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A new hydroxydiphosphine as a ligand for Rh(I)-catalyzed enantioselective hydrogenation

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Abstract—A new diphosphine ligand bearing a hydroxy group in the backbone was synthesized starting from 9-bromocamphor. The rhodium(I) complex based on this ligand was tested in the hydrogenation of α- and β-amino acid precursors. The activity and selectivity of the catalyst were found to be strongly dependent upon the nature of the substrate. Thus, β-acetylamino carboxylates were obtained with up to 97% ee. © 2002 Published by Elsevier Science Ltd.

1. Introduction

We have focused our research on the synthesis and application of chiral hydroxydiphosphine ligands in the rhodium(I)-catalyzed enantioselective hydrogenation for several years.[1] In these studies, we and other researchers have provided several pieces of evidence that the hydroxy group can actively participate in the catalytic process.[2] Thus, the additional functional group may significantly affect the activity and selectivity of these catalysts, even in cases where the hydroxy group was found to be remote from the metal in the relevant precatalysts.[3] This and other observations gave proof that the hydroxy group if appropriately placed in the catalyst can change the electronic and steric properties of the metal center and the substrate, well-known in enzyme catalysis as 'induced fit'.[4]

Herein, we describe a new hydroxy-substituted diphosphine and its performance in the enantioselective hydrogenation of functionalized olefins of pharmaceutical relevance. Our approach for the synthesis of the ligand takes advantage of the availability of the 'chiral pool' material (*R*)-camphor **1**. Simple protocols for the conversion of camphor to a variety of related bromo-substituted derivatives, originally developed by Money,[5] make this natural terpenoid attractive for the synthesis of functionalized diphosphines.[6] One of the most easily available bromosubstituted camphor derivatives, apart from the commercially available 3-bromocamphor **2**, is 9-bromocamphor **4** which can be derived from camphor by a simple three-step protocol via bromides **2** and **3** on large scale (Scheme 1).[5,7]

Subsequent oxidation of **4**, first using SeO_2 to form the 'quinone' **5**, followed by H_2O_2 gave the anhydride **6** in high yield. The latter was reduced with $LiAlH_4$ to give diol **8**. Compound **8** was also obtained from **4** using a Baeyer–Villiger rearrangement–$LiAlH_4$ reduction sequence. The rearrangement proceeded in the presence of the *p*-toluenesulfonic acid with the preferential formation of the desired lactone **7**.

We analyzed the enantiomeric purity of diol **8** by HPLC on a chiral stationary phase. It was found to be enantiomerically pure within experimental errors of the technique (>98% ee). In parallel, the enantiomer, (*R*)-**8**, was prepared starting from (*S*)-camphor. Surprisingly, the enantiomeric purity of (*R*)-**8** was also >98% ee, though the starting material, (*S*)-camphor, is known to be of relatively low enantiomeric purity (78.6–92.8% ee).[8] Obviously, this is the result of several recrystallizations of the intermediates throughout the synthesis.

