Synthesis and Evaluation of a Broad Range of New Chiral (Aminoalkyl)phosphane Ligands for Asymmetric Hydrogen-Transfer Reduction of Prochiral Ketones

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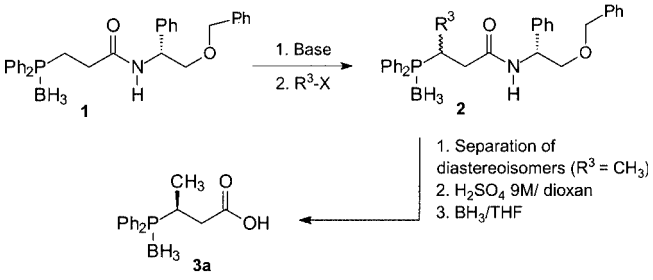
Twenty new chiral (aminoalkyl)phosphane ligands have been prepared from four enantiomerically pure advanced chiral compounds. We describe their use for asymmetric hydrogen-transfer reduction of three prochiral ketones. Enantioselectivities up to 90% were obtained. We investigated the influence on the enantioselectivity of each part of these new (aminoalkyl)phosphane ligands.

Introduction

Catalytic asymmetric reduction of prochiral ketones to produce chiral secondary alcohols is an important reaction in organic synthesis.[1] This enantioselective transformation can be carried out in several ways, including hydride reduction with an oxazaborolidine catalyst,[2] hydrogenation with chiral diphosphane ligands,[3] and transfer hydrogenation.[4] In view of the low cost of the reducing agent and its operational simplicity, transition-metal-catalyzed transfer hydrogenation either with 2-propanol or with an HCO_2H/Et_3N mixture[5] as a hydride source has emerged as an attractive alternative to asymmetric hydrogenation with H_2. Numerous catalytic systems of varying levels of efficiency have been developed involving, for example, ruthenium complexes modified by various di- or tridentate ligands such as diamines,[5] amino alcohols,[6] amidates,[7] oxazolines/amines,[8] phosphanes/amines,[9] or phosphane oxides.[10] One of the most efficient systems is based on the Ru^{II}–TsDPEN complex reported by Noyori,[11] who suggested that the presence of an NH moiety in the ligand structure may promote a cyclic transition state through hydrogen bonding to the ketone substrate. Moreover, it appeared that the formation of a metal–ligand bifunctional complex might induce high enantioselectivity because of a greater affinity of the substrate to the active site of the catalyst. Despite these developments, there is as yet no universal catalyst for the transfer hydrogenation of all prochiral ketones; in fact, though, it is highly desirable to have access to a variety of catalysts in order to optimize the reaction when applied to a wide range of substrates.

We have recently[12] described the synthesis of chiral α-substituted [β-(aminocarbonyl)alkyl]phosphane–boranes **2** by diastereoselective alkylation of [β-(aminocarbonyl)alkyl]phosphane–boranes **1**, using classical *O*-benzylated phenylglycinol as a chiral inducer (Scheme 1). Hydrolysis of these compounds afforded the advanced chiral pool compound **3**.



Scheme 1

The promising yields and diastereoselectivities obtained encouraged us to test these precursors (and related variants) in asymmetric catalytic processes. Here we present the synthesis and evaluation of a broad range of new chiral (aminoalkyl)phosphane ligands for asymmetric hydrogen-transfer reduction of prochiral ketones.

Results and Discussion

Ligand Synthesis

Our divergent approach to the design of new (aminoalkyl)phosphane ligands involved the generation of ad-

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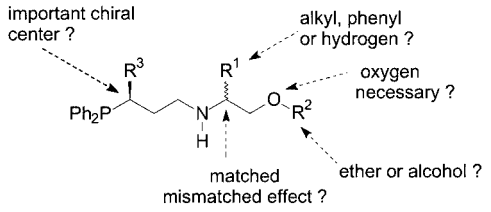
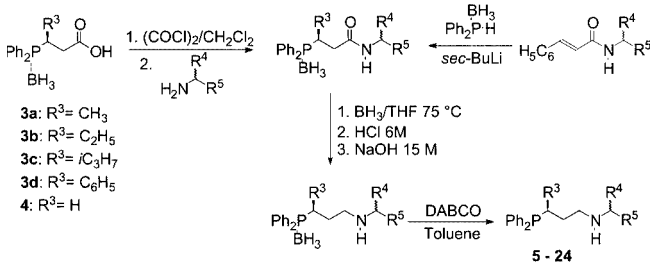
vanced chiral intermediates and their subsequent transformation into a series of functionalized chiral (aminoalkyl)-phosphanes **5**−**24**. We were then able to determine which part of the catalyst is essential for asymmetric transfer hydrogenation of prochiral ketones, as illustrated in Scheme 2.



Scheme 2

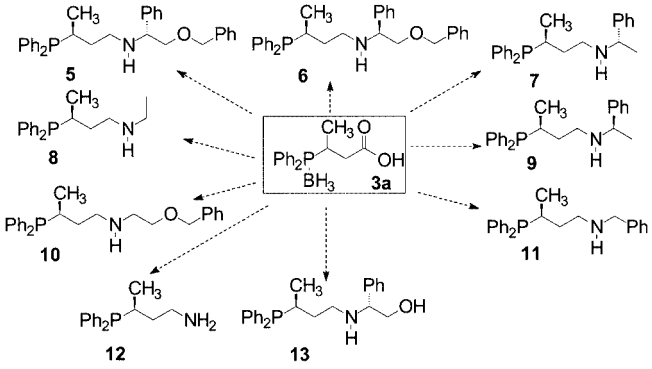
Specifically, we investigated the stereochemical influences of the chiral center next to the phosphane, the oxygen functionality, and the nature of R^1, R^2, and R^3.

The new (aminoalkyl)phosphane ligands were synthesized by the general procedure depicted in Scheme 3.

