Bis(phosphinite) with C_2-Symmetric Axis; Effects on the Ruthenium(II)-Catalyzed Asymmetric Transfer Hydrogenation of Acetophenone Derivatives

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Abstract: Chiral ruthenium catalyst systems generated in situ from $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ complex and chiral C_2-symmetric bis(phosphinite) ligands based on amino alcohol derivatives were employed in the asymmetric transfer hydrogenation of aromatic ketones to give the corresponding optically active alcohols in high yield. The best results were obtained in the $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ and (2*S*)-2-[benzyl(2-{benzyl[(2*S*)-1-[(diphenylphosphanyl)oxy]-3-phenyl propan-2-yl]amino}ethyl)amino]-3-phenylpropyl diphenylphosphinite or (2*R*)-2-[benzyl(2-{benzyl[(2*R*)-1-[(diphenylphosphanyl)oxy]-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropyl diphenylphosphinite catalytic systems, which gave enantioselectivities of up to 93% ee and 99% conversion.

Key words: phosphinites, enantioselectivity, hydrogenation, homogeneous catalysis, ruthenium, ketones

Asymmetric transfer hydrogenation of ketones has recently emerged as an alternative method to asymmetric hydrogenation for the production of chiral alcohols due to its operational simplicity and ready availability of reductants.[1–3] Chiral alcohols are very important building blocks and synthetic intermediates in organic synthesis and in the pharmaceutical industry.[4,5] Catalytic asymmetric synthesis using chiral metal complexes as catalyst precursors offers an ideal method for reducing ketones to chiral alcohols.[6,7] In general, the most easily designed and the most abundant ligands are C_2-symmetric bis(phosphines) due to their stereochemical redundancy. Significantly fewer in number are other arrangements, such as bidentate bis(phosphinites) systems.[8,9] Phosphine ligands have found widespread applications in transition-metal-catalyzed asymmetric transformations.[10,11] Phosphinites provide different chemical, electronic, and structural properties compared to phosphines. The metal–phosphorus bond is often stronger for phosphinites compared to the related phosphines due to the presence of the electron-withdrawing P-OR group. In addition, the empty σ*-orbital of the phosphinite $P(OR)R_2$ is stabilized, making the phosphinite a better electron acceptor.[12]

Chiral β-amino alcohols continue to be of importance in modern synthetic chemistry, not least because of their biological properties,[13] but also because of their wide range of synthetic applications.[14,15] Hence, the asymmetric synthesis of enantiomerically enriched amino alcohols has been extensively studied. Especially, catalysts derived from C_2-symmetric amino alcohols have received much attention and are used in many asymmetric catalytic reactions; furthermore, they have been shown to be powerful tools in the asymmetric reduction of prochiral ketones.[16,17] Because C_2-symmetric amino alcohols often give high levels of enantioselectivity in asymmetric reactions, as an extension of our ongoing research program, we wanted to synthesize novel C_2-symmetric bis(phosphinites) based on amino alcohol derivatives and use them with Ru(II) precursors as catalysts in the asymmetric transfer hydrogenation of aromatic ketones with *i*-PrOH under varying conditions.

The synthesis of the ligands was accomplished as illustrated in Scheme 1. First, the synthesis of L- and D-phenylglycinol, and L- and D-phenylalaninol were accomplished in one step from the corresponding phenylglycine or phenylalanine according to procedures described in the literature,[18,19] using $NaBH_4$–I_2 in anhydrous tetrahydrofuran (THF). The conversions of phenylglycinol and phenylalaninol into the corresponding *N*-benzyl amino alcohol derivatives were carried out at 110 °C, as shown in Scheme 1.[20] The C_2-symmetric chiral amino alcohols **13**–**16** were synthesized from ethylene glycol ditosylate with an excess of **9**–**12** in the presence of Na_2CO_3 in good yields. The structures of these chiral amino alcohols are consistent with the data obtained from ^{1}H NMR, ^{13}C NMR, IR spectra and elemental analyses (for details see the experimental section).

The C_2-symmetric chiral bis(phosphinite) ligands **17**–**24** were synthesized by hydrogen abstraction from the described C_2-symmetric chiral amino alcohols **13**–**16** by a base (Et_3N), and subsequent reaction with two equivalents of Ph_2PCl or $(i\text{-}Pr)_2PCl$, in anhydrous toluene or CH_2Cl_2 under an argon atmosphere, respectively. The progress of this reaction was conveniently followed by ^{31}P-{^{1}H} NMR spectroscopy. The ^{31}P NMR signals of the starting materials PPh_2Cl (δ = 81.0 ppm) and $(i\text{-}Pr)_2PCl$ (δ = 133.81 ppm) disappeared and new singlets appeared downfield due to the phosphinite ligands. The new ligands were characterized by ^{31}P-{^{1}H} NMR spectroscopy. Thus, the ^{31}P-{^{1}H} NMR spectra of **17**–**24** showed no unexpected features and a singlet was observed in the spectrum of each ligand due to the equivalent phosphorus nuclei.

The ^{31}P-{^{1}H} NMR spectra of the free ligands[21,22] are in line with the values previously observed for similar compounds.[23–26] Typical spectra of these ligands are il-

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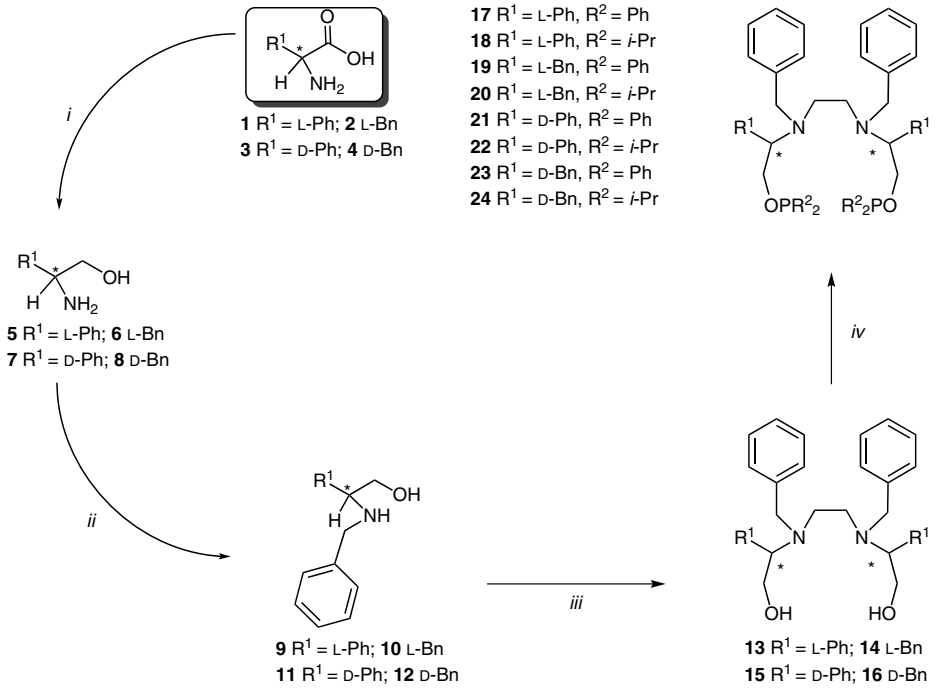


