RSC Advances

PAPER

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Cite this: *RSC Adv.*, 2023, **13**, 34439

Synthesis of *P*-stereogenic 1-phosphanorbornane-derived phosphine–phosphite ligands and application in asymmetric catalysis†‡

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Received 8th November 2023
Accepted 10th November 2023

DOI: 10.1039/d3ra07630j

rsc.li/rsc-advances

A convenient synthesis of enantiopure mixed donor phosphine–phosphite ligands has been developed incorporating *P*-stereogenic phosphanorbornane and axially chiral bisnaphthols into one ligand structure. The ligands were applied in Pd-catalyzed asymmetric allylic substitution of diphenylallyl acetate, Rh-catalyzed asymmetric hydroformylation of styrene and Rh-catalyzed asymmetric hydrogenation of an acetylated dehydroamino ester. Excellent branched selectivity was observed in the hydroformylation although low *ee* was found. Moderate *ee*'s of up to 60% in allylic substitution and 50% in hydrogenation were obtained using bisnaphthol-derived ligands.

Introduction

Phosphines have been the cornerstone of homogeneous catalysis for the last six decades.[1] Especially, chiral phosphines are still the dominating class of ligands used in asymmetric catalysis.[2,3] A plethora of *P*-stereogenic phosphines have already been reported; however, the search for better, more efficient and sustainable ligands is still ongoing as the topic remains demanding even in the present day. The discovery of the well-known cyclohexyl(*o*-anisyl)methylphosphine (CAMP) and (ethane-1,2-diyl)bis[(2-methoxyphenyl)(phenyl)phosphine] (DIPAMP) used in Rh-catalyzed asymmetric hydrogenation[4] boosted the scientific interest in *P*-stereogenic[5–9] (or *P*-chiral, *P*-chirogenic, *P**-) ligands. Despite the challenging synthesis of *P**-phosphines, a number of methods has been developed with pioneering contributions from Mislow,[10] Knowles,[4] Horner,[11] Börner,[12] Jugé,[13] van Leeuwen and Kamer[14] and many more.[1,3] Very often resolution of secondary or tertiary phosphine oxides,[15] use of bifunctional chiral auxiliaries ((−)-ephedrine or amino-alcohols),[13] chiral base ((−)-sparteine) mediated enantioselective deprotonation,[16] or chiral amine ((*R*/*S*)-1-phenylethylamine) as modifier[17,18] are used for the preparation of *P**-synthons. The *P**-phosphine-borane adduct reported by Imamoto *et al.* has opened the way to a number of benchmark *P**- phosphines which induce high enantioselectivity and can be used in various transition metal catalysed asymmetric transformations.[19,20] However, in most cases, acyclic *P**-synthons or ligands are used. Bidentate ligands based on *P**- phosphacycles are scarce in the literature. At the same time, mixed donor bidentate phosphines are quite successful in many enantioselective transformations.[21,22] The phosphine–phosphite ligand class developed by van Leeuwen *et al.*,[23] Pizzano *et al.*,[24] Vidal-Ferran *et al.*,[25] and others were successfully applied in several hydrofunctionalization reactions (selected examples of ligands are shown in Fig. 1). Hey-Hawkins and co-workers reported the first phospha-aza-Diels–Alder cycloaddition reactions to give *P**-phosphacycles (1-phospha-2-azanorbornenes)[26] and could show that the products undergo P–N bond cleavage to afford racemic and enantiopure 1-alkoxy-2,3-dihydrophosphole derivatives[27,28] or reduction to seven-membered phosphacycles.[29] Moreover, in 2012 we reported an unprecedented asymmetric phospha-Diels–Alder reaction between 2*H*-phosphole and (5*R*)-(L-menthyloxy)-2(5*H*)-furanone (MOxF) to give *P*-stereogenic 1-phosphanorbornenes in high diastereoselectivity (Scheme 1).[26] The diastereomers were separated *via* crystallization. Further functionalizations gave enantiomerically pure *P**-1-phosphanorbornane alcohol[30] (PNA; Scheme 1, 7) which was converted to silyl ethers *via* reaction with chlorosilanes. The resulting 1-phosphanorbornane silyl ethers were applied as ligands in asymmetric hydrogenations.[31] We therefore envisioned that further functionalization of the *P**-1-phosphanorbornane alcohol 7 could serve as the key step in the synthesis of various bidentate ligands.[30]

Herein, we report the synthesis of 1-phosphanorbornane-based *P*-stereogenic mixed donor bidentate ligands and their application in Pd-catalyzed asymmetric allylic substitution of

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† In memory of Prof. Paul C. J. Kamer.

