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Quinaphos and Dihydro-Quinaphos Phosphine–Phosphoramidite Ligands for Asymmetric Hydrogenation

Thomas Pullmann,[a] Barthel Engendahl,[a] Ziyun Zhang,[a] Markus Hölscher,[a] Antonio Zanotti-Gerosa,[b] Alan Dyke,[b] Giancarlo Franciò,*[a] and Walter Leitner*[a]

Dedicated to Professor Felice Faraone, for his inspiration in the development of Quinaphos, on the occasion of his retirement

Abstract: New derivatives of the Quinaphos ligands and the related Dihydro-Quinaphos ligands based on the more flexible 1,2,3,4-tetrahydroquinoline backbone have been prepared and fully characterised. A general and straightforward separation protocol was devised, which allowed for the gram-scale isolation of the R_a,S_c and S_a,R_c diastereomers. These new phosphine–phosphoramidite ligands have been applied in the Rh-catalysed asymmetric hydrogenation of functionalised olefins with the achievement of excellent enantioselectivities ($\geq$99%) in most cases and turnover frequency (TOF) values of up to $\geq$20000 h^{-1}. These results substantiate the practical utility of readily accessible Quinaphos-type ligands, which belong to the most active and selective category of ligands for Rh-catalysed hydrogenation known to date.

Keywords: asymmetric catalysis · bidentate ligands · enantioselectivity · hydrogenation · phosphoramidites

Introduction

Asymmetric hydrogenation with transition-metal complexes is one the most efficient methods for the synthesis of enantio-enriched compounds and the development of chiral phosphorus ligands plays a determining role for progress in this area.[1] Among the vast structural variety of ligands, bidentate-chelating P,P′-ligands with electronically different P-donor groups offer interesting potential for fine-tuning in transition-metal-catalysed asymmetric reactions.[2] Very successful hetero-combinations are those with one phosphino group combined with a less-electron-rich phosphoramidite or phosphite unit. A prominent representative of such electronically unsymmetrical P,P′-ligands, the phosphine–phosphite BINAPHOS, was reported by Nozaki in 1993.[3] This hybrid phosphorus ligand and its derivatives were successfully applied in Rh-catalysed asymmetric hydroformylation[4] and hydrogenation[5] reactions, as well as in Pd-catalysed copolymerisation[6] and hydrophosphorylation reactions.[7] More recently, several phosphine–phosphoramidite ligands[2,8] have been synthesised and used in asymmetric hydrogenation[9,10] and hydroformylation[9a,11] reactions with the production of good to excellent enantioselectivities. In some cases, mixtures of monodentate chiral phosphoramidites and achiral phosphines can mimic the corresponding bidentate ligands. This can lead to improved enantioselectivity and catalyst activity in hydrogenation reactions with respect to the use of chiral monodentate phosphoramidites only.[12]

In 2000, we reported the first example of a chiral phosphine–phosphoramidite ligand (Quinaphos) and showed the high potential of this class of ligands in asymmetric catalysis.[9a,10l,13] Quinaphos is based on the 1,2-dihydroquinoline backbone and is obtained through a modular synthetic approach as a diastereomeric mixture. The two diastereomers (R_a,R_c)-*n*Bu-Quinaphos ((R_a,R_c)-**5a**) and (R_a,S_c)-*n*Bu-Quinaphos ((R_a,S_c)-**5a**) were separated by column chromatography and a strong cooperation between the two stereo-elements was observed in asymmetric catalysis.[9] The relative

[a] Dr. T. Pullmann, B. Engendahl, Z. Zhang, Dr. M. Hölscher, Dr. G. Franciò, Prof. Dr. W. Leitner
Institut für Technische und Makromolekulare Chemie
RWTH Aachen University, Worringerweg 1
520274 Aachen (Germany)
Fax: (+49) 241-80-22177
E-mail: francio@itmc.rwth-aachen.de
leitner@itmc.rwth-aachen.de

[b] Dr. A. Zanotti-Gerosa, Dr. A. Dyke
Johnson Matthey, Unit 28, Cambridge Science Park
Cambridge, CB4 0FP (UK)

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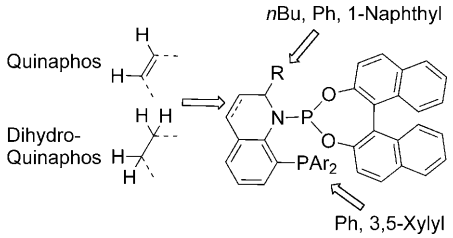
stereochemistry (R_a,R_c)-**5a** was found to correspond to the matched diastereomer for the enantioselective Rh-catalysed hydrogenation of olefins and led to excellent enantioselectivities and activities.[9a]

In the present study, we have investigated structural variations within the Quinaphos-family focusing on the group at the 2-position (R), the aryl group at the phosphine moiety (PAr_2) and the olefinic double bond within the heterocyclic backbone (Scheme 1).

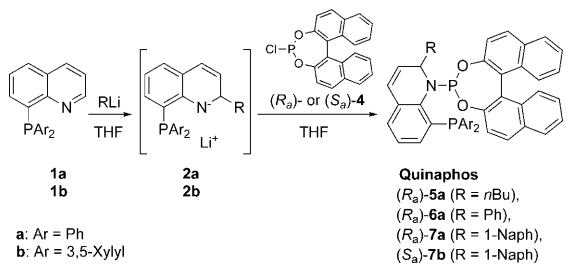


Scheme 1. Modifications to the Quinaphos-ligand framework.

All ligands have been fully characterised in solution. The structure of a free ligand and of a rhodium complex in the solid state has been determined by single-crystal X-ray analysis. The new ligands have been applied in the Rh-catalysed asymmetric hydrogenation of functionalised olefins and give excellent enantioselectivities (≥99% in almost all cases) and turnover frequency (TOF) values up to 21600 h^{-1}.

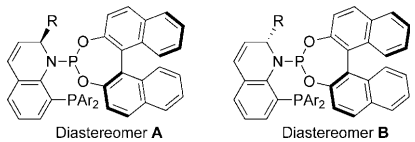
Results and Discussion

Synthesis of Quinaphos derivatives: Phosphine–phosphoramidites **6a** (R = Ph) and **7a** (R = 1-naphthyl) were synthesised by a one-pot, two-step procedure as shown in Scheme 2. The organolithium reagents PhLi and 1-naphthyllithium (**3**) were added to 8-diarylphosphinoquinoline (**1**) to result in the formation of the corresponding lithium amides **2**. The dark-red solutions were reacted directly with the enantiopure phosphorochloridite **4**[13a] and led to the selective formation (>90% by ^{31}P NMR spectroscopy) of the desired ligands as 1:1 mixtures of the corresponding (R_a,R_c) and (R_a,S_c) diastereomers. ^{31}P NMR chemical shifts and the P,P′-coupling constants for the different Quinaphos derivatives are summarised in Table 1.



Scheme 2. Synthetic route to Quinaphos ligands.

Table 1. ^{31}P NMR chemical shifts and coupling constants of Quinaphos derivatives (C_6D_6).



	R/Ar		Diastereomer configuration[a]	δ (^{31}P) [ppm] $NP(O)_2$	PAr_2	J(P,P′) [Hz]
1	*n*Bu/Ph	**5a**	**A** (R_a,R_c)	137.5	−17.8	191.7
2	*n*Bu/Ph	**5a**	**B** (R_a,S_c)	143.6	−16.4	131.2
3	Ph/Ph	**6a**	**A** (R_a,S_c)	132.8	−18.6	192.1
4	Ph/Ph	**6a**	**B** (R_a,R_c)	141.2	−21.3	140.5
5	1-Naph/Ph	**7a**	**A** (R_a,S_c)	138.1	−18.4	209.6
6	1-Naph/Ph	**7a**	**B** (R_a,R_c)	140.6	−20.9	151.5
7[b]	1-Naph/Xylyl	**7b**	$\mathbf{A}_{ent}$ (S_a,R_c)	137.7	−18.9	204.9
8[b]	1-Naph/Xylyl	**7b**	$\mathbf{B}_{ent}$ (S_a,S_c)	141.5	−20.3	158.2

[a] Due to priority change (CIP rules) the stereodescriptors of entries 1, 3, 5 and 2, 4, 6 correspond to the same spatial arrangement, **A** and **B**, respectively. [b] Measured in $CDCl_3$.