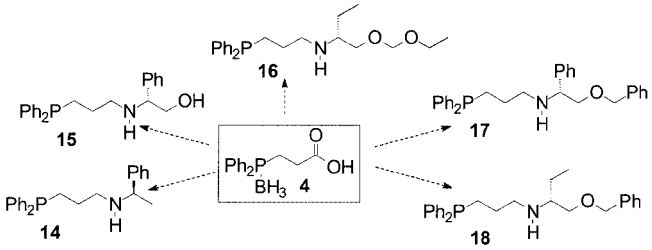


Scheme 3

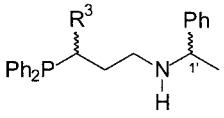
Racemic compounds **3b**, **3c**, and **3d** were prepared by a general procedure involving reaction between the α,β-unsaturated ester and the sodium salt of diphenylphosphane−borane, followed by saponification of the resulting esters. For all the ligands, the two final steps involved amide reduction and removal of borane. Ligand **5** was directly synthesized by a diastereoselective alkylation of **1**.[12] Eight ligands (**6**−**13**) were prepared by coupling of (*S*)-(+)-[2-carboxy-1-(methyl)ethyl]diphenylphosphane−borane (**3a**) with various amines. Five ligands (**14**−**18**) were synthesized from (2-carboxyethyl)diphenylphosphane−borane (**4**) through the coupling of **4** with (*R*)-phenylglycinol or (*R*)-aminobutanol derivatives. Ligands **19** and **20** were prepared by coupling of α-methylbenzylamine with (*S*)-(+)-(2-carboxy-1-ethylethyl)diphenylphospane−borane (**3b**), which was obtained by semi-preparative chiral HPLC separation.[13] Ligands **21** and **22** were obtained from (*R*)-(+)-(2-carboxy-1-isopropylethyl)diphenylphosphane−borane (**3c**), also obtained by semi-preparative chiral HPLC separation.[14] Ligands **23** and **24** were prepared by diastereoselective 1,4-addition,[15] followed by separation by flash chromatography through silica gel and recrystallisation from cyclohexane/ethyl acetate. The absolute configuration of the chiral center next to the phosphane was determined by X-ray diffraction analysis of **23**. (*R*)-(+)-(2-Carboxy-1-phenylethyl)diphenylphosphane−borane (**3d**) was also obtained by semi-preparative chiral HPLC separation,[16] its configuration being correlated to that of amide **23** after the coupling reaction between **3d** and α-methylbenzylamine. All the structures of the ligands **6**−**24** are shown in Schemes 4−6.



Scheme 4



Scheme 5



Ligand	R^3	Conf. at 1'
9	Me (*S*)	(*R*)
7	Me (*S*)	(*S*)
19	Et (*S*)	(*R*)
20	Et (*S*)	(*S*)
21	*i*Pr (*R*)	(R)
22	*i*Pr (*R*)	(S)
23	Ph (*R*)	(R)
24	Ph (*S*)	(R)

Scheme 6

In most cases, both the coupling reaction and the reduction of the amide moiety proceeded in moderate to very good yields. Removal of the borane protection (DABCO, toluene, reflux) in the final step gave the (aminoalkyl)phosphane ligands **5**−**24** in quantitative yields.

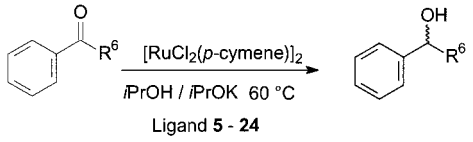
Optimization of the Asymmetric Hydrogen-Transfer Reduction of Prochiral Ketones

Three prochiral ketones − acetophenone, propiophenone, and isobutyrophenone − were investigated as asymmetric hydrogenation substrates. Ligand **17**, which was the most convenient to synthesize, was chosen for a more thorough study of the transfer hydrogenation conditions be-

cause this catalyst/ligand combination displayed a broad range of enantioselectivity for the three substrates (acetophenone 27.9% *ee*; propiophenone 56.2% *ee*; isobutyrophenone 80.9% *ee*). Under the standard conditions, we used a ligand/metal ratio of 2:1, 6 equiv. of base, and 100 equiv. of substrate. We then studied various parameters, first comparing the two bases *i*PrOK and KOH. Although the enantiomeric excesses were very similar for the three substrates ($\Delta ee < 2\%$), *i*PrOK was selected as it gave faster reaction rates.[17]

We next studied the influence of base stoichiometry (4, 6 or 8 equiv.), finding that the use of 6 equiv. *i*PrOK provides a modest improvement in enantioselectivity. ($\Delta ee < 10\%$). The reaction temperature appeared to have little effect upon *ee*, although reaction rates were greatly improved at 60 and 80 °C. We then studied the influence of the number of ligand equivalents relative to the metal (namely, **1**, **2**, or **4**). Use of 1 equiv. gave very low enantiomeric excesses, while the best results were obtained with the use of 4 equiv. of ligand. Finally, we tested two different "ruthenium" species: *p*-cymene and hexamethylbenzene. $[RuCl_2(p\text{-cymene})]_2$ gave higher *ee*s ($\Delta ee = 24\%$) when, for example, ligands **17** and **18** were tested.

After numerous assays, standard conditions were defined with a substrate/catalyst ratio (S/C) of 100 as follows: the chiral catalysts were prepared by heating 2 mol % of ligand with 0.5 mol % of $[RuCl_2(p\text{-cymene})]_2$ at reflux in 2-propanol for 30 min, and *i*PrOK (6 mol %) was added to the solution, which was then diluted with 2-propanol (in order to obtain [ketone] = 0.1 M). Finally, the prochiral ketone (100 equiv.) was added to the reaction mixture, and the transfer hydrogenations were performed at 60 °C.[18]



Scheme 7

In a first set of experiments, we examined the importance of the presence of a chiral center next to the phosphane moiety. Table 1 shows the results from a small screen of four ligands. In terms of the enantiopurity of the product, the best ligand for this first series was **17**. These initial results indicated that the introduction of a chiral center next to the phosphane had a dramatic effect on the stereochemical course of the reaction. Moreover, if we compare the *ee*s for ligands **5** and **6**, since the inversion was not complete this result does actually represent a match mismatched effect, although not a large one.

Table 1. Asymmetric hydrogen transfer reduction of prochiral ketones

Ligand	*ee* (%) R^6 = Me	R^6 = Et	R^6 = *i*Pr
17	27.9 (*S*)	56.2 (*S*)	80.9 (*S*)
18	30.7 (*S*)	50.6 (*S*)	73.6 (*S*)
5	4.5 (*S*)	14.9 (*S*)	27.6 (*S*)
6	12.9 (*R*)	01 (*R*)	18.8 (*R*)

It also seems that, for this type of ligand, the chiral center adjacent to the amine has the major influence on the sense of induction. Ligand **18** gave lower *ee*s than ligand **17** for the reactions with propiophenone and isobutyrophenone, indicating that the presence of an aromatic group on the chiral center has a beneficial effect, probably due either to π-stacking interactions (between the prochiral ketone and the ligand) or steric effects. It therefore appears that ligand **17** is an efficient ligand for the reduction of the most hindered prochiral ketone tested (isobutyrophenone) but a less efficient one for the other two ketones.

We next investigated the influence on the enantioselectivity of the group adjacent to the chiral center of ligand **17** (alcohol, ether, or hydrogen). Table 2 shows the results from a small screen of ligands **14**, **15**, and **16**. Replacement of the ether moiety in **17** by an alcohol reduced the *ee*s obtained in the reduction of isobutyrophenone (80.9% *ee* for **17** vs. 35.7% for **15**) and propiophenone (56.2% for **17** vs. 34.8% for **15**) and inverted the sense of induction. In the case of the acetophenone reduction, it appeared that the presence of an alcohol moiety has a beneficial influence (still with an inversion of induction), which could be due to modification of the chelating mode between the metal and the ligand giving rise to a mixture of amino alcohol, (hydroxyalkyl)phosphane, and (aminoalkyl)phosphane-type species. Indeed, ligand **15** gave the best *ee* for the reduction of acetophenone in this series [48.7% *ee*, (*R*) major]. On the other hand, removal of the oxygen atom (in case **14**, for example) resulted in very low *ee*. Likewise, introduction of a second oxygen atom as a MEM function (**16**) produced only moderate *ee*s. It therefore appeared that in the absence of a chiral center next to the phosphane, the best functional group on the opposite part of the catalyst is an alkoxy group; ligand **17** was the best catalyst for the reduction of isobutyrophenone, but was less efficient for less hindered ketones such as acetophenone and propiophenone.