‡ Electronic supplementary information (ESI) available. CCDC 2302227. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d3ra07630j

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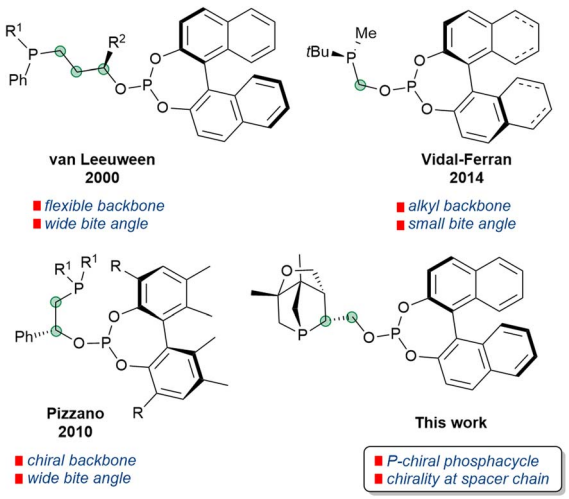
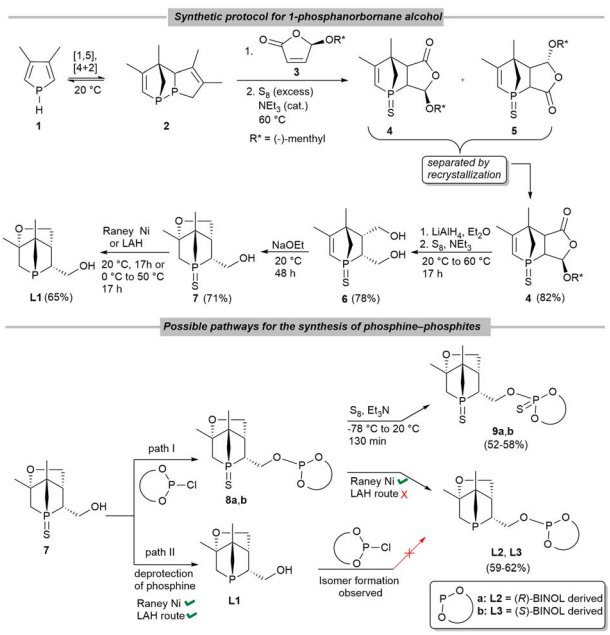


Fig. 1 Selected examples of mixed donor backbone-chiral and *P*-chiral phosphine–phosphites.



Scheme 1 Synthetic protocol for 1-phosphanorbornane alcohol **L1** (top) and pathway for the synthesis of phosphine–phosphite ligands **9a, b** and **L2**, **L3** (bottom).

benchmark diphenylallyl acetate, Rh-catalyzed asymmetric hydrogenation of methyl (*Z*)-2-acetamido-3-phenylacrylate and Rh-catalyzed asymmetric hydroformylation of styrene.

Results and discussion

Synthesis of mixed donor *P*-stereogenic phosphine–phosphites

The sulfur-protected *P*-stereogenic 1-phosphanorbornane alcohol (Scheme 1, **7**) was readily synthesized following the reported procedure in good yields (ESI, Fig. S1‡).[26,32,33] The unprotected compound **L1** can be obtained by reaction of **7** with either excess of freshly activated Raney nickel (Raney Ni) or with 4–5 eq. of $LiAlH_4$ at elevated temperatures for 17 h in THF (Scheme 1).

For the synthesis of bidentate (*R*)- or (*S*)-BINOL-based mixed donor ligands from **7**, two possible pathways were studied (Scheme 1, bottom). Path I involves the reaction of enantiopure BINOL-based chlorophosphites, which were prepared employing a general procedure for chlorophosphites,[34] with sulfur-protected PNA **7** in the presence of a mild base (such as NEt_3), followed by deprotection to give **L2, L3**. The mild reducing agent Raney Ni was used as desulfurizing reagent in this case in view of its high selectivity and facile work-up, as lithium aluminum hydride (LAH) also attacks the phosphite $P(OR)_3$ motif in **8a, b**. Path II started with deprotection of **7** to afford **L1** by either Raney Ni or LAH, followed by reaction with the corresponding chlorophosphites. However, the $^{31}P\{^1H\}$ NMR spectrum of the reaction mixture showed several signals for unidentified products, rendering this pathway unsuitable.