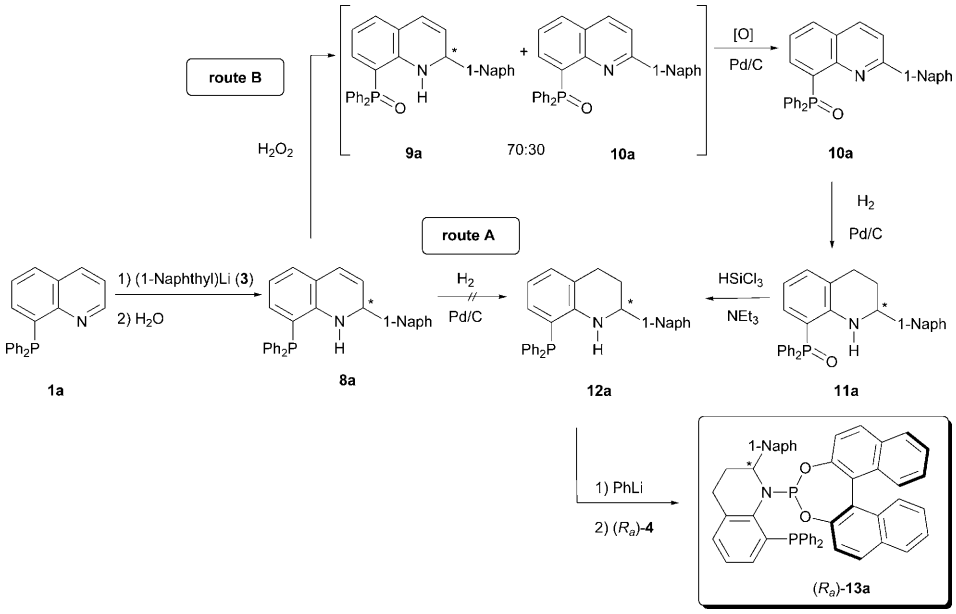
The assignment of signals to the corresponding diastereomers relies on the distinctive value of the P,P′-coupling constants. It is important to note that (R_a,R_c)-**5a** has the same spatial arrangement (**A**) as (R_a,S_c)-**6a** and (R_a,S_c)-**7a** because of the priority change in accordance with the Cahn–Ingold–Prelog (CIP) rules. Diastereomers **B** are characterised by smaller coupling constants (J = 130–160 Hz), whereas significantly larger splittings (J = 190–210 Hz) are observed for the corresponding diastereomers **A**.[9c]

Attempts to separate the diastereomeric mixtures of **6a** and **7a** by column chromatography, both on silica gel and on aluminium oxide, failed with a variety of eluent mixtures. Very poor separation and/or extensive decomposition were always observed. In contrast, we succeeded to separate the diastereomers of **7a** very readily by crystallisation. The addition of ethanol to a solution of **7a** in toluene led to the selective precipitation of the R_a,S_c diastereomer as a colourless powder with a diastereomeric excess (*de*) of 93–95%. The mother liquor contained the R_a,R_c diastereomer with a similar diastereomeric purity, together with other side products. Diastereomerically pure (R_a,S_c)-**7a**, inclusive of 5–10% of toluene, was obtained after a second precipitation using the same solvent combination. Precipitation from CH_2Cl_2/*n*-pentane afforded solvent-free (R_a,S_c)-**7a** with an overall yield of 62%. Since (R_a,S_c)-**7a** (diastereomer **A**) has the matched relative configuration for the Rh-catalysed hydrogenation,[9a] the isolation of the other diastereomer (R_a,R_c)-**7a** was not pursued in the present work.

Notably, the simple procedure described above for isolating pure (R_a,S_c)-**7a** could be applied successfully for the gram-scale separation of other 1-naphthyl-substituted Quinaphos derivatives. Starting from bis(3,5-xylyl)-substituted phosphine **1b**, the corresponding derivative (Xyl_2P,1-Naph)-Quinaphos (**7b**) was synthesised from (*S*)-**4** (Scheme 2). Chemically and diastereomerically pure (S_a,R_c)-**7b** could be obtained after three recrystallisation steps (1.5 g, 56% overall yield).

Synthesis of Dihydro-Quinaphos: The quinoline backbone of the Quinaphos-ligand family features an olefinic double bond, which may itself be subject to hydrogenation under catalytic conditions.[14] This would lead from an essentially planar arrangement to a more flexible backbone and, hence, to a change in coordination properties. To investigate this in more detail, we set out to synthesise saturated analogues, 3,4-dihydro-Quinaphos, for direct comparison.

Initial attempts to obtain Dihydro-Quinaphos **13a** directly from **7a** by hydrogenation of the C-3=C-4 double bond over Pd/C were not successful. Hence, we envisaged an alternative multi-step procedure as shown in Scheme 3. Firstly, 1-naphthyl-lithium (**3**) was added to 8-(diphenylphosphino)-quinoline (**1a**) to give the intermediate **2a**, which was subsequently quenched with water to give the phosphinoamine **8a**. Again, Pd/C hydrogenation of the free phosphinoamine **8a** failed to afford **12a** (route A). This indicated that the phosphino group should be protected to prevent strong coordination to the palladium catalyst and, hence, catalyst deactivation. A reaction sequence of phosphine oxidation, heterocycle hydrogenation, followed by phosphine reduction was devised to circumvent this problem (route B).



Scheme 3. Synthetic route to Dihydro-Quinaphos derivative **13a**.

The oxidation of **8a** with H_2O_2 led to the formation of 1,2-dihydroquinoline **9a** together with the re-aromatised quinoline **10a** in a ratio of 70:30, respectively. This mixture was completely oxidised in situ, over Pd/C in the presence of air, to **10a** with an overall yield of 76%.[15] The subsequent hydrogenation of **10a** was carried out over the same catalyst batch used for the dehydrogenation (Pd/C) to give the corresponding 1,2,3,4-tetrahydroquinoline **11a** in 91% yield. These transformations can be monitored conveniently by means of in situ ^{31}P NMR spectroscopy. The reduction of the phosphine oxide was carried out with trichlorosilane in the presence of NEt_3 to afford phosphine **12a** in 63% yield. In the final step, compound **12a** was deprotonated with phenyllithium and the resultant lithium amide intermediate was treated with phosphorochloridite (R_a)-**4** to afford Dihydro-Quinaphos **13a** with a high selectivity of 95% (as determined by ^{31}P NMR spectroscopy). It is interesting to note that the deprotonation in this last step could only be carried out successfully by using strong bases, such as phenyllithium or butyllithium. Neither the use of triethylamine or 4-(dimethylamino)pyridine (as HCl scavengers) nor stronger bases, for example, sodium hydride, led to the formation of the desired product **13a**. Similar observations were recently reported for the synthesis of INDOLPhos.[10h]

Again, the separation of the diastereomers of **13a** was carried out by the precipitation procedure described above for ligands **7a** and **7b**, which confirmed the generality of this approach. Accordingly, diastereomerically pure and solvent free (R_a,S_c)-**13a** was obtained in 57% overall yield.

Solid-state structure of ligand (R_a,S_c)-13a·CHCl$_3$: Single crystals of (R_a,S_c)-**13a**·$CHCl_3$ suitable for X-ray analysis could be obtained by slow diffusion from $CHCl_3$/Et_2O at room temperature (Figure 1).[16] Table 2 contains selected bond lengths and angles. The absolute configuration at C-40 was confirmed as *S*, which validated the initial assignment based on the P,P′-coupling constants and chemical shifts within the Quinaphos family.[9] The six-membered het-

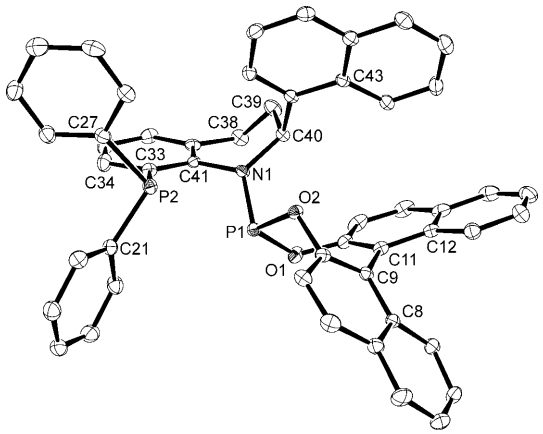
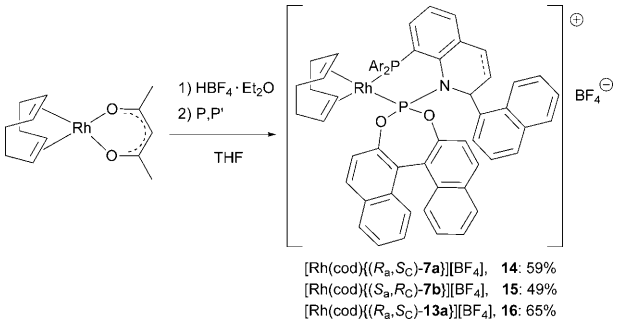


Figure 1. ORTEP representation of (R_a,S_c)-**13a**·$CHCl_3$ (50% probability level; hydrogen atoms and $CHCl_3$ are omitted for clarity).