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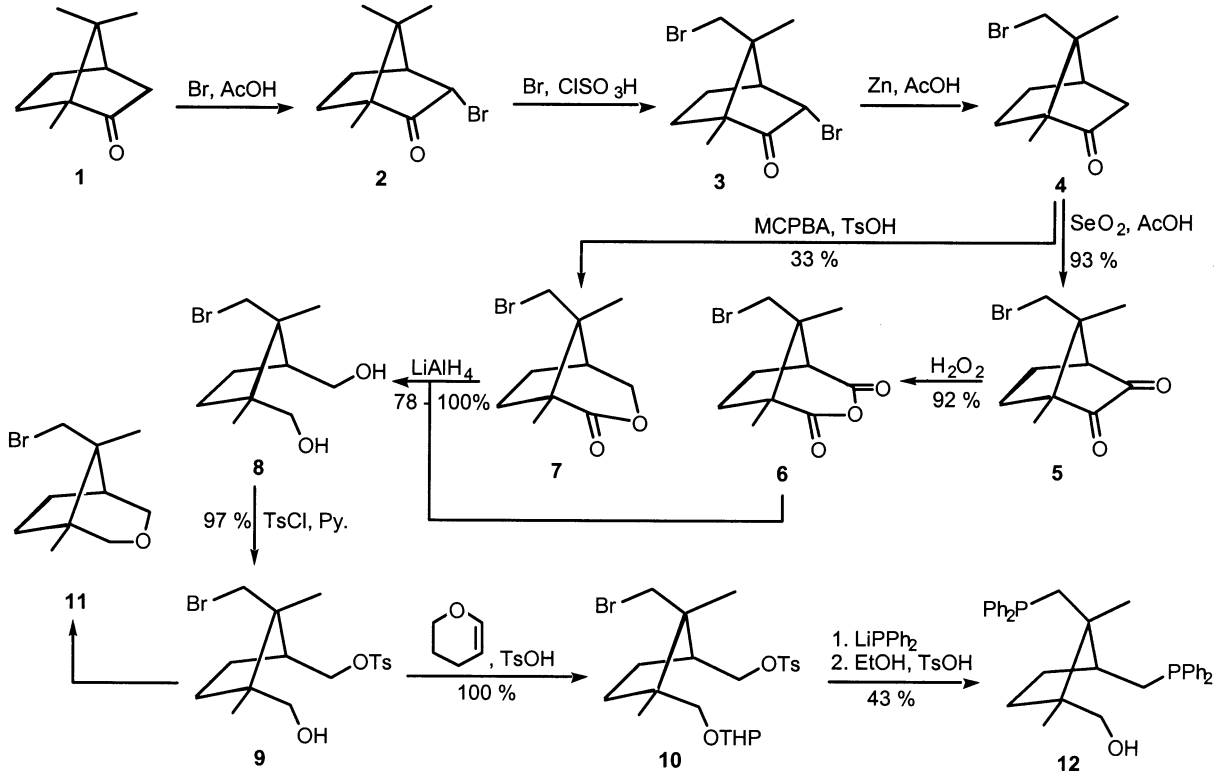


Scheme 1.

The diol **8** was selectively esterified at the less hindered OH group with TsCl to give the tosylate **9**. Subsequently, the remaining hydroxy group in **9** was protected as the THP–acetal **10**. Protection of the HO-group was necessary to avoid undesired cyclization of **9** that readily proceeds under basic conditions to yield the bicyclic ether **11**. Nucleophilic substitution of the tosylate group in **10** by Ph_2PLi followed by deprotection gave the target hydroxydiphosphine **12**. This ligand can form a seven-membered chelate ring upon coordination with a transition metal. It possesses no symmetry elements (C_1-symmetry group) and a hydroxy group on a conformationally flexible arm remote from the diphenylphosphine moiety.

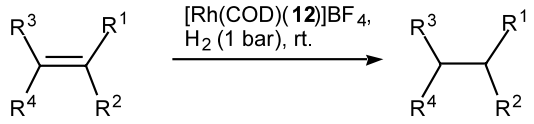
2. Synthesis and characterization of the precatalyst

The precatalyst [Rh(**12**)(COD)]BF_4 was synthesized by reaction of [Rh(COD)acac] with diphosphine **12** in THF and subsequent addition of HBF_4. The complex was precipitated from the mixture as a yellow powder by the addition of ether. Due to the presence of residual THF and ether the complex had no satisfactory microanalytical data, but was fully characterized by its spectroscopic data. The ^{31}P NMR spectrum contained two double doublets at δ 22.3 and 16.7 ($J_{PP}=41.6$, J_{P-Rh} 144.3 Hz). Such chemical shifts and coupling constants are characteristic of Rh(I) complexes bearing diphosphine ligands with C_1-symmetry.[9] In the ^{13}C NMR spectrum, the methine carbons of the COD ligands gave resonances between δ 96–106, which is indicative of their *trans*-relationship to the π-accepting phosphorus atoms. These NMR data allowed us to exclude structures with the OH group coordinated to the metal center, as this coordination would lead to significant changes in the ^{31}P and ^{13}C NMR spectra of the ligand.[10] Molecular modelling of the complex showed that such coordination is prevented by the 2-CH_3 group which acts as a barrier, meaning that coordination of the OH group to the metal center would lead to significant steric congestion.

