-1-one ((*S*)-L_A6)

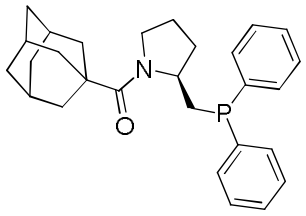


Product **(*S*)-L_A6** (26%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 3,3-dimethylbutanoyl chloride.

$C_{23}H_{30}NOP$ (367.46 $g \cdot mol^{-1}$):
m.p. 80-84 °C. **R_f** = 0.31 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (500 MHz, $CDCl_2$): δ = 8.11-7.22 (m, 10 H, Ph/Ph'-*H*), 4.39-4.15 (m, 1 H, Pyr-2-*H*), 3.57-3.32 (m, 2 H, Pyr-5-H_2), 2.44-1.74 (m, 8 H, CH_2P, CH_2 and Pyr-*H*), 1.13-0.71 (m, 9 H, *t*Bu-H_3) ppm. **$^{13}C\{^1H\}$ NMR** (126 MHz, $CDCl_3$): δ = 171.1-170.8 (br s, *C*=O), 137.9-137.5 (m, Ph-*i*-*C*), 135.6-135.3 (m, Ph'-*i*-*C*), 133.9-132.8 (m, Ph/Ph'-*C*H), 131.9-130.4 (m, Ph/Ph'-*C*H), 129.3-128.4 (m, Ph/Ph'-*C*H), 55.3-55.0 (br d, Pyr-2-*C*H), 48.3-47.9 (br d, Pyr-5-*C*H_2), 47.2 (br s, *C*H_2), 34.7-34.4 (br s, *t*Bu-*C*), 31.8-31.4 (m, *C*H_2P),

30.4-29.8 (m, Pyr-3-*C*H_2 and *t*Bu-*C*H_3), 24.5 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 25.3 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2958m, 2933m, 2867m, 1622s, 1463w, 1434m, 1413m, 1394m, 1211m, 1190m, 1120w, 995w, 796w, 742m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 368 (10, $[M + H]^+$), 285 (18), 284 (100), 217 (15), 215 (25), 202 (27), 201 (29), 182 (22), 166 (23), 84 (56), 83 (10), 70 (16). $[\alpha]_D^{20}$ = – 22.9 (*c* = 0.830, $CHCl_3$).

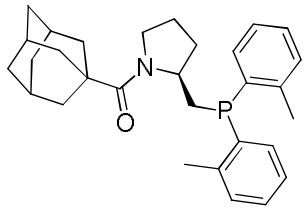
Adamantan-1-yl {(*S*)-2-[(diphenylphosphino)methyl]pyrrolidin-1-yl}methanone ((*S*)-L_A7)



Product **(*S*)-L_A7** (96%) was prepared according to **general procedure 1** from **(*S*)-Lc1** and 1-adamantanecarbonyl chloride.

$C_{28}H_{34}NOP$ (431.55 $g \cdot mol^{-1}$):
m.p. 118-120 °C. **R_f** = 0.49 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.66-7.60 (m, 2 H, Ph/Ph'-*H*), 7.42-7.26 (m, 8 H, Ph/Ph'-*H*), 4.36-4.27 (m, 1 H, Pyr-2-*H*), 3.89-3.78 (m, 1 H, Pyr-5-*H*H'), 3.59-3.49 (m, 1 H, Pyr-5-H*H'*), 2.99-2.82 (m, 1 H, C*H*H'P), 2.05-1.81 (m, 13 H, CH*H'*P, Pyr-4-*H*H', Pyr-3-H_2 and Adm-*H*), 1.80-1.54 (m, 7 H, Pyr-4-H*H'* and Adm-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 175.9 (s, *C*=O), 140.7 (br d, $^1J_{C,P}$ = 15 Hz, Ph-*i*-*C*), 137.6 (d, $^1J_{C,P}$ = 12 Hz, Ph'-*i*-*C*), 133.2 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.9 (d, $^2J_{C,P}$ = 20 Hz, Ph'-*o*-*C*H), 128.7 (s, Ph-*p*-*C*H), 128.7 (d, $^3J_{C,P}$ = 6.9 Hz, Ph-*m*-*C*H), 128.6 (s, Ph'-*p*-*C*H), 128.5 (d, $^3J_{C,P}$ = 6.9 Hz, Ph'-*m*-*C*H), 57.3 (br d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 48. (br s, Pyr-5-*C*H_2), 42.0 (s, Adm-1-*C*), 38.3 (s, Adm-2/8/10-*C*H_2), 36.8 (s, Adm-4/6/9-*C*H_2), 32.8 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 29.5 (br d, $^3J_{C,P}$ = 10 Hz, Pyr-3-*C*H_2), 28.5 (s, Adm-3/5/7-*C*H), 25.9 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = − 25.1 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 2909m, 2850m, 1689m, 1608s, 1393s, 1166m, 1107m, 749m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 431 (3, M^+), 231 (15), 230 (100), 201 (13), 135 (48), 79 (8). $[\alpha]_D^{20}$ = – 32.0 (*c* = 1.42, $CHCl_3$).

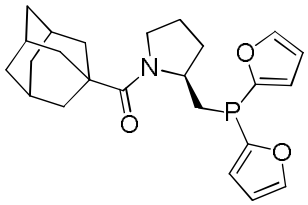
Adamantan-1-yl {(*S*)-2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}methanone ((*S*)-L_A8)



Product **(*S*)-L_A8** (83%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and 1-adamantanecarbonyl chloride.

$C_{30}H_{38}NOP$ (459.60 g·mol^{-1}):
m.p. 145-147 °C. **R_f** = 0.47 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.99-7.82 (m, 1 H, *o*Tol-3-*H*), 7.40-7.29 (m, 1 H, *o*Tol-5-*H*), 7.24 ("t", $^2J_{H,H}$ = 7.4 Hz, 1 H, *o*Tol-4-*H*), 7.22-7.10 (m, 3 H, *o*Tol'-4-*H* and *o*Tol/*o*Tol'-6-*H*), 7.09-6.95 (m, 2 H, *o*Tol'-3-*H* and *o*Tol'-5-*H*), 4.40-4.30 (m, 1 H, Pyr-2-*H*), 3.89-3.78 (m, 1 H, Pyr-5-*H*H'), 3.63-3.52 (m, 1 H, Pyr-5-H*H'*), 2.96-2.79 (m, 1 H, C*H*H'P), 2.53 (br s, 3 H, *o*Tol-*C*H_3), 2.30 (br s, 3 H, *o*Tol'-*C*H_3), 2.07-1.52 (m, 20 H, CH*H'*P, Pyr-*H* and Adm-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 175.9 (s, *C*=O), 142.2-141.6 (m, *o*Tol-2-*C*), 141.6 (d, $^2J_{C,P}$ = 27 Hz, *o*Tol'-2-*C*), 137.4 (d, $^1J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 135.7 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 132.5-131.6 (m, *o*Tol/*o*Tol'-3-*C*H), 130.1-129.9 (m, *o*Tol/*o*Tol'-6-*C*H),128.5 (br s, *o*Tol/*o*Tol'-4-*C*H), 126.7 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 57.6-57.0 (m, Pyr-2-*C*H), 48.0 (br s, Pyr-5-*C*H_2), 42.1 (s, Adm-1-*C*), 38.4 (s, Adm-2/8/9-*C*H_2), 36.8 (s, Adm-4/6/10-*C*H_2), 31.5-31.2 (m, *C*H_2P), 29.7-29.3 (m, Pyr-3-*C*H_2), 28.6 (s, Adm-3/5/7-*C*H), 26.0 (br s, Pyr-4-*C*H_2), 21.4 (d, $^3J_{C,P}$ = 10 Hz, *o*Tol-*C*H_3), 21.2 (d, $^3J_{C,P}$ = 12 Hz, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = − 41.0 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2902m, 2853m, 1693w, 1605s, 1450m, 1381s, 1310w, 1200w, 1161w, 1034w, 878w, 755s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 459 (3, M^+), 231 (18), 230 (100), 229 (13), 135 (38). $[\alpha]_D^{20}$ = – 48.4 (*c* = 0.520, $CHCl_3$). **HRMS** (ESI): calc. for $C_{30}H_{39}NOP$ ($[M + H]^+$): 460.2764; found: 460.2747.

Adamantan-1-yl ((*S*)-2-{[di(furan-2-yl)phosphine]methyl}pyrrolidin-1-yl)methanone ((*S*)-L_A9)

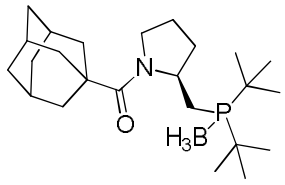


Product **(*S*)-L_A9** (61%) was prepared according to **general procedure 1** from **(*S*)-L_C3** and 1-adamantanecarbonyl chloride.

$C_{24}H_{30}NO_3P$ (411.47 g·mol^{-1}):

m.p. 127-129 °C. **R_f** = 0.43 (SiO_2, dichloromethane/ethyl acetate 200:1). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.63 ("dd", $^3J_{H,H}$ = 4.2 Hz, J = 1.7 Hz, 2 H, Fur/Fur'-5-*H*), 6.89-6.86 (m, 1 H, Fur-3-*H*), 6.74-6.71 (m, 1 H, Fur'-3-*H*), 6.43-6.40 (m, 1 H, Fur-4-*H*), 6.40-6.38 (m, 1 H, Fur'-4-*H*), 4.25-4.13 (m, 1 H, Pyr-2-*H*), 3.82-3.71 (m, 1 H, Pyr-5-*H*H'), 3.57-3.47 (m, 1 H, Pyr-5-H*H'*), 2.82-2.73 (m, 1 H, C*H*H'P), 2.10 (ddd, $^2J_{H,P}$ = 13 Hz, $^2J_{H,H}$ = 10 Hz, $^3J_{H,H}$ = 1.0 Hz, 1 H, CH*H'*P), 1.99 (br s, 3 H, Adm-3/5/7-*H*), 1.96-1.57 (m, 16 H, Pyr-*H* and Adm-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 175.4 (s, *C*=O), 151.8-151.5 (br d, Fur-2-*C*), 151.1-150.7 (br d, Fur'-2-*C*), 146.9 (br s, Fur/Fur'-5-*C*H), 120.0 (s, Fur-3-*C*H), 119.8 (s, Fur'-3-*C*H), 110.7 (s, Fur-4-*C*H), 110.7 (Fur'-4-*C*H), 57.1-56.3 (br m, Pyr-2-*C*H), 47.9 (s, Pyr-5-*C*H_2), 41.9 (s, Adm-1-*C*), 38.3 (s, Adm-2/8/9-*C*H_2), 36.7 (s, Adm-4/6/10-*C*H_2), 30.0-29.8 (br d, *C*H_2P), 29.0 (br s, Pyr-3-*C*H_2), 28.7 (s, Adm-3/5/7-*C*H), 25.8-25.4 (br s, Pyr-4-*C*H_2) ppm. **^{31}P NMR** (162 MHz, CD_2Cl_2): δ = − 70.0 (br d) ppm. **IR** (KBr): $\tilde{\nu}$ = 2919m, 2847m, 1690m, 1608s, 1393s, 1166m, 1160m, 1013s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 411 (8, M^+), 231 (15), 230 (100), 135 (64). $[\alpha]_D^{20}$ = –51.2 (*c* = 1.00, $CHCl_3$).

Adamantan-1-yl {(*S*)-2-[(di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}methanone borane adduct ((*S*)-L_A10·BH_3)

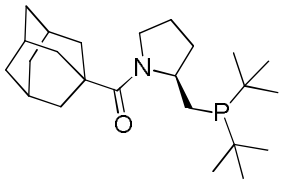


Product **(*S*)-L_A10·BH_3** (43%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and 1-adamantanecarbonyl chloride.

$C_{24}H_{45}BNOP$ (405.40 g·mol^{-1}):

m.p. 201-203 °C. **R_f** = 0.32 (hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.40-4.32 (m, 1 H, Pyr-2-*H*), 3.83-3.75 (m, 1 H, Pyr-5-*H*H'), 3.65-3.57 (m, 1 H, Pyr-5-H*H'*), 2.53 ("td", *J* = 14, 2.0 Hz, 1 H, C*H*H'P), 2.19-2.09 (m, 1 H, Pyr-3-*H*H'), 2.03 ("br d", 3 H, Adm-3/5/7-*H*), 1.99 (br s, 6 H, Adm-2/8/10-H_2), 1.99-1.86 (m, 2 H, Pyr-3-H*H'* and Pyr-4-*H*H'), 1.85-1.77 (m, 1 H, Pyr-4-H*H'*), 1.72 (br s, 6 H, Adm-4/6/9-H_2), 1.40 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.35-1.25 (m, 1 H, CH*H'*P), 1.23 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-*H*), 0.83-0.08 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 176.2 (s, *C*=O), 57.9 (d, $^2J_{C,P}$ = 5.4 Hz, Pyr-2-*C*H), 48.0 (s, Pyr-5-*C*H_2), 42.2 (s, Adm-1-*C*), 38.4 (s, Adm-2/8/10-*C*H_2), 36.8 (s, Adm-4/6/9-*C*H_2), 33.2 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.6 (d, $^1J_{C,P}$ = 28 Hz, *t*Bu'-*C*), 30.4 (s, Pyr-3-*C*H_2), 28.5 (s, Adm-3/5/7-*C*H), 28.3 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.2 Hz, *t*Bu'-CH_3), 25.6 (s, Pyr-4-*C*H_2), 21.9 (d, $^1J_{C,P}$ = 24 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 40.3 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2902m, 2870m, 2851m, 2378m, 2358m, 1689m, 1600s, 1468w, 1451w, 1386s, 1366m, 1347w, 1069m, 1023w, 925w, 879w, 815m, 666m, 623m cm^{-1}. **MS** (FAB, NBS + KCl): *m/z* (%) = 444 (28, $[M + K]^+$), 406 (19), 405 (27), 404 (90, $[M - H]^+$), 403 (24), 392 (34, $[M - BH_2]^+$), 377 (27), 376 (98), 334 (36), 320 (20), 278 (19), 270 (12), 242 (27), 241 (15), 240 (61), 184 (15), 135 (100), 128 (17), 93 (18), 91 (16), 79 (19), 67 (10), 57 (72), 41 (21). $[\alpha]_D^{20}$ = – 55.5 (*c* = 0.500, $CHCl_3$). **Elemental analysis**: calc. C 71.10%, H 11.19%, N 3.46%; found: C 71.06%, H 11.01%, N 3.38%.

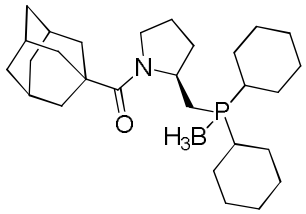
Adamantan-1-yl {(*S*)-2-[(di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}methanone ((*S*)-L_A10)



Product **(*S*)-L_A10** was prepared according to **general procedure 3** from **(*S*)-L_A10·BH_3**.

$C_{24}H_{42}NOP$ (391.57 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 22.2 (s) ppm.

Adamantan-1-yl {(*S*)-2-[(dicyclohexylphosphino)methyl]pyrrolidin-1-yl}methanone borane adduct ((*S*)-L_A11·BH_3)

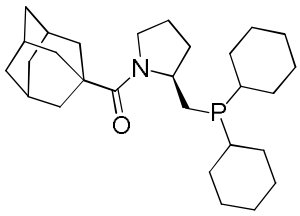


Product **(*S*)-L_A11·BH_3** (83%), isolated as a colorless semisolid, was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and 1-adamantanecarbonyl chloride.

$C_{28}H_{49}BNOP$ (457.48 g·mol^{-1}):
R_f = 0.10 (SiO_2, hexanes/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.37-4.26 (m, 1 H, Pyr-2-*H*), 3.81-3.73 (m, 1 H, Pyr-5-*H*H'), 3.63-3.54 (m, 1 H, Pyr-5-H*H'*), 2.37 ("t", *J* = 15 Hz, 1 H, C*H*H'P), 2.09-1.62 (m, 29 H), 1.56-1.16 (m, 13 H), 0.82-0.02 (br q, 3 H, B*H*$_3$) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 176.0 (s, *C*=O), 56.4 (br d, $^2J_{C,P}$ = 2.7 Hz, Pyr-2-*C*H), 46.9 (s, Pyr-5-*C*H$_2$), 42.1 (s, Adm-1-*C*), 38.3 (s, Adm-2/8/10-*C*H$_2$), 36.8 (s, Adm-4/6/9-*C*H$_2$), 32.6 (d, $^1J_{C,P}$ = 32 Hz, Cy-1-*C*H), 32.4 (d, $^1J_{C,P}$ = 37 Hz, Cy'-1-*C*H), 30.1 (s, Pyr-3-*C*H$_2$), 28.5 (s, Adm-3/5/7-*C*H), 27.3-26.8 (m, Cy/Cy'-*C*H$_2$), 25.9 (br s, Pyr-4-*C*H$_2$), 24.1 (d, $^1J_{C,P}$ = 27 Hz, *C*H$_2$P) ppm. **^{31}P{^{1}H} NMR** (202 MHz, $CDCl_3$): δ = 21.4 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2903s, 2861s, 2374m, 1614s, 1455m, 1377m, 1061m, 1010w, 880m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 457 (25), 456 (76, $[M - H]^+$), 455 (18), 444 (29, $[M - BH_2]^+$), 429 (30), 428 (100), 426 (12), 360 (35), 338 (26), 337 (10), 322 (11), 294 (28), 293 (21), 292 (75), 291 (19), 278 (12),

230 (14), 147 (12), 135 (86), 115 (21), 107 (10), 97 (12), 95 (15), 93 (24), 91 (22), 83 (31), 81 (42), 79 (29), 77 (10), 73 (26), 71 (12), 69 (31), 67 (27), 57 (37), 55 (66), 43 (34), 41 (42). $[\alpha]_D^{20}$ = – 14.7 (*c* = 0.692, $CHCl_3$). **Elemental analysis**: calc. C 73.51%, H 10.80%, N 3.06%; found: C 73.78%, H 10.60%, N 2.86%.

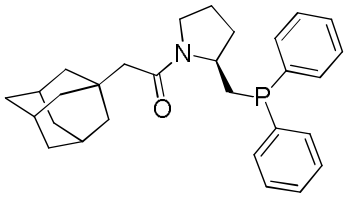
Adamantan-1-yl {(*S*)-2-[(dicyclohexylphosphino)methyl]pyrrolidin-1-yl}methanone ((*S*)-L_A11)



Product **(*S*)-L_A11** was prepared according to **general procedure 3** from **(*S*)-L_A11·BH_3**.

$C_{28}H_{46}NOP$ (443.64 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = – 10.3 (br) ppm.

2-(Adamantan-1-yl)-1-{(*S*)-2-[(diphenylphosphino)methyl]pyrrolidin-1-yl}ethanone ((*S*)-L_A12)

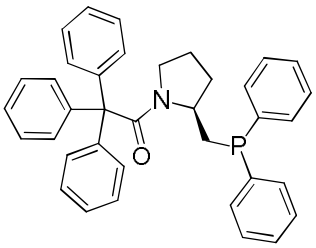


Compound **(*S*)-L_A12** (48%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 2-(adamantan-1-yl)acetyl chloride (**60**, prepared according to **general procedure 4**) and isolated as a colorless semisolid.

$C_{29}H_{36}NOP$ (445.58 g·mol^{-1}):
R_f = 0.20 (SiO_2, hexanes/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71-7.62 (m, 1 H, Ph/Ph'-*H*), 7.57-7.45 (m, 1 H, Ph/Ph'-*H*), 7.45-7.22 (m, 8 H, Ph/Ph'-*H*), 4.37-4.21/3.86-3.66* (m, 1 H, Pyr-2-*H*); 3.53-3.41 (m, 2 H, Pyr-5-*H*), 3.41-3.27/3.08-2.91* (m, 1 H, C*H*H'P), 2.34-1.24 (m, 22 H, CH*H'*P, CH_2, Pyr-*H* and Adm-*H*) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 170.1/169.7* (s, *C*=O), 139.5-138.8* (m, Ph-*i*-*C*), 137.7-136.9* (m, Ph'-*i*-*C*), 133.9* (d, $^2J_{C,P}$ = 20 Hz, Ph-*o*-*C*H), 133.2-132.7* (m,

Ph/Ph'-*C*H), 132.1* (d, $^{2}J_{C,P}$ = 18 Hz, Ph'-*o*-*C*H), 129.4-128.1 (m, Ph/Ph'-*C*H), 55.8/55.4* (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 48.7 (s, *C*H$_2$), 48.4/47.9* (s, Pyr-5-*C*H$_2$), 42.9/42.6* (s, Adm-2/8/9-*C*H$_2$), 37.0/36.9* (s, Adm-4/6/10-*C*H$_2$), 34.0-32.3* (m, *C*H$_2$P and Adm-1-*C*), 31.1-30.3* (m, Pyr-3-*C*H$_2$), 28.6 (br s, Adm-3/5/7-*C*H), 24.6 (br s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 24.6/– 24.9* (s) ppm. In the ^{1}H, ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 2:3 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (KBr): $\tilde{\nu}$ = 2897s, 2845m, 1622s, 1446w, 1433m, 1407s, 1360m, 1345w, 1313w, 1244w, 1183m, 1120w, 1102m, 1095m, 1027w, 987w, 917w, 878w, 790w, 738s, 693s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 445 (3, M^+), 284 (18), 245 (18), 244 (100), 243 (15), 201 (13), 135 (21), 70 (13), 69 (13). $[\alpha]_D^{20}$ = – 21.7 (*c* = 0.660, $CHCl_3$).

(*S*)-1-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone ((*S*)-L$_A$13)



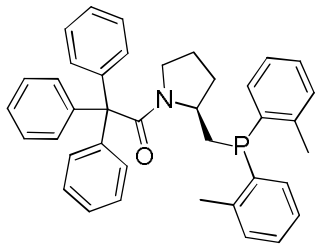
Product **(*S*)-L$_A$13** (96%) was prepared according to **general procedure 1** from **(*S*)-L$_C$1** and 2,2,2-triphenylacetyl chloride (prepared according to **general procedure 4**).

$C_{37}H_{34}NOP$ (539.65 g·mol^{-1}):

m.p. 105-107 °C. **R$_f$** = 0.28 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.65 ("t", *J* = 7.9 Hz, 2 H, PPh-*o*-*H*), 7.41-7.30 (m, 5 H, PPh'-*o*-*H* and PPh/Ph'-*H*), 7.29-7.23 (m, 9 H, PPh/Ph'-*H*, and CPh-*m*-*H*), 7.22-7.16 (m, 9 H, CPh-*o*/*p*-*H*), 4.47-4.38 (m, 1 H, Pyr-2-*H*), 3.34 ("dt", *J* = 13, 4.3 Hz, 1 H, C*H*H'P), 3.00-2.94 (m, 1 H, Pyr-5-*H*H'), 2.16-2.10 (m, 1 H, Pyr-5-H*H'*), 2.02-1.95 (m, 1 H, Pyr-3-*H*H'), 1.83-1.77 (m, 1 H, CH*H'*P), 1.71-1.63 (m, 1 H, Pyr-3-H*H'*), 1.56-1.48 (m, 1 H, Pyr-4-*H*H'), 1.40-1.30 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 171.0 (s, *C*=O), 143.0 (s, CPh-*i*-*C*), 139.5 (d, $^{1}J_{C,P}$ = 12 Hz, PPh-*i*-*C*), 137.2 (d, $^{1}J_{C,P}$ = 13 Hz, PPh'-*i*-*C*), 133.3 (d, $^{2}J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 132.9 (d, $^{2}J_{C,P}$ = 19 Hz, PPh'-*o*-*C*H), 130.5 (s, CPh-*m*-*C*H), 128.7 (d, $^{3}J_{C,P}$ = 9.2 Hz, PPh-*m*-*C*H), 128.6 (d,

$^{3}J_{C,P}$ = 7.3 Hz, PPh'-*m*-*C*H), 128.5 (s, PPh-*p*-*C*H), 128.4 (s, PPh'-*p*-*C*H), 127.8 (s, CPh-*o*-*C*H), 126.6 (s, CPh-*p*-*C*H), 68.0 (s, *C*Ph$_3$), 57.5 (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 48.6 (s, Pyr-5-*C*H$_2$), 32.2 (d, $^{1}J_{C,P}$ = 15 Hz, *C*H$_2$P), 30.6 (d, $^{3}J_{C,P}$ = 10 Hz, Pyr-3-*C*H$_2$), 25.1 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (202 MHz, CDCl$_3$): δ = – 21.1 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3053m, 2924s, 2850m, 1626s, 1599w, 1489m, 1445m, 1433m, 1381s, 1205w, 1180w, 1157m, 1086m, 1034w, 999w, 837m, 737s, 694s, 640m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 539 (5, M^+), 338 (24), 337 (25), 244 (20), 243 (100), 165 (18). $[\alpha]_D^{20}$ = – 57.2 (*c* = 0.620, CHCl$_3$). **Elemental analysis**: calc. C 82.35%, H 6.35%, N 2.60%; found: C 82.27%, H 7.36%, N 2.54%.

(*S*)-1-{2-[(Di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone ((*S*)-L$_A$14)



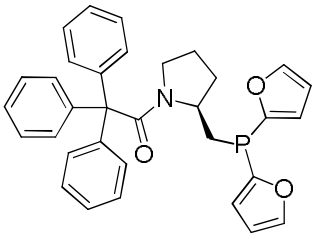
Product **(*S*)-L$_A$14** (67%) was prepared according to **general procedure 1** from **(*S*)-L$_C$2** and 2,2,2-triphenylacetyl chloride (prepared according to **general procedure 4**).

$C_{39}H_{38}NOP$ (567.70 g·mol^{-1}):

m.p. 92-95 °C. **R$_f$** = 0.39 (SiO$_2$, hexanes/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, CDCl$_3$): δ = 7.91-7.88 (m, 1 H, *o*Tol-3-*H*), 7.33-7.29 (m, 1 H, *o*Tol-6-*H*), 7.27-7.11 (m, 18 H, *o*Tol/*o*Tol'-*H* and Ph-*H*), 7.06-7.03 (m, 2 H, *o*Tol'-3-*H* and *o*Tol'-5-*H*), 6.95 (d, $^{3}J_{H,P}$ = 6.7 Hz, 1 H, *o*Tol'-6-*H*), 4.49-4.42 (m, 1 H, Pyr-2-*H*), 3.22 ("dt", *J* = 14, 3.8 Hz, 1 H, C*H*H'P), 2.95-2.90 (m, 1 H, Pyr-5-*H*H'), 2.52 (s, 3 H, *o*Tol-C*H*$_3$), 2.30 (s, 3 H, *o*Tol'-C*H*$_3$), 2.19-2.14 (m, 1 H, Pyr-5-H*H'*), 2.05-1.98 (m, 1 H, Pyr-3-*H*H'), 1.78-1.71 (m, 1 H, Pyr-3-H*H'*), 1.62 ("td", *J* = 13, 2.8 Hz, 1 H, CH*H'*P), 1.57-1.50 (m, 1 H, Pyr-4-*H*H'), 1.42-1.33 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CDCl$_3$): δ = 171.0 (s, *C*=O), 143.1 (s, Ph-*i*-*C*), 142.1 (d, $^{2}J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 141.8 (d, $^{2}J_{C,P}$ = 27 Hz, *o*Tol'-2-*C*), 137.3 (d, $^{1}J_{C,P}$ = 13 Hz, *o*Tol-1-*C*), 135.5 (d, $^{1}J_{C,P}$ = 12 Hz, *o*Tol'-1-*C*), 132.4 (s, *o*Tol-3-*C*H), 132.1 (s, *o*Tol'-3-*C*H), 130.6 (s, Ph-*m*-*C*H), 130.0-129.8 (m, *o*Tol/*o*Tol'-6-*C*H), 128.5 (s, *o*Tol-4-*C*H), 128.4 (s, *o*Tol'-4-*C*H), 127.8 (s,

Ph-*o*-*C*H), 126.6 (s, Ph-*p*-*C*H), 126.6 (s, *o*Tol-5-*C*H), 126.1 (s, *o*Tol'-5-*C*H), 68.0 (s, *C*Ph$_3$), 57.2 (d, $^2J_{C,P}$ = 22 Hz, Pyr-2-*C*H), 48.4 (s, Pyr-5-*C*H$_2$), 31.0 (d, $^1J_{C,P}$ = 14 Hz, *C*H$_2$P), 30.7 (d, $^3J_{C,P}$ = 9.6 Hz, Pyr-3-*C*H$_2$), 25.0 (d, $^4J_{C,P}$ = 1.1 Hz, Pyr-4-*C*H$_2$), 21.1 (d, $^3J_{C,P}$ = 6.5 Hz, *o*Tol-*C*H$_3$), 20.9 (d, $^3J_{C,P}$ = 5.8 Hz, *o*Tol'-*C*H$_3$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 42.4 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2943w, 911w, 1625s, 1595m, 1491m, 1443s, 1387m, 1178w, 1157m, 1136w, 1031m, 924w, 899w, 871, 740s, 697s, 641m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 567 (4, M^+), 338 (23), 337 (23), 244 (21), 243 (100), 229 (11), 165 (19). $[\alpha]_D^{20}$ = – 36.9 (*c* = 0.550, $CHCl_3$).

(*S*)-1-{2-[(Di(furan-2-yl)phosphino]methylpyrrolidin-1-yl}-2,2,2-triphenylethanone ((*S*)-L$_A$15)



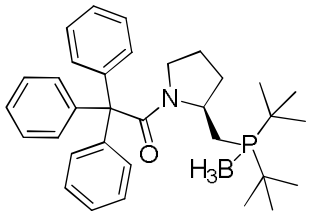
Product **(*S*)-L$_A$15** (80%) was prepared according to **general procedure 1** from **(*S*)-L$_C$3** and 2,2,2-triphenylacetyl chloride (prepared according to **general procedure 4**).

$C_{33}H_{30}NO_3P$ (519.57 g·mol^{-1}):

m.p. 175-179 °C. **R$_f$** = 0.19 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.62 (br s, 2 H, Fur/Fur'-5-*H*), 7.34-7.17 (m, 15 H, Ph-*H*), 6.82 (s, 1 H, Fur-3-*H*), 6.74 (s, 1 H, Fur'-3-*H*), 6.38 (s, 2 H, Fur/Fur'-4-*H*), 4.50-4.39 (m, 1 H, Pyr-2-*H*), 3.22-3.14 (m, 1 H, C*H*H'P), 2.97-2.87 (m, 1 H, Pyr-5-*H*H'), 2.19 (dd, *J* = 13 Hz, *J* = 10 Hz, 1 H, CH*H'*P), 2.15-2.05 (m, 1 H, Pyr-5-H*H'*), 1.90-1.80 (m, 1 H, Pyr-3-*H*H'), 1.54-1.44 (m, 1 H, Pyr-4-*H*H'), 1.41-1.23 (m, 1 H, Pyr-4-H*H'*), 1.32-1.22 (m, 1 H, Pyr-3-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 171.2 (*C*=O), 151.6 (d, $^1J_{C,P}$ = 18 Hz, Fur-2-*C*), 151.2 (d, $^1J_{C,P}$ = 13 Hz, Fur'-2-*C*), 147.1 (2 s, Fur/Fur'-5-*C*H), 143.0 (s, Ph-*i*-*C*), 130.6 (s, Ph-*m*-*C*H), 127.8 (s, Ph-*o*-*C*H), 126.6 (s, Ph-*p*-*C*H), 120.6 (d, $^2J_{C,P}$ = 27 Hz, Fur-3-*C*H), 120.0 (d, $^2J_{C,P}$ = 23 Hz, Fur'-3-*C*H), 110.8 (d, $^3J_{C,P}$ = 3.6 Hz, Fur-4-*C*H), 110.8 (d, $^3J_{C,P}$ = 2.6 Hz, Fur'-4-*C*H), 68.0 (s, *C*Ph$_3$), 57.6 (d, $^2J_{C,P}$ = 23 Hz,, Pyr-2-*C*H), 48.6 (s, Pyr-5-*C*H), 30.0 (d, $^1J_{C,P}$ = 6.3 Hz, *C*H$_2$P), 29.6 (d, $^3J_{C,P}$ = 4.1 Hz, Pyr-3-*C*H$_2$), 25.1 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz,

$CDCl_3$): δ = − 66.9 (br s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3122w, 3087w, 3056w, 3021w, 2972m, 2873w, 1959w, 1735w, 1627s, 1596m, 1491m, 1445m, 1420w, 1390s, 1346w, 1281w, 1254w, 1227w, 1211m, 1188w, 1163w, 1153m, 1118w, 1105w, 1074w, 1036w, 1005s, 943w, 902m, 875m, 838w, 799w,755s, 743s, 702s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 519 (13, M^+), 338 (18), 337 (15), 244 (20), 243 (100), 165 (45). $[\alpha]_D^{20}$ = – 77.9 (*c* = 1.00, $CHCl_3$). **HRMS** (ESI): calc. for $C_{33}H_{31}NO_3P$ ($[M + H]^+$): 520.2036; found: 520.2022.

(*S*)-1-{2-[(Di-*tert*-butylphosphino)methyl)]pyrrolidin-1-yl}-2,2,2-triphenylethanone borane adduct ((*S*)-L_A16·BH_3)



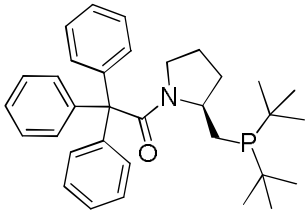
Product **(*S*)-L_A16·BH_3** (91%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and 2,2,2-triphenylacetyl chloride (prepared according to **general procedure 4**).

$C_{33}H_{45}BNOP$ (513.50 $g \cdot mol^{-1}$):

m.p. 207-210 °C. $\mathbf{R_f}$ = 0.33 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.32-7.25 (m, 6 H, Ph-*o*-*H*), 7.25-7.19 (m, 9 H, Ph-*m*-*H* and Ph-*p*-*H*), 4.59-4.52 (m, 1 H, Pyr-2-*H*), 2.90-2.82 (m, 1 H, Pyr-5-*H*H'), 2.77 ("td", *J* = 14, 2.3 Hz, 1 H, C*H*H'P), 2.24-2.13 (m, 2 H, Pyr-3-*H*H' and Pyr-5-H*H'*), 1.88-1.78 (m, 1 H, Pyr-3-H*H'*), 1.60-1.42 (m, 2 H, Pyr-4-H_2), 1.41 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.29-1.22 (m, 1 H, CH*H'*P), 1.24 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-*H*), 0.94-0.07 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 170.9 (s, *C*=O), 143.0 (s, Ph-*i*-*C*), 130.5 (s, Ph-*m*-*C*H), 127.8 (s, Ph-*o*-*C*H), 126.7 (s, Ph-*p*-*C*H), 68.0 (s, *C*Ph_3), 57.4 (d, $^2J_{C,P}$ = 5.0 Hz, Pyr-2-*C*H), 48.2 (s, Pyr-5-*C*H_2), 33.2 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.2 (d, $^1J_{C,P}$ = 28 Hz, *t*Bu'-*C*), 31.3 (s, Pyr-3-*C*H_2), 28.5 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.2 Hz, *t*Bu'-*C*H_3), 24.8 (s, Pyr-4-*C*H_2), 21.5 (d, $^1J_{C,P}$ = 24 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 40.1 ("br d", *J* = 54 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 3055m, 2924m, 2382m, 1620s, 1599w, 1489m, 1445m, 1385s, 1373s, 1252w, 1177w, 1155m, 1070m, 874w, 750s, 737s, 696s, 640m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 512

(100, $[M - H]^+$), 500 (21, $[M - BH_2]^+$), 484 (14), 442 (22), 270 (16), 243 (84), 240 (20), 184 (20), 165 (34), 128 (12), 57 (23). $[\alpha]_D^{20}$ = – 85.1 (c = 0.700, $CHCl_3$). **Elemental analysis**: calc. C 77.19%, H 8.83%, N 2.73%; found: C 77.02%, H 8.95%, N 2.85%.

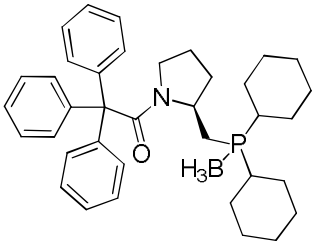
(*S*)-1-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone ((*S*)-L_A16)



Product **(*S*)-L_A16** was prepared according to **general procedure 3** from **(*S*)-L_A16·BH_3**.

$C_{33}H_{42}NOP$ (499.67 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 20.6 (s) ppm.

(*S*)-1-{2-([(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone borane adduct ((*S*)-L_A17·BH_3)

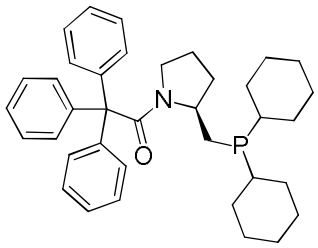


Product **(*S*)-L_A17·BH_3** (89%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and 2,2,2-triphenylacetyl chloride (prepared according to **general procedure 4**).

$C_{37}H_{49}BNOP$ (565.58 g·mol^{-1}):
m.p. 100-104 °C. **R_f** = 0.43 (SiO_2, cyclohexane/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.31-7.18 (m, 15 H, Ph-*H*), 4.50-4.42 (m, 1 H, Pyr-2-*H*), 2.89-2.82 (m, 1 H, Pyr-5-*H*H'), 2.71 ("td", J = 14, 2.3 Hz, 1 H, C*H*H'P), 2.19-2.09 (m, 2 H, Pyr-5-H*H'* and Pyr-3-*H*H'), 2.09-1.98 (m, 2 H, Cy/Cy'-1-*H*), 1.93-1.78 (m, 6 H, Cy/Cy'-*H*), 1.78-1.67 (m, 5 H, Pyr-3-H*H'* and Cy/Cy'-*H*), 1.59-1.38 (m, 4 H, Pyr-4-*H*H' and Cy/Cy'-*H*), 1.38-1.16 (m, 9 H, CH*H'*P, Pyr-4-H*H'* and Cy/Cy'-*H*), 0.82-0.07 (br q, 3 H, BH_3) ppm.

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 171.0 (s, *C*=O), 143.0 (s, Ph-*i*-*C*), 130.5 (s, Ph-*m*-*C*H), 127.8 (s, Ph-*o*-*C*H), 126.7 (s, Ph-*p*-*C*H), 68.0 (s, *C*Ph_3), 56.4 (d, $^{2}J_{C,P}$ = 4.6 Hz, Pyr-2-*C*H), 48.3 (s, Pyr-5-*C*H_2), 32.6 (d, $^{1}J_{C,P}$ = 32 Hz, Cy-1-*C*H), 32.5 (d, $^{1}J_{C,P}$ = 34 Hz, Cy'-1-*C*H), 31.3 (s, Pyr-3-*C*H_2), 27.2-26.8 (m, Cy/Cy'-*C*H_2), 26.8 (s, Cy/Cy'-*C*H_2), 26.4 (m, Cy/Cy'-*C*H_2), 26.1 (s, Cy/Cy'-*C*H_2), 25.0 (s, Pyr-4-*C*H_2), 23.7 (d, $^{1}J_{C,P}$ = 27 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 21.8 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2918s, 2849s, 2372m, 1626s, 1506m, 1489m, 1447m, 1373w, 1354m, 1339m, 1308m, 1157w, 1067m, 1000w, 891w, 876w, 762m, 746m, 698s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 564 (100, $[M - H]^+$), 552 (25, $[M - BH_2]^+$), 468 (17), 322 (19), 294 (28), 293 (16), 292 (19), 243 (74), 210 (22), 165 (23). $[\alpha]_D^{20}$ = – 61.6 (*c* = 0.532, $CHCl_3$). **Elemental analysis**: calc. C 78.57%, H 8.73%, N 2.48%; found: C 78.53%, H 8.98%, N 2.54%.

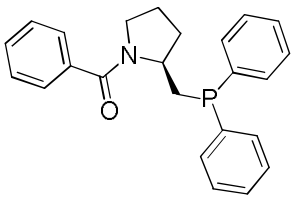
(*S*)-1-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone ((*S*)-L_A17)



Product **(*S*)-L_A17** was prepared according to **general procedure 3** from **(*S*)-L_A17·BH_3**.

$C_{37}H_{46}NOP$ (551.74 $g \cdot mol^{-1}$):
^{31}P{^{1}H} NMR (162 MHz, CD_2Cl_2): δ = – 10.3 (s) ppm.

(*S*)-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}(phenyl)methanone ((*S*)-L_A18)



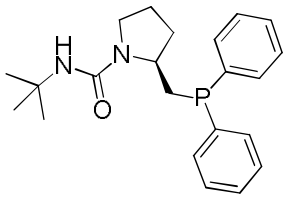
Compound **(*S*)-L_A18** (94%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and benzoyl chloride.

$C_{24}H_{24}NOP$ (373.43 g·mol^{-1}):

R_f = 0.30 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72-7.63 (m, 2 H, CPh-*H*), 7.48-7.25 (m, 13 H, CPh-*H* and PPh-*H*), 4.47-4.36 (m, 1 H, Pyr-2-*H*), 3.51-3.32 (m, 2 H, Pyr-5-H_2), 3.14-3.03 (d, $^2J_{H,P}$ = 13 Hz, 1 H, C*H*H'P), 2.23-2.13 (m, 5 H, CH*H'*P and Pyr-*H*) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 25.9 (s) ppm. **MS** (EI, 70 eV): *m/z* (%) = 373 (14, M^+), 248 (13), 206 (12), 202 (12), 201 (33), 183 (21), 173 (13), 172 (100), 171 (15), 158 (14), 121 (18), 105 (93), 104 (36), 77 (45), 69 (33). The spectroscopic data are consistent with those reported in the literature.[68f]

6.3.3
Trisubstituted Ureaphosphines (*S*)-L_{U3} and Precursors

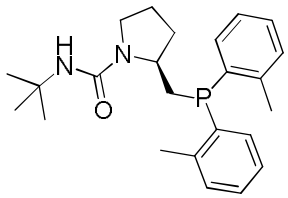
(*S*)-*N*-(*tert*-Butyl)-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}1)



Compound **(*S*)-L_{U3}1** (78%) was prepared according to **general procedure 1** from **(S)-L_C1** and *tert*-butyl isocyanate.

$C_{22}H_{29}N_2OP$ (368.45 g·mol^{-1}):
m.p. 92-95 °C. $\mathbf{R_f}$ = 0.26 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.55-7.49 (m, 2 H, Ph-*o*-*H*), 7.43-7.38 (m, 2 H, Ph-*o'*-*H*), 7.36-7.29 (m, 6 H, Ph-*H*), 3.94-3.84 (m, 2 H, Pyr-2-*H* and N*H*), 3.30-3.22 (m, 2 H, Pyr-5-H_2), 2.63 ("dt", J = 14, 3.7 Hz, 1 H, C*H*H'P), 2.17-2.10 (m, 1 H, CH*H'*P), 2.04-1.93 (m, 3 H, Pyr-3-H_2 and Pyr-4-*H*H'), 1.90-1.80 (m, 1 H, Pyr-4-H*H'*), 1.27 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 156.0 (s, *C*=O), 138.9 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*H), 138.1 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*H), 133.2 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 129.0 (s, Ph-*p*-*C*H), 128.8 (d, $^3J_{C,P}$ = 6.9 Hz, Ph-*m*-*C*H), 128.6 (s, Ph'-*p*-*C*H), 128.6 (d, $^2J_{C,P}$ = 6.9 Hz, Ph'-*m*-*C*H), 55.1 (d, $^2J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 50.7 (s, *t*Bu-*C*), 46.3 (s, Pyr-5-*C*H_2), 34.0 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.5 (d, $^3J_{C,P}$ = 8.4 Hz, Pyr-3-*C*H_2), 29.8 (s, *t*Bu-*C*H_3), 23.8 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 21.3 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3480w, 2968m, 2938m, 2919m, 2837m, 1641s, 1632s, 1507s, 1498m, 1448m, 1434m, 1387m, 1351m, 1342s, 1244w, 1217m, 1203m, 1182m, 1163w, 1067m, 1025m, 961m, 920m, 879m, 805m, 794m, 756s, 747s, 737s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 368 (24, M^+), 353 (16), 202 (14), 201 (17), 199 (11), 185 (13), 183 (27), 167 (48), 121 (12), 111 (31), 84 (39), 83 (23), 70 (100). $[\alpha]_D^{20}$ = – 53.4 (*c* = 1.05, $CHCl_3$). **HRMS** (ESI): calc. for $C_{22}H_{30}N_2OP$ ($[M+H]^+$): 369.2090; found: 369.2087.

(*S*)-*N*-(*tert*-Butyl)-2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}2)

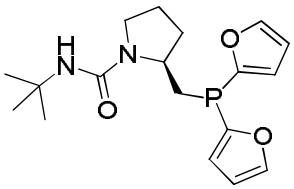


Compound **(*S*)-L_{U3}2** (56%) was prepared according to **general procedure 1** from **(S)-L_C2** and *tert*-butyl isocyanate.

$C_{24}H_{33}N_2OP$ (396.51 g·mol^{-1}):

R_f = 0.18 (SiO_2, hexanes/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.45-7.37 (m, 1 H, *o*Tol-*H*), 7.24-7.03 (m, 7 H, *o*Tol/*o*Tol'-*H*), 3.90 (s, 1 H, N*H*), 3.85-3.74 (m, 1 H, Pyr-2-*H*), 3.36-3.25 (m, 2 H, Pyr-5-H_2), 2.56-2.49 (m, 1 H, C*H*H'P), 2.49 (s, 3 H, *o*Tol-CH_3), 2.37 (s, 3 H, *o*Tol'-CH_3), 2.14-2.05 (m, 1 H, CH*H'*P), 2.02-1.84 (m, 4 H, Pyr-*H*), 1.25 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 156.0 (s, *C*=O), 142.5 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 141.7 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol'-2-*C*), 137.0 (d, $^1J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 136.0 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 131.8 (s, *o*Tol-6-*C*H), 131.2 (s, *o*Tol'-6-*C*H), 130.2 (d, $^3J_{C,P}$ = 4.6 Hz, *o*Tol-3-*C*H), 130.2 (d, $^3J_{C,P}$ = 4.7 Hz, *o*Tol'-3-*C*H), 128.8 (s, *o*Tol-4-*C*H), 128.5 (s, *o*Tol'-4-*C*H), 126.8 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 55.0 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 50.7 (s, *t*Bu-*C*), 46.1 (s, Pyr-5-*C*H_2), 32.8 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.7 (d, $^3J_{C,P}$ = 9.2 Hz, Pyr-3-*C*H_2), 29.7 (s, *t*Bu-*C*H_3), 23.7 (s, Pyr-4-*C*H_2), 21.5-21.1 (m, *o*Tol/*o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 42.9 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3344w, 2963m, 2929m, 2869m, 1634s, 1533s, 1447m, 1387m, 1657s, 1286m, 1203s, 1031w, 956w, 748m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 396 (4, M^+), 381 (22), 328 (13), 312 (39), 230 (14), 229 (47), 215 (23), 213 (24), 183 (17), 167 (52), 157 (16), 111 (14), 84 (100), 83 (21), 70 (84), 58 (96), 57 (17). $[\alpha]_D^{20}$ = – 12.3 (*c* = 0.470, $CHCl_3$).

(*S*)-*N*-(*tert*-Butyl)-2-{[di(furan-2-yl)phosphine]methyl}pyrrolidine-1-carboxamide ((*S*)-L_{U3}3)

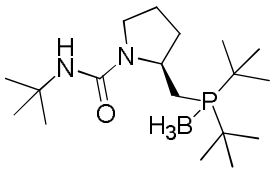


Compound **(*S*)-L_{U3}3** (65%) was prepared according to **general procedure 1** from **(S)-L_C3** and *tert*-butyl isocyanate.