Scheme 1 *Reagents and conditions*: (i) $NaBH_4$–I_2, THF; (ii) $PhCH_2Cl$, Na_2CO_3, 110 °C, 12 h; (iii) ethylene glycol ditosylate, Na_2CO_3, 110 °C, 12 h; (iv) Ph_2PCl (2 equiv), Et_3N (2 equiv), toluene (for **17**, **19**, **21**, and **23**); (*i*-Pr)$_2$PCl (2 equiv), Et_3N (2 equiv), CH_2Cl_2 (for **18**, **20**, **22**, and **24**).

lustrated in Figure 1 and Figure 2. Solutions of the ligands in $CDCl_3$, prepared under anaerobic conditions, were unstable and decomposed rapidly to give the oxide and the hydrolysis product diphenylphosphinous acid [$Ph_2P(O)H$; in 5 min).[27] Furthermore, the ^{31}P-{^1H} NMR spectrum also revealed the formation of PPh_2PPh_2 and $P(O)Ph_2PPh_2$, as indicated by signals at ca. δ = –15.8 ppm as a singlet and δ = 35.2 ppm and δ = –21.4 ppm as doublets ($^1J_{P–P}$ = 224 Hz), respectively.[28] In addition, the ^{31}P-{^1H} NMR spectrum also revealed the formation of P(O)(*i*-Pr)$_2$P(*i*-Pr)$_2$, as indicated by signals at ca. δ = 66.3 ppm and δ = –13.5 ppm as doublets ($^1J_{P–P}$ = 279 Hz), respectively. Because **17**–**24** are not stable enough in common solvents that contain trace amounts of water, the corresponding ruthenium(II) complexes were synthesized in situ. The starting ruthenium(II) complex, [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$, was prepared from the reaction of commercially available α-phellandrene (5-isopropyl-2-methylcyclohexa-1,3-diene) with $RuCl_3$.[29]

The excellent catalytic performance and the higher structural permutability of phosphinite-based transition metal catalysts[30–33] prompted us to develop new Ru(II) catalyst systems with well-defined ligands.[34–39] The most important advantage of chiral phosphinite ligands over the corresponding phosphine ligands is the ease of preparation.

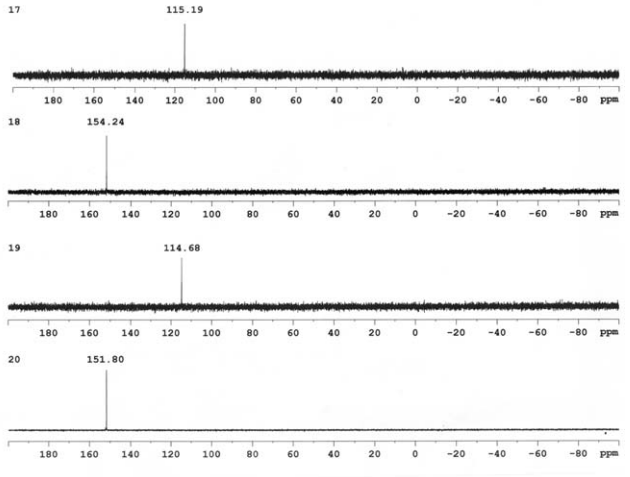


Figure 1 The ^{31}P-{^1H} NMR spectra of C_2-symmetric chiral bis(phosphinite) ligands **17**–**20**

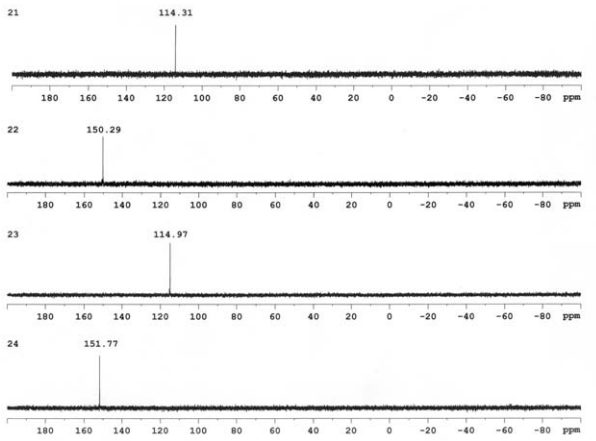
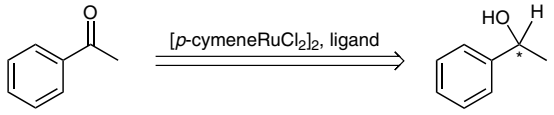


Figure 2 The ^{31}P-{^1H} NMR spectra of C_2-symmetric chiral bis(phosphinite) ligands **21**–**24**

From a practical standpoint, it is of substantial interest to develop highly effective chiral phosphinite ligands for asymmetric catalysis.[40,41] Noyori and co-workers suggested that the highly skewed position of the naphthyl rings in BINAP was the determining factor for the ligand to be so effective in asymmetric catalytic reactions.[42] Comparison of the structure of BINAP with that of the less effective BINAPO reveals two possible reasons for the difference in their effectiveness as chiral ligands in homogeneous catalysis:[43] (1) The oxygen atom in BINAPO increases the distance between the chiral binaphthyl moiety and the PPh_2 group. Consequently, there is less control of stereoselectivity in the catalyst–substrate interaction. (2) The presence of the C–O–P bond in BINAPO substantially increases the flexibility of the backbone and consequently decreases the enantioselectivity of the catalyst. In our recent pursuit of the design of new chiral and highly active ligands, we have found an opportunity both to test these hypotheses and to develop a class of effective chiral phosphinite ligands.

