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Asymmetric Catalysis

Bidentate Phosphine–Phosphoramidite Ligands of the BettiPhos Family for Rh-Catalyzed Asymmetric Hydrogenation

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Abstract: Phosphine–phosphoramidites comprising a stereogenic phosphorus atom at the phosphoramidite moiety and a Betti base as chiral backbone have been synthesized. Individual diastereomers have been benchmarked as ligands in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate to study the interplay of the different elements of chirality. The privileged diastereomer was applied to Rh-catalyzed asymmetric hydrogenation of several functionalized olefins, leading to high enantioselectivities between 91 and 97 % *ee*, which confirms the effectiveness of the BettiPhos ligand family in asymmetric catalysis.

Introduction

Since the seminal work of Knowles[1] and Horner[2] in the 1960s, asymmetric hydrogenation has impressively progressed to an efficient method for several substrate classes and is used for the preparation of chiral molecules on laboratory as well as industrial scale.[3] While Knowles and Horner used phosphine ligands with stereogenic phosphorus donor(s),[4] mainly diphosphine ligands with C_2-symmetric skeletons were employed later as stereoselectors.[4,5] In 2000, the contributions of Feringa and de Vries,[6] Reetz,[7] and Pringle[8] showed that also monodentate phosphorus compounds containing phosphorus heteroatom bonds are excellent ligands for the Rh-catalyzed asymmetric hydrogenation. Their efficiency together with their plain synthesis by simple condensation reactions of phosphorus trichloride with a broad variety of alcohols/diols and/or (di)amines[5] attracted great interest and stimulated structural exploitation leading to very diverse application in catalysis.[9] In the same year, we reported the first hybrid bidentate phosphine–phosphoramidite ligand QuinaPhos **L1**.[10,11] Because of the combination of two different phosphorus donor groups, QuinaPhos **L1** combined the high stereoselectivity observed with monodentate phosphoramidite ligands with the high activity found for the more electron-rich phosphine donors allowing for enantioselectivities of up to 99 % *ee* and TOF values of up to 36.000 h^{-1}.[10,12] In the following years, numerous phosphine–phosphoramidites were introduced by several groups providing powerful ligands for a variety of catalyzed reactions in combination with different metals, in particular for asymmetric hydrogenation (C=C, C=O, C=N), and for hydroformylation. Some prominent examples are depicted in Figure 1. Noteworthy, all phosphine–phosphoramidite ligands as well as the large majority of related ligand classes (phosphine–phosphite, phosphine–phosphonite, as well as most monodentate phosphoramidites, phosphites, and phosphonite mentioned above) rely on the atropoisomeric Binol moiety as essential structural feature for obtaining a high level of enantioselectivity in asymmetric catalysis and in asymmetric hydrogenation, in particular.

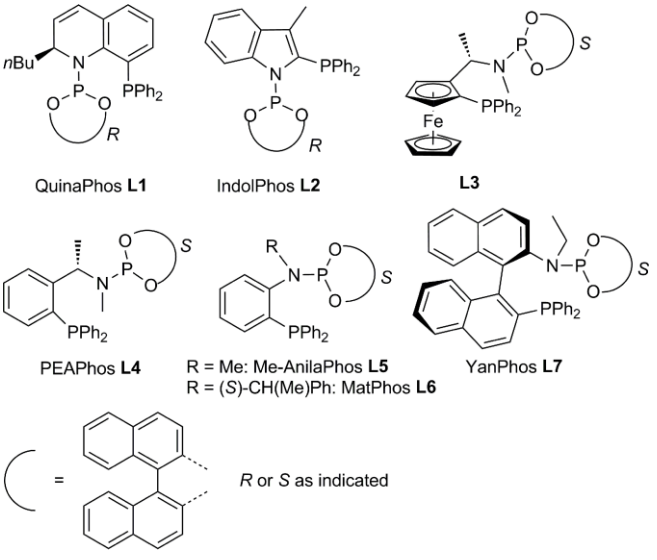

Figure 1. Examples of phosphine–phosphoramidite ligands: QuinaPhos **L1**,[10] IndolPhos **L2**,[13] **L3**,[14] PEAPhos **L4**,[15] Me-AnilaPhos **L5**,[16] MatPhos **L6**,[17] and YanPhos **L7**.[18]

We recently reported a series of modular monodentate phosphoramidite and phosphorodiamidite ligands **L8**[19] (see Figure 2) based on a chiral amino alcohol, a so-called Betti base.[20] In contrast to the Binol-based ligands, this structural motif leads to a stereogenic phosphorus donor. We further exploited the versatile chiral Betti base backbone to construct phosphine–phosphorodiamidite ligands **L9** (BettiPhos, Figure 2), which gave very high enantioselectivities accompanied by excellent

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regioselectivities in the asymmetric hydroformylation of various vinyl esters and vinyl amides.[21] The stereochemistry of the chiral P donor proved important for the catalytic performances of these Betti base-derived ligands providing an additional control element for tuning the activity and enantioselectivity of catalysts.

