Article

P-chirogenic Diphosphazanes with Axially Chiral Substituents and their Use in Rh-catalyzed Asymmetric Hydrogenation

Jan-Ole Moritz, Soumyadeep Chakrabortty, Bernd H. Müller, Anke Spannenberg, and Paul C.J. Kamer

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c01108 • Publication Date (Web): 14 Sep 2020

P-chirogenic Diphosphazanes with Axially Chiral Substituents and their Use in Rh-catalyzed Asymmetric Hydrogenation

Jan-Ole Moritz,‡ Soumyadeep Chakrabortty,‡ Bernd H. Müller, Anke Spannenberg, Paul C. J. Kamer*

Leibniz-Institut für Katalyse e.V., Albert-Einstein-Straße 29a, 18059 Rostock, Germany

Keywords: P-chirogenic, asymmetric catalysis, Rhodium, hydrogenation

Dedicated to Prof. Dr. Uwe Rosenthal on the occasion of his 70th birthday.

Abstract

A convenient synthesis of enantiopure P-chirogenic diphosphazanes incorporating bulky bisphenol and BINOL-derived substituents *via* functionalization of a readily accessible enantiopure lithium phosphinoamide with chlorophosphoridites was developed. Since the product requires no subsequent deprotection, the protocol provides an easy, convenient synthesis of P-chirogenic ligands on gram-scale. The ligands were applied in Rh-catalyzed asymmetric hydrogenation of benchmark substrates furnishing *ee*'s up to 96%.

Introduction

Chiral diphosphines are ubiquitous in asymmetric catalysis. The incorporation of a chiral center or axially chiral fragments into ligand scaffolds is well described in literature.[1,2] However, in most of the catalysts used in this field, the chiral information is located on a carbon and not on the coordinating phosphorus. After the success of Knowles and co-workers in asymmetric hydrogenation with PAMP and DiPAMP,[3] P-chirogenic ligands have gathered more attention. The work of Jugé,[4] Imamoto,[5] Horner,[6] Börner[7] and others have set milestones in the synthesis of P-chirogenic compounds. In the last two decades, examples like MaxPHOS,[8] MaxPHOX,[9a] ThaxPHOS,[9b] QuinoxP*,[10] or TCFP[11] shined light on the potential of ligands incorporating P-chirogenic moieties in asymmetric catalysis. In addition, the development of ligands like BINAP by Noyori[12] and the phosphoramidite MonoPhos by De Vries and Feringa[13a] gave rise to the use of axially chiral ligands in asymmetric catalysis. Another family of P-stereogenic N-phosphine-phosphinite ligands have been developed by Diéguez et al. based on readily available (1*R*,2*S*)-(−)-ephedrine and applied in asymmetric hydrogenation with very promising enantioselectivities up to >99%.[13b] To the best of our knowledge, the potential of the incorporation of P-chirogenic components in combination with axially chiral motifs has not been well explored. The design concept described in here takes this into account (Figure 1) where we combine the successful application of MaxPHOS with the powerful performance of axially chiral BINOL-based phosphites.[13a,c] This concept is based on the work by Krishnamurthy and

co-workers, who described the synthesis of diphosphazanes with an axially chiral BINOL-derived P-component.[14]

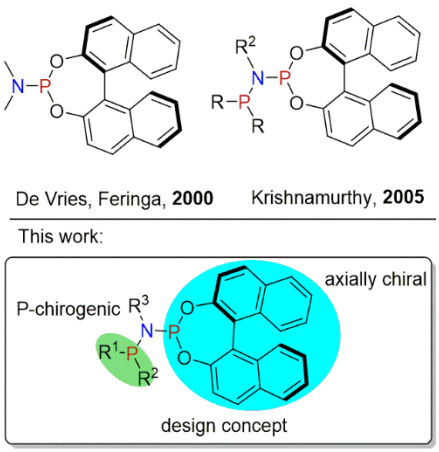


Figure 1 General structure of a PNP ligand incorporation a P-chirogenic center as well as an axially chiral structure compared to previous work by De Vries, Feringa and Krishnamurthy.

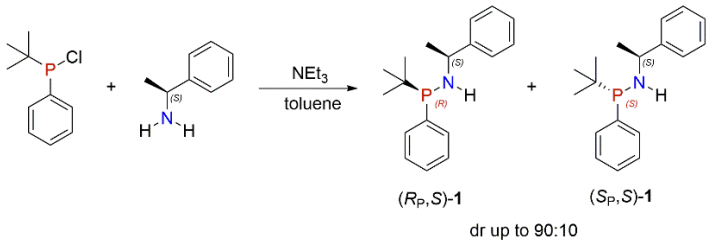
To gain simple access to this motif, a convenient synthesis of an enantiopure and easily functionalizable nucleophilic PN-synthon is needed. Two of such PN building blocks were described by Riera and Verdaguer.[8,15]

Herein, we report a convenient two-step synthesis of both enantiomers of an enantiopure lithium phosphinoamide, useable as nucleophilic PN-synthon, on multi-gram-scale and its functionalization towards diphosphazanes. The ligands have been applied in the Rh-catalyzed asymmetric hydrogenation of alkenes and the cooperativity between the two chiral modules has been investigated.

Results and Discussion

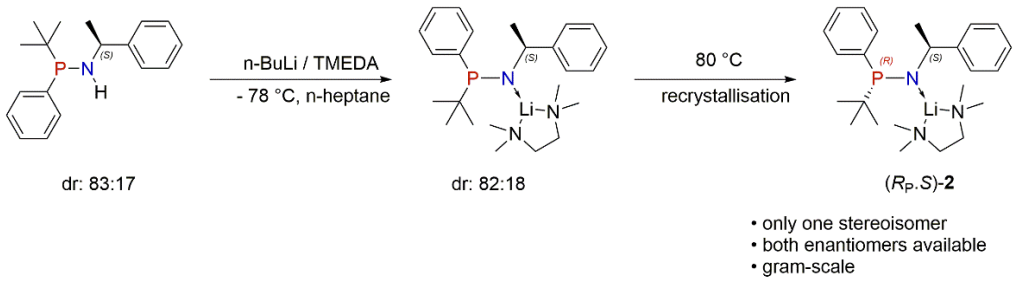
Preparation of the PN-synthon

Kolodyazhnyi et al. described that the base-assisted nucleophilic substitution of (*tert*-butyl)phenylchlorophosphine with enantiopure (*S*)-1-phenylethylamine furnishes a diastereomeric mixture of the corresponding phosphazane **1** with diastereomeric ratios up to 90:10 (Scheme 1). The use of (*R*)- instead of (*S*)-1-phenylethylamine leads to the corresponding opposite diastereomeric mixture.[16]



Scheme 1 Synthesis of P-chirogenic phosphazanes as diastereomeric mixture according to Gryshkun and co-workers.[16]

Reaction of the diastereomeric mixture of (R_P,S)-**1** (major) and (S_P,S)-**1** (minor) with *n*-BuLi in the presence of TMEDA in *n*-heptane at – 78 °C furnished a bright yellow precipitate, which can be dissolved completely upon immediate heating to 80 °C. After cooling down to recrystallize the compound, diastereomerically pure crystals of (R_P,*S*)-**2** were obtained (Scheme 2).



Scheme 2 Synthesis of enantiopure lithium phosphinoamide. Both enantiomers are available.