P-stereogenic 1-phosphanorbornane alcohol **L1** and the phosphine–phosphites **L2**, **L3** were fully characterized by NMR spectroscopy and high-resolution mass spectrometry. In the $^{31}P\{^1H\}$ NMR spectra ($CDCl_3$), **L1** exhibits a singlet at −45.9 ppm, while two singlets are observed for **L2** (135.4 and −44.7 ppm) and **L3** (139.4 and −44.7 ppm) which are characteristic signals for phosphites and phosphines, respectively.

Intermediates **8a, b** were sulfurized to obtain the double sulfur-protected air- and moisture-stable compounds **9a, b** (Scheme 1, bottom). The compounds were isolated by slowly cooling down a hot *i*PrOH solution and storing at −25 °C overnight. The structures of **9a, b** were confirmed by NMR spectroscopy and HRMS. Single crystals of **9b** (S-protected analogue of **L3**) suitable for X-ray crystal structure determination were obtained by slow evaporation of solvent from an ethyl acetate solution of **9b**; any other method resulted in formation of powder only due to rapid nucleation. Excellent chemical (98–100%) and optical purities of **9a, b** were verified by chiral HPLC (ESI, Fig. S23 and S24‡), thus also indirectly confirming the optical purities of **L2** and **L3**.

As shown in Fig. 2, both phosphorus atoms in compound **9b** have a distorted tetrahedral environment. The P–O bond lengths of the phosphite moiety are in the range of 156.6–159.8 pm in agreement with the literature.[35] Moreover, both P═S bond lengths (188.9 pm and 194.0 pm) are comparable to those reported previously.[36]

Application of *P*-chiral ligands in asymmetric catalysis

Monodentate PNA **L1** and bidentate BINOL-derived mixed donor phosphine–phosphites **L2**, **L3** were tested in several benchmark transformations in asymmetric catalysis.

The Pd-catalyzed enantioselective allylation[37] is an important method for C–C or C–heteroatom bond formation, where hybrid bidentate phosphines (P,P′), bulky monodentate phosphines (mostly phosphoramidites) and P,N ligands (P, oxazoline) have been employed successfully. The PNA (**L1**) and phosphine–phosphite ligands (**L2**, **L3**) were tested in the Pd-catalyzed asymmetric allylic alkylation of diphenylallyl acetate using

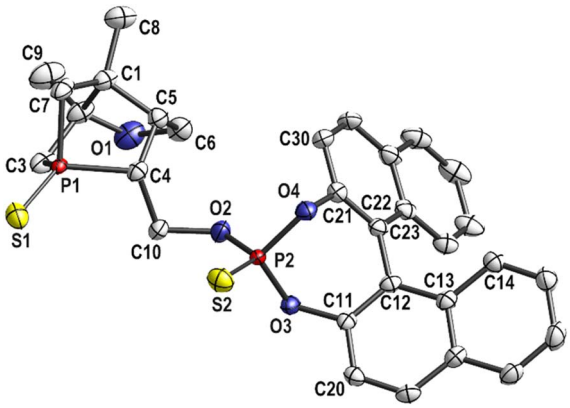
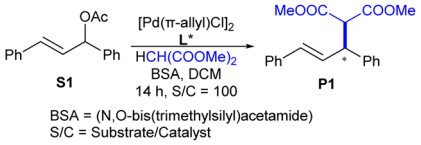


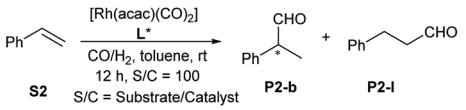
Fig. 2 Molecular structure of enantiopure sulfur-protected phosphine–phosphite **9b** analogue of **L3**. Hydrogen atoms are omitted for clarity. Displacement ellipsoids are drawn at the 50% probability level.

Table 1 Pd-catalyzed asymmetric allylic substitution of diphenylallyl acetate



Entry	Pd : L*	L*	Conversion (%)	*ee* (%)
1	1 : 2	**L1**	60%	15(*R*)
2	1 : 1	**L2**	>99%	26(*S*)
3	1 : 1	**L3**	>99%	60(*R*)

Table 2 Rh-catalyzed asymmetric hydroformylation of styrene

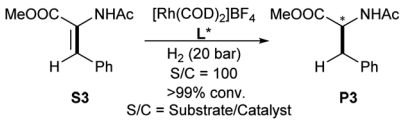


Entry	Rh : L*	CO/H_2 pressure (bar)	Conversion (%)	b/l	*ee* (%)
1	1 : 2 (**L1**)	20 (1 : 1)	>99	90/10	*rac*
2	1 : 1 (**L2**)	20 (1 : 1)	>99	99/1	3(*S*)
3	1 : 1 (**L3**)	20 (1 : 1)	>99	99/1	5(*R*)
4	1 : 2 (**L3**)	30 (1 : 1)	>99	99/1	11(*R*)
5	1 : 3 (**L3**)	30 (1 : 1)	>99	99/1	10(*R*)

dimethyl malonate as C-based nucleophile. Low conversion of diphenylallyl acetate was observed employing monodentate PNA (**L1**) (Pd/**L1** = 1 : 2) resulting in only 15% *ee* (entry 1, Table 1). Higher conversions (up to 60% *ee* in CH_2Cl_2) were obtained with the BINOL-derived ligands **L2** and **L3** (entries 2 and 3, Table 1).

