



# Novel bi- and tridentate phosphane and thioether ligands derived from chiral $\alpha$ -hydroxy acids

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## Abstract

Novel bi- and tridentate ligands with phosphane and thioether moieties have been prepared in enantiomerically pure form in good to excellent yields by substitution reactions with phosphorus and sulfur nucleophiles of easily available tosylates derived from natural chiral  $\alpha$ -hydroxy acids. © 1999 Elsevier Science Ltd. All rights reserved.

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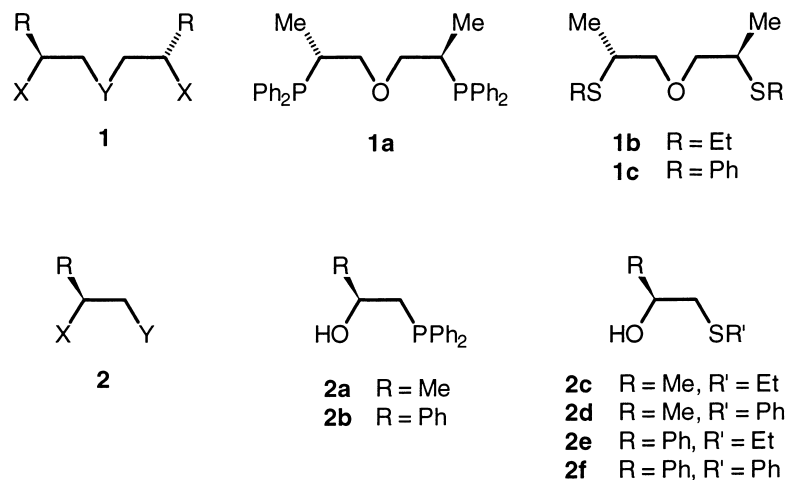
## 1. Introduction

We are interested in the development of new chiral multidentate ligands,<sup>1,2</sup> e.g. tridentate ligands of the general type **1** and bidentate ligands **2** (Scheme 1) with different donor moieties, such as phosphane and thioether groups, for transition metal catalyzed asymmetric C–C bond formations, with special interest in the transition metal catalyzed asymmetric Michael reaction.<sup>3</sup>

In this paper we report in continuation of our previous work<sup>1</sup> the synthesis of three new enantiomerically pure  $C_2$ -symmetric tridentate ligands with *P,O,P*- and *S,O,S*-donor sets (**1a–1c**) and an improved route to the enantiopure hydroxyalkyl phosphanes and thioethers **2a–2f** (Scheme 1). The hydroxy compounds **2a–2f** have already been prepared in racemic form as well as — in some cases — enantiopure materials by either epoxide opening or substitution of hydroxy alkyl halides with phosphorus or sulfur nucleophiles.<sup>4–10</sup> The route we present herein is an improvement on the reported procedures, since regioselectivity problems in epoxide opening reactions or stereoselectivity problems in the introduction of chirality by an asymmetric reaction are avoided. In our approach the stereo information is derived from natural, non-racemic  $\alpha$ -hydroxy acids. Unlike **1a–1c**, secondary alcohols **2a–2f** can not only be applied as chiral ligands, but play an important role as enantiopure building blocks or chiral auxiliaries.

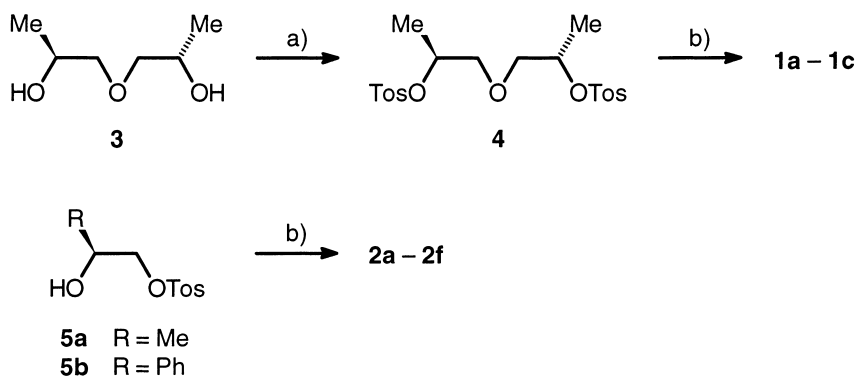
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Scheme 1. Tri- and bidentate ligands derived from natural  $\alpha$ -hydroxy acids