In a preliminary study, chiral ligands **17**–**24** combined with $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ were examined in the asymmetric transfer hydrogenation of acetophenone. The catalysts were generated in situ prior to hydrogen transfer by heating a mixture of $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ with the appropriate ligand in anhydrous *i*-PrOH. Our aim here was to compare the coordinating abilities of various functionalized phosphinites in $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ complexes in the catalytic asymmetric transfer hydrogenation. A comparison of the complexes with **17**–**24** as precatalysts for the asymmetric hydrogenation of acetophenone by *i*-PrOH in the presence of KOH is summarized in Table 1. Catalytic experiments were carried out under argon atmosphere using standard Schlenk techniques. These systems catalyzed the reduction of acetophenone to the corresponding alcohol [(*S*)-, (*R*)-1-phenylethanol] in the presence KOH as a promoter. To a solution of ruthenium complex and chiral ligand in *i*-PrOH, an appropriate amount of acetophenone, and KOH/*i*-PrOH solutions were added, respectively, at room temperature. The solution was stirred for several hours and then examined by capillary GC analysis. At room temperature, transfer hydrogenation of acetophenone occurred very slowly,[44] with low conversion (up to 40%) and moderate to high enantioselectivity (up to 80% ee) in

Table 1 Transfer Hydrogenation of Acetophenone with *i*-PrOH Catalyzed by $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$-**L**



Entry	Ligand (**L**)	Sub./Cat./KOH	Temp.	Time (h)[a]	Conversion (%)[a,b]	ee (%)[a,c]	Config.[d]	TOF (h^{-1})[e]
1	**17**	100:1:5	r.t.	24	32	76	*S*	<5
2	**18**	100:1:5	r.t.	24	14	70	*S*	<5
3	**19**	100:1:5	r.t.	24	30	80	*S*	<5
4	**20**	100:1:5	r.t.	24	10	74	*S*	<5
5	**21**	100:1:5	r.t.	24	36	74	*R*	<5
6	**22**	100:1:5	r.t.	24	12	69	*R*	<5
7	**23**	100:1:5	r.t.	24	32	78	*R*	<5
8	**24**	100:1:5	r.t.	24	14	72	*R*	<5
9	**17**	100:1:0	reflux	1	<5	–	–	–
10	**18**	100:1:0	reflux	1	<5	–	–	–
11	**19**	100:1:0	reflux	1	<5	–	–	–
12	**20**	100:1:0	reflux	1	<5	–	–	–
13	**21**	100:1:0	reflux	1	<5	–	–	–
14	**22**	100:1:0	reflux	1	<5	–	–	–
15	**23**	100:1:0	reflux	1	<5	–	–	–
16	**24**	100:1:0	reflux	1	<5	–	–	–
17	**17**	100:1:5	reflux	2 (2)	95 (94)	78 (77)	*S*	48
18	**18**	100:1:5	reflux	4 (4)	98 (97)	73 (71)	*S*	25
19	**19**	100:1:5	reflux	2 (2)	99 (98)	88 (87)	*S*	50
20	**20**	100:1:5	reflux	4 (4)	96 (96)	76 (76)	*S*	24
21	**21**	100:1:5	reflux	2 (2)	98 (96)	80 (77)	*R*	49
22	**22**	100:1:5	reflux	4 (4)	98 (97)	75 (72)	*R*	25
23	**23**	100:1:5	reflux	2 (2)	97 (99)	90 (89)	*R*	49
24	**24**	100:1:5	reflux	4 (4)	96 (96)	82 (78)	*R*	24

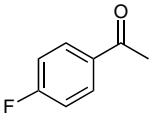
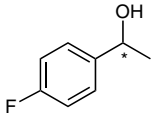
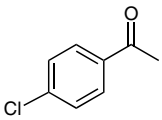
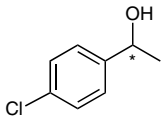
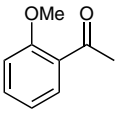
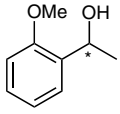
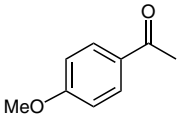
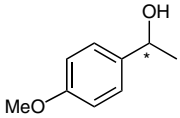
[a] Values obtained with NaOH as base are given in parentheses.
[b] Determined by GC analysis (three independent experiments).
[c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column.
[d] Determined by comparison of the retention times of the enantiomers on the GC traces with literature values, (*S*) or (*R*) configuration was obtained in all experiments.
[e] Referred to the reaction time indicated in column; TOF = (mol product/mol Ru(II)cat.) × h^{-1}.

all cases. During this period, the color changed from orange to deep-red. In addition, the ee values did not vary with time, as indicated by the results obtained with **17**–**24**. Furthermore, as can be inferred from the Table 1 (entries **9**–**16**) the presence of base was necessary to obtain appreciable conversions. The choice of base, such as KOH and NaOH, had little influence on the conversion or enantioselectivity. In addition, optimization studies of the catalytic reduction of acetophenone in *i*-PrOH showed that good activity was obtained with a base/ligand ratio of 5:1. Reduction of acetophenone into (*S*)- or (*R*)-1-phenylethanol could be achieved in high yield by increasing the temperature to 82 °C (Table 1, entries 17–24).

It is noteworthy that the catalytic system [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$-**L** (**L**: **17**–**24**) shows differences in reactivity. Interestingly, the reaction rate could be enhanced by changing the nature of the substituents on the phosphorus atom. Thus, replacing an isopropyl moiety by a phenyl group resulted in an increase in both the conversion and the enantioselectivity (Table 1). An examination of the results shows clearly that the best enantioselectivity was achieved when (2*S*)-2-[benzyl(2-{benzyl[(2*S*)-1-[(diphenylphosphanyl)oxy]-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropyl diphenylphosphinite (**19**) and (2*R*)-2-[benzyl(2-{benzyl[(2*R*)-1-[(diphenylphosphanyl)oxy]-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropyl diphenylphosphinite (**23**), were used as ligand (up to 88 and 90% ee, respectively). These results indicate that the structure of the bis(phosphinite) is a crucial factor for acceleration of the reaction. In the context of the results, it could be reasonably argued that the absolute configuration of the product is governed by the carbon-centered chirality.