As mixed donor phosphine–phosphite ligands have been used in the Rh-catalyzed asymmetric hydroformylation[38] of styrene, we also tested ligands **L1–L3** in this reaction. Excellent branch selectivity was observed for all ligands (Table 2), but poor *ee* values were obtained. The *ee* could be slightly improved by changing the **Rh**/**L3** ratio to 1 : 2 and increasing the syngas pressure to 30 bar. However, higher **L3**/**Rh** ratios did not afford higher *ee* values (Table 2).

Table 3 Rh-catalyzed asymmetric hydrogenation of methyl (*Z*)-2-acetamido-3-phenylacrylate



Entry	Rh : L*	L*	Solvent	*ee* (%)
1	1 : 2	**L1**	CH_2Cl_2	1
2	1 : 1	**L2**	CH_2Cl_2	3(*R*)
3	1 : 1	**L3**	CH_2Cl_2	5(*S*)
4	1 : 1	**L3**	MeOH	20(*S*)
5	1 : 1	**L3**	Toluene	n.r.
6	1 : 1	**L3**	THF	50(*S*)
7	1 : 1	**L3**	*n*-hexane	n.r.

Ligands **L1–L3** were also employed in the Rh-catalyzed asymmetric hydrogenation of the trisubstituted functionalized olefin methyl (*Z*)-2-acetamido-3-phenylacrylate as benchmark substrate (Table 3). Full conversion was achieved with $[Rh(COD)_2]BF_4$ and 2 eq. **L1** in CH_2Cl_2, albeit no *ee* was observed. However, a slight increase in *ee* (up to 50%, entry 6, Table 3) was observed with **L3** as bidentate ligand in THF.

Conclusions

The *P*-stereogenic enantiopure 1-phosphanorbornane-based mono- (**L1**) and bidentate ligands (**L2**, **L3**) combine different types of chiral information, namely *P*-chirality, backbone and axial chirality (for the BINOL derivatives). While monodentate **L1** gave up to 15% *ee* in the Pd-catalyzed allylic substitution of diphenylallyl acetate with dimethyl malonate as nucleophile, the BINOL-based backbone in **L2** and **L3** indeed improved the activity and enantioselectivity up to 60%. High branched selectivity was observed in the Rh-catalyzed asymmetric hydroformylation of styrene for **L1–L3**, albeit poor *ee* was observed. In the Rh-catalyzed asymmetric hydrogenation of a dehydroamino ester 50% *ee* was obtained with the mixed donor phosphine–phosphite ligand **L3** in THF. These results already show the potential of these ligands in asymmetric catalysis.

Experimental details

General consideration

The synthetic work was conducted using standard Schlenk and glovebox techniques. All reagents were purchased from commercial sources and used as received, unless stated otherwise. (*R*)- and (*S*)-BINOL were bought from Merck and used as received. Compound **7** was prepared according to the literature.[30] NEt_3 and $CDCl_3$ were dried over CaH_2, distilled prior to

use, and degassed with three freeze–pump–thaw cycles. THF was distilled from sodium/benzophenone and stored over activated 4 Å molecular sieves. Toluene and CH_2Cl_2 were bought from Acros Organics with 99.85% purity, <0.005% water content and stored under inert atmosphere over molecular sieves (3 Å). C_6D_6 was dried over Na/benzophenone and distilled prior to use. Samples for mass spectrometry were prepared in the glovebox and measured on a Finnigan MAT 95-XP (Thermo Electron) or Kratos MS-50 spectrometer 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, ^{13}C: 75.46, ^{31}P: 121.49 MHz), Bruker Fourier 300 (^{1}H: 300.13, ^{13}C: 75.46, ^{31}P: 121.49 MHz) or Avance 400 (^{1}H: 400.13, ^{13}C: 100.63, ^{31}P: 161.98 MHz) instruments operating at the denoted spectrometer frequency given in Megahertz (MHz) for the specified nucleus.