## 2. Synthesis

The synthesis of the tridentate ligands **1a–1c** starts from the recently published diol **3** (Scheme 2), which is easily prepared from (*S*)-(-)-ethyl lactate.<sup>1</sup> Compound **3** is tosylated with TosCl in pyridine to give the bistosylate **4** in 51% yield. Intermediate **4** can be easily substituted by  $\text{KPh}_2$  in DMF/THF or NaSR in DMF to give compounds **1a–1c** in good to excellent yields with an inversion of configuration (Table 1). It is important to mention that by NMR or GC no other diastereoisomers of **1a–1c** are detectable, which means that the substitution is stereospecific and no epimerization takes place. The <sup>13</sup>C spectrum of **1a** shows the expected phosphorus coupling and that the two Ph groups of each  $\text{Ph}_2\text{P}$  moiety are diastereotopic.



Scheme 2. Ligand synthesis: (a) TosCl, pyridine, 51%; (b) see Table 1

It is remarkable, that — in our hands — bisphosphane **1a** shows only a very low tendency to oxidize in air at room temperature, although at elevated temperatures, especially in solution, formation of phosphane oxides is detectable by <sup>31</sup>P NMR.

The hydroxyalkyl phosphanes **2a** and **2b** and thioethers **2c–2f** have been prepared from the corresponding hydroxy tosylates **5a** and **5b** (Scheme 2), which are derived in enantiomerically pure form from (*S*)-(-)-ethyl lactate and (*S*)-(+)-ethyl mandelate.<sup>1</sup> Substitution with  $\text{KPh}_2$  in DMF/THF or NaSR in DMF proceeds in high yields (Table 1). In the case of the phosphanes **2a** and **2b** all expected phosphorus couplings are observed in the NMR spectra. Moreover, the Ph groups of the  $\text{Ph}_2\text{P}$  moieties appear to be

Table 1  
Yields and reaction conditions

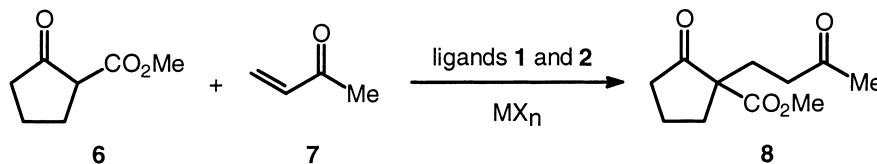
Product	Yield	Starting Material	Nucleophile	Conditions
<b>1a</b>	47%	<b>4</b>	KPh <sub>2</sub>	DMF/THF, 0°C → rt
<b>1b</b>	80%	<b>4</b>	NaSEt	DMF, rt
<b>1c</b>	66%	<b>4</b>	NaSPh	DMF, rt
<b>2a</b>	38%	<b>5a</b>	KPh <sub>2</sub>	DMF/THF, 0°C → rt
<b>2b</b>	44%	<b>5b</b>	KPh <sub>2</sub>	DMF/THF, 0°C → rt
<b>2c</b>	81%	<b>5a</b>	NaSEt	DMF, rt
<b>2d</b>	90%	<b>5a</b>	NaSPh	DMF, rt
<b>2e</b>	86%	<b>5b</b>	NaSEt	DMF, rt
<b>2f</b>	91%	<b>5b</b>	NaSPh	DMF, rt

diastereotopic. Besides that, it is remarkable that the specific rotation of compound **2a** shows a strong dependence on the solvent and concentration: it has a positive sign ( $[\alpha]_D^{20} +21.5$ , c 12.1) in CHCl<sub>3</sub>, while it is negative in AcOEt ( $[\alpha]_D^{20} -3.8$ , c 8.6).

Although there are already syntheses of compounds **2** reported in the literature, the presented route is superior to the others: the regioselectivity problem of the epoxide opening is avoided as well as the need for an asymmetric reaction to build up the stereogenic center, because the stereo information is derived from the chiral pool.