Table 2. Asymmetric hydrogen transfer reduction of prochiral ketones

Ligand	*ee* (%) R^6 = Me	R^6 = Et	R^6 = *i*Pr
17	27.9 (*S*)	56.2 (*S*)	80.9 (*S*)
15	48.7 (*R*)	34.8 (*R*)	35.7 (*R*)
14	11.5 (*S*)	10.7 (*S*)	5.8 (*S*)
16	20.2 (*R*)	45.1 (*R*)	63 (*R*)

As shown in Table 1, it appeared that the presence of a chiral center next to the phosphane group had a detrimental influence on the magnitude of asymmetric induction, so we went on to investigate the effect of modifying the group connected to the "right arm" of the catalyst through the amine. Table 3 shows the results of a small screening to de-

termine the best compromise between the functionality on either side of the ligand. All the catalysts in Table 3 have a methyl group next to the phosphane. Removal of the chiral center connected to the amine moiety resulted in very low levels of enantioselectivity regardless of the group on the amine (hydrogen in **12**, benzyl in **11**, *O*-benzyloxyethyl in **10**, ethyl in **8**). Condensation of **3** with (*R*)-α-methylbenzylamine afforded ligand **9**, which induced poor levels of *ee*. In contrast, ligand **7** [obtained from (*S*)-α-methylbenzylamine] is an efficient ligand for the reduction of acetophenone (82.9% *ee*) and propiophenone (77.5% *ee*), but a poor one for the asymmetric reduction of isobutyrophenone. Comparison of the results obtained for ligands **7** and **9** clearly demonstrates a "match-mismatched effect". Moreover, in this case, the chiral center adjacent to the phosphane governs the sense of induction.

Table 3. Asymmetric hydrogen transfer reduction of prochiral ketones

Ligand	*ee* (%) R^6 = Me	R^6 = Et	R^6 = *i*Pr
12	20.2 (*S*)	20.1 (*S*)	3.9 (*S*)
8	0	7.6 (*R*)	14.4 (*R*)
10	13.2 (*S*)	6.3 (*S*)	26 (*S*)
11	23.3 (*S*)	17.9 (*S*)	19 (*R*)
9	30.5 (*S*)	32.6 (*S*)	10.4 (*S*)
7	82.9 (*S*)	77.5 (*S*)	4.5 (*S*)

Of this limited screening of 13 ligands, two exhibited promising levels of asymmetric induction: ligand **17** for the asymmetric reduction of isobutyrophenone (80.9% *ee*), and ligand **7** for acetophenone (82.9% *ee*) and propiophenone (77.5% *ee*).

Finally, ligand **13** was synthesized [from (*S*)-phenylglycinol] in order to determine the influence on the enantioselectivity of a combination of a methyl group adjacent to the phosphane and an alcohol next to the amine. This combination produced poorer *ee*s and an inversion of the sense of induction (11% *ee* for acetophenone, 16% for propiophenone, and 7% for isobutyrophenone). This result probably means that a mixture of an (aminoalkyl)phosphane-type ligand and an amino alcohol ligand linked to the ruthenium metal was present during the reduction process.

We finally studied the influence of the nature of the substituent R^3 connected to the chiral center next to the phosphane moiety (Table 4). We first noticed that enantiomeric excesses were increased when the methyl group was replaced by an ethyl group (from **9** and **7** to **19** and **20**), no matter whether there was a matched or a mismatched effect (Table 4). The presence of an isopropyl group, however, did not produce any further increase in the enantiomeric excess: selectivity decreased with ligands **21** and **22**.

The chiral center next to the phosphane moiety shows correlation to the sense of the asymmetric induction observed, while it seems that the chiral center next to the amine moiety has little influence on the sense of asymmetric induction. The enantiomeric excesses obtained with diastereoisomeric ligands **19** and **20** are indeed similar, no matter whether (*R*)- or (*S*)-α-methylbenzylamine is used. However, the chiral center next to the amine moiety is a tertiary center, which seems to be necessary for the reaction to be selective. The results obtained with benzylamine **11** and ethylamine **8** are indeed very weak (Table 3; maximum *ee*: 23%). The results obtained with the ligands possessing a methyl group (**7** and **9**), an ethyl group (**19** and **20**), or an isopropyl group (**21** and **22**) on the chiral center next to the phosphane moiety are very similar. This implies that these ligands constitute a "specific family" for which the enantiomeric excesses are similar for acetophenone and propiophenone, and weaker for isobutyrophenone. With a phenyl group on the chiral center next to the phosphane moiety (**23** and **24**), however, the results were quite different, and low enantiomeric excesses were obtained. In this case the sense of induction is governed by the chiral center next to the amine moiety. This is probably due to electronic effects (π-stacking with the substrate, which also has an aromatic group) and/or a change in the three-dimensional structure of the ligand.

Table 4. Asymmetric hydrogen transfer reduction of prochiral ketones

Ligand	*ee* (%) R^6 = Me	R^6 = Et	R^6 = *i*Pr
9	30.5 (*S*)	32.6 (*S*)	10.4 (*S*)
7	82.9 (*S*)	77.5 (*R*)	4.5 (*R*)
19	75.5 (*S*)	75.3 (*S*)	12.8 (*S*)
20	84.8 (*S*)	90.1 (*S*)	12 (*S*)
21	44.2 (*S*)	54.2 (*S*)	7.6 (*S*)
22	59.4 (*S*)	64.8 (*S*)	7.4 (*R*)
23	7.7 (*R*)	22.8 (*R*)	30.3 (*R*)
24	21.5 (*R*)	16.7 (*R*)	7.7 (*R*)

Conclusion

In conclusion, we have investigated a small library of new (aminoalkyl)phosphane for asymmetric transfer hydrogenation of prochiral ketones. Two types of ligands have emerged from this study; the first, exemplified by ligand **17**, is effective for the reduction of isobutyrophenone, and the second (**20**) is better for the asymmetric reduction of acetophenone and propiophenone.

Further investigations, especially concerning X-ray structures of the complexes, mechanistic information, and application to other prochiral ketones are currently in progress in our laboratory and will be reported in due course.

Experimental Section

General: Solvents were purified by conventional methods prior to use. TLC was performed on Merck 60F-250 silica gel plates and column chromatography on silica gel SI 60 (230−240 mesh). Melting points were taken with a Kofler apparatus and were uncor-

rected. Elemental analyses were carried out with a Carlo−Erba EA 1100 analyzer. NMR spectra were recorded with a Bruker DXP 300 spectrometer operating at 300 MHz for ^{1}H, 75.4 MHz for ^{13}C and 121.5 MHz for ^{31}P. This probe is equipped with pulsed-field (*z*) gradients. Chemical shifts (δ) are expressed in ppm relative to TMS for ^{1}H and ^{13}C nuclei and to H_3PO_4 for ^{31}P nuclei; coupling constants (*J*) are given in Hertz; coupling multiplicities are reported as conventional abbreviations. All hydrogenation experiments were performed by use of standard Schlenk techniques under nitrogen.