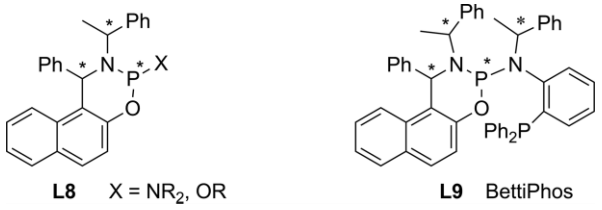
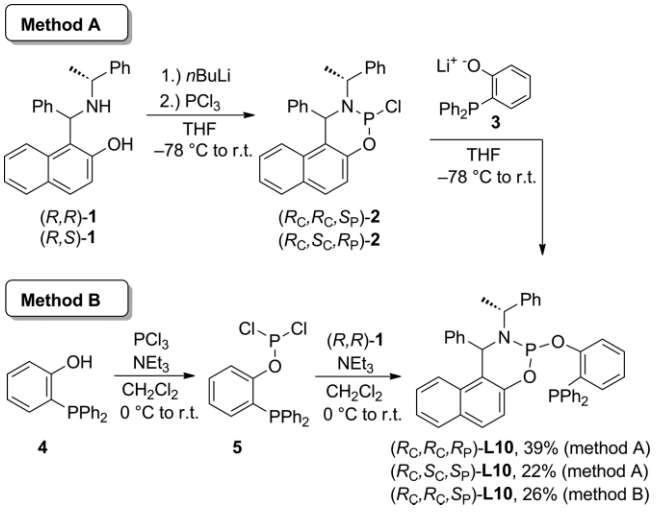


Figure 2. Monodentate[19] and bidentate[21] ligands based on chiral Betti bases bearing a stereogenic P atom.

Herein, we report the first phosphine–phosphoramidite ligands synthesized from a chiral Betti base amino alcohol backbone, therefore possessing a stereogenic phosphorus atom at the phosphoramidite moiety. The ligands were applied to the asymmetric hydrogenation of functionalized olefins achieving a high level of enantioselectivities comparable with that obtained with Binol-derived congeners.

Results and Discussion

The ligands were synthesized starting from the (*R*,*R*)- and (*R*,*S*)-Betti base **1** with use of 2-(diphenylphosphanyl)phenol **4** as the main synthon, by following methods previously explored for the preparation of BettiPhos **L9** (Scheme 1).[20]

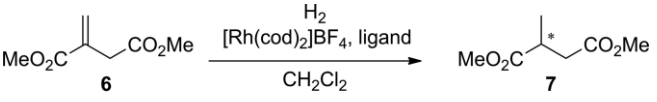


Scheme 1. Synthetic routes for the synthesis of **L10**.

Method A allows the stereoselective formation of phosphoramidochloridite **2** by treatment of the respective Betti base **1** with *n*-butyllithium in THF at –78 °C and subsequent reaction with phosphorus trichloride. Here, a single phosphorus epimer is obtained, whose configuration depends on the configuration of the Betti base starting material. When (*R*,*R*)-**1** is used (R_C,R_C,S_P)-**2** is obtained, whereas (*R*,*S*)-**1** leads to the formation of (R_C,S_C,R_P)-**2**. Subsequent treatment of **2** with the lithiated *ortho*-diphenyl-phosphinophenol **3** at –78 °C resulted in the substitution of the chloride under inversion of the configuration at the phosphorus. From compounds (R_C,R_C,S_P)-**2** and (R_C,S_C,R_P)-**2** the corresponding phosphine–phosphoramidite BettiPhosO ligands (R_C,R_C,R_P)-**L10** and (R_C,S_C,S_P)-**L10** were obtained in 39 and 22 % yield, respectively. Method B was applied to access (R_C,R_C,S_P)-**L10**. Here, phosphine **4** is first treated with phosphorus trichloride in the presence of triethylamine and then a reaction is performed beween the in situ formed dichloro-[2-(diphenylphosphanyl)phenoxy]phosphane **5** and (*R*,*R*)-**1**. The phosphine–phosphoramidite was obtained as a mixture of both P epimers in a ratio of (R_P)/(S_P) = 35:65. After recrystallization from toluene/ethanol the major diastereomer (R_C,R_C,S_P)-**L10** was isolated in 26 % yield.

The configuration of the phosphoramidite P atom was assigned by comparison of the characteristic chemical shifts in the ^{1}H, ^{13}C, and ^{31}P NMR spectra and the coupling constants $J_{H,P}$ and $J_{C,P}$ to the related monodentate phosphoramidite ligands, where the configuration at the phosphorus atom was conclusively determined by X-ray crystal structure analysis.[19]

The three obtained diastereomeric phosphine–phosphoramidites **L10** were then evaluated in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate **6** as a benchmark substrate. The catalysts were prepared in situ from $[Rh(cod)_2]BF_4$ and the respective ligand. The results are shown in Scheme 2.



ligand	conv. (%)	*ee* %
(R_C,R_C,S_P)-**L10**	85%	96 (*S*)
(R_C,S_C,R_P)-**L10**	>99%	73 (*R*)
(R_C,S_C,S_P)-**L10**	18%	82 (*S*)

Scheme 2. Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate with different **L10** diastereomers. Conditions: substrate (3.0 mmol), $[Rh(cod)_2]BF_4$ (3.0 µmol), ligand (3.15 µmol), CH_2Cl_2 (1.0 mL), 40 bar H_2, room temp., 1 h.