Encouraged by the enantioselectivities obtained in these preliminary studies, we next extended our investigations to include asymmetric hydrogenation of substituted aceto-

Table 2 Asymmetric Transfer Hydrogenation of Substituted Acetophenones with the Catalyst Systems Prepared from [Ru(η^6-*p*-cymene)(μ-Cl)Cl]$_2$ and C_2-Symmetric Bis(phosphinite) Ligands **17**–**24**[a]

Entry	Ligand (**L**)	Substrate	Product	Time (h)	Conv. (%)[b]	ee (%)[c]	Config.[d]	TOF (h^{-1})[e]
1	**17**			1	97	76	*S*	97
2	**18**			3	96	65	*S*	32
3	**19**			1	95	81	*S*	95
4	**20**			3	94	77	*S*	31
5	**21**			1	99	73	*R*	99
6	**22**			3	97	62	*R*	32
7	**23**			1	97	82	*R*	97
8	**24**			3	94	74	*R*	31
9	**17**			2	98	77	*S*	49
10	**18**			4	99	67	*S*	25
11	**19**			2	97	83	*S*	49
12	**20**			4	96	76	*S*	24
13	**21**			2	98	77	*R*	49
14	**22**			4	97	67	*R*	24
15	**23**			2	97	83	*R*	49
16	**24**			4	96	76	*R*	24
17	**17**			4	98	77	*S*	25
18	**18**			7	99	70	*S*	14
19	**19**			5	98	90	*S*	20
20	**20**			7	99	80	*S*	14
21	**21**			4	98	80	*R*	25
22	**22**			8	99	73	*R*	12
23	**23**			5	98	93	*R*	20
24	**24**			8	99	80	*R*	12
25	**17**			4	96	76	*S*	24
26	**18**			6	96	68	*S*	16
27	**19**			6	98	85	*S*	16
28	**20**			8	99	81	*S*	12
29	**21**			4	96	75	*R*	24
30	**22**			7	97	64	*R*	14
31	**23**			6	98	84	*R*	16
32	**24**			9 h	96	76	*R*	11

[a] Reaction conditions: Catalyst (0.005 mmol), substrate (0.5 mmol), *i*-PrOH (5 mL), KOH (0.025 mmol), 82 °C, the concentration of acetophenone was 0.1 M.
[b] The purity was checked by NMR and GC analyses (three independent experiments); yields are based on aryl ketone.
[c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column (30 m × 0.32 mm × 0.25 μm film thickness).
[d] Determined by comparison of the retention times of the enantiomers on the GC traces with literature values.
[e] Referred to the reaction time indicated in column; TOF = (mol product/mol Ru(II)Cat.) × h^{-1}.

phenone derivatives. The results presented in Table 2 demonstrate that a range of acetophenone derivatives can be hydrogenated with good to high enantioselectivities. The catalytic reduction of acetophenone derivatives were tested under the optimized conditions. Complexes **17**–**24** showed very high activity with most of the ketones, however, the position and electronic properties of the ring substituents influenced the hydrogenation results. The introduction of electron-withdrawing substituents, such as F and Cl, to the *para*-position of the aryl ring of the ketone decreased the electron density of the C=O bond so that the activity was improved, facilitating the hydrogenation.[45,46] The presence of an electron-withdrawing group, such as a fluoro group, on the *para*-position was helpful to obtain excellent conversion and moderate to good enantioselectivity (up to 82% ee, Table 2, entries 1–8), whereas the introduction of an electron-donating substituent such as a methoxy group on the *para*-position tended to lower activity (<24 h^{-1}), while maintaining satisfactory enantioselectivity (entries 25–32). The introduction of an electron-donating substituent such as a methoxy group to the *ortho*- or *para*-position decelerated the reaction (<25 h^{-1}), but substituents on the *ortho*-position especially increased the enantioselectivity ratio (difference up to 10% ee), more than substituents on the *para*-position (see Table 2). Among all the selected ketones, the best result was obtained in the reduction of *o*-methoxyacetophenone, giving up to 93% ee (Table 2, entry 23). The results indicated that strong electron-withdrawing substituents, such as fluoro and chloro groups, were capable of achieving higher conversion (up to 99 h^{-1}), but with slightly lower enantiomeric purity. Conversely, the most electron-donating substituent (methoxy) led to lower conversions with higher ee values (Table 2).

In conclusion, the $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ and C_2-symmetric bis(phosphinite) systems demonstrate remarkable catalytic activity and enantioselectivity in the asymmetric transfer hydrogenation of acetophenone derivatives. High conversion and good to excellent enantioselectivity were obtained in the catalytic reaction. The simplicity and efficiency clearly make it an excellent choice of catalyst for the practical preparation of highly valued alcohols through catalytic asymmetric transfer hydrogenation of ketones. Further studies are in progress to improve both activity and enantioselectivity and to extend the use of these novel ligands to other asymmetric catalytic reactions.

Unless otherwise stated, all reactions were carried out under an atmosphere of argon using conventional Schlenk glassware; solvents were dried using established procedures and distilled under argon immediately prior to use. Analytical grade and deuterated solvents were purchased from Merck. The starting materials L-, D-phenylglycine, L-, D-phenylalanine, PPh_2Cl, $(i\text{-}Pr)_2PCl$ and Et_3N, purchased from Fluka, and were used as received. $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$,[47] L-phenylglycinol [(2*S*)-2-amino-2-phenylethan-1-ol; **1**], L-phenylalaninol [(2*S*)-2-amino-3-phenylpropan-1-ol; **2**], D-phenylglycinol [(2*R*)-2-amino-2-phenylethan-1-ol; **3**], D-phenylalaninol [(2*R*)-2-amino-3-phenylpropan-1-ol; **4**],[18] and *N*-benzyl amino alcohols (2*S*)-2-(benzylamino)-2-phenylethan-1-ol (**5**) and (2*S*)-2-(benzylamino)-3-phenylpropan-1-ol (**6**), (2*R*)-2-(benzylamino)-2-phenylethan-1-ol (**7**), and (2*R*)-2-(benzylamino)-3-phenylpropan-1-ol] (**8**)[48] were prepared according to literature procedures.

IR spectra were recorded with a Mattson 1000 ATI UNICAM FT-IR spectrometer as KBr pellets. ^1H (400.1 MHz), ^{13}C NMR (100.6 MHz), and $^{31}P\text{-}\{^1H\}$ NMR (162.0 MHz) spectra were recorded with a Bruker AV 400 spectrometer, with δ referenced to external TMS and 85% H_3PO_4, respectively. Elemental analysis was carried out with a Fisons EA 1108 CHNS-O instrument. Melting points were recorded with a Gallenkamp apparatus with open capillaries.

GC analyses were performed with a Shimadzu GC 2010 Plus Gas Chromatograph equipped with cyclodex B (Agilent) capillary column (30 m × 0.32 mm, 0.25 μm film thickness). The GC parameters for asymmetric transfer hydrogenation of ketones were as follows: initial temperature 50 °C, initial time 1.1 min, solvent delay 4.48 min, temperature ramp 1.3 °C/min, final temperature 150 °C, initial time 2.2 min, temperature ramp 2.15 °C/min, final temperature 250 °C, initial time 3.3 min, final time 44.33 min, injector port temperature 200 °C, detector temperature 200 °C, injection volume 2.0 μL.