$C_{18}H_{25}N_2O_3P$ (348.38 g·mol^{-1}):

m.p. 162-165 °C. **R_f** = 0.15 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.61 (br s, 2 H, Fur/Fur'-5-*H*), 6.79 (br s, 1 H, Fur-3-*H*), 6.72 (br s, 1 H, Fur'-3-*H*), 6.40-6.36 (m, 2 H, Fur/Fur'-4-*H*), 4.32-4.04 (m, 1 H, N*H*), 3.89-3.78 (m, 1 H, Pyr-2-*H*), 3.32-3.22 (m, 2 H, Pyr-5-H_2), 2.80-2.72 (m, 1 H, C*H*H'P), 2.24-2.13 (m, 1 H, CH*H'*P), 2.01-1.70 (m, 4 H, Pyr-*H*), 1.34 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 155.9 (s, *C*=O), 151.3 (d, $^1J_{C,P}$ = 16 Hz, Fur-2-*C*), 151.0 (d, $^1J_{C,P}$ = 17 Hz, Fur'-2-*C*), 147.2 (s, Fur-5-*C*H), 147.1 (s, Fur'-5-*C*H), 120.7 (d, $^2J_{C,P}$ = 26 Hz, Fur-3-*C*H), 120.2 (d, $^2J_{C,P}$ = 26 Hz, Fur'-3-*C*H), 111.0 (d, $^3J_{C,P}$ = 6.4 Hz, Fur-4-*C*H), 110.8 (d, $^3J_{C,P}$ = 6.4 Hz, Fur'-4-*C*H), 54.9 (d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 50.8 (s, *t*Bu-*C*), 46.2 (s, Pyr-5-*C*H_2), 31.2 (d, $^1J_{C,P}$ = 6.4 Hz, *C*H_2P), 30.7 (d, $^4J_{C,P}$ = 3.7 Hz, Pyr-3-*C*H_2), 29.7 (s, *t*Bu-*C*H_3), 23.6 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = −70.0 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3450m, 3105m, 2966m, 2859m, 1732m, 1639s, 1518s, 1454m, 1392w, 1350w, 1213s, 1151w, 1065w, 1002m, 960w, 902w, 884w, 834w, 771s, 713w, 656w cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 348 (17, M^+), 291 (11), 181 (6), 167 (10), 165 (17), 127 (6), 111 (13), 109 (6), 84 (14), 83 (17), 71 (5), 70 (100), 57 (7), 41 (5). $[\alpha]_D^{20}$ = − 46.6 (*c* = 1.00, $CHCl_3$). **HRMS** (ESI): calc. for $C_{18}H_{26}N_2O_3P$ ($[M+H]^+$): 349.1676; found: 349.1669.

(*S*)-*N*-(*tert*-Butyl)-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}4·BH_3)

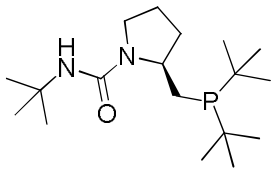


Compound **(*S*)-L_{U3}4·BH_3** (77%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and *tert*-butyl isocyanate.

$C_{18}H_{40}BN_2OP$ (342.31 g·mol^{-1}):

m.p. 176-178 °C. **R_f** = 0.25 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.27-4.20 (m, 1 H, Pyr-2-*H*), 4.10 (s, 1 H, N*H*), 3.30-3.24 (m, 1 H, Pyr-5-*H*H'), 3.17 ("q", $J_{H,H}$ = 8.1 Hz, 1 H, Pyr-5-H*H'*), 2.38 ("td", *J* = 14, 1.5 Hz, 1 H, C*H'*HP), 2.21-2.14 (m, 1 H, Pyr-3-*H*H'), 2.10-1.97 (m, 1 H, Pyr-3-H*H'*), 1.96-1.88 (m, 2 H, Pyr-4-H_2), 1.50-1.41 (m, 1 H, CH*H'*P), 1.38 (d, $^3J_{H,P}$ = 13 Hz, 9 H, P*t*Bu-*H*), 1.35 (s, 9 H, N*t*Bu-*H*), 1.24 (d, $^3J_{H,P}$ = 12 Hz, 9 H, P*t*Bu'-*H*), 0.83-0.03 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 156.0 (s, *C*=O), 55.2 (d, $^2J_{C,P}$ = 5.4 Hz, Pyr-2-*C*H), 50.8 (s, N*t*Bu-*C*), 46.1 (s, Pyr-5-*C*H_2), 33.1 (d, $^1J_{C,P}$ = 28 Hz, P*t*Bu-*C*), 32.5 (d, $^1J_{C,P}$ = 27 Hz, P*t*Bu'-*C*), 31.5 (s, Pyr-3-*C*H_2), 29.8 (s, N*t*Bu-*C*H_3), 28.3 (d, $^2J_{C,P}$ = 1.5 Hz, P*t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.5 Hz, P*t*Bu'-*C*H_3), 23.8 (s, Pyr-4-*C*H_2), 22.4 (d, $^1J_{C,P}$ = 23 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.9 ("br d", *J* = 75 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 3420w, 2969m, 2911m, 2871m, 1651s, 1508s, 1460m, 1452m, 1360s, 1344s, 1243m, 1216m, 1190m, 1149w, 1068m, 1025w, 963w, 918w, 858w, 814m, 791m, 768m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 341 (10, [M – H]$^+$), 272 (15), 271 (100), 259 (10), 242 (16), 240 (17), 215 (23), 139 (17), 84 (12), 70 (18), 57 (26). $[\alpha]_D^{20}$ = – 66.6 (*c* = 0.350, $CHCl_3$).

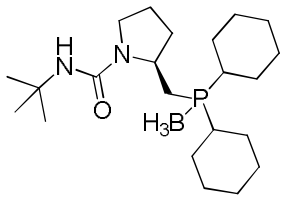
(*S*)-*N*-(*tert*-Butyl)-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}4)



Product **(*S*)-L_{U3}4** was prepared according to **general procedure 3** from **(*S*)-L_{U3}4·BH_3**.

$C_{18}H_{37}N_2OP$ (328.47 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 21.7 (s) ppm.

(*S*)-*N*-(*tert*-Butyl)-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}5·BH_3)

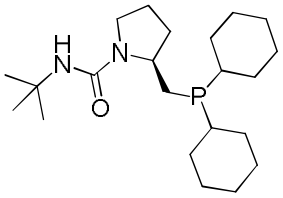


Compound **(*S*)-L_{U3}5·BH_3** (64%) was isolated as a colorless semisolid and prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and *tert*-butyl isocyanate.

$C_{22}H_{44}BN_2OP$ (394.38 g·mol^{-1}):
R_f = 0.27 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.18 (br s, 1 H, N*H*), 4.16-4.05 (m, 1 H, Pyr-2-*H*), 3.32-3.25 (m, 1 H, Pyr-5-*H*H'), 3.24-3.18 (m, 1 H, Pyr-5-H*H'*), 2.15 ("t", *J* = 14 Hz, 1 H, C*H*H'P), 2.02-1.62 (m, 15 H, Pyr-3-H_2, Pyr-4-H_2 and Cy/Cy'-*H*), 1.61-1.52 (m, 1 H, CH*H'*P), 1.47-1.37 (m, 2 H, Cy/Cy'-*H*), 1.35 (br s, 9 H, *t*Bu-*H*), 1.33-1.22 (m, 9 H, Cy/Cy'-*H*), 0.76-0.07 (br q, 3 H, BH_3) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 155.9 (s, *C*=O), 53.6 (d, $^2J_{C,P}$ = 4.2 Hz, Pyr-2-*C*H), 51.0 (s, *t*Bu-*C*), 46.0 (s, Pyr-5-*C*H_2), 32.5 (d, $^1J_{C,P}$ = 33 Hz, Cy-1-*C*H), 32.5 (d, $^1J_{C,P}$ = 33 Hz, Cy'-1-*C*H), 32.0 (s, Pyr-3-*C*H_2), 29.8 (s, *t*Bu-*C*H_3), 27.1-26.7 (m, Cy/Cy'-*C*H_2), 26.1 (s, Cy/Cy'-*C*H_2), 24.6 (d, $^1J_{C,P}$ = 26 Hz, *C*H_2P), 23.7 (s, Pyr-4-*C*H_2) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 21.9 ("br d", *J* = 73 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2963w, 2927s, 2916s, 2851s, 1614s, 1448s, 1415s, 1352m, 1312m, 1242w, 1221w, 1180m, 1155m, 1121m, 1004m, 894s, 875m, 746s, 719m, 695m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 394 (3), 393 (12, $[M - H]^+$), 311 (10), 298 (19), 297 (100), 294 (34),

293 (15), 292 (41), 139 (17), 114 (11), 84 (12), 83 (10), 70 (20), 58 (11), 55 (11). $[\alpha]_D^{20}$ = – 4.3 (*c* = 0.180, $CHCl_3$).

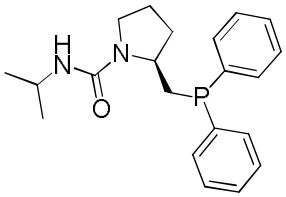
(*S*)-*N*-(*tert*-Butyl)-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}5)



Product **(*S*)-L_{U3}5** was prepared according to **general procedure 3** from **(*S*)-L_{U3}5·BH_3**.

$C_{12}H_{41}N_2OP$ (380.55 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = − 10.2 (s) ppm.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-isopropylpyrrolidine-1-carboxamide ((*S*)-L_{U3}6)

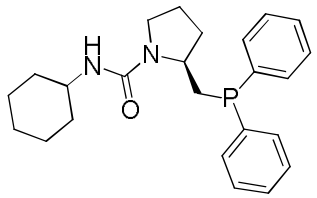


Compound **(*S*)-L_{U3}6** (71%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and isopropyl isocyanate.

$C_{21}H_{27}N_2OP$ (354.43 g·mol^{-1}):
m.p. 93-95 °C. **R_f** = 0.16 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.61-7.56 (m, 2 H, Ph-*o*-*H*), 7.44-7.27 (m, 8 H, Ph/Ph'-*H*), 3.97-3.86 (m, 2 H, Pyr-2-*H* and *i*Pr-C*H*), 3.73 (br d, 1 H, $^3J_{H,H}$ = 7.6 Hz, N*H*), 3.31-3.19 (m, 2 H, Pyr-5-H_2), 2.73 ("td", *J* = 14, 3.6 Hz, 1 H, C*H*H'P), 2.10-1.94 (m, 4 H, CH*H'*P, Pyr-4-*H*H' and Pyr-3-H_2), 1.93-1.84 (m, 1 H, Pyr-4-H*H'*), 1.08 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, *i*Pr-CH_3), 1.04 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, *i*Pr-CH_3) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 156.3 (s, *C*=O), 139.3 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 138.0 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 133.5 (d, $^2J_{C,P}$ = 20 Hz, Ph-*o*-*C*H), 132.9 (d, $^2J_{C,P}$ =19 Hz, Ph'-*o*-*C*H), 129.3 (s, Ph-*p*-*C*H), 129.1 (d, $^3J_{C,P}$ = 6.9 Hz, Ph-*m*-*C*H), 128.9 (s, Ph'-*p*-*C*H), 128.8 (d, $^3J_{C,P}$ = 6.9 Hz, Ph'-*m*-*C*H),

55.4 (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 46.4 (s, Pyr-5-*C*H_2), 42.4 (s, *i*Pr-*C*H), 34.2 (d, $^{1}J_{C,P}$ = 14 Hz, *C*H_2P), 31.5 (d, $^{3}J_{C,P}$ = 8.4 Hz, Pyr-3-*C*H_2), 24.1 (s, *i*Pr-*C*H_3), 24.0 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.4 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3480w, 2969w, 2932m, 2927m, 2918m, 2853m, 1613s, 1521w, 1469w, 1448m, 1415m, 1369m, 1352m, 1313m, 1306m, 1180m, 1156m, 1120m, 1027w, 1003w, 993w, 894m, 876m, 773m, 745s, 740s, 719m, 695s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 354 (22, M^+), 277 (12), 201 (14), 199 (10), 185 (12), 183 (26), 153 (97), 84 (47), 83 (19), 70 (100). $[\alpha]_D^{20}$ = – 47.8 (*c* = 1.03, $CHCl_3$). **HRMS** (ESI): calc. for $C_{21}H_{28}N_2OP$ ($[M+H]^+$): 355.1934; found: 355.1931.

(*S*)-*N*-Cyclohexyl-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}7)



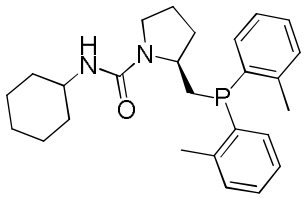
Compound **(*S*)-L_{U3}7** (76%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and cyclohexyl isocyanate.

$C_{24}H_{31}N_2OP$ (394.49 $g \cdot mol^{-1}$):

m.p. 129-131 °C. **R_f** = 0.11 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.62-7.55 (m, 2 H, Ph-*H*), 7.43-7.26 (m, 8 H, Ph/Ph'-*H*), 3.98-3.88 (m, 1 H, Pyr-2-*H*), 3.82 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1 H, N*H*), 3.65-3.55 (m, 1 H, Cy-1-*H*), 3.31-3.21 (m, 2 H, Pyr-5-H_2), 2.79 ("dt", *J* = 14, 3.8 Hz, 1 H, C*H*H'P), 2.11-1.94 (m, 4 H, Pyr-3-H_2, Pyr-4-*H*H' and CH*H*'P), 1.94-1.79 (m, 3 H, Pyr-4-H*H*' and Cy-*H*), 1.71-1.62 (m, 2 H, Cy-*H*), 1.62-1.53 (m, 1 H, Cy-*H*), 1.39-1.26 (m, 2 H, Cy-*H*), 1.15-1.06 (m, 1 H, Cy-*H*), 1.06-0.89 (m, 2 H, Cy-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 156.0 (s, *C*=O), 139.1 (d, $^{1}J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 137.7 (d, $^{1}J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 133.2 (d, $^{2}J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^{2}J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 129.0 (s, Ph-*p*-*C*H), 128.8 (d, $^{3}J_{C,P}$ = 6.9 Hz, Ph-*m*-*C*H), 128.6 (s, Ph'-*p*-*C*H), 128.5 (d, $^{3}J_{C,P}$ = 6.5 Hz, Ph'-*m*-*C*H), 55.1 (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 49.0 (s, Cy-1-*C*H), 46.1 (s, Pyr-5-CH_2), 34.4 (s, Cy-*C*H_2), 34.3 (s, Cy-*C*H_2), 33.8 (d, $^{1}J_{C,P}$ = 14 Hz, *C*H_2P), 31.1 (d, $^{3}J_{C,P}$ = 8.4 Hz, Pyr-3-*C*H_2), 25.8 (s, Cy-*C*H_2), 25.3 (s, Cy-*C*H_2), 25.2 (s, Cy-*C*H_2), 23.9 (s, Pyr-4-*C*H_2)

ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.4 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3315m, 2926m, 2849m, 1635m, 1608s, 1511s, 1480m, 1447w, 1432m, 1393m, 1353m, 1339m, 1288w, 1218w, 1190w, 1147w, 1068w, 917w, 871w, 809w, 771m, 737s, 694s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 394 (10, M^+), 317 (16), 285 (11), 284 (54), 216 (10), 201 (16), 200 (20), 199 (14), 194 (11), 193 (89), 185 (18), 183 (31), 121 (10), 111 (25), 110 (10), 84 (52), 83 (33), 70 (100). $[\alpha]_D^{20}$ = – 57.6 (*c* = 1.10, $CHCl_3$). **HRMS** (ESI): calc. for $C_{24}H_{32}N_2OP$ ($[M+H]^+$): 395.2247; found: 395.2244.

(*S*)-*N*-Cyclohexyl-2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}8)



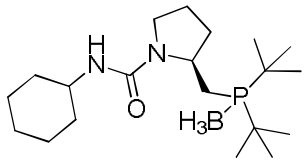
Compound **(*S*)-L_{U3}8** (52%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and cyclohexyl isocyanate.

$C_{26}H_{35}N_2OP$ (422.54 $g \cdot mol^{-1}$):

m.p. 145-149 °C. **R_f** = 0.14 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.66-7.55 (m, 1 H, *o*Tol-*H*), 7.30-7.09 (m, 7 H, *o*Tol/*o*Tol'-*H*), 3.94-3.76 (m, 2 H, Pyr-2-*H* and N*H*), 3.69-3.55 (m, 1 H, Cy-1-*H*), 3.39-3.20 (m, 2 H, Pyr-5-H_2), 2.76-2.64 (m, 1 H, C*H*H'P), 2.42 (s, 3 H, *o*Tol-CH_3), 2.41 (s, 3 H, *o*Tol'-CH_3), 2.20-2.11 (m, 1 H, CH*H'*P), 2.06-1.76 (m, 6 H, Pyr-*H* and Cy-*H*), 1.72-1.51 (m, 3 H, Cy-*H*), 1.40-1.22 (m, 2 H, Cy-*H*), 1.57-0.86 (m, 3 H, Cy-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 155.9 (s, *C*=O), 142.6 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 141.6 (d, $^2J_{C,P}$ = 25 Hz, *o*Tol'-2-*C*), 136.7-136.4 (br, *o*Tol-1-*C*), 135.5-135.0 (br, *o*Tol'-1-*C*), 132.0 (s, *o*Tol-6-*C*H), 131.5 (s, *o*Tol'-6-*C*H), 130.2 (br s, *o*Tol-3-*C*H), 130.2 (br s, *o*Tol'-3-*C*H), 129.0 (s, *o*Tol-4-*C*H), 128.7 (s, *o*Tol'-4-*C*H), 126.9 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 55.0 (d, $^2J_{C,P}$ = 24 Hz, Pyr-2-*C*H), 49.0 (s, Cy-1-*C*H), 46.1 (s, Pyr-5-*C*H_2), 34.4 (s, Cy-*C*H_2), 34.3 (s, Cy-*C*H_2), 32.5 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 31.3 (d, $^3J_{C,P}$ = 9.0 Hz, Pyr-3-*C*H_2), 25.8 (s, Cy-*C*H_2), 25.3 (Cy-*C*H_2), 25.3 (Cy-*C*H_2), 23.8 (s, Pyr-4-*C*H_2), 21.5 (d, $^3J_{C,P}$ = 19 Hz, *o*Tol-*C*H_3), 21.2 (d, $^3J_{C,P}$ = 19 Hz, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 42.0 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3307m, 2927m,

2850m, 1746w, 1615s, 1525s, 1448m, 1390m, 1352m, 1251w, 1197w, 1158w, 1076w, 1028w, 917w, 890w, 873w, 744s, 720m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 422 (7, M^+), 407 (19), 331 (32), 312 (26), 229 (14), 213 (26), 193 (72), 84 (61), 83 (12), 70 (100). $[\alpha]_D^{20}$ = – 59.6 (*c* = 0.99, $CHCl_3$).

(*S*)-*N*-Cyclohexyl-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}9·BH_3)

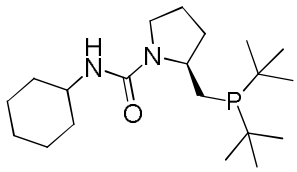


Compound **(*S*)-L_{U3}9·BH_3** (63%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and cyclohexyl isocyanate.

$C_{20}H_{42}BN_2OP$ (368.35 $g \cdot mol^{-1}$):

m.p. 79-83 °C. $\mathbf{R_f}$ = 0.20 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.27-4.21 (m, 1 H, Pyr-2-*H*), 4.08 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, N*H*), 3.71-3.61 (m, 1 H, Cy-1-*H*), 3.30-3.25 (m, 1 H, Pyr-5-*H*H'), 3.15 ("q", *J* = 8.0 Hz, 1 H, Pyr-5-H*H'*), 2.48 ("t", *J* = 14, 2.5 Hz, 1 H, C*H*H'P), 2.22-2.14 (m, 1 H, Pyr-3-*H*H'), 2.08-1.98 (m, 1 H, Pyr-3-H*H'*), 1.98-1.87 (m, 4 H, Cy-*H*), 1.76-1.64 (m, 2 H, Cy-*H*), 1.63-1.54 (m, 1 H, Pyr-4-*H*H'), 1.48-1.40 (m, 1 H, CH*H'*P), 1.38 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.39-1.28 (m, 2 H, Cy-*H*), 1.22 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-*H*), 1.17-0.91 (m, 3 H, Pyr-4-H*H'* and Cy-*H*), 0.81-0.06 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 156.1 (s, *C*=O), 55.6 (d, $^2J_{C,P}$ = 5.8 Hz, Pyr-2-*C*H), 48.9 (s, Cy-1-*C*H), 46.0 (s, Pyr-5-*C*H_2), 34.6 (s, Cy-*C*H_2), 34.3 (s, Cy-*C*H_2), 33.1 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.0 (d, $^1J_{C,P}$ = 28 Hz, *t*Bu'-*C*), 31.5 (s, Pyr-3-*C*H_2), 28.3 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.2 Hz, *t*Bu'-*C*H_3), 25.7 (s, Pyr-4-*C*H_2), 25.3 (s, Cy-*C*H_2), 25.2 (s, Cy-*C*H_2), 23.8 (s, Cy-*C*H_2), 22.5 (d, $^1J_{C,P}$ = 23 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.9 ("br d", *J* = 68 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 3324w, 2926m, 2852m, 1617s, 1513s, 1474m, 1448m, 1391m, 1345s, 1242w, 1188m, 1145m, 1070s, 1021m, 919w, 889w, 813m, 772m cm^{-1}. **MS** (EI, eV): *m/z* (%) =367 (8, $[M - H]^+$), 298 (18), 297 (100), 242 (13), 241 (13), 240 (12), 221 (12), 70 (13), 57 (11). $[\alpha]_D^{20}$ = – 31.0 (*c* = 0.581, $CHCl_3$). **HRMS** (ESI): calc. for $C_{20}H_{41}BN_2OP$ ($[M - H]^+$): 367.3044; found: 367.3041.

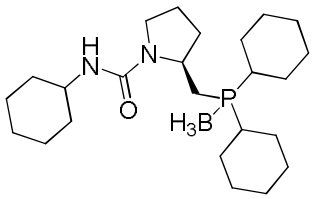
(*S*)-*N*-Cyclohexyl-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}9)



Product **(*S*)-L_{U3}9** was prepared according to **general procedure 3** from **(*S*)-L_{U3}9·BH_3**. $C_{20}H_{39}N_2OP$ (354.51 g·mol^{-1}):

$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 21.8 (s) ppm.

(*S*)-*N*-Cyclohexyl-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}10·BH_3)

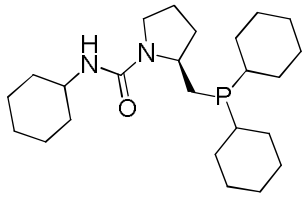


Compound **(*S*)-L_{U3}10·BH_3** (51%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and cyclohexyl isocyanate.

$C_{24}H_{46}BN_2OP$ (420.42 g·mol^{-1}):
m.p. 128-131 °C. **R_f** = 0.14 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.22-4.11 (m, 2 H, Pyr-2-*H* and N*H*), 3.69-3.60 (m, 1 H, NCy-1-*H*), 3.32-3.27 (m, 1 H, Pyr-5-*H*H'), 3.20 ("q", *J* = 8.0 Hz, 1 H, Pyr-5-H*H'*), 2.28 ("t", *J* = 14 Hz, 1 H, C*H*H'P), 2.05-1.57 (m, 21 H), 1.57-1.49 (m, 1 H, CH*H'*P), 1.49-1.05 (m, 15 H), 0.87-0.05 (br q, 3 H, B*H*$_3$) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 155.9 (s, *C*=O), 54.0 (d, $^2J_{C,P}$ = 4.2 Hz, Pyr-2-*C*H), 49.1 (s, NCy-1-*C*H), 45.9 (s, Pyr-5-*C*H_2), 34.5 (s, NCy-*C*H_2), 34.3 (s, NCy-*C*H_2), 32.6 (d, $^1J_{C,P}$ = 11 Hz, PCy-1-*C*H), 32.3 (d, $^1J_{C,P}$ = 12 Hz, PCy'-1-*C*H), 31.8 (s, Pyr-3-*C*H_2), 27.2-26.5 (m, PCy/Cy'-CH_2), 26.1 (s, PCy/Cy'-*C*H_2), 25.7 (NCy-4-*C*H_2), 25.4 (s, NCy-*C*H_2), 25.3 (s, NCy-*C*H_2), 24.8 (d, $^1J_{C,P}$ = 26 Hz, *C*H_2P), 23.8 (s, Pyr-4-*C*H_2) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 21.7 ("br d", *J* = 71 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 3339w, 2924m, 2850m, 1630s, 1516m, 1447m, 1432m, 1386m, 1349m, 1342m, 1172w, 1066m, 856w, 763m, 752m, 696m cm^{-1}. **MS** (EI,

70 eV): *m/z* (%) = 420 (2), 419 (9, $[M - H]^+$), 337 (11), 324 (20), 323 (100), 294 (28), 293 (11), 292 (23), 221 (14), 70 (11). $[\alpha]_D^{20}$ = – 19.3 (*c* = 0.580, $CHCl_3$).

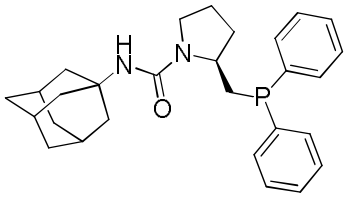
(*S*)-*N*-Cyclohexyl-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}10)



Product **(*S*)-L_{U3}10** was prepared according to **general procedure 3** from **(*S*)-L_{U3}10·BH_3**.

$C_{24}H_{43}N_2OP$ (406.58 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = −10.5 (s) ppm.

(*S*)-*N*-(Adamantan-1-yl)-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}11)

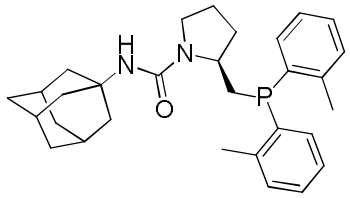


Compound **(*S*)-L_{U3}11** (94%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 1-adamantyl isocyanate.

$C_{28}H_{35}N_2OP$ (446.56 g·mol^{-1}):
m.p. 77-79 °C. **R_f** = 0.29 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.58-7.53 (m, 2 H, Ph-*H*), 7.42-7.29 (m, 8 H, Ph/Ph'-*H*), 3.93-3.86 (m, 1 H, Pyr-2-*H*), 3.84 (s, 1 H, N*H*), 3.25-3.19 (m, 2 H, Pyr-5-H_2), 2.69 ("dt", $^2J_{H,P}$ =13 Hz, $J_{H,H}$ = 3.8 Hz, 1 H, C*H*H'P), 2.06-1.93 (m, 7 H, CH*H*'P, Pyr-3-H_2, Pyr-4-*H*H' and Adm-3/5/7-*H*), 1.90 (s, 6 H, Adm-2/8/9-H_2), 1.88-1.78 (m, 1 H, Pyr-4-H*H*'), 1.66 (s, 6 H, Adm-4/6/10-H_2) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 155.7 (s, *C*=O), 139.0 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 138.1 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 133.2 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.9 (s, Ph-*p*-*C*H), 128.8 (d, $^3J_{C,P}$ = 6.9 Hz, Ph-*m*-*C*H), 128.6 (s, Ph'-*p*-*C*H), 128.6 (d, $^3J_{C,P}$ = 6.9 Hz, Ph'-*m*-*C*H),

55.1 (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 51.2 (s, Adm-1-*C*), 46.3 (s, Pyr-5-*C*H_2), 42.7 (s, Adm-2/8/9-*C*H_2), 36.6 (s, Adm-4/6/10-*C*H_2), 34.0 (d, $^{1}J_{C,P}$ = 15 Hz, *C*H_2P), 31.4 (d, $^{3}J_{C,P}$ = 8.8 Hz, Pyr-3-*C*H_2), 29.7 (s, Adm-3/5/7-*C*H), 23.8 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = − 21.1 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3441w, 3341m, 2904s, 2847m, 1640s, 1630s, 1504s, 1480m, 1452w, 1372w, 1352s, 1337m, 1306s, 1185m, 1160m, 1101w, 1081w, 738s, 715s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 446 (27, M^+), 284 (12), 246 (16), 245 (97), 215 (10), 204 (13), 201 (24), 200 (86), 199 (30), 185 (19), 183 (30), 177 (26), 151 (14), 135 (61), 121 (17), 120 (50), 94 (23), 93 (12), 91 (10), 84 (56), 83 (32), 79 (13), 70 (100). $[\alpha]_D^{20}$ = – 34.5 (*c* = 1.04, $CHCl_3$). **HRMS** (ESI): calc. for $C_{28}H_{36}N_2OP$ ($[M+H]^+$): 447.2560; found: 447.2553.

(*S*)-*N*-(Adamantan-1-yl)-2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}12)



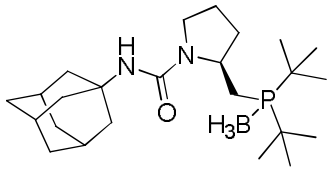
Compound **(*S*)-L_{U3}12** (79%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and 1-adamantyl isocyanate.

$C_{30}H_{39}N_2OP$ (474.62 g·mol^{-1}):

m.p. 80-84 °C. **R_f** = 0.33 (SiO_2, hexanes/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.47-7.40 (m, 1 H, *o*Tol-*H*), 7.24-7.11 (m, 7 H, *o*Tol/*o*Tol'-*H*), 3.87-3.78 (m, 2 H, Pyr-2-*H* and N*H*), 3.35-3.26 (m, 2 H, Pyr-5-H_2), 2.55 ("dt", *J* = 14, 3.2 Hz, 1 H, C*H*H'P), 2.44 (s, 3 H, *o*Tol-CH_3), 2.38 (s, 3 H, *o*Tol'-CH_3), 2.12-1.83 (m, 8 H, CH*H'*P, Pyr-*H* and Adm-3/5/7-*H*), 1.87 (s, 6 H, Adm-2/8/9-H_2), 1.64 (s, 6 H, Adm-4/6/10-H_2) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 155.7 (s, *C*=O), 142.5 (d, $^{2}J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 141.8 (d, $^{2}J_{C,P}$ = 26 Hz, *o*Tol'-2-*C*), 137.1 (d, $^{1}J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 136.0 (d, $^{1}J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 131.9 (s, *o*Tol-3-*C*H), 131.3 (s, *o*Tol'-3-*C*H), 130.3-130.1 (m, *o*Tol/*o*Tol'-6-*C*H), 128.7 (s, *o*Tol-4-*C*H), 128.5 (s, *o*Tol'-4-*C*H), 126.8 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 55.0 (d, $^{2}J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 51.2 (s, Adm-1-*C*), 46.1 (s, Pyr-5-*C*H_2), 42.7 (s, Adm-2/8/9-*C*H_2), 36.6 (s, Adm-4/6/10-*C*H_2), 32.8 (d, $^{1}J_{C,P}$ = 15 Hz, *C*H_2P), 31.6 (d, $^{3}J_{C,P}$ = 9.4 Hz, Pyr-3-*C*H_2), 29.7 (s,

Adm-3/5/7-*C*H), 23.7 (s, Pyr-4-*C*H_2), 21.6-21.1 (m, *o*Tol/*o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 42.1 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3353w, 2902s, 2846s, 1632s, 1506s, 1450m, 1371m, 1352s, 1338m, 1306m, 1186w, 1159w, 1130w, 1080w, 1031w, 957w, 919w, 875w, 802w, 745s, 719m cm^{-1}. **MS** (EI, eV): *m/z* (%) = 474 (7, M^+), 459 (24), 383 (21), 246 (19), 245 (100), 229 (16), 228 (32), 227 (14), 214 (11), 213 (61), 177 (16), 151 (17), 135 (49), 120 (29), 94 (23), 93 (12), 84 (68), 83 (16), 79 (12), 70 (95). $[\alpha]_D^{20}$ = – 28.8 (*c* = 0.600, $CHCl_3$). **HRMS** (ESI): calc. for $C_{30}H_{40}N_2OP$ ($[M + H]^+$): 475.2873; found: 475.2862.

(*S*)-*N*-(Adamantan-1-yl)-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}13·BH_3)



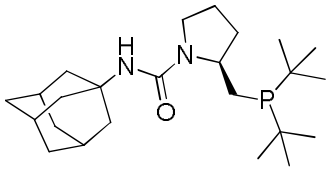
Product **(*S*)-L_{U3}13·BH_3** (72%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and 1-adamantyl isocyanate.

$C_{24}H_{46}BN_2OP$ (420.42 g·mol^{-1}):

m.p. 98-100 °C. **R_f** = 0.27 (SiO_2, cyclohexane/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.27-4.18 (m, 1 H, Pyr-2-*H*), 3.98 (s, 1 H, N*H*), 3.30-3.24 (m, 1 H, Pyr-5-*H*H'), 3.17 ("q", $J_{H,H}$ = 8.1 Hz, 1 H, Pyr-5-H*H'*), 2.36 ("t", *J* = 15 Hz, 1 H, C*H'*HP), 2.22-2.14 (m, 1 H, Pyr-3-*H*H'), 2.05 (br s, 3 H, Adm-3/5/7-*H*), 1.98 (br s, 7 H, Pyr-3-H*H'* and Adm-2/8/9-H_2), 1.95-1.87 (m, 2 H, Pyr-4-H_2), 1.66 (br s, 6 H, Adm-4/6/10-H_2), 1.50-1.41 (m, 1 H, CH*H'*P), 1.37 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.23 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-*H*), 0.82-0.13 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 155.6 (s, *C*=O), 55.1 (d, $^2J_{C,P}$ = 5.4 Hz, Pyr-2-*C*H), 51.4 (s, Adm-1-*C*), 46.2 (s, Pyr-5-*C*H_2), 42.7 (s, Adm-2/8/9-*C*H_2), 36.6 (s, Adm-4/6/10-*C*H_2), 33.6 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.6 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu'-*C*), 31.5 (s, Pyr-3-*C*H_2), 29.7 (s, Adm-3/5/7-*C*H), 28.4 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.1 Hz, *t*Bu'-*C*H_3), 23.7 (s, Pyr-4-*C*H_2), 22.4 (d, $^1J_{C,P}$ = 23 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.8 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2904s, 2851m, 2363m, 1644s, 1510s, 1475m, 1454m, 1351m, 1306m, 1255w, 1191m, 1153w, 1072m, 1020w, 958w, 926w, 816m, 758m cm^{-1}. **MS** (FAB, NBS + KCl): *m/z* (%) = 459 (18, $[M + K]^+$),

421 (24), 420 (31), 419 (100, $[M - H]^+$), 418 (27), 407 (23, $[M - BH_2]^+$), 349 (17), 242 (25), 240 (18), 135 (35), 128 (10), 70 (12), 57 (34). $[\alpha]_D^{20}$ = – 48.1 (c = 0.520, $CHCl_3$). **Elemental analysis**: calc. C 68.57%, H 11.03%, N 6.66%; found: C 68.33%, H 11.01%, N 6.66%.

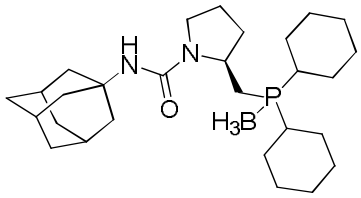
(*S*)-*N*-(Adamantan-1-yl)-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}13)



Product **(*S*)-L_{U3}13** was prepared according to **general procedure 3** from **(*S*)-L_{U3}13·BH_3**.

$C_{24}H_{43}N_2OP$ (406.58 g·mol^{-1}):
^{31}P{^{1}H} NMR (162 MHz, CD_2Cl_2): δ = 21.7 (s) ppm.

(*S*)-*N*-(Adamantan-1-yl)-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}14·BH_3)

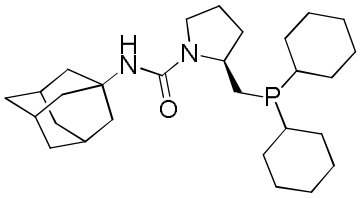


Product **(*S*)-L_{U3}2·BH_3** (87%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and 1-adamantyl isocyanate.

$C_{28}H_{50}BN_2OP$ (472.49 g·mol^{-1}):
m.p. 79-82 °C. **R_f** = 0.19 (SiO_2, cyclohexane/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.16-4.08 (m, 1 H, Pyr-2-*H*), 4.08 (s, 1 H, N*H*), 3.30-3.26 (m, 1 H, Pyr-5-*H*H'), 3.21 ("q", J = 8.1 Hz, 1 H, Pyr-5-H*H'*), 2.19-2.12 (m, 1 H, C*H*H'P), 2.06 (br s, 3 H, Adm-3/5/7-*H*), 2.01-1.75 (m, 19 H, Pyr-*H*, Adm-2/8/9-H_2 and Cy/Cy'-*H*), 1.73-1.68 (m, 4 H, Cy/Cy'-*H*), 1.66 (br s, 6 H, Adm-4/6/10-H_2), 1.59-1.53 (m, 1 H, CH*H'*P), 1.49-1.37 (m, 2 H, Cy/Cy'-*H*), 1.37-1.16 (m, 7 H, Cy/Cy'-*H*), 0.73-0.04 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 155.6 (s, *C*=O), 53.6 (d, $^2J_{C,P}$ = 3.7 Hz,

Pyr-2-*C*H), 51.5 (s, Adm-1-*C*), 46.0 (s, Pyr-5-*C*H_2), 42.7 (s, Adm-2/8/9-*C*H_2), 36.6 (s, Adm-4/6/10-*C*H_2), 32.5 (d, $^1J_{C,P}$ = 34 Hz, Cy-1-*C*H), 32.4 (d, $^1J_{C,P}$ = 32 Hz, Cy'-1-*C*H), 32.0 (s, Pyr-3-*C*H_2), 29.8 (s, Adm-3/5/7-*C*H), 27.1-26.6 (m, Cy/Cy'-*C*H_2), 26.1 (s, Cy/Cy'-*C*H_2), 24.6 (d, $^1J_{C,P}$ = 26 Hz, *C*H_2P), 23.6 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 21.8 (br d) ppm. **IR** (neat): $\tilde{\nu}$ = 2907s, 2849s, 2374m, 1651s, 1506s, 1447m, 1350m, 1339m, 1306m, 1195w, 1065m, 1003w, 854w cm^{-1}. **MS** (ESI): *m/z* (%) = 483 (46), 481 (100, [M – BH_3 + Na]$^+$), 480 (50), 473 (11, [M + H]$^+$), 466 (21), 399 (17), 322 (13), 321 (16), 304 (37), 281 (30), 253 (25), 252 (78), 224 (11), 184 (29). $[\alpha]_D^{20}$ = – 21.4 (*c* = 0.186, $CHCl_3$). **Elemental analysis**: calc. C 71.18%, H 10.67%, N 5.93%; found: C 71.20%, H 10.41%, N 6.07%.

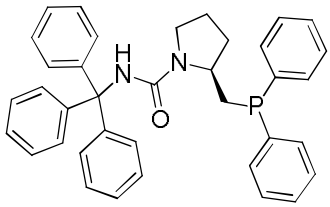
(*S*)-*N*-(Adamantan-1-yl)-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U3}14)



Product **(*S*)-L_{U3}14** was prepared according to **general procedure 3** from **(*S*)-L_{U3}14·BH_3**.

$C_{28}H_{47}N_2OP$ (458.66 g·mol^{-1}):
^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ = – 10.2 (s) ppm.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide ((*S*)-L_{U3}15)

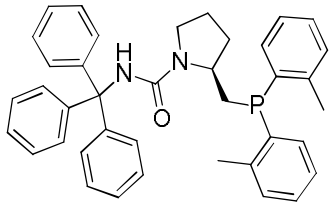


Product **(*S*)-L_{U3}15·BH_3** (92%), isolated as a colorless semisolid, was prepared according to **general procedure 1** from **(*S*)-L_C1** and triphenylmethyl isocyanate (**66**).[82]

$C_{37}H_{35}N_2OP$ (554.66 g·mol^{-1}):
R_f = 0.26 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.36-7.11 (m, 25 H, PPh/Ph'-*H* and CPh-*H*), 5.42 (s, 1 H, N*H*), 4.06-3.95 (m, 1 H, Pyr-2-*H*),

3.37-3.21 (m, 2 H, Pyr-5-H_2), 3.87 ("dt", J = 14, 3.8 Hz, 1 H, CHH'P), 2.07 (dd, J = 14, 9.3 Hz, 1 H, CHH'P), 1.93-1.79 (m, 2 H, Pyr-3-HH' and Pyr-4-HH'), 1.79-1.69 (m, 2 H, Pyr-3-HH' and Pyr-4-HH') ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 155.4 (s, C=O), 146.0 (s, CPh-i-C), 139.2 (d, $^{1}J_{C,P}$ = 12 Hz, PPh-i-C), 138.0 (d, $^{1}J_{C,P}$ = 12 Hz, PPh'-i-C), 133.0 (d, $^{2}J_{C,P}$ = 5.6 Hz, PPh-o-CH), 132.8 (d, $^{2}J_{C,P}$ = 5.6 Hz, PPh'-o-CH), 128.9 (s, CPh-o-CH), 128.7-128.4 (m, PPh-CH), 127.9 (s, CPh-m-CH), 126.7 (s, CPh-p-CH), 70.1 (s, CPh$_3$), 55.9 (d, $^{2}J_{C,P}$ = 13 Hz, Pyr-2-CH), 46.4 (s, Pyr-5-CH$_2$), 33.8 (d, $^{1}J_{C,P}$ = 15 Hz, CH$_2$P), 31.3 (d, $^{3}J_{C,P}$ = 8.2 Hz, Pyr-3-CH$_2$), 24.0 (s, Pyr-4-CH$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.6 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3055m, 2920m, 2864m, 1663s, 1489s, 1474m, 1445m, 1433m, 1339s, 1184m, 1026m, 744m, 696s cm^{-1}. **MS** (ESI): m/z (%) = 577 (20, [M + Na]$^+$), 555 (39, [M + H]$^+$), 244 (22), 243 (100), 165 (19). $[\alpha]_D^{20}$ = – 28.8 (c = 1.71, $CHCl_3$). **Elemental analysis**: calc. C 80.12%, H 6.36%, N 5.05%; found: C 79.86%, H 6.98%, N 4.65%.

(*S*)-2-[(Di-*ortho*-tolylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide ((*S*)-L$_{U3}$16)



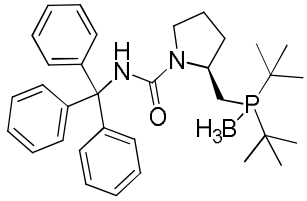
Product **(*S*)-L$_{U3}$16** (42%) was prepared according to **general procedure 1** from **(*S*)-L$_C$2** and triphenylmethyl isocyanate (**66**).[82]

$C_{39}H_{39}N_2OP$ (582.71 g·mol^{-1}):

R$_f$ = 0.36 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.32-7.06 (m, 23 H, oTol/oTol'-H and Ph-H), 5.65 (s, 1 H, NH), 4.12-4.02 (m, 1 H, Pyr-2-H), 3.49-3.39 (m, 1 H, Pyr-5-HH'), 3.88-3.30 (m, 1 H, Pyr-5-HH'), 2.58-2.49 (m, 1 H, CHH'P), 2.37 (s, 3 H, oTol-CH_3), 2.30 (s, 3 H, oTol'-CH_3), 2.01-1.83 (m, 5 H, CHH'P and Pyr-H) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 155.6 (s, C=O), 146.0 (s, Ph-i-C), 142.2 (d, $^{2}J_{C,P}$ = 7.3 Hz, oTol-2-C), 142.0 (d, $^{2}J_{C,P}$ = 7.7 Hz, oTol'-2-C), 136.9 (d, $^{1}J_{C,P}$ = 12 Hz, oTol-1-C), 135.7 (d, $^{1}J_{C,P}$ = 12 Hz, oTol'-1-C), 131.6 (br s, oTol/oTol'-3-CH), 130.2 (d, $^{2}J_{C,P}$ = 5.0 Hz, oTol-6-CH), 130.1 (d, $^{2}J_{C,P}$ = 5.0 Hz, oTol'-6-CH), 128.8 (s, Ph-m-CH), 128.6 (s, oTol-4-CH), 128.6 (s, oTol'-4-CH), 127.9 (s,

Ph-*o*-*C*H), 126.7 (s, Ph-*p*-*C*H), 126.5 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 70.1 (s, *C*Ph$_3$), 56.0 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 46.2 (s, Pyr-5-*C*H$_2$), 32.8 (d, $^1J_{C,P}$ = 15 Hz, *C*H$_2$P), 31.8 (d, $^3J_{C,P}$ = 9.2 Hz, Pyr-3-*C*H$_2$), 23.8 (s, Pyr-4-*C*H$_2$), 21.4 (d, $^3J_{C,P}$ = 8.4 Hz, *o*Tol-*C*H$_3$), 21.2 (d, $^3J_{C,P}$ = 8.0 Hz, *o*Tol'-*C*H$_3$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CDCl$_3$): δ = – 42.2 (s) ppm.

(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide borane adduct ((*S*)-L$_{U3}$17·BH$_3$)

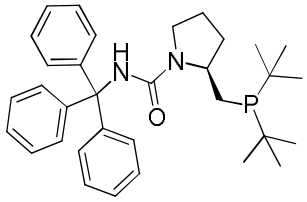


Product **(*S*)-L$_{U3}$17·BH$_3$** (88%) was prepared according to **general procedure 2** from **(*S*)-L$_C$4·BH$_3$** and triphenylmethyl isocyanate (**66**).[82]

$C_{33}H_{46}BN_2OP$ (528.52 g·mol^{-1}):

m.p. 104-107 °C. **R$_f$** = 0.43 (SiO$_2$, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, CDCl$_3$): δ = 7.30-7.18 (m, 15 H, Ph-*H*), 5.40 (s, 1 H, N*H*), 4.25-4.18 (m, 1 H, Pyr-2-*H*), 3.44-3.36 (m, 2 H, Pyr-5-*H*$_2$), 2.20-1.93 (m, 5 H, Pyr-*H* and C*H*H'P), 1.35-1.20 (m, 1 H, CH*H*'P), 1.19 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu-*H*), 1.17 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu'-*H*), 0.88-0.04 (br q, 3 H, B*H*$_3$) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CDCl$_3$): δ = 155.2 (s, *C*=O), 146.0 (s, Ph-*i*-*C*), 128.9 (s, Ph-*m*-*C*H), 127.9 (s, Ph-*o*-*C*H), 126.8 (s, Ph-*p*-*C*H), 70.4 (s, *C*Ph$_3$), 55.4 (d, $^2J_{C,P}$ = 5.0 Hz, Pyr-2-*C*H), 46.0 (s, Pyr-5-*C*H$_2$), 33.5 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.0 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu'-*C*), 31.2 (s, Pyr-3-*C*H$_2$), 28.2 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H$_3$), 27.9 (d, $^2J_{C,P}$ = 0.8 Hz, *t*Bu'-*C*H$_3$), 24.0 (s, Pyr-4-*C*H$_2$), 22.2 (d, $^1J_{C,P}$ = 23 Hz, *C*H$_2$P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CDCl$_3$): δ = 39.3 (br d, *J* = 61 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2930m, 2852m, 2372m, 1489s, 1447s, 1339s, 1308m, 1186w, 1157w, 1064m, 1000w, 748m, 696s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 527 (16, [M – H]$^+$), 244 (21), 243 (100), 165 (12), 57 (12). $[\alpha]_D^{20}$ = + 17.0 (*c* = 0.493, CHCl$_3$). **Elemental analysis**: calc. C 74.99%, H 8.77%, N 5.30%; found: C 74.78%, H 9.00%, N 5.40%.

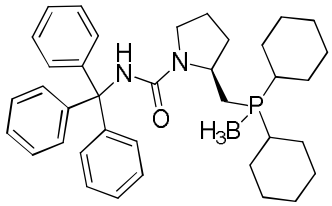
(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide ((*S*)-L_{U3}17)



Product **(*S*)-L_{U3}17** was prepared according to **general procedure 3** from **(*S*)-L_{U3}17·BH_3**.