Table 2. Selected bond lengths, angles and dihedral angles of **13a** in crystals of **13a**·$CHCl_3$.

Distances	[Å]	Angles	[°]
P1–N1	1.6725(17)	O2-P1-O1	97.36(7)
P1–O1	1.6679(15)	C41-N1-C40	118.71(16)
P1–02	1.6679(15)	C41-N1-P1	117.35(13)
P2–C33	1.8371(21)	C40-N1-P1	122.96(13)
P2–C21	1.8264(20)	C8-C9-C11-C12	57.1
P2–C27	1.8410(20)	C40-N1-P1-O2	47.2
N1–C40	1.4823(25)	C39-C40-C42-C43	95.5
N1–C41	1.4242(25)	C27-P2-C33-C34	47.7
C9–C11	1.487(3)		



Scheme 4. Synthesis of Rh-complexes from a [Rh(acac)(cod)] precursor.

erocycle of the 1,2,3,4-tetrahydroquinoline backbone adopts a boat conformation and the carbon atoms C-39 and C-40 reside out of the plane defined by the aromatic carbon atoms of the heterocyclic backbone. This puckered arrangement is significantly different from the parent Quinaphos backbone, as expected.[9]

The nitrogen atom has a trigonal planar arrangement with an angle sum of 359°, indicative of pronounced sp^2 character. The quite short P–N distance of 1.6725(17) Å hints at a partial double-bond character and confirms sp^2 hybridisation of the nitrogen atom. The phosphoramidite phosphorus atom, P1, is located slightly out of the plane defined by the aromatic carbon atoms of the 1,2,3,4-tetrahydroquinoline backbone (dihedral angle P1-N1-C41-C33 = 51.2°), probably to minimize repulsion with the 1-naphthyl substituent.

The free electron pairs at the phosphorus atoms point in approximately the same direction, already in good alignment for metal chelation. Moreover, the through-space distance between the two phosphorus atoms of 3.19 Å supports that the P,P′-coupling is caused by a through-space interaction rather than a through-bond coupling.[17] The torsion angle of the binaphthyl moiety is in the expected range (57.1°).

Synthesis of rhodium-Quinaphos complexes: Addition 1 equiv of (R_a,S_c)-**7a** to $[Rh(cod)_2][BF_4]$ (cod = 1,5-cyclooctadiene) in CH_2Cl_2 or THF led to a mixture (≈20:1) of the desired compound [Rh(cod){(R_a,S_c)-**7a**}][BF_4] (**14**) and the homoleptic complex [Rh{(R_a,S_c)-**7a**}$_2$][BF_4].[18] In contrast, the addition of 1 equiv of the ligand to a solution of [Rh(cod)$(thf)_2$][BF_4] in THF (generated in situ by protonation of [Rh(acac)(cod)] (acac = acetylacetonate) with HBF_4·Et_2O) resulted in the exclusive formation of **14** in 59% yield after recrystallisation from CH_2Cl_2/Et_2O (Scheme 4). This reactivity is in line with the observation that Quinaphos-type ligands typically exhibit better catalytic performance in isolated precursors or systems generated in situ from [Rh(acac)(cod)]/HBF_4 compared with use of the $[Rh(cod)_2][BF_4]$ precursor.

By using the same procedure, the complexes [Rh(cod)-{(S_a,R_c)-**7b**}][BF_4] (**15**) and [Rh(cod){(R_a,S_c)-**13a**}][BF_4] (**16**) were obtained in 49 and 65% yield, respectively. As expected, two signals were present in each of the ^{31}P NMR spectra, both as doublet of doublets due to the P,P′- and Rh,P-couplings (Table 3). Interestingly, a considerable coordination shift of δ = 40–43 ppm was observed for the phosphine moieties, whereas no significant change in the chemical shift was noticeable for the phosphoramidite moieties. Moreover, a large decrease of the P,P-coupling constants from around 200 to about 62 Hz occurred upon coordination for all ligands, due to the change of the coupling mode from through-space to through-bond coupling.

Table 3. ^{31}P NMR chemical shifts and coupling constants of [Rh(cod)-(P,P′)] complexes ($CDCl_3$).

Complex	δ (^{31}P) [ppm]		J [Hz]		
	PAr_2	$NP(O)_2$	Rh,PAr_2	Rh,$NP(O)_2$	P,P′
14	24.8	138.3	135.9	258.4	61.3
15	23.7	138.0	135.8	259.5	62.0
16	22.7	136.9	133.4	252.6	62.4

Solid-state structure of 14·CH_2Cl_2: Single crystals of [Rh(cod){(R_a,S_c)-**7a**}][BF_4]·CH_2Cl_2 (**14**·CH_2Cl_2) suitable for X-ray diffraction analysis were obtained by slow diffusion from CH_2Cl_2/Et_2O at room temperature.[16] Figure 2 shows

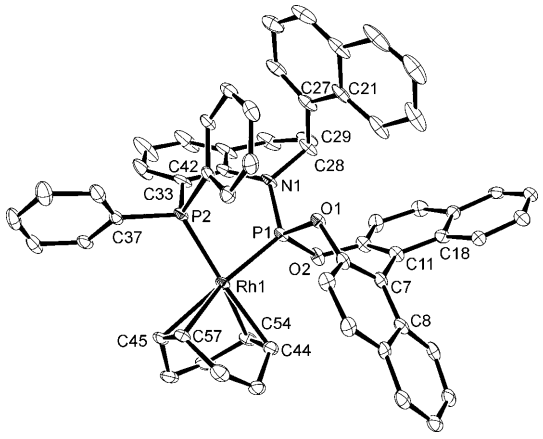


Figure 2. ORTEP representation of [Rh(cod){(R_a,S_c)-**7a**}]$^+$ in **14**·CH_2Cl_2 (30% probability level; hydrogen atoms, the BF_4^- anion and CH_2Cl_2 are omitted for clarity).

the molecular structure of the cationic metal complex and Table 4 contains selected bond lengths and angles.

Table 4. Selected bond lengths and angles of complex **14** in crystals of **14**·CH_2Cl_2.

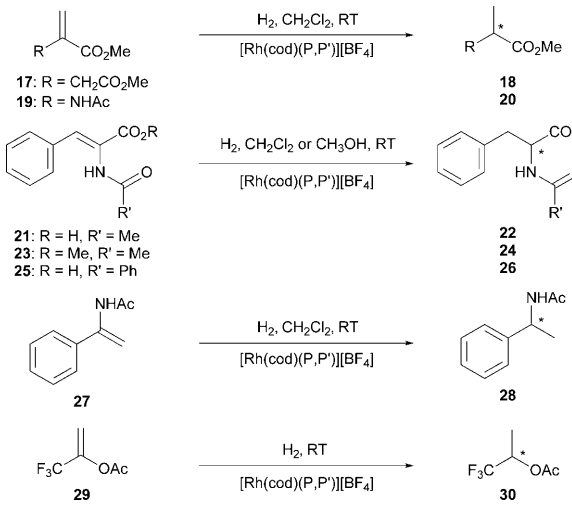
Bond	[Å]	Angle	[°]
Rh1–P1	2.1984(13)	P1-Rh1-P2	84.97(5)
Rh1–P2	2.2939(14)	C32-N1-C28	115.9(4)
Rh1–C57	2.263(5)	C32-N1-P1	120.8(3)
Rh1–C45	2.315(5)	C28-N1-P1	119.8(4)
Rh1–C44	2.271(6)	C8-C7-C11-C18	64.6
Rh1–C54	2.228(6)	C28-N1-P1-O1	52.5
C44–C54	1.375(8)	C27-C28-C27-C21	131.1
C45–C57	1.369(9)	C42-P2-C33-C34	118.5
P1–N1	1.662(4)		
P2–C33	1.805(6)		
C7–C11	1.512(8)		

The rhodium centre displays a typical square-planar geometry and the bite angle of the two phosphorus donors amounts to 84.97(5)°. As already observed for another phosphine–phosphoramidite rhodium complex,[10j] the phosphoramidite–rhodium bond is significantly shorter than the phosphine–rhodium bond (2.1984(13) versus 2.2939(14) Å, respectively). The two phenyl rings at phosphorus atom P2 adopt the characteristic face–edge conformation. The dihedral angle of the binaphthyl moiety in the phosphoramidite portion is approximately 64.6°. The 1-naphthyl substituent at the stereogenic C28 is quite far from the rhodium centre, which is in line with the observation that the substituents in this position only have a moderate influence on the stereocontrol exerted by Quinaphos ligands.[13d] The coordinated 1,5-cyclooctadiene ligand shows a clockwise twist of about 13°.