Transfer Hydrogenation of Ketones; General Procedure

A flame-dried Schlenk flask was charged with $[Ru(\eta^6\text{-}p\text{-cymene})(\mu\text{-Cl})Cl]_2$ (0.005 mmol), excess bis(phosphinite) ligand (0.02 mmol) and a stir bar. To these components was added *i*-PrOH (5 mL, dried and degassed), and the resultant solution was heated to 82 °C for 20 min, followed by cooling to ambient temperature. A solution of ketone (0.5 mmol) in *i*-PrOH (5 mL) was then added to the catalyst mixture and the solution was heated to the desired temperature (generally, 25 or 82 °C). The reaction was initiated by the addition of a solution of KOH (2.5 mL, 0.1 M *i*-PrOH). As soon as the reaction was complete, an aliquot of the solution (1 mL) was removed by using a syringe and evaporated under reduced pressure. The resultant oil was subjected to flash chromatography (silica gel 60; Et_2O) and subsequent evaporation under reduced pressure yielded clear liquids in each case. After this time a sample of the reaction mixture was taken, diluted with acetone, and analyzed immediately by GC. Reported conversions are related to the residual unreacted ketone. ^1H NMR spectral data for the resultant products were consistent with previously reported results.

Preparation of the Chiral, C_2-Symmetric *N*-Benzyl Amino Alcohols and the Corresponding Chiral Bis(phosphinite) Ligands

(2*S*)-2-(Benzylamino)-2-phenylethan-1-ol (9): (*S*)-Phenylglycinol (43.90 g, 320 mmol), benzyl chloride (10.13 g, 80 mmol), and anhydrous Na_2CO_3 (8.48 g, 80 mmol) were placed in a 250 mL two-necked, round-bottomed flask. The mixture was stirred at 110 °C for 12 h under dry Ar, then cooled to r.t. and $CHCl_3$ (150 mL) was added and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (3 × 150 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and evaporated. The product was then distilled under reduced pressure (160–170 °C/0.8 mmHg) to give **9** (15.5 g, 85%); mp 83–84 °C; $[\alpha]_D^{20}$ +56.9 (*c* 0.5, MeOH). ^1H NMR ($CDCl_3$): δ = 7.28–7.37 (m, 10 H, ArH), 3.62–3.89 (m, 5 H, C*H*-N, CH_2OH and CH_2Ph), 3.23 (br, 2 H, N*H* and O*H*). ^{13}C NMR ($CDCl_3$): δ = 139.71, 139.19, 128.78, 128.52, 128.46, 127.86, 127.50, 127.30 (-CHC_6H_5 and -$CH_2C_6H_5$), 66.49 (-CH_2OH), 63.76 (-CH-N), 50.95 (-CH_2Ph). IR (KBr): 3392 (OH), 3353 (NH), 3030 (CH), 2915, 2838 cm^{-1}. Anal. Calcd for $C_{15}H_{17}NO$ (227.3): C, 79.26; H, 7.54; N, 6.16. Found: C, 79.18; H, 7.47; N, 6.09.

(2*S*)-2-(Benzylamino)-3-phenylpropan-1-ol (10): (*S*)-Phenylalaninol (48.40 g, 320 mmol), benzyl chloride (10.13 g, 80 mmol), and anhydrous Na_2CO_3 (8.48 g, 80 mmol) were placed in a 250 mL two-necked, round-bottomed flask. The mixture was stirred at 110 °C for 12 h under dry Ar, then cooled to r.t. and $CHCl_3$ (150 mL) was added and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-ex-

tracted with $CHCl_3$ (3 × 150 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and evaporated. The product was then distilled under reduced pressure (165–170 °C/0.8 mmHg) to give **10** (14.9 g, 77%); mp 54–56 °C; $[\alpha]_D^{20}$ –11.1 (*c* 1.2, MeOH). ^{1}H NMR ($CDCl_3$): δ = 7.17–7.27 (m, 10 H, ArH), 3.57–3.99 (m, 4 H, -C*H*$_2$OH and N-C*H*$_2$-Ph), 2.99 (br, 1 H, C*H*-N), 2.80 (br, 2 H, -C*H*$_2$Ph), 2.14 (br, 2 H, N*H* and O*H*). ^{13}C NMR ($CDCl_3$): δ = 140.15, 139.17, 129.78, 129.75, 128.51, 128.14, 126.72, 126.40 (-$CH_2C_6H_5$ and -N-$CH_2C_6H_5$), 53.32, 51.44 (-*C*H$_2$OH and N-*C*H$_2$-Ph), 59.42 (-*C*H-N), 38.19 (-*C*H$_2$Ph). IR (KBr): 3550 (OH), 3323 (NH), 3061 (CH), 3023, 2930, 2861, 1653 (C=C), 1601, 1523 cm^{-1}. Anal. Calcd for $C_{16}H_{19}NO$ (241.3): C, 79.63; H, 7.94; N, 5.80. Found: C, 79.59; H, 7.83; N, 5.76.

(2*R*)-2-(Benzylamino)-2-phenylethan-1-ol (11): (*R*)-Phenylglycinol (43.90 g, 320 mmol), benzyl chloride (10.13 g, 80 mmol), and anhydrous Na_2CO_3 (8.48 g, 80 mmol) were placed in a 250 mL two-necked, round-bottomed flask. The mixture was stirred at 110 °C for 12 h under dry Ar, then cooled to r.t. and $CHCl_3$ (150 mL) was added and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (3 × 150 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and evaporated. The product was then distilled under reduced pressure (160–170 °C/0.8 mmHg) to give **11** (14.2 g, 78.1%); mp 83–84 °C; $[\alpha]_D^{20}$ –56.9 (*c* 0.5, MeOH). ^{1}H NMR ($CDCl_3$): δ = 7.28–7.44 (m, 10 H, ArH), 3.86 (m, 1 H, C*H*-N), 3.81 [m 1 H, C*H*$_2$Ph(a)], 3.65 [m 1 H, C*H*$_2$Ph(b)], 3.72 [m, 1 H, C*H*$_2$OH(b)], 3.61 [m, 1 H, C*H*$_2$OH(b)]. ^{13}C NMR ($CDCl_3$): δ = 140.50, 140.06, 128.73, 128.49, 128.30, 127.71, 127.42, 127.13 (-CHC_6H_5 and -$CH_2C_6H_5$), 66.80 (-*C*H$_2$OH), 63.85 (-*C*H-N), 51.23 (-*C*H$_2$Ph). IR (KBr): 3390 (OH), 3348 (NH), 3026 (CH), 2912, 2835 cm^{-1}. Anal. Calcd for $C_{15}H_{17}NO$ (227.3): C, 79.26; H, 7.54; N, 6.16. Found: C, 79.19; H, 7.49; N, 6.12.