$C_{33}H_{43}N_2OP$ (514.68 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 21.8 (s) ppm.

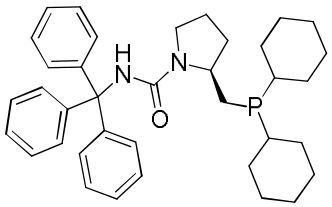
(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}18·BH_3)



Product **(*S*)-L_{U3}18·BH_3** (87%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and triphenylmethyl isocyanate (**66**).[82]

$C_{37}H_{50}BN_2OP$ (580.59 g·mol^{-1}):
m.p. 58-60 °C. **R_f** = 0.38 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33-7.17 (m, 15 H, Ph-*H*), 5.42 (s, 1 H, N*H*), 4.17-4.08 (m, 1 H, Pyr-2-*H*), 3.38 ("t", *J* = 6.3 Hz, 2 H, Pyr-5-C*H*$_2$), 2.09-1.04 (m, 28 H, Pyr-*H*, Cy/Cy'-*H* and C*H*$_2$P), 0.80-0.07 ("br q", 3 H, B*H*$_3$) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 155.0 (s, *C*=O), 145.9 (s, Ph-*i*-*C*), 128.9 (s, Ph-*m*-*C*H), 127.9 (s, Ph-*o*-*C*H), 126.8 (s, Ph-*p*-*C*H), 70.3 (s, *C*Ph$_3$), 54.1 (br d, $^2J_{C,P}$ = 4.6 Hz, Pyr-2-*C*H), 45.9 (s, Pyr-5-*C*H$_2$), 32.5 (d, $^1J_{C,P}$ = 14 Hz, Cy-1-*C*H), 32.2 (d, $^1J_{C,P}$ = 12 Hz, Cy'-1-*C*H), 31.5 (s, Pyr-3-*C*H$_2$), 27.1-25.9 (m, Cy/Cy'-*C*H$_2$), 24.0 (s, Pyr-4-*C*H$_2$) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 20.8 ("br d") ppm. **IR** (neat): $\tilde{\nu}$ = 2930m, 2918m, 2851m, 2372m, 1655s, 1489s, 1447s, 1339s, 1308m, 1186w, 1065m, 899m, 746m, 696s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 580 (11), 579 (22, [M – H]$^+$), 244 (20), 243 (100), 165 (16), 149 (12). $[\alpha]_D^{20}$ = + 3.0 (*c* = 1.30, $CHCl_3$). **Elemental analysis**: calc. C 76.54%, H 8.68%, N 4.83%; found: C 76.22%, H 8.65%, N 5.05%.

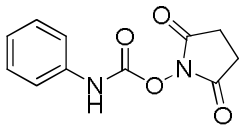
(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide ((*S*)-L_{U3}18)



Product **(*S*)-L_{U3}18** was prepared according to **general procedure 3** from **(*S*)-L_{U3}18·BH_3**.

$C_{37}H_{47}N_2OP$ (566.76 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (203 MHz, CD_2Cl_2): δ = – 10.9 (s) ppm.

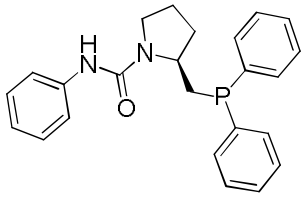
2,5-Dioxopyrrolidin-1-yl phenyl carbamate (70)



A mixture of aniline (**69**, 140 µL, 1.52 mmol, 1.0 eq.) and triethylamine (220 µL, 1.58 mmol, 1.0 eq.) in dichloromethane (16 mL) was added to a solution of *N*,*N*'-disuccinimidyl carbonate (DSC, 614 mg, 2.40 mmol, 1.6 eq.) in dichloromethane (32 mL) at 0 °C. The reaction mixture was then allowed to stir at room temperature for 30 minutes, before it was reduced to dryness under reduced pressure. The residue was purified by column chromatography on silica gel (3 x 10 cm), eluting with hexanes/ethyl acetate (3:5). The title compound **70** (292 mg, 1.25 mmol, 82%) was obtained as a colorless solid.

$C_{11}H_{10}N_2O_4$ (234.21 g·mol^{-1}):
R_f = 0.28 (SiO_2, hexanes/ethyl acetate 3:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.55 (br s, 1 H, N*H*), 7.37 (d, $^3J_{H,H}$ = 8.5 Hz, 2 H, Ph-*o*-*H*), 7.31 ("t", $^3J_{H,H}$ = 7.9 Hz, 2 H, Ph-*m*-*H*), 7.13 (d, $^3J_{H,H}$ = 7.3 Hz, 1 H, Ph-*p*-*H*), 2.87 (s, 4 H, CH_2) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $(CD_3)_2SO$): δ = 171.7 (s, *C*=O), 150.0 (*C*=O), 138.1 (s, Ph-*i*-*C*), 129.7 (s, Ph-*p*-*C*H), 124.9 (s, Ph-*m*-*C*H), 119.6 (s, Ph-*o*-*C*H), 26.2 (s, *C*H_2) ppm.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-phenylpyrrolidine-1-carboxamide ((*S*)-L_{U3}19)

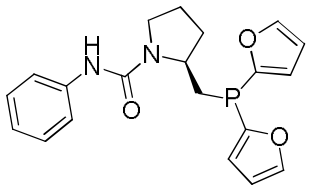


Compound **(*S*)-L_{U3}19** (49%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 2,5-dioxopyrrolidin-1-yl phenyl carbamate (**70**).

$C_{24}H_{25}N_2OP$ (388.44 g·mol^{-1}):

m.p. 166-169 °C. **R_f** = 0.16 (SiO_2, hexanes/ethyl acetate 7:3). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.56 (s, 1 H, N*H*), 7.60-7.57 (m, 2 H, PPh-*o*-*H*), 7.44-7.40 (m, 2 H, PPh'-*o*-*H*), 7.39-7.34 (m, 3 H, PPh/Ph'-*H*), 7.31-7.27 (m, 3 H, NPh-*o*-*H* and PPh/Ph'-*H*), 7.27-7.24 (m, 4 H, NPh-*m*-*H* and PPh/Ph'-*H*), 7.03-6.97 (m, 1 H, NPh-*p*-*H*), 4.13-4.00 (m, 1 H, Pyr-2-*H*), 3.42 ("t", *J* = 1.6 Hz, 2 H, Pyr-5-H_2), 2.79 ("dt", *J* = 14, 2.8 Hz, 1 H, C*H*H'P), 2.20-2.14 (m, 1 H, CH*H*'P), 2.14-2.04 (m, 3 H, Pyr-3-H_2 and Pyr-4-*H*H'), 1.99-1.91 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 153.8 (s, *C*=O), 139.1 (s, NPh-*i*-*C*), 138.6 (d, $^1J_{C,P}$ = 12 Hz, PPh-*i*-*C*), 137.6 (d, $^1J_{C,P}$ = 12 Hz, PPh'-*i*-*C*), 133.2 (d, $^2J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, PPh'-*o*-*C*H), 129.1 (s, PPh-*p*-*C*H), 128.9 (d, $^3J_{C,P}$ = 6.4 Hz, PPh-*m*-*C*H), 128.9 (s, NPh-*o*-*C*H), 128.8 (s, PPh'-*p*-*C*H), 128.6 (d, $^2J_{C,P}$ = 6.4 Hz, PPh'-*m*-*C*H), 122.9 (s, NPh-*p*-*C*H), 119.8 (s, NPh-*m*-*C*H), 55.6 (d, $^2J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 46.5 (s, Pyr-5-CH_2), 33.8 (s, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.4 (d, $^3J_{C,P}$ = 8.2 Hz, Pyr-3-CH_2), 24.0 (s, Pyr-4-CH_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 22.3 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3270m, 2945w, 2906w, 2880w, 1627s, 1592m, 1523s, 1497m, 1432s, 1379s, 1353m, 1293w, 1242m, 1215m, 1190m, 1093w, 1027w, 918w, 880w, 842w, 736s, 692s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 388 (10, M^+), 387 (10), 296 (11), 201 (18), 200 (52), 199 (20), 188 (13), 187 (100), 185 (28), 183 (31), 119 (20), 91 (11), 84 (49), 83 (10), 70 (78). $[\alpha]_D^{20}$ = – 31.8 (*c* = 0.592, $CHCl_3$). **HRMS** (ESI): calc. for $C_{24}H_{26}N_2OP$ ($[M+H]^+$): 389.1777; found: 389.1772.

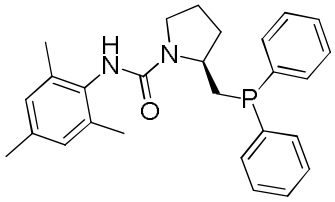
(*S*)-2-{[Di(furan-2-yl)phosphine]methyl}-*N*-phenylpyrrolidine-1-carboxamide ((*S*)-L_{U3}20)



Compound **(*S*)-L_{U3}20** (61%) was prepared according to **general procedure 1** from **(*S*)-L_C3** and 2,5-dioxopyrrolidin-1-yl phenyl carbamate (**70**).

$C_{20}H_{21}N_2O_3P$ (368.37 g·mol^{-1}):
m.p. 97-99 °C. $\mathbf{R_f}$ = 0.18 (SiO_2, cyclohexane/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $(CD_3)_2CO$): δ = 8.34 (s, 1 H, N*H*), 7.86 (d, *J* = 9.8 Hz, 1 H, Fur-*H*), 7.70-7.58 (m, 3 H, Fur/Fur'-*H* and Ph/Ph'-*H*), 7.41-7.26 (m, 4 H, Fur/Fur'-*H* and Ph/Ph'-*H*), 7.12-7.00 (m, 2 H, Fur/Fur'-*H* and Ph/Ph'-*H*), 6.57 (d, *J* = 16 Hz, 1 H, Fur'-*H*), 4.37-4.22 (m, 1 H, Pyr-2-*H*), 3.69-3.51 (m, 2 H, Pyr-5-H_2), 3.06-2.97 (m, 1 H, C*H*H'P), 2.41 (dd, $^2J_{H,P}$ = 13 Hz, *J* = 10 Hz 1 H, CH*H'*P), 2.18-1.97 (m, 3 H, Pyr-3-H_2 and Pyr-4-*H*H'), 1.89-1.78 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $(CD_3)_2CO$): δ = 155.7 (s, *C*=O), 153.7-153.4 (br, Ph-1-*C*), 149.2-149.0 (m, Fur/Fur'-2-*C*), 142.6 (s, Fur-5-*C*H), 142.1 (Fur'-5-*C*H), 130.6/130.2* (s, Ph-*m*-*C*H), 123.9/123.7* (s, Ph-*p*-*C*H), 121.5 (d, $^2J_{C,P}$ = 25 Hz, Fur-3-*C*H), 121.1 (d, $^2J_{C,P}$ = 19 Hz, Fur'-3-*C*H), 121.3/120.4* (s, Ph-*o*-*C*H), 112.7-112.5 (m, Fur/Fur'-4-*C*H), 57.2 (d, $^2J_{C,P}$ = 22 Hz, Pyr-2-*C*H), 48.0 (s, Pyr-5-*C*H_2), 32.3 (d, $^3J_{C,P}$ = 3.4 Hz, Pyr-3-*C*H_2), 32.1 (d, $^1J_{C,P}$ = 6.9 Hz, *C*H_2P), 25.8 (s, Pyr-4-*C*H_2) ppm. In the ^{13}C NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:1 and therefore nuclei, which are detected twice are marked with an asterisk. **^{31}P{^{1}H} NMR** (162 MHz, $(CD_3)_2CO$): δ = − 66.8 ("br d") ppm. **IR** (KBr): $\tilde{\nu}$ = 3286m, 3110w, 2958w, 2871w, 1945w, 1872w, 1719m, 1655s, 1598s, 1534s, 1495m, 1441s, 1366m, 1308s, 1231s, 1150m, 1070m, 1010m, 894m, 840w, 752s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 368 (5, M^+), 276 (37), 212 (22), 187 (10), 165 (16), 119 (12), 94 (7), 93 (100), 92 (9), 77 (11), 70 (46), 65 (10). $[\alpha]_D^{20}$ = − 29.2 (*c* = 0.200, $CHCl_3$). **HRMS** (ESI): calc. for $C_{20}H_{22}N_2O_3P$ ($[M+H]^+$): 369.1363; found: 369.1358.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-mesitylpyrrolidine-1-carboxamide ((*S*)-L_{U3}21)

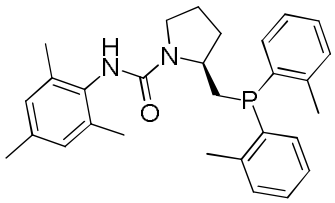


Product **(*S*)-L_{U3}21** (82%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 2,4,6-trimethylphenyl isocyanate.

$C_{27}H_{31}N_2OP$ (430.52 g·mol^{-1}):

m.p. 163-166 °C. **R_f** = 0.14 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.59 ("dt", *J* = 7.7, 1.5 Hz, 2 H, Ph-*o*-*H*), 7.42-7.38 (m, 2 H, Ph'-*o*-*H*), 7.32-7.23 (m, 6 H, Ph/Ph'-*H*), 6.85 (br s, 2 H, Mes-*H*), 5.26 (br s, 1 H, N*H*), 4.08-3.95 (m, 1 H, Pyr-2-*H*), 3.51-3.40 (m, 2 H, Pyr-5-H_2), 2.91 ("dt", *J* = 14, 3.6 Hz, 1 H, C*H*H'P), 2.25 (s, 3 H, Mes-4-CH_3), 2.15 (s, 6 H, Mes-2/6-CH_3), 2.10-2.01 (m, 4 H, CH*H'*P, Pyr-3-H_2 and Pyr-4-*H*H'), 2.01-1.83 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 154.7 (s, *C*=O), 139.1 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 137.4 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 136.1 (s, Mes-4-*C*), 135.5 (s, Mes-2/6-*C*), 133.3 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.6 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 132.6 (s, Mes-1-*C*), 129.1 (s, Ph-*p*-*C*H), 128.9 (s, Mes-3/5-*C*H), 128.8 (d, $^3J_{C,P}$ = 6.3 Hz, Ph-*m*-*C*H), 128.6 (s, Ph'-*p*-*C*H), 128.6 (d, $^3J_{C,P}$ = 6.9 Hz, Ph'-*m*-*C*H), 55.6 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 46.5 (s, Pyr-5-*C*H_2), 34.1 (d, $^1J_{C,P}$ = 14 Hz, *C*H_2P), 31.5 (d, $^3J_{C,P}$ = 7.3 Hz, Pyr-3-*C*H_2), 24.1 (s, Pyr-4-*C*H_2), 21.0 (s, Mes-4-*C*H_3), 18.7 (s, Mes-2/6-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 21.1 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3271m, 970m, 2949m, 2922m, 1735m, 1622s, 1608m, 1505s, 1482m, 1433m, 1418m, 1362s, 1235m, 1210m, 1121w, 1094w, 1068w, 845m, 747s, 736s, 694s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 430 (4, M^+), 415 (10), 353 (12), 286 (35), 284 (14), 229 (17), 215 (18), 201 (22), 200 (100), 199 (32), 185 (23), 183 (38), 161 (45), 146 (30), 133 (10), 91 (12), 84 (45), 83 (38), 70 (99). $[\alpha]_D^{20}$ = – 76.4 (*c* = 0.372, $CHCl_3$).

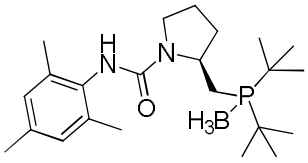
(*S*)-2-[(Di-*ortho*-tolylphosphino)methyl]-*N*-mesitylpyrrolidine-1-carboxamide ((*S*)-L_{U3}22)



Product **(*S*)-L_{U3}22** (67%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and 2,4,6-trimethylphenyl isocyanate.

$C_{29}H_{35}N_2OP$ (458.57 g·mol^{-1}):
m.p. 169-173 °C. **R_f** = 0.15 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.58-7.50 (m, 1 H, *o*Tol-*H*), 7.24-7.00 (m, 7 H, *o*Tol/*o*Tol'-*H*), 6.84 (s, 2 H, Mes-*H*), 5.13 (s, 1 H, N*H*), 3.98-3.87 (m, 1 H, Pyr-2-*H*), 3.55-3.40 (m, 2 H, Pyr-5-H_2), 2.84-2.75 (m, 1 H, C*H*H'P), 2.44 (s, 3 H, *o*Tol-CH_3), 2.41 (s, 3 H, *o*Tol'-CH_3), 2.24 (s, 3 H, Mes-4-CH_3), 2.20-1.87 (m, 5 H, Pyr-*H* and CH*H'*P), 2.13 (s, 6 H, Mes-2/6-CH_3) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 154.6 (s, *C*=O), 142.6 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 41.6 (d, $^2J_{C,P}$ = 25 Hz, *o*Tol'-2-*C*), 137.1 (d, $^1J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 136.1 (s, Mes-4-*C*), 135.7 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 135.5 (s, Mes-2/6-*C*), 132.6 (s, Mes-1-*C*), 131.9 (s, *o*Tol-3-*C*H), 131.3 (s, *o*Tol'-3-*C*), 130.3-130.0 (m, *o*Tol/*o*Tol'-6-*C*H), 128.9 (s, Mes-3/5-*C*H), 128.9 (s, *o*Tol-4-*C*H), 128.6 (s, *o*Tol'-4-*C*H), 126.8 (s, *o*Tol-5-*C*H), 126.3 (s, *o*Tol'-5-*C*H), 55.3 (d, $^2J_{C,P}$ = 22 Hz, Pyr-2-*C*H), 46.5 (s, Pyr-5-*C*H_2), 33.1 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.6 (d, $^3J_{C,P}$ = 6.9 Hz, Pyr-3-*C*H_2), 24.0 (s, Pyr-4-*C*H_2), 21.6-21.1 (m, *o*Tol/*o*Tol'-*C*H_3), 21.0 (s, Mes-4-*C*H_3), 18.6 (s, Mes-2/6-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 42.3 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 32559m, 2962m, 2922m, 2874m, 1623s, 1609m, 1502s, 1498s, 1450m, 1352s, 1235m, 1202m, 1070w, 1029w, 947w, 917w, 844m, 755s, 742s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 458 (8, M^+), 443 (17), 367 (35), 314 (30), 312 (12), 229 (60), 228 (45), 227 (19), 214 (14), 213 (80), 161 (33), 146 (21), 91 (12), 84 (74), 83 (21), 70 (100). $[\alpha]_D^{20}$ = – 30.5 (*c* = 0.322, $CHCl_3$).

(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*-mesitylpyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}23·BH_3)

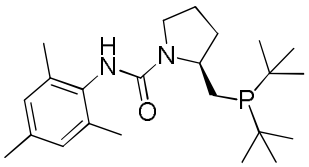


Product **(*S*)-L_{U3}23·BH_3** (90%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and 2,4,6-trimethylphenyl isocyanate.

$C_{23}H_{42}BN_2OP$ (404.38 g·mol^{-1}):

m.p. 206-208 °C. **R_f** = 0.19 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 6.87 (s, 2 H, Mes-*H*), 5.55 (br s, 1 H, N*H*), 4.40-4.27 (m, 1 H, Pyr-2-*H*), 3.54-3.44 (m, 1 H, Pyr-5-*H*H'), 3.44-3.36 (m, 1 H, Pyr-5-H*H'*), 2.57 ("t", *J* = 15 Hz, 1 H, C*H*H'P), 2.24 (s, 3 H, Mes-4-C*H*$_3$), 2.22 (s, 6 H, Mes-2/6-C*H*$_3$), 2.21-2.11 (m, 2 H, Pyr-3-*H*$_2$), 2.06-1.98 (m, 2 H, Pyr-4-*H*$_2$), 1.54-1.44 (m, 1 H, CH*H'*P), 1.35 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.25 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu'-*H*), 0.90-0.06 (br q, 3 H, B*H*$_3$) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 154.7 (s, *C*=O), 136.3 (s, Mes-4-*C*), 135.5 (s, Mes-2/6-*C*), 132.4 (s, Mes-1-*C*), 129.1 (s, Mes-3/5-*C*H), 55.9 (d, $^2J_{C,P}$ = 5.5 Hz, Pyr-2-*C*H), 46.4 (s, Pyr-5-*C*H$_2$), 33.2 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.0 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu'-*C*), 31.6 (s, Pyr-3-*C*H$_2$), 28.2 (br s, *t*Bu-*C*H$_3$), 28.0 (br s, *t*Bu'-*C*H$_3$), 24.1 (s, Pyr-4-*C*H$_2$), 22.4 (d, $^1J_{C,P}$ = 24 Hz, *C*H$_2$P), 21.0 (s, Mes-4-*C*H$_3$), 18.6 (s, Mes-2/6-*C*H$_3$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 39.8 ("br d", *J* = 67 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2926m, 2852m, 2376m, 1620s, 1514s, 1475m, 1450w, 1389m, 1346s, 1236w, 1190m, 1147m, 1070m, 1020m, 813m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 405 (23), 404 (32), 403 (100, $[M - H]^+$), 402 (25), 391 (15, $[M - BH_2]^+$), 333 (22), 277 (12), 270 (36), 242 (21), 186 (12), 128 (10), 70 (15), 57 (46). $[\alpha]_D^{20}$ = – 56.2 (*c* = 1.01, $CHCl_3$). **Elemental analysis**: calc. C 68.31%, H 10.47%, N 6.93%; found: C 68.33%, H 10.32%, N 7.00%.

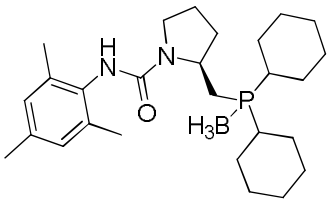
(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*-mesitylpyrrolidine-1-carboxamide ((*S*)-L_{U3}23)



Product **(*S*)-L_{U3}23** was prepared according to **general procedure 3** from **(*S*)-L_{U3}23·BH_3**.

$C_{23}H_{39}N_2OP$ (390.54 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 21.3 (s) ppm.

(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*-mesitylpyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U3}24·BH_3)

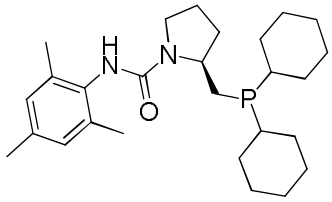


Product **(*S*)-L_{U3}24·BH_3** (82%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and 2,4,6-trimethylphenyl isocyanate.

$C_{27}H_{46}BN_2OP$ (456.45 g·mol^{-1}):
m.p. 141-143 °C. **R_f** = 0.23 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 6.68 (s, 2 H, Mes-*H*), 5.65 (s, 1 H, N*H*), 4.29-4.22 (m, 1 H, Pyr-2-*H*), 3.48-3.43 (m, 1 H, Pyr-5-*H*H'), 3.93 ("q", 1 H, *J* = 7.9 Hz, Pyr-5-H*H*'), 2.38 ("t", *J* = 14 Hz, 1 H, C*H*H'P), 2.24 (s, 3 H, Mes-4-CH_3), 2.21 (s, 6 H, Mes-2/6-CH_3), 2.14-2.08 (m, 1 H, Pyr-3-*H*H'), 2.09-1.93 (m, 5 H, Pyr-*H* and Cy/Cy'-1-*H*), 1.92-1.64 (m, 10 H, Cy/Cy'-*H*), 1.58 ("q", *J* = 11 Hz, 1 H, CH*H*'P), 1.48-1.38 (m, 2 H, Cy/Cy'-*H*), 1.38-1.28 (m, 2 H, Cy/Cy'-*H*), 1.28-1.18 (m, 6 H, Cy/Cy'-*H*), 0.78-0.06 (br q, 3 H, BH_3) ppm. **$^{13}C\{^1H\}$ NMR** (126 MHz, $CDCl_3$): δ = 154.5 (s, *C*=O), 136.1 (s, Mes-1-*C*), 135.5 (s, Mes-2/6-*C*), 132.4 (s, Mes-4-*C*), 129.0 (s, Mes-3/5-*C*H), 54.4 (br s, Pyr-2-*C*H), 46.3 (s, Pyr-5-*C*H_2), 32.5 (d, $^1J_{C,P}$ = 29 Hz, Cy-1-*C*H), 32.2 (d, $^1J_{C,P}$ = 29 Hz, Cy'-1-*C*H), 31.9 (br s, Pyr-3-*C*H_2), 27.1 (s, Cy/Cy-*C*H_2), 27.0 (s, Cy/Cy-*C*H_2), 26.9 (d, *J* = 3.7 Hz, Cy/Cy'-*C*H_2), 26.8 (d, *J* = 5.5 Hz, Cy/Cy'-*C*H_2), 26.8 (s, Cy/Cy'-*C*H_2), 26.7 (s, Cy/Cy'-*C*H_2), 26.5 (br s, Cy/Cy'-*C*H_2), 26.4 (br d, *J* = 1.8 Hz, Cy/Cy'-*C*H_2), 26.1 (s,

Cy-4-*C*H_2), 26.0 (s, Cy'-4-*C*H_2), 24.6 (d, $^1J_{C,P}$ = 27 Hz, *C*H_2P), 24.0 (s, Pyr-4-*C*H_2), 21.0 (s, Mes-4-*C*H_3), 18.6 (s, Mes-2/6-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 21.8 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2928m, 2851m, 2372m, 1653s, 1628s, 1504m, 1489s, 1447m, 1339m, 1186w, 1065m, 746m, 696s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 457 (28), 456 (42), 455 (100, $[M - H]^+$), 454 (31), 443 (18, $[M - BH_2]^+$), 359 (24), 322 (42), 294 (38), 293 (11), 292 (18), 277 (10), 70 (10), 55 (12). $[\alpha]_D^{20}$ = – 35.5 (*c* = 0.774, $CHCl_3$). **Elemental analysis**: calc. C 71.05%, H 10.16%, N 6.14%; found: C 70.90%, H 10.08%, N 6.07%.

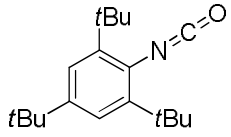
(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*-mesitylpyrrolidine-1-carboxamide ((*S*)-L_{U3}24)



Product **(*S*)-L_{U3}24** was prepared according to **general procedure 3** from **(*S*)-L_{U3}24·BH_3**.

$C_{27}H_{43}N_2OP$ (442.31 g·mol^{-1}):
^{31}P{^{1}H} NMR (203 MHz, CD_2Cl_2): δ = – 10.1 (s) ppm.

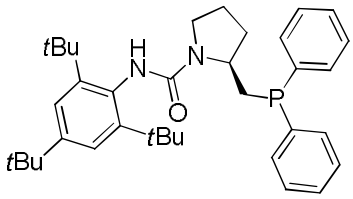
2,4,6-Tri-*tert*-butylmethylphenyl isocyanate (68)[83]



A solution of di-*tert*-butyl carbonate (339 mg, 1.55 mmol, 1.4 eq.) in acetonitrile (2 mL) was successively with a solution of 4-(dimethylamino)pyridine (DMAP, 136 mg, 1.11 mmol, 1.0 eq.) in acetonitrile (3 mL) and a solution of 2,4,6-tri-*tert*-butylaniline (**67**, 290 mg, 1.11 mmol, 1.0 eq.) in acetonitrile (2 mL). The resulting yellowish mixture was stirred at room temperature for 10 minutes. The reaction mixture was treated with H_2SO_4 (7.0 eq.) as a 40% solution in acetonitrile and then stirred for 5 minutes. The mixture was extracted with *n*-hexanes (3 x 30 mL). The combined hexanes layers were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure, to afford **68** (225 mg, 783 µmol, 71%**)** as a yellowish solid. The compound was used without

further purification. The spectroscopic data were consistent with those reported in the literature.[135]

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-(2,4,6-tri-*tert*-butylphenyl)pyrrolidine-1-carboxamide ((*S*)-L_{U3}25)

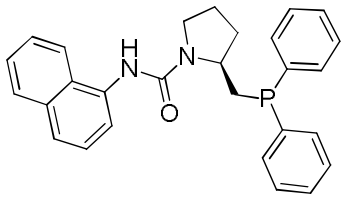


Product **(*S*)-L_{U3}25** (34%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 2,4,6-tri-*tert*-butylmethylphenyl isocyanate (**68**).

$C_{36}H_{49}N_2OP$ (556.76 g·mol^{-1}):
m.p. 186-188 °C. **R_f** = 0.34 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.65 ("t", $^3J_{H,H}$ = 7.1 Hz, 2 H, Ph-*o*-*H*), 7.44 (s, 2 H, Ar-3/5-*H*), 7.43-7.27 (m, 8 H, Ph/Ph'-*H*), 5.56 (s, 1 H, N*H*), 4.14-4.03 (m, 1 H, Pyr-2-*H*), 3.58-3.43 (m, 2 H, Pyr-5-H_2), 2.98 (br d, *J* = 13 Hz, 1 H, CHH'P), 2.20-1.97 (m, 4 H, Pyr-*H*), 1.97-1.83 (m, 1 H, CH*H*'P), 1.37 (s, 18 H, *t*Bu/*t*Bu'-H_3), 1.35 (s, 9 H, *t*Bu''-H_3) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ = 155.8 (s, *C*=O), 149.2 (s, Ar-4-*C*), 149.0 (s, Ar-2/6-*C*), 148.8 (s, Ar-2/6-*C*), 139.7 (br s, Ph-*i*-*C*), 137.6 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 133.0 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.6 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 132.4 (s, Ar-1-*C*), 128.7 (s, Ph-*p*-*C*H), 128.5 (d, $^3J_{C,P}$ = 6.8 Hz, Ph-*m*-*C*H), 128.5 (Ph'-*p*-*C*H), 128.4 (d, $^3J_{C,P}$ = 7.0 Hz, Ph'-*m*-*C*H), 123.0 (2s, Ar-3/5-*C*H), 55.6 (d, $^2J_{C,P}$ = 22 Hz, Pyr-2-*C*H), 46.1 (s, Pyr-5-*C*H_2), 36.4 (s, *t*Bu-*C*), 36.3 (s, *t*Bu'-*C*), 34.9 (s, *t*Bu''-*C*), 33.5 (br d, $^1J_{C,P}$ = 14 Hz, *C*H_2P), 31.9 (s, *t*Bu/*t*Bu'-*C*H_3), 31.2 (s, *t*Bu''-*C*H_3), 30.7 (br s, Pyr-3-*C*H_2), 24.3 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = − 22.0 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3305w, 2959m, 2904m, 2867m, 1740m, 1628s, 1598m, 1516s, 1507s, 1474m, 1433m, 1361s, 1349s, 1217m, 1204m, 1085w, 1030w, 913w, 876m, 738s, 696s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 556 (1, M^+), 500 (14), 499 (42), 479 (19), 355 (25), 273 (21), 272 (100), 256 (11), 216 (11), 201 (11), 200 (38), 199 (11), 185 (23), 183 (20), 84 (40), 83 (28), 70 (44), 57 (18). $[\alpha]_D^{20}$ = – 70.9 (*c* = 1.18, $CHCl_3$).

[135] J. F. W. Keana, A. P. Guzikowski, D. D. Ward, C. Morat, F. L. Van Nice, *J. Org. Chem.* **1983**, *48*, 2654-2660.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-(naphthalene-1-yl)pyrrolidine-1-carboxamide ((*S*)-L_{U3}26)



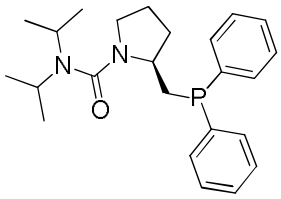
Product **(*S*)-L_{U3}26** (81%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and 1-naphthyl isocyanate.

$C_{28}H_{27}N_2OP$ (438.50 g·mol^{-1}):

R_f = 0.19 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.88-7.81 (m, 1 H, Naph-2-*H*), 7.80-7.70 (m, 2 H, Ar-*H*), 7.66-7.56 (m, 3 H, Ar-*H*), 7.50-7.40 (m, 5 H, Ar-*H*), 7.33-7.22 (m, 6 H, Naph-8-*H* and Ph/Ph'-*H*), 6.38 (s, 1 H, N*H*), 4.28-4.18 (m, 1 H, Pyr-2-*H*), 3.57-3.48 (m, 2 H, Pyr-5-H_2), 2.97-2.89 (m, 1 H, C*H*H'P), 2.27-2.19 (m, 1 H, CH*H'*P), 2.19-2.07 (m, 3 H, Pyr-3-H_2 and Pyr-4-*H*H'), 2.05-1.96 (m, 1H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 154.5 (s, *C*=O), 138.5 (br d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*H), 137.1 (d, $^1J_{C,P}$ = 10 Hz, Ph'-*i*-*C*H), 134.3 (s, Naph-1-*C*), 133.7 (s, Naph-5a-*C*), 133.1 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 129.1 (s, Ph-*p*-*C*H), 129.2-128.9 (m, Ph'-*p*-*C*H, Ph-*m*-*C*H and Naph-*C*H), 128.9 (d, $^3J_{C,P}$ = 7.2 Hz, Ph'-*m*-*C*H), 127.9 (s, Naph-1a-*C*), 126.6 (br s, 2 Naph-*C*H), 125.8 (s, Naph-*C*H), 124.7 (s, Naph-*C*H), 121.0 (s, Naph-*C*H), 120.6 (s, Naph-*C*H), 56.0 (d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 46.6 (s, Pyr-5-*C*H_2), 33.7 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 31.3 (d, $^3J_{C,P}$ = 8.9 Hz, Pyr-3-*C*H_2), 24.2 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 21.5 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3239w, 3049w, 2938w, 2874w, 1622s, 1596m, 1524m, 14945m, 1480m, 1432m, 1372m, 1328m, 1271m, 1243w, 1184w, 1117w, 1070w, 1016w, 926w, 851w, 784s, 766s, 756m, 740s, 694s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 438 (3, M^+), 237 (16), 201 (17), 200 (100), 199 (29), 185 (14), 183 (23), 170 (10), 169 (77), 141 (19), 140 (18), 70 (69). $[\alpha]_D^{20}$ = – 48.3 (*c* = 0.582, $CHCl_3$). **HRMS** (ESI): calc. for $C_{28}H_{28}N_2OP$ ($[M+H]^+$): 439.1934; found: 439.1927. The spectroscopic data were consistent with those reported in the literature.[68f]

6.3.4
Tetrasubstituted Ureaphosphines (*S*)-L_{U4} and Precursors

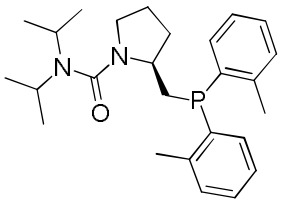
(*S*)-2[(Diphenylphosphino)methyl]-*N*,*N*-di-isopropylpyrrolidine-1-carboxamide ((*S*)-L_{U4}1)



Compound **(*S*)-L_{U4}1** (75%), isolated as a colorless semisolid, was prepared according to **general procedure 1** from **(*S*)-L_C1** and *N*,*N*-di-isopropylcarbamoyl chloride.

$C_{24}H_{33}N_2OP$ (396.51 g·mol^{-1}):
R_f = 0.21 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.50-7.44 (m, 2 H, Ph-*o*-*H*), 7.43-7.38 (m, 2 H, Ph'-*o*-*H*), 7.34-7.25 (m, 6 H, Ph/Ph'-*H*), 4.29-4.19 (m, 1 H, Pyr-2-*H*), 3.56 (sept, $^3J_{H,H}$ = 6.7 Hz, 2 H, *i*Pr/*i*Pr'-C*H*), 3.38-3.30 (m, 1 H, Pyr-5-*H*H'), 3.23-3.15 (m, 1 H, Pyr-5-H*H'*), 2.52 ("dt", *J* = 14, 3.9 Hz, 1 H, C*H*H'P), 2.30 (dd, $^2J_{H,P}$ = 14 Hz, $^2J_{H,H}$ = 8.1 Hz, 1 H, CH*H'*P), 2.07-1.99 (m, 1 H, Pyr-*H*), 1.85-1.77 (m, 1 H, Pyr-*H*), 1.75-1.62 (m, 2 H, Pyr-*H*), 1.20 (d, $^3J_{H,H}$ = 6.6 Hz, 6 H, *i*Pr-CH_3), 1.18 (d, $^3J_{H,H}$ = 6.8 Hz, 6 H, *i*Pr'-CH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 162.6 (*C*=O), 139.9 (d, $^1J_{C,P}$ = 13 Hz, Ph-*i*-*C*), 139.5 (d, $^1J_{C,P}$ = 12Hz, Ph'-*i*-*C*), 133.1 (d, $^2J_{C,P}$ = 20 Hz, Ph-*o*-*C*H), 132.8 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.6-128.3 (m, Ph/Ph'-*m*/*p*-*C*H), 56.3 (d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 51.3 (s, Pyr-5-*C*H_2), 47.1 (s, *i*Pr/*i*Pr'-*C*H), 34.2 (d, $^1J_{C,P}$ = 12 Hz, *C*H_2P), 32.3 (d, $^3J_{C,P}$ = 9.6 Hz, Pyr-3-*C*H_2), 25.6 (s, Pyr-4-*C*H_2), 22.5 (s, *i*Pr-*C*H_3), 21.1 (s, *i*Pr'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 22.7 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3051w, 2961m, 2925m, 2869m, 1623s, 1424s, 1374m, 1337s, 1315s, 1205m, 1156m, 1129m, 1071m, 1037m, 908w, 873w, 776m, 737s, 694s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 398 (21), 397 (55, $[M + H]^+$), 354 (20), 353 (74), 319 (10), 312 (18), 311 (21), 296 (40), 286 (11), 284 (11), 217 (13), 201 (26), 196 (13), 195 (89), 185 (42), 153 (10), 128 (72), 91 (12), 86 (100), 73 (33), 70 (23), 43 (65). Partial oxidation was observed while measuring. $[\alpha]_D^{20}$ = + 34.8 (*c* = 0.642, $CHCl_3$).

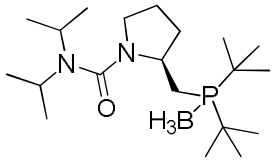
(*S*)-2-[(Di-*ortho*-tolylphosphino)methyl]-*N*,*N*-di-isopropylpyrrolidine-1-carboxamide ((*S*)-L_{U4}2)



Product **(*S*)-L_{U4}2** (93%), isolated as a colorless semisolid, was prepared according to **general procedure 1** from **(*S*)-L_C2** and *N*,*N*-di-isopropylcarbamoyl chloride.

$C_{26}H_{37}N_2OP$ (424.56 g·mol^{-1}):
R_f = 0.43 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.47-7.44 (m, 1 H, *o*Tol-*H*), 7.23-7.07 (m, 7 H, *o*Tol/*o*Tol'-*H*), 4.24-4.15 (m, 1 H, Pyr-2-*H*), 3.56 (sept, $^3J_{H,H}$ = 6.6 Hz, 2 H, *i*Pr/*i*Pr'-C*H*), 3.38-3.32 (m, 1 H, Pyr-5-*H*H'), 3.21-3.15 (m, 1 H, Pyr-5-H*H'*), 2.47-2.43 (m, 1 H, C*H*H'P), 2.46 (s, 3 H, *o*Tol-CH_3), 2.37 (s, 3 H, *o*Tol'-CH_3), 2.11-2.02 (m, 2 H, Pyr-3-H_2), 1.86-1.78 (m, 1 H, Pyr-4-*H*H'), 1.74-1.63 (m, 2 H, Pyr-4-H*H'* and CH*H'*P), 1.22 (d, $^3J_{H,H}$ = 6.6 Hz, 6 H, *i*Pr-CH_3), 1.18 (d, $^3J_{H,H}$ = 6.9 Hz, 6 H, *i*Pr'-CH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 162.7 (s, *C*=O), 142.1-141.7 (m, *o*Tol/*o*Tol'-2-*C*), 137.6 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol-1-*C*), 137.1 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 131.9 (s, *o*Tol-3-*C*H), 131.8 (s, *o*Tol'-3-*C*H), 130.0 (br s, *o*Tol-6-*C*H), 129.9 (br s *o*Tol'-6-*C*H), 128.3 (s, *o*Tol-4-*C*H), 128.3 (s, *o*Tol'-4-*C*H), 126.3 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 56.3 (d, $^2J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 51.1 (s, Pyr-5-*C*H_2), 47.1 (s, *i*Pr/*i*Pr'-*C*H), 32.6 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 32.4 (d, $^3J_{C,P}$ = 10 Hz, Pyr-3-*C*H_2), 25.4 (s, Pyr-4-*C*H_2), 22.5 (s, *i*Pr-*C*H_3), 21.4 (d, $^3J_{C,P}$ = 9.1 Hz, *o*Tol-*C*H_3), 21.3 (d, $^3J_{C,P}$ = 8.2 Hz, *o*Tol'-*C*H_3), 21.1 (s, *i*Pr'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 43.0 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3051w, 2962m, 2867m, 1626s, 1423s, 1337s, 1315m, 1204w, 1157m, 1128m, 1072w, 1036w, 746s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 424 (1, M^+), 382 (24), 381 (100), 340 (31), 339 (50), 324 (31), 312 (10), 229 (40), 213 (26), 211 (11), 196 (11), 195 (92), 128 (44), 86 (41), 84 (11), 70 (14), 43 (31). $[\alpha]_D^{20}$ = + 13.7 (*c* = 0.881, $CHCl_3$). **Elemental analysis**: calc. C 73.55%, H 8.78%, N 6.60%; found: C 73.57%, H 8.85%, N 6.38%.

(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*,*N*-di-isopropylpyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U4}3·BH_3)

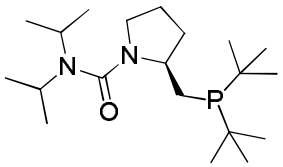


Product **(*S*)-L_{U4}3·BH_3** (47%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and *N*,*N*-di-isopropylcarbamoyl chloride.

$C_{20}H_{44}BN_2OP$ (370.36 g·mol^{-1}):

m.p. 144-146 °C. **R_f** = 0.37 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.23-4.14 (m, 1 H, Pyr-2-*H*), 3.64 (sept, $^3J_{H,H}$ = 6.7 Hz, 2 H, *i*Pr/*i*Pr'-C*H*), 3.30 (ddd, $^2J_{H,H}$ = 16 Hz, $^3J_{H,H}$ = 10, 6.4 Hz, 1 H, Pyr-5-*H*H'), 3.13 ("t", *J* = 8.7 Hz, 1 H, Pyr-5-H*H'*), 2.55 ("q", *J* = 6.2 Hz, 1 H, Pyr-3-*H*H'), 2.29 ("td", *J* = 15, 2.5 Hz, 1 H, C*H*H'P), 1.86-1.67 (m, 2 H, Pyr-4-H_2), 1.54-1.44 (m, 1 H, Pyr-3-H*H'*), 1.44-1.37 (m, 1 H, CH*H'*P), 1.35 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.31 (d, $^3J_{H,H}$ = 6.5 Hz, 6 H, *i*Pr-CH_3), 1.23 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-*H*), 1.22 (d, $^3J_{H,H}$ = 6.2 Hz, 6 H, *i*Pr'-CH_3) 0.93-0.06 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 162.4 (s, *C*=O), 56.4 (d, $^2J_{C,P}$ = 5.4 Hz, Pyr-2-*C*H), 50.8 (s, Pyr-5-*C*H_2), 47.1 (s, *i*Pr/*i*Pr'-*C*H), 33.4 (s, Pyr-3-*C*H_2), 33.0 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.1 (d, $^1J_{C,P}$ = 28 Hz, *t*Bu'-*C*), 28.3 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu'-*C*H_3), 25.9 (s, Pyr-4-*C*H_2), 24.2 (d, $^1J_{C,P}$ = 25 Hz, *C*H_2P), 22.5 (s, *i*Pr-*C*H_3), 21.1 (s, *i*Pr'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.6 ("br d", *J* = 77 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2967m, 2947m, 2931m, 2870m, 2394w, 2362m, 2342m, 1623s, 1470w, 1426m, 1369m, 1340s, 1317m, 1206m, 1157m, 1132m, 1070m, 1021m, 879w, 814w cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 369 (11, $[M - H]^+$), 300 (18), 299 (100), 271 (13), 270 (78), 269 (20), 243 (11), 242 (44), 241 (14), 240 (14), 128 (44), 86 (50), 57 (21), 43 (24). $[\alpha]_D^{20}$ = – 25.4 (*c* = 0.520, $CHCl_3$). **Elemental analysis**: calc. C 64.86%, H 11.97%, N 7.56%; found: C 65.10%, H 11.76%, N 7.49%.

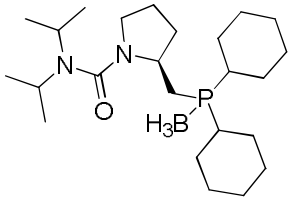
(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*,*N*-di-isopropylpyrrolidine-1-carboxamide ((*S*)-L_{U4}3)



Product **(*S*)-L_{U4}3** was prepared according to **general procedure 3** from **(*S*)-L_{U4}3·BH_3**.

$C_{20}H_{41}N_2OP$ (356.53 g·mol^{-1}):
^{31}P{^{1}H} NMR (162 MHz, CD_2Cl_2): δ = 21.0 (s) ppm.

(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*,*N*-di-isopropylpyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U4}4·BH_3)

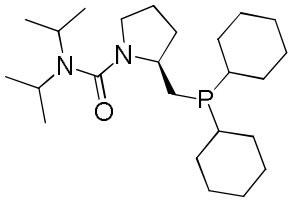


Product **(*S*)-L_{U4}4·BH_3** (86%) was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and *N*,*N*-di-isopropylcarbamoyl chloride.

$C_{24}H_{48}BN_2OP$ (422.44 g·mol^{-1}):
m.p. 127-129 °C. **R_f** = 0.38 (SiO_2, cyclohexane/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.21-4.11 (m, 1 H, Pyr-2-*H*), 3.64 (sept, $^3J_{H,H}$ = 6.7 Hz, 2 H, *i*Pr/*i*Pr'-C*H*), 3.36-3.29 (m, 1 H, Pyr-5-*H*H'), 3.12 ("t", *J* = 8.4 Hz, 1 H, Pyr-5-H*H'*), 2.32-2.23 (m, 1 H, Pyr-3-*H*H'), 2.06 ("td", *J* = 14, 2.9 Hz, 1 H, C*H*H'P), 1.98-1.53 (m, 15 H, Pyr-4-H_2, Pyr-3-H*H'* and Cy/Cy'-*H*), 1.48-1.14 (m, 11 H, CH*H'*P and Cy/Cy'-*H*), 1.31 (d, $^3J_{H,H}$ = 6.6 Hz, 6 H, *i*Pr-CH_3), 1.21 (d, $^3J_{H,H}$ = 6.7 Hz, 6 H, *i*Pr'-CH_3), 0.88-0.04 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 162.4 (s, *C*=O), 55.1 (d, $^2J_{C,P}$ = 3.2 Hz, Pyr-2-*C*H), 50.8 (s, *i*Pr-*C*H), 47.0 (s, Pyr-5-*C*H_2), 33.0 (s, Pyr-3-*C*H_2), 32.7 (d, $^1J_{C,P}$ = 27 Hz, Cy-1-*C*H), 32.3 (d, $^1J_{C,P}$ = 29 Hz, Cy'-1-*C*H), 27.2-26.4 (m, Cy/Cy'-*C*H_2), 26.2 (s, Cy/Cy'-*C*H_2), 26.1 (s, Cy/Cy'-*C*H_2), 25.7 (s, Pyr-4-*C*H_2), 25.3 (d, $^1J_{C,P}$ = 28 Hz, *C*H_2P), 22.6 (s, *i*Pr-*C*H_3), 21.1 (s, *i*Pr'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 20.8 ("br d", *J* = 75 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2962m, 2920s, 2853m, 2382m, 2338w, 1663m, 1622s, 1489m, 1445m, 1431m, 1339s, 1313m, 1202w,

1157m, 1065m, 1038m, 1002w, 916w, 748m, 696s cm^{-1}. **MS** (ESI): *m/z* (%) = 423 (100, $[M + H]^+$), 410 (13), 409 (17, $[M – BH_2]^+$), 257 (10). $[\alpha]_D^{20}$ = – 48.0 (*c* = 0.510, $CHCl_3$). **Elemental analysis**: calc. C 68.24%, H 11.45%, N 6.63%; found: C 68.49%, H 11.27%, N 6.47%.