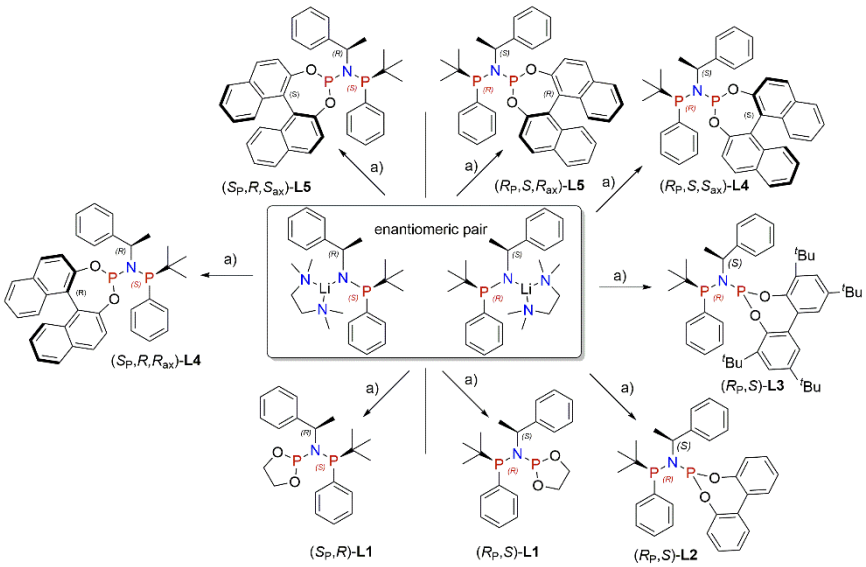
The molecular structure of (R_P,S)-**2** in the solid state revealed the (*R*)-configuration of the phosphorus atom (Figure S 63, for thermal ellipsoid plots of all molecular structures, crystal parameters and refinement metrics see ESI). As intended with the addition of TMEDA, no aggregates were observed and the lithium phosphinoamide forms a well-defined monomeric species (for comparison of lithiation with TMEDA and without see Figures S48 vs S49).

In order to access the enantiomer of (R_P,S)-**2**, (S_P,R)-**2**, the diastereomeric mixture consisting of (S_P,R)-**1** (major) and (R_P,R)-**1** (minor) is used as starting material for the previously described reaction sequence.

Synthesis of PNP-ligands and Coordination Behavior

Generally, **2** can provide easy access to a wide variety of bidentate ligands and was reacted with phosphorochloridites containing bisphenol and BINOL-moieties. Additionally, reaction with 2-chloro-1,3,2-dioxaphospholane was also performed to study the interaction of the P-chirogenic center and the axially chiral BINOL-fragment (Scheme 3). All further modifications

in the ligand backbone, run smoothly at – 78 °C in toluene and the desired product is obtained in high purity after separation from LiCl and the removal of the solvent. All the PNP ligands (**L1-L5**) are characterized by NMR and mass



Scheme 3 Synthesized set of optically pure ligands for Rh-catalyzed asymmetric hydrogenation utilizing stereopure lithium phosphinoamide as PN-building block. Reaction conditions: a) 1.) – 78 °C, 1 eq. of chlorophosphoridite dissolved in toluene is added to 1 eq. of (R_P,S)-**2** or (S_P,R)-**2** (crude) dissolved in toluene; 2.) filtration and removal of solvent.

spectrometry. $^{31}P\{^{1}H\}$ NMR of the ligands shows two signals (doublets) for the phosphine within the range of 55-58 ppm and for the $P(OR)_2$ of 141-147 ppm (Figure S 45). The coupling constant is also in accordance to the $^{2}J_{P\text{-}P}$ constant in the range of 32-38 Hz. Additionally, the thermal stability of the ligands was also investigated. The P-chirogenic moiety is stable at room temperature but tends to epimerize above 80°C, which results in the formation of the other diastereomer as the $P(OR)_2$ moiety and the substituent at the amine remain stereo-chemically fixed (Figure S 46 and S 47).

The crystal structure of (R_P,S)-**L1** reveals (*R*)-configuration of P1 (Figure S 64). Crystals suitable for X-ray analysis of (S_P,R)-**L1** (Figure S 65) were obtained applying the synthetic procedure with (S_P,R)- instead of (R_P,S)-**2** and used for confirmation of the configuration. As expected, the molecular structures of (R_P,S)-**L1** and (S_P,R)-**L1** are enantiomeric and bond lengths and angles differ just slightly. Hence, only the structure of (R_P,S)-**L1** is discussed herein.

The geometrical environment of N1 is planar as indicated by the sum of the relevant bond angles (ΣN1 = 359.6(2)°). Additionally, P1-N1 bond distance (1.7304(16) Å) is longer than the P2-N1 bond (1.6860(16) Å).

The $^{31}P\{^1H\}$ NMR spectrum of the mixture of one equivalent of (R_P,S)-**L1** (dissolved in CH_2Cl_2) and one equivalent of $[Rh(nbd)_2]BF_4$ (also dissolved in CH_2Cl_2) indicates a 2:1 complex with an AA'XX' spin system in which *J*(AX) and *J*(AX') are almost equal as main component (Figure 2). A similar behavior was observed by Vidal-Ferran and co-workers for Rh(I) species ligated by two P-OP ligands.[17] An experiment with a 2:1 ligand to Rh ratio furnished an almost identical NMR spectrum and the AA'XX' spin system was confirmed by simple spin system simulation with coupling constants *J*(AX) and *J*(AX') of 43.1 Hz and 45.0 Hz, respectively.

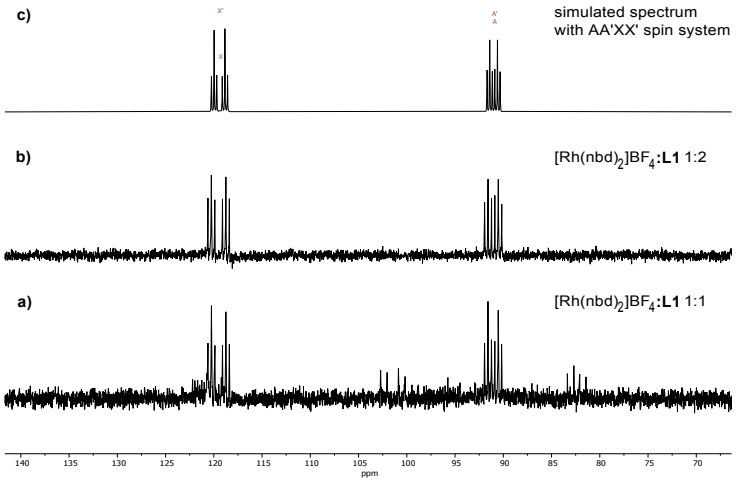


Figure 2 in situ $^{31}P\{^{1}H\}$ NMR spectra of reaction mixtures with $[Rh(nbd)_2]BF_4$: (R_P,S)-**L1** ratios of 1:1 (a) and 1:2 (b) in CH_2Cl_2 and simulated $^{31}P\{^{1}H\}$ NMR AA'XX' spectrum (MestReNova 14, spectrometer frequency: 161 MHz) (c).

Crystals suitable for X-ray diffraction were obtained from the reaction mixture with a $[Rh(nbd)_2]BF_4$: (R_P,S)-**L1** ratio 1:2 in CH_2Cl_2 *via* gas diffusion of Et_2O into the solution. The crystal structure reveals a homoleptic bis-diphosphine complex of rhodium exhibiting a distorted square planar complex geometry (Figure S 66). The ligand bite angles in the complex are 69.63(3)° and 69.91(3)°, respectively, and in good accordance with bite angles enforced by examples of similar PNP ligands coordinated to Rh(I) in a 1:1 fashion[8c,18] or 2:1 fashion.[19]

However, the coordination chemistry of ligand and metal described here does not necessarily reflect the actual situation during the catalytic reaction as solvents and concentrations are different.[20]

Application in Rh-catalyzed asymmetric hydrogenation

We evaluated the catalytic activity of these P-chirogenic PNP ligands in the asymmetric hydrogenation of alkenes. In general, the complexes were prepared *in situ* by the addition of corresponding PNP ligands to the metal precursor, $[Rh(cod)_2]BF_4$, prior to the catalysis.

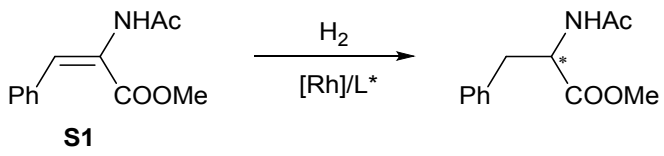
Tables 1 and 2 show the results of the asymmetric hydrogenation of substrates 1 to 4 using chiral PNP ligands. **L1-L5,** have been tested in Rh-catalyzed enantioselective hydrogenation of the benchmark substrate methyl (Z)-α-acetamidocinnamate (S1) in a series of catalytic experiments. Hydrogenation of the C-C double bond occurred in MeOH at 10 bar of H_2 pressure (catalyst/substrate =1:100) at room temperature (25 °C) with complete conversion but with moderate *ee* up to 46% (Table 1, entries 1-2, S1, MeOH).