3. Enantioselective hydrogenation

The complex [Rh(**12**)(COD)]BF_4 was used as a precatalyst in the hydrogenation of different prochiral substrates. The results are listed in the Table 1. As clearly to be seen activity and enantioselectivity of the catalyst are highly dependent on the nature of the substrate. The enantioselectivities range from 9% ee for the 'standard' substrate itaconic acid **16** to 97% ee for (*E*)-methyl-3-acetylaminocrotonate **17**.[11] The high activity observed in the hydrogenation of standard substrates indicates that, in accordance with the conclusion derived from the analysis of the ^{31}P NMR spectrum of the precatalyst, there is no interaction between the hydroxy group and the metal in catalytically relevant intermediates.[10] The new catalyst is also suitable for the hydrogenation of β-amino acid precursors **17**–**20**. In the hydrogenation of the latter, the enantioselectivity for the (*E*)-isomers was good, but is only moderate for the (*Z*)-isomers.

Table 1. Hydrogenation results of prochiral substrates **13**–**22** with Rh[(**12**)(COD)]BF_4[a]



	Substrate				Solvent	Time	Con. (%)	ee (%)
No.	R_1	R_2	R_3	R_4				
13	COOMe	NHAc	H	Ph	MeOH	1.5 min	100	11 (*S*)
					CH_2Cl_2	5 min	100	24 (*S*)
14	COOH	NHAc	H	Ph	MeOH	1.5 min	100	57 (*S*)
					CH_2Cl_2	8 min	100	49 (*S*)
15	CH_2COOMe	COOMe	H	H	MeOH	6 min	100	70 (*S*)
					CH_2Cl_2	3.5 min	100	75 (*S*)
16	CH_2COOH	COOH	H	H	MeOH	1.5 min	100	9 (*S*)
					CH_2Cl_2	300 min	62	10 (*S*)
17	COOMe	H	CH_3	NHAc	MeOH	40 min	100	93 (*R*)
					CH_2Cl_2	12 min	100	95 (*R*)
					Toluene	300 min	98	97 (*R*)
18	COOMe	H	NHAc	CH_3	MeOH	20 min	100	46 (*R*)
					CH_2Cl_2	45 min	72	58 (*R*)
					toluene	700 min	7	50 (*R*)
19	COOH	H	CH_3	NHAc	MeOH	120 min	82	81 (*R*)
					CH_2Cl_2	>24 h	54	82 (*R*)
20	COOH	H	NHAc	CH_3	MeOH	13 h	53	54 (*R*)
					CH_2Cl_2	>24 h	8	12 (*R*)

[a] Conditions for the hydrogenation: molar catalyst–substrate ratio 1:100, 1 bar H_2, 25°C.

In general, the difference in enantioselectivity observed in the hydrogenation of carboxylic acids and their corresponding esters is notable. For example, itaconic acid **16** was reduced with poor enantioselectivity whereas its methyl ester **15** was obtained with good ee, irrespective of the solvent used. In contrast, the hydrogenation of (*Z*)-2-acetamidocinnamic acid **14** was superior than the reaction with its methyl ester **13** as substrate. A clear dependence of the enantioselectivity and the rates of the hydrogenation on the solvent polarity was noted. In most cases the enantioselectivities were higher in solvents with low polarity (CH_2Cl_2, toluene), than in methanol. The rate followed an opposite tendency.

In summary, a new chiral hydroxyphosphine has been synthesised starting from (*R*)-camphor. Its utility as a ligand in the Rh(I)-catalysed asymmetric hydrogenation of α- and β-acetyl dehydroamino acids has been demonstrated. Remarkable differences were noted when carboxylic acids or their esters were used as substrates. Work is now in progress in order to elucidate the reasons for this observation.