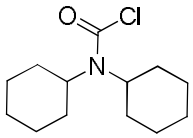
(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*,*N*-di-isopropylpyrrolidine-1-carboxamide ((*S*)-L_{U4}4)



Product **(*S*)-L_{U4}4** was prepared according to **general procedure 3** from **(*S*)-L_{U4}4·BH_3**.

$C_{24}H_{45}N_2OP$ (408.60 $g \cdot mol^{-1}$):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = – 12.6 (s) ppm.

N,*N*-Dicyclohexylcarbamoyl chloride (72)

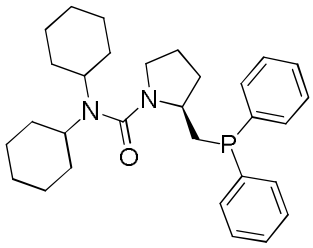


Dicyclohexylcarbamoyl chloride was prepared in analogy to the procedure reported for the synthesis of di-isopropylcarbamoyl chloride.[85] To a solution of bis(trichloromethyl) carbonate (451 mg, 1.52 mmol, 0.33 eq.) in abs. toluene (5 mL) was added dicyclohexylamine (**71**, 1.00 mL, 5.02 mmol, 1.1 eq.) drop wise at – 5° C. The mixture was then stirred for 48 hours at room temperature. The solids were filtered of and washed with toluene (3 x 10 mL). The filtrate was reduced to dryness under reduced pressure to afford dicyclohexylcarbamoyl chloride (**72**, 549 mg, 2.07 mmol, 45%) as a colorless solid, which was used without further purification.

$C_{13}H_{22}ClNO$ (243.77 $g \cdot mol^{-1}$):
^1H NMR (400 MHz, $CDCl_3$): δ = 4.21-3.99 (m, 1 H, Cy-1-*H*), 3.21-2.94 (m, 1 H, Cy'-1-H), 2.30-2.07 (m, 2 H, Cy-*H*), 1.89-1.01 (m, 18 H, Cy-*H*) ppm. **MS** (ESI):

m/z (%) = 243 (7, M^+), 208 (18), 162 (37), 126 (36), 118 (15), 83 (52), 82 (50), 67 (36), 55 (100), 54 (27), 41 (84).

(*S*)-*N*,*N*-Dicyclohexyl-2-[(diphenylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U4}5)



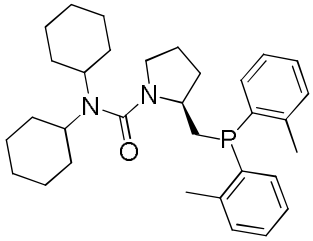
Compound **(*S*)-L_{U4}5** (83%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and *N*,*N*-dicyclohexylcarbamoyl chloride (**72**).

$C_{30}H_{41}N_2OP$ (476.63 g·mol^{-1}):

m.p. 142-143 °C. $\mathbf{R_f}$ = 0.39 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.41-7.34 (m, 4 H, Ph/Ph'-*o*-*H*), 7.26-7.18 (m, 6 H, Ph/Ph'-*H*), 4.20-4.12 (m, 1 H, Pyr-2-*H*), 3.27-3.22 (m, 1 H, Pyr-5-*H*H'), 3.12 ('"t", *J* = 8.4 Hz, 1 H, Pyr-5-H*H'*), 2.98-2.92 (m, 2 H, Cy/Cy'-1-*H*), 2.38 ("dt", *J* = 14, 3.6 Hz, 1 H, C*H*H'P), 2.31 (ddd, $^2J_{H,P}$ = 14 Hz, $^3J_{H,H}$ = 7.9 Hz, $^3J_{H,H}$ = 1.9 Hz, 1 H, CH*H'*P), 1.99-1.95 (m, 1 H, Pyr-3-*H*H'), 1.89-1.81 (m, 2 H, Cy-*H*), 1.78-1.56 (m, 9 H, Pyr-3-HH', Pyr-4-H_2 and Cy/Cy'-*H*), 1.54-1.49 (m, 2 H, Cy/Cy'-*H*), 1.49-1.43 (m, 2 H, Cy/Cy'-*H*), 1.38-1.33 (m, 2 H, Cy/Cy'-*H*), 1.23-1.13 (m, 2 H, Cy/Cy'-*H*), 1.11-0.99 (m, 4 H, Cy/Cy'-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 162.8 (s, *C*=O), 139.8 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 139.5 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 133.0 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.8 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.5 (d, $^3J_{C,P}$ = 7.3 Hz, Ph-*m*-*C*H), 128.4 (d, $^3J_{C,P}$ = 7.3 Hz, Ph'-*m*-*C*H), 128.4 (s, Ph/Ph'-*p*-*C*H), 56.9 (s, Cy/Cy'-1-*C*H), 56.5 (d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 51.4 (s, Pyr-5-*C*H_2), 33.7 (d, $^1J_{C,P}$ = 12 Hz, *C*H_2P), 32.8 (s, Cy/Cy'-*C*H_2), 32.3 (d, $^3J_{C,P}$ = 10 Hz, Pyr-3-*C*H_2), 31.3 (s, Cy/Cy'-*C*H_2), 26.8 (s, Cy/Cy'-*C*H_2), 25.7 (s, Cy/Cy'-*C*H_2), 25.5 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 23.1 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3051w, 2923s, 2849s, 1741w, 1626s, 1583m, 1481m, 1451m, 1421s, 1365s, 1341s, 1315s, 1243m, 1182s, 1124m, 1071w, 1026m, 1004m, 894m, 871m, 750s, 715m, 697s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 477 (22, $[M + H]^+$), 393 (11), 296 (14), 275 (27), 208 (13), 201 (12), 193 (14), 192 (45), 185 (24), 183 (11), 126 (26),

84 (16), 83 (100), 81 (10), 70 (20), 55 (35), 41 (14). Partial oxidation was observed while measuring. $[\alpha]_D^{20}$ = + 52.6 (c = 0.510, $CHCl_3$). **Elemental analysis**: calc. C 75.60%, H 8.67%, N 5.88%; found: C 75.31%, H 8.64%, N 5.78%.

(*S*)-*N*,*N*-Dicyclohexyl-2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U4}6)



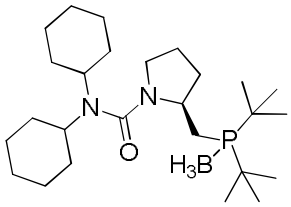
Compound **(*S*)-L_{U4}6** (81%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and *N*,*N*-dicyclohexylcarbamoyl chloride (**72**).

$C_{32}H_{45}N_2OP$ (504.69 g·mol^{-1}):

m.p. 134-136 °C. $\mathbf{R_f}$ = 0.51 (SiO_2, hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.36-7.32 (m, 1 H, *o*Tol-6-*H*), 7.25-7.20 (m, 1 H, *o*Tol'-6-*H*), 7.20-7.15 (m, 3 H, *o*Tol/*o*Tol'-*H*), 7.15-7.08 (m, 3 H, *o*Tol/*o*Tol'-*H*), 4.24-4.15 (m, 1 H, Pyr-2-*H*), 3.37-3.28 (m, 1 H, Pyr-5-*H*H'), 3.19 ("t", J = 8.1 Hz, 1 H, Pyr-5-H*H'*), 3.01 (m, 2 H, Cy/Cy'-1-*H*), 2.43 (s, 3 H, *o*Tol-CH_3), 2.40 (s, 3 H, *o*Tol'-CH_3), 2.35 ("dt", J = 14, 3.3 Hz, 1 H, C*H*H'P), 2.16 (dd, $^2J_{H,P}$ = 14 Hz, $^3J_{H,H}$ = 8.6 Hz, 1 H, CH*H'*P), 2.12-2.04 (m, 1 H, Pyr-3-*H*H'), 1.99-1.86 (m, 2 H, Cy/Cy'-*H*), 1.85-1.61 (m, 9 H, Pyr-3-H*H'*, Pyr-4-H_2 and Cy/Cy'-*H*), 1.61-1.53 (m, 2 H, Cy/Cy'-*H*), 1.53-1.39 (m, 4 H, Cy/Cy'-*H*), 1.30-1.19 (m, 2 H, Cy/Cy'-*H*), 1.19-1.05 (m, 4 H, Cy/Cy'-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 163.0 (s, *C*=O), 141.9 (d, $^2J_{C,P}$ = 25 Hz, *o*Tol-2-*C*), 141.8 (d, $^2J_{C,P}$ = 25 Hz, *o*Tol'-2-*C*), 137.5 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol-1-*C*), 137.4 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 132.1 (s, *o*Tol-6-*C*H), 131.7 (s, *o*Tol'-6-*C*H), 130.0 (s, *o*Tol-3-C*H*), 129.9 (s, *o*Tol'-3-*C*H), 128.3 (s, *o*Tol-4-*C*H), 128.2 (s, *o*Tol'-4-*C*H), 126.3 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 57.0 (s, Cy/Cy'-1-*C*H), 56.5 (s, $^2J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 51.2 (s, Pyr-5-*C*H_2), 32.9 (s, Cy/Cy'-*C*H_2), 32.4 (d, $^3J_{C,P}$ = 9.6 Hz, Pyr-3-*C*H_2), 32.2 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 31.3 (s, Cy/Cy'-*C*H_2), 26.9 (s, Cy/Cy'-*C*H_2), 26.8 (s, Cy/Cy'-*C*H_2), 25.8 (s, Cy/Cy'-*C*H_2), 25.4 (s, Pyr-4-*C*H_2), 21.5 (d, $^3J_{C,P}$ = 1.2 Hz, *o*Tol-*C*H_3), 21.3 (d, $^3J_{C,P}$ = 1.9 Hz, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 43.8 (s) ppm.

IR (neat): $\tilde{\nu}$ = 2968w, 2927m, 2915m, 2852m, 1615s, 1448m, 1416s, 1369m, 1310s, 1242w, 1179m, 1155m, 1121m, 1028w, 1003w, 893m, 746s, 719m, 695m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 504 (1, M^+), 423 (3), 422 (20), 421 (65), 339 (19), 324 (16), 276 (16), 275 (80), 229 (17), 213 (23), 193 (46), 192 (100), 84 (19), 83 (38), 70 (15), 55 (18). $[\alpha]_D^{20}$ = + 41.3 (*c* = 1.13, $CHCl_3$).

(*S*)-*N*,*N*-Dicyclohexyl-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U4}7·BH_3)

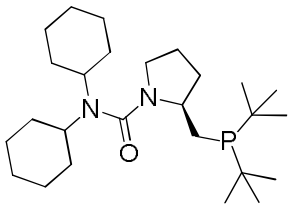


Product **(*S*)-L_{U4}7·BH_3** (69%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and *N*,*N*-dicyclohexylcarbamoyl chloride (**72**).

$C_{26}H_{52}BN_2OP$ (450.49 g·mol^{-1}):

m.p. 117-118 °C. **R_f** = 0.47 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.24-4.13 (m, 1 H, Pyr-2-*H*), 3.31-3.23 (m, 1 H, Pyr-5-*H*H'), 3.18-3.07 (m, 3 H, Pyr-5-H*H'* and Cy/Cy'-1-*H*), 2.57-2.48 (m, 1 H, Pyr-3-*H*H'), 2.27 ("td", *J* = 14, 2.7 Hz, 1 H, C*H*H'P), 2.08-1.96 (m, 2 H, Cy/Cy'-*H*), 1.87-1.53 (m, 14 H, Pyr-4-H_2 and Cy/Cy'-*H*), 1.53-1.46 (m, 1 H, Pyr-3-H*H'*), 1.46-1.09 (m, 25 H, *t*Bu/*t*Bu'-*H*, CH*H'*P and Cy/Cy'-*H*), 0.80-0.08 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 162.8 (s, *C*=O), 57.0 (s, Cy/Cy'-1-*C*H), 56.4 (d, $^2J_{C,P}$ = 5.4 Hz, Pyr-2-*C*H), 50.8 (s, Pyr-5-*C*H_2), 33.3 (s, Pyr-3-*C*H_2), 33.0 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.9 (s, Cy/Cy'-*C*H_2), 32.1 (d, $^1J_{C,P}$ = 28 Hz, *t*Bu'-*C*), 31.2 (s, Cy/Cy'-*C*H_2), 28.3 (d, $^2J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H_3), 28.0 (d, $^2J_{C,P}$ = 1.2 Hz, *t*Bu'*C*H_3), 26.8 (s, Cy/Cy'-*C*H_2), 26.7 (s, Cy/Cy'-*C*H_2), 25.9 (s, Pyr-4-*C*H_2), 25.7 (s, Cy/Cy'-*C*H_2), 24.1 (d, $^1J_{C,P}$ = 25 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.7 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2928s, 2860m, 2393m, 2364m, 1625s, 1451w, 1419m, 1365m, 1311s, 1243w, 1236w, 1181m, 1157w,1068m, 1024w, 999w, 894m, 871m, 813m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 449 (6, $[M - H]^+$), 379 (82), 270 (100), 242 (31), 208 (11), 126 (15), 83 (34), 57 (15). $[\alpha]_D^{20}$ = + 0.6 (*c* = 0.500, $CHCl_3$). **Elemental analysis**: calc. C 69.32%, H 11.63%, N 6.22%; found: C 69.30%, H 11.60%, N 6.00%.

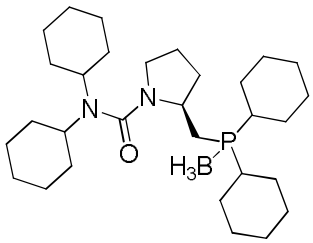
(*S*)-*N*,*N*-Dicyclohexyl-2-[(di-*tert*-butylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U4}7)



Product **(*S*)-L_{U4}7** was prepared according to **general procedure 3** from **(*S*)-L_{U4}7·BH_3**.

$C_{26}H_{49}N_2OP$ (436.65 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 21.1 (s) ppm.

(*S*)-*N*,*N*-Dicyclohexyl-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U4}8·BH_3)

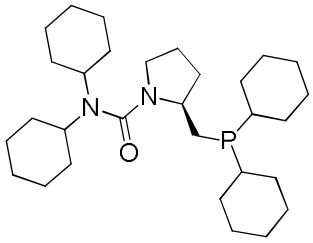


Product **(*S*)-L_{U4}8·BH_3** (61%), isolated as a colorless semisolid, was prepared according to **general procedure 2** from **(*S*)-L_C5·BH_3** and *N*,*N*-dicyclohexylcarbamoyl chloride (**72**).

$C_{30}H_{56}BN_2OP$ (502.56 g·mol^{-1}):
m.p. 54-57 °C. **R_f** = 0.28 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.23-4.03 (m, 1 H, Pyr-2-*H*), 3.37-3.24 (m, 1 H, Pyr-5-*H*H'), 3.19-3.05 (m, 3 H, Pyr-5-H*H'* and NCy/Cy'-1-*H*), 2.32-2.19 (m, 1 H, Pyr-3-*H*H'), 2.11-1.04 (m, 47 H), 0.83-0.10 (br q, 3 H, B*H*$_3$) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 162.7 (s, *C*=O), 56.8 (s, NCy/Cy'-1-*C*H), 55.2 (br d, $^2J_{C,P}$ = 3.0 Hz, Pyr-2-*C*H), 50.8 (s, Pyr-5-*C*H$_2$), 33.0 (s, NCy/Cy'-*C*H$_2$), 33.9 (s, Pyr-3-*C*H$_2$), 32.7 (d, $^1J_{C,P}$ = 22 Hz, PCy-1-*C*H), 32.4 (d, $^1J_{C,P}$ = 23 Hz, PCy'-1-*C*H), 31.3 (s, *C*H$_2$), 27.2-26.1 (m, *C*H$_2$), 25.7 (s, *C*H$_2$), 25.1 (d, $^1J_{C,P}$ = 28 Hz, *C*H$_2$P) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 20.7 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2924s, 2851m, 2370m, 1691m, 1628s, 1448m, 1421m, 1360m, 1310s, 1180w, 1065m, 1005w, 893m, 854m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 501 (3, [M – H]$^+$), 406 (27), 407 (100), 323 (22), 322 (65), 321 (17), 294 (44), 293 (16), 292 (34), 242 (28),

83 (16), 55 (9). $[\alpha]_D^{20}$ = + 8.5 (c = 0.961, $CHCl_3$). **Elemental analysis**: calc. C 71.70%, H 11.23%, N 5.57%; found: C 71.73%, H 11.16%, N 5.54%.

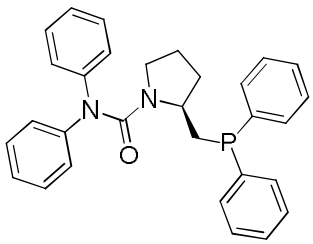
(*S*)-*N*,*N*-Dicyclohexyl-2-[(dicyclohexylphosphino)methyl]pyrrolidine-1-carboxamide ((*S*)-L_{U4}8)



Product **(*S*)-L_{U4}8** was prepared according to **general procedure 3** from **(*S*)-L_{U4}8·BH_3**.

$C_{30}H_{53}N_2OP$ (488.73 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = – 12.5 (s) ppm.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*,*N*-diphenylpyrrolidine-1-carboxamide ((*S*)-L_{U4}9)

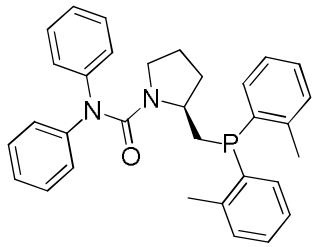


Compound **(*S*)-L_{U4}9** (77%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and diphenylcarbamoyl chloride.

$C_{30}H_{29}N_2OP$ (464.54 g·mol^{-1}):
m.p. 128-129 °C. **R_f** = 0.30 (hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.62 (t, J = 7.8 Hz, 2 H, PPh-*o*-*H*), 7.46-7.40 (m, 2 H, PPh'-*o*-*H*), 7.36-7.26 (m, 10 H, NPh/Ph'-*m*-*H*, PPh/Ph'-*m*-*H* and PPh/Ph'-*p*-*H*), 7.12 ("t", $^3J_{H,H}$ = 7.5 Hz, 2 H, NPh/Ph'-*p*-*H*), 7.06 (d, $^3J_{H,H}$ = 8.5 Hz, 4 H, NPh/Ph'-*o*-*H*), 4.20-4.09 (m, 1 H, Pyr-2-*H*), 3.34-3.21 (m, 2 H, Pyr-5-*H*'H and *CH*'HP), 2.68-2.58 (m, 1 H, Pyr-5-H'*H*), 2.19-2.09 (m, 1 H, Pyr-3-*H*'H), 1.93-1.86 (m, 1 H, *C*H'*H*P), 1.76-1.61 (m, 3 H, Pyr-3-H'*H* and Pyr-4-CH_2) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 158.7 (s, *C*=O), 144.8 (s,

NPh/Ph'-*i*-*C*), 139.5 (d, $^{1}J_{C,P}$ = 12 Hz, PPh-*i*-*C*), 137.2 (d, $^{1}J_{C,P}$ = 12 Hz, PPh'-*i*-*C*), 133.2 (d, $^{2}J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 132.9 (d, $^{2}J_{C,P}$ = 20 Hz, PPh'-*o*-*C*H), 129.3 (s, NPh/Ph'-*m*-*C*H), 128.8 (d, $^{3}J_{C,P}$ = 8.1 Hz, PPh-*m*-*C*H), 128.7 (s, PPh/Ph'-*p*-*C*H), 128.6 (d, $^{3}J_{C,P}$ = 7.0 Hz, PPh'-*m*-*C*H), 126.0 (s, NPh/Ph'-*o*-*C*H), 124.9 (s, NPh/Ph'-*p*-*C*H), 56.9 (d, $^{2}J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 49.3 (s, Pyr-5-*C*H_2), 33.2 (d, $^{1}J_{C,P}$ = 14 Hz, *C*H_2P), 32.2 (d, $^{3}J_{C,P}$ = 9.2 Hz, Pyr-3-*C*H_2), 25.2 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 25.7 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3050m, 2981m, 2913m, 2880m, 1647s, 1592m, 1491m, 1389s, 1288w, 1234m, 1170w, 1095w, 1030w, 903w, 741m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 464 (14, M^+), 463 (27), 297 (20), 296 (100), 264 (16), 263 (75), 232 (14), 223 (27), 201 (14), 196 (47), 195 (16), 185 (49), 183 (52), 180 (12), 173 (12), 169 (27), 168 (34), 167 (19), 77 (13). $[\alpha]_D^{20}$ = + 282.6 (*c* = 0.993, $CHCl_3$). **Elemental analysis**: calc. C 77.57%, H 6.29%, N 6.03%; found: C 77.37%, H 6.55%, N 6.06%.

(*S*)-2-[(Di-*ortho*-tolylphosphino)methyl]-*N*,*N*-diphenylpyrrolidine-1-carboxamide ((*S*)-L_{U4}10)



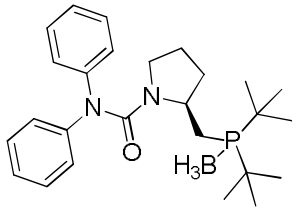
Compound **(*S*)-L_{U4}10** (61%) was prepared according to **general procedure 1** from **(*S*)-L_C2** and diphenylcarbamoyl chloride.

$C_{32}H_{33}N_2OP$ (492.59 $g \cdot mol^{-1}$):

m.p. 193-197 °C. $\mathbf{R_f}$ = 0.38 (hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.82-7.76 (m, 1 H, *o*Tol-6-C*H*), 7.31-7.25 (m, 5 H, *o*Tol-5-C*H* and Ph/Ph'-*m*-C*H*), 7.24-7.15 (m, 3 H, *o*Tol-3/4-C*H* and *o*Tol'-4-C*H*), 7.14-7.07 (m, 5 H, *o*Tol'-3/5/6-C*H* and Ph/Ph'-*p*-C*H*), 7.05 (d, $^{3}J_{H,H}$ = 7.3 Hz, 4 H, Ph/Ph'-*o*-C*H*), 4.26-4.16 (m, 1 H, Pyr-2-C*H*), 3.34-3.25 (m, 1 H, Pyr-5-C*H*H'), 3.12 ("dt", *J* = 14, 3.6 Hz, 1 H, C*H*H'P), 2.71-2.61 (m, 1 H, Pyr-5-CH*H'*P), 2.53 (s, 3 H, *o*Tol-CH_3), 2.31 (s, 3 H, *o*Tol'-CH_3), 2.24-2.14 (m, 1 H, CH*H'*P), 1.79-1.64 (m, 4 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 158.7 (s, *C*=O), 144.8 (s, Ph/Ph'-*i*-*C*), 142.1 (d, $^{2}J_{C,P}$ = 24 Hz, *o*Tol-2-*C*),

141.9 (d, $^{2}J_{C,P}$ = 25 Hz, *o*Tol'-2-*C*), 137.3 (d, $^{1}J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 135.6 (d, $^{1}J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 132.2 (s, *o*Tol-6-*C*H), 131.8 (s, *o*Tol'-6-*C*H), 130.1 (d, $^{3}J_{C,P}$ =5.0 Hz, *o*Tol-3-*C*H), 130.0 (d, $^{3}J_{C,P}$ = 5.0 Hz, *o*Tol'-3-*C*H), 129.3 (s, Ph/Ph'-*m*-*C*H), 128.6 (s, *o*Tol-4-*C*H), 128.5 (s, *o*Tol'-4-*C*H), 126.7 (s, *o*Tol-5-*C*H), 126.3 (s, *o*Tol'-5-*C*H), 126.0 (s, Ph/Ph'-*o*-*C*H), 124.8 (s, Ph/Ph'-*p*-*C*H), 56.9 (d, $^{2}J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 49.2 (s, Pyr-5-*C*H_2), 32.3 (d, $^{3}J_{C,P}$ = 9.6 Hz, Pyr-3-*C*H_2), 31.9 (d, $^{1}J_{C,P}$ = 14 Hz, *C*H_2P), 252 (s, Pyr-4-*C*H_2), 21.4 (d, $^{3}J_{C,P}$ = 19 Hz, *o*Tol-*C*H_3), 21.2 (d, $^{3}J_{C,P}$ = 18 Hz, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 42.5 ppm. **IR** (neat): $\tilde{\nu}$ = 3057w, 2911m, 1637m, 1601m, 1489m, 1448m, 1382s, 1345s, 1235m, 1164m, 1029w, 759s, 695m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 492 (12, M^+), 491 (24), 477 (20), 401 (21), 325 (21), 324 (97), 264 (19), 263 (100), 246 (19), 213 (31), 197 (12), 196 (98), 169 (11), 167 (12). $[\alpha]_D^{20}$ = + 241.0 (*c* = 1.04, $CHCl_3$).

(*S*)-2-[(Di-*tert*-butyl-phosphino)methyl]-*N*,*N*-diphenylpyrrolidine-1-carboxamide borane adduct ((*S*)-L_{U4}11·BH_3)



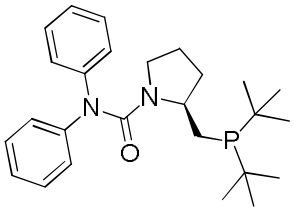
Compound **(*S*)-L_{U4}11** (43%) was prepared according to **general procedure 2** from **(*S*)-L_C4·BH_3** and diphenylcarbamoyl chloride.

$C_{26}H_{40}BN_2OP$ (438.39 g·mol^{-1}):

m.p. 154-155 °C. **R_f** = 0.14 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.31 (dd, $^{3}J_{H,H}$ = 7.5 Hz, 4 H, Ph/Ph'-*m*-*H*), 7.12 ("t", $^{3}J_{H,H}$ = 7.5 Hz, 2 H, Ph/Ph'-*p*-*H*), 7.06 (dd, $^{3}J_{H,H}$ = 8.5 Hz, $^{4}J_{H,H}$ = 1.3 Hz, 4 H, Ph/Ph'-*o*-*H*), 4.39-4.30 (m, 1 H, Pyr-2-*H*), 3.28-3.22 (m, 1 H, Pyr-5-*H*H'), 2.82 (td, *J* = 15 Hz, *J* = 2.3 Hz, 1 H, C*H*H'P), 2.62-2.47 (m, 2 H, Pyr-5-H*H*' and Pyr-3-*H*H'), 1.76-1.57 (m, 3 H, Pyr-3-H*H*' and Pyr-4-H_2), 1.45-1.34 (m, 1 H, CH*H*'P), 1.38 (d, $^{3}J_{H,P}$ = 13 Hz, 9 H, *t*Bu-H_3), 1.27 (d, $^{3}J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-H_3), 0.92-0.03 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 158.8 (s, *C*=O), 144.7 (s, Ph/Ph'-*i*-*C*), 129.4 (s, Ph/Ph'-*m*-*C*H), 125.7 (s, Ph/Ph'-*o*-*C*H), 124.9 (s, Ph/Ph'-*p*-*C*H), 57.1 (d, $^{2}J_{C,P}$ = 5.6 Hz, Pyr-2-*C*H), 49.2 (s, Pyr-5-*C*H_2), 33.3 (d, $^{1}J_{C,P}$ = 27 Hz, *t*Bu-*C*), 33.3 (s, Pyr-3-*C*H_2), 32.1 (d, $^{1}J_{C,P}$ = 28 Hz,

*t*Bu'-*C*), 28.3.3 (d, $^{2}J_{C,P}$ = 1.5 Hz, *t*Bu-*C*H$_3$), 28.0 (d, $^{2}J_{C,P}$ = 1.2 Hz, *t*Bu'-*C*H$_3$), 25.3 (s, Pyr-4-*C*H$_2$), 22.7 (d, $^{1}J_{C,P}$ = 24 Hz, *C*H$_2$P) ppm. **^{31}P NMR** (162 MHz, CDCl$_3$, 300 K): δ = 40.0 (br s) ppm. **IR** (neat): $\tilde{\nu}$ = 2956m, 2943m, 2870m, 1648s, 1588m, 1488m, 1471m, 1378s, 1342m, 1285w, 1226m, 1174m, 1150w, 1068m, 1021w, 902w, 876m, 817m, 755s, 697s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 437 (6, [M − H]$^+$), 367 (100), 311 (16), 270 (52), 242 (12), 196 (19), 168 (17), 57 (14). $[\alpha]_D^{20}$ = + 217.0 (c = 0.550, CHCl$_3$). **Elemental analysis:** calc. C 71.23%, H 9.20%, N 6.39%; found: C 71.19%, H 9.40%, N 6.35%.

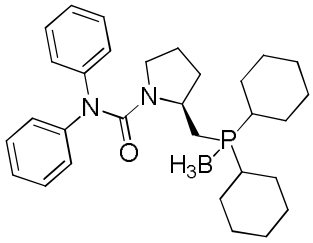
(*S*)-2-[(Di-*tert*-butylphosphino)methyl]-*N*,*N*-diphenylpyrrolidine-1-carboxamide ((*S*)-L$_{U4}$11)



Product **(*S*)-L$_{U4}$11** was prepared according to **general procedure 3** from **(*S*)-L$_{U4}$11·BH$_3$**. C$_{26}$H$_{37}$N$_2$OP (424.56 g·mol^{-1}):

^{31}P{^{1}H} NMR (162 MHz, CDCl$_3$): δ = 21.0 (s) ppm.

(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*,*N*-diphenylpyrrolidine-1-carboxamide borane adduct ((*S*)-L$_{U4}$12·BH$_3$)



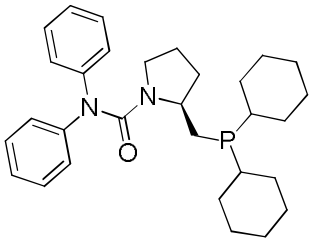
Compound **(*S*)-L$_{U4}$12·BH$_3$** (92%) was prepared according to **general procedure 2** from **(*S*)-L$_C$5·BH$_3$** and diphenylcarbamoyl chloride.

C$_{30}$H$_{44}$BN$_2$OP (490.47 g·mol^{-1}):

R$_f$ = 0.20 (SiO$_2$, hexanes/ethyl acetate 9:1). **^{1}H NMR** (500 MHz, CDCl$_3$): δ = 7.31 ("t", $^{2}J_{H,H}$ = 7.8 Hz, 4 H, Ph/Ph'-*m*-*H*), 7.14 ("t", $^{2}J_{H,H}$ = 7.5 Hz, 2 H, Ph/Ph'-*p*-*H*), 7.06 ("t",

$^{2}J_{H,H}$ = 7.5 Hz, 4 H, Ph/Ph'-*o*-*H*), 4.28-4.20 (m, 1 H, Pyr-2-*H*), 3.25-3.19 (m, 1 H, Pyr-5-*H*H'), 2.75-2.67 (m, 1 H, C*H*H'P), 2.60-2.53 (m, 1 H, Pyr-5-H*H'*), 2.40-2.30 (m, 1 H, Pyr-3-*H*H'), 2.05-1.15 (m, 26 H, CH*H'*P, Pyr-3-H*H'*, Pyr-4-H_2 and Cy/Cy'-*H*), 0.75-0.04 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 158.6 (s, *C*=O), 144.6 (s, Ph/Ph'-*i*-*C*), 129.4 (s, Ph/Ph'-*o*-*C*H), 125.9 (s, Ph/Ph'-*m*-*C*H), 125.0 (s, Ph/Ph'-*p*-*C*H), 56.1 (d, $^{2}J_{C,P}$ = 4.6 Hz, Pyr-2-*C*H), 49.1 (s, Pyr-5-*C*H_2), 33.0 (s, Pyr-3-*C*H_2), 32.7 (d, $^{1}J_{C,P}$ = 29 Hz, Cy-1-*C*H), 32.5 (d, $^{1}J_{C,P}$ = 31 Hz, Cy'-1-*C*H), 27.2-26.0 (m, Cy/Cy'-*C*H_2), 25.3 (s, Pyr-4-*C*H_2), 24.5 (d, $^{1}J_{C,P}$ = 27 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 21.5 (br s) ppm.

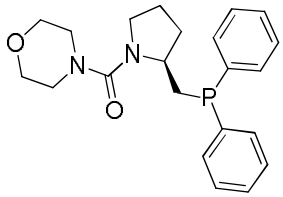
(*S*)-2-[(Dicyclohexylphosphino)methyl]-*N*,*N*-diphenylpyrrolidine-1-carboxamide ((*S*)-L$_{U4}$12)



Product **(*S*)-L$_{U4}$12** was prepared according to **general procedure 3** from **(*S*)-L$_{U4}$12·BH$_3$**.

$C_{30}H_{41}N_2OP$ (476.63 g·mol^{-1}):
^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ =− 10.5 (s) ppm.

(*S*)-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}(morpholino)methanone ((*S*)-L$_{U4}$13)

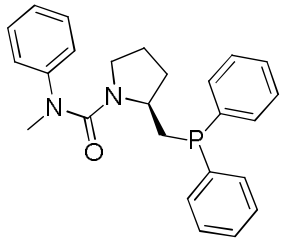


Compound **(*S*)-L$_{U4}$13** (60%) was prepared according to **general procedure 1** from **(*S*)-L$_{C}$1** and 4-morpholinocarbonyl chloride.

$C_{22}H_{27}N_2O_2P$ (382.44 g·mol^{-1}):

m.p. 113-114 °C. $\mathbf{R_f}$ = 0.31 (hexanes/ethyl acetate 1:1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.53-7.50 (m, 2 H, Ph-*o*-*H*), 7.44-7.40 (m, 2 H, Ph'-*o*-*H*), 7.35-7.26 (m, 6 H, Ph/Ph'-*H*), 4.25-4.18 (m, 1 H, Pyr-2-*H*), 3.67-3.60 (m, 2 H, Morph-*H*), 3.54-3.50 (m, 2 H, Morph-*H*), 3.36-3.31 (m, 2 H, Pyr-5-H_2), 3.20 ("ddd", $^2J_{H,H}$ = 13 Hz, $^3J_{H,H}$ = 6.6, 2.8 Hz, 2 H, Morph-*H*), 2.99 ("ddd", $^2J_{H,H}$ = 13 Hz, $^3J_{H,H}$ = 6.4, 2.8 Hz, 2 H, Morph-*H*), 2.65 ("dt", $^2J_{H,P}$ = 14 Hz, $J_{H,H}$ = 3.4 Hz, 1 H, C*H*H'P), 2.26 (dd, $^2J_{H,P}$ = 14 Hz, $J_{H,H}$ = 8.8 Hz, 1 H, CH*H'*P), 2.20-2.16 (m, 1 H, Pyr-*H*), 1.88-1.63 (m, 3 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 162.8 (*C*=O), 139.4 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 138.6 (d, $^1J_{C,P}$ = 12 Hz, Ph'-*i*-*C*), 133.8 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 133.0 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.9 (s, Ph-*p*-*C*H), 128.9 (s, Ph'-*p*-*C*H), 128.8 (d, $^3J_{C,P}$ = 6.8 Hz, Ph-*m*-*C*H), 128.7 (d, $^3J_{C,P}$ = 7.1 Hz, Ph'-*m*-*C*H), 67.0 (s, Morph-2/6-*C*H_2), 56.9 (d, $^2J_{C,P}$ = 18 Hz, Pyr-2-*C*H), 51.4 (s, Pyr-5-*C*H_2), 46.6 (s, Morph-3/5-*C*H_3), 34.0 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 32.5 (d, $^3J_{C,P}$ = 9.7 Hz, Pyr-3-*C*H_2), 26.1 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 27.4 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3045m, 2977m, 2895m, 2855m, 1967w, 1635s, 1569w, 1480m, 1413s, 1351m, 1306m, 1265m, 1215m, 1178m, 1115s, 1025m, 948m, 872m, 785m, 744s, 699s, 607m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 383 (100, [M + H]$^+$), 312 (16), 296 (59), 185 (73), 181 (92), 114 (95), 70 (73), 39 (14). $[\alpha]_D^{20}$ = + 1.6 (*c* = 1.01, $CHCl_3$). **Elemental analysis**: calc. C 69.09%, H 7.12%, N 7.33%; found: C 69.13%, H 7.09%, N 7.25%.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-methyl-*N*-phenylpyrrolidine-1-carboxamide ((*S*)-L_{U4}14)

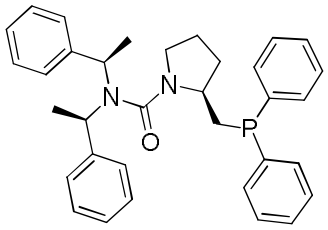


Compound **(*S*)-L_{U4}14** (39%) was prepared according to **general procedure 1** from **(*S*)-L_C1** and *N*-methyl-*N*-phenylcarbamoyl chloride.

$C_{25}H_{27}N_2OP$ (402.47 g·mol^{-1}):

m.p. 139-141 °C. $\mathbf{R_f}$ = 0.25 (hexanes/ethyl acetate 4:1). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.66-7.60 (m, 2 H, NPh-*o*-*H*), 7.47-7.25 (m, 10 H, PPh/Ph'-*H*), 7.13-7.07 (m, 3 H, NPh-*H*), 4.09-3.97 (m, 1 H, Pyr-2-*H*), 3.17 (s, 3 H, C*H*$_3$), 3.08-3.10 (m, 2 H, Pyr-5-*H*H' and C*H*H'P), 2.55-2.46 (m, 1 H, Pyr-5-H*H'*), 2.11-2.01 (m, 1 H, Pyr-3-*H*H'), 1.96-1.88 (m, 1 H, CH*H'*P), 1.66-1.49 (m, 3 H, Pyr-3-H*H'* and Pyr-4-*H*$_2$) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 159.6 (s, *C*=O), 146.6 (s, NPh-*i*-*C*), 139.8 (d, $^1J_{C,P}$ = 13 Hz, PPh-*i*-*C*), 138.2 (d, $^1J_{C,P}$ = 14 Hz, PPh'-*i*-*C*), 133.0 (d, $^2J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, PPh'-*o*-*C*H), 129.3 (s, NPh-*m*-*C*H), 128.7 (s, PPh-*p*-*C*H), 128.5 (d, $^3J_{C,P}$ = 2.6 Hz, PPh-*m*-*C*H), 128.4 (d, $^2J_{C,P}$ = 1.6 Hz, PPh'-*m*-*C*H), 128.4 (s, PPh'-*p*-*C*H), 124.8 (s, NPh-*o*-*C*H), 124.2 (s, NPh-*p*-*C*H), 56.7 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 49.4 (s, Pyr-5-*C*H$_2$), 39.2 (s, *C*H$_3$), 33.6 (d, $^1J_{C,P}$ = 14 Hz, *C*H$_2$P), 32.1 (d, $^3J_{C,P}$ = 8.1 Hz, Pyr-3-*C*H$_2$), 25.2 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = − 22.1 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2975w, 2943w, 2905w, 2881w, 1634s, 1595m, 1581m, 1492m, 1432s, 1386s, 1351m, 1334m, 1298m, 1165m, 1108m, 1073m, 1025m, 998w, 932w, 906w, 875w, 851w, 763m, 752s, 696s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 402 (12, M^+), 401 (12), 401 (25), 325 (11), 296 (42), 203 (18), 202 (14), 201 (100), 199 (11), 183 (31), 161 (29), 134 (83), 133 (14), 106 (21), 77 (15). $[\alpha]_D^{20}$ = + 169.7 (*c* = 0.623, $CHCl_3$).

(*S*)-2-[(Diphenylphosphino)methyl]-*N*,*N*-bis((*R*)-1-phenylethyl)pyrrolidine-1-carboxamide ((*S*,*R*,*R*)-L$_{U4}$15)

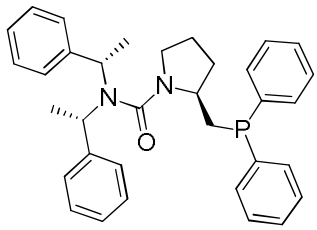


To a solution of (+)-bis[(*R*)-1-phenylethyl]amine (**(*R*,*R*)-73**, 100 µL, 437 µmol, 1.00 eq.) in abs. tetrahydrofuran (5 mL) was added drop wise a 1.6 M solution of *n*-butyllithium (300 µL, 480 µmol, 1.1 eq.) at −78 °C in a dry ice/acetone bath. The resulting solution was allowed to stir for 30 minutes at – 78 °C and then for 1 hour at 0 °C in an ice bath, before a solution of bis(trichloromethyl)carbonate (45.4 mg, 153 µmol, 0.35 eq.) in abs. tetrahydrofuran (3 mL) was added at 0 °C. The reaction mixture was

allowed to warm to room temperature over 12 hours, before the solvent was removed *in vacuo*. The residual colorless solid was again dissolved in abs. tetrahydrofuran (2 mL). Triethylamine (400 µL, 2.87 mmol, 6.6 eq.) and a solution of (*S*)-2-[(diphenylphosphino)methyl]pyrrolidine hydrochloride (**(*S*)-52·HCl**, 170 mg, 458 µmol, 1.0 eq.) in tetrahydrofuran (2 mL) were then added successively at 0 °C. The resulting mixture was allowed to warm to room temperature over 20 hours, before it was reduced to dryness *in vacuo*. The crude was purified by column chromatography on silica gel (3 x 15 cm), eluting with hexanes/ethyl acetate (9:1). The product **(*S*,*R*,*R*)-L_{U4}15** was isolated as yellowish semisolid (54.4 mg, 104 µmol, 24%).

$C_{34}H_{37}N_2OP$ (520.64 g·mol^{-1}):
R_f = 0.18 (SiO_2, hexanes/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.73-6.97 (m, 20 H, PPh/Ph'-*H* and C/C'Ph-*H*), 4.58-4.39 (m, 2 H, NC/C'*H*), 4.23-4.07 (m, 1 H, Pyr-2-*H*), 3.50-3.22 (m, 2 H, Pyr-5-H_2), 2.60 (d, $^2J_{H,P}$ = 13 Hz, 1 H, C*H*H'P), 2.01-1.36 (m, 11 H, CH*H'*P, Pyr-*H* and CH_3/CH_3') ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 163.1 (*C*=O), 143.3 (s, C/C'Ph-*i*-*C*), 140.0 (d, $^1J_{C,P}$ = 12 Hz, PPh-*i*-*C*), 138.7 (d, $^1J_{C,P}$ = 13 Hz, PPh'-*i*-*C*), 133.2 (d, $^2J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 133.2 (d, $^2J_{C,P}$ = 19 Hz, PPh'-*o*-*C*H), 128.8 (d, $^3J_{C,P}$ = 6.9 Hz, PPh-*m*-*C*H), 128.8 (s, PPh-*p*-*C*H), 128.7 (s, PPh'-*p*-*C*H), 128.7 (d, $^3J_{C,P}$ = 6.9 Hz, PPh'-*m*-*C*H), 128.4 (s, C/C'Ph-*m*-*C*H), 127.8 (s, C/C'Ph-*o*-*C*H), 127.1 (s, C/C'Ph-*p*-*C*H), 56.9 (s, N*C*/*C*'H), 56.4 (d, $^2J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 50.8 (s, Pyr-5-*C*H_2), 33.6 (d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 32.1 (d, $^3J_{C,P}$ = 9.0 Hz, Pyr-3-*C*H_2), 25.6 (s, Pyr-4-*C*H_2), 21.2 (s, *C*H_3/*C*H_3') ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 26.0 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 3058w, 3028w, 2969m, 2868m, 1633s, 1493m, 1446m, 1433m, 1410s, 1368m, 1333m, 1282m, 1184m, 1156w, 1118w, 1071w, 1025m, 908m, 794w, 739s, 693s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 521 (20, $[M + H]^+$), 433 (9), 415 (46), 311 (24), 286 (19), 185 (21), 105 (100), 57 (7). $[\alpha]_D^{20}$ = + 30.9 (*c* = 1.00, $CHCl_3$).

(*S*)-2-[(Diphenylphosphino)methyl]-*N*,*N*-bis((*S*)-1-phenylethyl)pyrrolidine-1-carboxamide ((*S*,*S*,*S*)-L_{U4}15)



A 1.6 M solution of phosgene in toluene (600 µL, 960 µmol, 1.1 eq.) was added drop wise to a stirred solution of (−)-bis[(*S*)-1-phenylethyl]amine (**(*S*,*S*)-73**, 200 µL, 876 µmol, 1.0 eq.) and *N*-ethyldiisopropylamine (500 µL, 2.58 mmol, 3.0 eq.) in toluene (3 mL) at 0 °C under argon atmosphere. Stirring was continued for 1 hour before addition of a solution of (*S*)-2-[(diphenylphosphino)methyl]pyrrolidine hydrochloride (**(*S*)-52·HCl**, 299 mg, 976 µmol, 1.1 eq.) in dichloromethane (2 mL) and 4-(dimethylamino)pyridine (DMAP, 21.4 mg, 175 µmol, 0.20 eq.). The reaction mixture was then heated at reflux for 22 hours. After cooling to room temperature, H_2O (20 mL) and conc. HCl (2 mL) were added. The phases were separated and the aqueous layer was extracted with toluene (20 mL). The combined organic extracts were washed with H_2O (20 mL), dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (3 x 18 cm, pre-treated with 10% NEt_3), eluting with dichloromethane (100%). The product **(*S*,*S*,*S*)-L_{U4}15** was obtained as yellowish semisolid (121 mg, 323 µmol, 27%).

$C_{34}H_{37}N_2OP$ (520.64 g·mol^{-1}):

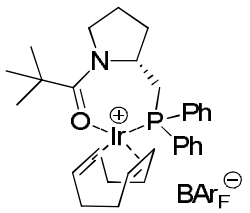
R_f = 0.75 (SiO_2, dichloromethane 100%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.57 ("t", $^3J_{H,H}$ = 7.3 Hz, 2 H, Ar-*H*), 7.40-7.30 (m, 5 H, Ar-*H*), 7.30-7.26 (m, 3 H, Ar-*H*), 7.24-7.10 (m, 10 H, Ar-*H*), 4.85 (q, $^3J_{H,H}$ = 7.1 Hz, 2 H, NC/C'*H*), 4.21-4.10 (m, 1 H, Pyr-2-*H*), 3.57-3.48 (m, 1 H, Pyr-5-*H*H'), 3.34-3.23 (m, 1 H, Pyr-5-H*H'*), 2.89 ("dt", *J* = 14, 4.0 Hz, 1 H, C*H*H'P), 2.07-1.97 (m, 1 H, Pyr-*H*), 1.94 ("dd", *J* = 13, 10 Hz, 1 H, CH*H'*P), 1.86-1.76 (m, 1 H, Pyr-*H*), 1.71-1.48 (m, 2 H, Pyr-*H*), 1.50 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3') ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 163.6 (s, *C*=O), 143.8 (s, CPh-*i*-*C*), 139.8 (d, $^1J_{C,P}$ = 13 Hz, C'PPh-*i*-*C*), 138.2 (d, $^1J_{C,P}$ = 12 Hz, PPh'-*i*-*C*), 133.1 (d, $^2J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 132.9 (d, $^2J_{C,P}$ = 19 Hz, PPh'-*o*-*C*H), 128.7 (s, PPh-*p*-*C*H), 128.6 (d, $^3J_{C,P}$ = 4.0 Hz, PPh-*m*-*C*H), 128.5 (s, PPh'-*p*-*C*H), 128.4 (d, $^3J_{C,P}$ = 8.4 Hz, PPh'-*m*-*C*H), 128.1 (s, C/C'Ph-*m*-*C*H), 127.6 (s, C/C'Ph-*o*-*C*H), 126.7 (s,

C/C'Ph-*p*-*C*H), 56.7 (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 55.8 (s, N*C*/*C*'H), 50.5 (s, Pyr-5-*C*H_2), 33.7 (d, $^{1}J_{C,P}$ = 14 Hz, *C*H_2P), 32.1 (d, $^{3}J_{C,P}$ = 8.7 Hz, Pyr-3-*C*H_2), 25.5 (s, Pyr-4-*C*H_2), 19.8 (s, *C*H_3/*C*H_3') ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 25.9 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3056w, 3025w, 2969m, 2935w, 2866w, 1623s, 1415m, 1375m, 1340m, 1310m, 1199m, 1181m, 1170m, 1091m, 1070m, 1025m, 997w, 907m, 873m, 794m, 739s, 693s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 521 (20, $[M + H]^+$), 433 (9), 415 (46), 311 (24), 286 (19), 185 (21), 105 (100), 57 (7). $[\alpha]_D^{20}$ = + 2.9 (*c* = 1.28, $CHCl_3$).