Synthesis of chlorophosphites. The synthesis was carried out according to the general procedure for chlorophosphites. The analytical data were in agreement with those reported.[34]

*Synthesis of phosphanorbornane alcohol (**L1**).* LAH route: A suspension of 4–6 eq. of lithium aluminium hydride in 5 ml THF was slowly portion-wise transferred at 0 °C to a solution of **7** (100 mg, 0.43 mmol) in 2 ml THF. The reaction mixture was stirred for 10 min at 0 °C then warmed to room temperature. After stirring the mixture overnight, the excess of LAH was quenched with an aqueous KOH solution (20%, 5 ml) at 0 °C with vigorous stirring. After stirring for an additional 15 min at 0 °C, the reaction mixture was heated to 50 °C for 1 h (this compacts the precipitate and facilitates faster and better filtration in the next step). The precipitate is isolated by filtration and washed 2–3 times with 10 ml THF each. Then the solvent was removed under reduced pressure to give a light beige oil.

Raney nickel route. Raney nickel was activated and destroyed according to the literature.[31] S-protected alcohol **7** (43 mg, 0.185 mmol) was added to a suspension of freshly activated Raney nickel (*ca.* 0.5 g, excess) in 2 ml THF and stirred for 17 h at room temperature. The clear solution was filtered and the black solid was washed four times with 3 ml THF each. The solution was concentrated to give 24 mg of **L1** as a beige oil (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92–3.72 (m, 3H), 2.58–2.43 (m, 1H), 2.28–2.21 (m, 1H), 1.73–1.69 (m, 1H), 1.60–1.52 (m, 1H), 1.44–1.38 (m, 1H), 1.20 (s, 3H), 1.15 (s, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 88.9, 64.4, 61.3, 51.5, 45.0, 38.6, 36.7, 24.6, 17.2 ppm. ^{31}P{^{1}H} NMR (161 MHz, $CDCl_3$): δ −45.9 (s) ppm. HRMS (ESI-TOF): m/z calculated for $C_{10}H_{18}O_2P$: 201.2367 $[M + H]^+$; observed 201.2249.

*Synthesis of **L2** and **L3**.* Triethylamine (0.33 mmol) was added at −78 °C to a THF solution of (*R*)- or (*S*)-BINOL chlorophosphite (0.3 mmol). Optically pure sulfur-protected **7** (0.3 mmol, 70 mg) was dissolved in 10 ml THF and added dropwise to the NEt_3–chlorophosphite mixture maintaining the low temperature. The reaction mixture was stirred at this temperature for 5 min and then warmed to room temperature and stirred overnight. The THF solution was filtered to remove the ammonium salt and the solvent evaporated under vacuum yielding an off-white solid. The solid was dissolved in 10 ml THF again and added to a THF suspension of freshly activated Raney Ni (1 g for 50 mg of **8a, b**) and stirred for 25 h at room temperature. The THF solution was filtered off and the black solid was washed 2–3 times with THF (5 ml). The combined solutions were evaporated under vacuum yielding **L2**, **L3** as off-white solid in 59–62% yield. The products were characterized by NMR spectroscopy and HRMS.

L2 (*R*-BINOL-derived): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08–7.91 (m, 4H), 7.59–7.27 (m, 8H), 4.61–4.50 (m, 1H), 3.93–3.90 (m, 1H), 3.78–3.73 (m, 2H), 2.79–2.58 (m, 1H), 2.49–2.40 (m, 1H), 2.20–1.97 (m, 2H), 1.90–1.82 (m, 2H), 1.26 (s, 3H), 1.19 (s, 3H). ^{13}C{^{1}H} (75 MHz, $CDCl_3$): δ 130.6, 128.5, 128.3, 128.0, 127.6, 127.2, 126.4, 125.2, 87.8, 68.1, 64.5, 45.9, 43.5, 38.5, 25.8, 24.7, 18.5. ^{31}P{^{1}H} NMR (122 MHz, $CDCl_3$): δ 135.4 (s) ppm, −44.7 (s) ppm. HRMS (ESI-TOF): m/z calculated for $C_{30}H_{29}O_4P_2$: 515.1270 $[M + H]^+$; observed 515.1255. EA: calcd. for $C_{30}H_{28}O_4P_2$: C: 70.05, H: 5.50. Found: C: 70.23, H: 5.47.