MeOH can be a detrimental solvent for P-N as well as P-O bonds.[21] However, when mimicking the conditions of the catalyst formation in MeOH, only minor decomposition of the ligand was observed (based on the $^{31}P\{^1H\}$ NMR spectrum, Figure S50). In addition, the reactions with S1 were performed in dichloromethane in order to check whether there is any notable solvent effect or not. No significant differences in *ee's* have been observed (Table 1, entries 1-2, S1, CH_2Cl_2). As we could afford to use MeOH, since the ligands are unexpectedly stable in this environmentally more benign solvent, further experiments were performed in MeOH.

To investigate the influence of chirality in the ligand backbone atropoisomerically flexible biphenyl ligands (R_P,S)-**L2** was applied in the hydrogenation of S1 leading to moderate

enantiomeric excess (Table 1, entry 3). The stereoselectivity of the hydrogenation could be increased up to 20% upon modification on the biaryl part. The *ortho*-di-substituted biphenyl (R_P,*S*)-**L3** ligand gave rise to 51% *ee* (Table 1, entry 4) following the same reaction condition. Finally, the effect of a fixed axial chirality in the $P(OR)_2$ motif was studied in the catalytic performance using (*S*) and (*R*)-BINOL moiety. (R_P,*S*,S_{ax})-**L4** was applied in the hydrogenation of S1 leading to high enantiomeric excess of 94% (entry 5, table 1). As expected, application of (S_P,*R*,R_{ax})-**L4** resulted in formation of the opposite *S*-enantiomer of the product with similar *ee* of 96% (Table 1, entry 6). Changing the configuration of the BINOL moiety, forming the diastereomeric ligand (R_P,*S*,R_{ax})-**L5**, resulted in the formation of *S*-product albeit in lower *ee* of 78%. Clearly, **L4** is the matched diastereomer for the asymmetric hydrogenation of S1, where **L5** represents the mismatched combination of chiral entities.[22]

Table 1. *ee* (%) in Rh-catalyzed asymmetric hydrogenation using **L1-L5** and S1 in MeOH and CH_2Cl_2



S1

Entry	Ligand	S1 (MeOH)	S1 (CH_2Cl_2)
1	(R_P,*S*)-**L1**	46% (*R*)	46% (*R*)

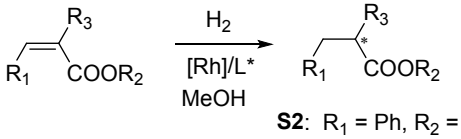
2	(S_P,R)-**L1**	40% (S)	38% (S)
3	(R_P,S)-**L2**	30% (R)	33% (R)
4	(R_P,S)-**L3**	51% (R)	50% (R)
5	(R_P,S,S_{ax})-**L4**	94% (R)	94% (R)
6	(S_P,R,R_{ax})-**L4**	96% (S)	94% (S)
7	(R_P,S,R_{ax})-**L5**	78% (S)	78% (S)
8	(S_P,R,S_{ax})-**L5**	80% (R)	82% (R)

Reaction condition: In a stainless steel autoclave, Rh:substrate =1:100 , Rh/L = 1: 1.1, $[Rh(cod)_2]BF_4$ (0.005 mmol) as metal precursor, H_2 (10 bar),12 h, appropriate solvent (2mL), T = 25 °C, all reactions are performed in duplicate, full conversion was achieved in all cases as determined by GC. Enantiomeric excess of the product was determined by chiral HPLC (absolute configuration drawn in parenthesis).

Similarly, (Z)-α-acetamido cinnamic acid (S2) and methyl 2-acetamidoacrylate (S3) were also asymmetrically hydrogenated (Table 2, entries 1-8). The enantiomeric pairs of (R_P,S)-

L1/(S_P,*R*)-**L1** and the PNP-BINOL ligands (R_P,*S*,S_{ax})-**L4**/(S_P,*R*,R_{ax})-**L4** and (R_P,*S*,R_{ax})-**L5**/(S_P,*R*,S_{ax})-**L5** were tested. Again, both enantiomers of **L1** resulted in low *ee* for S2 and even lower for S3. In comparison, enantioselectivity was also increased in the case of S2 and S3 using (R_P,*S*)-**L2** and (R_P,*S*)-**L3** (Table 2, entry 3 vs entry 4). The (S_{ax})-BINOL derivatives ((R_P,*S*,S_{ax})-**L4** and (S_P,*R*,S_{ax})-**L5**) give rise to (*R*)-enantiomer (entries 5 and 8, Table 1 and 2) and (R_{ax})-BINOL moiety (R_P,*S*,R_{ax})-**L5** and (S_P,*R*,R_{ax})-**L4**) produces the (*S*)-enantiomer (entries 6 and 7, Table 1 and 2) in asymmetric hydrogenation of both S2 and S3. A similar matched-mismatched effect[22] as for S1 was observed for these substrates as the degree of enantioselection again largely depends on the chiral information in the BINOL moiety. The matched combinations gave up to 30% higher *ee* than the mismatched ones, as illustrated by (R_P,*S*,S_{ax})-**L4** and (R_P,*S*,R_{ax})-**L5** for S3. In addition to that, the match effect has also been observed in the hydrogenation of dimethyl itaconate (S4) under the same reaction condition (Table 2, entry 5 and 6 vs 7 and 8). The intrinsic additional chirality (axially chiral BINOL moiety) in the PNP-ligand backbone apparently plays a pivotal role to achieve high enantioselectivity in asymmetric hydrogenation.

Table 2. *ee* (%) in Rh-catalyzed asymmetric hydrogenation using **L1-L5** and **S2-S4** in MeOH.



S2: R_1 = Ph, R_2 = H, R_3 = NHAc
S3: R_1 = H, R_2 = Me, R_3 = NHAc
S4: R_1 = H, R_2 = Me, R_3 = CH_2COOMe

Entry	Ligand	S2	S3	S4
1	(R_P,*S*)-**L1**	23% (*R*)	20% (*R*)	-
2	(S_P,*R*)-**L1**	16% (*S*)	10% (*S*)	-
3	(R_P,*S*)-**L2**	14% (*R*)	14% (*R*)	nd[a]
4	(R_P,*S*)-**L3**	22% (*R*)	32% (*R*)	nd[a]
5	(R_P,*S*,S_{ax})-**L4**	88% (*R*)	92% (*R*)	32% (*R*)
6	(S_P,*R*,R_{ax})-**L4**	92% (*S*)	92% (*S*)	28% (*S*)
7	(R_P,*S*,R_{ax})-**L5**	84% (*S*)	60% (*S*)	-
8	(S_P,*R*,S_{ax})-**L5**	80% (*R*)	72% (*R*)	-

Reaction condition: In a stainless steel autoclave, Rh:substrate =1:100 , Rh/L = 1: 1.1, $[Rh(cod)_2]BF_4$ (0.005 mmol) as metal precursor, H_2 (10 bar),12 h, MeOH (2 mL), T = 25 °C, all reactions are performed in duplicate, full conversion was achieved in all cases as determined by GC. Enantiomeric excess of the product was determined by chiral HPLC (absolute configuration drawn in parenthesis). [a] Not determined.

From the results of the present set of ligands it is clear that steric bulk on the diol part of the phosphoramidite moiety contributes to improved enantioselectivity but fixing the biaryl axis in the matched position has the highest impact. Obvious next step is to introduce bisnaphthol moieties with increasing steric bulk at ortho-positions. This approach has been reported previously[23] and is currently being pursued by us (for further testing of substrates cf. reference [26]).

Conclusions

A series of P-chirogenic diphosphazanes incorporating diol, bisphenol and BINOL-derived substituents has been prepared on gram-scale. The incorporation of bulky, axially chiral BINOL-derived moiety into the ligand structure leads to a significant increase of the enantioselectivity of the catalyst. Additionally, the sole change from (R_{ax})- to (S_{ax})-configurated BINOL-fragments is sufficient to invert the stereoselectivity of the reaction, which reveals a dominant role of the axially chiral part of the ligand in the presented cases. However, the P-chirogenic fragment is still of importance in this matter, indicated by the observed match-mismatched interaction. Careful arrangement of both chirogenic sites of the presented system is required to achieve high enantioselectivity.