6.4

Proline-Based P,O Ligand/Iridium Complexes: Preparation and Analytical Data

[(η^4-1,5-Cyclooctadiene)-((*R*)-1-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}-2,2-dimethylpropan-1-one)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*R*)-C_A1)

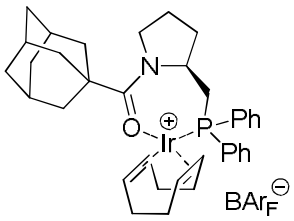


Complex **(*R*)-C_A1** (98%) was prepared according to **general procedure 5** from ligand **(*R*)-L_A1** and [Ir(cod)$_2$]BAr$_F$.[73] Crystals suitable for X-ray diffraction were obtained by crystallization from dichloromethane layered with *n*-pentane in an NMR tube.

$C_{62}H_{52}NOPIrBF_{24}$ (1517.03 g·mol^{-1}):
m.p. 98-102 °C. **^{1}H NMR** (500 MHz, CD_2Cl_2): δ = 7.96-7.90 (m, 1 H, Ph-*o*-*H*), 7.76 (s, 8 H, Ar$_F$-*o*-*H*), 7.69-7.33 (m, 12 H, Ph/Ph'-*H* and Ar$_F$-*p*-*H*), 7.05-6.96 (m, 1 H, Ph'-*m*-*H*), 5.38-5.28 (m, 1 H, Pyr-2-*H*), 5.25-5.16 (m, 1 H, cod-C*H*), 5.11-5.04 (m, 1 H, cod-C*H*), 3.78-3.69 (m, 1 H, Pyr-5-*H*H'), 3.31-3.22 (m, 1 H, Pyr-5-H*H'*), 3.12-3.00 (m, 1 H, C*H*H'P), 2.97-2.85 (m, 2 H, cod-C*H*), 2.85-2.77 (m, 1 H, CH*H'*P), 2.50-2.39 (m, 2 H, cod-CH_2), 2.31-1.73 (m, 9 H, cod-CH_2 and Pyr-*H*), 1.60-1.48 (m, 1 H, Pyr-3-H*H'*), 0.84 (s, 9 H, *t*Bu-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ = 184.7 (s, *C*=O), 161.9 (q, $^1J_{C,B}$ = 50 Hz, Ar$_F$-*i*-*C*), 134.9 (s, Ar$_F$-*o*-*C*H), 134.7 (d, $^2J_{C,P}$ = 13 Hz, Ph-*o*-*C*H), 132.9 (s, Ph-*p*-*C*H), 131.3 (d, $^3J_{C,P}$ = 9.4 Hz, Ph-*m*-*H*), 131.2 (s, Ph'-*p*-*C*H), 130.3 (d, $^1J_{C,P}$ = 51 Hz, Ph-*i*-*C*), 129.9 (d, $^2J_{C,P}$ = 11 Hz, Ph'-*o*-*C*H), 129.5-128.5 (m, Ar$_F$-*m*-*C* and Ph'-*m*-*C*H), 125.3 (d, $^1J_{C,P}$ = 53 Hz, Ph'-*i*-*C*), 124.7 (q, $^1J_{C,F}$ = 272 Hz, Ar$_F$-*C*F$_3$), 117.8-117.4 (m, Ar$_F$-*p*-*C*H), 69.1 (s, *t*Bu-*C*), 59.4 (d, $^2J_{C,P}$ = 4.2 Hz, Pyr-2-*C*H), 52.3 (s, cod-*C*H), 51.5 (s, cod-*C*H), 48.6 (s, Pyr-5-*C*H$_2$), 36.9 (d, $^1J_{C,P}$ = 30 Hz, *C*H$_2$P), 35.3 (br d, $^3J_{C,P}$ = 3.8 Hz, cod-*C*H$_2$), 31.9 (br d, $^3J_{C,P}$ = 2.1 Hz, cod-*C*H$_2$), 31.5 (d, $^3J_{C,P}$ = 14 Hz, Pyr-3-*C*H$_2$), 29.7 (br s, cod-*C*H$_2$), 27.2 (br s, cod-*C*H$_2$), 26.7 (s, *t*Bu-*C*H$_3$), 23.4 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 9.1 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 63.5 (s) ppm. **IR** (KBr): $\tilde{\nu}$ = 2974m, 1781w, 1612s, 1535s, 1487m, 1438s, 1358s, 1279s, 1131s, 1000w, 950w, 926w, 888s, 839m cm^{-1}. **MS** (FAB,

NBA): *m/z* (%) = 655 (13), 654 (36, $[M + H]^+$), 652 (25), 488 (27), 486 (21), 458 (12), 456 (10). $[\alpha]_D^{20}$ = + 9.3 (*c* = 1.10, $CHCl_3$). **Elemental analysis**: calc. C 49.09%, H 3.45%, N 0.92%; found: C 49.16%, H 3.47%, N 0.85%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-Adamantan-1-yl {(*S*)-2-[(diphenylphosphino)methyl] pyrrolidin-1-yl}methanone)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_A7)

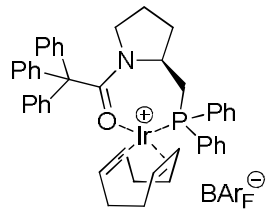


Complex **(*S*)-C_A7** (98%) was prepared according to **general procedure 5** from ligand **(*S*)-L_A7** and $[Ir(cod)_2]BAr_F$.[73]

$C_{68}H_{58}NOPIrBF_{24}$ (1595.16 g·mol^{-1}):

m.p. 89-91 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.96-7.88 (m, 1 H, Ph-*H*), 7.73 (s, 8 H, Ar_F-*o*-*H*), 7.69-7.24 (m, 12 H, Ar_F-*p*-*H* and Ph/Ph'-*H*), 7.04-6.95 (m, 1 H, Ph'-*H*), 5.41-5.32 (m, 1 H, Pyr-2-*H*), 5.27-5.18 (m, 1 H, cod-C*H*), 5.12-5.03 (m, 1 H, cod-C*H*), 4.00-3.88 (m, 1 H, Pyr-5-*H*H'), 3.39-3.24 (m, 1 H, Pyr-5-H*H'*), 3.11-2.95 (m, 1 H, C*H*H'P), 2.95-2.83 (m, 2 H, cod-C*H*), 2.83-2.72 (m, 1 H, CH*H'*P), 2.54-2.38 (m, 2 H, cod-*H*), 2.34-1.15 (m, 25 H, cod-*H*, Pyr-*H* and Adm-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ = 183.6 (s, *C*=O), 161.9 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 134.9 (s, Ar_F-*o*-*C*H), 134.7 (s, Ph-*o*-*C*H), 131.7-130.5 (m, Ph-*m*-*C*H, Ph/Ph'-*p*-*C*H and Ph-*i*-*C*), 129.9 (d, $^2J_{C,P}$ = 11 Hz, Ph'-*o*-*C*H), 129.6-128.0 (m, Ph'-*m*-*C*H and Ar_F-*m*-*C*), 124.7 (q, $^1J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 125.3 (br d, Ph'-*i*-*C*), 117.5 (br s, Ar_F-*p*-*C*H), 99.2 (d, $^2J_{C,P}$ = 13 Hz, cod-*C*H), 98.8 (d, $^2J_{C,P}$ = 13 Hz, cod-*C*H), 59.2 (br d, $^2J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 52.1 (s, cod-*C*H), 51.3 (s, cod-*C*H), 48.5 (s, Pyr-5-*C*H_2), 43.8 (s, Adm-1-*C*), 37.1 (s, Adm-2/8/10-*C*H_2), 36.0 (br s, cod-*C*H_2), 35.9 (s, Adm-4/6/9-*C*H_2), 33.1 (d, $^1J_{C,P}$ = 35 Hz, *C*H_2P), 31.9 (br d, cod-*C*H_2), 31.3 (d, $^3J_{C,P}$ = 8.1 Hz, Pyr-3-*C*H_2), 29.8 (s, cod-*C*H_2), 28.0 (s, Adm-3/5/7-*C*H), 27.2 (s, cod-*C*H_2), 23.6 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 12.5 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 62.3 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2912m, 2856m, 1734m, 1610w, 1522m, 1436m, 1354s, 1271s, 1112s, 885m, 839m, 744m, 711m, 680s, 667m cm^{-1}. **MS** (ESI): *m/z* (%) = 732 (100, M^+). $[\alpha]_D^{20}$ = − 3 (*c* = 0.270, $CHCl_3$).

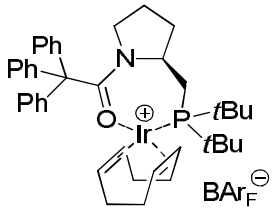
[(η^4-1,5-Cyclooctadiene)-((*S*)-1-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_A13)



Complex **(*S*)-C_A13** (99%) was prepared according to **general procedure 5** from ligand **(*S*)-L_A13** and $[Ir(cod)_2]BAr_F$.[73]

$C_{77}H_{58}NOPIrBF_{24}$ (1703.25 g·mol^{-1}):
m.p. 80-84 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.10-8.01 (m, 2 H, Ph-*H*), 7.81-7.01 (m, 30 H, Ph/Ph'-*H*, CPh-*H* and Ar_F-*H*), 6.80-6.70 (m, 5 H, PPh/Ph'-*H*), 5.50-5.39 (m, 1 H, Pyr-2-*H*), 4.81-4.73 (m, 1 H, cod-C*H*), 4.26-4.17 (m, 1 H, cod-C*H*), 3.18-3.03 (m, 3 H, Pyr-5-H_2 and C*H*H'P), 2.92-2.79 (m, 2 H, cod-*C*H), 2.65-2.54 (m, 1 H, CH*H'*P), 2.42-0.94 (m, 12 H, Pyr-*H* and cod-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ = 178.7 (s, *C*=O), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 140.4 (s, CPh-*i*-*C*), 135.8 (d, $^2J_{C,P}$ = 11 Hz, PPh-*o*-*C*H), 134.9 (s, Ar_F-*o*-*C*H), 133.3 (s, PPh-*p*-*C*H), 131.5 (d, $^3J_{C,P}$ = 11 Hz, PPh-*m*-*C*H), 131.2 (s, PPh'-*p*-*C*H), 131.1 (br d, PPh-*i*-*C*), 130.0 (d, $^3J_{C,P}$ = 10 Hz, PPh'-*m*-*C*H), 129.8 (s, CPh-*m*-*C*H), 129.5-128.4 (m, PPh'-*o*-*C*H, CPh-*o*-*C*H and Ar_F-*m*-*C*), 127.5 (s, CPh-*p*-*C*H), 125.9 (br d, PPh'-*i*-*C*), 124.7 (q, $^1J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 117.7-117.4 (m, Ar_F-*p*-*C*H), 100.7 (d, $^2J_{C,P}$ = 12 Hz, cod-*C*H), 98.0 (d, $^2J_{C,P}$ = 12 Hz, cod-*C*H), 69.8 (s, *C*Ph_3), 60.1 (d, $^2J_{C,P}$ = 6.8 Hz, Pyr-2-*C*H), 53.7 (s, cod-*C*H), 53.5 (s, cod-*C*H), 51.6 (s, Pyr-5-*C*H_2), 43.0 (d, $^1J_{C,P}$ = 28 Hz, *C*H_2P), 34.5 (s, cod-*C*H_2), 33.1 (d, $^3J_{C,P}$ = 14 Hz, Pyr-3-*C*H_2), 38.4 (s, cod-*C*H_2), 29.2 (s, cod-*C*H_2), 27.5 (s, cod-*C*H_2), 23.3 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 14.9 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2927m, 2854m, 1610m, 1552m, 1488m, 1438m, 1354s, 1273s, 1115s, 1000m, 929w, 885m, 839m, 742m, 700m, 680s cm^{-1}. **MS** (ESI): *m/z* (%) = 840 (100, M^+). $[\alpha]_D^{20}$ = + 6.1 (*c* = 1.271, $CHCl_3$).

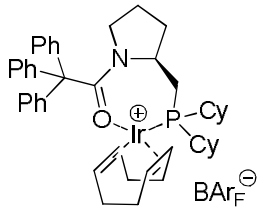
[(η^4-1,5-Cyclooctadiene)-((*S*)-1-{2-[(di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_A16)



Complex **(*S*)-C_A16** (99%) was prepared according to **general procedure 5** from ligand **(*S*)-L_A16** and [Ir(cod)$_2$]BAr$_F$.[73]

$C_{73}H_{66}NOPIrBF_{24}$ (1663.27 g·mol^{-1}):
m.p. 66-70 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.70 (s, 8 H, Ar$_F$-*o*-*H*), 7.51 (s, 4 H, Ar$_F$-*p*-*H*), 7.38-6.97 (m, 15 H, Ph-*H*), 5.03-4.93 (m, 1 H, Pyr-2-*H*), 4.24-4.16 (m, 1 H, cod-C*H*), 4.16-4.07 (m, 1 H, cod-C*H*), 4.07-4.00 (m, 1 H, cod-C*H*), 3.48-3.39 (m, 1 H, cod-C*H*), 3.10-2.98 (m, 1 H, Pyr-5-*H*H'), 2.81-2.70 (m, 1 H, C*H*H'P), 2.30-2.07 (m, 5 H, Pyr-5-H*H*' and cod-CH_2), 2.07-1.96 (m, 1 H, CH*H*'P), 1.83-1.45 (m, 8 H, Pyr-*H* and cod-CH_2), 1.32 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.19 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu'-*H*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 174.7 (s, *C*=O), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar$_F$-*i*-*C*), 140.5 (br s, Ph-*i*-*C*), 134.9 (s, Ar$_F$-*o*-*C*H), 130.1 (s, Ph-*m*-*C*H), 129.4-128.6 (m, Ar$_F$-*m*-*C*), 128.6 (s, Ph-*o*-*C*H), 128.2 (s, Ph-*p*-*C*H), 124.7 (q, $^1J_{C,F}$ = 273 Hz, Ar$_F$-*C*F$_3$), 117.7-117.4 (m, Ar$_F$-*p*-*C*H), 95.9 (d, $^2J_{C,P}$ = 11 Hz, cod-*C*H), 90.8 (d, $^2J_{C,P}$ = 13 Hz, cod-*C*H), 69.1 (s, *C*Ph$_3$), 60.2 (d, $^2J_{C,P}$ = 9.3 Hz, Pyr-2-*C*H), 52.4 (s, Pyr-5-*C*H$_2$), 52.2 (s, cod-*C*H), 50.5 (s, cod-*C*H), 39.6 (d, $^1J_{C,P}$ = 19 Hz, *t*Bu-*C*), 37.5 (d, $^1J_{C,P}$ = 20 Hz, *C*H$_2$P), 36.5 (d, $^1J_{C,P}$ = 17 Hz, *t*Bu'-*C*), 34.7 (s, cod-*C*H$_2$), 34.3 (s, cod-*C*H$_2$), 33.4 (s, Pyr-3-*C*H$_2$), 30.5 (d, $^2J_{C,P}$ = 4.0 Hz, *t*Bu-*C*H$_3$), 28.9 (br s, *t*Bu'-*C*H$_3$), 28.0 (s, cod-*C*H$_2$), 26.8 (s, cod-*C*H$_2$), 25.2 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (202 MHz, $CDCl_3$): δ = 55.8 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 62.6 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2966w, 2889w, 1553m, 1353s, 1272s, 1115s, 1095m, 884m, 838m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 801 (43), 800 (100, [M + H]$^+$), 799 (28), 798 (59), 392 (11), 360 (16), 244 (10), 243 (47), 165 (22). $[\alpha]_D^{20}$ = + 7.8 (*c* = 0.460, $CHCl_3$). **Elemental analysis**: calc. C 52.72%, H 4.00%, N 0.84%; found: C 52.54%, H 4.02%, N 0.95%.

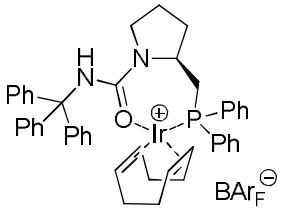
[(η^4-1,5-Cyclooctadiene)-((*S*)-1-{2-[(dicyclohexylphosphino)methyl]pyrrolidin-1-yl}-2,2,2-triphenylethanone)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_A17)



Complex **(*S*)-C_A17** (97%) was prepared according to **general procedure 5** from ligand **(*S*)-L_A17** and [Ir(cod)$_2$]BAr$_F$.[73]

$C_{77}H_{70}NOPIrBF_{24}$ (1715.35 g·mol^{-1}):
m.p. 88-93 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.70 (s, 8 H, Ar$_F$-*o*-*H*), 7.25 (m, 4 H, Ar$_F$-*p*-*H*), 7.26-6.96 (m, 15 H, Ph-*H*), 4.82-4.66 (m, 1 H, cod-C*H*), 4.44-4.29 (m, 1 H, Pyr-2-*H*), 3.76-3.68 (m, 1 H, cod-C*H*), 3.50-3.33 (m, 2 H, cod-C*H*), 3.14-2.98 (m, 1 H, Pyr-5-*H*H'), 2.98-0.76 (m, 37 H, C*H*$_2$P, Pyr-*H*, cod-*H* and Cy/Cy'-*H*) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 35.9 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2945m, 2869m, 1606m, 1481m, 1434m, 1352m, 1272s, 1122s, 1105s, 1054m, 1027m, 999m, 885m, 732m, 703m, 669m cm^{-1}. **MS** (ESI): *m/z* (%) = 852 (100, M$^+$). $[\alpha]_D^{20}$ = − 7.0 (*c* = 0.300, $CHCl_3$).

[(η^4-1,5-Cyclooctadiene)-((*S*)-{2-[(diphenylphosphino)methyl]-*N*-tritylpyrrolidine-1-carboxamide}-2,2,2-triphenylethanone)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl) phenyl]borate ((*S*)-C_{U3}15)

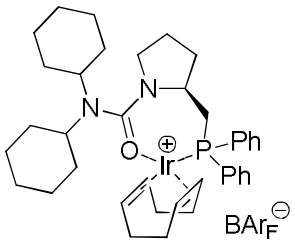


Complex **(*S*)-C_{U3}15** (97%) was prepared according to **general procedure 5** from ligand **(*S*)-L_{U3}15** and [Ir(cod)$_2$]BAr$_F$.[73] [**((*S*)-L$_{U3}$15**)Ir(cod)]PF$_6$ was prepared from **(*S*)-L$_{U3}$15** and [Ir(cod)$_2$]PF$_6$. Crystals suitable for X-ray diffraction were obtained by crystallization from dichloromethane layered with *n*-pentane in an NMR tube.

$C_{77}H_{59}N_2OPIrBF_{24}$ (1718.26 g·mol^{-1}):

m.p. 84-88 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.00-6.97 (m, 37 H, PPh/Ph'-*H*, CPh-*H* and Ar_F-*H*), 5.56 (s, 1 H, N*H*), 4.76-4.67 (m, 1 H, Pyr-2-*H*), 4.47-4.39 (m, 1 H, cod-C*H*), 3.76-3.64 (m, 1 H, cod-C*H*), 3.21-3.13 (m, 1 H, Pyr-5-*H*H'), 3.09-2.93 (m, 2 H, Pyr-5-H*H'* and C*H*H'P), 2.82-2.74 (m, 1 H, cod-*C*H), 2.68-2.53 (m, 2 H, CH*H'*P and cod-*C*H), 2.36-2.09 (m, 3 H, cod-CH_2), 2.08-1.79 (m, 5 H, Pyr-*H* and cod-CH_2), 1.75-1.22 (m, 4 H, cod-CH_2) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 163.7 (s, *C*=O), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 143.6 (s, CPh-*i*-*C*), 135.0 (s, Ar_F-*o*-*C*H), 133.9 (d, $^2J_{C,P}$ = 12 Hz, PPh-*o*-*C*H), 132.8 (d, $^4J_{C,P}$ = 2.3 Hz, PPh-*p*-*C*H), 131.5 (d, $^3J_{C,P}$ = 9.0 Hz, PPh-*m*-*C*H), 131.3 (br d, $^4J_{C,P}$ = 2.2 Hz, PPh'-*p*-*C*H), 130.1 (d, $^1J_{C,P}$ = 50 Hz, PPh-*i*-*C*), 129.7 (d, $^2J_{C,P}$ = 10 Hz, PPh'-*o*-*C*H), 129.6-128.5 (m, Ar_F-*m*-*C* and PPh'-*m*-*C*H), 128.5 (s, CPh-*m*-*C*H), 128.3 (s, CPh-*o*-*C*H), 128.0 (s, CPh-*p*-*C*H), 125.4 (d, $^1J_{C,P}$ = 50 Hz, PPh'-*i*-*C*), 124.7 (q, $^1J_{C,F}$ = 273 Hz, Ar_F-*C*F_3), 117.7-117.5 (m, Ar_F-*p*-*C*H), 99.7 (d, $^2J_{C,P}$ = 12 Hz, cod-*C*H), 99.6 (d, $^2J_{C,P}$ = 13 Hz, cod-*C*H), 72.2 (s, *C*Ph_3), 57.6 (d, $^2J_{C,P}$ = 3.0 Hz, Pyr-2-*C*H), 51.3 (s, cod-*C*H), 50.7 (s, cod-*C*H), 47.4 (s, Pyr-5-*C*H_2), 35.3 (d, $^2J_{C,P}$ = 4.4 Hz, cod-*C*H_2), 34.4 (d, $^1J_{C,P}$ = 31 Hz, *C*H_2P), 32.7 (d, $^2J_{C,P}$ = 12 Hz, Pyr-3-*C*H_2), 31.5 (br d, $^2J_{C,P}$ = 2,5 Hz, cod-*C*H_2), 29.6 (br s, cod-*C*H_2), 26.8 (br s, cod-*C*H_2), 23.5 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 11.2 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 62.6 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3450w, 2959w, 1572m, 1569m, 1486w, 1436w, 1353s, 1272s, 1115s, 1036m, 885m, 839m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 856 (21), 855 (45, $[M + H]^+$), 854 (14), 853 (27), 244 (21), 243 (100), 165 (34). $[\alpha]_D^{20}$ = – 37.7 (*c* = 0.700, $CHCl_3$). **HRMS** (ESI): calc. for $C_{45}H_{47}N_2OIrP$ (M^+): 855.3050; found: 855.3063.

[(η^4-1,5-Cyclooctadiene)-{(*S*)-*N*,*N*-Dicyclohexyl-2-[(diphenylphosphino)methyl] pyrrolidine-1-carboxamide}-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl] borate ((*S*)-C_{U4}5)

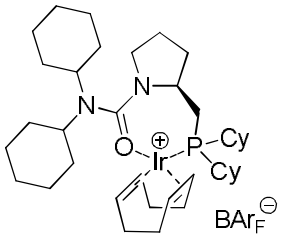


Complex **(*S*)-C_{U4}5** (97%) was prepared according to **general procedure 5** from ligand **(*S*)-L_{U4}5** and $[Ir(cod)_2]BAr_F$.[73]

$C_{70}H_{65}N_2OPIrBF_{24}$ (1640.24 g·mol^{-1}):

m.p. 80-84 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.98-7.89 (m, 2 H, Ph-*o*-*H*), 7.72 (s, 8 H, Ar_F-*o*-*H*), 7.64-7.51 (m, 7 H, ArF-*p*-*H* and Ph/Ph'-*H*), 7.40-7.32 (m, 3 H, Ph/Ph'-*H*), 6.99-6.91 (m, 2 H, Ph-*m*-*H*), 5.32-5.20 (m, 1 H, Pyr-2-*H*), 5.18-5.11 (m, 1 H, cod-C*H*), 5.11-4.97 (m, 1 H, cod-C*H*), 3.47-3.38 (m, 1 H, Pyr-5-*H*H'), 3.33-3.25 (m, 1 H, Pyr-5-H*H'*), 2.96-2.67 (m, 5 H), 2.62-2.42 (m, 3 H), 2.25-1.93 (m, 4 H), 1.86-1.39 (m, 17 H), 1.33-1.04 (m, 3 H), 1.11-0.95 (m, 4 H), 0.73-0.62 (m, 2 H) ppm. **^{13}C{^{1}H} NMR** (126 MHz, CD_2Cl_2): δ = 168.4 (s, *C*=O), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 135.5 (d, $^2J_{C,P}$ = 12 Hz, Ph-*o*-*C*H), 134.9 (s, Ar_F-*o*-*C*H), 134.2 (s, Ph-*p*-*C*H), 131.3 (d, $^2J_{C,P}$ = 10 Hz, Ph'-*o*-*C*H), 130.9 (br d, $^3J_{C,P}$ = 2.6 Hz, Ph-*m*-*C*H), 130.3 (s, Ph'-*p*-*C*H), 130.1-128.3 (m, Ph-*i*-*C*, Ph'-*m*-*C*H and Ar_F-*m*-*C*), 124.4 (br d, Ph'-*i*-*C*), 124.7 (q, $^1J_{C,F}$ = 273 Hz, Ar_F-*C*F_3),117.7-117.4 (m, Ar_F-*p*-*C*H), 97.2 (d, $^2J_{C,P}$ = 10 Hz, cod-*C*H), 96.2 (d, $^2J_{C,P}$ = 13 Hz, cod-*C*H), 59.2 (br d, Pyr-2-*C*H), 58.9 (br s, Cy/Cy'-1-*C*H), 55.1 (s, Pyr-5-*C*H_2), 51.4 (s, cod-*C*H), 49.7 (s, cod-*C*H), 35.9 (br s, cod-*C*H_2), 35.0 (br d, Pyr-3-*C*H_2), 32.6 (s, Cy/Cy'-*C*H_2), 31.1 (br s, cod-*C*H_2), 30.4 (s, Cy/Cy'-*C*H_2), 30.3 (br s, cod-*C*H_2), 26.8 (br s, cod-*C*H_2), 26.3 (s, Cy/Cy'-*C*H_2), 26.2 (s, Cy/Cy'-*C*H_2), 25.4 (s, Pyr-4-*C*H_2), 25.3 (s, Cy/Cy'-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 14.6 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 62.4 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2939m, 2862m, 1733w, 1610w, 1521m, 1452m, 1436m, 1353s, 1271s, 1113s, 1093s, 1000m, 885m, 836m, 742m, 711m, 680s, 669m cm^{-1}. **MS** (ESI): *m/z* (%) = 777 (100, M^+). $[\alpha]_D^{20}$ = + 36.5 (*c* = 0.320, $CHCl_3$).

[(η^4-1,5-Cyclooctadiene)-{(*S*)-*N*,*N*-Dicyclohexyl-2-[(dicyclohexylphosphino)methyl] pyrrolidine-1-carboxamide}-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl] borate ((*S*)-C_{U4}8)



Complex **(*S*)-C_{U4}8** (98%) was prepared according to **general procedure 5** from ligand **(*S*)-L_{U4}8** and [Ir(cod)$_2$]BAr_F.[73]

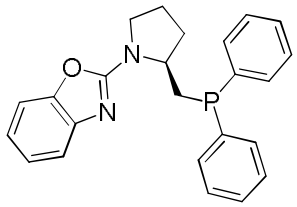
$C_{70}H_{77}N_2OPIrBF_{24}$ (1652.33 g·mol^{-1}):

m.p. 83-87 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.72 (s, 8 H, Ar_F-*o*-*H*), 7.56 (s, 4 H, Ar_F-*p*-*H*), 5.05-4.94 (m, 1 H, cod-C*H*), 4.84-4.76 (m, 1 H, cod-C*H*), 4.49-4.36 (m, 1 H, Pyr-2-*H*), 3.77-3.69 (m, 1 H, cod-C*H*), 3.58-3.48 (m, 1 H, Pyr-5-*H*H'), 3.33-3.26 (m, 1 H, Pyr-5-H*H'*), 3.25-3.09 (m, 3 H, cod-C*H* and Cy-*H*), 2.54-1.07 (m, 56 H) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 165.1 (s, *C*=O), 161.8 (q, $^{1}J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 134.9 (s, Ar_F-*o*-*C*H), 129.3-128.6 (m, Ar_F-*m*-*C*), 124.7 (q, $^{1}J_{C,F}$ = 273 Hz, Ar_F-*C*F_3), 117.7-117.5 (m, Ar_F-*p*-*C*H), 93.2 (m, 2 cod-*C*H), 59.9 (d, $^{2}J_{C,P}$ = 9.0 Hz, Pyr-2-*C*H), 59.0 (br s, NCy/Cy'-1-*C*H), 53.0 (s, Pyr-5-*C*H_2), 51.9 (s, cod-*C*H), 49.2 (s, cod-*C*H), 37.0-36.3 (m, PCy/Cy'-1-*C*H and cod-*C*H_2), 34.5 (d, $^{3}J_{C,P}$ = 10 Hz, Pyr-3-*C*H_2), 33.5 (s, Cy/Cy'-*C*H_2), 30.9-29.4 (m, Cy/Cy'-*C*H_2 and cod-*C*H_2), 28.1 (d, $^{1}J_{C,P}$ = 28 Hz, *C*H_2P), 26.8-25.1 (m, Pyr-4-*C*H_2, Cy/Cy'-*C*H_2 and cod-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (202 MHz, $CDCl_3$): δ = 26.6 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, $CDCl_3$): δ = − 62.6 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2935m, 2858m, 1533m, 1448w, 1353s, 1271s, 1113s, 884m, 839m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 790 (41), 789 (100, $[M + H]^+$), 788 (28), 787 (64), 677 (15), 675 (18), 501 (15), 470 (17), 468 (18), 466 (18), 386 (16), 384 (14), 302 (11), 126 (14), 83 (51), 55 (25). $[\alpha]_D^{20}$ = + 62.3 (*c* = 0.591, $CHCl_3$). **Elemental analysis**: calc. C 50.88%, H 4.70%, N 1.70%; found: C 50.59%, H 4.73%, N 1.81%.

6.5
Proline-Based P,N Ligands: Preparation and Analytical Data

6.5.1
Benzoxazole phosphines (*S*)-L_{Ox} and Precursors

(*S*)-2-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole ((*S*)-L_{Ox}1)

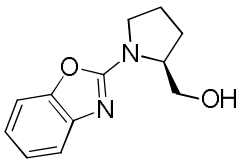


Compound **(*S*)-L_{Ox}1** (82%) was prepared according to **general procedure 6** from **(*S*)-L_C1** and 2-chlorobenzoxazole (**81**).

$C_{24}H_{23}N_2OP$ (386.43 g·mol^{-1}):

m.p. 87-89 °C. $\mathbf{R_f}$ = 0.26 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.68-7.59 (m, 2 H, Ph-*H*), 7.45-7.33 (m, 6 H, BzOx-7-*H* and Ph-*H*), 7.26-7.20 (m, 3 H, Ph-*H*), 7.20-7.10 (m, 2 H, BzOx-4-*H* and BzOx-5-*H*), 6.99 ("t", $^3J_{H,H}$ = 7.7 Hz, 1 H, BzOx-6-*H*), 4.31-4.16 (m, 1 H, Pyr-2-*H*), 3.72-3.56 (m, 2 H, Pyr-5-H_2), 2.86 ("dt", J = 14, 3.0 Hz, 1 H, C*H*H'P), 2.33 ("t", J = 12 Hz, 1 H, CH*H*'P), 2.23-2.05 (m, 3 H, Pyr-3-H_2 and Pyr-4-*H*H'), 2.05-1.91 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 160.5 (s, BzOx-2-*C*), 148.9 (s, BzOx-7a-*C*), 143.4 (br s, BzOx-3a-*C*), 138.6 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 137.7 (d, $^1J_{C,P}$ = 12 Hz, Ph'-*i*-*C*), 133.1 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 129.0 (s, Ph-*p*-*C*H), 128.7 (d, $^3J_{C,P}$ = 7.0 Hz, Ph-*m*-*C*H), 128.6 (s, Ph'-*p*-*C*H), 128.5 (d, $^3J_{C,P}$ = 7.0 Hz, Ph'-*m*-*C*H), 123.9 (s, BzOx-5-*C*H), 120.2 (s, BzOx-6-*C*H), 116.2 (s, BzOx-4-*C*H), 108.6 (s, BzOx-7-*C*H), 57.5 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 48.4 (s, Pyr-5-*C*H_2), 33.7 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.7 (d, $^3J_{C,P}$ = 7.6 Hz, Pyr-3-*C*H_2), 24.1 (br s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 22.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3054w, 2951w, 2875w, 1636s, 1576s, 1458m, 1383m, 1355m, 1243m, 1149w, 1002w, 912m, 794w, 736s, 695s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 386 (4, M^+), 310 (20), 309 (100), 187 (27). $[\alpha]_D^{20}$ = − 85.2 (*c* = 0.520, $CHCl_3$).

(*S*)-[1-(Benzo[*d*]oxazol-2-yl)pyrrolidin-2-yl]methanol ((*S*)-90)



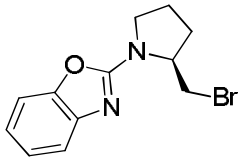
(*S*)-2-{[(*tert*-butyldimethylsilyl)oxy]methyl}pyrrolidine[106] (**(*S*)-87**, 1.00 g, 4.64 mmol, 1.0 eq.) was dissolved in tetrahydrofuran (15 mL) and a 1.6 M solution of *n*-butyllithium (3.30 mL, 5.28 mmol, 1.1 eq.) in hexanes was slowly added at – 78 °C in a acetone/dry ice bath. The resulting solution was then stirred for 30 minutes at – 78 °C and for 1 hour at room temperature. After cooling the solution again to – 78 °C, 2-chlorobenzoxazole (**81**, 700 µL, 6.13 mmol, 1.3 eq.) was added and the reaction mixture was allowed to warm to room temperature over 14 hours. At 0 °C in an ice bath, aqueous saturated $NaHCO_3$ (10 mL) was added drop wise. Ethyl acetate (30 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 x 30 mL). The combined organic layers were washed with brine (40 mL) and dried over $MgSO_4$. The solvents were evaporated under reduced pressure and the crude product, (*S*)-2-(2-{[(*tert*-butyldimethylsilyl)oxy]methyl}pyrrolidin-1-yl)benzo[*d*]oxazole (**(*S*)-88**), was dried *in vacuo*. The residue was then dissolved in tetrahydrofuran (10 mL) and tetrabutylammonium fluoride trihydrate (TBAF·3 H_2O, 2.93 g, 9.29 mmol, 2.0 eq.) was added portion wise, at 0 °C in an ice bath. The resulting mixture was allowed to stir at room temperature for 3 hours. Ethyl acetate (30 mL) and H_2O (50 mL) were added. The resulting layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, washed with brine (70 mL) and dried over $MgSO_4$. The solvents were removed under reduced pressure and the residue was filtered over a plug of silica gel (5 x 5 cm), eluting with ethyl acetate (100%). After evaporation of the solvent the product was purified by column chromatography on silica gel (5 x 15 cm), eluting with cyclohexane/ethyl acetate (1:1 → 3:7). The title compound **(*S*)-90** was obtained as a yellowish semisolid (576 mg, 2.64 mmol, 57%).

$C_{12}H_{14}N_2O_2$ (218.25 g·mol^{-1}):

R_f = 0.11 (SiO_2, cyclohexane/ethyl acetate 7:3). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.31 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, BzOx-7-*H*), 7.24 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, BzOx-4-*H*), 7.15 (“t”, $^3J_{H,H}$ = 7.8 Hz, 1 H, BzOx-6-*H*), 7.00 (“t”, $^3J_{H,H}$ = 7.8 Hz, 1 H, BzOx-5-*H*), 5.99-5.76 (br s, 1 H, O*H*), 4.19-4.08 (m, 1 H, Pyr-2-*H*), 3.86-3.71 (m, 3 H, CH_2O and

Pyr-5-*H*H'), 3.70-3.59 (m, 1 H, Pyr-5-H*H'*), 2.24-2.14 (m, 1 H, Pyr-*H*), 2.09-1.99 (m, 1 H, Pyr-*H*), 1.99-1.89 (m, 1 H, Pyr-*H*), 1.82-1.68 (m, 1 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 162.0 (s, BzOx-2-*C*), 148.9 (s, BzOx-7a-*C*), 142.4 (s, BzOx-3a-*C*), 124.2 (s, BzOx-5-*C*H), 120.7 (s, BzOx-6-*C*H), 116.1 (s, BzOx-4-*C*H), 108.9 (s, BzOx-7-*C*H), 66.6 (s, Pyr-2-*C*H), 63.1 (s, *C*H_2O), 48.8 (s, Pyr-5-*C*H_2), 29.6 (s, Pyr-4-*C*H_2), 24.4 (s, Pyr-3-*C*H_2) ppm. **IR** (neat): $\tilde{\nu}$ = 3270w, 2929w, 2873m, 1631s, 1573s, 1458s, 1386m, 1354m, 1242s, 1168w, 1151w, 1052m, 1003m, 962w, 912m, 793w, 753m, 737s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 218 (20, M^+), 188 (20), 187 (100). $[\alpha]_D^{20}$ = − 70.6 (*c* = 0.720, $CHCl_3$).

(*S*)-2-[2-(Bromomethyl)pyrrolidin-1-yl]benzo[*d*]oxazole ((*S*)-92)



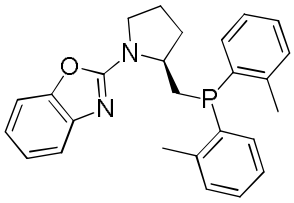
(*S*)-90 (336 mg, 1.54 mmol, 1.0 eq.), tetrabromomethane (765 mg, 2.31 mmol, 1.5 eq.) and triphenylphosphine (605 mg, 2.31 mmol, 1.5 eq.) were mixed in dichloromethane (10 mL) at 0 °C in an ice bath. The resulting mixture was allowed to warm to room temperature overnight. The solvent was evaporated and the crude was purified by column chromatography on silica gel (4 x 17 cm), eluting with cyclohexane/ethyl acetate (8:2). The title compound **(*S*)-92** was obtained as a colorless solid (417 mg, 1.48 mmol, 96%).

$C_{12}H_{13}BrN_2O$ (281.15 g·mol^{-1}):

m.p. 51-54 °C. **R_f** = 0.25 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.38 (d, $^{3}J_{H,H}$ = 8.3 Hz, 1 H, BzOx-4-*H*), 7.28 (d, $^{3}J_{H,H}$ = 7.9 Hz, 1 H, BzOx-7-*H*), 7.17 ("td", $^{3}J_{H,H}$ = 7.7 Hz, $^{4}J_{H,H}$ = 1.0 Hz, 1 H, BzOx-5-*H*), 7.02 ("td", $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1 H, BzOx-6-*H*), 4.39-4.31 (m, 1 H, Pyr-2-*H*), 3.79-3.67 (m, 3 H, Pyr-5-H_2 and C*H*H'Br), 3.61 (dd, $^{2}J_{H,H}$ = 9.9 Hz, $^{3}J_{H,H}$ = 8.3 Hz, 1 H, CH*H'*Br), 2.24-1.95 (m, 4 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 160.5 (s, BzOx-2-*C*), 149.0 (s, BzOx-7a-*C*), 143.3 (s, BzOx-3a-*C*), 124.1 (s, BzOx-5-*C*H), 120.8 (s, BzOx-6-*C*H), 116.5 (s, BzOx-4-*C*H), 109.9 (s, BzOx-7-*C*H), 59.6 (s, Pyr-2-*C*H), 49.0 (s, Pyr-5-*C*H_2), 34.4 (s, *C*H_2Br), 30.2 (s, Pyr-4-*C*H_2), 23.8 (s, Pyr-3-*C*H_2) ppm. **IR** (neat): $\tilde{\nu}$ = 2956w, 2875w, 1630s, 1569s, 1456s, 1435m, 1381m, 1345m, 1328m,

1281m, 1244s, 1224m, 1203m, 1189m, 1137m, 1085w, 1004m, 902m, 824m, 795m, 739s, 644s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 282 (17), 280 (17, M^+), 201 (20), 188 (13), 187 (100). $[\alpha]_D^{20} = -59.1$ (c = 0.981, $CHCl_3$).

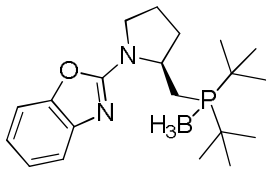
(*S*)-2-{2-[(Di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole ((*S*)-L_{Ox}2)



Product **(*S*)-L_{Ox}2** (83%) was prepared according to **general procedure 7** from bromide **(*S*)-92** and di-*ortho*-tolylphosphine (**94**) and isolated as a colorless semisolid.

$C_{26}H_{27}N_2OP$ (414.48 $g \cdot mol^{-1}$):
R_f = 0.35 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.78-7.73 (m, 1 H, *o*Tol-*H*), 7.38-7.28 (m, 3 H, BzOx-7-*H* and *o*Tol/*o*Tol'-*H*), 7.22-7.10 (m, 6 H, BzOx-4-*H*, BzOx-5-*H* and *o*Tol/*o*Tol'-*H*), 7.08-6.97 (m, 2 H, BzOx-6-*H* and *o*Tol/*o*Tol'-*H*), 4.28-4.16 (m, 1 H, Pyr-2-*H*), 3.77-3.69 (m, 1 H, Pyr-5-*H*H'), 3.68-3.61 (m, 1 H, Pyr-5-H*H'*), 2.87-2.80 (m, 1 H, C*H*H'P), 2.49 (s, 3 H, *o*Tol-CH_3), 2.44 (s, 3 H, *o*Tol'-CH_3), 2.39-1.96 (m, 5 H, CH*H'*P and Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 160.6 (s, BzOx-2-*C*), 148.9 (s, BzOx-7a-*C*), 143.4 (s, BzOx-3a-*C*), 142.6 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 141.8 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol'-2-*C*), 136.6 (d, $^1J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 135.6 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 131.8 (s, *o*Tol-6-*C*H), 131.6 (s, *o*Tol'-6-*C*H), 130.2 (d, $^3J_{C,P}$ = 4.8 Hz, *o*Tol-3-*C*H), 130.1 (d, $^3J_{C,P}$ = 5.0 Hz, *o*Tol'-3-*C*H), 128.8 (s, *o*Tol-4-*C*H), 128.6 (s, *o*Tol'-4-*C*H), 126.3 (s, *o*Tol-5-*C*H), 126.1 (s, *o*Tol'-5-*C*H), 123.9 (s, BzOx-5-*C*H), 120.2 (s, BzOx-6-*C*H), 116.2 (s, BzOx-4-*C*H), 108.6 (s, BzOx-7-*C*H), 57.4 (d, $^2J_{C,P}$ = 23 Hz, 1 H, Pyr-2-*C*H), 48.2 (s, Pyr-5-CH_2), 32.7 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.6 (d, $^3J_{C,P}$ = 7.7 Hz, Pyr-3-CH_2), 24.0 (s, Pyr-4-CH_2), 21.4 (d, $^3J_{C,P}$ = 5.9 Hz, *o*Tol-CH_3), 21.2 (s, *o*Tol'-CH_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): $\delta = -43.2$ (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3054w, 2969w, 2875w, 1636s, 1576s, 1457s, 1381m, 1355m, 1283w, 1243m, 1148w, 1031w, 1003w, 917m, 739s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 414 (5, M^+), 324 (21), 323 (100), 187 (27). $[\alpha]_D^{20} = -87.1$ (c = 0.421, $CHCl_3$).

(*S*)-2-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole borane adduct ((*S*)-L_{Ox}3·BH_3)

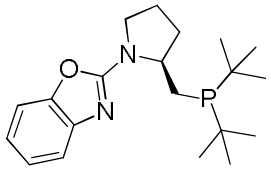


Compound **(*S*)-L_{Ox}3·BH_3** (89%) was prepared according to **general procedure 7** from **(*S*)-92** and di-*tert*-butylphosphine borane adduct (**50·BH_3**).

$C_{20}H_{34}BN_2OP$ (360.28 g·mol^{-1}):

m.p. 52-56 °C. **R_f** = 0.36 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, BzOx-7-*H*), 7.20 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, BzOx-4-*H*), 7.17-7.10 (m, 1 H, BzOx-5-*H*), 7.03-6.94 (m, 1 H, BzOx-6-*H*), 4.44-4.32 (m, 1 H, Pyr-2-*H*), 3.77-3.67 (m, 1 H, Pyr-5-*H*H'), 3.67-3.56 (m, 1 H, Pyr-5-H*H'*), 2.64 ("t", *J* = 14 Hz, 1 H, C*H*H'P), 2.37-2.26 (m, 1 H, Pyr-3-*H*H'), 2.26-2.24 (m, 1 H, Pyr-3-H*H'*), 2.06-1.94 (m, 2 H, Pyr-4-H_2), 1.63-1.51 (m, 1 H, CH*H'*P), 1.45 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.25 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu'-*H*), 0.93-0.08 (br m, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 160.5 (s, BzOx-2-*C*), 148.9 (s, BzOx-7a-*C*), 143.6 (s, BzOx-3a-*C*), 124.0 (s, BzOx-5-*C*H), 120.4 (s, BzOx-6-*C*H), 116.3 (s, BzOx-4-*C*H), 108.5 (s, BzOx-7-*C*H), 57.3 (d, $^2J_{C,P}$ = 6.2 Hz, Pyr-2-*C*H), 48.1 (s, Pyr-5-*C*H_2), 33.4 (d, $^1J_{C,P}$ = 29 Hz, *t*Bu-*C*), 32.8 (s, Pyr-3-*C*H), 32.1 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu'-*C*), 28.2 (br s, *t*Bu-*C*H_3), 27.9 (br s, *t*Bu'-*C*H_3), 23.6 (s, Pyr-4-*C*H_2), 21.9 (d, $^1J_{C,P}$ = 23 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.8 (br d, $^1J_{P,B}$ = 68 Hz) ppm. **IR** (neat): $\tilde{\nu}$ = 2953m, 2874m, 1637s, 1578s, 1458m, 1382m, 1373m, 1284w, 1244m, 1147w, 1072m, 1023w, 919w, 813m, 740s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 360 (14), 359 (22, [M – H]$^+$), 343 (32), 303 (33), 290 (17), 289 (100), 247 (27), 245 (17), 233 (26), 232 (15), 213 (14), 201 (22), 187 (21), 178 (10), 57 (28). $[\alpha]_D^{20}$ = − 68.4 (*c* = 0.252, $CHCl_3$). **Elemental analysis**: calc. C 66.67%, H 9.51%, N 7.78%; found: C 66.39%, H 9.52%, N 7.30%.

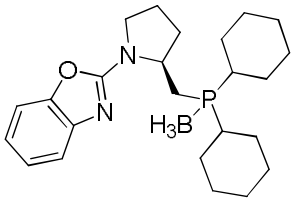
(*S*)-2-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole ((*S*)-L_{Ox}3)



Product **(*S*)-L_{Ox}3** was prepared according to **general procedure 3** from **(*S*)-L_{Ox}3·BH_3**.

$C_{20}H_{31}N_2OP$ (346.45 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ = 21.2 (s) ppm.