Asymmetric hydrogenation: Complexes **14**, **15**, **16** and [Rh(cod){(S_a,R_c)-**7b**}][BF_4], generated in situ by the procedure described above, were applied in the asymmetric hydrogenation of functionalised olefins. The reactions were carried out at room temperature under hydrogen pressures between 30 and 70 bar. Dichloromethane was the solvent of choice, except for the hydrogenation of α-acetamido cinnamic acid (**21**), for which methanol was used for solubility reasons, and for hydrogenation of trifluoromethylvinyl acetate (**29**), for which no additional solvent was added. The results are summarised in Table 5.

In the presence of complex **14** (0.1 mol%), both dimethylitaconate (**17**) and acetamidomethylacrylate (**19**) were hydrogenated quantitatively within 30 min with almost perfect enantioselectivity (>99%), which corresponds to a TOF of ≥2000 h^{-1} (Table 5, entries 1 and 7). Full conversion of substrates **17** and **19**, within 30 min and with excellent enantioselectivities (>99%), was also obtained with ligand **7b** (at a catalyst loading of 0.1 mol%), which bears the sterically more demanding bis(3,5-xylyl)phosphino group (Table 5, entries 4 and 8). A broad range of substrates can be hydrogenated with these ligands with uniformly excellent levels of enantioselectivity. The cinnamic acid derivative **21** was converted quantitatively in methanol to **22** with 97% *ee*, which demonstrated that the catalyst is stable towards free acid (Table 5, entry 10). The corresponding methyl ester **23** and the more bulky benzoyl-protected derivative **25** could be hy-

Table 5. Asymmetric hydrogenation of functionalised olefins with Quinaphos-type ligands in catalysts [Rh(cod)(P,P′)][BF_4].[a]



	Substrate	P,P′ ligand	*t* [min]	S/C[b]	Conversion [%]	TOF [h^{-1}]	*ee*[c] [%]
1	**17**	(R_a,S_c)-**7a**	30	1000	>99	≥2000	>99 (*R*)
2[d]	**17**	(R_a,S_c)-**7a**	45	10000	94	12600	>99 (*R*)
3	**17**	(R_a,S_c)-**7a**	30	20000	25	10000	>99 (*R*)
4[e]	**17**	(S_a,R_c)-**7b**	30	1000	>99	≥2000	>99 (*S*)
5	**17**	(R_a,S_c)-**13a**	3	1000	>99	≥20000	>99 (*R*)
6	**17**	(R_a,S_c)-**13a**	30	20000	54	21600	>99 (*R*)
7	**19**	(R_a,S_c)-**7a**	30	1000	>99	≥2000	99 (*S*)
8[e]	**19**	(S_a,R_c)-**7b**	30	1000	>99	≥2000	99 (*R*)
9	**19**	(R_a,S_c)-**13a**	5	1000	99	11900	99 (*S*)
10[f]	**21**	(R_a,S_c)-**7a**	30	1000	>99	≥2000	97 (*S*)
11	**23**	(R_a,S_c)-**7a**	60	1000	>99	≥1000	>99 (*S*)
12[f]	**25**	(R_a,S_c)-**7a**	60	1000	>99	≥1000	99 (*S*)
13	**27**	(R_a,S_c)-**7a**	30	1000	>99	≥2000	>99 (*S*)
14[g]	**29**	(S_a,R_c)-**7b**	240	1000	>99	≥250	98 (*R*)

[a] CH_2Cl_2 (2 mL), RT, 30 bar H_2, 500 rpm. [b] Substrate/catalyst ratio. [c] *ee* = enantiomeric excess. [d] 70 bar H_2. [e] Catalyst generated in situ. [f] MeOH used as solvent. [g] Reaction performed neat.

drogenated quantitatively with enantioselectivities ≥99% (Table 5, entries 11 and 12, respectively). Full conversion after 30 min with >99% *ee* was also achieved in the hydrogenation of enamide **27** (Table 5, entry 13). The hydrogenation of trifluoromethylvinyl acetate **29** was carried out in the neat substrate with complex **15** as the catalyst. The hydrogenated product **30** was obtained in 98% *ee* (Table 5, entry 14).

To estimate the activity of complex **14**, the hydrogenation of **17** was carried out with a reduced catalyst loading of 0.01 mol%. At 70 bar of H_2, product **18** was formed almost quantitatively (conversion = 94%) in >99% *ee* within 45 min, which corresponded to a TOF of 12600 h^{-1} (Table 5, entry 2). A further reduction of the catalyst loading shows that this represents an upper limit for the TOF of this system (Table 5, entry 3). Compared with ligand (R_a,R_c)-**5a**,[9a] complex **14** leads to very similar activities and enantioselectivities in the hydrogenation of **17**.

The Dihydro-Quinaphos derivative (R_a,S_c)-**13a**, the more flexible analogue of (R_a,S_c)-**7a**, was tested in the hydrogenation of itaconate **17** and acrylate **19**. Again, excellent enantioselectivities ≥99% were obtained. At a substrate/catalyst ratio of 1000, full conversion was achieved after 3 and 5 min (equivalent to TOF values of ≥20000 and 11900 h^{-1}), respectively (Table 5, entries 5 and 9). To evaluate the activity of complex **16** more precisely and to have a direct comparison with **14**, a hydrogenation experiment was carried out with **16** under exactly the same conditions used in Table 5, entry 3 for **14**. At a catalyst loading of 0.005 mol%, the reaction was stopped after 30 min by venting the autoclave. Relative to **14**, catalyst **16** led to almost two-fold conversion (54%), which corresponds to a TOF of 21600 h^{-1} (Table 5, entries 6 versus 3). These results show clearly that the saturation modification of the double bond in the heterocyclic part of the backbone causes a significant increase of the catalyst activity,[14] without a negative effect on the enantioselectivity.

Conclusion

We have reported the synthesis of new ligands of the Quinaphos family, which include the first examples of Dihydro-Quinaphos ligands based on the conformationally more flexible 1,2,3,4-tetrahydroquinoline backbone. Exploiting a modular synthetic approach to Quinaphos, a 1-naphthyl substituent was introduced at C-2, which significantly affects the solubility profile of the diastereomers and enables a facile separation. Hence, a general, simple and reliable protocol was developed and allowed the isolation of pure R_a,S_c and S_a,R_c diastereomers on a gram scale.[20] This procedure could be applied successfully to all derivatives with a 1-naphthyl group, irrespective of the nature of the phosphine group and of the dihydro- or tetrahydroquinoline backbone.

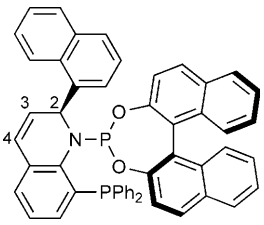
The new Quinaphos-type ligands showed remarkably high enantioselectivities and activities in the rhodium-catalysed asymmetric hydrogenation of functionalised olefins, dehydroamino acid derivatives (including a free acid) and enamides. In almost all cases *ee* values ≥99% were obtained, combined with TOF values of up to 12600 h^{-1}. A two-fold enhancement of catalyst activity, TOF values ≥20000 h^{-1} and the same excellent level of enantioselectivity were observed when using the Dihydro-Quinaphos ligand (R_a,S_c)-**13a** compared with the corresponding Quinaphos ligand (R_a,S_c)-**7a**. These results substantiate the practical utility of readily accessible Quinaphos-type ligands, which belong to the most active and selective ligands for the rhodium-catalysed hydrogenation known to date.

Experimental Section

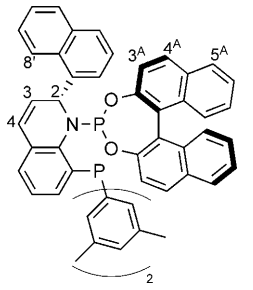
General: All reactions and manipulations were performed by using standard Schlenk techniques or in a glove box (M. Braun MB 150B-G) under an inert argon atmosphere unless otherwise noted. Argon 4.6 was purchased from Messer and traces of water and oxygen were removed with an M. Braun MB 100-HP apparatus. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker AV 600 (600, 150 and 243 MHz, respectively) or a Bruker DPX-300 spectrometer (300, 75 and 121 MHz, respectively). Chemical shifts (δ) were referenced to residual solvent peaks (^{1}H NMR, ^{13}C NMR) or to external standard 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on a Varian 1200L Quadrupole GC-MS, Finnigan MAT 8200 (MS and HRMS-EI) or a Bruker FTICR-Apex III spectrometer (HRMS-ESI). IR spectra were recorded on a Perkin–Elmer PE-1760 FT or a Thermo Electron Avatar 380 spectrometer. Optical rotations were measured on a Jasco P-1020 polarimeter. The concentrations used for measuring specific rotations are given as g/100 mL. THF, toluene and *n*-pentane were dried over alumina with a solvent purification system from Innovative Technology. Et_2O, MeOH and EtOH were distilled and then dried over molecular sieves. All other organic solvents were purged with argon for 2 h prior to use. Deuterated solvents were degassed through freeze–pump–thaw cycles and stored over molecular sieves. The following substances were been synthesised according to literature procedures: [Rh(acac)(cod)],[20] phosphorochloridite (R_a)-**4** and (S_a)-**4**,[13a] enamide (**29**)[21] and *N*-benzoylamino cinnamic acid (**27**).[22] For the synthesis of **1a** and **1b** see the Supporting Information. 8-Bromoquinoline was purchased from Frontier Scientific Europe. All other chemicals were purchased from Sigma–Aldrich, Acros or Alfa Aesar and used as received.