(2*R*)-2-(Benzylamino)-3-phenylpropan-1-ol (12): (*R*)-Phenylalaninol (48.40 g, 320 mmol), benzyl chloride (10.13 g, 80 mmol), and anhydrous Na_2CO_3 (8.48 g, 80 mmol) were placed in a 250 mL two-necked round-bottomed flask. The mixture was stirred at 110 °C for 12 h under dry Ar, then cooled to r.t. and $CHCl_3$ (150 mL) was added and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (3 × 150 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and evaporated. The product was then distilled under reduced pressure (165–170 °C/0.8 mmHg) to give **12** (14.2 g, 73.5%); mp 54–56 °C; $[\alpha]_D^{20}$ +11.1 (*c* 1.2, MeOH). ^{1}H NMR ($CDCl_3$): δ = 7.10–7.24 (m, 10 H, ArH), 3.64–3.77 (m, 4 H, -C*H*$_2$OH and N-C*H*$_2$-Ph), 2.92 (br, 1 H, C*H*-N), 2.72 (br, 2 H, -C*H*$_2$Ph), 2.14 (br, 2 H, N*H* and O*H*). ^{13}C NMR ($CDCl_3$): δ = 140.07, 139.22, 129.32, 129.08, 128.53, 128.18, 126.14, 126.42 (-$CH_2C_6H_5$ and -N-$CH_2C_6H_5$), 53.35, 51.38 (-*C*H$_2$OH and N-*C*H$_2$-Ph), 59.46 (-*C*H-N), 38.16 (-*C*H$_2$Ph). IR (KBr): 3550 (OH), 3384 (NH), 3061 (CH), 3023, 2938, 2861, 1615 (C=C), 1561, 1525 cm^{-1}. Anal. Calcd for $C_{16}H_{19}NO$ (241.3): C, 79.63; H, 7.94; N, 5.80. Found: C, 79.60; H, 7.90; N, 5.76.

(2*S*)-2-[Benzyl(2-{benzyl[(1*S*)-2-hydroxy-1-phenylethyl]amino}ethyl)amino]-2-phenylethan-1-ol (13): Compound **9** (22.73 g, 100 mmol), ethylene glycol ditosylate (6.18 g, 16.67 mmol) and Na_2CO_3 (3.03 g, 28.57 mmol) were stirred at 110 °C for 12 h under an Ar atmosphere. The mixture was cooled to r.t. and $CHCl_3$ (100 mL) was added and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (3 × 25 mL). The combined $CHCl_3$ layers were dried (Na_2SO_4) and evaporated. After the excess amino alcohol **9** was distilled at reduced pressure (150–160 °C/0.1 mmHg), the product was purified by flash column chromatography on silica gel (toluene–EtOAc, 5:3) to give **13** (4.01 g, 50.1%); $[\alpha]_D^{20}$ +59.2 (*c* 0.5, MeOH). ^{1}H NMR ($CDCl_3$): δ = 7.13–7.52 (m, 20 H, NCH*Ph* and NCH$_2$*Ph*), 4.16 [m, 2 H, C*H*$_2$OH(a)], 3.94 (m, 2 H, NC*H*Ph), 3.83 [d, *J* = 13.2 Hz, 2 H, NC*H*$_2$Ph(a)], 3.69 [m, 2 H, C*H*$_2$OH(b)], 3.07 [d, *J* = 13.2 Hz, 2 H, NC*H*$_2$Ph(b)], 2.95 [d, *J* = 9.2 Hz, 2 H, NC*H*$_2$CH$_2$N(a)], 2.30 [d, *J* = 9.2 Hz, 2 H, NC*H*$_2$CH$_2$N(b)], ^{13}C NMR ($CDCl_3$): δ = 138.88, 135.63, 129.34, 129.08, 128.62, 128.35, 127.94, 127.29 (NCH*Ph* and NCH$_2$*Ph*), 64.37 (NCHPh), 61.06 (-*C*H$_2$OH), 55.04 (NC*H*$_2$Ph), 47.40 (NC*H*$_2$CH$_2$N). IR (KBr): 3415 (OH), 3055, 3027 [aromatic υ(CH)], 2924, 2837 [aliphatic υ(CH)], 1487, 1451, 1407 [aromatic υ(C=C)], 1031 (C-0) cm^{-1}. Anal. Calcd for $C_{32}H_{36}N_2O_2$ (480.7): C, 79.97; H, 7.55; N, 5.83. Found: C, 79.68; H, 7.37; N, 5.61.

(2*S*)-2-[Benzyl(2-{benzyl[(2*S*)-1-hydroxy-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropan-1-ol (14): Compound **10** (24.13 g, 100 mmol), ethylene glycol ditosylate (6.18 g, 16.67 mmol), and Na_2CO_3 (3.03 g, 28.57 mmol) were stirred at 110 °C for 12 h under an Ar atmosphere. The mixture was cooled to r.t., $CHCl_3$ (100 mL) was added and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (2 × 50 mL). The combined $CHCl_3$ layers were dried (Na_2SO_4) and evaporated. After the excess amino alcohol **10** was distilled at reduced pressure (160–170 °C/0.1 mmHg), the desired product was purified by flash column chromatography on silica gel (toluene–EtOAc, 5:3) to give **14** (3.76 g, 44.3%); mp 106–108 °C; $[\alpha]_D^{20}$ –28.6 (*c* 1.2, MeOH). ^{1}H NMR ($CDCl_3$): δ = 7.07–7.38 (m, 20 H, NCH$_2$*Ph* and CHCH$_2$*Ph*), 4.00 (br, 2 H, CH$_2$O*H*), 3.83 [d, *J* = 13.2 Hz, 2 H, NC*H*$_2$Ph(a)], 3.49 [d, *J* = 10.8 Hz, 2 H, C*H*$_2$OH(a)], 3.37 [m, 4 H, NC*H*$_2$Ph(b) and C*H*$_2$OH(b)], 2.97 [m, 2 H, -C*H*N and 2 H, -CHC*H*$_2$Ph(a)], 2.83 [d, *J* = 8.8 Hz, 2 H, NC*H*$_2$CH$_2$N(a)], 2.53 [d, *J* = 7.6 Hz, 2 H, NC*H*$_2$CH$_2$N(b)], 2.31 [m, 2 H, -CHC*H*$_2$Ph(b)]. ^{13}C NMR ($CDCl_3$): δ = 139.20, 138.84, 129.34, 128.97, 128.61, 128.60, 127.36, 126.24 (NCH$_2C_6H_5$ and CHCH$_2C_6H_5$), 62.54 (-*C*H-N), 60.57 (-*C*H$_2$OH), 54.55 (NC*H*$_2$Ph), 47.56 (NC*H*$_2$CH$_2$N), 31.51 (-CHC*H*$_2$Ph). IR (KBr): 3363 (OH), 3053, 3023 [aromatic υ(CH)], 2939, 2858 [aliphatic υ(CH)], 1489, 1452, 1411 [aromatic υ(C=C)], 1027 [υ(C-0)] cm^{-1}. Anal. Calcd for $C_{34}H_{40}N_2O_2$ (508.7): C, 80.28; H, 7.93; N, 5.51. Found: C, 80.18; H, 7.63; N, 5.44.