L3 (*S*-BINOL-derived): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99–7.96 (m, 4H), 7.47–7.32 (m, 8H), 4.38–4.28 (m, 1H), 3.88–3.73 (m, 2H), 3.03 (br, 1H), 2.61–2.54 (m, 1H), 2.32–2.24 (m, 1H), 1.90–1.86 (m, 2H), 1.66–1.52 (m, 2H), 1.22 (s, 3H), 1.17 (s, 3H). ^{13}C{^{1}H} (75 MHz, $CDCl_3$) δ 130.7, 128.3, 128.0, 127.6, 126.4, 87.8, 68.1, 63.1, 45.5, 44.0, 35.3, 25.9, 24.1, 19.3. ^{31}P{^{1}H} NMR (122 MHz, $CDCl_3$): δ 139.4 (s) ppm, −44.7 (s) ppm. HRMS (ESI-TOF): m/z calculated for $C_{30}H_{29}O_4P_2$: 515.1271 $[M + H]^+$; observed 515.1193. EA: calcd. for $C_{30}H_{28}O_4P_2$: C: 70.05, H: 5.50. Found: C: 70.31, H: 5.37.

*Synthesis of **9a**.* Triethylamine (0.48 mmol, 67 μl) was added at −78 °C to a solution of (*R*)-1,1′-binaphthyl-2,2′-diyl chlorophosphite (0.48 mmol, 169.5 mg) in 10 ml THF. Optically pure sulfur-protected **7** (0.44 mmol, 102 mg) was dissolved in THF and added dropwise to the NEt_3–chlorophosphite mixture maintaining the low temperature. The reaction mixture was stirred at this temperature for 10 min and then for 1 h at room temperature. Elemental sulfur (21 mg, 0.66 mmol) and NEt_3 (5 drops) were added to the reaction mixture and stirred for 1 h at 20 °C. The solvent was evaporated to give a white solid. The crude product was washed 3 times with 5 ml Et_2O each and then dissolved in 10 ml EtOAc followed by washing with 6 ml saturated aq. NH_4Cl solution. The organic phase was separated and further washed 3 times with 5 ml H_2O each. The organic phase was dried over $MgSO_4$ and then the solvent was evaporated. The crude product was dissolved in boiling *i*PrOH (*ca.* 40 ml). After standing overnight at room temperature, **9a** was obtained as a white powder (133 mg, 52%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09–7.93 (m, 4H, H-aryl), 7.58 (m, 1H, H-aryl), 7.55–7.44 (m, 3H, H-aryl), 7.44–7.28 (m, 4H, H-aryl), 4.98 (m, 1H, H-6a), 4.54 (m, 1H, H-6a), 4.11–4.05 (m, 1H, H-5a), 3.90 (m, 1H, H-5a), 2.84 (m, 1H, H-6), 2.40 (m, 1H, H-5), 2.19 (m, 1H, H-2 or 7), 2.10–2.02 (m, 4H, H-2 or 7), 1.97–1.84 (m, 2H, H-2 and 7), 1.25 (s, 3H, H-3a or 4a), 1.18 (s, 3H, H-3a or 4a) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 132.3 (s, C-quart. aryl), 131.9 (s, C-quart. aryl), 131.6 (s, C-quart. aryl), 131.2 (s, C-aryl), 130.9 (s, C-aryl), 128.5 (s, C-aryl), 128.4 (s, C-aryl), 127.2 (s, C-aryl), 127.0 (s, C-aryl), 126.8 (s, C-aryl), 126.6 (s, C-aryl), 125.8 (s, C-aryl), 121.1 (s, C-aryl), 120.3 (s, C-aryl), 86.1 (d, J = 1.3 Hz, C-quart.), 51.2 (d, J = 18.7 Hz, C-quart.), 66.1 (s, C-5a), 65.6 (dd, C-6a), 46.8 (s, C-5), 42.9 (dd, C-6), 41.6 (d, J = 44.6 Hz, C-2 or 7), 40.3 (d, J = 52.4 Hz, C-2 or 7), 23.8 (d, J = 7.6 Hz, C-3a or 4a), 18.1 (d, J = 16.5 Hz, C-3a or 4a) ppm; ^{31}P{^{1}H}