Ligand (R_a,S_c)-7a: A solution of 1-naphthyllithium (1 equiv, 17.5 mL, c = 0.385 M in THF) was added slowly with a syringe at −20 °C to a solution of **1a** (2.112 g, 6.741 mmol) in THF (50 mL). The reaction mixture was stirred for 1 h at 0 °C and then cooled to −20 °C before phosphorochloridite (*R*)-**4** (1 equiv, 6.741 mmol, 2.364 g) in THF (20 mL) was added dropwise. The mixture was allowed to warm to RT and stirred for 1 h. The solvent was removed under reduced pressure and the resulting solid was extracted with toluene (80 mL). The extracted phase was filtered through a plug of alumina (25 mL), concentrated under reduced pressure and the resulting solid was dried in vacuo (4.808 g). A portion of this solid (1.873 g) was dissolved in toluene (11 mL) and ethanol (37 mL) was added dropwise, whereupon a colourless solid (821.6 mg) precipitated (in some cases the precipitation was delayed and the mixture was allowed to stir overnight), which contained (R_a,S_c)-**7a** (95–97%) and (R_a,R_c)-**7a** (3–5%). This solid was recrystallised from toluene/ethanol (10:50 mL) to afford diastereomerically pure (R_a,S_c)-**7** with included toluene. Solvent-free (R_a,S_c)-**7a** was obtained as a colourless powder after recrystallisation of (R_a,S_c)-**7** from CH_2Cl_2/*n*-pentane (5:30 mL). Yield: 62% (496.2 mg); $[\alpha]_D^{20} = -694°$ (c = 0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.18 (d, J = 8.7 Hz, 1H; Ar), 8.13 (d, J = 8.2 Hz, 1H; Ar), 7.89 (d, J = 8.8 Hz, 1H; Ar), 7.86 (d, J = 8.2 Hz, 1H; Ar), 7.71 (d, J = 8.7 Hz, 1H; Ar), 7.62–7.53 (m, 6H; Ar), 7.46–7.28 (m, 14H; Ar), 7.24 (m, 1H; Ar), 7.17–7.12 (m, 2H; Ar), 7.07–7.03 (m, 2H; Ar), 6.56 (d, J = 9.6 Hz, 1H; H-4), 6.41 (m, 1H; Ar), 6.35 (d, J = 8.5 Hz, 1H; Ar), 5.97 (dd, J = 9.6, 5.8 Hz 1H; H-3), 5.88 ppm (m, 1H; H-2); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.71 (m; C_q),

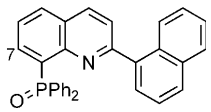
149.51 (C_q), 143.76 (dd, J=24.1, 20.5 Hz; C_q), 140.47 (t, J=18.1 Hz; C_q), 138.62 (C_q), 137.73 (CH), 137.13 (d, J=5.6 Hz; C_q), 133.55 (C_q), 133.53 (CH), 133.50 (CH), 133.39 (CH), 133.37 (CH), 133.22 (C_q), 132.72 (C_q), 131.59 (C_q), 130.99 (C_q), 130.59 (CH), 130.50 (CH), 129.60 (CH), 128.50 (2CH), 128.50 (C_q), 128.47 (CH), 128.45 (2CH), 128.42 (CH), 128.40 (CH), 128.34 (C_q), 128.30 (CH), 128.29 (C_q), 128.27 (CH), 128.23 (CH), 127.66 (CH), 127.43 (CH), 126.98 (CH), 126.58 (CH), 126.27 (CH), 125.68 (CH), 125.52 (CH), 125.11 (CH), 125.06 (CH), 125.02 (CH), 124.07 (CH), 124.00 (CH), 123.76 (d, J=5.0 Hz; C_q), 123.40 (CH), 123.35 (CH), 122.32 (CH), 122.25 (CH), 122.09 (C_q), 51.10 ppm (CH); ^{31}P NMR (243 MHz, $CDCl_3$): δ=137.9 (d, J=205.6 Hz; NP(O)$_2$), −18.8 ppm (d, J=205.6 Hz; PPh_2); HRMS (ESI): m/z: calcd for $C_{51}H_{35}NNaO_2P_2$: 778.203530 $[M+Na]^+$; found: 778.204537.



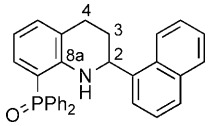
Ligand (S_a,R_c)-7b: A solution of 1-naphthyllithium (1 equiv, 21.8 mL, c=0.301 M in THF) was slowly added with a syringe at −20 °C to a solution of **1b** (2.471 g, 6.693 mmol) in THF (50 mL). The reaction mixture was stirred for 1 h at 0 °C and then cooled to −20 °C. Phosphorochloridite (S_a)-**4** (1 equiv, 6.693 mmol, 2.348 g) in THF (20 mL) was added dropwise. After stirring overnight at RT, the volatile compounds were removed under reduced pressure and the remaining solid was dried in vacuo. Toluene (24 mL) and ethanol (5 mL) were added to the obtained solid and the resulting mixture was heated to 40 °C to give a clear solution. After cooling to RT, ethanol (85 mL) was added slowly with a syringe, whereupon a colourless solid precipitated containing (S_a,R_c)-**7b** with approximately 93% *de* (as determined by ^{31}P NMR spectroscopy). The obtained solid was filtered off and dissolved in hot (70–80 °C) toluene (70 mL). Ethanol (60 mL) was added and resulted in the formation of a colourless powder that contained (S_a,R_c)-**7b** in diastereomerically pure form (as determined by ^{31}P NMR spectroscopy). The obtained solid included residual toluene, which could not be removed, even by heating in vacuo overnight. Solvent-free (S_a,R_c)-**7b** was obtained after precipitation from CH_2Cl_2/*n*-pentane (11:70 mL). After removal of the mother liquor, the solid was dried in vacuo at 60 °C to give (S_a,R_c)-**7b** as a white powder. Yield: 56% (1.53 g, 1.88 mmol); >99% *de*; $[\alpha]_D^{20}$=+576° (c=0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.17 (d, J=8.7 Hz, 1H; Ar), 8.11 (d, J=8.2 Hz, 1H; Ar), 7.87 (d, J=8.9 Hz, 1H; Ar), 7.85 (d, J=8.2 Hz, 1H; Ar), 7.70 (d, J=8.7 Hz, 1H; H-3^A), 7.60–7.51 (m, 4H; Ar), 7.42–7.29 (m, 6H; Ar), 7.22 (m, 1H; Ar), 7.17–7.07 (m, 4H; Ar), 7.05 (m, 1H; Ar), 7.00 (t, J=7.5 Hz, 1H; Ar), 6.93 (s, 1H; Ar), 6.91 (s, 1H; Ar), 6.90 (s, 2H; Ar), 6.54 (d, J=9.6 Hz, 1H; H-4), 6.38 (m, 1H; Ar), 6.33 (d, J=8.6 Hz, 1H; H-8′), 5.96 (dd, J=9.6, 5.7 Hz, 1H; H-3), 5.85 (m, 1H; H-2), 2.27 (s, 6H; CH_3), 2.26 ppm (s, 6H; CH_3); ^{13}C NMR (150 MHz, CD_2Cl_2): δ=151.20 (m; C_q), 149.80 (C_q), 144.06 (dd, J=24.3, 20.6 Hz; C_q), 140.91 (dd, J=17.4, 16.8 Hz; C_q), 139.21 (C_q), 138.40 (C_q), 138.38 (CH), 138.36 (2C_q), 138.31 (C_q), 137.05 (d, J=3.5 Hz; C_q), 134.04 (C_q), 133.65 (C_q), 133.16 (C_q), 132.17 (C_q), 131.78 (CH), 131.64 (CH), 131.61 (d, J=2.5 Hz; CH), 131.56 (C_q), 131.49 (d, J=2.3 Hz; CH), 131.08 (CH), 130.62 (CH), 130.60 (CH), 130.54 (CH), 130.34 (CH), 129.05 (C_q), 128.98 (CH), 128.96 (CH), 128.89 (CH), 128.78 (CH), 128.70 (2C_q), 128.18 (CH), 127.63 (CH), 127.19 (CH), 127.06 (CH), 126.80 (CH), 126.29 (CH), 125.87 (CH), 125.72 (CH), 125.58 (CH), 125.57 (CH), 124.68 (CH), 124.47 (d, J=4.9 Hz; C_q), 124.35 (CH), 123.80 (CH), 123.63 (CH), 122.68 (CH), 122.38 (CH), 122.35 (C_q), 51.57 (d, J=3.2 Hz; C-2), 21.76 (2CH_3), 21.73 ppm (2CH_3); ^{31}P NMR (243 MHz, $CDCl_3$): δ=137.7 (d, J=204.9 Hz; NP(O)$_2$), −18.9 ppm (d, J=204.9 Hz; PXyl$_2$); MS (EI): m/z (%): 813 (18), 812 (55), 811 (100), 810 (26), 707 (45), 706 (88), 685 (38), 684 (76), 527 (39), 526 (98), 496 (22), 495 (12), 406 (22), 391 (33), 390 (33), 316 (23), 315 (76), 284 (15), 269 (16), 268 (70), 264 (38), 254 (15), 252 (27); HRMS (ESI): m/z: calcd for $C_{55}H_{44}NO_2P_2$: 812.284182 $[M+H]^+$; found: 812.284121.