(2*R*)-2-[Benzyl(2-{benzyl[(1*R*)-2-hydroxy-1-phenylethyl]amino}ethyl)amino]-2-phenylethan-1-ol (15): Compound **11** (22.73 g, 100 mmol), ethylene glycol ditosylate (6.18 g, 16.67 mmol) and Na_2CO_3 (3.03 g, 28.57 mmol) were stirred at 110 °C for 12 h under an Ar atmosphere. The mixture was cooled, $CHCl_3$ (100 mL) was added at r.t., and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (3 × 25 mL). The combined $CHCl_3$ layers were dried (Na_2SO_4) and evaporated. After the excess amino alcohol **11** was distilled at reduced pressure (150–160 °C/0.1 mmHg), the desired product was purified by flash column chromatography on silica gel (toluene–EtOAc, 5:3) to give **15** (3.98 g, 49.7%); $[\alpha]_D^{20}$ –59.2 (*c* 0.5, MeOH). ^{1}H NMR ($CDCl_3$): δ = 7.12–7.42 (m, 20 H, NCH*Ph* and NCH$_2$*Ph*), 4.15 [m, 2 H, C*H*$_2$OH(a)], 3.94 (m, 2 H, NC*H*Ph), 3.82 [d, *J* = 13.2 Hz, 2 H, NC*H*$_2$Ph(a)], 3.68 [m, 2 H, C*H*$_2$OH(b)], 3.06 [d, *J* = 13.2 Hz, 2 H, NC*H*$_2$Ph(b)], 2.94 [d, *J* = 8.8 Hz, 2 H, NC*H*$_2$CH$_2$N(a)], 2.29 [d, *J* = 8.8 Hz, 2 H, NC*H*$_2$CH$_2$N(b)]. ^{13}C NMR ($CDCl_3$): δ = 138.93, 135.67, 129.32, 129.06, 128.61, 128.34, 127.92, 127.27 (NCH*Ph* and NCH$_2$*Ph*), 64.34 (NCHPh), 61.06 (-*C*H$_2$OH), 55.05 (NC*H*$_2$Ph), 47.44 (NC*H*$_2$CH$_2$N). IR (KBr): 3413 [υ(OH)], 3057, 3027 [aromatic υ(CH)], 2930, 2833 [aliphatic υ(CH)], 1484, 1452, 1412 [aromatic υ(C=C)], 1033 [υ(C-O)]. Anal. Calcd for $C_{32}H_{36}N_2O_2$ (480.7): C, 79.97; H, 7.55; N, 5.83. Found: C, 79.78; H, 7.39; N, 5.59.

(2*R*)-2-[Benzyl(2-{benzyl[(2*R*)-1-hydroxy-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropan-1-ol (16): Compound **12** (24.13 g, 100 mmol), ethylene glycol ditosylate (6.18 g, 16.67 mmol) and Na_2CO_3 (3.03 g, 28.57 mmol) were stirred at 110 °C for 12 h under an Ar atmosphere. The mixture was cooled to r.t., $CHCl_3$ (100 mL) was added, and the mixture was heated at reflux for 2 h. The $CHCl_3$ layer was separated from the solid phase, which was re-extracted with $CHCl_3$ (2 × 50 mL). The combined $CHCl_3$ layers were dried (Na_2SO_4) and evaporated. After the excess amino alcohol **12** was distilled at reduced pressure (160–170 °C/0.1 mmHg),

the desired product was purified by flash column chromatography on silica gel (toluene–EtOAc, 5:3) to give **16** (3.52 g, 41.5%); bp 106–108 °C; $[\alpha]_D^{20}$ +28.6 (*c* 1.2, MeOH). ^{1}H NMR ($CDCl_3$): δ = 6.94–7.28 (m, 20 H, NCH_2*Ph* and $CHCH_2$*Ph*), 3.70 [d, *J* = 13.2 Hz, 2 H, NCH_2Ph(a)], 3.53 [t, *J* = 10.6 Hz, 2 H, CH_2OH(a)], 3.26 [m, 4 H, NCH_2Ph(b) and CH_2OH(b)], 2.87 [m, 2 H, -C*H*N and 2 H, -$CHCH_2$Ph(a)], 2.71 [d, *J* = 8.4 Hz, 2 H, NCH_2CH_2N(a)], 2.39 [d, *J* = 8.4 Hz, 2 H, NCH_2CH_2N(b)], 2.20 [m, 2 H, -$CHCH_2$Ph(b)]. ^{13}C NMR ($CDCl_3$): δ = 139.19, 138.84, 129.32, 128.96, 128.60, 128.58, 127.35, 126.22 ($NCH_2C_6H_5$ and $CHCH_2C_6H_5$), 62.56 (-*C*H-N), 60.66 (-CH_2OH), 54.56 (NCH_2Ph), 47.59 (NCH_2CH_2N), 31.52 (-$CHCH_2$Ph). IR (KBr): 3358 [υ(OH)], 3053, 3023 [aromatic υ(CH)], 2939, 2857 [aliphatic υ(CH)], 1488, 1452, 1411 [aromatic υ(C=C)], 1027 [υ(C-O)]. Anal. Calcd for $C_{34}H_{40}N_2O_2$ (508.7): C, 80.28; H, 7.93; N, 5.51. Found: C, 80.14; H, 7.64; N, 5.28.