Experimental Section

All synthetic work was performed under oxygen- and moisture free conditions using standard Schlenk and glovebox techniques. All reagents were purchased from commercial sources and used as received, unless otherwise stated. TMEDA, NEt_3, (*S*)-1-phenylethylamine, (R)-1-phenylethylamine, CD_3Cl and CD_2Cl_2 were dried over CaH_2, distilled prior to use, and degassed with three freeze-pump-thaw cycles. THF was distilled from Na/benzophenone. Toluene and CH_2Cl_2 (amylene stabilized (50 ppm)) were bought from Acros Organics with 99.85% purity, <0.005% water content and stored under inert atmosphere over molecular sieves. *n*-Heptane and C_6D_6 were dried over Na/benzophenone and tetraglyme and distilled prior to use. *n*-Pentane was purified using Grubbs-type column system Pure Solv MD-5.[24] 2-Chloro-1,3,2-dioxaphospholidine was bought from TCI and degassed via freeze-pump-thaw cycles. (*R*)- and (*S*)-BINOL were bought from Merck and used as received. Samples for mass spectrometry were prepared in the glove box and measured on a Finnigan MAT 95-XP (Thermo Electron) or Kratos MS-50 spectrometer and measurements were carried out in HRMS (ESI-TOF) mode. Fragment signals are given in mass per charge number (m/z). NMR spectra were recorded on Bruker Avance 300 (^{1}H: 300, ^{13}C: 75, ^{31}P: 121 MHz), Bruker Fourier 300 (^{1}H: 300, ^{13}C: 75, ^{31}P: 121 MHz) or Avance 400 (^{1}H: 400, ^{13}C: 100, ^{31}P: 161 MHz) instruments operating at the denoted spectrometer frequency given in Megahertz (MHz) for the specified nucleus. Samples for measurement of melting points were prepared under argon

in a capillary tube sealed with grease. The measurements were conducted on a Mettler-Toledo MP-70 melting point apparatus. Optical rotations were measured on an Anton Paar MCP 200. Experimental details of the X-ray single crystal analysis are described in the ESI.

Synthesis of (R_P,*S*)-1/(S_P,*S*)-1 (diastereomeric mixture) A 50 mL Schlenk-tube was filled with (*S*)-1-phenylethylamine (0.9 mL, 7.07 mmol), which was subsequently dissolved in toluene (20 mL). After addition of NEt_3 (1.0 mL, 7.17 mmol), *tert*-butylphenylchlorophosphine (1.3 mL, 6.90 mmol) was added dropwise into the mixture. Upon heating in an oil bath to 90 °C (16 h), a white precipitate was formed. The supernatant was filtered off and the precipitate was washed with toluene (2.5 mL). The solvent was completely removed from the filtrate, yielding **1** as colorless oil (1.8 g, 6.31 mmol). Yield: 91%. ^{1}H (300 MHz, CD_2Cl_2): δ 7.51-7.18 (m, 10H, Ar*H*), 4.32-4.16 (m, 1H, C*H*), 2.16 (m, 1H, N*H*), 1.56 (major) and 1.47 (minor) (d, $^2J_{HH}$ = 6.6 Hz, 3H [integrated as one signal], CH_3), 0.99 (major) and 0.95 (minor) (d, $^3J_{PH}$ = 12.8 Hz, 9H [integrated as one signal], (CH_3)$_3$); ^{13}C{^{1}H} NMR (75 MHz, CD_2Cl_2): δ 147.9 (d, $^3J_{PC}$ = 3.8 Hz, *ipso*-N*Ph*, major), 147.6 (d, $^3J_{PC}$ = 5.2 Hz, *ipso*-N*Ph*, minor), 140.9 (d, $^1J_{PC}$ = 28.5 Hz, *ipso*-P*Ph*, minor), 140.4 (d, $^1J_{PC}$ = 25.0 Hz, *ipso*-P*Ph*, major), 131.5, 131.2, 128.6, 128.4, 127.9 (d, *J* = 6.6 Hz, Ar*C*), 127.8 (d, *J* = 6.7 Hz, Ar*C*), 127.1 – 126.5 (m, Ar*C*), 57.4 (d, $^2J_{PC}$ = 26.7 Hz, *C*H, major), 57.1 (d, $^2J_{PC}$ = 25.6 Hz, *C*H, minor) 31.5 (d, *J* = 7.4 Hz), 31.3 (d, *J* = 6.0 Hz), 26.2

(d, $^{1}J_{PC}$ = 14.9 Hz, C(CH$_3$)$_3$), 25.8 (d, $^{3}J_{PC}$ = 8.1 Hz, NCH$_3$); ^{31}P{^{1}H} (121 MHz, CD_2Cl_2): δ 48.22 (minor, 17%), 47.58 (major, 83 %)

Analytical data match previously reported data.[16]

The opposite product **(S_P,R)-1/(R_P,R)-1 (diastereomeric mixture)** was obtained in the same way: ^{31}P{^{1}H} (121 MHz, CD_2Cl_2): δ = 48.21 (minor, 17%), 47.58 (major, 83 %)

Analytical data match previously reported data.[16]

Synthesis of phosphorochloridites

The synthesis was carried out according to the general procedure for phosphorochloridites formation and the analytical data matched with the reported procedure.[25]

2,2′-biphenol phosphochloridite

A solution of 2,2′-biphenol (1.61g, 8.75 mmol) in THF (25mL) was slowly added to a mixture of PCl_3 (1.0 mL, 11.4 mmol) and Et_3N (2.7 mL, 19.25 mmol) in THF (10 mL) at 0 °C. After 22 h, the reaction mixture was filtered under inert atmosphere and the solvent was evaporated to yield the white-yellowish powder (1.75g, 80%).

^{1}H NMR (300 MHz, C_6D_6): δ 7.1-7.0 (m, 2H), 6.9-6.8 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ 149.8, 131.4, 130.8, 129.7, 126.3, 122.5. ^{31}P{^{1}H} NMR (122 MHz, C_6D_6): δ 180.1.

3,3',5,5'-tetra-tert-butyl-[1,1'-biphenyl]-2,2'-diol phosphochloridite

A solution of 3,3',5,5'-tetra-tert-butyl-[1,1'-biphenyl]-2,2'-diol (3.5g, 8.75 mmol) in THF (25mL) was slowly added to a mixture of PCl_3 (1.0 mL, 11.4 mmol) and Et_3N (2.7 mL, 19.25 mmol) in THF (10 mL) at 0 °C. After 22 h, the reaction mixture was filtered under inert atmosphere and the solvent was evaporated to yield the white-yellowish powder (3.30g, 82%).

^1H NMR (400 MHz, $CDCl_3$): δ 7.4 (s, 2 H), 7.1 (s, 2 H), 1.4 (s, 18H), 1.3 (s, 18H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 147.7, 145.7, 140.6, 133.7, 128.2, 128.0, 127.7, 126.9, 124.5, 35.7, 34.9, 31.7. $^{31}P\ \{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 171.6.

(*S*)/(*R*)-BINOL-phosphorochloridites

A solution of (*S*) or (*R*)-1,1'-bi-2-naphthol (2.5 g, 8.75 mmol) in THF (25mL) was slowly added to a mixture of PCl_3 (1.0 mL, 11.4 mmol) and Et_3N (2.7 mL, 19.25 mmol) in THF (10 mL) at 0 °C. After 22 h, the reaction mixture was filtered under inert atmosphere and the solvent was evaporated to yield the white-yellowish powder (2.60g, 85%).

^1H NMR (300 MHz, $CDCl_3$): δ 8.07-7.98 (m, 4H), 7.58-7.30 (m, 8H) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 148.0, 147.5, 132.3, 131.7, 131.1, 130.2, 128.6, 128.2, 127.9, 127.6, 127.2, 127.1, 126.7, 126.6, 125.9, 125.6, 121.8, 121.3 ppm. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): δ 178.4 ppm.