General Procedure for the Coupling Reaction between *O*-Protected Amino Alcohols, Amino Alcohols, Amines, or α-Methylbenzylamine and 3a, 3b, 3c, 3d, or 4: Oxalyl chloride (1.4 g, 11 mmol) was added dropwise under nitrogen to a stirred, cooled (0 °C) solution of (2-carboxyethyl)diphenylphosphane−borane (**4**, 1.5 g, 5.5 mmol) or enantiomeric pure [2-carboxy-1-alkyl (or -1-phenyl)]-diphenylphosphane−borane (**3a**, **3b**, **3c**, or **3d**) (5.5 mmol) in dichloromethane (30 mL). The reaction mixture was stirred at room temperature for 4 h. Removal of solvent and excess of oxalyl chloride under reduced pressure (0.05 Torr) afforded the corresponding acid chloride in quantitative yield as a red oil. Sodium hydroxide (0.176 g, 4.39 mmol), dissolved in water (0.5 mL), was added slowly, at room temperature, to a stirred solution of 3-(diphenylphosphanyl)propanoyl chloride (1.06 g, 3.9 mmol) or (boranato−diphenylphosphanyl)acetyl chloride (1.12 g, 3.9 mmol) and *O*-protected amino alcohol, amino alcohol, amine, or α-methylbenzylamine (3.9 mmol) in dichloromethane (30 mL). The reaction mixture was stirred at room temperature for 4 h and was then washed with water (3 × 10 mL). The organic layer was dried ($MgSO_4$) and the solvents were evaporated under reduced pressure to afford [(aminocarbonyl)alkyl]phosphane−boranes. The crude product was purified by chromatography (each eluent is specified in the Supporting Information).

General Procedure for the Reduction of the [(Aminocarbonyl)alkyl]phosphane−Boranes to (Aminoalkyl)phosphane−Boranes: A THF/BH_3 solution (1 M, 4 mmol) was added dropwise under nitrogen to a stirred, cooled (0 °C) solution of [(aminocarbonyl)alkyl]phosphane−boranes (1 mmol) in tetrahydrofuran (18 mL). The reaction mixture was stirred at room temperature for 1 h and then heated at reflux overnight. The reaction mixture was then cooled to 0 °C and hydrolyzed with HCl (6 N, 12 mL). Stirring was continued for 15 min, and sodium hydroxide (15 M, 12 mL) was then added. The mixture was stirred for 2 h and then extracted with ethyl acetate (3 × 15 mL). The organic layer was dried ($MgSO_4$) and the solvents were evaporated under reduced pressure to afford (aminoalkyl)phosphane−boranes. The crude product was purified by chromatography (each eluent is specified in the Supporting Information).

General Procedure for the Reduction of the (Aminoalkyl)phosphane−Boranes to (Aminoalkyl)phosphane Ligands 5−24: 1,4-Diazabicyclo[2.2.2]octane (6 mmol) was added under nitrogen to a stirred solution of (aminoalkyl)phosphane−borane (0.5 mmol) in toluene (7.5 mL). The reaction mixture was stirred at 40 °C for 8 h. The reaction solvents were evaporated under reduced pressure to afford (aminoalkyl)phosphane. The crude product was purified by chromatography (each eluent is specified in the Supporting Information).

Catalytic Hydrogenation: The standard procedure was as follows: $[RuCl_2(p\text{-cymene})]_2$ (1 equiv.) and the ligand (2 equiv.) were dissolved in 2-propanol (5 mL) under nitrogen. The solution was stirred at 80 °C for 30 min, and then cooled to 60 °C. *i*PrOK (6 equiv.) was added to the solution, which was then diluted with 2-propanol (in order to obtain [ketone] = 0.1 M). Finally the prochiral ketone (100 equiv.) was added to the reaction mixture. After completion of the reaction, the degree of conversion was determined by gas chromatography, and the product was recovered by filtration of the reaction solution on a plug of silica to remove the catalyst. The determination of the enantiomeric excesses was determined with a Varian 3300 capillary gas chromatograph with a Supelco β-Dex column (15 m × 0.25 mm i.d.), nitrogen as carrier gas, and a flame ionization detector. The GC separation was calibrated with the racemic material: for acetophenone T = 110 °C, R_{t1} = 12.1, R_{t1} = 12.8; for propiophenone T= 110 °C, R_{t1} = 17.7, R_{t1} = 18.3; for isobutyrophenone T = 110 °C, R_{t1} = 23.8, R_{t1} = 24.1. The optical rotation of the product was compared to a literature value to assign the absolute configuration.[19]

(*S*)-(2-Carboxy-1-ethylethyl)diphenylphospane−Borane (3b): Separation was by chiral HPLC (ref.[13]): White powder; m.p. = 98 °C; R_f = 0.5 (cyclohexane/ethyl acetate, 7:3). $[\alpha]_D^{20}$ = +47.7 (*c* = 1.06, $CHCl_3$). ^{1}H NMR: δ = 0.5−1.5 (m, 3 H), 0.9 (t, *J* = 7 Hz, 3 H), 2.4−2.7 (m, 2 H), 3.0−3.2 (m, 1 H), 7.4−7.6 (m, 6 H), 7.7−7.9 (m, 4 H) ppm. ^{31}P NMR: δ = 24.6 ppm. ^{13}C NMR: δ = 13 (d, *J* = 10.3 Hz), 23.8 (d, *J* = 3.4 Hz), 31.4 (d, *J* = 37.1 Hz), 34.4 (d, *J* = 5.7 Hz), 128−129.4, 131.9−133.1, 178.5 (d, *J* = 13.1 Hz) ppm. $C_{17}H_{22}BO_2P$ (300.15): calcd. C 68.03, H 7.39; found C 68.08, H 7.43.

(*R*)-3-(2-Carboxy-1-isopropylethyl)diphenylphospane−Borane (3c): Separation was by chiral HPLC (ref [14]):White powder; m.p. = 109 °C; R_f = 0.35 (cyclohexane/ethyl acetate, 7:3). $[\alpha]_D^{20}$ = +27.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.5−1.5 (m, 3 H), 0.85 (d, *J* = 6.7 Hz, 3 H), 0.91 (d, *J* = 6.7 Hz, 3 H), 1.9−2.1 (m, 1 H), 2.4−2.7 (m, 2 H), 3.1−3.3 (m, 1 H), 7.2−7.5 (m, 6 H), 7.6−7.8 (m, 4 H) ppm. ^{31}P NMR: δ = 23.8 ppm. ^{13}C NMR: δ = 17.5 (d, *J* = 2.8 Hz), 22.5 (d, *J* = 10.3 Hz), 26.7 (d, *J* = 4 Hz), 29 (d, *J* = 5.7 Hz), 33.9 (d, *J* = 34.8 Hz), 126.9−127.7, 129.5−133.7, 177.2 (d, *J* = 12 Hz) ppm. $C_{18}H_{24}BO_2P$ (314.18): calcd. C 68.82, H 7.70; found C 68.63, H 7.50.