4. Experimental

4.1. General

All reagents were obtained from Aldrich and Merck. Solvents were dried and freshly distilled under argon before use. Reactions using phosphines and organometallic compounds were performed under an Ar atmosphere by using standard Schlenk techniques. Thin-layer chromatography was performed on precoated TLC plates (silica gel 60 F_{254}, Merck). Flash chromatography was carried out with silica gel 60 (particle size 0.040–0.063 mm, Merck). Melting points are not corrected. NMR spectra were recorded at the following frequencies: 400.13 MHz (^{1}H), 100.63 MHz (^{13}C), 161.98 MHz (^{31}P). Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in ppm downfield from TMS as internal standard. Chemical shifts of ^{31}P NMR spectra are referred to H_3PO_4 as external standard. Elemental analyses were performed with a LEGO CHNS-932.

Hydrogenation experiments were carried out under normal pressure and isobaric conditions with an automatically registering gas measuring device (1.0 atm overall pressure over the solution). The experiments were performed in 15.0 mL of solvent at 25.0°C. The conversion of the dehydroamino acids as well as the enantioselectivity of the products were determined by GC. The acids were esterified with trimethylsilyldiazomethane before the GC-measurements: FID, Carrier gas: Ar: 1 mL/min; methyl *N*-acetylphenylalaninate: fused silica, 10 m, XE-60-L-valin-*tert*-butylamide, ID 0.2 mm; oven temperature: 150°C; dimethyl methylsuccinate: fused silica, Lipodex E (Machery and Nagel), 25 m, ID 0.25 mm, oven temperature: 85°C; methyl 3-*N*-acetylamino butanoate: Chiraldex β-PM 50 m×0.25 mm (astec), 130°C. The enantiomeric purity of **8** and its enantiomer was determined using HPLC on a chiral stationary phase (Chiralpack AD; eluent hexane:*iso*-PrOH = 9:1).

4.2. (1*R*,7*R*)-7-(Bromomethyl)-1,7-dimethylbicyclo-[2.2.1]heptane-2,3-dione, 5

A solution of (+)-9-bromocamphor[7] (20 g, 86.5 mmol) and SeO_2 (freshly sublimed, 20 g, 180.2 mmol; toxic—all operations were carried out in a good fumecupboard) in AcOH (150 mL) was heated under reflux under stirring for 12 h (the reaction was followed by TLC, EtOAc–benzene, 8:1, $R_f = 0.76$). After cooling to room temperature, the mixture was filtered through Celite. The Celite pad was washed with methanol. The volatile products were removed on a rotary evaporator (fumehood!). The residue was mixed with Et_2O (200 mL), washed with water (2×50 mL), saturated $NaHCO_3$ solution (100 mL), water (2×50 mL), and dried over Na_2SO_4. Diethyl ether was distilled off and the product was recrystallized from heptane. Yellow crystals (19.69 g, 80.3 mmol, 93% yield), mp 123–124°C (subl.). $[\alpha]_D^{30} = +77.5$ (*c* 0.0213, MeOH). Anal. calcd for $C_{10}H_{13}BrO_2$: C, 49.00; H, 5.35. Found: C, 49.29; H, 5.37%. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 3.62 (dd, $J = 10.7$ and 0.8 Hz, 1H), 3.30 (d, $J = 10.7$ Hz, 1H), (7-CH_2Br); 3.01 (d, $J = 5.2$ Hz, 1H) (4-H); 2.10–2.20 (m, 1H), 1.90–2.00 (m, 1H), 1.65–1.75 (m, 2H), (5-CH_2, 6-CH_2); 1.17 (s, 3H), (1-CH_3); 1.10 (d, $J = 0.8$ Hz, 3H), (7-CH_3). ^{13}C NMR (100.63 MHz, $CDCl_3$) δ: 203.30 (C=O), 201.61 (C=O), 59.73 (C), 56.40 (CH), 47.49 (C), 35.90 (CH_2), 29.25 (CH_2), 22.26 (CH_2), 18.16 (CH_3), 9.58 (CH_3).