Synthesis of PNP ligands

(R_P,S)-L1. (R_P,S)-**1**/(S_P,S)-**1** (diastereomeric mixture (83:17); 1.74 g; 6.09 mmol) was dissolved in heptane (38 mL). TMEDA (1.00 mL, 6.70 mmol) was added and subsequently the solution was cooled down to –78 °C. Next, *n*BuLi (2.5 M in n-hexane; 2.44 mL) was added dropwise into the mixture. Immediately after addition, a yellow precipitate occurred and the cooling bath was removed, allowing the solution to reach room temperature. Upon heating in an oil bath to 80 °C the yellow solid was dissolved and recrystallized at room temperature overnight. Afterwards, the supernatant was removed via cannula followed by drying of the yellow crystals in vacuo and the solid was weighed (1.64 g, 4.02 mmol). The yellow solid was dissolved in toluene (30 mL) and brought to reaction with 2-chloro-1,3,2-dioxaphospholidine (536 mg, 4.20 mmol) leading to formation of a white precipitate. The solid was filtered off and the solvent was removed *in vacuo*. The obtained white solid was dissolved again in toluene (35 mL) to remove the last percentage of insoluble compounds. Again, the solids were filtered off and the solvent were completely removed *in vacuo*. A white powder was obtained, which was washed with n-pentane at –78 °C. Upon drying, 1.09 g (2.90 mmol) of the optically pure product (R_P,S)-**L1** was received as a colorless powder. Crystals suitable for X-ray analysis were collected from the washing solution at 6 °C. Yield: 48% (1.09 g). M.p. 121°C. $[\alpha]_D^{298} = +28.2°$ (c 0.5, CH_2Cl_2)

^{1}H NMR (400 MHz, C_6D_6): δ 8.02-7.95 (m, 2H), 7.63-7.55 (m, 2H), 7.28-7.18 (m, 4H), 7.14-

7.02 (m, 2H), 4.76-4.64 (m, 1H), 3.87-3.76 (m, 1H), 3.69-3.60 (m, 1H), 3.52-3.36 (m, 2H), 1.5 (dd, 3H, $^3J_{HH}$ = 7.02 Hz, J = 0.86 Hz), 1.06 (d, 9H, ^3J = 13.77 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, C_6D_6): δ 142.6 (d, J = 3.5 Hz), 140.5 (dd, J = 30.3 Hz), 132.9 - 132.0 (m), 129.4 (d, J = 2.8 Hz), 128.3 - 126.9 (m), 126.8, 64.4, 64.0 (d, J = 8.5 Hz), 53.0 (dd, J = 27.0 Hz, J = 2.1 Hz), 32.7 (dd, J = 18.6 Hz, J = 4.3 Hz), 29.0 (dd, J = 17.5 Hz, J = 9.7 Hz), 20.2 (d, J = 14.5 Hz); ^{15}N (30 MHz, C_6D_6): δ = –279.6 (m); $^{31}P\{^1H\}$ (161 MHz, C_6D_6): δ 146.30 (d, ^2J = 33 Hz), 54.38 (d, ^2J = 33 Hz). HRMS (ESI-TOF): m/z calculated for $C_{20}H_{27}NO_2P_2$: 376.1595 [M+H]+; observed 376.1595. EA: Anal. calcd. for $C_{20}H_{27}NO_2P_2$: C: 63.99, H: 7.25, N: 3.73. Found: C: 63.93, H: 7.46, N:3.79

(S_P,R)-L1. (S_P,R)-**L1** was synthesized according to the procedure described for (R_P,S)-**L1**. Crystals suitable for X-ray analysis were collected from the washing solution at 6 °C. Yield: 37% (0.84 g). M.p. 121°C. $[\alpha]_D^{298} = -28.8°$ (c 0.5, CH_2Cl_2) ^1H NMR (400 MHz, C_6D_6): δ 8.03-7.96 (m, 2H), 7.64-7.55 (m, 2H), 7.28-7.18 (m, 4H), 7.14-7.01 (m, 2H), 4.76-4.64 (m, 1H), 3.85-3.76 (m, 1H), 3.69-3.60 (m, 1H), 3.52-3.36 (m, 2H), 1.5 (dd, 3H, $^3J_{HH}$ = 7.06 Hz, J = 0.88 Hz), 1.06 (d, 9H, ^3J = 13.80 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, C_6D_6) δ 142.6, 140.5, 132.5, 129.8, 125.7, 64.4, 64.0, 53.0, 32.7, 29.0, 20.2; $^{31}P\{^1H\}$ NMR (161 MHz, C_6D_6): δ 146.22 (d, ^2J = 32.9 Hz), 54.38 (d, ^2J = 32.8 Hz). HRMS (ESI-TOF): m/z calculated for $C_{20}H_{27}NO_2P_2$: 376.1595 [M+H]+;

observed 376.1596. EA: Anal. calcd. for $C_{20}H_{27}NO_2P_2$: C: 63.99, H: 7.25, N: 3.73. Found: C: 64.06, H: 7.26, N: 3.85

(*R*P,*S*)-L2. Optically pure (*R*P,*S*)-**2** was prepared according the previously mentioned protocol and used as crude material. A solution of pure 2,2′-biphenol phosphochloridite (0.36 mmol, 90 mg) dissolved in toluene (10 mL) was slowly added to (*R*P,*S*)-**2** (0.36 mmol, 150 mg) in toluene (10 mL) at - 78 °C. The mixture was allowed to reach room temperature and stirred for 10 h. The resulting solution was filtered, and the solvent was removed *in vacuo*. A white solid was formed, which was again washed with *n*-pentane to obtain (*R*P,*S*)-**L2** in optically pure form. Yield: 54% (0.098g). M.p. 153°C. $[\alpha]_D^{298} = +90.8°$ (c 0.5,CH_2Cl_2) ^{1}H NMR (300 MHz, C_6D_6): δ 8.11 (m, 2H), 7.67 (d, 2H, *J* = 8.7 Hz), 7.31-7.19 (m, 8H), 7.12- 6.92 (m, 6H), 5.30- 5.23(m, 1H), 1.58 (d, 3H, *J* = 7 Hz), 1.09 (d, 9H, *J* = 14 Hz). ^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ 133.6 (Ar*C*), 133.3 (Ar*C*), 132.7 (Ar*C*), 130.6 (Ar*C*), 130.4 (Ar*C*H), 130.1 (Ar*C*H), 129.8 (Ar*C*), 129.7 (Ar*C*), 129.4 (Ar*C*H), 129.0 (Ar*C*H), 127.3 (Ar*C*H), 125.4 (Ar*C*H), 124.4 (Ar*C*H), 122.9 (Ar*C*H), 120.7 (Ar*C*H), 53.9 (N*C*CH$_3$), 34.0 (P*C*(CH$_3$)$_3$), 29.2 (PC(*C*H$_3$)$_3$), 20.8 (NC*C*H$_3$). ^{31}P{^{1}H} NMR (122 MHz, C_6D_6) δ 142.7 (d, ^2J = 37.9 Hz), 54.9 (d, ^2J = 37.9 Hz). HRMS (ESI-TOF): *m/z* calculated for $C_{30}H_{31}NO_2P_2$: 500.1908 $[M+H]^+$; observed 500.1900.