(*R*)-3-(2-Carboxy-1-phenylethyl)diphenylphospane−Borane (3d): Separation was by chiral HPLC (ref. [16]):White powder; m.p. = 179 °C; R_f = 0.52 (cyclohexane/ethyl acetate, 5:5). $[\alpha]_D^{20}$ = +197.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.5−1.5 (m, 3 H), 2.7−2.9 (m, 1 H), 3.1−3.3 (m, 1 H), 4.1−4.3 (m, 1 H), 6.9−7.4 (m, 10 H), 7.4−7.6 (m, 3 H), 7.8−8 (m, 2 H) ppm. ^{31}P NMR: δ = 25.6 ppm. ^{13}C NMR: δ = 35.6 (d, *J* = 7.4 Hz), 39.2 (d, *J* = 32.4 Hz), 128−134.9, 178.2 (d, *J* = 15.3 Hz) ppm. $C_{21}H_{22}BO_2P$ (348.19): calcd. C 72.44, H 6.37; found C 71.92, H 6.02.

[(1*R*)-2-Benzyloxy-1-phenylethyl][(3*S*)-3-(diphenylphosphanyl)-butyl]amine (5): White oil; R_f = 0.56 (cyclohexane/ethyl acetate, 6:4). ^{1}H NMR: δ = 0.83 (dd, *J* = 6.9, *J* = 15.1 Hz, 3 H), 1.1−1.3 (m, 1 H), 1.5−1.7 (m, 1 H), 1.8 (s, 1 H), 2.3−2.5 (m, 3 H), 3.34 (dd, *J* = 9.2, *J* = 9.2 Hz, 1 H), 3.40 (dd, *J* = 3.9, *J* = 9.5 Hz, 1 H), 3.75 (dd, *J* = 3.8, *J* = 9.0 Hz, 1 H), 4.38 (d, *J* = 15.9 Hz, 1 H), 4.43 (d, *J* = 15.9 Hz, 1 H), 7.1−7.3 (m, 16 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = 0.58 ppm. ^{13}C NMR: δ = 14.9 (d, *J* = 16.0 Hz), 26.3 (d, *J* = 9.1 Hz), 32.3 (d, *J* = 16.6 Hz), 43.8 (d, *J* = 12.6 Hz), 61.6, 72.2, 74.5, 126.3, 126.5, 126.6, 126.7, 127.15 (d, *J* = 6.8), 127.2 (d, *J* = 6.8 Hz), 127.21, 127.4, 127.5 (d, *J* = 4.0 Hz), 132.5 (d, *J* = 18.8 Hz), 132.6 (d, *J* = 18.8 Hz), 136.2 (d, *J* = 15.0 Hz), 136.3 (d, *J* = 15.0 Hz), 137.0, 139.7 ppm.

[(1*S*)-2-Benzyloxy-1-phenylethyl][(3*S*)-3-(diphenylphosphanyl)-butyl]amine (6): White oil; R_f = 0.56 (cyclohexane/ethyl acetate, 6:4). ^{1}H NMR: δ = 0.88 (dd, *J* = 6.7, *J* = 14.8 Hz, 3 H), 1.2−1.4 (m, 1 H), 1.5−1.7 (m, 1 H), 1.88 (s, 1 H), 2.2−2.3 (m, 1 H), 2.3−2.4

(m, 1 H), 2.5−2.6 (m, 1 H), 3.35 (dd, *J* = 9.0, *J* = 9.2 Hz, 1 H), 3.43 (dd, *J* = 3.8, *J* = 9.4 Hz, 1 H), 3.78 (dd, *J* = 3.8, *J* = 8.7 Hz, 1 H), 4.37 (d, *J* = 15.6 Hz, 1 H), 4.42 (d, *J* = 15.9 Hz, 1 H), 7.15−7.25 (m, 16 H), 7.3−7.4 (m, 4 H) ppm. ^{31}P NMR: δ = 0.20 ppm. ^{13}C NMR: δ = 15.3 (d, *J* = 16.0 Hz), 27.0 (d, *J* = 10.3 Hz), 32.8 (d, *J* = 16.6 Hz), 44.6 (d, *J* = 12.6 Hz), 61.9, 72.2, 74.4, 126.3, 126.5, 126.6, 126.7, 127.2 (d, *J* = 6.3 Hz), 127.3, 127.4, 127.6 (d, *J* = 8.6), 132.4 (d, *J* = 21.7 Hz), 132.7 (d, *J* = 21.7 Hz), 136.0 (d, *J* = 14.8 Hz), 136.2 (d, *J* = 14.3 Hz), 137.0, 139.7 ppm.

[(3*S*)-3-(Diphenylphosphanyl)butyl][(1*S*)-1-phenylethyl]amine (7): White oil; R_f = 0.46 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR: δ = 0.85 (dd, *J* = 6.9, *J* = 15.1 Hz, 3 H), 1.23 (d, *J* = 6.6 Hz, 3 H), 1.25−1.4 (m, 1 H), 1.5−1.7 (m, 2 H), 2.2−2.4 (m, 2 H), 2.5−2.6 (m, 1 H), 3.58 (q, *J* = 6.6 Hz, 1 H), 7.1−7.3 (m, 11 H), 7.4−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = 0.40 ppm. ^{13}C NMR: δ = 16.6 (d, *J* = 16.0 Hz), 24.8, 28.1 (d, *J* = 9.7 Hz), 34.0 (d, *J* = 17.1 Hz), 45.8 (d, *J* = 12.6 Hz), 58.5, 127.0, 127.3, 128.7 (d, *J* = 6.8 Hz), 128.8 (d, *J* = 8.0 Hz), 128.83, 129.4 (d, *J* = 4.6 Hz), 134.0 (d, *J* = 18.8 Hz), 134.0 (d, *J* = 19.4 Hz), 137.5 (d, *J* = 14.3 Hz), 137.7 (d, *J* = 13.7 Hz), 145 ppm.

[(3*S*)-3-(Diphenylphosphanyl)butyl]ethylamine (8): Colorless oil; R_f = 0.37 (methanol/dichloromethane, 6:4). ^{1}H NMR: δ = 0.87 (t, *J* = 7.1 Hz, 3 H), 0.95 (dd, *J* = 6.9, *J* = 14.6 Hz, 3 H), 1.18 (s, 1 H), 1.2−1.4 (m, 1 H), 1.5−1.7 (m, 1 H), 2.1−2.3 (m, 1 H), 2.7−2.9 (m, 1 H), 2.9−3.2 (m, 2 H), 7.1−7.3 (m, 6 H), 7.3−7.6 (m, 4 H) ppm. ^{31}P NMR: δ = −0.57 ppm. ^{13}C NMR: δ = 13.0, 16.2 (d, *J* = 14.9 Hz), 27.9 (d, *J* = 12.6 Hz), 31.4 (d, *J* = 17.7 Hz), 42.6, 45.6 (d, *J* = 13.7 Hz), 128.2 (d, *J* = 6.8 Hz), 128.3 (d, *J* = 5.7 Hz), 128.7 (d, *J* = 6.3 Hz), 129.2 (d, *J* = 9.7 Hz), 133.3 (d, *J* = 18.8 Hz), 133.6 (d, *J* = 19.4 Hz), 136.8 (d, *J* = 13.7 Hz), 137.1 (d, *J* = 13.7 Hz) ppm.