Comparing the conversions and enantioselectivities obtained, significant influences of both the relative configuration of the phosphorus atom and the ligand backbone can be observed. With use of (R_C,R_C,S_P)-**L10** 85 % conversion after 1 h and 96 % *ee* (*S*) were obtained, whereas the epimer at phosphorus (R_C,R_C,R_P)-**L10** afforded preferentially the opposite enantiomer in 73 % *ee* (*R*) at full conversion.[22] Thus, the relative configuration of the stereogenic phosphorus is the major factor for controlling the enantiodiscrimination. In contrast to the ligands derived from (R_C,R_C)-Betti base, ligand (R_C,S_C,S_P)-**L10** derived from (R_C,S_C)-Betti base provided a far less active catalyst, and just 18 % conversion was obtained after 14 h. Again the stereochemistry at the P donor dictates the product configuration leading to an enantiomeric excess of 82 % (*S*).[21] Hence, whereas the stereochemistry at the P atom exerts the main control for the enantioselectivity, the configuration of the Betti base backbone seems to have a crucial influence on the activity.

Next, the substrate scope of the privileged BettiPhosO diastereomer (R_C,R_C,S_P)-**L10** in the asymmetric hydrogenation of

functionalized olefins was explored by using the isolated catalyst complex [Rh(cod){(R_C,R_C,S_P)-**L10**}]BF_4 (**9**), which was synthesized from [Rh(cod)acac] (**8**), HBF_4/Et_2O and (R_C,R_C,S_P)-**L10** in 89 % yield. The results of the substrate screening are summarized in Figure 3.

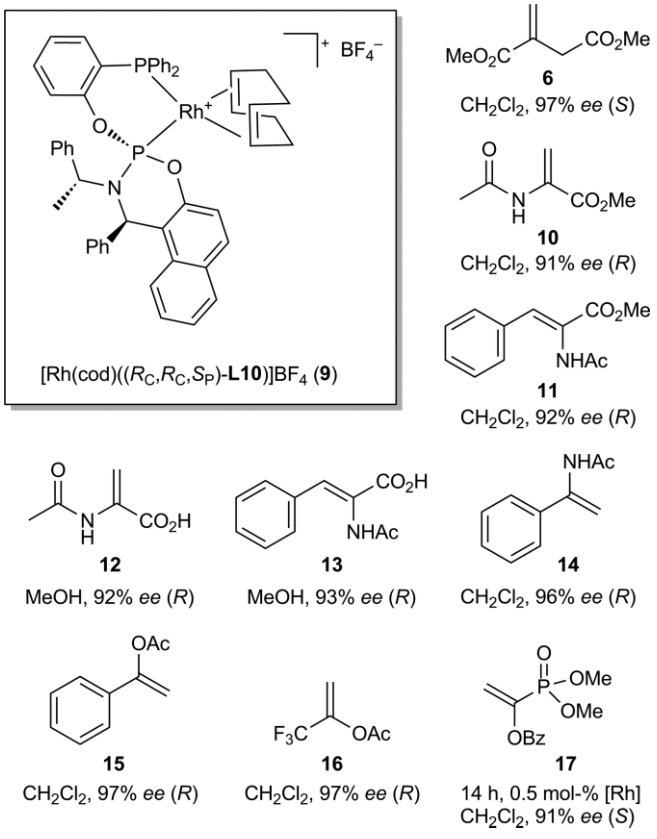


Figure 3. Asymmetric hydrogenation of functionalized olefins with complex **9**. Conditions: substrate (1.5 mmol), complex **9** (1.5 µmol), solvent (1.0 mL), 15 bar H_2, room temp., 3 h. Quantitative conversion for each substrate was obtained.