Compound 10a: Hydrogen peroxide (8 mL, 35% w/w) was added slowly at 0 °C to a solution of **8a** (1.504 g, 3.407 mmol) in CH_2Cl_2 (25 mL). The reaction mixture was stirred overnight at RT. The mixture was cooled with an ice bath and Pd on charcoal (10% w/w, 750 mg) was added in small portions while excess H_2O_2 was decomposed. The suspension was stirred for 3 d at RT. The solid was allowed to settle and the supernatant was filtered through basic Celite (25 mL). The organic phase was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The remaining solid was dried under vacuum at 60 °C. Compound **10a** was obtained as a yellow solid. Yield: 1.175 g (2.579 mmol, 76%); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.77 (ddd, J=13.8, 7.1, 1.5 Hz, 1H; H-7), 8.25 (dd, J=8.5, 1.7 Hz, 1H; Ar), 8.10 (dt, J=8.1, 1.2 Hz, 1H; Ar), 7.89 (m, 2H; Ar), 7.81–7.73 (m, 6H; Ar), 7.67 (d, J=8.4 Hz, 1H; Ar), 7.46 (m, 1H; Ar), 7.41–7.33 (m, 3H; Ar), 7.23–7.15 (m, 5H; Ar), 6.82 ppm (dd, J=7.1, 1.2 Hz, 1H; Ar); ^{13}C NMR (150 MHz, $CDCl_3$): δ=158.64 (C_q), 147.75 (d, J=6.0 Hz; C_q), 137.96 (d, J=6.5 Hz; C-7), 137.78 (C_q), 136.29 (CH), 133.78 (d, J=108.5 Hz; 2C_q), 133.75 (C_q), 132.64 (d, J=10.6 Hz; 4CH), 132.58 (CH), 131.47 (d, J=101.1 Hz; C_q), 131.22 (d, J=3.0 Hz; 2CH), 130.80 (C_q), 129.16 (CH), 128.54 (CH), 128.46 (CH), 127.91 (d, J=12.6 Hz; 4CH), 127.00 (d, J=7.5 Hz; C_q), 126.60 (CH), 126.41 (d, J=12.5 Hz; CH), 125.88 (CH), 125.27 (CH), 125.25 (CH), 123.70 ppm (CH); ^{31}P NMR (243 MHz, $CDCl_3$): δ=28.5 ppm; MS (EI): m/z (%): 456 (20), 455 (76), 454 (100), 377 (8), 376 (29), 330 (5), 328 (9), 300 (8), 254 (11), 253 (13), 252 (9); HRMS (ESI): m/z; calcd for $C_{31}H_{23}NOP$: 456.151175 $[M+H]^+$; found: 456.150816.

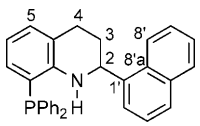


Compound 11a: A suspension of **10a** (219.3 mg, 0.481 mmol) and Pd on charcoal (50 mg, 5% w/w) in CH_2Cl_2 (4 mL) was placed in a 10 mL stainless-steel autoclave equipped with a glass inlet and a magnetic stirrer. Hydrogen was added (30 bar) and the reaction mixture was stirred for 16 h. The autoclave was vented and the reaction mixture was filtered through a plug of basic Celite. The filter material was washed with CH_2Cl_2 (5 mL) and the combined organic filtrates were concentrated under reduced pressure. The remaining solid was dried under vacuum at 60 °C. Compound **11a** was obtained as a yellow solid. Yield: 201.3 mg (0.438 mmol, 91%); ^{1}H NMR (600 MHz, $CDCl_3$): δ=7.99–7.95 (m, 1H; Ar), 7.86–7.82 (m, 1H; Ar), 7.76–7.66 (m, 5H; Ar), 7.60 (dt, J=7.3, 1.2 Hz, 1H; Ar), 7.56 (dt, J=7.3, 1.2 Hz, 1H; Ar), 7.54–7.43 (m, 6H; Ar), 7.23 (br s, 1H; NH), 7.18 (t, J=7.7 Hz, 1H; Ar), 7.11 (d, J=7.2 Hz, 1H; Ar), 7.07 (d, J=7.2 Hz, 1H; Ar), 6.71 (m, 1H; Ar), 6.51 (dt, J=7.5, 2.8 Hz, 1H; Ar), 5.40 (m, 1H; H-2), 2.87 (m, 1H; H_A-4), 2.63 (m, 1H; H_B-4), 2.29 (m, 1H; H_A-3), 1.99 ppm (m, 1H; H_B-3); ^{13}C NMR (150 MHz, $CDCl_3$): δ=149.97 (d, J=2.3 Hz; C_q), 139.83 (C-1′), 133.90 (C_q), 132.95 (d, J=103.3 Hz; C_q), 133.18 (d, J=2.2 Hz; CH), 132.51 (d, J=104.4 Hz; C_q), 132.31 (d, J=9.7 Hz; 4CH), 132.00 (d, J=2.9 Hz; CH), 131.92 (d, J=2.9 Hz; CH), 131.77 (d, J=11.2 Hz; CH), 130.18 (C-8a), 129.05 (CH), 128.58 (d, J=12.1 Hz; 4CH), 127.45 (CH), 126.00 (CH), 125.60 (CH), 125.41 (CH), 123.62 (CH), 122.63 (CH), 121.84 (d, J=7.9 Hz; C_q), 114.57 (d, J=13.8 Hz; CH), 110.60 (d, J=105.9 Hz; C_q), 51.71 (C-2), 28.01 (C-3), 26.09 ppm (C-4); ^{31}P NMR (243 MHz, $CDCl_3$): δ=35.9 ppm; MS (EI): m/z (%): 461 (6), 460 (33), 459 $[M]^+$ (100), 458 (20), 333 (17), 332 (73), 331 (15), 330 (12), 305 (10), 255 (5), 254 (23), 230 (11), 201 (9), 199 (5), 191 (7), 152 (5), 141 (6); HRMS (ESI): m/z: calcd for $C_{31}H_{22}NNaOP$: 482.164421 $[M+Na]^+$; found: 482.164413.