[(3*S*)-3-(Diphenylphosphanyl)butyl][(1*R*)-1-phenylethyl]amine (9): White oil; R_f = 0.4 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR: δ = 0.88 (dd, *J* = 6.9, *J* = 14.8 Hz, 3 H), 1.2 (d, *J* = 6.4 Hz, 3 H), 1.1−1.4 (m, 1 H), 1.5−1.7 (m, 1 H), 1.96 (s, 1 H), 2.2−2.3 (m, 1 H), 2.3−2.5 (m, 1 H), 2.5−2.6 (m, 1 H), 3.58 (q, *J* = 6.4 Hz, 1 H), 7.1−7.3 (m, 11 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = 0.00 ppm. ^{13}C NMR: δ = 18.9 (d, *J* = 16.0 Hz), 26.5, 30.5 (d, *J* = 9.7 Hz), 36.2 (d, *J* = 16.6 Hz), 48.1 (d, *J* = 12.0 Hz), 60.5, 129.0, 129.4, 130.7 (d, *J* = 6.8 Hz), 130.8 (d, *J* = 6.8 Hz), 130.9, 131.1 (d, *J* = 6.3 Hz), 135.9 (d, *J* = 18.3 Hz), 136.2 (d, *J* = 18.9 Hz), 139.5 (d, *J* = 14.8 Hz), 139.7 (d, *J* = 14.8 Hz), 147.9 ppm.

[2-(Benzyloxy)ethyl][(3*S*)-3-(diphenylphosphanyl)butyl]amine (10): White oil; R_f = 0.25 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR: δ = 0.92 (dd, *J* = 6.9, *J* = 14.6 Hz, 3 H), 1.3−1.4 (m, 1 H), 1.5−1.7 (m, 1 H), 2.3−2.4 (m, 1 H), 2.5−2.8(m, 2 H), 2.66 (t, *J* = 5.1 Hz, 2 H), 3.15 (s, 1 H), 3.48 (t, *J* = 5.1 Hz, 2 H), 4.4 (s, 2 H), 7.1−7.3 (m, 11 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = −0.07 ppm. ^{13}C NMR: δ = 16.7 (d, *J* = 16.0 Hz), 28.3 (d, *J* = 9.7 Hz), 33.5 (d, *J* = 17.1 Hz), 47.9 (d, *J* = 12.6 Hz), 49.4, 69.6, 73.6, 128.1, 128.2, 128.8, 128.9 (d, *J* = 7.4 Hz), 129.0 (d, *J* = 6.3 Hz), 129.1 (d, *J* = 5.7 Hz), 134.0 (d, *J* = 21.1 Hz), 134.1 (d, *J* = 21.7 Hz), 137.4 (d, *J* = 13.7 Hz), 137.6 (d, *J* = 13.7 Hz), 138.6 ppm.

Benzyl[(3*S*)-3-(diphenylphosphanyl)butyl]amine (11): White oil; R_f = 0.26 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR: δ = 0.93 (dd, *J* = 6.9, *J* = 15.1 Hz, 3 H), 1.2−1.4 (m, 1 H), 1.5−1.7 (m, 1 H), 1.51 (s, 1 H), 2.3−2.4 (m, 1 H), 2.5−2.65 (m, 1 H), 2.65−2.8 (m, 1 H), 3.6 (d, *J* = 15.9 Hz, 1 H), 3.64 (d, *J* = 15.6 Hz, 1 H), 7.1−7.3 (m, 11 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = 0.17 ppm. ^{13}C NMR: δ = 18.7 (d, *J* = 16.0 Hz), 30.2 (d, *J* = 9.7 Hz), 35.9 (d, *J* = 17.1 Hz), 49.5 (d, *J* = 12.6 Hz), 56.2, 129.3, 130.5, 130.65 (d, *J* = 6.3 Hz), 130.72 (d, *J* = 4.6 Hz), 130.75, 131.1 (d, *J* = 4.6 Hz), 135.9 (d, *J* = 18.3 Hz), 135.1 (d, *J* = 19.4 Hz), 139.5 (d, *J* = 13.7 Hz), 139.6 (d, *J* = 13.7 Hz), 142.7 ppm.

[(3*S*)-3-(Diphenylphosphanyl)butyl]amine (12): White oil; R_f = 0.15 (methanol). ^{1}H NMR: δ = 0.97 (dd, *J* = 6.9, *J* = 16.9 Hz, 3 H), 1.3−1.5 (m, 1 H), 1.5−1.7 (m, 3 H), 2.2−2.4 (m, 1 H), 2.5−2.6 (m, 1 H), 2.6−2.7 (m, 1 H), 7.1−7.3 (m, 6 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = 0.1 ppm. ^{13}C NMR: δ = 16.8 (d, *J* = 15.4 Hz), 28.5 (d, *J* = 10.3 Hz), 34.2 (d, *J* = 17.1 Hz), 47.7 (d, *J* = 12.6 Hz), 128.6 (d, *J* = 7.4 Hz), 128.8 (d, *J* = 6.3 Hz), 129.1 (d, *J* = 5.7 Hz), 133.9 (d, *J* = 18.8 Hz), 134.2 (d, *J* = 18.8 Hz), 137.4 (d, *J* = 13.1 Hz), 137.6 (d, *J* = 13.1 Hz) ppm.

2-[(3*S*)-3-(Diphenylphosphanyl)butylamino]-2-(2*R*)-phenylethanol (13): White oil; R_f = 0.5 (ethyl acetate). ^{1}H NMR: δ = 0.86 (dd, *J* = 6.9, *J* = 14.8 Hz, 3 H), 1.2−1.4 (m, 1 H), 1.5−1.7 (1 H), 2.32 (s, 2 H), 2.4−2.6 (m, 3 H), 3.3−3.45 (m, 1 H), 3.5−3.6 (m, 2 H), 7.1−7.3 (m, 11 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = 0.26 ppm. ^{13}C NMR: δ = 16.6 (d, *J* = 15.4 Hz), 28.2 (d, *J* = 9.7 Hz), 34.0 (d, *J* = 16.6 Hz), 45.4 (d, *J* = 12.0 Hz), 64.8, 67.1, 127.6, 128.0, 128.7 (d, *J* = 6.8 Hz), 128.8 (d, *J* = 6.8 Hz), 129.0, 129.1 (d, *J* = 4.0 Hz), 134.0 (d, *J* = 18.8 Hz), 134.1 (d, *J* = 19.4 Hz), 137.4 (d, *J* = 14.8 Hz), 137.6 (d, *J* = 14.8 Hz) ppm.