The asymmetric hydrogenation using Rh complex **9** led to full conversion for all selected substrates within 3 h at room temperature with a catalyst loading of 0.1 mol-%. A prolonged reaction time (14 h) and higher catalyst loading (0.5 mol-%) were needed for full hydrogenation of the more reluctant substrate 1-(dimethoxyphosphoryl)vinyl benzoate **17**, as the only exception. In the case of dimethyl itaconate **6** the use of isolated Rh-catalyst **9** gave slightly higher enantiomeric excess than the in situ generated catalyst (97 vs. 96 %). In the hydrogenation of methyl 2-acetamidoacrylate **10** and (*Z*)-acetamidocinnamate **11** enantiomeric excesses of 91 % (*R*) and 92 % (*R*) were achieved, respectively. The corresponding free acids, that is 2-acetamidoacrylic acid **12** and (*Z*)-acetamidocinnammic acid **13**, were hydrogenated in methanol with comparable enantioselectivities of 92 % *ee* (*R*) and 93 % *ee* (*R*) indicating that the catalyst is equally effective in both aprotic (CH_2Cl_2) and protic solvents (MeOH). *N*-(1-phenylvinyl)acetamide **14** was hydrogenated with 96 % *ee* (*R*), and a similar result was achieved with the structurally related 1-phenylvinyl acetate **15** [97 % *ee* (*R*)]. The hydrogenation of 1-trifluoromethylvinyl acetate **16** proceeded with 97 % *ee* (*R*), while somehow lower enantioselectivity was achieved in the reduction of 1-(dimethoxyphosphoryl)vinyl benzoate **17** with an enantiomeric excess of 91 % *ee* (*S*). Notably, with related phosphine–phosphite ligands bearing the Binol backbone in place of the Betti base moiety lower enantioselectivities were achieved. For instance, 74 % *ee* (vs. 97 % *ee* with **9**) was obtained in the hydrogenation of 1-phenylvinyl acetate **15** under similar conditions,[23] while with use of a Rh complex supported on sulfonated polystyrene resins values of up to 84 % *ee* (vs. 91 % *ee* with **9**) and up to 88 % *ee* (vs. 92 % *ee* with **9**) were attained in aqueous medium in the hydrogenation of methyl 2-acetamidoacrylate **10** and (*Z*)-acetamidocinnamate **11**, respectively.[24]

Conclusions

New phosphine–phosphoramidites bearing a chiral phosphorus atom at the phosphoramidite moiety were synthesized starting from a chiral Betti base. They are a rare example of this class of compounds[25] and new members of the BettiPhos ligand family. The different diastereomeric ligands have been applied to the asymmetric hydrogenation of dimethyl itaconate to evaluate the impact of the single chiral elements. Interestingly, whereas the configuration of the stereogenic phosphorus atom was mainly responsible for steering the enantioselectivity, the configuration in the ligand backbone had a major influence on the catalyst activity. The most efficient ligand has been used in the hydrogenation of a range of functionalized olefins achieving high enantioselectivities of 91–97 % *ee*. Corroborated by the results obtained in the asymmetric hydroformylation with the related phosphine–phosphorodiamidite ligands,[21,22] these findings demonstrate the effectiveness of the chiral amino alcohol (Betti base), easily accessible on gram scale, as a useful scaffold for efficient chiral-at-phosphorus hybrid bidentate ligands and as a valid alternative to the well-established Binol backbone.

Experimental Section

General Considerations: All reactions and manipulations were performed by using standard Schlenk techniques or in a glovebox under an argon atmosphere. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded with a Bruker AV 600 (600, 150 and 243 MHz, respectively), Bruker AV 400 (400, 100, 162 MHz, respectively), Bruker AV 300 (300, 75, 121 MHz, respectively). Chemical shifts were referenced to residual solvent peaks (^1H NMR, ^{13}C NMR) or H_3PO_4 (85 %) as an external standard (^{31}P NMR). Mass spectra were recorded with a Finnigan MAT 8200 (MS + HRMS-EI) or a Bruker FTICR-Apex III (HRMS-ESI). Optical rotations were measured with a Jasco P-1020 polarimeter. The concentrations used for measuring specific rotations are given in g per 100 mL. CH_2Cl_2, toluene, and *n*-pentane were dried with alumina and molecular sieves with a solvent purification system from Innovative Technology. THF, ether, and NEt_3 were distilled from KOH and dried with molecular sieves. Ethanol was dried with molecular sieves. PCl_3 was freshly distilled. $CDCl_3$ and CD_2Cl_2 were degassed through freeze-pump-thaw cycles and stored over molecular sieves. Basic alumina (Al_2O_3 90 basic, pH 8.5–10.5, 0.063–0.2 mm) was purchased from Roth. (R_C,R_C)-**1**[19,26] and (R_C,S_C)-**1**[26] were prepared according to published procedures. All other chemi-

cals were purchased from Sigma–Aldrich, ABCR, TCI, or AlfaAesar and used as received.