NMR (162 MHz, $CDCl_3$): δ 73.3 (d, J = 2.4 Hz, P-exocyclic), 43.0 (d, J = 2.4 Hz, P-endocyclic) ppm; ^{31}P NMR (162 MHz, $CDCl_3$): δ 73.3 (m, P-exocyclic), 43.0 (m, P-endocyclic) ppm; HRMS (ESI(+), MeCN/CH_2Cl_2), m/z: found: 579.0986, calculated for $[M + H]^+$: 579.0977; found: 596.1242, calculated for $[M + NH_4]^+$: 596.1243; found: 601.0799, calculated for $[M + Na]^+$: 601.0797; found: 1174.2156, calculated for $[2\ M + NH_4]^+$: 1174.2147; infrared spectrum (KBr): $\tilde{\nu}$ = 3061 (w, C–H aryl), 2923 (w, C–H alkyl), 2855 (w, C–H alkyl), 1740 (w), 1620 (w), 1588 (w), 1505 (w), 1462 (w), 1433 (w), 1375 (w), 1322 (w), 1218 (m), 1199 (m), 1143 (m), 1084 (s), 1068 (s), 1026 (s, C–O stretching in P–O–CH_2–C fragment), 1007 (s), 980 (s), 957 (s, P–O stretching in P^V–O–Ar fragment), 900 (s), 866 (s), 812 (s), 787 (s), 772 (s), 749 (s), 720 (s), 706 (s), 695 (s), 682 (s), 671 (s, possibly P=S exocyclic), 652 (s, possibly P=S exocyclic), 629 (s, possibly P=S exocyclic), 566 (s), 548 (s), 527 (s), 470 (s), 447 (s) cm^{-1}.

Synthesis of ***9b****.* The same procedure was employed as for **9a** with triethylamine (0.57 mmol, 80 μl), (*S*)-1,1′-binaphthyl-2,2′-diyl chlorophosphite (0.57 mmol, 201 mg) in 8 ml THF, **7** (0.52 mmol, 120 mg) in 5 ml THF, elemental sulfur (25 mg, 0.78 mmol) and NEt_3 (5 drops).

Yield **9b**: 172 mg (58%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (m, 2H, H-aryl), 7.97 (m, 2H, H-aryl), 7.62–7.52 (m, 1H, H-aryl), 7.51–7.48 (m, 3H, H-aryl), 7.45–7.28 (m, 4H, H-aryl), 4.91 (m, 1H, H-6a), 4.57 (m, 1H, H-6a), 4.01 (m, 1H, H-5a), 3.83 (m, 1H, H-5a), 2.82 (m, 1H, H-6), 2.42 (m, 1H, H-5), 2.30–2.16 (m, 1H, H-2 or 7), 2.13–2.04 (m, 1H, H-2 or 7), 1.99–1.88 (m, 2H, H-2 and 7), 1.26 (s, 3H, H-3a or 4a), 1.19 (s, 3H, H-3a or 4a) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 132.3 (s, C-quart. aryl), 131.9 (s, C-quart. aryl), 131.6 (s, C-quart. aryl), 131.2 (s, C-aryl), 131.0 (s, C-aryl), 128.5 (s, C-aryl), 128.4 (s, C-aryl), 127.2 (s, C-aryl), 127.0 (s, C-aryl), 126.8 (s, C-aryl), 126.7 (s, C-aryl), 125.8 (s, C-aryl), 122.0 (s, C-aryl), 121.0 (d, J = 3.0 Hz), 120.2 (d, J = 2.7 Hz), 86.1 (s, C-quart.), 65.8 (s, C-5a), 65.3 (dd, C-6a), 51.3 (d, J = 18.5 Hz, C-quart.), 46.8 (s, C-5), 43.0 (dd, C-6), 41.5 (d, J = 44.9 Hz, C-2 or 7), 40.2 (d, J = 52.3 Hz, C-2 or 7), 23.8 (d, J = 7.4 Hz, C-3a or 4a), 18.1 (d, J = 16.1 Hz, C-3a or 4a) ppm; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 73.1 (d, J = 3.5 Hz), 43.2 (d, J = 3.5 Hz) ppm; ^{31}P NMR (162 MHz, $CDCl_3$): δ 73.1 (m, P-endocyclic), 43.2 (m, P-exocyclic) ppm; HRMS (ESI(+), MeCN), m/z: found: 579.0983, calculated for $[M + H]^+$: 579.0977; found: 596.1241, calculated for $[M + NH_4]^+$: 596.1243; found: 601.0809, calculated for $[M + Na]^+$: 601.0797; found: 1174.2142, calculated for $[2\ M + NH_4]^+$: 1174.2147; infrared spectrum (KBr): $\tilde{\nu}$ = 3047 (w, C–H aryl), 2964 (w, C–H alkyl), 2876 (w, C–H alkyl), 1729 (m), 1589 (m), 1508 (m), 1462 (m), 1434 (w), 1371 (w), 1322 (w), 1222 (m), 1198 (w), 1156 (w), 1128 (w), 1072 (m), 1023 (m, C–O stretching in P–O–CH_2–C fragment), 980 (s), 954 (s, P–O stretching in P^V–O–Ar fragment), 865 (s), 845 (s), 813 (s), 784 (s), 772 (s), 748 (s), 717 (s), 680 (s), 670 (s, possibly P=S exocyclic), 650 (s, possibly P=S exocyclic), 630 (s, possibly P=S exocyclic), 567 (s), 546 (s), 527 (s), 495 (s), 470 (s) cm^{-1}.