(*R*P,*S*)-L3 was synthesized following the same protocol as mentioned for (*R*P,*S*)-**L2** using 3,3',5,5'-tetra-tert-butyl-[1,1'-biphenyl]-2,2'-diol phosphochloridite and crude (*R*P,*S*)-**2.** Yield:

53% (0.138 g). M.p. 175°C. $[\alpha]_D^{298} = 124.5°$ (c 0.5, CH_2Cl_2) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (m, 2H), 7.35- 7.29 (m, 3H),7.24- 7.20 (m, 3H), 7.13 (m, 1H), 7.07- 6.94 (m, 5H), 4.70 (m, 1H), 1.36 (s, 9H), 1.24 (s, 9H), 1.17 (s, 9H), 1.14 (d, 3H, *J* = 8 Hz) , 0.89 (s, 9H), 0.72 (d, 9H, *J* = 14 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 148.0 (Ar*C*), 147.9 (Ar*C*), 147.5 (Ar*C*), 146.1 (Ar*C*), 145.8 (Ar*C*), 144.1 (Ar*C*), 140.6 (Ar*C*), 139.5 (Ar*C*), 133.3 (Ar*C*H), 132.2 (Ar*C*H), 130.2 (Ar*C*H), 129.6 (Ar*C*), 129.2 (Ar*C*), 128.4 (Ar*C*H), 128.2 (Ar*C*H), 128.0 (Ar*C*H), 127.7 (Ar*C*H), 127.4 (Ar*C*H), 127.0 (Ar*C*H), 125.8 (Ar*C*H), 125.5 (Ar*C*H), 124.4 (Ar*C*H), 124.3 (Ar*C*H), 55.6(N*C*CH$_3$), 35.3 *C*(CH$_3$)$_3$, 34.8(P*C*(CH$_3$)$_3$), 33.6 (*C*(CH$_3$)$_3$), 31.7 (C(*C*H$_3$)$_3$), 31.1 (C(*C*H$_3$)$_3$), 28.3(PC(*C*H$_3$)$_3$), 21.6 (NC*C*H$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 145.9 (d, ^2J = 34.1 Hz), 53.9 (d, ^2J = 36.5 Hz). HRMS (ESI-TOF): *m/z* calculated for $C_{46}H_{63}NO_2P_2$: 724.4412 $[M+H]^+$; observed 724.4419.

(R_P,*S*,S_{ax})-L4. Optically pure (R_P,*S*)-**2** was prepared according the previously mentioned protocol and used as crude material. A solution of optically pure (*S*)-BINOL phosphochloridite (0.36 mmol, 133 mg) dissolved in toluene (10 mL) was slowly added to (R_P,*S*)-**2** (0.36 mmol, 150 mg) in toluene (10 mL) at - 78 °C. The mixture was allowed to reach at room temperature and stirred for 10 h. The resulting solution was filtered, and the solvent was removed *in vacuo*. A white solid was formed, which was again washed with pentane to obtain (R_P,*S*,S_{ax})-**L4** in optically pure form. Yield: 49% (0.105 g). M.p. 147°C. $[\alpha]_D^{298} = +188.1°$ (c 0.5, CH_2Cl_2) ^{1}H NMR

(400 MHz, $CDCl_3$): δ 8.06 (d, 1H, *J* = 8.74 Hz), 7.99-7.93 (m, 3H), 7.88 (d, 1H, *J* = 8.97), 7.81 (d, 1H, *J* = 8.29 Hz), 7.57-7.28 (m, 16H), 4.90 (m, 1H), 1.51 (d, 3H, *J* = 6.12 Hz), 1.00 (d, 9H, *J* = 14.04 Hz) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.0 (Ar*C*), 149.0 (Ar*C*), 143.3 (Ar*C*), 133.3 (Ar*C*), 133.1 (Ar*C*), 132.6 (Ar*C*), 130.8 (Ar*C*H), 130.5 (Ar*C*H), 129.9 (Ar*C*), 129.2 (Ar*C*), 128.7 (Ar*C*H), 128.5 (Ar*C*H), 128.3 (Ar*C*H), 128.2 (Ar*C*H), 128.0 (Ar*C*H), 128.0 (Ar*C*H), 127.7 (Ar*C*H), 127.5 (Ar*C*H), 127.4 (Ar*C*H), 127.0 (Ar*C*H), 126.5 (Ar*C*H), 126.4 (Ar*C*H), 126.1 (Ar*C*H), 125.1(Ar*C*H), 124.6 (Ar*C*H), 122.5 (Ar*C*), 122.2 (Ar*C*), 54.6(N*C*CH_3), 34.2 (P*C*$(CH_3)_3$), 29.4(PC(CH_3)$_3$) , 21.9 (NCH_3) ppm. $^{31}P\{^1H\}$ NMR (161 MHz, $CDCl_3$): δ 144.63 (d, ^2J = 37 Hz), 58.64 (d, ^2J = 37 Hz) ppm. HRMS (ESI-TOF): *m/z* calculated for $C_{38}H_{35}NO_2P_2$: 600.2221 $[M+H]^+$; observed 600.2236.

(*S*$_P$,*R*,*R*$_{ax}$)-L4. (*S*$_P$,*R*,*R*$_{ax}$)-**L4** was synthesized following the same protocol as mentioned for (*R*$_P$,*S*,*S*$_{ax}$)-**L4** using (*R*)-BINOL phosphochloridite and crude (*S*$_P$,*R*)-**2**. Yield: 39% (0.083 g). M.p. 148°C. $[\alpha]_D^{298} = -188.7°$ (c 0.5, CH_2Cl_2) ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, 1H, *J* = 8.08 Hz) , 7.84-7.75 (m, 3H), 7.71 (d, 1H, *J* = 7.70 Hz), 7.65 (d, 1H, *J* = 9.33 Hz), 7.42-7.07 (m, 16H), 4.73 (m, 1H), 1.27 (d, 3H, *J* = 6.02 Hz), 1.01 (d, 9H, *J* = 12.91 Hz) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.2 (Ar*C*), 149.4 (Ar*C*), 142.8 (Ar*C*), 134.4 (Ar*C*), 133.0 (Ar*C*), 131.6 (Ar*C*), 130.8 (Ar*C*H), 130.5 (Ar*C*H), 129.9 (Ar*C*), 129.2 (Ar*C*), 128.7 (Ar*C*H), 128.5 (Ar*C*H), 128.2 (Ar*C*H), 128.0 (Ar*C*H), 127.7 (Ar*C*H), 127. 5 (Ar*C*H), 127.0 (Ar*C*H), 126.4 (Ar*C*H), 125.1

(Ar*C*H), 124.6 (Ar*C*H), 122.5 (Ar*C*H), 122.2 (Ar*C*), 120.1 (Ar*C*), 54.4 (N*C*CH_3), 34.3 (P*C*$(CH_3)_3$), 29.3 (PC(*C*$H_3)_3$), 21.8 (NC*C*H_3) ppm. $^{31}P\{^1H\}$ NMR (161 MHz, $CDCl_3$): δ 144.63 (d, ^2J = 36.96 Hz), 58.64 (d, ^2J = 37.05 Hz) ppm. HRMS (ESI-TOF): *m/z* calculated for $C_{38}H_{35}NO_2P_2$: 600.2221 $[M+H]^+$; observed 600.2223.

(R_P,*S*,R_{ax})-L5. (R_P,*S*,R_{ax})-**L5** was synthesized following the same protocol as mentioned for (R_P,*S*,S_{ax})-**L4** using (*R*)-BINOL phosphochloridite and crude (R_P,*S*)-**2** adduct. Yield: 50% (0.107 g). M.p. 156°C. $[\alpha]_D^{298} = -167.2°$ (c 0.5, CH_2Cl_2) ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, 1H, *J* = 8.56 Hz), 7.87-7.83 (m, 3H), 7.78 (d, 1H, *J* = 8.56 Hz), 7.61 (d, 1H, *J* = 9.10 Hz), 7.40-7.05 (m, 16H) , 4.65 (m, 1H), 1.53 (d, 3H, *J* = 6.73 Hz) , 1.00 (d, 9H, *J* = 13.04 Hz) ppm.$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.4 (Ar*C*), 149.5 (Ar*C*), 142.2 (Ar*C*), 133.01 (Ar*C*), 133.0 (Ar*C*), 132.9 (Ar*C*), 131.5 (Ar*C*H), 131.4 (Ar*C*H), 129.7 (Ar*C*), 129.6 (Ar*C*), 129.1 (Ar*C*H), 128.6 (Ar*C*H), 128.4 (Ar*C*H), 128.2 (Ar*C*H), 128.1 (Ar*C*H), 127.9 (Ar*C*H), 127.2 (Ar*C*H), 126.9 (Ar*C*H), 126.3 (Ar*C*H), 126.2 (Ar*C*H), 125.0 (Ar*C*H), 124.7 (Ar*C*H), 122.2 (Ar*C*), 122.0 (Ar*C*), 53.8 (N*C*CH_3), 33.4 (P*C*$(CH_3)_3$), 28.8 (PC(*C*$H_3)_3$), 21.0 (NC*C*H_3) ppm. $^{31}P\{^1H\}$ NMR (161 MHz, $CDCl_3$): δ 141.83 (d, ^2J = 38 Hz) , 55.33 (d, ^2J = 38 Hz) ppm. HRMS (ESI-TOF): *m/z* calculated for $C_{38}H_{35}NO_2P_2$: 600.2221 $[M+H]^+$; observed 600.2232.