Synthetic Procedures

(1*R*,3*R*)-3-[2-(Diphenylphosphanyl)phenoxy]-1-phenyl-2-[(*R*)-1-phenylethyl]-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3,2]oxazaphosphinine [(R_C,R_C,R_P)-L10]: *Method A* in Scheme 1. 1-((*R*)-Phenyl{[(*R*)-1-phenylethyl]amino}methyl)naphthalen-2-ol (706.9 mg, 2.0 mmol, 1.0 equiv.) was dissolved in THF (10 mL) and the solution cooled to –78 °C. Afterwards *n*-butyllithium (1.6 M in hexanes, 2.53 mL, 4.04 mmol, 2.02 equiv.) was added dropwise within 15 min, and the mixture was stirred for 1 h at –78 °C and 1 h at room temperature. The solution was cooled again to –78 °C, and a solution of phosphorus trichloride (175 µL, 2.0 mmol, 1.0 equiv.) in THF (6 mL) was added dropwise within 15 min. The mixture was stirred for 1 h at –78 °C and another 1.5 h at room temperature. In another Schlenk flask, 2-(diphenylphosphanyl)phenol (545.4 mg, 1.96 mmol, 0.98 equiv.) was dissolved in THF (10 mL), and TMEDA (300 µL, 2.0 mmol, 1.0 equiv.) was added. The solution was cooled to –78 °C and *n*-butyllithium (1.6 M in hexanes, 1.25 mL, 2.0 mmol, 1.0 equiv.) was added dropwise within 15 min. The mixture was stirred for 1 h at –78 °C and 1 h at 0 °C. The solution was cooled again to –78 °C, and the solution of the phosphoramidochloridite (R_C,R_C,S_P)-**2** was added dropwise within 15 min. The mixture was stirred for 2 h at –78 °C and then allowed to reach room temperature overnight. All volatiles were removed at high vacuum, and the residue was redissolved in THF (10 mL) and filtered through basic alumina. After elution with THF (10 mL), all volatiles were removed under reduced pressure to give a colorless solid. The residue was recrystallized from toluene/ethanol. The precipitate was collected, washed with small amounts of ethanol, and dried to yield the product as a colorless solid. Yield: 508.0 mg (0.77 mmol, 39 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 4.74 (dq, $^3J_{H,H}$ = 6.8, $^3J_{H,P}$ = 13.4 Hz, 1 H, CH), 5.61 (d, $^3J_{H,P}$ = 6.4 Hz, 1 H, CH), 6.60 (ddd, J = 7.4, J = 3.7, J = 1.4 Hz, 1 H, Ar), 6.73 (dd, J = 7.9, J = 4.4 Hz, 1 H, Ar), 6.82–6.94 (m, 6 H, Ar), 7.05–7.27 (m, 20 H, Ar), 7.59 (m, 2 H, Ar) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 20.8 (d, $J_{C,P}$ = 9.2 Hz, CH_3), 54.7 (d, $J_{C,P}$ = 4.6 Hz, CH), 58.1 (d, $J_{C,P}$ = 40.9 Hz, CH), 120.2 (dd, $J_{C,P}$ = 1.3, $J_{C,P}$ = 11.7 Hz, CH, Ar), 120.4 (d, $J_{C,P}$ = 6.4 Hz, C_q, Ar), 120.6 (d, $J_{C,P}$ = 3.4 Hz, CH, Ar), 121.9 (CH, Ar), 123.57 (CH, Ar), 123.61 (CH, Ar), 126.2 (CH, Ar), 126.6 (CH, Ar), 127.0 (CH, Ar), 127.30 (CH, Ar), 127.32 (CH, Ar), 127.8 (2 × CH, Ar), 128.0 (2 × CH, Ar), 128.21 (CH, Ar), 128.26 (CH, Ar), 128.33 (2 × CH, Ar), 128.39 (CH, Ar), 128.41 (CH, Ar), 128.45 (CH, Ar), 128.8 (3 × CH, Ar), 129.0 (C_q, Ar), 129.6 (C_q, Ar), 129.9 (CH, Ar), 130.8 (C_q, Ar), 133.82 (CH, Ar), 133.86 (CH, Ar), 133.95 (CH, Ar), 134.02 (CH, Ar), 134.06 (CH, Ar), 137.0 (d, $J_{C,P}$ = 12.2 Hz, C_q, Ar), 137.1 (d, $J_{C,P}$ = 12.4 Hz, C_q, Ar), 141.5 (d, $J_{C,P}$ = 6.2 Hz, C_q, Ar), 141.9 (C_q, Ar), 147.7 (d, $J_{C,P}$ = 9.0 Hz, C_q, Ar), 155.8 (dd, $J_{C,P}$ = 8.0, $J_{C,P}$ = 18.8 Hz, C_q, Ar) ppm. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ = –17.0 (d, $J_{P,P}$ = 19.3 Hz), 131.5 (d, $J_{P,P}$ = 19.3 Hz) ppm. EI-MS: *m/z* (%) = 294.1 (10), 279.1 (22), 278.1 (100), 277.1 (46), 232.1 (12), 231.1 (33), 200.1 (13), 199.1 (58), 183.1 (38), 152.1 (12), 149.1 (15), 107.1 (12), 106.1 (93), 105.1 (32), 92.1 (31), 91.1 (45), 79.1 (19), 78.1 (12), 77.1 (27), 74.1 (10). HRMS (ESI): calcd. for $C_{43}H_{36}NO_2P_2^+$ $[M + H]^+$ 660.22158; found 660.22207. $[\alpha]_D^{25}$ = –50.5 (c = 0.5, CH_2Cl_2).