(2*S*)-2-{Benzyl[2-(benzyl{(1*S*)-2-[(diphenylphosphanyl)oxy]-1-phenylethyl}amino)ethyl]amino}-2-phenylethyldiphenylphosphinite (17): Chlorodiphenylphosphine (0.097 g, 0.416 mmol) was added to a stirred solution of **13** (0.100 g, 0.208 mmol) and Et_3N (0.043 g, 0.416 mmol) in toluene (25 mL) at r.t. with vigorous stirring. The mixture was stirred at r.t. for 1 h and the white precipitate (triethylammonium chloride) was filtered off under argon and the remaining organic phase was dried in vacuo to produce **17** (172 mg, 92%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 115.19 [s, O-P-$(C_6H_5)_2$].

(2*S*)-2-(Benzyl{2-[benzyl((1*S*)-2-{[bis(propan-2-yl)phosphanyl]oxy}-1-phenylethyl)amino] ethyl}amino)-2-phenylethylbis(propan-2-yl)phosphinite (18): (*i*-Pr)$_2$PCl (0.067 g, 0.416 mmol) was added to a stirred solution of **13** (0.10 g, 0.208 mmol) and Et_3N (0.043 g, 0.416 mmol) in CH_2Cl_2 (25 mL) at r.t. with vigorous stirring. The mixture was stirred at r.t. for 72 h, and the solvent was removed under reduced pressure. After addition of anhydrous toluene, the white precipitate (triethylammonium chloride) was filtered off under argon and remaining organic phase was dried in vacuo to give **18** (141 mg, 95%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 154.24 [s, O-P-(*i*-Pr)$_2$].

(2*S*)-2-{Benzyl[2-(benzyl{(2*S*)-1-[(diphenylphosphanyl)oxy]-3-phenylpropan-2-yl}amino)ethyl]amino}-3-phenylpropyldiphenylphosphinite (19): Chlorodiphenylphosphine (0.092 g, 0.394 mmol) was added to a stirred solution of **14** (0.100 g, 0.197 mmol) and Et_3N (0.04 g, 0.394 mmol) in toluene (25 mL) at r.t. with vigorous stirring. The mixture was stirred at r.t. for 1 h and the white precipitate (triethylammonium chloride) was filtered off under argon and remaining organic phase was dried in vacuo to produce **19** (166 mg, 97%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 114.68 [s, O-P-$(C_6H_5)_2$].

(2*S*)-2-[Benzyl(2-{benzyl[(2*S*)-1-{[bis(propan-2-yl)phosphanyl]oxy}-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropylbis(propan-2-yl)phosphinite (20): (*i*-Pr)$_2$PCl (0.063 g, 0.394 mmol) was added to a stirred solution of **14** (0.100 g, 0.197 mmol) and Et_3N (0.040 g, 0.394 mmol) in CH_2Cl_2 (25 mL) at 0 °C with vigorous stirring. The mixture was stirred at r.t. for 72 h, and the solvent was removed under reduced pressure. After addition of anhydrous toluene, the white precipitate (triethylammonium chloride) was filtered off under argon and the remaining organic phase was dried in vacuo to produce **20** (140 mg, 96%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 151.80 [s, O-***P***-(*i*-Pr)$_2$].

(2*R*)-2-[Benzyl(2-{benzyl[(1*R*)-2-[(diphenylphosphanyl)oxy]-1-phenylethyl]amino}ethyl)amino]-2-phenylethyldiphenylphosphinite (21): Chlorodiphenylphosphine (0.097 g, 0.416 mmol) was added to a stirred solution of **15** (0.100 g, 0.208 mmol) and Et_3N (0.043 g, 0.416 mmol) in toluene (25 mL) at r.t. with vigorous stirring. The mixture was stirred at r.t. for 1 h and the white precipitate (triethylammonium chloride) was filtered off under argon and the remaining organic phase was dried in vacuo to produce **21** (170 mg, 96.1%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 114.31 [s, O-P-$(C_6H_5)_2$].

(2*R*)-2-[Benzyl(2-{benzyl[(1*R*)-2-{[bis(propan-2-yl)phosphenyl]oxy}-1-phenylethyl] amino}ethyl)amino]-2-phenylethylbis(propan-2-yl)phosphinite (22): (*i*-Pr)$_2$PCl (0.067 g, 0.416 mmol) was added to a stirred solution of **15** (0.100 g, 0.208 mmol) and Et_3N (0.043 g, 0.416 mmol) in CH_2Cl_2 (25 mL) at r.t. with vigorous stirring. The mixture was stirred at room r.t. for 48 h, and the solvent was removed under reduced pressure. After addition of anhydrous toluene, the white precipitate (triethylammonium chloride) was filtered off under argon and the remaining organic phase was dried in vacuo to produce **22** (138 mg, 93.2%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 150.29 [s, O-P-(*i*-Pr)$_2$].

(2*R*)-2-[Benzyl(2-{benzyl[(2*R*)-1-[(diphenylphosphanyl)oxy]-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropyldiphenylphosphinite (23): Chlorodiphenylphosphine (0.092 g, 0.394 mmol) was added to a stirred solution of **16** (0.100 g, 0.197 mmol) and Et_3N (0.040 g, 0.394 mmol) in toluene (25 mL) at r.t. with vigorous stirring. The mixture was stirred at r.t. for 1 h and the white precipitate (triethylammonium chloride) was filtered off under argon and the remaining organic phase was dried in vacuo to produce **23** (165 mg, 95.9%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 114.97 [s, O-P-$(C_6H_5)_2$].

(2*R*)-2-[Benzyl(2-{benzyl[(2*R*)-1-{[bis(propan-2-yl)phosphanyl]oxy}-3-phenylpropan-2-yl]amino}ethyl)amino]-3-phenylpropylbis(propan-2-yl)phosphinite (24): (*i*-Pr)$_2$PCl (0.063 g, 0.394 mmol) was added to a stirred solution of **16** (0.100 g, 0.197 mmol) and Et_3N (0.040 g, 0.394 mmol) in CH_2Cl_2 (25 mL) at 0 °C with vigorous stirring. The mixture was stirred at r.t. for 48 h, and the solvent was removed under reduced pressure. After addition of anhydrous toluene, the white precipitate (triethylammonium chloride) was filtered off under argon and remaining organic phase was dried in vacuo to produce **24** (138 mg, 94.5%) as a white viscous oil. ^{31}P-{^{1}H} NMR ($CDCl_3$): δ = 151.77 [s, O-P-(*i*-Pr)$_2$].

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