(S_P,*R*,S_{ax})-L5. (S_P,*R*,S_{ax})-**L5** was synthesized following the same protocol as mentioned for (R_P,*S*,S_{ax})-**L4** using (*S*)-BINOL phosphochloridite and crude (S_P,*R*)-**2**. Yield: 40% (0.085 g).

M.p. 155°C. $[\alpha]_D^{298} = +167.9°$ (c 0.5, CH_2Cl_2) ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, 1H, *J* = 9.02 Hz), 7.99 (m, 3H), 7.93-7.90 (m, 1H), 7.62 (d, 1H, *J* = 7.76 Hz), 7.53-7.17 (m, 16H), 1.52 (d, 3H, *J* = 8.05 Hz), 1.00 (d, 9H, *J* = 14.81 Hz) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.0 (Ar*C*), 149.2 (Ar*C*), 141.8 (Ar*C*), 138.6 (Ar*C*), 134.5 (Ar*C*), 132.9 (Ar*C*), 131.5 (Ar*C*H), 130.7 (Ar*C*H), 129.8 (Ar*C*), 129.7 (Ar*C*), 128.7 (Ar*C*H), 128.5 (Ar*C*H), 128.3 (Ar*C*H), 128.2 (Ar*C*H), 128.0 (Ar*C*H), 127.7 (Ar*C*H), 127.6 (Ar*C*H), 127.3 (Ar*C*H), 127.0 (Ar*C*H), 126.4 (Ar*C*H), 126.2 (Ar*C*H), 125.5 (Ar*C*H), 125.1 (Ar*C*H), 124.8 (Ar*C*H), 122.3 (Ar*C*), 122.1 (Ar*C*), 53.8 (N*C*CH$_3$), 33.7 (P*C*(CH$_3$)$_3$), 29.2 (PC(*C*H$_3$)$_3$, 21.2 (NC*C*H$_3$) ppm. ^{31}P{^{1}H} NMR (161 MHz, $CDCl_3$): δ 141.83 (d, ^2J = 38 Hz), 55.33 (d, ^2J = 38 Hz) ppm. HRMS (ESI-TOF): *m/z* calculated for $C_{38}H_{35}NO_2P_2$: 600.2221 $[M+H]^+$; observed 600.2228.

General procedure for asymmetric hydrogenation

All the hydrogenation experiments were performed in stainless steel autoclave charged with an insert suitbale for up to 8 reaction vessels (4 mL) with teflon mini stirring bars. In a typical experiment, a reaction vessel is charged with $[Rh(cod)_2]BF_4$ (1.9 mg, 5μmol) and ligand (5.5μmol, M/L= 1/1.1) and stirred for 10-15 mins in the appropiate solvent (2 mL). Then the desired substrates (0.5 mmol) were added to the reaction vessel maintaining the inert atmosphere and the vessels were placed in a high pressure autoclave. First the autoclave was

purged two times with nitrogen and three times with hydrogen. Finally it was pressurized at 10 bar of H_2 pressure at 25 ° C for 12 hrs. After the desired reaction time, the autoclave was depressurized and the reaction vessels were diluted with EtOAc and filtered through a short pad of silica. The conversion was determined by GC measurement and the enantiomeric exess was measured by chiral HPLC.

In situ $^{31}P\{^1H\}$ NMR experiments of (R_P,*S*)-L1 and $[Rh(nbd)_2]BF_4$

To a solution of (R_P,*S*)-**L1** (0.20 mmol, 70 mg) in CH_2Cl_2 (10 mL) a solution of $[Rh(nbd)_2]BF_4$ (0.05 M) in CH_2Cl_2 (1.8 mL for M:L ratio 1:2; 3.4 mL for 1:1 ratio) was added at room temperature. After 1h, a sample was taken (0.4 mL) and submitted for NMR measurement (solvent: 0.2 mL CD_2Cl_2).

ASSOCIATED CONTENT

Supporting information

NMR spectra, detailed structural information of the synthesized compounds and HPLC traces, thermal ellipsoid plots, crystal data and refinement metrics of reported crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

Paul C. J. Kamer - Leibniz-Institut für Katalyse e.V. Albert-Einstein-Straße 29a 18059 Rostock, Germany;

Email: Paul.Kamer@catalysis.de

Authors

Jan-Ole Moritz - Leibniz-Institut für Katalyse e.V. Albert-Einstein-Straße 29a 18059 Rostock, Germany.

Soumyadeep Chakrabortty - Leibniz-Institut für Katalyse e.V. Albert-Einstein-Straße 29a 18059 Rostock, Germany.

Bernd H. Müller - Leibniz-Institut für Katalyse e.V. Albert-Einstein-Straße 29a 18059 Rostock, Germany.

Anke Spannenberg - Leibniz-Institut für Katalyse e.V. Albert-Einstein-Straße 29a 18059 Rostock, Germany.

Notes

The authors declare no competing financial interest.

Author Contributions

‡J.-O.M. and S.D.C. contributed equally.

Acknowledgement

We thank Deutsche Forschungsgemeinschaft e.V. (KA 2936/1-1) for financial support. We would also like to thank Prof. Johannes G. de Vries for fruitful discussions and LIKAT for the analytical facilities.

References

(1) Börner, A., Ed. *Phosphorus Ligands in Asymmetric Catalysis - Synthesis and Application*; Wiley-VCH: Weinheim, 2008.

(2) McCarthy, M.; Guiry, P. J. Axially chiral bidentate ligands in asymmetric catalysis. *Tetrahedron* **2001**, *57*, 3809.

(3) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. Asymmetric hydrogenation with a complex of rhodium and a chiral bisphosphine. *J. Am. Chem. Soc*. **1975**, *97*, 2567.

(4) a) Jugé, S.; Stephan, M.; Laffitte, J. A.; Genet, J. P. Efficient asymmetric synthesis of optically pure tertiary mono and diphosphine ligands. *Tetrahedron Lett.* **1990**, *31*, 6357. b) Dutartre, M.; Bayardon, J.; Jugé, S. Applications and stereoselective syntheses of P-chirogenic phosphorus compounds. *Chem. Soc. Rev.* **2016**, *45*, 5771.

(5) a) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. Synthesis and reactions of phosphine-boranes. Synthesis of new bidentate ligands with homochiral phosphine centers

via optically pure phosphine-boranes. *J. Am. Chem. Soc.* **1990**, *112*, 5244. b) Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. P-Chiral Bis(trialkylphosphine) Ligands and Their Use in Highly Enantioselective Hydrogenation Reactions. *J. Am. Chem. Soc.* **1998**, *120*, 1635.

(6) Horner, L.; Jordan, M. Zur Stereochemie und zum chemischen Verhalten optisch aktiver Amidophosphoniumsalze und optisch aktiver Phosphinigsaureamide. *Phosphorus Sulfur Relat. Elem.* **1980**, *8*, 225.

(7) Dubrovina, N. V.; Börner, A. Enantioselective Catalysis with Chiral Phosphine Oxide Preligands. *Angew. Chem. Int. Ed.* **2004**, *43*, 5883.

(8) a) Revés, M.; Ferrer, C.; León, T.; Doran, S.; Etayo, P.; Vidal-Ferran, A.; Riera, A.; Verdaguer, X. Primary and Secondary Aminophosphines as Novel P-Stereogenic Building Blocks for Ligand Synthesis. *Angew. Chem. Int. Ed*. **2010**, *49*, 9452. b) Grabulosa, A.; Doran, S.; Brandariz, G.; Muller, G.; Benet-Buchholz, J.; Riera, A.; Verdaguer, X. Nickel(II) and Palladium(II) Complexes of the Small-Bite-Angle P-Stereogenic Diphosphine Ligand MaxPHOS and Its Monosulfide. *Organometallics* **2014**, *33*, 692. c) Cristóbal-Lecina, E.; Constantino, A. R.; Grabulosa, A.; Riera, A.; Verdaguer, X. Rhodium-Catalyzed Pauson–Khand Reaction Using a Small-Bite-Angle P-Stereogenic C_1-Diphosphine Ligand. *Organometallics* **2015**, *34*, 4989 d) the MaxPHOS-family was recently reviewed in Cabré, A.; Riera, A.; Verdaguer, X. P-Stereogenic Amino-Phosphines as Chiral Ligands: From Privileged Intermediates to Asymmetric Catalysis. *Acc. Chem. Res.* **2020**, *53*, 676.