(1*R*,3*S*)-3-[2-(Diphenylphosphanyl)phenoxy]-1-phenyl-2-[(*R*)-1-phenylethyl]-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3,2]oxazaphosphinine [(R_C,R_C,S_P)-L10]: *Method B* in Scheme 1. To a solution of phosphorus trichloride (357 µL, 4.08 mmol, 1.02 equiv.) in CH_2Cl_2 (8 mL) was added triethylamine (1.12 mL, 8.0 mmol, 2.0 equiv.), and the solution was cooled to 0 °C. A solution of 2-(diphenylphosphanyl)phenol (1.113 g, 4.0 mmol, 1.0 equiv.) in CH_2Cl_2 (12 mL) was added dropwise within 5 min, and the mixture was stirred for 30 min at 0 °C and overnight at room temperature. The solution was cooled to 0 °C, and a solution of 1-((*R*)-phenyl{[(*R*)-1-phenylethyl]amino}methyl)naphthalen-2-ol (1.386 g, 3.92 mmol, 0.98 equiv.) and triethylamine (1.68 mL, 12.0 mmol, 3.0 equiv.) in CH_2Cl_2 (10 mL) was added dropwise within 30 min. The mixture was stirred for 30 min at 0 °C and 16 h at room temperature. Toluene (2 mL) was added, and all volatiles were removed at high vacuum. The residue was redissolved in toluene (12 mL) and the suspension filtered through a PTFE membrane and basic alumina consecutively. After elution with THF (10 mL) all volatiles were removed under reduced pressure to give a colorless solid. The residue was recrystallized from toluene/ethanol. The precipitate was collected, washed with small amounts of ethanol, and dried to yield the product as a colorless solid. Yield: 683.4 mg (1.04 mmol, 26 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3), 4.33 (dq, $^3J_{H,H}$ = 6.8, $^3J_{H,P}$ = 18.5 Hz, 1 H, CH), 5.58 (s, 1 H, CH), 6.50 (m, 1 H, Ar), 6.80 (m, 5 H, Ar), 7.02–7.42 (m, 21 H, Ar), 7.55 (d, $^3J_{H,H}$ = 8.7 Hz, 1 H, Ar), 7.65 (m, 2 H, Ar) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 18.9 (dd, $J_{C,P}$ = 6.4, $J_{C,P}$ = 4.7 Hz, CH_3), 55.0 (d, $J_{C,P}$ = 27.7 Hz, CH), 56.6 (d, $J_{C,P}$ = 5.4 Hz, CH), 117.7 (d, $J_{C,P}$ = 14.4 Hz, CH, Ar), 120.4 (CH, Ar), 121.6 (d, $J_{C,P}$ = 8.1 Hz, C_q, Ar), 122.5 (CH, Ar), 122.8 (CH, Ar), 124.0 (CH, Ar), 126.1 (CH, Ar), 127.1 (CH, Ar), 127.2 (CH, Ar), 127.66 (CH, Ar), 127.73 (CH, Ar), 127.93 (CH, Ar), 128.04 (2 × CH, Ar), 128.22 (2 × CH, Ar), 128.25 (CH, Ar), 128.27 (2 × CH, Ar), 128.31 (CH, Ar), 128.48 (CH, Ar), 128.59 (3 × CH, Ar), 128.60 (C_q, Ar), 129.2 (CH, Ar), 129.9 (CH, Ar), 130.5 (C_q, Ar), 130.8 (C_q, Ar), 132.9 (CH, Ar), 133.1 (CH, Ar), 133.4 (CH, Ar), 134.1 (CH, Ar), 134.3 (CH, Ar), 136.0 (d, $J_{C,P}$ = 11.5 Hz, C_q, Ar), 137.0 (d, $J_{C,P}$ = 12.1 Hz, C_q, Ar), 141.1 (d, $J_{C,P}$ = 5.2 Hz, C_q, Ar), 143.5 (d, $J_{C,P}$ = 2.2 Hz, C_q, Ar), 144.2 (d, $J_{C,P}$ = 2.8 Hz, C_q, Ar), 155.7 (dd, $J_{C,P}$ = 17.3, $J_{C,P}$ = 4.8 Hz, C_q, Ar) ppm. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ = –15.5 (d, $J_{P,P}$ = 6.1 Hz), 112.1 (d, $J_{P,P}$ = 6.1 Hz) ppm. EI-MS: *m/z* (%) = 555.2 (34), 554.1 (100), 540.1 (14), 278.0 (36), 276.0 (18), 199.0 (10), 105.1 (34). HRMS (ESI): calcd. for $C_{43}H_{36}NO_2P_2^+$ $[M + H]^+$ 660.22158; found 660.22218. $[\alpha]_D^{25}$ = –240.4 (c = 0.5, CH_2Cl_2).