(*S*)-2-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole borane adduct ((*S*)-L_{Ox}4·BH_3)

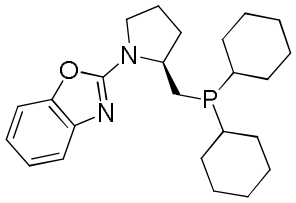


Compound **(*S*)-L_{Ox}4·BH_3** (78%) was prepared according to **general procedure 7** from **(*S*)-92** and dicyclohexylphosphine borane adduct (**51·BH_3**).

$C_{24}H_{38}BN_2OP$ (412.36 g·mol^{-1}):
m.p. 159-162 °C. **R_f** = 0.16 (SiO_2, cyclohexane/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, BzOx-7-*H*), 7.21 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, BzOx-4-*H*), 7.15 ("td", $^3J_{H,H}$ = 7.7 Hz, $^4J_{H,H}$ = 1.0 Hz, 1 H, BzOx-5-*H*), 7.00 ("td", $^3J_{H,H}$ = 7.7 Hz, $^4J_{H,H}$ = 1.1 Hz, 1 H, BzOx-6-*H*), 4.37-4.25 (m, 1 H, Pyr-2-*H*), 3.75-3.69 (m, 1 H, Pyr-5-*H*H'), 3.63-3.56 (m, 1 H, Pyr-5-H*H'*), 2.41 ("t", *J* =15 Hz, 1 H, C*H*H'P), 2.32-1.17 (m, 27 H, CH*H'*P, Pyr-*H* and Cy/Cy'-*H*), 0.82-0.05 (br q, 3 H, BH_3) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 160.4 (s, BzOx-2-*C*), 149.0 (s, BzOx-7a-*C*), 143.5 (s, BzOx-3a-*C*), 124.1 (s, BzOx-5-*C*H), 120.4 (s, BzOx-6-*C*H), 116.3 (s, BzOx-4-*C*H), 108.6 (s, BzOx-7-*C*H), 56.4 (d, $^2J_{C,P}$ = 6.3 Hz, 1 H, Pyr-2-*C*H), 48.1 (s, Pyr-5-*C*H_2), 33.1 (d, $^1J_{C,P}$ = 33 Hz, 1 H, Cy-1-*C*H), 32.8 (s, Pyr-3-*C*H_2), 31.9 (d, $^1J_{C,P}$ = 34 Hz, 1 H, Cy'-1-*C*H), 27.3-26.0 (m, Cy/Cy'-*C*H_2), 23.9 (d, $^1J_{C,P}$ = 26 Hz, *C*H_2P), 23.7 (s, Pyr-4-*C*H_2) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 21.0 (br d) ppm. **IR** (neat): $\tilde{\nu}$ = 3288m, 2926m, 2849m, 1635s, 1627s, 1593m, 1523s, 1516s, 1493m, 1381m, 1355m, 1346m, 1331w, 1240m, 1217w, 1192w, 1174m, 1068w, 951w, 916w,

8816w, 737s, 692s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 412 (17, M^+), 411 (29, $[M - H]^+$), 396 (13), 395 (50), 394 (12), 329 (11), 316 (20), 315 (100), 313 (25), 292 (10), 247 (11), 233 (13), 215 (17), 213 (17), 201 (12), 187 (13). $[\alpha]_D^{20} = -60.7$ (*c* = 0.560, $CHCl_3$).

(*S*)-2-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole ((*S*)-L_{Ox}4)



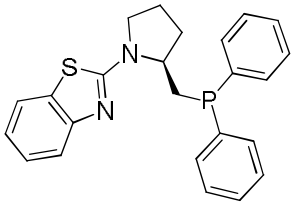
Product **(*S*)-L_{Ox}4** was prepared according to **general procedure 3** from **(*S*)-$L_{Ox}4 \cdot BH_3$**.

$C_{24}H_{35}N_2OP$ (398.52 $g \cdot mol^{-1}$):

$^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): $\delta = -11.2$ (s) ppm.

6.5.2
Benzothiazole phosphines (*S*)-L_{Th} and Precursors

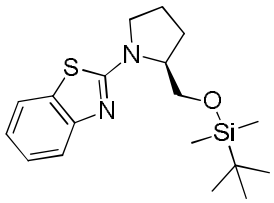
(*S*)-2-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole ((*S*)-L_{Th}1)



Compound **(*S*)-L_{Th}1** (75%) was prepared according to **general procedure 6** from **(*S*)-L_C1** and 2-chlorobenzothiazole (**82**).

$C_{24}H_{23}N_2PS$ (402.49 g·mol^{-1}):
m.p. 101-105 °C. $\mathbf{R_f}$ = 0.23 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.70 (m, 2 H, Ph-*o*-*H*), 7.57 (d, $^2J_{H,H}$ = 8.0 Hz, 1 H, BzTh-4-*H*), 7.54 (d, $^2J_{H,H}$ = 7.8 Hz, 1 H, BzTh-7-*H*), 7.45-7.34 (m, 5 H, Ph/Ph'-*H*), 7.28 (m, 1 H, BzTh-5-*H*), 7.24 (m, 3 H, Ph/Ph'-*H*), 7.03 (m, 1 H, BzTh-6-*H*), 4.02-4.08 (m, 1 H, Pyr-2-*H*), 3.62-3.44 (m, 2 H, Pyr-5-H_2), 2.99 (br d, $^2J_{H,P}$ = 14 Hz, 1 H, C*H*H'P), 2.24-2.09 (m, 4 H, CH*H*'P and Pyr-3-H_2 and Pyr-4-*H*H'), 2.02 (m, 1 H, Pyr-4-H*H'*) ppm. **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ = 164.6 (s, BzTh-2-*C*), 153.1 (s, BzTh-3a-*C*), 138.6 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 137.4 (d, $^1J_{C,P}$ = 12 Hz, Ph'-*i*-*C*), 133.4 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 130.7 (s, BzTh-7a-*C*), 128.9-128.5 (m, Ph/Ph'-*C*H), 125.8 (s, BzTh-5-*C*H), 120.8 (d, BzTh-6-*C*H), 120.7 (BzTh-7-*C*H), 118.8 (s, BzTh-4-*C*H), 59.3 (d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 50.2 (s, Pyr-5-*C*H_2), 32.3 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.4 (d, $^3J_{C,P}$ = 7.5 Hz, Pyr-3-*C*H_2), 23.9 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (202 MHz, $CDCl_3$): δ = − 21.6 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3066w, 2964w, 2918w, 2867w, 1595m, 1564m, 1533s, 1481m, 1452m, 1441s, 1431m, 1363m, 1313m, 1269m, 1254w, 1186w, 1124m, 1066m, 1018m, 914m, 852m, 734s cm^{-1}. **MS** (ESI): *m/z* (%) = 403 (100, $[M + H]^+$). Partial oxidation was observed while measuring. $[\alpha]_D^{20}$ = − 61.6 (*c* = 0.530, $CHCl_3$).

(*S*)-2-(2-{[(*tert*-Butyldimethylsilyl)oxy]methyl}pyrrolidin-1-yl)benzo[*d*]thiazole ((*S*)-89)

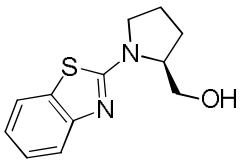


(*S*)-2-{[(*tert*-butyldimethylsilyl)oxy]methyl}pyrrolidine[106] (**(*S*)-87**, 750 mg, 3.48 mmol, 1.0 eq.) was dissolved in tetrahydrofuran (5 mL) and a 1.6 M solution of *n*-butyllithium (2.50 mL, 4.00 mmol, 1.2 eq.) in hexanes was slowly added at – 78 °C in a acetone/dry ice bath. The resulting solution was then stirred for 30 minutes at – 78 °C and for 1 hour at room temperature. After cooling the solution again to – 78 °C, 2-chlorobenzothiazole (**82**, 540 µL, 4.15 mmol, 1.2 eq.) was added and the reaction mixture was allowed to warm to room temperature over 14 hours. At 0 °C in an ice bath, aqueous saturated $NaHCO_3$ (10 mL) was added drop wise. Ethyl acetate (20 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic extracts were washed with brine (30 mL) and dried over $MgSO_4$. The solvents were evaporated under reduced pressure and the crude was purified by column chromatography on silica gel (4 x 15 cm), eluting with cyclohexane/ethyl acetate (19:1). The title compound **(*S*)-89** was obtained as a colorless semisolid (837 mg, 2.64 mmol, 69%).

$C_{18}H_{28}N_2OSSi$ (348.58 g·mol^{-1}):

R_f = 0.31 (SiO_2, cyclohexane/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.62-7.53 (m, 2 H, BzTh-4-*H* and BzTh-7-*H*), 7.31-7.25 (m, 1 H, BzTh-5-*H*), 7.09-7.00 (m, 1 H, BzTh-6-*H*), 4.12-4.00 (m, 1 H, Pyr-2-*H*), 3.87-3.78 (m, 2 H, C*H*$_2$O), 3.66-3.57 (m, 1 H, Pyr-5-*H*H'), 3.57-3.47 (m, 1 H, Pyr-5-H*H'*), 2.22-1.93 (m, 4 H, Pyr-*H*), 0.88 (s, 9 H, *t*Bu-*H*), 0.05 (s, 3 H, C*H*$_3$), 0.00 (s, 3 H, C*H*$_3$') ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 165.4 (s, BzTh-2-*C*), 153.4 (s, BzTh-3a-*C*), 130.9 (s, BzTh-7a-*C*), 125.9 (s, BzTh-5-*C*H), 120.9 (s, BzTh-6-*C*H), 120.7 (s, BzTh-7-*C*H), 118.9 (s, BzTh-4-*C*H), 62.9 (s, *C*H$_2$O), 62.7 (s, Pyr-2-*C*H), 50.9 (s, Pyr-5-*C*H$_2$), 28.6 (s, Pyr-4-*C*H$_2$), 26.1 (s, *t*Bu-*C*H$_3$), 24.0 (s, Pyr-3-*C*H$_2$), 18.4 (s, *t*Bu-*C*), − 5.2 (2 s, *C*H$_3$/*C*H$_3$') ppm. **IR** (neat): $\tilde{\nu}$ = 2953m, 2929m, 2856m, 1597m, 1535s, 1445m, 1362m, 1277m, 1252m, 1096m, 1016w, 835s, 776m, 750s, 724m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 348 (11, M$^+$), 291 (37), 216 (12), 204 (14), 203 (100). $[\alpha]_D^{20}$ = − 100 (*c* = 0.100, $CHCl_3$).

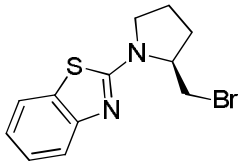
(*S*)-[1-(Benzo[*d*]thiazol-2-yl)pyrrolidin-2-yl]methanol ((*S*)-91)



(*S*)-89 (331 mg, 949 µmol, 1.0 eq.) was dissolved in tetrahydrofuran (7 mL) and tetrabutylammonium fluoride trihydrate (TBAF·3 H_2O, 599 mg, 1.90 mmol, 2.0 eq.) was added at 0 °C in an ice bath. The resulting mixture was allowed to stir at room temperature for 3 hours. Ethyl acetate (10 mL) and H_2O (20 mL) were added. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The organic layers were combined, washed with brine (15 mL) and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel (4 x 10 cm), eluting with cyclohexane/ethyl acetate (1:1), to afford **(*S*)-91** (199 mg, 849 µmol, 89%) as a yellowish semisolid.

$C_{12}H_{14}N_2OS$ (234.32 $g \cdot mol^{-1}$):
R_f = 0.24 (SiO_2, cyclohexane/ethyl acetate 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.60 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, BzTh-4-*H*), 7.54 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, BzTh-7-*H*), 7.31 ("t", $^3J_{H,H}$ = 7.7 Hz, 1 H, BzTh-5-*H*), 7.09 ("t", $^3J_{H,H}$ = 7.7 Hz, 1 H, BzTh-6-*H*), 6.65-6.45 (br s, 1 H, O*H*), 4.30-4.20 (m, 1 H, Pyr-2-*H*), 3.86-3.71 (m, 2 H, CH_2O), 3.60-3.51 (m, 1 H, Pyr-5-*H*H'), 3.50-3.40 (m, 1 H, Pyr-5-H*H'*), 2.27-2.16 (m, 1 H, Pyr-*H*), 2.13-2.193 (m, 2 H, Pyr-*H*), 1.83-1.70 (m, 1 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 167.2 (s, BzTh-2-*C*), 151.7 (s, BzTh-3a-*C*), 130.2 (s, BzTh-7a-*C*), 130.2 (BzTh-5-*C*H), 126.1 (s, BzTh-6-*C*H), 120.7 (s, BzTh-7-*C*H), 118.6 (s, BzTh-4-*C*H), 66.8 (s, Pyr-2-*C*H), 64.8 (s, *C*H_2O), 51.8 (s, Pyr-5-*C*H_2), 29.8 (s, Pyr-4-*C*H_2), 21.0 (s, Pyr-3-*C*H_2) ppm. **IR** (neat): $\tilde{\nu}$ = 3265m, 2906m, 2869m, 1594m, 1564m, 1528s, 1473w, 1442s, 1359s, 1314m, 1274m, 1253m, 1238m, 1185w, 1153w, 1124w, 1067w, 1047m, 1016m, 925w, 902w, 848w, 749s, 724s, 684w cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 234 (20, M^+), 204 (21), 203 (100). $[\alpha]_D^{20}$ = − 104 (*c* = 0.989, $CHCl_3$).

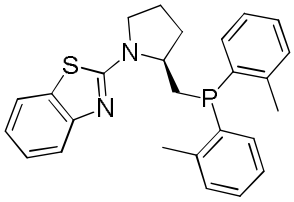
(*S*)-2-[2-(Bromomethyl)pyrrolidin-1-yl]benzo[*d*]thiazole ((*S*)-93)



(*S*)-91 (321 mg, 1.37 mmol, 1.0 eq.), tetrabromomethane (683 mg, 2.06 mmol, 1.5 eq.) and triphenylphosphine (539 mg, 2.05 mmol, 1.5 eq.) were mixed in dichloromethane (8 mL) at 0 °C in an ice bath. The resulting mixture was allowed to warm to room temperature overnight. The solvent was evaporated and the crude was purified by column chromatography on silica gel (4 x 17 cm), eluting with cyclohexane/ethyl acetate (8:2). The title compound **(*S*)-93** was obtained as a colorless solid (180 mg, 606 μmol, 44%).

$C_{12}H_{13}BrN_2S$ (297.21 g·mol^{-1}):
m.p. 130-133 °C. $\mathbf{R_f}$ = 0.47 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.53 ("t", $^3J_{H,H}$ = 7.4 Hz, 2 H, BzTh-*H*), 7.27-7.16 (m, 1 H, BzTh-*H*), 7.00 ("t", $^3J_{H,H}$ = 7.4 Hz, 1 H, BzTh-*H*), 4.38-4.25 (m, 1 H, Pyr-2-*H*), 5.76 (d, *J* = 9.8 Hz, 1 H, C*H*H'Br), 3.62-3.52 (m, 2 H, CH*H'*Br and Pyr-5-*H*H'), 3.47-3.38 (m, 1 H, Pyr-5-H*H'*), 2.20-1.98 (m, 4 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 164.9 (s, BzTh-2-*C*), 153.0 (s, BzTh-3a-*C*), 130.8 (s, BzTh-7a-*C*), 126.1 (s, BzTh-5-*C*H), 121.3 (s, BzTh-6-*C*H), 120.8 (s, BzTh-7-*C*H), 119.2 (s, BzTh-4-*C*H), 61.3 (s, Pyr-2-*C*H), 51.2 (s, Pyr-5-*C*H_2), 34.0 (s, *C*H_2Br), 30.1 (s, Pyr-3-*C*H_2), 23.8 (s, Pyr-4-*C*H_2) ppm. **IR** (neat): $\tilde{\nu}$ = 3439w, 2959w, 2872w, 1594m, 1558m, 1530s, 1473m, 1442m, 1418m, 1358m, 1325m, 1269m, 1246m, 1120m, 1065w, 1017w, 912w, 880w, 751s, 727s, 684m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 298 (17), 296 (17, M^+), 217 (30), 216 (18), 204 (13), 203 (100). $[\alpha]_D^{20}$ = − 113 (*c* = 0.123, $CHCl_3$).

(*S*)-2-{2-[(Di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole ((*S*)-L_{Th}2)

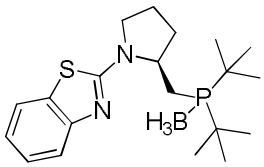


Compound **(*S*)-L_{Th}2** (59%) was prepared according to **general procedure 7** from bromide **(*S*)-93** and di-*ortho*-tolylphosphine (**94**).

$C_{26}H_{27}N_2PS$ (430.54 g·mol^{-1}):

m.p. 114-118 °C. **R_f** = 0.47 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.99-7.91 (m, 1 H, *o*Tol-6-*H*), 7.62 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, BzTh-7-*H*), 7.57 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, BzTh-4-*H*), 7.40 ("t", *J* = 7.2 Hz, 1 H, *o*Tol-5-*H*), 7.36-7.29 (m, 2 H, *o*Tol-4-*H* and BzTh-6-*H*), 7.24-7.20 (m, 1 H, *o*Tol-3-*H*), 7.20-7.14 (m, 3 H, *o*Tol'-3/4/6-*H*), 7.10-7.07 (m, 1 H, *o*Tol'-5-*H*), 7.07-7.03 (m, 1 H, BzTh-5-*H*), 4.23-4.09 (m, 1 H, Pyr-2-*H*), 3.67-3.60 (m, 1 H, Pyr-5-*H*H'), 3.56-3.47 (m, 1 H, Pyr-5-H*H'*), 3.04-2.95 (m, 1 H, C*H*H'P), 2.49 (s, 3 H, *o*Tol-H_3), 2.46 (s, 3 H, *o*Tol'-H_3), 2.31-2.24 (m, 1 H, Pyr-3-*H*H'), 2.22-2.13 (m, 2 H, Pyr-3-H*H'* and Pyr-4-*H*H'), 2.10-2.01 (m, 1 H, Pyr-4-H*H'*), 1.99-1.91 (m, 1 H, CH*H'*P) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 164.7 (s, BzTh-2-*C*), 153.3 (s, BzTh-7a-*C*), 142. (d, $^2J_{C,P}$ = 26 Hz, *o*Tol-2-*C*), 141.7 (d, $^2J_{C,P}$ = 26 Hz, *o*Tol'-2-*C*), 137.0 (d, $^1J_{C,P}$ = 12 Hz, *o*Tol-1-*C*), 135.6 (d, $^1J_{C,P}$ = 13 Hz, *o*Tol'-1-*C*), 132.5 (s, *o*Tol-6-*C*H), 131.6 (s, *o*Tol'-6-*C*H), 131.0 (s, BzTh-3a-*C*), 130.2-130.1 (m, *o*Tol/*o*Tol'-3-*C*H), 128.8 (s, *o*Tol-4-*C*H), 128.6 (s, *o*Tol'4-*C*H), 126.4 (s, *o*Tol-5-*C*H), 126.2 (s, *o*Tol'-5-*C*H), 125.9 (s, BzTh-6-*C*H), 120.8 (s, BzTh-5-*C*H), 120.7 (s, BzTh-4-*C*H), 118.9 (s, BzTh-7-*C*H), 59.4 (d, $^2J_{C,P}$ = 23 Hz, Pyr-2-*C*H), 50.1 (s, Pyr-5-*C*H_2), 31.4 (d, $^3J_{C,P}$ = 7.9 Hz, Pyr-3-*C*H_2), 31.2 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 24.0 (s, Pyr-4-*C*H_2), 21.4 (d, $^3J_{C,P}$ = 12 Hz, *o*Tol-*C*H_3), 21.3 (d, $^3J_{C,P}$ = 12 Hz, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 42.5 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3055w, 2966w, 2930w, 2874w, 1593m, 1560m, 1531s, 1444s, 1359m, 1318m, 1272m, 1254m, 1184w, 1141w, 1065w, 1016m, 925m, 909m, 847m, 754s, 748s, 725m, 680m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 430 (6, M^+), 340 (22), 339 (100), 267 (13), 217 (13), 215 (11), 203 (61). $[\alpha]_D^{20}$ = − 80.7 (*c* = 0.851, $CHCl_3$).

(*S*)-2-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole borane adduct ((*S*)-L_{Th}3·BH_3)

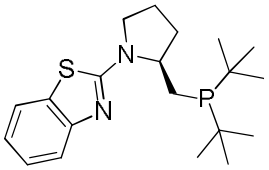


Compound **(*S*)-L_{Th}3·BH_3** (81%) was prepared according to **general procedure 7** from **(*S*)-93** and di-*tert*-butylphosphine borane adduct (**50·BH_3**).

$C_{20}H_{34}BN_2PS$ (376.35 g·mol^{-1}):

m.p. 171-176 °C. $\mathbf{R_f}$ = 0.54 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.61 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, BzTh-7-*H*), 7.48 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, BzTh-4-*H*), 7.31-7.22 (m, 1 H, BzTh-6-*H*), 7.05 ("t", $^1J_{H,H}$ = 7.4 Hz, 1 H, BzTh-5-*H*), 4.52-4.39 (m, 1 H, Pyr-2-*H*), 3.60-3.47 (m, 1 H, Pyr-5-*H*H'), 3.46-3.33 (m, 1 H, Pyr-5-H*H'*), 3.06-2.91 (m, 1 H, C*HH'*P), 2.41-2.19 (m, 2 H, Pyr-*H*), 2.13-1.97 (m, 2 H, Pyr-*H*), 1.62-1.37 (m, 1 H, CH*H'*P), 1.52 (d, $^3J_{H,P}$ = 13 Hz, 9 H, *t*Bu-*H*), 1.25 (d, $^3J_{H,P}$ = 12 Hz, 9 H, *t*Bu'-*H*), 0.93-0.12 (br q, 3 H, BH_3) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 164.5 (s, BzTh-2-*C*), 153.4 (s, BzTh-3a-*C*), 131.0 (s, BzTh-7a-*C*), 126.0 (s, BzTh-6-*C*H), 120.9 (s, BzTh-5-*C*H), 120.9 (s, BzTh-7-*C*H), 118.8 (s, BzTh-4-*C*H), 59.3 (d, $^2J_{C,P}$ = 5.7 Hz, Pyr-2-*C*H), 50.5 (s, Pyr-5-*C*H_2), 33.7 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu-*C*), 32.7 (s, Pyr-3-*C*H_2), 32.2 (d, $^1J_{C,P}$ = 27 Hz, *t*Bu'-*C*), 28.4 (br s, *t*Bu-*C*H_3), 28.0 (br s, *t*Bu'-*C*H_3), 23.9 (s, Pyr-4-*C*H_2), 20.7 (d, $^1J_{C,P}$ = 23 Hz, *C*H_2P) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = 39.7 (br d) ppm. **IR** (neat): $\tilde{\nu}$ = 2948m, 2906m, 2871m, 1597m, 1538s, 1444s, 1393w, 1354m, 1316w, 1274m, 1184m, 1147m, 1123m, 1070s, 1019m, 921m, 815m, 753s, 678m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 376 (24), 375 (63, $[M - H]^+$), 374 (14), 343 (12), 320 (12), 319 (60), 318 (14), 306 (18), 305 (100), 263 (21), 261 (13), 249 (30), 248 (15), 231 (15), 229 (17), 217 (20), 215 (13), 203 (33), 57 (24). $[\alpha]_D^{20}$ = − 120 (*c* = 0.210, $CHCl_3$).

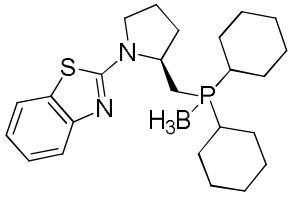
(*S*)-2-{2-[(Di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole ((*S*)-L_{Th}3)



Product **(*S*)-L_{Th}3** was prepared according to **general procedure 3** from **(*S*)-L_{Th}3·BH_3**.

$C_{20}H_{31}N_2PS$ (362.51 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 20.8 (s) ppm.

(*S*)-2-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole borane adduct ((*S*)-L_{Th}4·BH_3)

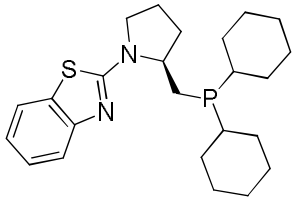


Compound **(*S*)-L_{Th}4·BH_3** (66%) was prepared according to **general procedure 7** from **(*S*)-93** and dicyclohexylphosphine borane adduct (**51·BH_3**).

$C_{24}H_{38}BN_2PS$ (428.42 g·mol^{-1}):
m.p. 120-123 °C. **R_f** = 0.40 (SiO_2, cyclohexane/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.61 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, BzTh-7-*H*), 7.50 (d, $^3J_{H,H}$ = 7.3 Hz, 1 H, BzTh-4-*H*), 7.29 ("t", $^3J_{H,H}$ = 7.8 Hz, 1 H, BzTh-6-*H*), 7.06 ("t", $^3J_{H,H}$ = 7.5 Hz, 1 H, BzTh-5-*H*), 4.46-4.33 (m, 1 H, Pyr-2-*H*), 3.61-3.48 (m, 1 H, Pyr-5-*H*H'), 3.48-3.34 (m, 1 H, Pyr-5-H*H'*), 2.72-2.58 (m, 1 H, C*H*H'P), 2.33-1.11 (m, 27 H, CH*H'*P, Pyr-*H* and Cy/Cy'-*H*), 0.79-0.10 (br q, 3 H, BH_3) ppm. **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ = 164.5 (s, BzTh-2-*C*), 153.4 (s, BzTh-3a-*C*), 131.0 (s, BzTh-7a-*C*), 126.1 (s, BzTh-6-*C*H), 121.0 (s, BzTh-5-*C*H), 120.9 (s, BzTh-7-*C*H), 118.8 (s, BzTh-4-*C*H), 58.1 (br s, Pyr-2-*C*H), 50.4 (s, Pyr-5-*C*H_2), 33.2 (d, $^1J_{C,P}$ = 32 Hz, Cy-1-*C*H), 32.6 (s, Pyr-3-*C*H_2), 32.0 (d, $^1J_{C,P}$ = 33 Hz, Cy'-1-*C*H), 27.4-25.9 (m, Cy/Cy'-*C*H_2), 23.8 (s, Pyr-4-*C*H_2), 22.8 (d, $^1J_{C,P}$ = 27 Hz, *C*H_2P) ppm. **$^{31}P\{^1H\}$ NMR** (162 MHz, $CDCl_3$): δ = 21.5 (br) ppm. **IR** (neat): $\tilde{\nu}$ = 2922m, 2915m, 2849m, 2369m, 1595m, 1560w, 1536s, 1442s, 1361m, 1318m, 1272m, 1252m, 1180w, 1125m, 1067m, 1016m, 1006m, 931m, 858m, 801m, 754s, 726s, 6778m cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 428 (26), 427 (85,

$[M - H]^+$), 426 (19), 395 (17), 345 (14), 332 (21), 331 (100), 292 (12), 249 (11), 231 (20), 217 (13), 203 (18). $[\alpha]_D^{20} = -53.8$ (c = 0.131, $CHCl_3$).

(*S*)-2-{2-[(Dicyclohexylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole ((*S*)-L_{Th}4)

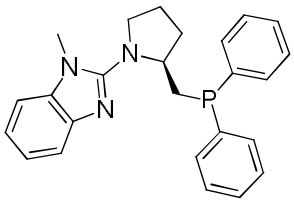


Product **(*S*)-L_{Th}4** was prepared according to **general procedure 3** from **(*S*)-L_{Th}4·BH_3**.

$C_{24}H_{35}N_2PS$ (414.59 g·mol^{-1}):
$^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): $\delta = -10.9$ (s) ppm.

6.5.3
Benzimidazole phosphines (*S*)-L_{Im}

(*S*)-2-{2-[(Diphenylphosphino)methyl]pyrrolidin-1-yl}-1-methyl-1*H*-benzo[*d*]imidazole ((*S*)-L_{Im}1)



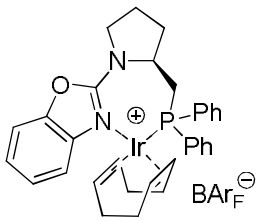
Compound **(*S*)-L_{Im}1** (83%) was prepared according to **general procedure 6** from **(*S*)-L_C1** and 2-chlorobenzimidazole (**83**).[105]

$C_{25}H_{26}N_3P$ (399.47 g·mol^{-1}):
R_f = 0.17 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.54 (d, $^3J_{H,H}$ = 7.7 Hz, 1 H, BzIm-4-*H*), 7.46-7.38 (m, 2 H, Ph/Ph'-*H*), 7.33-7.23 (m, 7 H, Ph/Ph'-*H*), 7.17-7.06 (m, 2 H, Ph/Ph'-*H* and BzIm-*H*), 7.02-6.92 (m, 2 H, BzIm-*H*), 4.61-4.48 (m, 1 H, Pyr-2-*H*), 3.75-3.66 (m, 1 H, Pyr-5-*H*H'), 3.49 (s, 3 H, NCH_3), 3.34-3.26 (m, 1 H, Pyr-5-H*H'*), 2.82-2.71 (m, 1 H, C*H*H'P), 2.38 (br d, $^2J_{H,P}$ = 14 Hz, 1 H, CH*H'*P), 2.30-2.12 (m, 2 H, Pyr-*H*), 2.09-1.98 (m, 1 H, Pyr-*H*), 1.96-1.84 (m, 1 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 160.0 (s, BzIm-2-*C*), 143.1 (s, BzIm-3a-*C*), 138.6 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 137.5 (d, $^1J_{C,P}$ = 12 Hz, Ph'-*i*-*C*), 133.9 (s, BzIm-7a-*C*), 133.2 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 129.0-128.5 (m, Ph/Ph'-*C*H), 122.9 (s, BzIm-*C*H), 121.0 (s, BzIm-*C*H), 118.4 (s, BzIm-4-*C*H), 109.7 (s, BzIm-7-*C*H), 63.3 (d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 52.2 (s, Pyr-5-*C*H_2), 35.1 (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 33.8 (s, *C*H_3), 31.5 (d, $^3J_{C,P}$ = 7.7 Hz, Pyr-3-*C*H_2), 28.8 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = − 23.2 (s) ppm.

6.6

Proline-Based P,N Ligand/Iridium Complexes: Preparation and Analytical Data

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(diphenylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Ox}1)



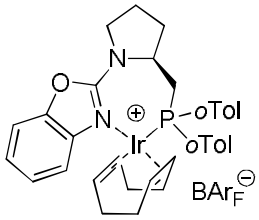
Complex **(*S*)-C_{Ox}1** (89%) was prepared according to **general procedure 8** from ligand **(*S*)-L_{Ox}1** and $[Ir(cod)Cl]_2$.

$C_{64}H_{47}N_2OPIrBF_{24}$ (1550.05 g·mol^{-1}):

m.p. 131-133 °C. **^{1}H NMR** (500 MHz, CD_2Cl_2): δ = 7.76 (br s, 9 H, BzOx-4-*H* and Ar_F-*o*-*H*), 7.58 (br s, 4 H, Ar_F-*p*-*H*), 7.50-7.44 (m, 2 H, Ph-*o*-*H*), 7.44-7.38 (m, 4 H, BzOx-5-*H* and Ph/Ph'-*H*), 7.32-7.27 (m, 1 H, Ph/Ph'-*p*-*H*), 7.23-7.11 (m, 6 H, BzOx-6/7-*H* and Ph/Ph'-*H*), 5.87-5.77 (m, 1 H, Pyr-2-*H*), 5.13-5.06 (m, 1 H, cod-C*H*), 4.97-4.88 (m, 1 H, cod-C*H*), 3.96-3.88 (m, 1 H, cod-C*H*), 3.74-3.65 (m, 1 H, Pyr-5-*H*H'), 3.65-3.56 (m, 1 H, Pyr-5-H*H'*), 3.31 (ddd, *J* = 15, 10, 2.2 Hz, 1 H, C*H*H'P), 3.10-2.98 (m, 2 H, CH*H'*P and cod-C*H*), 2.71-2.56 (m, 2 H, Pyr-3-*H*H' and cod-*H*), 2.44-2.36 (m, 1 H, cod-*H*), 2.33-2.08 (m, 7 H, Pyr-4-H_2, Pyr-3-H*H'* and cod-*H*), 1.75-1.65 (m, 1 H, cod-*H*), 1.65-1.56 (m, 1 H, cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 161.9 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 158.9 (s, BzOx-2-*C*), 147.6 (s, BzOx-7a-*C*), 138.7 (s, BzOx-3a-*C*), 134.9 (s, Ar_F-*o*-*C*H), 133.6 (d, $^2J_{C,P}$ = 13 Hz, Ph-*o*-*C*H), 131.9 (d, $^4J_{C,P}$ = 2.3 Hz, Ph-*p*-*C*H), 131.2 (d, $^4J_{C,P}$ = 2.5 Hz, Ph'-*p*-*C*H), 130.9 (d, $^3J_{C,P}$ = 9.4 Hz, Ph-*m*-*C*H), 130.4 (d, $^1J_{C,P}$ = 51 Hz, Ph-*i*-*C*), 129.5-128.5 (m, Ph'-*C*H and Ar_F-*m*-*C*), 127.4 (d, $^1J_{C,P}$ = 50 Hz, Ph'-*i*-*C*), 125.4 (s, BzOx-5-*C*H), 124.7 (q, $^1J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 123.7 (s, BzOx-6-*C*H), 117.7-117.4 (m, Ar_F-*p*-*C*H), 117.4 (s, BzOx-4-*C*H), 110.3 (s, BzOx-7-*C*H), 97.7 (d, $^2J_{C,P}$ = 9.6 Hz, cod-*C*H), 88.1 (d, $^2J_{C,P}$ = 15 Hz, cod-*C*H), 66.1 (s, cod-*C*H), 61.1 (s, cod-*C*H), 60.5 (d, $^2J_{C,P}$ = 5.8 Hz, Pyr-2-*C*H), 49.9 (s, Pyr-5-*C*H_2), 41.1 (d, $^1J_{C,P}$ = 29 Hz, *C*H_2P), 36.1 (d,$^3J_{C,P}$ = 4.3 Hz, cod-*C*H_2), 34.8 (d, $^3J_{C,P}$ = 13 Hz, Pyr-3-*C*H_2), 33.5 (s, cod-*C*H_2), 29.2 (d, $^3J_{C,P}$ = 1.6 Hz, cod-*C*H_2), 26.2 (d,

$^{3}J_{C,P}$ = 2.6 Hz, cod-*C*H_2), 23.5 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 15.6 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2928w, 2848w, 1643m, 1618m, 1589m, 1467m, 1436w, 1402w, 1353s, 1271s, 1251m, 1113s, 999w, 885m, 838m, 742m, 711m, 680s, 667s cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 688 (34), 687 (100, M^+), 686 (27), 685 (67), 577 (23), 575 (23), 573 (10). $[\alpha]_D^{20}$ = − 36.3 (*c* = 0.860, $CHCl_3$). **Elemental analysis**: calc. C 49.59%, H 3.06%, N 1.81%; found: C 49.40%, H 3.39%, N 1.81%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Ox}2)



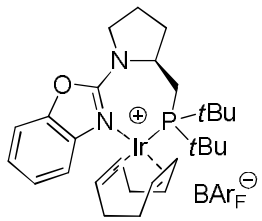
Complex **(*S*)-C_{Ox}2** (55%) was prepared according to **general procedure 9** from ligand **(*S*)-L_{Ox}2** and [Ir(cod)$_2$]BAr_F.

$C_{66}H_{51}N_2OPIrBF_{24}$ (1578.31 g·mol^{-1}):

m.p. 72-77 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.32-8.19 (br m, 1 H, *o*Tol-6-*H*), 7.81 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1 H, BzOx-4-*H*), 7.73 (br s, 8 H, Ar_F-*o*-*H*), 7.56 (s, 4 H, Ar_F-*p*-*H*), 7.48-6.80 (m, 10 H, *o*Tol/*o*Tol'-*H* and BzOx-*H*), 5.96-5.85 (m, 1 H, Pyr-2-*H*), 4.98-4.89 (m, 1 H, cod-C*H*), 4.68-4.53 (m, 1 H, cod-C*H*), 3.98-3.89 (m, 1 H, cod-C*H*), 3.89-3.74 (m, 2 H, cod-*H*), 3.61-3.52 (m, 1 H, C*H*H'P), 2.77-2.58 (m, 3 H, CH*H'*P, Pyr-5-*H*H' and Pyr-3-*H*H'), 2.58-1.98 (m, 11 H, cod-C*H*, cod-*H*, Pyr-*H* and *o*Tol-H_3), 1.93 (s, 3 H, *o*Tol'-H_3), 1.67-1.43 (m, 3 H, Pyr-4-H*H'* and cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 161.8 (q, $^{1}J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 158.0 (s, BzOx-2-*C*), 147.7 (s, BzOx-7a-*C*), 141.7 (br, *o*Tol-2-*C*), 141.2 (br, *o*Tol'-2-*C*), 140.3 (br d, *o*Tol-6-*C*H), 138.8 (s, BzOx-3a-*C*), 134.9 (s, Ar_F-*o*-*C*H), 132.8-132.3 (m, *o*Tol-4-*C*H, *o*Tol/*o*Tol'-3-*C*H), 131.6 (br s, *o*Tol'-6-*C*H),130.0 (br, *o*Tol-1-*C*), 129.3-128.4 (m, Ar_F-*m*-*C*), 128.4 (q, $^{1}J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 127.9-125.0 (m, *o*Tol'-1-*C*, *o*Tol'-4-*C*H, *o*Tol/*o*Tol'-5-*C*H and BzOx-5-*C*H), 123.7 (s, BzOx-6-*C*H), 117.8-117.4 (m, Ar_F-*p*-*C*H and BzOx-4-*C*H), 110.4 (s, BzOx-7-*C*H), 96.9 (br d, cod-*C*H), 87.2 (d, $^{2}J_{C,P}$ = 15 Hz,

cod-*C*H), 66.7 (s, cod-*C*H), 62.6 (s, cod-*C*H), 59.6 (br d, $^{2}J_{C,P}$ = 4.0 Hz, Pyr-2-*C*H), 50.0 (s, cod-*C*H_2), 43.9 (d, $^{1}J_{C,P}$ = 26 Hz, *C*H_2P), 36.8 (br s, Pyr-5-*C*H_2), 36.0 (d, $^{3}J_{C,P}$ = 11 Hz, Pyr-3-*C*H_2), 33.9 (s, cod-*C*H_2), 28.4 (s, cod-*C*H_2), 25.6 (s, Pyr-4-*C*H_2), 24.0 (br s, *o*Tol-*C*H_3), 23.1 (s, cod-*C*H_2), 21.8 (br s, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 26.1/10.2*(br s) ppm. In ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 25:1. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2965w, 2888w, 1647m, 1620m, 1468m, 1404w, 1355m, 1274s, 1117s, 1003w, 887m, 840m, 745m, 713m, 680m cm^{-1}. **MS** (ESI): *m/z* (%) = 715 (100, M+). $[\alpha]_D^{20}$ = − 37 (*c* = 0.140, $CHCl_3$). **Elemental analysis**: calc. C 50.23%, H 3.26%, N 1.78%; found: C 50.69%, H 3.94%, N 1.93%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Ox}3)



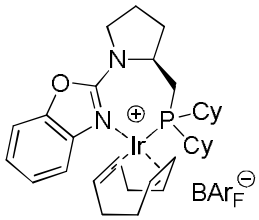
Complex **(*S*)-C_{Ox}3** (95%) was prepared according to **general procedure 9** from ligand **(*S*)-L_{Ox}3** and [Ir(cod)$_2$]BAr$_F$.

$C_{60}H_{55}N_2OPIrBF_{24}$ (1510.05 g·mol^{-1}):

m.p. 210-213 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.73 (br s, 8 H, Ar$_F$-*o*-*H*), 7.59-7.52 (m, 5 H, Ar$_F$-*p*-*H* and BzOx-4-*H*), 7.40-7.33 (m, 2 H, BzOx-5-*H* and BzOx-7-*H*), 7.23 ("td", $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1 H, BzOx-6-*H*), 5.32-5.20 (m, 2 H, cod-C*H*), 4.45-4.37 (m, 1 H, cod-C*H*), 4.13-4.05 (m, 1 H, Pyr-2-*H*), 3.97-3.76 (m, 3 H, Pyr-5-*H*$_2$ and cod-C*H*), 2.82 (ddd, $^{2}J_{H,P}$ = 16 Hz, $^{2}J_{H,H}$ = 12 Hz, $J_{H,H}$ = 1.8 Hz, 1 H, C*H*H'P), 2.70-2.57 (m, 2 H, cod-*H*), 2.42-2.34 (m, 1 H, cod-*H*), 2.34-2.22 (m, 1 H, Pyr-3-*H*H'), 2.20-1.95 (m, 5 H, Pyr-3-H*H'*, Pyr-4-*H*$_2$ and cod-*H*), 1.95-1.77 (m, 2 H, CH*H'*P and cod-*H*), 1.46-1.22 (m, 11 H, *t*Bu-*H* and cod-*H*), 1.17 (d, $^{3}J_{H,P}$ = 14 Hz, 9 H, *t*Bu'-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 161.8 (q, $^{1}J_{C,B}$ = 50 Hz, Ar$_F$-*i*-*C*), 157.5 (s, BzOx-2-*C*), 148.0 (s, BzOx-7a-*C*), 138.9 (s, BzOx-3a-*C*), 134.9 (s, Ar$_F$-*o*-*C*H), 129.5-128.4 (m, Ar$_F$-*m*-*C*), 125.2 (s, BzOx-5-*C*H), 124.7 (q, $^{1}J_{C,F}$ = 272 Hz, Ar$_F$-*C*F$_3$), 123.8 (s,

BzOx-6-*C*H), 118.8 (s, BzOx-4-*C*H), 117.5 (br s, Ar_F-*p*-*C*H), 110.4 (s, BzOx-7-*C*H), 92.0 (d, $^2J_{C,P}$ = 8.5 Hz, cod-*C*H), 82.9 (d, $^2J_{C,P}$ = 15 Hz, cod-*C*H), 65.7 (s, cod-*C*H), 58.5 (s, cod-*C*H), 57.9 (d, $^2J_{C,P}$ = 7.4 Hz, Pyr-2-*C*H), 49.7 (s, Pyr-5-*C*H_2), 38.5 (d, $^3J_{C,P}$ = 4.2 Hz, cod-*C*H_2), 38.3 (d, $^1J_{C,P}$ = 17 Hz, *t*Bu-*C*), 36.5 (d, $^3J_{C,P}$ = 8.1 Hz, cod-*C*H_2), 36.0 (d, $^1J_{C,P}$ = 18 Hz, *t*Bu'-*C*), 34.3 (d, $^1J_{C,P}$ = 21 Hz, *C*H_2P), 33.7 (s, Pyr-3-*C*H_2), 30.7 (d, $^2J_{C,P}$ = 4.5 Hz, *t*Bu-*C*H_3), 30.0-29.2 (br m, *t*Bu'-*C*H_3), 28.8 (s, cod-*C*H_2), 24.6 (s, Pyr-4-*C*H_2), 24.1 (s, cod-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 46.8 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.9 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2968w, 2892w, 1650m, 1622m, 1469m, 1406w, 1354m, 1272s, 1162s, 1121s, 1005w, 887m, 840m, 714m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 648 (32), 647 (100, M^+), 646 (21), 645 (61), 537 (12), 423 (12). $[\alpha]_D^{20}$ = + 7.1 (*c* = 0.220, $CHCl_3$).

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(dicyclohexylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]oxazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Ox}4)



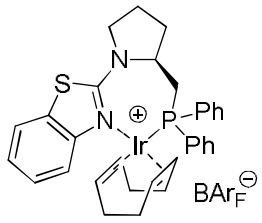
Complex **(*S*)-C_{Ox}4** (84%) was prepared according to **general procedure 9** from ligand **(*S*)-L_{Ox}4** and $[Ir(cod)_2]BAr_F$.

$C_{64}H_{59}N_2OPIrBF_{24}$ (1562.13 $g \cdot mol^{-1}$):

m.p. 142-146 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.74 (s, 8 H, Ar_F-*m*-*H*), 7.61 (d, $^2J_{H,H}$= 8.0 Hz, 1 H, BzOx-4-*H*), 7.57 (s, 4 H, Ar_F-*p*-*H*), 7.40-7.34 (m, 2 H, BzOx-5-*H* and BzOx-7-*H*), 7.24 ("td", $^2J_{H,H}$= 7.9 Hz, $^3J_{H,H}$= 1.1 Hz, 1 H, BzOx-6-*H*), 5.21-5.08 (m, 1 H, Pyr-2-*H*), 4.77-4.70 (m, 1 H, cod-C*H*), 4.70-4.62 (m, 1 H, cod-C*H*), 4.20-4.10 (m, 1 H, cod-C*H*), 3.93-3.77 (m, 2 H, Pyr-5-H_2), 3.54-3.44 (m, 1 H, cod-C*H*), 2.66-2.54 (m, 3 H, C*H*H'P and cod-*H*), 2.40-2.24 (m, 2 H, Pyr-3-*H*H' and cod-*H*), 2.21-1.84 (m, 11 H, CH*H*'P, Pyr-*H*, cod-*H* and Cy/Cy'-*H*), 1.84-1.67 (m, 5 H, Cy/Cy'-*H*), 1.64-1.01 (m, 14 H, cod-*H* and Cy/Cy'-*H*), 0.95-0.82 (m, 1 H, cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 158.0 (s, BzOx-2-*C*), 147.8 (s, BzOx-7a-*C*), 138.8 (s, BzOx-3a-*C*), 134.9 (s, Ar_F-*o*-*C*H), 129.6-128.4 (m, Ar_F-*m*-*C*H),

125.4 (s, BzOx-5-*C*H), 124.6 (q, $^{1}J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 123.9 (s, BzOx-6-*C*H), 118.0 (s, BzOx-4-*C*H), 117.6 (br s, Ar_F-*p*-*C*H), 110.4 (s, BzOx-7-*C*H), 95.3 (d, $^{2}J_{C,P}$ = 9.5 Hz, cod-*C*H), 86.8 (d, $^{2}J_{C,P}$ = 15 Hz, cod-*C*H), 65.8 (s, cod-*C*H), 58.8 (s cod-*C*H), 58.8 (d, $^{2}J_{C,P}$ = 6.1 Hz, Pyr-2-*C*H), 49.9 (s, Pyr-5-*C*H_2), 37.5 (d, $^{3}J_{C,P}$ = 3.9 Hz, cod-*C*H_2), 37.0 (d, $^{1}J_{C,B}$ = 26 Hz, Cy-1-*C*H), 35.9 (d, $^{3}J_{C,P}$ = 10 Hz, cod-*C*H_2), 33.4 (s, Pyr-3-*C*H_2), 33.0 (d, $^{1}J_{C,P}$ = 26 Hz, *C*H_2P), 31.6 (d, $^{1}J_{C,B}$ = 26 Hz, Cy'-1-*C*H), 30.1 (s, Cy/Cy'-*C*H_2), 29.8 (s, Cy/Cy'-*C*H_2), 29.5 (s, Cy/Cy'-*C*H_2), 29.0 (s, Cy/Cy'-*C*H_2), 26.9-26.7 (m, cod-*C*H_2 and Cy/Cy'-*C*H_2), 26.1 (s, Cy/Cy'-*C*H_2), 25.9 (s, Cy/Cy'-*C*H_2), 24.8 (d, $^{3}J_{C,P}$ = 2.5 Hz, cod-*C*H_2), 24.3 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 24.9 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.7 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2937w, 2860w, 1648m, 1620w, 1596w, 1467w, 1402w, 1354m, 1273s, 1119s, 1005w, 887m, 840w, 745m, 713m, 681m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 700 (34), 699 (100, M^+), 698 (25), 697 (62), 587 (18), 585 (11). $[\alpha]_D^{20}$ = + 60.9 (*c* = 0.330, $CHCl_3$). **Elemental analysis**: calc. C 49.21%, H 3.81%, N 1.79%; found: C 48.89%, H 4.11%, N 1.73%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(diphenylphosphino)methyl]pyrrolidin-1-yl} benzo[*d*]thiazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Th}1)

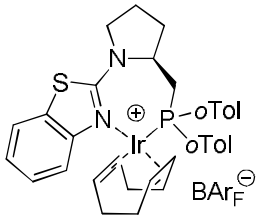


Complex **(*S*)-C_{Th}1** (81%) was prepared according to **general procedure 8** from ligand **(*S*)-L_{Th}1** and $[Ir(cod)Cl]_2$.