[(3*S*)-3-(Diphenylphosphanyl)propyl][(1*R*)-1-phenylethyl]amine (14): White oil; R_f = 0.4 (cyclohexane/ethyl acetate, 5:5). ^{1}H NMR: δ = 1.4−1.5 (m, 2 H), 1.8−2.0 (m, 2 H), 2.4−2.6 (m, 2 H), 2.96 (s, 2 H), 3.4 (dd, *J* = 8.7, *J* = 10.5 Hz, 1 H), 3.51 (dd, *J* = 4.1, *J* = 10.5 Hz, 1 H), 3.58 (dd, *J* = 4.1, *J* = 8.5 Hz, 1 H), 7.0−7.2 (m, 11 H), 7.2−7.3 (m, 4 H) ppm. ^{31}P NMR: δ = −15.0 ppm. ^{13}C NMR: δ = 26.8 (d, *J* = 11.4 Hz), 27.6 (d, *J* = 16.0 Hz), 49.5 (d, *J* = 13.7 Hz), 65.8, 67.8, 128.6, 128.8, 129.6 (d, *J* = 6.8 Hz), 129.8, 133.9 (d, *J* = 18.8 Hz), 139.9 (d, *J* = 12.6 Hz), 141.75 ppm.

2-[(3*S*)-3-(Diphenylphosphanyl)propylamino]-2-(2*R*)-phenylethanol (15): Colorless oil; R_f = 0.15 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR: δ = 1.4 (d, *J* = 6.6 Hz, 3 H), 1.5−1.6 (m, 1 H), 1.6−1.8 (m, 2 H), 2.0−2.2 (m, 2 H), 2.6−2.8 (m, 2 H), 3.8 (q, *J* = 6.6 Hz, 1 H), 7.3−7.5 (m, 11 H), 7.5−7.56 (m, 4 H) ppm. ^{31}P NMR: δ = −14.7 ppm. ^{13}C NMR: δ = 24.9, 26.2 (d, *J* = 11.4 Hz), 27.2 (d, *J* = 16.0 Hz), 49.3 (d, *J* = 13.7 Hz), 58.6, 127.1, 127.4, 128.85, 128.88 (d, *J* = 6.8 Hz), 128.95, 128.97 (d, *J* = 9.7 Hz), 133.2 (d, *J* = 18.3 Hz), 133.3 (d, *J* = 18.3), 139.3 (d, *J* = 13.1 Hz), 139.3 (d, *J* = 13.1 Hz), 146.2 ppm.

[(3*S*)-3-(Diphenylphosphanyl)propyl][(1*R*)-1-(ethoxymethoxymethyl)propyl]amine (16): White oil; R_f = 0.48 (cyclohexane/ethyl acetate, 5:5). ^{1}H NMR: δ = 0.81 (t, *J* = 7.4 Hz, 3 H), 1.1 (t, *J* = 7.0 Hz, 3 H), 1.25−1.5 (m, 2 H), 1.5−1.7 (m, 3 H), 1.9−2.1 (m, 2 H), 2.4−2.6 (m, 1 H), 2.6−2.7 (m, 2 H), 3.3 (dd, *J* = 6.4, *J* = 9.7, 1 H), 3.5 (q, *J* = 7.1 Hz, 2 H), 3.6 (dd, *J* = 3.8, *J* = 10.0 Hz, 1 H), 4.58 (s, 2 H), 7.2−7.3 (m, 6 H), 7.3−7.5 (m, 4 H) ppm. ^{31}P NMR: δ = −14.9 ppm. ^{13}C NMR: δ = 10.7, 15.6, 24.6, 26.2 (d, *J* = 12.0 Hz), 27.2 (d, *J* = 16.0 Hz), 48.6 (d, *J* = 13.7 Hz), 59.0, 63.6, 69.7, 95.7, 128.8 (d, *J* = 6.8 Hz), 133.1 (d, *J* = 18.3), 139.1 (d, *J* = 12.6 Hz) ppm.

[(1*R*)-2-Benzyloxy-1-phenylethyl][(3*S*)-3-(diphenylphosphanyl)-propyl]amine (17): White oil; R_f = 0.30 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR: δ = 0.75 (t, *J* = 7.4 Hz, 3 H), 1.2−1.4 (m, 2 H), 1.4−1.67 (m, 3 H), 1.9−2.0 (m, 2 H), 2.5−2.7 (m, 3 H), 3.23 (dd, *J* = 6.9, *J* = 9.2 Hz, 1 H), 3.37 (dd, *J* = 4.3, *J* = 9.2 Hz, 1 H), 4.38 (s, 2 H), 7.1−7.25 (m, 11 H), 7.3−7.45 (m, 4 H) ppm. ^{31}P NMR: δ = −14.8 ppm. ^{13}C NMR: δ = 10.7, 24.7, 26.2 (d, *J* = 12.0 Hz), 27.2 (d, *J* = 16.0 Hz), 48.7 (d, *J* = 13.7 Hz), 59.0, 72.6,

73.6, 128.1, 128.8, 128.85 (d, J = 6.3 Hz), 128.9, 129.0, 133.2, 138.9, 139.2 (d, J = 13.1 Hz), 139.3 (d, J = 12.6 Hz) ppm.

[(1*R*)-1-Benzyloxymethylpropyl][(3*S*)-3-(diphenylphosphanyl)-propyl]amine (18): Colorless oil; R_f = 0.56 (cyclohexane/ethyl acetate, 6:4). ^{1}H NMR: δ = 1.5−1.7 (m, 2 H), 1.9−2.1 (m, 3 H), 2.5−2.6 (m, 2 H), 3.4 (dd, J = 9.2, J = 9.2 Hz, 1 H), 3.5 (dd, J = 4.0, J = 9.5 Hz, 1 H), 3.85 (dd, J = 3.9, J = 9.0 Hz, 1 H), 4.48 (d, J = 16.1 Hz, 1 H), 4.54 (d, J = 15.9 Hz, 1 H), 7.1−7.3 (m, 16 H), 7.3−7.4 (m, 4 H) ppm. ^{31}P NMR: δ = −14.6 ppm. ^{13}C NMR: δ = 26.2 (d, J = 11.4 Hz), 27.0 (d, J = 16.0 Hz), 49.1 (d, J = 13.7 Hz), 63.3, 73.8, 76.0, 128.0, 128.2, 128.25, 128.3, 128.85, 128.9, 128.92 (d, J = 6.3 Hz), 128.95, 128.97 (d, J = 5.1 Hz), 133.2 (d, J = 18.3 Hz), 138.6, 139.3 (d, J = 13.1 Hz), 139.4 (d, J = 13.1 Hz), 141.3 ppm.