(1*S*,3*S*)-3-[2-(Diphenylphosphanyl)phenoxy]-1-phenyl-2-[(*R*)-1-phenylethyl]-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3,2]oxazaphosphinine [(R_C,S_C,S_P)-L10]: *Method A* in Scheme 1. 1-((*S*)-Phenyl{[(*R*)-1-phenylethyl]amino}methyl)naphthalen-2-ol (706.9 mg, 2.0 mmol, 1.0 equiv.) was dissolved in THF (10 mL) and the solution cooled to –78 °C. Afterwards *n*-butyllithium (1.6 M in hexanes, 2.53 mL, 4.04 mmol, 2.02 equiv.) was added dropwise within 15 min, and the mixture was stirred for 1 h at –78 °C and 1 h at room temperature. The solution was cooled again to –78 °C, and a solution of phosphorus trichloride (175 µL, 2.0 mmol, 1.0 equiv.) in THF (6 mL) was added dropwise within 15 min. The mixture was stirred for 1 h at –78 °C and another 1.5 h at room temperature. In another Schlenk flask 2-(diphenylphosphanyl)phenol (545.4 mg, 1.96 mmol, 0.98 equiv.) was dissolved in THF (10 mL), and TMEDA (300 µL, 2.0 mmol, 1.0 equiv.) was added. The solution was cooled to –78 °C, and *n*-butyllithium (1.6 M in hexanes, 1.25 mL, 2.0 mmol, 1.0 equiv.) was added dropwise within 15 min. The mixture was stirred for 1 h at –78 °C and 1 h at 0 °C. The solution was cooled again to –78 °C, and the solution of the phosphoramidochloridite (R_C,S_C,R_P)-**2** was added dropwise within 15 min. The mixture was stirred for 2 h at –78 °C and then allowed to reach room temperature overnight. All volatiles were removed at high vacuum, and the residue was redissolved in THF (10 mL) and filtered through basic alumina. After elution with THF (10 mL), all volatiles were removed under reduced pressure to give a colorless solid. The residue was recrystallized from toluene/ethanol. The precipitate was collected, washed with small amounts of ethanol, and dried to yield the product as a colorless solid. Yield: 287.0 mg (0.44 mmol, 22 %). ^{1}H NMR (400 MHz,

$CDCl_3$): δ = 1.33 (dd, $^3J_{H,H}$ = 6.8, $J_{H,P}$ = 4.3 Hz, 3 H, CH_3), 4.66 (dq, $^3J_{H,H}$ = 6.8, $^3J_{H,P}$ = 6.6 Hz, 1 H, CH), 5.40 (d, $^3J_{H,P}$ = 6.3 Hz, 1 H, CH), 6.63 (ddd, *J* = 7.5, *J* = 3.7, *J* = 1.5 Hz, 1 H, Ar), 6.67 (dd, *J* = 7.9, *J* = 4.5 Hz, 1 H, Ar), 6.82–6.97 (m, 6 H, Ar), 7.04–7.26 (m, 18 H, Ar), 7.33 (d, *J* = 7.4 Hz, 2 H, Ar), 7.62 (d, *J* = 7.8 Hz, 1 H, Ar), 7.64 (d, *J* = 8.8 Hz, 1 H, Ar) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 23.2 (d, $J_{C,P}$ = 28.7 Hz, CH_3), 55.5 (d, $J_{C,P}$ = 4.2 Hz, CH), 58.4 (d, $J_{C,P}$ = 30.4 Hz, CH), 117.1 (d, $J_{C,P}$ = 6.3 Hz, C_q, Ar), 119.9 (dd, $J_{C,P}$ = 1.4, 10.6 Hz, CH, Ar), 120.6 (d, $J_{C,P}$ = 3.3 Hz, CH, Ar), 122.8 (CH, Ar), 123.5 (CH, Ar), 123.6 (CH, Ar), 126.2 (CH, Ar), 126.8 (CH, Ar), 127.0 (2 × CH, Ar), 127.4 (CH, Ar), 127.9 (2 × CH, Ar), 128.17 (CH, Ar), 128.24 (CH, Ar), 128.27 (CH, Ar), 128.34 (3 × CH, Ar), 128.46 (CH, Ar), 128.8 (2 × CH, Ar), 129.2 (CH, Ar), 129.5 (2 × CH, Ar), 129.9 (CH, Ar), 130.0 (C_q, Ar), 130.1 (d, $J_{C,P}$ = 13.6 Hz, C_q, Ar), 131.0 (C_q, Ar), 133.8 (CH, Ar), 133.9 (2 × CH, Ar), 134.0 (CH, Ar), 134.1 (CH, Ar), 136.9 (d, $J_{C,P}$ = 6.9 Hz, C_q, Ar), 137.0 (d, $J_{C,P}$ = 6.5 Hz, C_q, Ar), 141.1 (C_q, Ar), 143.7 (d, $J_{C,P}$ = 5.9 Hz, C_q, Ar), 147.0 (d, $J_{C,P}$ = 8.1 Hz, C_q, Ar), 155.7 (dd, $J_{C,P}$ = 18.6, $J_{C,P}$ = 7.4 Hz, C_q, Ar) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = –17.6 (d, $J_{P,P}$ = 19.1 Hz), 120.6 (d, $J_{P,P}$ = 19.1 Hz) ppm. EI-MS: *m/z* (%) = 554.1 (10), 356.1 (10), 350.1 (13), 322.1 (11), 294.1 (23), 279.1 (25), 278.1 (100), 277.1 (42), 231.1 (16), 218.1 (13), 200.1 (14), 199.1 (48), 183.1 (35), 167.1 (11), 152.1 (11), 149.1 (24), 106.1 (13), 105.1 (46), 77.1 (10). HRMS (ESI): calcd. for $C_{43}H_{36}NO_2P_2^+$ $[M + H]^+$ 660.22158; found 660.22234. $[\alpha]_D^{25}$ = 2.3 (*c* = 0.5, CH_2Cl_2).