(9) a) Orgué, S.; Flores-Gaspar, A.; Biosca, M.; Pámies, O.; Dieguez, M.; Riera, A.; Verdaguer, X. Stereospecific S(N)2@P reactions: novel access to bulky P-stereogenic ligands. *Chem. Commun*. **2015**, *51*, 17548. b) Orgué, S.; León, T.; Riera, A.; Verdaguer, X. Asymmetric Intermolecular Cobalt-Catalyzed Pauson-Khand Reaction Using a P-Stereogenic Bis-Phosphane. *Org. Lett.* **2015**, *17*, 250.

(10) Imamoto, T.; Sugita, K.; Yoshida, K. An Air-Stable P-Chiral Phosphine Ligand for Highly Enantioselective Transition-Metal-Catalyzed Reactions. *J. Am. Chem. Soc*. **2005**, *127*, 11934.

(11) Hoge, G.; Wu, H.-P.; Kissel, W. S.; Pflum, D. A.; Greene, D. J.; Bao, J. Highly Selective Asymmetric Hydrogenation Using a Three Hindered Quadrant Bisphosphine Rhodium Catalyst. *J. Am. Chem. Soc*. **2004**, *126*, 5966.

(12) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. Synthesis of 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), an atropisomeric chiral bis(triaryl)phosphine, and its use in the rhodium(I)-catalyzed asymmetric hydrogenation of α-(acylamino)acrylic acids. *J. Am. Chem. Soc*. **1980**, *102*, 7932.

(13) a) van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. Highly Enantioselective Rhodium-Catalyzed Hydrogenation with Monodentate Ligands. *J. Am. Chem. Soc*. **2000**, *122*, 11539. b) Biosca, M.; de la Cruz-Sánchez, P.; Pàmies, O.; Dieguez M. P-Stereogenic *N*-Phosphine–Phosphite Ligands for the Rh-Catalyzed Hydrogenation of Olefins. *J. Org. Chem.* **2020,** *85* (7), 4730. c) Etayo, P.; Núñez-Rico, J. L.; Vidal-Ferran, A. Chiral Rhodium Complexes Derived From Electron-Rich Phosphine-Phosphites as Asymmetric Hydrogenation Catalysts. *Organometallics* **2011**, *30*, 6718

(14) Mandal, S. K.; Nagana Gowda, G. A.; Krishnamurthy, S. S.; Stey, T.; Stalke, D. Chiral "P–N–P" ligands, (C20H12O2)PN(R)PY2 [R=CHMe$_2$, Y=C$_6$H$_5$, OC$_6$H$_5$, OC$_6$H$_4$-4-Me, OC$_6$H$_4$-4-OMe or OC$_6$H$_4$-4-tBu] and their allyl palladium complexes *J. Organomet. Chem*. **2005**, *690*, 742.

(15) León, T.; Riera, A.; Verdaguer, X. Stereoselective Synthesis of P-Stereogenic Aminophosphines: Ring Opening of Bulky Oxazaphospholidines. *J. Am. Chem*. Soc. **2011**, *133*, 5740.

(16) a) Kolodyazhnyi, O. I.; Andrushko, N. V.; Gryshkun, E. V. Stereoselective Reactions of Optically Active Derivatives of α-Methylbenzylaminophosphine *Russ. J. Gen. Chem*. **2004**, *74*, 515. b) Andrushko, N. V.; Kolodyazhnyi, O. I.; Gryshkun, E. V.; Stereoselective reactions of chiral amines with racemic chlorophosphines. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1027.

(17) Fernandez-Perez, H.; Donald, S. M.; Munslow, I. J.; Benet-Buchholz, J.; Maseras, F.; Vidal-Ferran, A. Highly Modular P–OP Ligands for Asymmetric Hydrogenation: synthesis, Catalytic Activity, and Mechanism *Chem. - Eur. J.* **2010**, *16*, 6495.

(18) Simón-Manso, E.; Valderrama, M. Group VIII transition metal complexes with the chiral diphosphazane ligand (*S*)-α-$(Ph_2P)_2N$(CHMePh): Synthesis and structural characterization *J. Organomet. Chem.* **2006**, *691*, 380.

(19) Ganesamoorthy, C.; Mague, J. T.; Balakrishna, M. S. Synthesis and structural studies of Rh^{I}, Pd^{I}, Ni^{II} complexes and one-pot synthesis of binuclear Ru^{II} complex [(η^6-*p*-cymene)Ru(μ_2-Cl)$_3$Ru{PhN(P(OC_6H_4OMe-*o*)$_2$)$_2$}Cl] *J. Organomet. Chem.* **2007**, *692*, 3400.

(20) Alberico, E.; Möller, S.; Horstmann, M.; Drexler, H.-J.; Heller, D. Activation, Deactivation and Reversibility Phenomena in Homogeneous Catalysis: A Showcase Based on the Chemistry of Rhodium/Phosphine Catalysts. *Catalysts* **2019**, *9*, 582.

(21) Baker, M. J.; Harrison, K. N.; Orpen, A. G.; Pringle, P. G.; Shaw, G. Chelating diphosphite complexes of nickel(0) and platinum(0): their remarkable stability and hydrocyanation activity. *J. Chem. Soc., Chem. Commun.* **1991**, 803.

(22) Burk, M. J.; Pizzano, A.; Martin, J. A. Bis(phospholane) Ligands Containing Chiral Backbones. Matching and Mismatching Effects in Enantioselective Hydrogenation of α-Keto Esters. *Organometallics* **2000**, *19*, 250.

(23) Buisman, G. J. H.; van der Veen, L. A.; Klootwijk, A.; de Lange, W. G. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. Chiral Cooperativity in Diastereomeric Diphosphite Ligands: Effects on the Rhodium-Catalyzed Enantioselective Hydroformylation of Styrene. *Organometallics* **1997**, *16*, 2929.

(24) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification, *Organometallics* **1996**, *15*, 1518.

(25) Scherera J.; Huttnera, G.; Büchnera, M., Bakosb, J. Chirale tripod-rhodium-komplexe: Ligandsynthese, komplexchemie, katalyse. *J. Organomet. Chem*. **1996**, *520*, 45.

(26) Further testing with the presented set of ligands under the same reaction conditions as described yielded following results: Hydrogenation of atropic acid: (R_P,*S*)-**L1**: >99% conv., 0% *ee*; (S_P,*R*,R_{ax})-**L4**: >99% conv., 0% *ee*; (R_P,*S*,S_{ax})-**L4**: >99% conv., 0% *ee*; Hydrogenation of *N*-(3,4-dihydronaphthalen-1-yl)acetamide: (R_P,*S*)-**L1**: >99% conv., 0% *ee*; (S_P,*R*)-**L1**: >99% conv., 0% *ee*; (R_P,*S*,S_{ax})-**L4**: >99% conv., 0% *ee*; Hydrogenation of (*E*)-3-acetylamino-2-

methyl-2-butenoic acid ethyl ester: (R_P,S)-**L1**: NR (no reaction); (S_P,R)-**L1**: NR; (R_P,S,S_{ax})-**L4**: NR; Hydrogenation of dimethyl itaconate: (R_P,S)-**L1**: >99% conv., 0% *ee*; (S_P,R)-**L1**: >99% conv., 0% *ee*; (S_P,R,R_{ax})-**L4**: >99% conv., 28% *ee* (*S*); (R_P,S,S_{ax})-**L4**: >99% conv., 32% *ee* (*R*); (R_P,S,R_{ax})-**L5**: >99% conv., 0% *ee*; (S_P,R,S_{ax})-**L5**: >99% conv., 0% *ee*

Table of Contents graphic