$C_{64}H_{47}N_2PSIrBF_{24}$ (1566.10 g·mol^{-1}):
m.p. 69-71 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.34 (d, $^{2}J_{H,H}$ = 8.2 Hz, 1 H, BzTh-4-*H*), 7.77 (s, 8 H, Ar_F-*m*-*H*), 7.56 (s, 4 H, Ar_F-*p*-*H*), 7.55-7.51 (m, 1 H, BzTh-5-*H*), 7.49 (d, $^{2}J_{H,H}$ = 7.9 Hz, 1 H, BzTh-7-*H*), 7.47-7.37 (m, 5 H, Ph/Ph'-*H*), 7.32-7.28 (m, 1 H, Ph/Ph'-*H*), 7.28-7.22 (m, 1 H, BzTh-6-*H*), 7.20-7.10 (m, 4 H, Ph/Ph'-*H*), 6.35-6.22 (m, 1 H, Pyr-2-*H*), 4.85-4.77 (m, 1 H, cod-C*H*), 4.51-4.42 (m, 1 H, cod-C*H*), 4.12-4.06 (m, 1 H, cod-C*H*), 3.52-3.34 (m, 3 H, Pyr-5-H_2 and C*H*H'P), 3.02-2.87 (m,

2 H, CH*H'*P and cod-C*H*), 2.78-2.63 (m, 2 H, Pyr-3-*H*H' and cod-*H*), 2.36-2.10 (m, 7 H, Pyr-3-H*H'*, Pyr-4-H_2 and cod-*H*), 2.10-1.97 (m, 1 H, cod-*H*), 1.63-1.45 (m, 2 H, cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 165.8 (s, BzTh-2-*C*), 162.0 (q, $^{1}J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 148.6 (s, BzTh-3a-*C*), 135.0 (s, Ar_F-*o*-*C*H), 133.2 (d, $^{2}J_{C,P}$ = 13 Hz, Ph-*o*-*C*H), 132.1 (s, Ph-*p*-*C*H), 131.5 (s, Ph'-*p*-*C*H), 130.7 (d, $^{3}J_{C,P}$ = 9.4 Hz, Ph-*m*-*C*H), 130.1 (d, $^{1}J_{C,P}$ = 51 Hz, Ph-*i*-*C*), 129.5-128.6 (m, Ph'-*o*-*C*H, Ph'-*m*-*C*H and Ar_F-*m*-*C*), 128.0 (d, $^{1}J_{C,P}$ = 50 Hz, Ph'-*i*-*C*), 127.1 (s, BzTh-5-*C*H), 126.8 (s, BzTh-7a-*C*), 128.4 (q, $^{1}J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 124.2 (s, BzTh-6-*C*H), 122.1 (s, BzTh-4-*C*H), 121.9 (s, BzTh-7-*C*H), 117.1 (s, Ar_F-*p*-*C*H), 97.3 (d, $^{2}J_{C,P}$ = 9.4 Hz, cod-*C*H), 89.6 (d, $^{2}J_{C,P}$ = 15 Hz, cod-*C*H), 65.3 (s, cod-*C*H), 61.9 (s, cod-*C*H), 61.9 (d, $^{2}J_{C,P}$ = 6.7 Hz, Pyr-2-*C*H), 53.5 (s, Pyr-5-*C*H_2), 40.8 (d, $^{1}J_{C,P}$ = 31 Hz, *C*H_2P), 36.7 (d, $^{3}J_{C,P}$ = 3.6 Hz, cod-*C*H_2), 35.8 (d, $^{3}J_{C,P}$ = 13 Hz, Pyr-3-*C*H_2), 33.6 (s, cod-*C*H_2), 28.7 (s, cod-*C*H_2), 25.9 (s, cod-*C*H_2), 23.8 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 15.6 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2889w, 1610w, 1534m, 1452m, 1352s, 1272s, 1113s, 1024w, 999w, 937w, 885m, 838m, 744m, 711m, 686m, 669m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 705 (11), 704 (37), 703 (100), 702 (27), 701 (60), 595 (12), 594 (16), 593 (30), 592 (10), 591 (18). $[\alpha]_D^{20}$ = + 17.9 (*c* = 1.08, $CHCl_3$). **Elemental analysis**: calc. C 49.08%, H 3.02%, N 1.79%; found: C 49.06%, H 2.94%, N 2.02%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(di-*ortho*-tolylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Th}2)

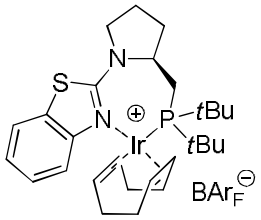


Complex **(*S*)-C_{Th}2** (97%) was prepared according to **general procedure 9** from ligand **(*S*)-L_{Th}2** and $[Ir(cod)_2]BAr_F$.

$C_{66}H_{51}N_2PSIrBF_{24}$ (1594.15 g·mol^{-1}):
m.p. 118-121 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.52 (d, $^{3}J_{H,H}$ = 8.3 Hz, 1 H, BzTh-4-*H*), 8.18-8.08 (m, 1 H, *o*Tol-6-*H*), 7.75 (s, 8 H, Ar_F-*o*-*H*), 7.69-7.60 (m, 2 H,

BzTh-5-*H* and BzTh-7-*H*), 7.57 (s, 4 H, Ar_F-*p*-*H*), 7.44-7.22 (m, 5 H, BzTh-6-*H*, *o*Tol'-6-*H*, *o*Tol-5-*H*, *o*Tol-4-*H* and *o*Tol-3-*H*), 7.18-7.10 (m, 1 H, *o*Tol'-3-*H*), 7.08-6.95 (m, 1 H, *o*Tol'-4-*H*), 6.94-6.85 (m, 1 H, *o*Tol'-5-*H*), 6.54-6.41 (m, 1 H, Pyr-2-*H*), 4.82-4.72 (m, 1 H, cod-C*H*), 4.31-4.20 (m, 1 H, cod-C*H*), 4.14-4.05 (m, 1 H, cod-C*H*), 3.77-3.64 (m, 1 H, C*H*H'P), 3.63-3.52 (m, 2 H, cod-*H*), 2.85-2.65 (m, 3 H, Pyr-5-H_2 and CH*H'*P), 2.65-2.55 (m, 1 H, cod-C*H*), 2.46-2.15 (m, 9 H, Pyr-3-H_2, Pyr-4-H_2, *o*Tol-H_3 and cod-*H*), 2.15-1.95 (m, 3 H, cod-*H*), 1.90 (s, 3 H, *o*Tol'-H_3), 1.57-1.44 (m, 1 H, cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 165.2 (s, BzTh-2-*C*), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 148.8 (s, BzTh-3a-*C*), 141.5 (br s, *o*Tol-2-*C*), 140.6 (br d, *o*Tol'-2-*C*), 139.4 (d, $^2J_{C,P}$ = 30 Hz, *o*Tol-6-*C*H), 134.9 (s, Ar_F-*o*-*C*H), 132.7-132.3 (m, *o*Tol-4-*C*H, *o*Tol/*o*Tol'-3-*C*H), 131.5 (br s, *o*Tol'-6-*C*H), 131.0 (br s, *o*Tol'-4-*C*H), 130.3 (br d, *o*Tol-1-*C*), 129.5-128.4 (m, Ar_F-*m*-*C*), 127.2 (s, BzTh-7a-*C*), 127.0 (s, BzTh-5-*C*H), 126.7 (d, $^3J_{C,P}$ = 9.6 Hz, *o*Tol-5-*C*H), 125.6 (d, $^3J_{C,P}$ = 9.6 Hz, oTol'-5-*C*H), 125.0 (q, $^1J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 125.2 (br d, *o*Tol'-1-*C*), 124.0 (s, BzTh-6-*C*H), 120.6 (s, BzTh-7-*C*H), 121.8 (s, BzTh-4-*C*H), 117.7-117.4 (m, Ar_F-*p*-*C*H), 96.2 (d, $^2J_{C,P}$ = 8.1 Hz, cod-*C*H), 87.9 (d, $^2J_{C,P}$ = 16 Hz, cod-*C*H), 66.3 (s, cod-*C*H), 63.1 (s, cod-*C*H), 62.2 (d, $^2J_{C,P}$ = 9.0 Hz, Pyr-2-*C*H), 53.9 (s, cod-*C*H_2), 43.7 (d, $^1J_{C,P}$ = 29 Hz, *C*H_2P), 37.2 (br s, Pyr-5-*C*H_2), 36.7 (d, $^3J_{C,P}$ = 13 Hz, Pyr-3-*C*H_2), 34.0 (s, cod-*C*H_2), 28.3 (s, cod-*C*H_2), 25.5 (s, cod-*C*H_2), 24.3 (s, Pyr-4-*C*H_2), 23.0 (d, $^3J_{C,P}$ = 5.6 Hz, *o*Tol-*C*H_3), 21.6 (br s, *o*Tol'-*C*H_3) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 22.4/3.32* (br s) ppm. In ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 17:1. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3064w, 2964w, 2889w, 1787w, 1545m, 1453m, 1355m, 1275s, 1116s, 888m, 839m, 744m, 714m, 681m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 733 (12), 732 (38), 731 (100, M^+), 730 (24), 729 (59), 623 (11), 622 (11), 621 (21), 620 (11), 619 (19), 617 (13). $[\alpha]_D^{20}$ = − 1.0 (*c* = 0.271, $CHCl_3$).

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(di-*tert*-butylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Th}3)

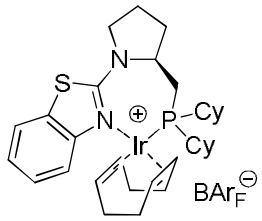


Complex **(*S*)-C_{Th}3** (94%) was prepared according to **general procedure 9** from ligand **(*S*)-L_{Th}3** and [Ir(cod)$_2$]BAr$_F$.

$C_{60}H_{55}N_2PSIrBF_{24}$ (1526.12 g·mol^{-1}):
m.p. 228-231 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.35 (d, $^3J_{H,H}$ = 8.2 Hz, 1 H, BzTh-4-*H*), 7.73 (br s, 8 H, Ar$_F$-*o*-*H*), 7.65 (d, $^3J_{H,H}$ = 7.9 Hz, 1 H, BzTh-7-*H*), 7.59-7.51 (m, 5 H, BzTh-5-*H* and Ar$_F$-*p*-*H*), 7.30 ("t", $^3J_{H,H}$ = 7.7 Hz, 1 H, BzTh-6-*H*), 5.76-5.65 (m, 1 H, Pyr-2-*H*), 5.37-5.29 (m, 1 H, cod-C*H*), 4.43-4.34 (m, 1 H, cod-C*H*), 4.07-3.97 (m, 1 H, cod-C*H*), 3.78-3.58 (m, 2 H, Pyr-5-*H*$_2$), 3.37-3.26 (m, 1 H, cod-C*H*), 2.86 (ddd, $^2J_{H,P}$ = 16 Hz, $^2J_{H,H}$ = 11 Hz, $^3J_{H,H}$ = 1.9 Hz, 1 H, C*H*H'P), 2.75-2.62 (m, 2 H, cod-*H*), 2.33-2.16 (m, 3 H, Pyr-3-*H*H', Pyr-4-*H*H' and cod-*H*), 2.16-1.91 (m, 5 H, CH*H'*P, Pyr-3-H*H'*, Pyr-4-H*H'* and cod-*H*), 1.82-1.71 (m, 1 H, cod-*H*), 1.50-1.17 (m, 11 H, *t*Bu-*H* and cod-*H*), 1.11 (d, $^3J_{H,P}$ = 14 Hz, 9 H, *t*Bu'-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 164.6 (s, BzTh-2-*C*), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar$_F$-*i*-*C*), 149.2 (s, BzTh-3a-*C*), 134.9 (s, Ar$_F$-*o*-*C*H), 129.5-128.2 (m, Ar$_F$-*m*-*C*H), 127.2 (s, BzTh-7a-*C*), 126.8 (s, BzTh-5-*C*H), 124.7 (q, $^1J_{C,F}$ = 272 Hz, Ar$_F$-*C*F$_3$), 124.0 (s, BzTh-6-*C*H), 123.5 (s, BzTh-4-*C*H), 121.7 (s, BzTh-7-*C*H), 117.5 (br s, Ar$_F$-*p*-*C*H), 91.2 (d, $^2J_{C,P}$ = 7.6 Hz, cod-*C*H), 83.8 (d, $^2J_{C,P}$ = 16 Hz, cod-*C*H), 67.3 (s, cod-*C*H), 59.6 (d, $^2J_{C,P}$ = 7.7 Hz, Pyr-2-*C*H), 57.5 (s, cod-*C*H), 53.4 (s, Pyr-5-*C*H$_2$), 38.7 (d, $^3J_{C,P}$ = 4.4 Hz, cod-*C*H$_2$), 37.6 (d, $^1J_{C,P}$ = 16 Hz, *t*Bu-*C*), 37.3 (d, $^3J_{C,P}$ = 8.1 Hz, cod-*C*H$_2$), 35.7 (d, $^1J_{C,P}$ = 18 Hz, *t*Bu'-*C*), 34.2 (s, Pyr-3-*C*H$_2$), 34.0 (d, $^1J_{C,P}$ = 21 Hz, *C*H$_2$P), 30.4 (d, $^2J_{C,P}$ = 4.6 Hz, *t*Bu-*C*H$_3$), 28.3 (br s, *t*Bu'-*C*H$_3$), 27.0 (s, cod-*C*H$_2$), 24.8 (s, Pyr-4-*C*H$_2$), 24.0 (d, $^3J_{C,P}$ = 2.9 Hz, cod-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 46.7 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.7 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2962w, 2888w, 1611w, 1546m, 1455w, 1353m, 1272s, 1163s, 1122s, 1021w, 887m, 839w, 747w, 714m,681m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 664 (31), 663 (100, M$^+$), 662 (21),

661 (59), 555 (11), 553 (15), 497 (12), 441 (11), 439 (14). $[\alpha]_D^{20}$ = + 140 (c = 1.30, $CHCl_3$). **Elemental analysis**: calc. C 47.22%, H 3.63%, N 1.84%; found: C 46.78%, H 3.92%, N 1.91%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(dicyclohexylphosphino)methyl]pyrrolidin-1-yl}benzo[*d*]thiazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ((*S*)-C_{Th}4)



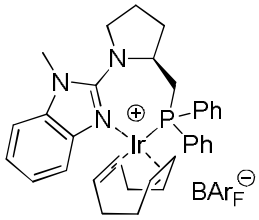
Complex **(*S*)-C_{Th}4** (98%) was prepared according to **general procedure 9** from ligand **(*S*)-L_{Th}4** and [Ir(cod)$_2$]BAr$_F$.

$C_{64}H_{59}N_2PSIrBF_{24}$ (1578.20 g·mol^{-1}):

m.p. 120-124 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.29 (d, $^2J_{H,H}$ = 8.1 Hz, 1 H, BzTh-4-*H*), 7.74 (br s, 8 H, Ar$_F$-*o*-*H*), 7.66 (d, $^2J_{H,H}$ = 7.9 Hz, 1 H, BzTh-7-*H*), 7.62-7.50 (m, 5 H, BzTh-5-*H* and Ar$_F$-*p*-*H*), 7.31 ("t", $^2J_{H,H}$ = 8.1 Hz, 1 H, BzTh-6-*H*), 5.63-5.51 (m, 1 H, Pyr-2-*H*), 4.89-4.80 (m, 1 H, cod-C*H*), 4.58-4.50 (m, 1 H, cod-C*H*), 3.71-3.52 (m, 4 H, Pyr-5-H_2 and cod-C*H*), 2.74-2.54 (m, 3 H, C*H*H'P and cod-*H*), 2.38-2.22 (m, 2 H, Pyr-3-*H*H' and cod-*H*), 2.22-1.82 (m, 11 H, CH*H'*P, Pyr-3-H*H'*, Pyr-4-H_2, cod-*H* and Cy/Cy'-*H*), 1.82-1.55 (m, 7 H, Cy/Cy'-*H*), 1.55-1.45 (m, 2 H, cod-*H* and Cy/Cy'-*H*), 1.45-1.20 (m, 8 H, cod-*H* and Cy/Cy'-*H*), 1.20-1.02 (m, 2 H, Cy/Cy'-*H*), 0.97-0.81 (m, 1 H, cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 165.2 (s, BzTh-2-*C*), 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar$_F$-*i*-*C*), 148.8 (s, BzTh-3a-*C*), 134.9 (s, Ar$_F$-*m*-*C*H), 129.6-128.3 (m, Ar$_F$-*m*-*C*H), 127.0 (s, BzTh-5-*C*H), 127.0 (s, BzTh-7a-*C*), 124.7 (q, $^1J_{C,F}$ = 272 Hz, Ar$_F$-*C*F$_3$), 124.1 (s, BzTh-6-*C*H), 122.2 (s, BzTh-4-*C*H), 121.7 (s, BzTh-7-*C*H), 117.6 (s, Ar$_F$-*p*-*C*H), 94.4 (d, $^2J_{C,P}$ = 9.2 Hz, cod-*C*H), 92.9 (d, $^2J_{C,P}$ = 14 Hz, cod-*C*H), 65.7 (s, cod-*C*H), 60.9 (d, $^2J_{C,P}$ = 6.4 Hz, Pyr-2-*C*H), 58.1 (s, cod-*C*H), 53.6 (s, Pyr-5-*C*H$_2$), 37.7 (d, $^3J_{C,P}$ = 3.8 Hz, cod-*C*H$_2$), 37.2 (d, $^1J_{C,P}$ = 25 Hz, Cy-1-*C*H), 36.7 (d, $^3J_{C,P}$ = 10 Hz, cod-*C*H$_2$), 33.6 (s, Pyr-3-*C*H$_2$), 32.9 (d, $^1J_{C,P}$ = 27 Hz, *C*H$_2$P), 32.2 (d, $^1J_{C,P}$ = 25 Hz, Cy'-1-*C*H), 29.5-29.2 (m, Cy/Cy'-*C*H$_2$), 28.8 (s, Cy/Cy'-*C*H$_2$), 27.2-26.6 (m, cod-*C*H$_2$ and Cy/Cy'-*C*H$_2$), 26.1 (s, Cy/Cy'-*C*H$_2$), 25.8 (s,

Cy/Cy'-CH_2), 24.8 (br d, $^3J_{C,P}$ = 2.4 Hz, cod-CH_2), 24.6 (s, Pyr-4-CH_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 22.9 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.8 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2936m, 2859m, 1611w, 1544m, 1453m, 1354s, 1273s, 1115s, 1003w, 887m, 839m, 747m, 713m, 680m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 716 (36), 715 (100, M^+), 714 (23), 713 (59), 605 (13), 604 (14), 603 (27), 601 (16). $[\alpha]_D^{20}$ = + 123 (*c* = 0.450, $CHCl_3$). **Elemental analysis**: calc. C 48.71%, H 3.77%, N 1.78%; found: C 48.78%, H 4.06%, N 1.91%.

[(η^4-1,5-Cyclooctadiene)-((*S*)-2-{2-[(diphenylphosphino)methyl]pyrrolidin-1-yl}-1-methyl-1*H*-benzo[*d*]imidazole)-iridium(I)]-tetrakis[3,5-bis(trifluoromethyl)phenyl] borate ((*S*)-C_{Im}1)



Complex **(*S*)-C_{Im}1** (92%) was prepared according to **general procedure 8** from ligand **(*S*)-L_{Im}1** and $[Ir(cod)Cl]_2$.

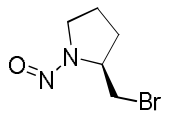
$C_{65}H_{50}N_3PIrBF_{24}$ (1563.08 g·mol^{-1}):

m.p. 88-91 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.95 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, BzIm-4-*H*), 7.73 (br s, 8 H, Ar_F-*o*-*H*), 7.58-7.51 (m, 6 H, Ph-*o*-*H* and Ar_F-*p*-*H*), 7.47-7.40 (m, 3 H, Ph'-*o*-*H* and Ph-*p*-*H*), 7.38-7.29 (m, 2 H, Ph'-*p*-*H* and BzIm-5-*H*), 7.29-7.19 (m, 3 H, Ph-*m*-*H* and BzIm-6-*H*), 7.18-7.08 (m, 3 H, Ph'-*m*-*H* and BzTh-7-*H*), 5.89-5.76 (m, 1 H, Pyr-2-*H*), 4.71-4.63 (m, 1 H, cod-C*H*), 4.63-4.55 (m, 1 H, cod-C*H*), 4.13-4.02 (m, 2 H, Pyr-5-*H*H' and cod-C*H*), 3.54 (s, 3 H, NCH_3), 3.56-3.41 (m, 2 H, Pyr-5-H*H'* and C*H*H'P), 2.82-2.67 (m, 3 H, Pyr-3-*H*H', cod-C*H* and cod-*H*), 2.54-2.44 (m, 1 H, CH*H*'P), 2.43-2.34 (m, 1 H, cod-*H*), 2.34-2.21 (m, 3 H, Pyr-4-*H*H' and cod-*H*), 2.19-1.93 (m, 4 H, Pyr-3-H*H'*, Pyr-4-H*H'* and cod-*H*), 1.64-1.41 (m, 2 H, cod-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 161.8 (q, $^1J_{C,B}$ = 50 Hz, Ar_F-*i*-*C*), 154.5 (s, BzIm-2-*C*), 138.0 (s, BzIm-3a-*C*), 134.9 (s, Ar_F-*o*-*C*H), 134.6 (s, BzIm-7a-*C*), 133.9 (d, $^2J_{C,P}$ = 13 Hz, Ph-*o*-*C*H), 131.8 (s, Ph-*p*-*C*H), 131.2-130.3 (m, Ph'-*p*-*C*H, Ph-*m*-*C*H and Ph-*i*-*C*), 129.7-128.2 (m, Ph'-*i*-*C*, Ph'-*o*-*C*H, Ph'-*m*-*C*H, and Ar_F-*m*-*C*H), 124.6 (q, $^1J_{C,F}$ = 272 Hz, Ar_F-*C*F_3), 123.4 (s, BzIm-6-*C*H), 123.3 (s, BzIm-5-*C*H),

119.3 (s, BzIm-4-*C*H), 117.6 (br s, Ar_F-*p*-*C*H), 109.6 (s, BzIm-7-*C*H), 95.6 (d, $^2J_{C,P}$ = 10 Hz, cod-*C*H), 88.7 (d, $^2J_{C,P}$ = 15 Hz, cod-*C*H), 64.2 (s, cod-*C*H), 62.0 ($^2J_{C,P}$ = 10 Hz, Pyr-2-*C*H), 60.9 (d, cod-*C*H), 53.4 (s, Pyr-5-*C*H_2), 37.4 (d, $^1J_{C,P}$ = 34 Hz, *C*H_2P), 36.8 (s, cod-*C*H_2), 35.1 (d, $^3J_{C,P}$ = 12 Hz, Pyr-3-*C*H_2), 33.9 (s, cod-*C*H_2), 32.3 (s, N*C*H_3), 28.6 (s, cod-*C*H_2), 26.0 (s, cod-*C*H_2), 24.9 (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = 18.6 (s) ppm. **^{19}F{^{1}H} NMR** (377 MHz, CD_2Cl_2): δ = − 62.6 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2970w, 2883w, 1610w, 1541m, 1481m, 1456w, 1352s, 1273s, 1115s, 999w, 885m, 838m, 742m, 711m cm^{-1}. **MS** (FAB, NBA): *m/z* (%) = 701 (39), 700 (100, M^+), 699 (25), 698 (63), 590 (21), 589 (15), 588 (37), 587 (13), 586 (32), 585 (11), 584 (13), 508 (12). $[\alpha]_D^{20}$ = + 15.8 (*c* = 1.13, $CHCl_3$).

6.7 Phosphinohydrazones and Precursors: Preparation and Analytical Data

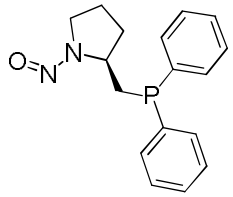
(*S*)-2-(Bromomethyl)-1-nitrosopyrrolidine ((*S*)-123)



(*S*)-(1-Nitrosopyrrolidin-2-yl)methanol[118] (6.30 g, 48.4 mmol, 1.0 eq.) and tetrabromomethane (24.6 g, 74.2 mmol, 1.5 eq.) were mixed in dichloromethane (95 mL) at 0 °C in an ice bath. Triphenylphosphine (19.0 g, 72.4 mmol, 1.5 eq.) was then added portion wise. The yellowish reaction mixture was then allowed to warm to room temperature overnight, where it turned brownish. The mixture was reduced to dryness under rotatory evaporation. The crude was purified by column chromatography on silica gel (7.5 x 19 cm), eluting with cyclohexane/ethyl acetate (8:2). The product **(*S*)-123** was isolated as a yellowish solid (8.50 g, 44.0 mmol, 91%).

$C_5H_9BrN_2O$ (193.04 g·mol^{-1}):
m.p. 45-47 °C. **R_f** = 0.18 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.76-4.66/4.52-4.44* (m, 1 H, Pyr-2-*H*), 4.44-4.36/3.87-3.82* (m, 1 H, C*H*H'Br), 4.14-4.04/3.72-3.66* (m, 1 H, CH*H'*Br), 3.75-3.70/3.60-3.50* (m, 1 H, Pyr-5-*H*H'), 3.57-3.52 (m, 1 H, Pyr-5-H*H'*), 2.87-1.82 (m, 4 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 60.9/56.8* (Pyr-2-*C*H), 51.0/46.2* (s, Pyr-5-*C*H_2), 34.3/32.1* (s, *C*H_2Br), 29.2/28.5 (s, Pyr-3-*C*H_2), 22.5/20.7* (s, Pyr-4-*C*H_2) ppm. In the ^{1}H and ^{13}C NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:1 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (neat): $\tilde{\nu}$ = 2986m, 2953m, 2934m, 2884m, 1472m, 1417m, 1399s, 1364s, 1336s, 1319m, 1272s, 1196m, 1170m, 1138m, 1007s, 963m, 927m, 878m, 809s, 706s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 194 (18), 192 (18, M^+), 113 (100), 99 (97), 83 (22), 82 (32), 69 (28), 68 (12), 55 (30), 42 (11), 41 (20), 39 (11). $[\alpha]_D^{20} = -103$ (*c* = 2.04, $CHCl_3$).

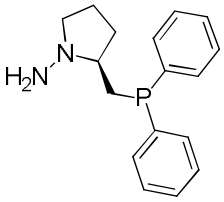
(*S*)-2-[(Diphenylphosphino)methyl]-1-nitrosopyrrolidine ((*S*)-122)



To a solution of (*S*)-2-(bromomethyl)-1-nitrosopyrrolidine (**(*S*)-123**, 500 mg, 2.59 mmol, 1.0 eq.) in abs. tetrahydrofuran (5 mL) was added under argon atmosphere a 0.5 M solution of potassium diphenylphosphide in tetrahydrofuran (6.70 mL, 3.37 mmol, 1.3 eq.) at 0 °C in an ice bath. The reaction mixture was then allowed to stir at 0 °C for 30 minutes before it was filtered through celite under inert atmosphere. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel (4 x 17 cm), eluting with cyclohexane/ethyl acetate (8:2). The title compound **(*S*)-122** was obtained as a colorless semisolid (698 mg, 2.34 mmol, 90%).

$C_{17}H_{19}N_2OP$ (298.32 g·mol^{-1}):
R_f = 0.26 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.66-7.27 (m, 10 H, Ph/Ph'-*H*), 4.49-4.36 (m, 1 H, Pyr-2-*H*), 4.36-4.26/3.74-3.62* (m, 1 H, Pyr-5-*H*H'), 4.18-4.08/3.56-3.46* (m, 1 H, Pyr-5-H*H'*), 3.22-3.14/2.96-2.89* (m, 1 H, C*H*H'P), 2.38-1.79 (m, 5 H, CH*H'*P and Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 138.0 (d, $^1J_{C,P}$ = 11 Hz, Ph-*i*-*C*), 136.8 (d, $^1J_{C,P}$ = 12 Hz, Ph'-*i*-*C*), 133.1/133.0* (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7/132.6* (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 129.2/129.3* (s, Ph-*p*-*C*H), 129.1-128.5 (m, Ph/Ph'-*C*H), 59.8/55.3* (d, $^2J_{C,P}$ = 22 Hz, Pyr-2-*C*H), 50.4/45.7* (s, Pyr-5-*C*H_2), 34.6/30.9* (d, $^1J_{C,P}$ = 15 Hz, *C*H_2P), 31.2/30.1* (d, $^3J_{C,P}$ = 7.4/8.4 Hz, Pyr-3-*C*H_2), 22.8/21.1* (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 22.2/– 22.8* (s) ppm. In the ^{1}H, ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:5 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (neat): $\tilde{\nu}$ = 3052w, 2967m, 2943m, 2877m, 1480, 1432s, 1413s, 1301s, 1271s, 1167w, 1095w, 999w, 740m, 696s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) =298 (1, M^+), 268 (20), 202 (19), 201 (100), 199 (21), 183 (29), 121 (35). $[\alpha]_D^{20}$ = − 67.8 (*c* = 1.56, $CHCl_3$).

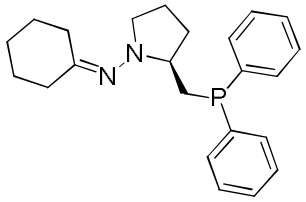
(*S*)-2-[(Diphenylphosphino)methyl]pyrrolidin-1-amine ((*S*)-114)



To a solution of **(*S*)-122** (200 mg, 670 μmol, 1.0 eq.) in abs. tetrahydrofuran (8 mL) was added drop wise at 0°C in an ice bath, under argon atmosphere, a 1 M solution of $LiAlH_4$ (2.00 mL, 2.00 mmol, 3.0 eq.) in tetrahydrofuran. The mixture was allowed to warm up to room temperature overnight (18 hours). Aqueous saturated Na_2SO_4 (8 mL) was added drop wise at 0°C and the biphasic mixture was stirred for 15 minutes at room temperature. The solids were filtered off and washed with tetrahydrofuran (3 x 10 mL). The filtrate was concentrated under reduced pressure to afford **(*S*)-114** as a colorless semisolid in quantitative yield. The title compound was used in the next step without further purification.

$C_{17}H_{21}N_2P$ (284.34 $g \cdot mol^{-1}$):
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45-7.12 (m, 10 H, Ph/Ph'-*H*), 3.19-3.10 (m, 1 H, Pyr-2-*H*), 2.80 (br s, 2 H, N*H*$_2$), 2.65 (br d, $^2J_{H,P}$ = 13 Hz, 1 H, C*H*H'P), 2.20-2.03 (m, 2 H, Pyr-5-*H*$_2$), 2.01-1.80 (m, 2 H, CH*H'*P and Pyr-4-*H*H'), 1.70-1.48 (m, 2 H, Pyr-4-*HH'* and Pyr-3-*H*H'), 1.47-1.35 (m, 1 H, Pyr-3-H*H'*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 139.2 (d, $^1J_{C,P}$ = 12 Hz, Ph-*i*-*C*), 138.6 (d, $^1J_{C,P}$ = 13 Hz, Ph'-*i*-*C*), 132.9 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.7 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.8-128.2 (m, Ph/Ph'-*C*H), 66.9 (d, $^2J_{C,P}$ = 18 Hz, Pyr-2-*C*H), 60.0 (s, Pyr-5-*C*H$_2$), 32.9 (d, $^1J_{C,P}$ = 12 Hz, *C*H$_2$P), 30.1 (d, $^3J_{C,P}$ = 6.7 Hz, Pyr-3-*C*H$_2$), 20.1 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.6 (s) ppm. **MS** (EI, 70 eV): *m/z* (%) = 285 (18), 284 (100, M^+), 217 (10), 215 (15), 202 (17), 201 (41), 98 (40), 85 (30), 77 (13).

(*S*)-*N*-Cyclohexylidene-2-[(diphenylphosphino)methyl]pyrrolidin-1-amine ((*S*)-L_H1)

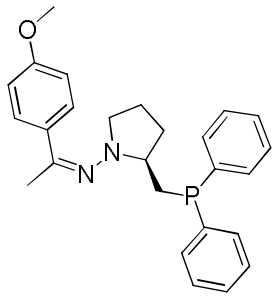


(*S*)-2-[(Diphenylphosphino)methyl]pyrrolidin-1-amine (**(*S*)-114**, 95.3 mg, 335 µmol, 1.0 eq.) and cyclohexanone (100 µL, 965 µmol, 2.9 eq.) were mixed in abs. tetrahydrofuran (1 mL) in a flame-dried Young tube. The resulting mixture was then heated at reflux for 17 hours, before the solvent was removed *in vacuo*. The crude was purified by column chromatography on silica gel (2 x 15 cm), eluting with cyclohexane/ethyl acetate (9:1 → 8:2). The title compound **(*S*)-L_H1** was obtained as a colorless semisolid (98.0 mg, 269 µmol, 80%).

$C_{23}H_{29}N_2P$ (364.46 g·mol^{-1}):

R_f = 0.37 (SiO_2, cyclohexane/ethyl acetate 8:2). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.52-7.37 (m, 4 H, Ph/Ph'-*o*-*H*), 7.37-7.23 (m, 6 H, Ph/Ph'-*H*), 3.11-2.33 (m, 2 H, Pyr-5-*H*H' and Pyr-2-*H*), 2.55-2.40 (m, 2 H, C*H*H'P and Cy-*H*), 2.37-2.10 (m, 4 H, Pyr-5-H*H'* and Cy-*H*), 2.10-1.89 (m, 2 H, CH*H'*P and Pyr-3-*H*H'), 1.82-1.33 (m, 9 H, Pyr-3-H*H'*, Pyr-4-H_2 and Cy-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 168.6/162.5* (s, C=N), 140.1/139.9* (d, $^1J_{C,P}$ = 14 Hz, Ph-*i*-*C*), 139.6/139.5* (d, $^1J_{C,P}$ = 14 Hz, Ph'-*i*-*C*), 132.8 (br d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.8 (br d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.5-128.1 (m, Ph/Ph'-*C*H), 64.9 (br d, $^2J_{C,P}$ = 19 Hz, Pyr-2-*C*H), 54.1/53.7* (s, Pyr-5-*C*H_2), 36.2/35.9* (s, Cy-2/6-*C*H_2), 33.9 (br d, $^1J_{C,P}$ = 12 Hz, *C*H_2P), 29.8 (br d, $^3J_{C,P}$ = 7.2 Hz, Pyr-3-*C*H_2), 29.4/29.1* (s, Cy-2/6-*C*H_2), 28.4/27.7* (Cy-3/5-*C*H_2), 26.6 (s, Cy-4-*C*H_2), 25.6/25.0* (s, Cy-3/5-*C*H_2), 21.7/21.5* (s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$): δ = – 21.8/– 22.1* (s) ppm. In the ^{13}C and ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 4:1 and therefore nuclei, which are detected twice are marked with an asterisk. **IR** (neat): $\tilde{\nu}$ = 2930m, 2854m, 2835m, 1695w, 1635w, 1447m, 1433s, 1184m, 1119m, 1037w, 906w, 740m, 696s cm^{-1}. **MS** (EI, 70 eV): *m/z* (%) = 364 (4, M^+), 322 (25), 321 (100), 295 (39), 294 (51), 285 (15), 284 (86), 282 (20), 281 (64), 280 (24), 268 (19), 201 (35), 200 (54), 199 (10), 185 (26), 183 (39), 172 (19), 165 (63), 121 (13), 96 (58), 91 (12), 70 (16), 69 (17), 55 (23), 41 (14). $[\alpha]_D^{20}$ = + 91.1 (*c* = 0.320, $CHCl_3$).

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-[1-(4-methoxyphenyl)ethylidene]pyrrolidin-1-amine ((*S*)-L_H2)

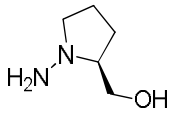


(*S*)-2-[(Diphenylphosphino)methyl]pyrrolidin-1-amine (**(*S*)-114**, 167 mg, 587 µmol, 1.0 eq.) and *para*-methoxyacetophenone (106 mg, 706 µmol, 2.2 eq.) were mixed in abs. toluene (4 mL) in a flame-dried Young tube charged with molecular sieves. A tip of a spatula of *para*-toluenesulfonic acid was added and the resulting mixture was heated at reflux for 2 days. The solids were then filtered of and the solvent was evaporated *in vacuo*. The crude was purified by column chromatography on silica gel (2 x 15 cm), eluting with cyclohexane/ethyl acetate (19:1) to afford product **(*S*)-L_H2** (41.0 mg, 98.4 µmol, 17%), as a colorless semisolid.

$C_{26}H_{29}N_2OP$ (416.50 g·mol^{-1}):
R_f = 0.20 (SiO_2, cyclohexane/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.70 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, OPh-3/5-*H*), 7.58-7.51 (m, 2 H, PPh-*o*-*H*), 7.47-7.40 (m, 2 H, PPh'-*o*-*H*), 7.38-7.23 (m, 6 H, PPh/Ph'-*H*), 6.84 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, OPh-2/6-*H*), 3.83 (s, 3 H, OCH_3), 3.43-3.26 (m, 2 H, Pyr-2-*H* and Pyr-5-*H*H'), 2.64 ("dt", *J* = 14, 3.3 Hz, 1 H, C*H*H'P), 2.45-2.35 (m, 1 H, Pyr-5-H*H'*), 2.17-2.03 (m, 5 H, CH*H'*P, Pyr-*H* and CH_3), 1.96-1.74 (m, 2 H, Pyr-*H*), 1.72-1.58 (m, 1 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 160.3 (s, OPh-1-*C*), 157.5 (s, *C*=N), 140.0 (d, $^1J_{C,P}$ = 13 Hz, PPh-*i*-*C*), 139.4 (d, $^1J_{C,P}$ = 14 Hz, PPh'-*i*-*C*), 132.9 (d, $^2J_{C,P}$ = 19 Hz, PPh-*o*-*C*H), 132.8 (d, $^2J_{C,P}$ = 19 Hz, PPh'-*o*-*C*H), 132.2 (s, OPh-4-*C*), 128.4-128.1 (m, PPh/PPh'-*C*H), 127.4 (s, OPh-3/5-*C*H), 113.4 (s, OPh-2/6-*C*H), 65.5 (d, $^2J_{C,P}$ = 18 Hz, Pyr-2-*C*H), 55.3 (s, O*C*H$_3$), 53.9 (s, Pyr-5-*C*H$_2$), 34.2 (d, $^1J_{C,P}$ = 12 Hz, *C*H$_2$P), 30.0 (d, $^3J_{C,P}$ = 7.2 Hz, Pyr-3-*C*H$_2$), 22.3 (s, Pyr-4-*C*H$_2$), 15.9 (s, *C*H$_3$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 22.2 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 2997w, 2954m, 2933m, 2833m, 1735m, 1606m, 1510s, 1433m, 1360m, 1308m, 1247s, 1174m, 1089w, 1032m, 831m, 739m, 696m cm^{-1}. **MS** (ESI): *m/z* (%) = 418 (30), 417 (100, $[M + H]^+$), 297 (21),

295 (56), 282 (17), 228 (19), 216 (49), 172 (37), 161 (70), 156 (24). Partial oxidation was observed while measuring. $[\alpha]_D^{20}$ = + 311 (*c* = 0.270, $CHCl_3$).

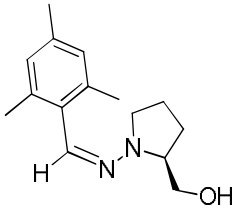
(*S*)-(1-Aminopyrrolidin-2-yl)methanol ((*S*)-131)



A solution of (*S*)-(1-nitrosopyrrolidin-2-yl)methanol[118] (640 mg, 4.92 mmol, 1.0 eq.) in abs. tetrahydrofuran (2 mL) was added drop wise to a suspension of $LiAlH_4$ (380 mg, 10.0 mmol, 2.0 eq.) in abs. tetrahydrofuran (17 mL) at 0°C in an ice bath, under argon atmosphere. The mixture was allowed to stir at 0°C for 30 minutes and then at room temperature for 3 hours. Aqueous saturated Na_2SO_4 (40 mL) was added drop wise at 0°C and the biphasic mixture was allowed to stir for 15 minutes at room temperature, where it turned colorless. The solids were filtered off and washed with tetrahydrofuran (3 x 20 mL). The filtrate was concentrated under reduced pressure to afford **(*S*)-131** as a colorless solid, which was used in the next step without further purification.

$C_5H_{12}N_2O$ (116.16 g·mol^{-1}):
^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.60-4.61 (m, 2 H, N*H*$_2$), 3.80-3.72 (m, 1 H, C*H*H'O), 3.65-3.57 (m, 1 H, CH*H'*O), 3.30-3.21 (m, 1 H, Pyr-2-*H*), 3.20-3.08 (m, 1 H, O*H*), 2.57-2.47 (m, 1 H, Pyr-5-*H*H'), 2.33-2.23 (m, 1 H, Pyr-5-H*H'*), 1.86-1.71 (m, 3 H, Pyr-*H*), 1.48-1.36 (m, 1 H, Pyr-*H*) ppm. The spectroscopic data were consistent with those reported.[136]

(*S*)-{1-[(2,4,6-Trimethylbenzylidene)amino]pyrrolidin-2-yl}methanol ((*S*)-134)



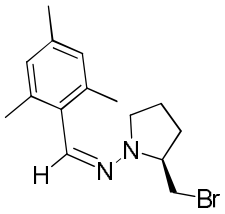
2,4,6-Trimethylbenzaldehyde (400 µL, 2.71 mmol, 1.6 eq.) and (*S*)-(1-aminopyrrolidin-2-yl)methanol (**(*S*)-131**, 191 mg, 1.64 mmol, 1.0 eq.) were mixed in abs. toluene (6 mL) and

[136] S. E. Denmark, J. P. Edwards, T. Weber, D. W. Piotrowski, Tetrahedron: Asymmetry, **2010**, *21*, 1278-1302.

heated at reflux overnight. The mixture was reduced to dryness under reduced pressure and purified by column chromatography on silica gel (4 x 15 cm), eluting with cyclohexane/ethyl acetate (9:1). The title compound was obtained as a colorless semisolid (199 mg, 808 µmol, 49%).

$C_{15}H_{22}N_2O$ (246.35 g·mol^{-1}):
R_f = 0.12 (SiO_2, cyclohexane/ethyl acetate 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.42 (s, 1 H, C*H*=N), 6.86 (s, 2 H, Mes-*H*), 3.92-3.82 (m, 1 H, O*H*), 3.80-3.64 (m, 2 H, Pyr-2-*H* and C*H*H'O), 3.62-3.47 (m, 2 H, CH*H'*O and Pyr-5-*H*H'), 3.07-2.96 (m, 1 H, Pyr-5-H*H'*), 2.38 (s, 6 H, Mes-2/6-H_3), 2.27 (s, 3 H, Mes-4-H_3), 2.12-1.90 (m, 3 H, Pyr-*H*), 1.68-1.55 (m, 1 H, Pyr-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ = 136.9 (s, Mes-4-*C*), 136.2 (s, Mes-2/6-*C*), 134.6 (s, *C*H=N), 130.5 (s, Mes-1-*C*), 129.5 (s, Mes-3/5-*C*H), 66.7 (s, *C*H_2O), 64.6 (Pyr-2-*C*H), 48.8 (Pyr-5-*C*H_2), 25.8 (s, Pyr-3-*C*H_2), 22.0 (s, Pyr-4-*C*H_2), 21.3 (s, Mes-2/6-*C*H_3), 21.1 (s, Mes-4-*C*H_3) ppm. **IR** (neat): $\tilde{\nu}$ = 3346m, 3261m, 2949m, 2914m, 2875m, 2808m, 1679m, 1610m, 1583m, 1431s, 1369s, 1339s, 1298m, 1236m, 1194m, 1141m, 1105m, 1020s, 993m, 889s, 854s, 729m cm^{-1}. **MS** (ESI): *m/z* (%) = 248 (17), 247 (100, [M + H]$^+$), 235 (27), 229 (11). $[\alpha]_D^{20}$ = − 147 (*c* = 1.10, $CHCl_3$).

(*S*)-2-(Bromomethyl)-*N*-(2,4,6-trimethylbenzylidene)pyrrolidin-1-amine ((*S*)-135)

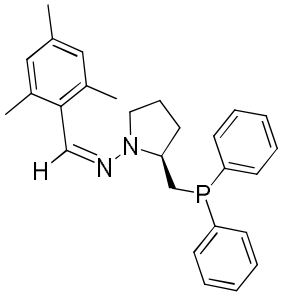


(*S*)-{1-[(2,4,6-Trimethylbenzylidene)amino]pyrrolidin-2-yl}methanol (**(*S*)-134**, 160 mg, 649 µmol, 1.0 eq.) and tetrabromomethane (323 mg, 974 µmol, 1.5 eq.) were mixed in dichloromethane (7 mL) at 0 °C in an ice bath. Triphenylphosphine (356 mg, 976 µmol, 1.5 eq.) was added and the resulting yellowish reaction mixture was stirred at room temperature for 3 hours. The mixture was then reduced to dryness under rotatory evaporation. The crude was purified by column chromatography on silica gel (4 x 17 cm), eluting with cyclohexane/ethyl acetate (100:0 → 19:1) to afford product **(*S*)-135** (139 mg, 449 mmol, 69%).

$C_{15}H_{21}BrN_2$ (309.24 g·mol^{-1}):

R_f = 0.61 (SiO_2, cyclohexane/ethyl acetate 19:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.42 (s, 1 H, C*H*=N), 6.85 (s, 2 H, Mes-*H*), 3.77-3.66 (m, 2 H, Pyr-2-*H* and C*H*H'Br), 3.58-3.45 (m, 2 H, CH*H'*P and Pyr-5-*H*H'), 3.10-3.00 (m, 1 H, Pyr-5-H*H'*), 2.39 (s, 6 H, Mes-2/6-H_3), 2.26 (s, 3 H, Mes-4-H_3), 2.16-1.81 (m, 4 H, Pyr-*H*) ppm.

(*S*)-2-[(Diphenylphosphino)methyl]-*N*-(2,4,6-trimethylbenzylidene)pyrrolidin-1-amine ((*S*)-L_H4)



To a solution of (*S*)-2-(bromomethyl)-*N*-(2,4,6-trimethylbenzylidene)pyrrolidin-1-amine **((*S*)-135**, 120 mg, 388 µmol, 1.0 eq.) in abs. tetrahydrofuran (2 mL) was added under argon atmosphere a 0.5 M solution of potassium diphenylphosphide in tetrahydrofuran (1.00 mL, 500 µmol, 1.3 eq.) at 0 °C. The reaction mixture was allowed to stir at 0 °C for 1 hour before the solvent was removed *in vacuo*. The residue was purified by column chromatography on silica gel (3 x 17 cm), eluting with cyclohexane/ethyl acetate (30:1). The product **(*S*)-L_H4** was isolated as a colorless semisolid (155 mg, 374 µmol, 96%).