General procedure for asymmetric allylic substitution. In a Schlenk tube, [Pd(π-allyl)Cl]$_2$ (0.005 mmol) and the ligand **L1** (0.02 mmol, 2 eq.), **L2** (0.01 mmol, 1 eq.) or **L3** (0.01 mmol, 1 eq.) were dissolved in dichloromethane (1.5 ml) in an M : L = 1 : x ratio (x = 2 for monodentate **L1**, 1 for bidentate **L2** and **L3**) and degassed. (*E*)-1,3-Diphenylprop-2-ene-1-yl acetate (1 mmol, 1 eq., C/S = 1/100), was added and stirred for 10 min followed by the addition of dimethyl malonate (1.5 mmol, 3 eq.), BSA (*N*,*O*-bis(trimethylsilyl)acetamide) (1.5 mmol, 3 eq.) and a catalytic amount of KOAc (0.024 mmol). The reaction mixture was stirred at room temperature for 14 h. When TLC indicated no further conversion, the reaction was quenched by dilution with Et_2O (10 ml); the organic layer was washed twice with saturated NH_4Cl solution (8–10 ml each) and dried over Na_2SO_4. Filtration and removal of solvent left a red oil, which was chromatographed (SiO_2; petroleum ether/CH_2Cl_2 = 1 : 1) to give analytically pure products. The enantioselectivity was determined by chiral HPLC. Absolute configuration of the products was determined by the known elution order. The analytical data of the product were in agreement with literature reports.[39]

General procedure for asymmetric hydroformylation. The hydroformylation reactions were performed in a stainless-steel autoclave (300 ml) equipped with 8 reaction vials. In a typical experiment, [Rh(acac)(CO)$_2$] (1 eq.) and ligands **L1**, **L2** or **L3** (desired eq.) were transferred to 4 ml reaction vials in a glovebox. Toluene (2 ml) was added under inert conditions and stirred for 5–10 min. The substrate was added to the catalyst solution and transferred to the autoclave. The autoclave was flushed with N_2 two times and pressurized with the desired syngas pressure at the desired temperature. After the required reaction time, the autoclave was depressurized carefully (Caution! There might be some CO left even after the evacuation. To be on the safe side, the autoclave can also be flushed a few times with N_2). The reaction mixture was analyzed with GC, GC-MS or NMR spectroscopy. Absolute configuration of the products was determined by the known elution order.

General procedure for asymmetric hydrogenation. The hydrogenation experiments were performed in a stainless-steel autoclave charged with an insert suitable for up to 8 reaction vessels (4 ml) with Teflon mini stirring bars. In a typical experiment, a reaction vessel was charged with [Rh(cod)$_2$]BF_4 (5 μmol) and ligands **L1** or **L3** (5 μmol, M : L = 1 : 1) and stirred for 10–15 min in the appropriate solvent (2 ml). The substrate methyl (*Z*)-2-acetamido-3-phenylacrylate (0.5 mmol) was added to the reaction vessels maintaining the inert atmosphere and the vessels were placed in the autoclave. The autoclave was purged two times with nitrogen and three times with hydrogen. Finally, it was pressurized at the desired H_2 pressure at 25 °C for the desired reaction time. After the required reaction time, the autoclave was depressurized, and the contents of the reaction vessels were diluted with EtOAc (5 ml) and filtered through a short pad of silica. The conversion was determined by GC, GC-MS and NMR measurements, and the enantiomeric excess was determined by GC or HPLC using a chiral column. Absolute configuration of the products was determined by the known elution order. The analytical data were in agreement with literature reports.[39]

Author contributions

Conceptualization: E. H. H., (late) Prof. Paul C. J. Kamer, J. G. d. V.; Synthetic and catalytic work: K. R., S. C.; B. M. assisted

with result analysis; manuscript preparation and correction: S. C., K. R., E. H. H., J. G. d. V.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We acknowledge the valuable contribution of (late) Prof. Dr Paul C. J. Kamer in the start-up phase of this project and research. We thank the Deutsche Forschungsgemeinschaft (DFG) for financial support (project number HE 1376/46-1 and 411421782). The analytical facilities at LIKAT are highly acknowledged. We thank Mara Wolniewicz for her help with chiral HPLC measurements. Funded by the Open Access Publishing Fund of Leipzig University, supported by the German Research Foundation within the program Open Access Publication Funding.

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