{Rh(cod)[(R_C,R_C,S_P)-L10]}BF_4 (9): To a solution of [Rh(cod)(acac)] (24.8 mg, 80.0 µmol, 1.0 equiv.) in THF (4 mL) was added a solution of HBF_4-etherate (54 %, 20.6 µL, 81.6 µmol, 1.02 equiv.), and then the reaction mixture was stirred for 20 min at room temperature. A solution of (R_C,R_C,S_P)-**L10** (53.8 mg, 81.6 µmol, 1.02 equiv.) in THF (2 mL) was added, and the solution stirred for 1 h at room temperature. All volatiles were removed under reduced pressure, and the residue was redissolved in THF (0.8 mL). Under vigorous stirring the solution was added dropwise to *n*-pentane (30 mL), leading to a yellow precipitate. The supernatant was decanted and the yellow solid washed with *n*-pentane (2 × 10 mL) and diethyl ether (2 × 10 mL). The solid was dried at high vacuum to yield the desired Rh complex as yellow-orange powder. Yield: 68.2 mg (71.2 µmol, 89 %). ^1H NMR (300 MHz, CD_2Cl_2): δ = 1.42 (d, $^3J_{H,H}$ = 7.1 Hz, 3 H, CH_3), 2.07–2.51 (m, 4 H, CH_2), 2.60–2.98 (m, 4 H, CH_2), 4.84 (m, 1 H, CH), 5.00 (dq, $^3J_{H,H}$ = 7.1, $^3J_{H,P}$ = 13.7 Hz, 1 H, CH), 5.20 (m, 1 H, CH), 5.71 (d, $^3J_{H,P}$ = 6.8 Hz, 1 H, CH), 5.82 (m, 1 H, CH), 6.36 (m, 1 H, CH, 1 H, Ar), 6.93 (d, *J* = 7.5 Hz, 2 H, Ar), 7.07–7.64 (m, 25 H, Ar), 7.83 (m, 1 H, Ar), 7.88 (d, *J* = 8.9 Hz, 1 H, Ar) ppm. $^{31}P\{^1H\}$ NMR (121 MHz, CD_2Cl_2): δ = 16.5 (dd, $J_{P,P}$ = 50.0, $J_{P,Rh}$ = 140.0 Hz), 121.7 (dd, $J_{P,P}$ = 50.0, $J_{P,Rh}$ = 255.7 Hz) ppm. HRMS (ESI pos.): calcd. for $C_{51}H_{47}NO_2P_2Rh^+$ $[M - BF_4]^+$ 870.21316; found 870.21375.

General Procedure for the Catalytic Hydrogenation of Dimethyl Itaconate Using in Situ Generated Catalysts: To a solution of $[Rh(cod)_2]BF_4$ (1.22 mg, 3.0 µmol, 1.0 equiv.) in CH_2Cl_2 (1 mL) was added a solution of the ligand (3.15 µmol, 1.05 equiv.) in CH_2Cl_2 (1 mL). The mixture was stirred for 30 min at room temperature and then transferred into a 10 mL stainless steel autoclave, equipped with a glass inlet, magnetic stirring bar, and dimethyl itaconate (474.5 mg, 3.0 mmol, 1000 equiv.), under an argon atmosphere. The autoclave was pressurized with hydrogen and the mixture stirred for 1 h at room temperature. After carefully releasing the pressure, the reaction mixture was filtered through a short plug of silica and analyzed by NMR and chiral GC.

General Procedure for the Catalytic Hydrogenation of C–C Double Bonds Using Isolated Rh Complex 9: A solution of **9** in CH_2Cl_2 or MeOH (1 mL, 1.5 mM, 1.5 µmol) was transferred into a 10 mL stainless steel autoclave, equipped with a glass inlet, magnetic stirring bar, and the respective substrate (1.5 mmol, 1000 equiv.), under an argon atmosphere. The autoclave was pressurized with hydrogen and the mixture stirred for the indicated time at room temperature. Further details and modifications of the conditions are given in Figure 3. After carefully releasing the pressure, the reaction mixture was analyzed by NMR spectroscopy. A small sample was filtered through a short plug of silica and analyzed by chiral GC or HPLC. The absolute configuration of the hydrogenation products was assigned by comparison of the sign of optical rotation with those reported in the literature.

NMR spectra of **L10** and **9** as well as the characterization of the hydrogenation products can be found in the Supporting Information.

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