[(3*S*)-3-(Diphenylphosphanyl)pentyl][(1*R*)-1-phenylethyl]amine (19): White oil; R_f = 0.42 (cyclohexane/ethyl acetate/triethylamine, 8.5:1.5:0.5). ^{1}H NMR: δ = 0.82 (t, J = 7.2 Hz, 3 H), 1.2 (d, J = 6.4 Hz, 3 H), 1.0−1.6 (m, 5 H), 2.0−2.2 (m, 1 H), 2.3−2.5 (m, 2 H), 3.55 (q, J = 6.6 Hz, 1 H), 7.0−7.5 (m, 15 H) ppm. ^{31}P NMR: δ = − 5.45 ppm. ^{13}C NMR: δ = 10.8 (d, J = 11.4 Hz), 22.1 (d, J = 14.8 Hz), 23.3, 29.2 (d, J = 14.3 Hz), 33.8 (d, J = 11.4 Hz), 44.7 (d, J = 10.3 Hz), 57.0, 125.4−136.3, 144.6 ppm.

[(3*S*)-3-(Diphenylphosphanyl)pentyl][(1*S*)-1-phenylethyl]amine (20): White oil; R_f = 0.42 (cyclohexane/ethyl acetate/triethylamine, 8.5:1.5:0.5). ^{1}H NMR: δ = 0.82 (t, J = 7.2 Hz, 3 H), 1.2 (d, J = 6.4 Hz, 3 H), 1.0−1.6 (m, 5 H), 2.1−2.3 (m, 1 H), 2.3−2.4 (m, 2 H), 3.55 (q, J = 6.6 Hz, 1 H), 7.0−7.5 (m, 15 H) ppm. ^{31}P NMR: δ = − 5.29 ppm. ^{13}C NMR: δ = 10.8 (d, J = 11.4 Hz), 22.1 (d, J = 14.8 Hz), 23.3, 29.2 (d, J = 14.3 Hz), 33.8 (d, J = 11.4 Hz), 44.7 (d, J = 10.3 Hz), 57.0, 125.4−136.3, 144.6 ppm.

[(3*R*)-3-(Diphenylphosphanyl)-4-methylpentyl][(1*R*)-1-phenylethyl]-amine (21): White oil; R_f = 0.72 (cyclohexane/ethyl acetate/triethylamine, 8:2:0.5). ^{1}H NMR: δ = 0.82 (t, J = 7.4 Hz, 3 H), 0.85 (t, J = 7.4 Hz, 3 H), 1.04 (s, 1 H), 1.1 (d, J = 6.7 Hz, 3 H), 1.3−1.6 (m, 2 H), 1.7−1.8 (m, 1 H), 1.9−2.0 (m, 1 H), 2.0−2.2 (m, 2 H), 3.4 (q, J = 6.6 Hz, 1 H), 7.0−7.5 (m, 15 H) ppm. ^{31}P NMR: δ = − 6.75 ppm. ^{13}C NMR: δ = 17.4 (d, J = 10.8 Hz), 21 (d, J = 8.6 Hz), 23.3, 27.0 (d, J = 15.4 Hz), 27.9 (d, J = 16 Hz), 38.4 (d, J = 14.6 Hz), 46.8 (d, J = 6.8 Hz), 57.0, 125.4−136.9, 144.7 ppm.

[(3*R*)-3-(Diphenylphosphanyl)-4-methylpentyl][(1*S*)-1-phenylethyl]-amine (22): White oil; R_f = 0.72 (cyclohexane/ethyl acetate/triethylamine, 8:2:0.5). ^{1}H NMR: δ = 0.82 (t, J = 7.4 Hz, 3 H), 0.85 (t, J = 7.4 Hz, 3 H), 1.04 (s, 1 H), 1.1 (d, J = 6.7 Hz, 3 H), 1.3−1.6 (m, 2 H), 1.7−1.8 (m, 1 H), 1.9−2.0 (m, 1 H), 2.0−2.2 (m, 2 H), 3.4 (q, J = 6.6 Hz, 1 H), 7.0−7.5 (m, 15 H) ppm. ^{31}P NMR: δ = − 6.72 ppm. ^{13}C NMR: δ = 17.4 (d, J = 10.8 Hz), 21 (d, J = 8.6 Hz), 23.3, 27.0 (d, J = 15.4 Hz), 27.9 (d, J = 16 Hz), 38.4 (d, J = 14.6 Hz), 46.8 (d, J = 6.8 Hz), 57.0, 125.4−136.9, 144.7 ppm.

[(3*R*)-3-(Diphenylphosphanyl)-3-phenylpropyl][(1*R*)-1-phenylethyl]-amine (23): White powder; R_f = 0.40 (cyclohexane/ethyl acetate/triethylamine, 8.5:1.5:0.5). ^{1}H NMR: δ = 1.7−2.0 (m, 2 H), 2.0−2.4 (m, 3 H), 3.3−3.5 (m, 1 H), 3.5−3.7 (m, 1 H), 6.8−7.9 (m, 20 H) ppm. ^{31}P NMR: δ = 1.15 ppm. ^{13}C NMR: δ = 28.5, 32.1 (d, J = 9.4), 42.1 (d, J = 12.6), 44.4 (d, J = 11.4), 56.5, 125.1−135.9, 144.2, 144.5.

[(3*S*)-3-(Diphenylphosphanyl)-3-phenylpropyl][(1*R*)-1-phenylethyl]-amine (24): White powder; R_f = 0.40 (cyclohexane/ethyl acetate/triethylamine, 8.5:1.5:0.5). ^{1}H NMR: δ = 1.7−2.0 (m, 2 H), 2.0−2.4 (m, 3 H), 3.3−3.5 (m, 1 H), 3.5−3.7 (m, 1 H), 6.8−7.9 (m, 20 H) ppm. ^{31}P NMR: δ = 1.36 ppm. ^{13}C NMR: δ = 28.5, 32.1 (d, J = 9.4 Hz), 42.1 (d, J = 12.6 Hz), 44.4 (d, J = 11.4 Hz), 56.5, 125.1−135.9, 144.2, 144.5 ppm.

Supporting Information Available (see footnote on the first page of this article): Yields, spectroscopic and analytical data for the amides and amines precursors of ligands (PDF).

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[13] Chiralcel OJ-H Column 250 × 20 mm; flow: 8 mL/min., 19 °C, UV detector (250 nm), eluent: heptane/2-propanol/formic acid, 93:7:0.5. Retention times: (*R*)-(−): R_t = 25.3 min, (*S*)-(+): R_t = 29.2 min.

[14] Chiralcel OJ-H Column 250 × 20 mm; flow: 8 mL/min, 19 °C, UV detector (250 nm), eluent: heptane/2-propanol/formic acid, 93:7:0.5. Retention times: (*S*)-(−): R_t = 22.4 min, (R)-(+): R_t = 26.5 min.

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[16] Chiralcel OJ-H Column 250 × 20 mm; flow: 6 mL/min., 19 °C, UV detector (250 nm), eluent: heptane/2-propanol/formic acid, 80:20:0.5. Retention times: (*S*)-(−): R_t = 22.4 min, (*R*)-(+): R_t = 27.0 min.

[17] A slow background epimerization of the product was observed; short reaction times were therefore highly advantageous.

[18] In 93% of the experiments, conversion rates of 80% or more are obtained in less than 9 h (all the conversions rates (for each ketone) and for each ligand are collected in the Supporting Information).

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