4.3. (1*R*,8*R*)-8-(Bromomethyl)-1,8-dimethyl-3-oxabicyclo[3.2.1]octane-2,4-dione, 6

Hydrogen peroxide (30% solution in water, 50 mL) was added to a yellow solution of (1*R*,7*R*)-7-(bromomethyl) - 1,7 - dimethylbicyclo[2.2.1]heptane - 2,3 - dione **5** (10 g, 40.8 mmol) in AcOH (250 mL) under stirring. The mixture was stirred at room temperature till it became colourless (approx. 3.6 h). Then it was poured into water (1 L). The white solid product was collected by filtration, washed with water and air-dried. It was sufficiently pure to be used directly in the next step. An analytical sample was prepared by recrystallization from diethyl ether. White crystals (9.75 g, 37.3 mmol, 92% yield), mp 152–153°C (subl.). $[\alpha]_D^{30} = +365$ (*c* 7.25×10^{-3}, MeOH). Anal. calcd for $C_{10}H_{13}BrO_3$: C, 46.00; H, 5.02. Found: C, 46.16; H, 5.03%. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 3.37 (d, $J = 8$ Hz, 1H), (5-H); 3.31 (ABq, $J = 10.7$ Hz, 2H), (8-CH_2Br); 2.10–2.25 (m, 2H), 1.95–2.05 (m, 2H), (6-CH_2, 7-CH_2); 1.28 (s, 3H), (CH_3); 1.19 (s, 3H), (CH_3). ^{13}C NMR (100.63 MHz, $CDCl_3$) δ: 171.7 (C=O), 169.3 (C=O), 53.9 (C), 51.7 (CH), 47.8 (C), 36.9 (CH_2), 33.4 (CH_2), 24.3 (CH_2), 17.3 (CH_3), 14.3 (CH_3).

4.4. (1*R*,5*R*,8*R*)-8-(Bromomethyl)-1,8-dimethyl-3-oxabicyclo[3.2.1]octan-2-one, 7

A solution of (+)-9-bromocamphor (1 g, 4.3 mmol), *m*-chloroperbenzoic acid (MCPBA) (1.12 g, 6.5 mmol) and *p*-toluenesulfonic acid (0.1 g) in CH_2Cl_2 (40 mL) was heated under reflux for 4 days. Each day an additional portion of MCPBA (~40 mg) was added. The mixture was diluted with ether (100 mL), washed with sat. $NaHCO_3$, 10% aqu. Na_2SO_3, again with sat. $NaHCO_3$ and finally with water (2×50 mL). The ether solution was dried (Na_2SO_4) and evaporated. The isomeric lactones (2:1 ratio of **7** to its regioisomer according to the ^{1}H NMR of the crude mixture) were separated by a flash chromatography (eluent: $CHCl_3$), to give the desired product **7** (0.35 g, 33% yield, mp 132–133°C, $[\alpha]_D^{30} = +7.4$, *c* 9.85×10^{-3}, MeOH), then its isomer. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 4.41 (ddd, $J = 11.1$, 3.2 and 1.4 Hz, 1H) (4-H_{exo}); 4.15 (d, $J = 11.1$ Hz, 1H) (4-H_{endo}); 3.39 (dq, $J = 10.3$ and 1.2 Hz, 1H), 3.25 (d, $J = 10.3$ Hz, 1H) (CH_2Br); 2.46 (dd, $J = 6.7$ and 3.2 Hz, 1H) (5-H); 2.08 (m 2H) (6-CH_2); 1.95 (m, 2H) (7-CH_2); 1.18 (d, $J = 1.2$ Hz, 3H) (8-CH_3); 1.16 (s, 3H) (1-CH_3). ^{13}C NMR (100.63 MHz, $CDCl_3$) δ: 175.9 (C=O), 74.4 (CH_2O), 54.0 (C), 47.0 (C), 41.2 (CH), 40.4 (CH_2), 35.9 (CH_2), 26.7 (CH_2), 17.1 (CH_3), 14.4 (CH_3).