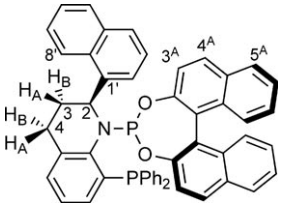


Compound 12a: Trichlorosilane was added with a syringe to a solution of **11a** (5.002 g, 10.98 mmol) and triethylamine (24.16 mmol, 2.2 equiv, 2.43 mL) in toluene (120 mL) under vigorous stirring and the reaction mixture was heated at reflux temperature for 3 h. The mixture was allowed to cool to RT and a solution of aqueous NaOH (37 mL, 4 M) was

added. The organic phase was diluted with ethyl acetate (50 mL) and the aqueous phase separated. The organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4 and evaporated to dryness under reduced pressure. The obtained solid was dissolved in CH_2Cl_2 (50 mL) and the solution was filtered through a plug of silica (25 mL). The filter cake was eluted with additional CH_2Cl_2 (3×50 mL) and the combined organic layers were evaporated under reduced pressure. The remaining solid was dried in vacuo to afford **12a** as a bright yellow solid. Yield: 3.183 g (65%); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.01 (d, J=8.2 Hz, 1H; H-8′), 7.87 (d, J=8.1 Hz, 1H; Ar), 7.73 (d, J=8.1 Hz, 1H; Ar), 7.51–7.34 (m, 12H; Ar), 7.29 (m, 1H; Ar), 7.24 (m, 1H; Ar), 7.07 (d, J=7.4 Hz, 1H; H-5), 6.72 (m, 1H; Ar), 6.62 (t, J=7.5 Hz, 1H; Ar), 5.34 (m, 1H; H-2), 5.12 (d, J=7.3 Hz, 1H; NH), 2.97 (m, 1H; H-4), 2.74 (dt, J=16.2, 5.5 Hz, 1H; H-4), 2.34 (m, 1H; H-3), 2.08 ppm (m, 1H; H-3); ^{13}C NMR (150 MHz, $CDCl_3$): δ=147.49 (d, J=17.1 Hz; C_q), 139.97 (C-1′), 135.76 (d, J=7.0 Hz; $C_{Ph,ipso}$), 135.54 (d, J=7.3 Hz; $C_{Ph,ipso}$), 134.16 (CH), 134.03 (CH), 133.97 (CH), 133.93 (C_q), 133.85 (CH), 132.46 (d, J=3.3 Hz; CH), 130.53 (C-5), 130.37 (C-8′a), 129.09 (CH), 128.99 (CH), 128.83 (CH), 128.72 (2CH), 128.67 (2CH), 127.67 (CH), 126.13 (CH), 125.68 (CH), 125.56 (CH), 123.51 (CH), 122.75 (C-8′), 120.58 (d, J=3.0 Hz; C_q), 117.87 (d, J=7.4 Hz; C_q), 116.68 (d, J=3.0 Hz; CH), 52.45 (C-2), 28.89 (C-4), 26.51 ppm (C-3); ^{31}P NMR (243 MHz, $CDCl_3$): δ=−20.9 ppm; MS (EI): m/z: 445 (5), 444 (33), 443 $[M]^+$ (100), 442 (14), 316 (13), 290 (9), 258 (6), 238 (13), 222 (7), 221 (6), 183 (10); HRMS (ESI): m/z: calcd for $C_{31}H_{27}NP$: 444.187565 $[M+H]^+$; found: 444.187779.



Ligand (R_a,S_c)-13a: A solution of phosphine **12a** (1.729 g, 3.898 mmol) in THF (40 mL) was cooled to −20 °C and phenyllithium (1 equiv, 2.12 mL, c=1.84 M in di-*n*-butylether/cyclohexane, 30:70) was added slowly with a syringe. After complete addition, the reaction mixture was stirred for 1 h at 0 °C and then cooled to −20 °C. Phosphorochloridite (*R*)-**4** (1 equiv, 7.8 mL, c=0.5 M in toluene) was added slowly and the mixture was allowed to warm to RT. After stirring for 1 h at RT the mixture was concentrated under reduced pressure and the remaining solid was dried in vacuo (4.256 g). Toluene (40 mL) and ethanol (2 mL) were added to a portion of this solid (3.915 g) and the resulting mixture was heated to 40 °C, which resulted in a clear solution. After cooling to RT, ethanol (48 mL) was added slowly with a syringe, whereupon a colourless solid precipitated that contained (R_a,S_c)-**13a** with approximately 93% *de* (as determined by ^{31}P NMR spectroscopy). The obtained solid was filtered off and dissolved in hot (40–80 °C) toluene (32 mL). Ethanol (50 mL) was added and resulted in the formation of a colourless powder that contained (R_a,S_c)-**13a** in diastereomerically pure form (as determined by ^{31}P NMR spectroscopy). The obtained solid included residual toluene, which could not be removed, even by heating in vacuo overnight. Solvent-free (R_a,S_c)-**13a** was obtained after precipitation from CH_2Cl_2/*n*-pentane (50:70 mL). After removal of the mother liquor, the solid was dried in vacuo at 60 °C to yield (R_a,S_c)-**13a** as a white powder. Yield: 57% (774.5 mg, 1.022 mmol); >99% *de*; $[\alpha]_D^{20}$=−256° (c=0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.25 (d, J=8.8 Hz, 1H; H-4^A), 8.16 (d, J=8.16 Hz, 1H; H-5^A), 7.84 (d, J=8.8 Hz, 2H; Ar), 7.80 (d, J=8.70 Hz, 1H; H-3^A), 7.60–7.52 (m, 4H; Ar), 7.51–7.35 (m, 9H; Ar), 7.35–7.25 (m, 8H; Ar), 7.22 (m, 1H; Ar), 7.13 (m, 1H; Ar), 7.06–6.99 (m, 2H; Ar), 6.16 (d, J=8.5 Hz, 1H; H-8′), 6.11 (m, 1H; Ar), 5.66 (m, 1H; H-2), 3.14 (m, 1H; H_A-4), 2.77 (m, 1H; H_B-4), 2.64 (m, 1H; H_A-3), 1.60 ppm (m, 1H; H_B-3); ^{13}C NMR (150 MHz, $CDCl_3$): δ=151.48 (t, J=4.1 Hz; C_q), 149.62 (C_q), 146.92 (dd, J=24.6, 20.4 Hz; C_q), 142.58 (C-1′), 140.46 (m; C_q), 138.17 (d, J=7.1 Hz; C_q), 136.46 (CH), 136.09 (m; C_q), 133.58 (CH), 133.51 (d, J=3.1 Hz; CH), 133.46 (CH), 133.46 (C_q), 133.39 (d, J=3.1 Hz; CH), 133.27 (C_q), 132.64 (C_q), 131.45 (C_q), 130.69 (C_q), 130.38 (CH), 130.01 (C-4^A), 129.66 (dd, J=8.6, 4.9 Hz; C_q), 129.33 (C_q), 129.10 (CH), 128.55 (d, J=6.0 Hz; 2CH), 128.41 (CH), 128.36 (d, J=6.5 Hz; 2CH), 128.28 (CH), 128.25 (CH), 128.24 (CH), 128.12 (CH), 127.68 (CH), 126.97 (CH), 126.52 (CH), 126.36 (CH), 126.09 (CH), 125.35 (CH), 125.15 (CH), 124.93 (CH), 124.85 (CH), 124.81 (CH), 124.08 (CH), 123.76 (d, J=5.2 Hz; C_q), 123.48 (d, J=3.7 Hz; CH), 122.41 (C-3^A), 122.30 (CH), 122.16 (C_q), 122.05 (CH), 51.99 (d, J=3.1 Hz; C-2), 34.73 (C-3), 27.86 ppm (C-4); ^{31}P NMR (243 MHz, $CDCl_3$): δ=138.2 (d, J=184.9 Hz; $NP(O)_2$), −19.9 ppm (d, J=184.9 Hz; PPh_2); MS (EI): m/z (%): 759 (5), 758 (16), 757 $[M]^+$ (29), 682 (12), 681 (50), 680 (100), 617 (8), 603 (6), 527 (12), 526 (32), 472 (7), 458 (5), 379 (11), 365 (14), 335 (17), 334 (5), 318 (5), 315 (5), 302 (7), 301 (9), 268 (7), 252 (15), 242 (6), 240 (6); HRMS (ESI): m/z: calcd for $C_{51}H_{37}NNaO_2P_2$: 780.219180 $[M+Na]^+$; found: 780.218943.



Compound (R_a,R_c)-13a: ^{31}P NMR (121 MHz, $CDCl_3$): δ=141.1 (d, J=151.5 Hz; NP $(O)_2$), −18.7 ppm (d, J=151.5 Hz; PPh_2).