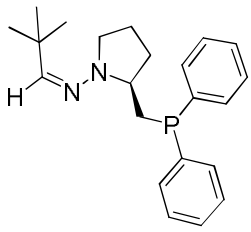
Compound **(*S*)-L_H4** (62%) was as well prepared according to **general procedure 10** from **(*S*)-114** and 2,4,6-trimethylbenzaldehyde.

$C_{27}H_{31}N_2P$ (414.52 g·mol^{-1}):

R_f = 0.25 (SiO_2, cyclohexane/ethyl acetate 30:1). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.55-7.48 (m, 2 H, Ph-*o*-*H*), 7.47-7.39 (m, 2 H, Ph'-*o*-*H*), 7.37-7.26 (m, 7 H, Ph/Ph'-*H* and NC*H*), 6.83 (s, 2 H, Mes-*H*), 3.48-3.34 (m, 2 H, Pyr-2-*H* and Pyr-5-*H*H'), 3.03 ("dt", *J* = 13, 3.5 Hz, 1 H, C*H*H'P), 2.98-2.89 (m, 1 H, Pyr-5-H*H'*), 2.37 (s, 6 H, Mes-2/6-CH_3), 2.25 (s, 3 H, Mes-4-CH_3), 2.12-1.97 (m, 3 H, CH*H'*P, Pyr-3-*H*H' and Pyr-4-*H*H'), 1.97-1.84 (m, 1 H, Pyr-4-H*H'*), 1.77-1.64 (m, 1 H, Pyr-3-H*H'*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 139.7 (d, $^1J_{C,P}$ = 13 Hz, Ph-*i*-*C*), 138.6 (d, $^1J_{C,P}$ = 14 Hz,

Ph'-*i*-*C*), 136.0 (s, Mes-4-*C*), 135.9 (s, Mes-2/6-*C*), 132.9 (d, $^{2}J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.9 (s, *C*H=N), 132.6 (d, $^{2}J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 130.9 (s, Mes-1-*C*), 129.3 (s, Mes-3/5-*C*H), 128.6 (s, Ph-*p*-*C*H), 128.4 (d, $^{3}J_{C,P}$ = 6.9 Hz, Ph-*m*-*C*H), 128.4 (s, Ph'-*p*-*C*H), 128.3 (d, $^{3}J_{C,P}$ = 6.6 Hz, Ph'-*m*-*C*H), 62.2 (d, $^{1}J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 48.2 (s, Pyr-5-*C*H$_2$), 33.6 (d, $^{1}J_{C,P}$ = 13 Hz, *C*H$_2$P), 30.1 (d, $^{3}J_{C,P}$ = 6.5 Hz, Pyr-3-*C*H$_2$), 21.8 (s, Pyr-4-*C*H$_2$), 21.5 (s, Mes-2/6-*C*H$_3$), 20.7 (s, Mes-4-*C*H$_3$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 22.7 (s) ppm. **IR** (neat): $\tilde{\nu}$ = 3069w, 2961m, 2911m, 2850w, 1584w, 1480m, 1457m, 1432s, 1336w, 1319m, 1259w, 1240w, 1197w, 1164w, 1120m, 1094m, 1027m, 743m, 674m cm^{-1}. **MS** (ESI): *m/z* (%) = 415 (100, $[M + H]^+$). $[\alpha]_D^{20}$ = − 11.2 (*c* = 0.501, $CHCl_3$).

(*S*)-*N*-(2,2-Dimethylpropylidene)-2-[(diphenylphosphino)methyl]pyrrolidin-1-amine ((*S*)-L$_H$5)



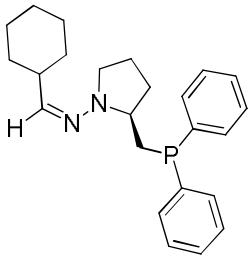
Product **(*S*)-L$_H$5** (51%), isolated as a colorless semisolid, was prepared according to **general procedure 10** from **(*S*)-114** and trimethylacetaldehyde.

$C_{22}H_{29}N_2P$ (352.45 g·mol^{-1}):

R$_f$ = 0.22 (SiO_2, cyclohexane/ethyl acetate 30:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.60-7.53 (m, 2 H, Ph-*o*-*H*), 7.46-7.38 (m, 2 H, Ph'-*o*-*H*), 7.38-7.24 (m, 6 H, Ph/Ph'-*H*), 6.50 (s, 1 H, C*H*=N), 3.29-3.21 (m, 1 H, Pyr-5-*H*H'), 3.15-3.04 (m, 1 H, Pyr-2-*H*), 3.01 ("dt", *J* = 13, 3.1 Hz, 1 H, C*H*H'P), 2.63-2.53 (m, 1 H, Pyr-5-H*H'*), 2.04-1.86 (m, 3 H, CH*H'*P, Pyr-3-*H*H' and Pyr-4-*H*H'), 1.86-1.73 (m, 1 H, Pyr-4-H*H'*), 1.66-1.52 (m, 1 H, Pyr-3-H*H'*), 1.07 (s, 9 H, *t*Bu-*H$_3$*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 146.8 (s, *C*H=N), 140.1 (d, $^{1}J_{C,P}$ = 13 Hz, Ph-*i*-*C*), 138.7 (d, $^{1}J_{C,P}$ = 14 Hz, Ph'-*i*-*C*), 133.0 (d, $^{2}J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.6 (d, $^{2}J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.5 (s, Ph-*p*-*C*H), 128.4 (d, $^{3}J_{C,P}$ = 6.7 Hz, Ph-*m*-*C*H), 128.3 (d, $^{3}J_{C,P}$ = 6.6 Hz, Ph'-*m*-*C*H), 128.3 (s, Ph'-*p*-*C*H), 62.6 (d, $^{2}J_{C,P}$ = 20 Hz, Pyr-2-*C*H), 49.0 (s, Pyr-5-*C*H$_2$), 34.5 (s, *t*Bu-*C*), 33.0 (d, $^{1}J_{C,P}$ = 12 Hz, *C*H$_2$P), 30.0 (d, $^{3}J_{C,P}$ = 5.7 Hz, Pyr-3-*C*H$_2$), 28.2 (s, *t*Bu-*C*H$_3$), 21.4 (s, Pyr-4-*C*H$_2$) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 22.4

(s) ppm. **IR** (neat): $\tilde{\nu}$ = 2953m, 2898m, 2862m, 2820m, 1593m, 1435s, 1362m, 1371m, 1186m, 1117m, 1109m, 1070m, 1027m, 736s, 692s cm^{-1}. **MS** (ESI): *m/z* (%) = 353 (36, $[M + H]^+$), 334 (23), 333 (100). Partial oxidation was observed while measuring. $[\alpha]_D^{20}$ = − 67.8 (*c* = 0.310, $CHCl_3$).

(*S*)-*N*-(Cyclohexylmethylene)-2-[(diphenylphosphino)methyl]pyrrolidin-1-amine ((*S*)-L_H6)



Product **(*S*)-L_H6** (49%), isolated as a colorless semisolid, was prepared according to **general procedure 10** from **(*S*)-114** and cyclohexanecarboxaldehyde.

$C_{24}H_{31}N_2P$ (378.49 $g \cdot mol^{-1}$):

R_f = 0.23 (SiO_2, cyclohexane/ethyl acetate 30:1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.57-7.49 (m, 2 H, Ph-*o*-*H*), 7.47-7.38 (m, 2 H, Ph'-*o*-*H*), 7.37-7.24 (m, 6 H, Ph/Ph'-*H*), 6.43 ("d", 1 H, C*H*=N), 3.28-3.19 (m, 1 H, Pyr-5-*H*H'), 3.17-3.07 (m, 1 H, Pyr-2-*H*), 2.95-2.87 (m, 1 H, C*H*H'P), 2.64-2.52 (m, 1 H, Pyr-5-H*H'*), 2.17-2.06 (m, 1 H, Cy-1-*H*), 2.06-1.53 (m, 10 H, CH*H'*P, Pyr-*H* and Cy-*H*), 1.38-1.11 (m, 5 H, Cy-*H*) ppm. **^{13}C{^{1}H} NMR** (101 MHz, CD_2Cl_2): δ = 144.3 (s, *C*H=N), 140.3-139.3 (br, Ph-*i*-*C*), 139.0-138.0 (br, Ph'-*i*-*C*), 133.1 (d, $^2J_{C,P}$ = 19 Hz, Ph-*o*-*C*H), 132.9 (d, $^2J_{C,P}$ = 19 Hz, Ph'-*o*-*C*H), 128.9-127.9 (m, Ph/Ph'-*C*H), 62.4 (br d, $^2J_{C,P}$ = 21 Hz, Pyr-2-*C*H), 49.6 (s, Pyr-5-*C*H_2), 41.4 (s, Cy-*C*H), 33.2 (br d, $^1J_{C,P}$ = 13 Hz, *C*H_2P), 31.4 (br d, $^3J_{C,P}$ = 5.5 Hz, Pyr-3-*C*H_2), 30.1 (s, Cy-*C*H_2), 26.3 (s, Cy-*C*H_2), 25.9 (br s, Cy-*C*H_2), 21.5 (br s, Pyr-4-*C*H_2) ppm. **^{31}P{^{1}H} NMR** (162 MHz, CD_2Cl_2): δ = – 19.9/− 22.2* (s) ppm. In the ^{31}P NMR spectra the title compound can be seen as a mixture of rotamers in a ratio close to 1:5. **IR** (neat): $\tilde{\nu}$ = 2920m, 2849m, 1373m, 1229m, 1206m, 1089m, 783m, 738m, 696m cm^{-1}. **MS** (ESI): *m/z* (%) = 380 (23), 379 (100, $[M + H]^+$), 235 (18), 193 (25), 149 (12), 130 (11). $[\alpha]_D^{20}$ = − 36.4 (*c* = 0.420, $CHCl_3$).

6.8
Hydrogenation Reactions: Procedures and Analytical Data

6.8.1
General Information, Working Techniques, and Standard Procedures

General Information:

The product yields obtained in the hydrogenation of any substrate presented in this thesis were determined by GC analysis and the products were not isolated.

Working Techniques:

The hydrogenation experiments were set up in a glove box, except otherwise noted below the respective table showing the hydrogenation results. In these cases the hydrogenations were prepared in air. The standard procedure is described below. When the temperature, the concentration, the reaction time, the pressure (5 bar) or the solvent was varied, the same procedure was followed taking into account the changes in reaction conditions. For reactions at elevated temperature the autoclave containing the reaction vials was immersed in a pre-heated oil bath for 5 minutes prior to the exposure to hydrogen. The solvents used for hydrogenation experiments were stored over aluminium oxide and filtered through a syringe filter prior to usage.

Standard procedure for catalytic hydrogenations at elevated pressure (50 bar):

The preparation of the reactions was carried out in a glove box under inert atmosphere. A stock solution of the individual ligand and $[Ir(cod)_2]BAr_F$ (1:1) or of the precatalyst was prepared in dichloromethane (5 mM in precatalyst). The substrate (250 µmol) was weighed into a separate vial and 0.5 mL of the stock solution (1 mol% of precatalyst) were added. A stir bar was added and four vials (1.5 mL) were placed into a 60-mL autoclave (Premex AG, Lengnau, Switzerland) which was closed in the glove box. The autoclave was purged, pressurized with H_2 gas (Carbagas, Switzerland, 99.995%) and placed on a stirring plate. The mixtures were stirred at room temperature for 2 hours. After pressure release, the solution was concentrated in a stream of nitrogen and taken up in *n*-heptane (3 mL) and filtered through a short plug of silica gel (0.5 x 6 cm), eluting

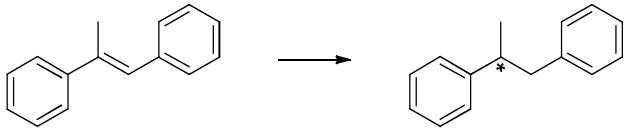
with *n*-heptane/isopropanol (7:3). The filtrates were analyzed by GC and HPLC (see below for detailed analytical procedures).

Standard procedure for catalytic hydrogenations at ambient pressure:

The preparation of the reactions was carried out in a glove box under inert atmosphere and the reaction mixtures were prepared like in the procedure described above. The four vials (1.5 mL) were then placed into a flask equipped with a 24/40 joint which was closed with a rubber septum. A H_2-filled balloon equipped with a needle was put on the septum, the flask was flushed with H_2 by pulling vacuum and placed on a stirring plate. The mixtures were stirred at room temperature for the indicated time. After pressure release, the workup and analysis were carried out as described above.

6.8.2
Hydrogenation Substrates and Products

(*E*)-1,2-Diphenyl-1-propene (S1)



S1 **P1**

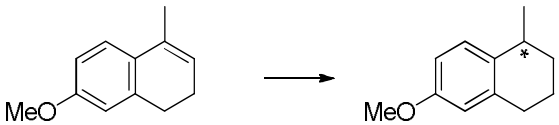
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[60a]

HPLC (Daicel Chiracel OJ, *n*-heptane/isopropanol 99:1, 0.5 mL·min^{-1}, 20 °C, 212 nm): t_R = 14.1 min (**(*R*)-P1**), t_R = 23.1 min (**(*S*)-P1**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 18.2 min (**P1**), t_R = 21.0 min (**S1**).

Substrate **S1** is commercially available.

6-Methoxy-1-methyl-3,4-dihydronaphthalene (S2)



S2 **P2**

The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[60a]

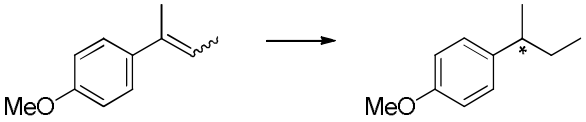
HPLC* (Daicel Chiracel OD-H, *n*-heptane 100%, 0.5 mL·min^{-1}, 20 °C, 212 nm): t_R = 20.4 min (**(*R*)-P2**), t_R = 27.0 min (**(*S*)-P2**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 16.9 min (**P1**), t_R = 18.3 min (**S1**).

Substrate **S2** was synthesized according to the reported procedure.[137]

[137] P. Schnider, Dissertation, University of Basel, **1996**, pp.149-149.

(*E*)- and (Z)-2-(4-methoxyphenyl)-2-butene ((*E*)- and (*Z*)-S3)



(*E*)- or (*Z*)-S3 P3

The enantiomeric excess was determined by HPLC or GC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[60a]

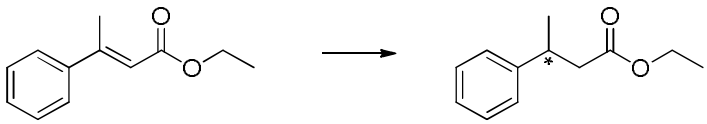
HPLC* (Daicel Chiracel OD-H, *n*-heptane 100%, 0.5 mL·min^{-1}, 20 °C, 220 nm): t_R = 12.9 min (**(*S*)-P3**), t_R = 14.3 min (**(*R*)-P3**).

GC* (*Chiraldex* γ-cyclodextrin TFA G-TA, 0.25 mm x 0.12 µm x 30 m, 60 kPa H_2, 60 °C/30 min, 5 °C·min^{-1}, 100 °C, 20 °C·min^{-1}, 160 °C/10 min) : t_R = 38.6 min (**(*R*)-P3**), t_R = 38.4 min (**(*S*)-P3**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 11.9 min (**P3**), t_R = 11.8 min (**(*Z*)-S3**), t_R = 14.2 min (**(*E*)-S3**).

Substrates **(*E*)-** and **(*Z*)-S3** were synthesized according to the reported procedure.[138]

(*E*)-Ethyl 3-phenylbut-2-enoate (S4)



S4 P4

The enantiomeric excess was determined by GC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[60a]

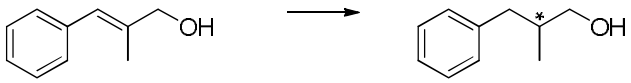
GC* (*Chiraldex* γ-cyclodextrin TFA G-TA, 0.25 mm x 0.12 µm x 30 m, 100 kPa H_2, 85 °C/50 min, 10 °C·min^{-1}, 160 °C/10 min) : t_R = 41.4 min (**(*R*)-P4**), t_R = 43.2 min (**(*S*)-P4**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 15.0 min (**P4**), t_R = 17.2 min (**S4**).

Substrate **S4** is commercially available.

[138] P. Schnider, Dissertation, University of Basel, **1996**, pp.147-147.

(*E*)-2-Methyl-3-phenylprop-2-en-1-ol (**S5**)



S5 **P5**

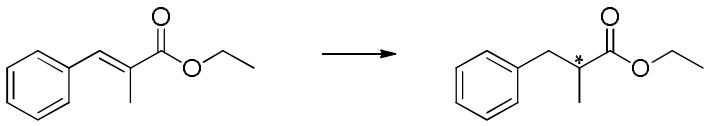
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase.[139] The conversion was determined by GC analysis.[60a]

HPLC* (Daicel Chiracel OD-H, *n*-heptane/isopropanol 95:5, 0.5 mL·min^{-1}, 40 °C, 205 nm): t_R = 14.8 min (**(*R*)-P5**), t_R = 16.8 min (**(*S*)-P5**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 14.0 min (**P5**), t_R = 15.7 min (**S5**).

Substrate **S5** is commercially available.

(*E*)-Ethyl 2-methyl-3-phenylacrylate (**S6a**)



S6a **P6a**

The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase.[140] The conversion was determined by GC analysis.[95a]

HPLC* (Daicel Chiracel OB-H, *n*-heptane 100%, 0.5 mL·min^{-1}, 20 °C, 210 nm): t_R = 22.7 min (**(*R*)-P6a**), t_R = 25.3 min (**(*S*)-P6a**).

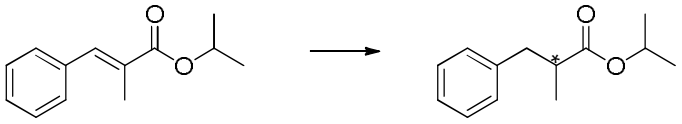
GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 14.5 min (**P6a**), t_R = 17.2 min (**S6a**).

The synthesis of substrate **S6a** is reported.[95a]

[139] The absolute configuration of the products was assigned according to: G. Fronza, C. Fuganti, S. Serra, *Eur. J. Org. Chem.* **2009**, 6160-6171.

[140] The absolute configuration of the products was assigned according to: D. J. Shermer, P. A. Slatford, D. D. Edney, J. M. J. Williams, *Tetrahedron: Asymmetry* **2007**, *18*, 2845-2848.

(*E*)-Isopropyl 2-methyl-3-phenylacrylate (**S6b**)



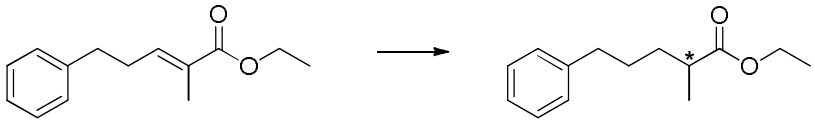
S6b **P6b**

The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase the absolute configuration of the products was assigned by correlation with previously reported data.[80] The conversion was determined by GC analysis.

HPLC* (Daicel Chiracel OB-H, *n*-heptane 100%, 0.5 mL·min^{-1}, 20 °C, 210 nm): t_R = 15.2 min (**(*R*)-P6b**), t_R = 17.1 min (**(*S*)-P6b**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 15.3 min (**P6b**), t_R = 18.5 min (**S6b**).

(*E*)-Ethyl 2-methyl-5-phenylpent-2-enoate (**S7**)



S7 **P7**

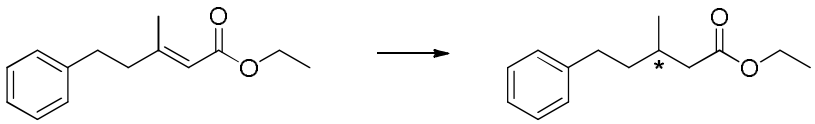
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[80]

HPLC* (Daicel Chiracel OB-H, *n*-heptane/isopropanol 97:3, 0.8 mL·min^{-1}, 20 °C, 210 nm): t_R = 9.7 min ((+)-**P7**), t_R = 13.8 min ((–)-**P7**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 19.1 min (**P7**), t_R = 20.9 min (**S7**).

The synthesis of substrate **S7** is reported.[80]

(*E*)-Ethyl 3-methyl-5-phenylpent-2-enoate (**S8**)



S8 **P8**

The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase

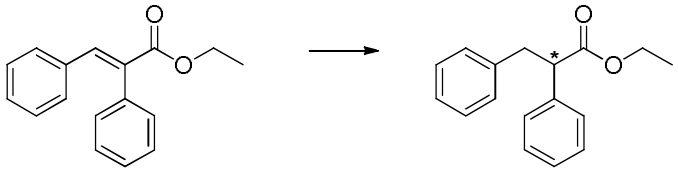
and the conversion was determined by GC analysis.[80,95]

HPLC* (Daicel Chiracel OJ-H, *n*-heptane/isopropanol 98:2, 0.5 mL·min^{-1}, 20 °C, 210 nm): t_R = 15.2 min (**(*R*)-P8**), t_R = 16.3 min (**(*S*)-P8**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 19.5 min (**P8**).

The synthesis of substrate **S8** is reported.[80,95]

(*E*)-Ethyl 2,3-diphenylacrylate (**S9**)



S9 **P9**

The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the conversion was determined by GC analysis.

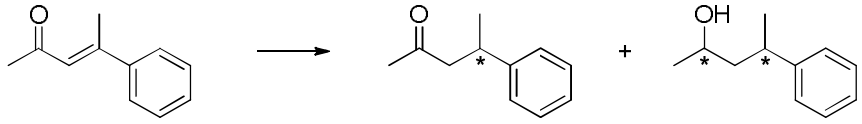
HPLC* (Daicel Chiracel OD-H, *n*-heptane/isopropanol 99:1, 0.5 mL·min^{-1}, 20 °C, 254 nm): t_R = 12.6 min ((–)-**P9**), t_R = 15.0 min ((+)-**97**). $[\alpha]_D^{20}$ = + 50.7 (*c* = 1.31, $CHCl_3$) for 56% *ee*.

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 24.3 min (**P9**), t_R = 25.9 min (**S9**).

(*E*)-Ethyl 2,3-diphenylacrylate (**S9**): α-phenylcinnamic acid (2.00 g, 8.92 mmol) was mixed with ethanol (3 mL), a drop of H_2SO_4 and a tip of a spatula of $MgSO_4$ were added, before the mixture was heated at reflux overnight. The excess ethanol was evaporated, the residue was dissolved in diethyl ether (30 mL) and washed with aqueous saturated $NaHCO_3$ (2 x 30 mL). The ethereal solution was dried over $MgSO_4$ and reduced to dryness. Column chromatography on silica gel (4 x 18 cm), eluting with cyclohexane/ethyl acetate (19:1), afforded the compound as an oil (1.73 g, 6.85 mmol, 77%). The spectroscopic data were consistent with those reported.[141]

[141] L. Boros, K. Felföldi, I. Pálinko, *Molecules* **2004**, *9*, 256-263.

(*E*)-4-Phenylpent-3-en-2-one (**S10a**)



S10a **P10a** **P10'**

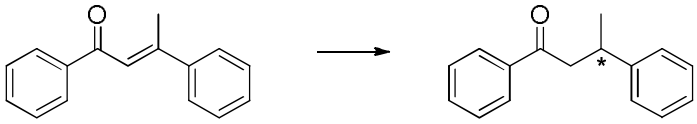
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the absolute configuration of the products was assigned by correlation with previously reported data.[34d] The conversion was determined by GC analysis.

HPLC* (Daicel Chiracel AS-H, *n*-heptane/isopropanol 99.3:0.7, 0.5 mL·min^{-1}, 20 °C, 210 nm): t_R = 20.5 min (**(*S*)-P10a**), t_R = 24.7 min (**(*R*)-P10a**) t_R = 26.6/31.2/34.2 min (**P10'**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 13.9 min (**P10a**), t_R = 16.0 min (**S10a**), t_R = 13.7/14.3 min (**P10'**).

The synthesis of substrate **S10a** was carried out according to the reported procedure.[34d]

(*E*)-1,3-Diphenylbut-2-en-1-one (S10b)



S10b **P10b**

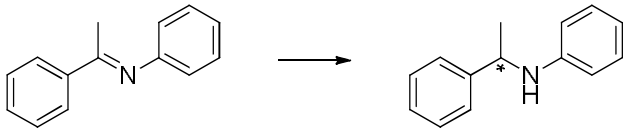
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the absolute configuration of the products was assigned according to previously reported data.[34d] The conversion was determined by GC-analysis.

HPLC* (Daicel Chiracel AD-H, *n*-heptane/isopropanol 97:3, 0.5 mL·min^{-1}, 20 °C, 230 nm): t_R = 13.4 min (**(*S*)-P10b**), t_R = 15.7 min (**(*R*)-P10b**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 25.2 min (**P10b**), t_R = 28.2 min (**S10b**).

The synthesis of substrate **S10b** was carried out according to the reported procedure.[34d]

N-(1-Phenylethylidene)-aniline (S11)



S11 **P11**

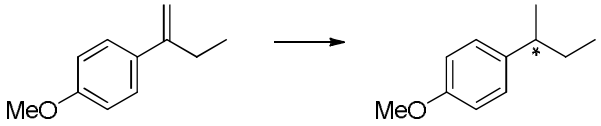
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[60a]

HPLC* (Daicel Chiracel OD-H, *n*-heptane/isopropanol 99:1, 0.5 mL·min^{-1}, 20 °C, 210 nm): t_R = 24.6 min (**(*S*)-P11**), t_R = 33.0 min (**(*R*)-P11**).

GC (Macherey-Nagel Optima 5-Amin, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/8 min, 5 °C·min^{-1}, 250 °C/10 min): t_R = 35.3 min (**P1**), t_R = 36.0 min (**S11**).

Substrate **S11** is commercially available.

2-(4-Methoxyphenyl)-1-butene (S12)



S12 **P3**

The enantiomeric excess was determined by HPLC on a chiral stationary phase and the conversion was determined by GC analysis.[60a]

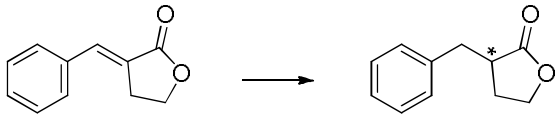
HPLC* (Daicel Chiracel OD-H, *n*-heptane 100%, 0.5 mL·min^{-1}, 20 °C, 220 nm): t_R = 12.9 min (**(*S*)-P3**), t_R = 14.3 min (**(*R*)-P3**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 11.9 min (**P3**), t_R = 13.0 min (**S12**).

Substrate **S12** was synthesized according to the reported procedure.[142]

[142] P. Schnider, Dissertation, University of Basel, **1996**, pp.148-148.

(*E*)-3-Benzylidenedihydrofuran-2(3*H*)-one (**S13**)



S13 **P13**

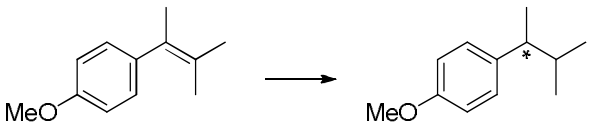
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase.[34e] The conversion was determined by GC analysis.

HPLC* (Daicel Chiracel OB-H, *n*-heptane/isopropanol 90:10, 0.8 mL·min^{-1}, 35 °C, 210 nm): t_R = 21.3 min ((+)-**P13**), t_R = 23.7 min ((−)-**P13**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 22.5 min (**P13**), t_R = 26.5 min (**S13**).

The synthesis of substrate **S13** is reported.[34e]

1-Methoxy-4-(3-methylbut-2-en-2-yl)-benzene (**S16**)



S16 **P16**

The enantiomeric excess was determined by GC analysis on a chiral stationary phase and the conversion was determined by GC analysis.[32]

GC* (*Brechbühler* *β*-cyclodextrin DEtTButSil (SE54), 0.25 mm x 0.25 µm x 25 m, 60 kPa H_2, 80 °C/0 min, 1 °C·min^{-1}, 120 °C/0 min, 10 °C·min^{-1}, 180 °C/2 min): t_R = 14.1 min ((+)-**P16**), t_R = 14.4 min ((−)-**P16**).

GC (Restek Rxt-1701, 0.25 mm x 0.25 µm x 30 m, 60 kPa He, 100 °C/2 min, 7 °C·min^{-1}, 250 °C/10 min): t_R = 13.6 min (**P16**), t_R = 14.1 min (**S16**).

Substrate **S16** was synthesized according to the reported procedure.[32,143]

[143] M. V. Troutman, D. H. Appella, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 4916-4917.

6.9
Allylic Alkylation Reactions: Procedures and Analytical Data

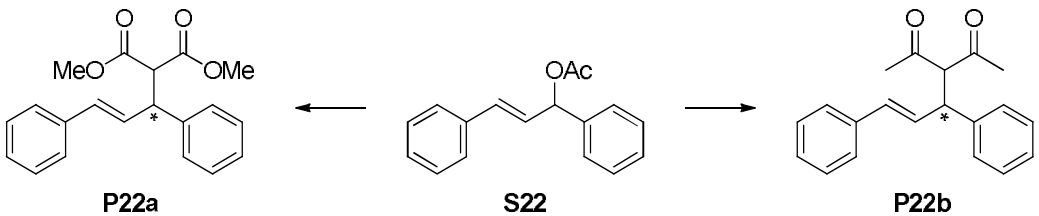
6.9.1
Standard Procedure

Standard procedure for catalytic allylic alkylation reactions:

A solution of $[(\pi\text{-}C_3H_5)PdCl]_2$ (2.50 mol%) and the individual ligand (2.50 mol%) in dichloromethane (2.0 mL) was degassed in a Young tube by three freeze-pump-thaw cycles and afterwards stirred at 50 °C for 2 hours. In a second Young tube the desired allylic alkylation substrate (200-300 μmol, 1.0 eq.) was dissolved in dichloromethane (250 μM). To this solution *N*,*O*-Bis(trimethylsilyl)acetamide (BSA, 3.0 eq.), the nucleophile (**109** or **138**, 3.0 eq.) and catalytic amounts of KOAc were added. After three freeze-pump-thaw cycles the catalyst solution was added *via* syringe and the resulting mixture was stirred at room temperature for the indicated time. After this time, the reaction was diluted with diethyl ether (20 mL) and washed with ice-cold aqueous saturated NH_4Cl (10 mL).The aqueous phase was extracted with diethyl ether (3 x20 mL), the combined organic extracts were dried over MgSO4 and the solvent was removed under reduced pressure. The products were purified by column chromatography on silica gel, eluting with hexanes/ethyl acetate/NEt_3 (18:1:1).[144]

6.9.2
Allylic Alkylation Substrates and Products

Allylic Alkylation of (*E*)-1,3-di-phenylallyl acetate (**S22**)



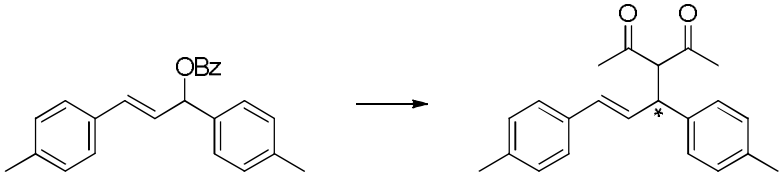
The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase. **HPLC*** (Daicel Chiracel AD-H, *n*-heptane/isopropanol 97:3, 1.0 mL·min^{-1}, 20 °C, 254 nm): t_R = 22.7 min (**(*R*)-P22a**), t_R = 32.8 min (**(*S*)-P22a**).

[144] C. Ebner, Dissertation, University of Basel **2012**, pp 146-146.

HPLC* (Daicel Chiracel AD-H, *n*-heptane/isopropanol 97:3, 0.9 mL·min^{-1}, 20 °C, 254 nm): t_R = 16.3 min (**(*R*)-P22b**), t_R = 18.0 min (**(*S*)-P22b**).

Substrate **S22** is commercially available.

Allylic Alkylation of (*E*)-1,3-di-*para*-tolylallyl benzoate (S23)



S23 **P23**

The enantiomeric excess was determined by HPLC analysis on a chiral stationary phase.[144]

HPLC* (Daicel Chiracel AD-H, *n*-heptane/isopropanol 97:3, 0.9 mL·min^{-1}, 20 °C, 254 nm): t_R = 16.2 min (**(*R*)-P23**), t_R = 17.5 min (**(*S*)-P23**).

The synthesis of substrate **S23** is reported.[144]

6.10 Crystallographic Data

The X-ray structures were measured by DR. MARKUS NEUBURGER and DR. SILVIA SCHAFFNER at the Department of Chemistry of the University of Basel. Data collection was performed with a Nonius KappaCCD, Brucker Kappa Apex2 or Area diffractometer using graphite-monochromated Mo *K*α-radiation. The structure was solved with SIR92[145] and refined with Crystals.[146] Chebychev polynominal weights were used to complete the refinement.[147] Hydrogen were added geometrically. The absolute configuration and enantiopurity was determined by refinement of the flack parameter.[148] Plots were produced using Mercury.

Compound	**(*R*)-C_A1**	[(**(*S*)-L_{U3}15)**Ir(cod)]PF_6	**(S)-C_H6**
molecular formula	$C_{63}H_{54}BF_{24}IrNOP$	$C_{45}H_{47}F_6IrN_2OP_2$	$C_{64}H_{55}BF_{24}IrN_2P$
molecular weight [g·mol^{-1}]	1601.99	1000.04	1542.10
shape	plate	block	block
color	red	orange	orange
temperature [K]	173	123	123
radiation	Mo K_α	Mo K_α	Mo K_α
wavelength [Å]	0.71073	0.71073	0.71073
crystal system	monoclinic	monoclinic	trigonal
space group	P 2_1	P 2_1	P 3_1
crystal size [mm^3]	0.02 x 0.12 0.29	0.13 x 0.17 x 0.23	0.060 x 0.140 x 0.240
a [Å]	12.4504(5)	10.5337(4)	13.0070(3)
b [Å]	17.8211(7)	17.8052(7)	13.0070(3)
c [Å]	14.5518(6)	10.5342(4)	31.8014(8)
α [°]	90	90	90
β [°]	91.605	96.692(2)	90
γ [°]	90	90	120
unit cell volume [Å^3]	3227.5(2)	1962.28(13)	4659.41(19)
Z	2	2	3
F(000)	1588	1000	2298
θ-range for data collection [°]	26.829	39.388	32.575
calculated density [Mg·cm^{-3}]	1.648	1.692	1.649
adsorption coefficient μ [mm^{-1}]	2.288	3.552	2.290
measured reflections	27501	92339	46182
independent reflexions	13056	22164	20770
used reflections	9783	20688	13566
parameter refined	920	515	839
$R^{[a]}$	0.0344	0.0124	0.0452
R_w[b]	0.0505	0.0135	0.0582
goodness-of-fit	1.2318	1.0832	1.0898
Flack parameter	0.004(6)	0.0069(13)	− 0.008(5)

[a] $R = \Sigma||F_0|-|F_C||/\Sigma|F_0|$; [b] $R_w = \{\Sigma[w(F_0-F_C)^2]/\Sigma[w(F_0)^2]\}^{1/2}$

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SUMMARY

Iridium complexes with chiral P,N ligands are highly efficient catalysts for the asymmetric hydrogenation of a broad range of substrates. Since the highest enantioselectivities achieved vary strongly depending on the substrate type, it is important to developed new ligands, which have various features, even if many catalysts have already been designed. Herein were presented various proline-based ligands, which coordinate to iridium in a bidentate fashion involving two different coordinating atoms. First were described proline-based P,O ligands followed by two types of proline-based P,N ligands (Figure 29).

In chapter 2, proline-based P,O ligands were investigated as ligands for the iridium-catalyzed asymmetric hydrogenation. These ligands were clearly identified to coordinate in a bidentate fashion to iridium, forming a seven-membered metallacycle upon binding of both the carbonyl oxygen atom and the phosphorus atom. L-Proline proved to be a convenient enantiopure modular scaffold and allowed to prepare in a few steps a broad library of chiral compounds in good yields, possessing a wide range of steric and electronic properties. Three subclasses of these ligands were developed and investigated: carbamatophosphines, amidophosphines and ureaphosphines.

These P,O ligand/iridium complexes were evaluated in the asymmetric hydrogenation of a series of substrates spanning a range of coordinating properties. Especially trisubstituted functionalized and unfunctionalized alkenes were reduced with good enantioselectivities within short reaction times. Depending on both the structure of the coordinating carbonyl substituent and the phosphine substituents, moderate to high enantioselectivities were achieved. The catalysts, which were identified to allow for the highest enantioselectivities in the asymmetric hydrogenation of routinely tested substrates (*e.g.* (*E*)-1,2-diphenyl-1-propene, (*E*)-ethyl 3-phenylbut-2-enoate, (*E*)-2-methyl-3-phenylprop-2-en-1-ol) were also tested in the asymmetric hydrogenation of more challenging prochiral trisubstituted alkenes, such as *α*,*β*-unsaturated carboxylic esters and ketones. Excellent conversions and enantiomeric excesses up to 95% were obtained when amidophosphines or ureaphosphines were employed as ligands in the iridium-catalyzed asymmetric hydrogenation of trisubstituted *α*,*β*-unsaturated, *α*-substituted carboxylic esters (see Figure 29). Even more impressive is the level of enantioselectivity obtained for *α*,*β*-unsaturated ketones, which were reduced with several catalysts that afforded enantioselectivities much higher than previously reported P,N-based systems.

Inspired by the structure of these P,O ligands, analogous proline-based P,N ligands were investigated. It was thought to combine two features: the well known chelation of P,N ligands to iridium and the proline-based structure. Also these P,N ligands were easily prepared and steric and electronic properties were studied by varying the substituents at the phosphorus atom and the pyrrolidine nitrogen. These P,N ligands form a seven-membered metallacycle when bound to iridium. Previous reports suggest that the size of the metallacycle strongly influences the enantioselectivity of the asymmetric reduction, therefore these ligands were investigated. These novel complexes showed excellent activities in the asymmetric reduction of unfunctionalized and functionalized trisubstituted standard substrates, albeit with slightly lower enantioselectivities than those achieved with P,O ligand/iridium complexes.

Furthermore, a second type of proline-based P,N ligand was investigated (Figure 29). This scaffold involves a hydrazone moiety in combination with a phosphorus donor and forms a six-membered metallacycle, upon binding to iridium. The synthesis of these ligands proved to be more difficult. Only aldhydrazones could be synthesized efficiently and complexed to iridium. These complexes were tested as catalysts for the hydrogenation of alkenes and proved to be quite unstable. Nevertheless, these complexes reduced some substrates with full conversions, but fluctuating enantioselectivities.

Finally, in chapter 5, the proline-based P,O ligands presented in chapter 1 were investigated as chiral ligands for the palladium-catalyzed allylic alkylation reaction. This project was carried out in collaboration with DR. CHRISTIAN EBNER. Good activities were achieved but the enantioselectivities were low and can not compete with previously reported ligands for this transformation.

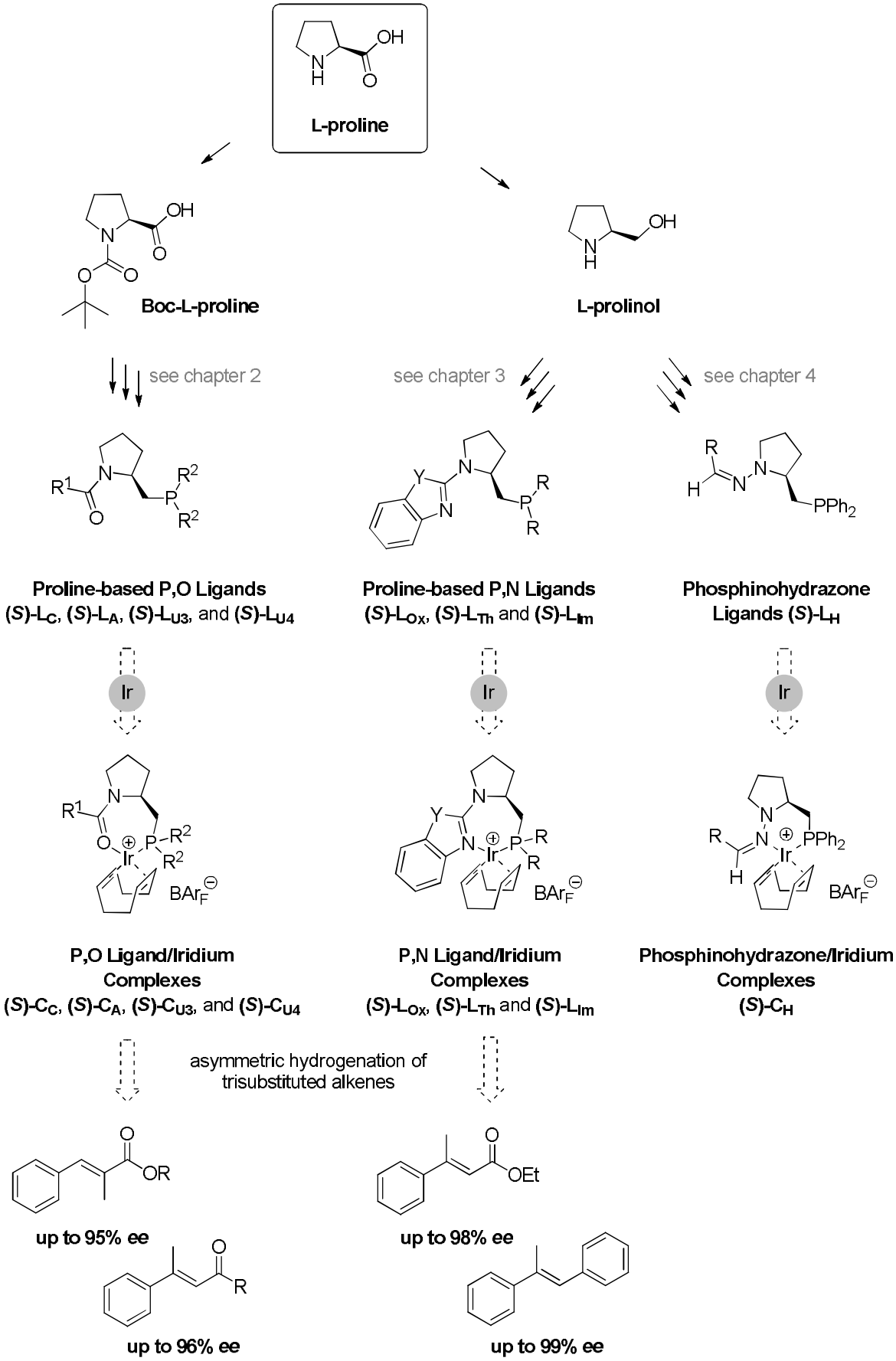

Figure 29. Proline-based ligands and iridium complexes investigated herein.

DENISE RAGEOT

Date of Birth	June 28, 1985
Place of Birth	Basel, Switzerland
Nationality	Swiss, French

EDUCATION AND TRAINING

June 2008-June 2012	**Ph. D. work** under the supervision of Prof. Dr. Andreas Pfaltz University of Basel, Switzerland Thesis: *Chiral proline-Based Ligands for Iridium-Catalyzed Asymmetric Hydrogenation*
Apr 2008	**M. Sc. in Chemistry**, University of Basel, Switzerland
Oct 2007-Apr 2008	Master work under the supervision of Prof. Dr. Andreas Pfaltz University of Basel, Switzerland Thesis: *Amidophosphine Derivatives of Proline: a New Class of P,O Ligands for Iridium(I) Catalyzed Hydrogenation*
Apr-Sep 2007	**Research Intern** under the supervision of Dr. Christina Hebach Novartis Pharma AG, Basel Research: Hit to Lead Optimization of a specific scaffold to improve selective kinase inhibition
Oct 2003-Sep 2006	**B. Sc. in Chemistry**, University of Basel, Switzerland
Oct 2003-Apr 2008	Studies in chemistry at the University of Basel, Switzerland
June 2003	**Baccalauréat** (type S), Lycée J. Mermoz, Saint-Louis, France

AWARDS

Poster Prize, Catalysis Research Laboratory Winter School 2011, Heidelberg, Germany, March 2011
Denise Rageot, Andreas Pfaltz
Ureaphosphines: New P,O Ligands for the Iridium Catalyzed Asymmetric Hydrogenation of Various Olefins.

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2) Adnan Ganić, Denise Rageot, Lars Tröndlin, Andreas Pfaltz, *Chimia* **2012**, 187-191.
Recent Advances in Iridium-Catalyzed Asymmetric Hydrogenation: New Catalysts, Substrates and Applications in Total Synthesis.

1) Denise Rageot, David H. Woodmansee, Benoît Pugin, Andreas Pfaltz, *Angew. Chem. Int. Ed.* **2011**, *50*, 9598-9601; *Angew. Chem.* **2011**, *123*, 9772-9775.
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Highlighted in: *Synfacts* **2012**, *8*, 53-53 and *Chimia* **2011**, *65*, 977-977.

CONFERENCE ABSTRACTS

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4) Denise Rageot, Andreas Pfaltz
Iridium Catalyzed Asymmetric Hydrogenation of Trisubstituted α,β-unsaturated Ketones and Esters using L-Proline derived P,O Ligands.
▪ **4th International Symposium on Advances in Synthetic and Medicinal Chemistry**, St. Petersburg, Russia, August 2011

3) Denise Rageot, Andreas Pfaltz
Ureaphosphines: New P,O Ligands for the Iridium Catalyzed Asymmetric Hydrogenation of Various Olefins (emphasis on substrate scope).
▪ **Catalysis Research Laboratory Winter School 2011**, Heidelberg, Germany, March 2011

2) Denise Rageot, Andreas Pfaltz
Ureaphosphines: New P,O Ligands for the Iridium Catalyzed Asymmetric Hydrogenation of Various Olefins (emphasis on ligand screening).
▪ **30th Regio Symposium**, Mittelwihr, France, September 2010
▪ **Fall Meeting of the Swiss Chemical Society 2010**, Zürich, Switzerland, September 2010
▪ **12th Belgian Organic Synthesis Symposium**, Namur, Belgium, July 2010

1) Denise Rageot, David H. Woodmansee, Andreas Pfaltz
Iridium Complexes with P,O Ligands as New Catalysts for the Asymmetric Hydrogenation of Olefins.
▪ **Fall Meeting of the Swiss Chemical Society 2009**, Lausanne, Switzerland, September 2009
▪ **10th Tetrahedron Symposium**, Paris, France, June 2009

TEACHING EXPERIENCES AND OTHER PROFESSIONAL ACTIVITIES

2009-2010	**Laboratory teaching assistant**, Department of Chemistry, University of Basel, supervision of chemistry, pharmacy or biology students in basic and organic chemistry
2009-2011	Individual supervision of chemistry students in scientific laboratory, Department of Chemistry, University of Basel
Summer 2010	Member of the organizing team of the activities of Department of Chemistry on the occasion of the celebration of the 550 years of the University of Basel: "*Markt des Wissens*" (simple chemistry experiments for children)
Fall 2009	Checking of a procedure to be published in *Organic Syntheses* Andrej Vinogradov, Simon Woodward, *Org. Synth.* **2010**, *87*, 104-114. *Palladium-Catalyzed Cross-Coupling using an Air-Stable Trimethylaluminium Source. Preparation of Ethyl 4-methylbenzoate.*
Feb 2009	Supervision of a *„Schweizer Jugend forscht"* project entitled: *Synthèse et Hydrogénation Homogène Asymétrique d'un Alcène au moyen de différents Complexes Chiraux d'Iridium*

During my education at the University of Basel, I attended lectures given by:

W. Bonrath, E. C. Constable, K. M. Fromm, B. Giese, P. C. Hauser, C. E. Housecroft, J. P. Maier, W. P. Meier, M. Meuwly, M. Oehme, C. Palivan, A. Pfaltz, C. Schönenberger, M. Schwarz, U. Séquin, E. Stulz, A. Vedani, H. Wennemers, H.-J. Wirz, W.-D. Woggon.