4.5. (1*R*,2*R*,3*S*)-(2-Bromomethyl-3-hydroxymethyl-2,3-dimethylcyclopentyl)methanol, 8

Method A. Lithium aluminium hydride (3 g, 79 mmol) was cautiously added in small portions to a suspension of (1*R*,8*R*)-8-(bromomethyl)-1,8-dimethyl-3-oxabicyclo[3.2.1]octane-2,4-dione **6** (5 g, 19.1 mmol) in diethyl ether (200 ml) under stirring. The mixture was heated under reflux for 1 h, diluted with THF (150 ml) and cooled in an ice bath. Under vigorous stirring and cooling, water was carefully added to quench the excess lithium aluminium hydride. The white precipitate of hydroxides was filtered off and washed on the filter several times with THF. The filtrate was evaporated, dissolved in a CH_2Cl_2–MeOH (9:1) mixture, and filtered through a small column packed with SiO_2 (approx. 100 g). The eluate containing the product ($R_f = 0.41$) was collected, evaporated, and used for the next step. An analytical sample was prepared by crystallization from $CHCl_3$. White crystals (3.72 g, 14.8 mmol, 78% yield), mp 116–117°C, $[\alpha]_D^{30} = +33.4$ (*c* 1.0, MeOH). The enantiomeric purity was confirmed by HPLC, where the opposite enantiomer was not detected. The enantiomer was prepared starting from (*S*)-camphor. Also in this case the other enantiomer was not detected.

Method B. The bromolactone **7** (150 mg, 0.61 mmol) was dissolved in ether (10 mL), and $LiAlH_4$ was added cautiously (46.1 mg, 1.22 mmol) under stirring. The mixture was stirred for 15 min. at ambient temperature. The excess lithium aluminium hydride was quenched with water, the precipitate filtered off and washed several times with ether. The filtrate and washings combined were dried (Na_2SO_4) and evaporated. The product (153.2 mg, 100% yield) was sufficiently pure to be used in the next step. Anal. calcd for $C_{10}H_{19}BrO_2$: C, 47.82; H, 7.62. Found: C, 47.56; H, 7.40. ^{1}H NMR (400.13 MHz, CD_3OD) δ: 3.48–3.65 (m, 4H), 3.22–3.33 (m, 4H), (CH_2O, CH_2O, CH_2Br); 2.08 (m, 1H), (1-H); 1.75–1.86 (m, 1H), 1.60–1.70 (m, 1H), 1.26–1.38 (m, 2H), (4-CH_2, 5-CH_2); 0.97 (s, 3H), (CH_3); 0.88 (s, 3H), (CH_3). ^{13}C NMR (100.63 MHz, CD_3OD) δ: 69.31 (CH_2OH), 65.30 (CH_2OH), 52.4 (C), 51.10 (CH), 49.5 (C, overlapped with the solvent residue signal), 45.50

(CH_2Br), 36.15 (CH_2), 27.35 (CH_2), 20.39 (CH_3), 16.36 (CH_3).

4.6. [(1*R*,2*R*,3*S*)-2-(Bromomethyl)-3-(hydroxymethyl)-2,3-dimethylcyclopentyl]methyl-4-methylbenzene sulfonate, 9