Complex 14: HBF_4·Et_2O (1.2 equiv, 0.294 mmol, 40 μL) was added to a solution of (acetylacetonato)-(1,5-cyclooctadiene)-rhodium(I) (75.9 mg, 0.245 mmol) in dry THF (10 mL). After stirring for 10 min, a solution of (R_a,S_c)-**7a** (1 equiv, 0.294 mmol, 185.0 mg) in THF (5 mL) was added, whereupon the colour of the solution turned from yellow to orange. After stirring for 30 min, the mixture was concentrated to half of the volume under reduced pressure. *n*-Pentane (25 mL) was added, whereupon a yellow solid formed, which was separated from the mother liquor. To remove included THF, this solid was dissolved in CH_2Cl_2 (8 mL) and precipitated by adding Et_2O (25 mL). The mother liquor was removed and the remaining yellow solid was dried under reduced pressure at 50 °C to give **14**. Yield: 151.7 mg (59%); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.35 (d, J=8.9 Hz, 1H; Ar), 8.22 (d, J=8.8 Hz,1H; Ar), 8.10 (d, J=8.1 Hz, 1H; Ar), 8.06 (d, J=8.2 Hz, 1H; Ar), 7.81 (d, J=8.9 Hz, 1H; Ar), 7.70 (d, J=7.2 Hz, 1H; Ar), 7.69 (d, J=7.8 Hz, 1H; Ar), 7.63 (d, J=8.8 Hz, 1H; Ar), 7.60 (m, 1H; Ar), 7.54–7.48 (m, 5H; Ar), 7.43–7.26 (m, 10H; Ar), 7.26–7.20 (m, 3H; Ar), 7.06 (m, 1H; Ar), 6.67 (t, J=7.8 Hz, 1H; Ar), 6.63 (d, J=9.4 Hz, 1H; H-4), 6.35–6.30 (m, 2H; Ar), 6.20 (d, J=8.7 Hz, 1H; Ar), 5.91 (t, J=6.8 Hz, 1H; CH_{cod}), 5.81 (t, J=7.0 Hz, 1H; CH_{cod}), 5.77 (t, J=7.1 Hz, 1H; H-2), 5.61 (dd, J=9.4, 6.1 Hz, 1H; H-3), 4.21 (m, 1H; CH_{cod}), 3.68 (m, 1H; CH_{cod}), 2.85 (m, 1H; CH_2), 2.69–2.48 (m, 3H; CH_2), 2.01 (m, 1H; CH_2), 1.95–1.82 (m, 2H; CH_2), 1.35–1.18 ppm (m, 1H; CH_2); ^{31}P NMR (243 MHz, $CDCl_3$): δ=138.3 (dd, $J_{P,P'}$=61.3 Hz, J(Rh,P)=258.4 Hz; $NP(O)_2$), 24.8 ppm (dd, J(P,P′)=61.3 Hz, J(Rh,P)=135.9 Hz; PPh_2); HRMS (ESI): m/z: calcd for $C_{59}H_{47}NO_2P_2Rh$: 966.212458 $[M]^+$; found: 966.211939.

Complex 15: HBF_4·Et_2O (1.2 equiv, 0.144 mmol, 20 μL) was added to a solution of (acetylacetonato)(1,5-cyclooctadiene)rhodium(I) (37.4 mg, 0.120 mmol) in dry THF (5 mL). After stirring for 10 min a solution of (S_a,R_c)-**7b** (1 equiv, 0.120 mmol, 98.0 mg) in THF (5 mL) was added. The resulting orange solution was stirred for 30 min and then concentrated to half volume under reduced pressure. *n*-Pentane (30 mL) was added, whereupon a yellow solid formed, which was separated from the mother liquor by filtration. To remove included THF, the solid was dissolved in CH_2Cl_2 (1 mL) and precipitated by adding Et_2O (15 mL). The mother liquor was removed and the remaining yellow solid was dried under reduced pressure at 50 °C to afford **15**. Yield: 65.9 mg (49%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.24 (d, J=8.9 Hz, 1H; Ar), 8.16 (d, J=8.9 Hz, 1H; Ar), 8.05 (d, J=8.1 Hz, 1H; Ar), 8.01 (d, J=8.1 Hz, 1H; Ar), 7.73 (d, J=8.9 Hz, 1H; Ar), 7.58–7.51 (m, 2H; Ar), 7.50–7.43 (m, 2H; Ar), 7.41 (m, 1H; Ar), 7.36–7.24 (m, 6H; Ar), 7.23–7.16 (m, 4H; Ar), 7.09 (s, 1H; Ar), 7.03 (t, J=7.3 Hz, 1H; Ar), 6.86 (s, 1H; Ar), 6.80 (d, J=11.3 Hz, 2H; Ar), 6.52–6.43 (m, 2H; Ar), 6.30 (t, J=8.0 Hz, 1H; Ar), 6.15 (d, J=8.5 Hz, 1H; Ar), 6.09 (d, J=7.5 Hz, 1H; Ar), 5.86 (m, 1H), 5.78–5.71 (m, 2H; CH_{cod}), 3.92 (m, 1H; CH_{cod}), 3.60 (m, 1H; CH_{cod}), 2.75–2.61 (m, 2H; CH_2), 2.54–2.47 (m, 2H; CH_2), 2.27 (s, 6H; CH_3), 2.15 (s, 6H; CH_3) 2.03–1.89 (m, 2H; CH_2), 1.77–1.72 ppm (m, 2H; CH_2); ^{31}P NMR (162 MHz, $CDCl_3$): δ=138.0 (dd, J(P,P)=62.0 Hz, J(P,Rh)=

259.5 Hz; $NP(O)_2$), 23.7 ppm (dd, $J(P,P)=62.0$ Hz, $J(P,Rh)=135.8$ Hz; $PXyl_2$); HRMS (ESI): m/z: calcd for $C_{63}H_{55}NO_2P_2Rh$: 1022.27576 $[M]^+$; found: 1022.27660.

Complex 16: $HBF_4{\cdot}Et_2O$ (1.2 equiv, 0.120 mmol, 16 μL) was added to a solution of (acetylacetonato)(1,5-cyclooctadiene)rhodium(I) (31.0 mg, 0.100 mmol) in dry THF (5 mL). After stirring for 10 min, a solution of (R_a,S_c)-**13a** (1 equiv, 0.100 mmol, 75.8 mg) in THF (5 mL) was added. The resulting orange solution was stirred for 30 min and then concentrated to half of the volume under reduced pressure. *n*-Pentane (30 mL) was added, whereupon a yellow solid formed, which was separated from the mother liquor. To remove included THF, the solid was dissolved in CH_2Cl_2 (3 mL) and precipitated by the addition of Et_2O (30 mL). The mother liquor was removed by filtration and the remaining yellow solid was dried under reduced pressure at 50 °C to give **16**. Yield: 61.1 mg (65 %); ^1H NMR (600 MHz, $CDCl_3$): $\delta=8.24$ (d, $J=8.8$ Hz, 1H; Ar), 8.21 (d, $J=9.0$ Hz, 1H; Ar), 8.15 (d, $J=8.2$ Hz, 1H; Ar), 7.98 (d, $J=8.0$ Hz, 1H; Ar), 7.83 (m, 2H; Ar), 7.69 (m, 2H; Ar), 7.66–7.61 (m, 2H; Ar), 7.61–7.56 (m, 2H; Ar), 7.53–7.49 (m, 4H; Ar), 7.47–7.28 (m, 8H; Ar), 7.28–7.23 (m, 1H; Ar), 7.21–7.15 (m, 2H; Ar), 7.11 (d, $J=8.5$ Hz, 1H; Ar), 7.02 (t, $J=7.5$ Hz, 1H; Ar), 6.62 (t, $J=7.6$ Hz, 1H; Ar), 6.13 (m, 2H), 5.92 (m, 2H), 5.72–5.61 (m, 2H), 4.16 (m, 1H), 3.59 (m, 1H), 2.76 (m, 1H), 2.56–2.44 (m, 4H), 2.38 (m, 1H), 1.99 (m, 1H), 1.89–1.77 (m, 2H), 1.61 (m, 1H), 0.99 ppm (m, 1H); ^{31}P NMR (243 MHz, $CDCl_3$): $\delta=136.9$ (dd, $J_{PP'}=62.4$ Hz, $J(Rh,P)=252.6$ Hz; $NP(O)_2$), 22.7 ppm (dd, $J(P,P)=62.4$ Hz, $J(Rh,P)=133.4$ Hz; PPh_2); HRMS (ESI): m/z: calcd for $C_{59}H_{49}NO_2P_2Rh$: 968.228808 $[M]^+$; found: 968.230606.

General procedure for asymmetric hydrogenation: A 10 mL stainless-steel autoclave equipped with a glass inlet and a magnetic stirring bar was charged under an argon atmosphere with the substrate (1 mmol). The desired Rh complex (1 μmol) was added by syringe as a stock solution in CH_2Cl_2 or MeOH. The total amount of solvent was adjusted to 2 mL by the addition of the appropriate quantity of the same solvent and the autoclave was pressurised with hydrogen (see Table 5 for details). The reaction was started by switching on the stirrer. The reaction mixture was stirred at RT for the desired reaction time then the pressure was carefully released. The conversion was determined by ^1H NMR spectroscopy of the concentrated reaction mixture. The *ee* value was determined by chiral GC or HPLC analysis after filtration through a plug of silica. The absolute configurations of the hydrogenation products were assigned by comparison of the sign of optical rotation to those reported in the literature.

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be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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