4-Methylbenzenesulfonyl chloride (2.05 g, 10.7 mmol) was added within 15 min to a solution of (1*R*,2*R*,3*S*)-(2-bromomethyl-3-hydroxymethyl-2,3-dimethylcyclopentyl)methanol **8** (2.7 g, 10.7 mmol) in dry pyridine (10 mL) at −10°C under stirring. Then the mixture was stirred at −10°C for 45 min. Water (70 mL) was added, and the product was extracted with diethyl ether (150 ml). The ether layer was washed with water (50 ml), 5% HCl (50 mL), water (3×50 mL), and dried over Na_2SO_4. The solvent was evaporated (not raising the bath temperature higher than 40°C), and the residue was purified by column chromatography (eluent: CH_2Cl_2–MeOH, 18:1). The ditosylate and the cyclic ether **11** were eluted first, following by the desired product **9** (R_f=0.5). The latter being a colourless oil (2.96 g, 7.3 mmol, 69% yield) was immediately used for the next step. The non-converted diol **8** could finally be eluted by CH_2Cl_2–MeOH (9:1) (0.8 g). The yield of the product **9**, calculated taking into account the recovered starting diol was 97.2%. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.77 (d, J=8.4 Hz, 2H); 7.34 (d, J=8.4 Hz, 2H); 4.30 (d, J=9.4 Hz, 1H); 4.01 (d, J=9.4 Hz, 1H); 3.75 (dd, J=10.6 and 7.1 Hz, 1H); 3.67 (d, J=10.6 Hz, 1H); 3.58 (dd, J=10.6 and 7.1 Hz, 1H); 3.54 (d, J=10.6 Hz, 1H); 2.44 (s, 3H); 2.15 (m, 1H); 1.85 (m, 2H); 1.62 (m, 1H); 1.48 (m, 1H); 1.29 (m, 1H); 1.00 (s, 3H); 0.93 (s, 3H). ^{13}C NMR (100.63 MHz, $CDCl_3$) δ: 145.20 (C), 133.23 (C), 130.27 (CH), 128.35 (CH), 76.52 (CH_2O), 64.19 (CH_2O), 49.42 (CH, C), 48.97 (C), 43.16 (CH_2), 34.92 (CH_2), 25.40 (CH_2), 22.11 (CH_3), 19.86 (CH_3), 15.95 (CH_3).

4.7. [(1*R*,2*R*,3*S*)-2-(Bromomethyl)-2,3-(dimethyl)-3[(tetrahydro-2*H*-pyran-2-yloxy)methyl]cyclopentyl]-methyl-4-methylbenzenesulfonate, 10

Compound **9** (2.96 g, 7.3 mmol) was dissolved in CH_2Cl_2 (20 mL). 3,4-Dihydro-2*H*-pyran (1 mL, 10.95 mmol) and pyridinium *p*-toluenesulfonate (PPTS) were added. The mixture was stirred overnight at room temperature. Diethyl ether (100 ml) was added and the solution was washed with brine (50 mL) and water (50 mL). Then it was dried over Na_2SO_4, evaporated and dried in high vacuum at 40°C for 2 h. The viscous oil (3.57 g, 100% yield) was used in the next step without further purification. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.76 (two d, 2H); 7.33 (d, J=8.5 Hz, 2H); 4.5 (m, 2H); 4.28 (dd, 1H); 3.0–4.0 (m, 6H); 2.44 (s, 3H); 1.1–2.4 (m, 11H); 0.85–1.05 (m, 6H). ^{13}C NMR (100.63 MHz, $CDCl_3$) δ: 145.1/144.3, 136.1, 133.5, 130.3, 129.5, 128.4, 100.1/99.1, 73.9/73.3, 68.6/67.4, 62.9/63.3, 59.1, 50.1, 48.4, 47.1/46.6, 35.09, 31.0, 26.5, 25.8, 22.1, 20.7, 20.1, 19.7, 16.5

4.8. [(1*S*,2*S*,3*R*)-1,2-Dimethyl-2,3-bis(diphenylphosphinomethyl)cyclopentyl]methanol, 12

A solution of Ph_2PLi (prepared from Ph_2PCl (0.41 mL, 2.3 mmol) and Li (65 mg, 9.4 mmol) in 10 mL THF, stirring at room temperature, 1 h, reflux, 2 h) was added within 1 h to a solution of the *O*-protected tosylate **10** (0.46 g, 0.94 mmol) in THF (5 mL) at 0–5°C (ice bath) under stirring. The reaction mixture was stirred first at room temperature for 2 h, and then heated under reflux for 1.5 h. Water (20 mL) was added, and the product was extracted with diethyl ether (70 mL). The ether solution was washed twice with water, evaporated and dried in high vacuum at 50°C for 4 h. The residue was dissolved in ethanol (8 mL) and pyridinium *p*-toluenesulfonate (25 mg) was added. The solution was stirred at 55°C (bath temperature) for 2 days (TLC control, hexane–EtOAc, 1:1). The ethanol was removed in vacuum, and the residue (dissolved in acetone) was subjected to a flash chromatography. The product **12** was eluted with pentane–Et_2O (1:1), R_f=0.4. Viscous oil (210 mg, 43% yield). ^{1}H NMR (400.13 MHz, C_6D_6) δ: 7.75 (t, J=5.1 Hz, 2H), 7.58–7.62 (m, 4H), 7.57 (t, J=5.1 Hz, 2H), 6.95–7.10 (m, 12H), (arom. protons); 3.75 (d, J=10.9 Hz, 1H), 3.30 (d, J=10.9 Hz, 1H), (CH_2O); 3.48 (br. s, 1H), (OH); 3.12 (dq, J=13 and 3 Hz, 1H), 1.9–2.0 (m, 1H), (2-CH_2P); 2.63 (dd, J=14.9 and 3.4 Hz, 1H), 2.32 (dd, J=14.9 and 3.4 Hz, 1H), (3-CH_2P); 2.19–2.30 (m, 2H), (4-CH_2, 3-CH); 1.15–1.50 (m, 3H), (4-CH_2, 5-CH_2); 1.02 (s, 3H), (1-CH_3); 0.92 (s, 3H), (2-CH_3). ^{13}C NMR (100.63 MHz, C_6D_6) δ: 140–142, 133–134, 127–129 (m, arom.), 69.27 (s, O-CH_2), 50.33 (s, 1-C), 49.08 (t, J=7.62 Hz, 2-C), 47.86 (dd, J=13.4 and 4.8 Hz, 3-CH), 37.37 (d, J=16.2 Hz, P-CH_2), 34.92 (s, 5-CH_2), 31.85 (dd, J=14.3 and 9.5 Hz, P-CH_2), 29.48 (d, J=8.6 Hz, 4-CH_2), 21.42 (s, 1-CH_3), 17.80 (d, J=13.4 Hz, 2-CH_3. ^{31}P NMR (161.98 MHz, C_6D_6), δ: −15.7, −22.7.

4.9. Preparation of [Rh(COD)(12)]BF_4

To a stirred solution of the diphosphine **12** (1 mmol) in THF (2 mL) [Rh(COD)(acac)] (311 mg, 1 mmol) was added. The solution was stirred for 15 min. Then a stoichiometric amount of aq. 40% HBF_4 was added, and stirring continued for another 15 min. The complex was precipitated by ether (20 mL), dissolved in CH_2Cl_2 (0.5 mL), and precipitated by ether again. Dried in vacuum for 5 h at 50°C. Yellow powder, contained nonstoichiometric amount of THF and ether. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 8.05–8.20 (m, 4H), 7.1–7.8 (m, 16H), 4.30–4.48 (br. m, 3H), 4.06 (br. m, 1H), 3.72 (t, J=3.8 Hz, 1H), 3.41 (d, J=11 Hz, 1H), 3.22 (m, 1H), 3.17 (d, J=11 Hz, 1H), 2.77 (dd, J=10 and 16 Hz, 1H), 1.95–2.45 (m, 9H), 1.55 (m, 2H), 1.35–1.5 (m, 4H), 0.79 (s, 3H), 0.48 (s, 3H). ^{13}C NMR (100.63 MHz, $CDCl_3$) δ: 125–135 (arom), 106.6, 102.1, 99.5, 96.6 (=CH); 69.3 (OCH_2), 51.4 (d, J=10.5 Hz, C), 47.6 (C), 44.7 (CH), 41.9 (d, J=17 Hz, P-CH_2), 34.2 (d, J=17 Hz, P-CH_2), 33.9 (CH_2), 31.6 (CH_2), 31.5 (CH_2), 30.7 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 21.8 (CH_3), 17.7 (CH_3). ^{31}P NMR (161.98 MHz, $CDCl_3$), δ: 22.3 (dd, J=41.6 and 144.3 Hz), 16.7 (dd, J=41.6 and 144.3 Hz). IR (KBr, cm^{-1}): 3550 [ν(OH)].

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