### 3. Asymmetric Michael reactions

Recently, Shibasaki has introduced an excellent heterobimetallic catalyst for the Michael reaction of  $\beta$ -dicarbonyl compounds with  $\alpha,\beta$ -unsaturated ketones.<sup>11,12</sup> However, the reaction conditions are strongly basic, thus often causing a number of unwanted side- and subsequent processes. The need for a neutral transition metal catalyst has been — more or less successfully — addressed by a number of groups in the past years.<sup>13–17</sup> As our contribution to this topic we screened all nine ligands **1a–1c** and **2a–2f** with 12 metal salts<sup>†</sup> (which we knew would catalyze the Michael reaction, shown in Scheme 3, at least to some extent at room temperature) in a combinatorial approach: separately, 108 (9 ligands  $\times$  12 metal salts) catalytic systems were formed in situ and screened for enantioselectivity in the catalysis of the Michael reaction of oxoester **6** with methyl vinyl ketone **7** (Scheme 3). Analysis of the product **8** was performed by chiral GC. Details are given in the experimental section. Unfortunately, in none of our experiments was an enantioselectivity of more than 10% *ee* detectable.



Scheme 3. Metal catalyzed Michael reaction, screening of ligands **1** and **2** with metal compounds MX<sub>n</sub>

<sup>†</sup> List of applied metal salts: CrCl<sub>3</sub>·6H<sub>2</sub>O, Mn(OAc)<sub>2</sub>·4H<sub>2</sub>O, FeCl<sub>3</sub>·6H<sub>2</sub>O, Ni(OAc)<sub>2</sub>·4H<sub>2</sub>O, NiCl<sub>2</sub>·6H<sub>2</sub>O, CoCl<sub>2</sub>·6H<sub>2</sub>O, RhCl<sub>3</sub>·3H<sub>2</sub>O, Cu(OAc)<sub>2</sub>·H<sub>2</sub>O, AgOAc, ZnCl<sub>2</sub>, SnCl<sub>2</sub>, Pb(OAc)<sub>2</sub>·3H<sub>2</sub>O.

## 4. Summary

Three new chiral tridentate ligands with *P,O,P*- and *S,O,S*-donor sets and six enantiopure hydroxyethyl phosphanes and thioethers have been prepared from commercially available natural chiral  $\alpha$ -hydroxy acids and tested as ligands in the asymmetric catalysis of the Michael reaction.

## 5. Experimental

### 5.1. General

Column chromatography was accomplished with Merck silica gel (Type 60, 0.063–0.200 mm).  $^1\text{H}$  NMR spectra were recorded on a Bruker AM 400 (400 MHz), and reported in parts per million (ppm) using the residual proton solvent peak of  $\text{CDCl}_3$  at 7.26 ppm as an internal standard, with coupling constants (J) in hertz (Hz).  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AC 200 (50 MHz,  $^1\text{H}$  decoupled), and reported in parts per million (ppm) using the solvent triplet of  $\text{CDCl}_3$  at 77.0 ppm as an internal standard. Assignments were made using DEPT experiments.  $^{31}\text{P}$  NMR spectra were recorded on a Bruker AC 200 (80 MHz) using  $\text{PPh}_3$  (–6 ppm) in  $\text{CDCl}_3$  as an external standard. MS spectra were obtained with Varian MAT 711 and MAT 955Q (high resolution) instruments. IR spectra were recorded on a Nicolet Magna IR 750. Elemental analyses were obtained with an Analytik Jena Vario EL. Optical rotations were measured with a Perkin–Elmer polarimeter 341. Chiral GC analysis was performed on a Packard 437A with FI detection, a Shimadzu C-R6A integrator and a Macherey–Nagel column FS-LIPODEX E (25 m, 0.25 mm) with nitrogen carrier gas.

Starting compounds **3**, **5a** and **5b** were synthesized according to literature procedures.<sup>1</sup> DMF (HPLC grade), NaSEt (90% technical quality), NaSPh (90% technical quality) and  $\text{KPPH}_2$  (0.5 M solution in THF) were purchased from the Aldrich Chemical Co. and used as received.

### 5.2. Abbreviations

ATR: attenuated total reflection; MTB: *tert*-butyl methyl ether; Tos: *p*-tolylsulfonyl.

### 5.3. (*S,S*)-(–)-Bis[2-(*p*-tolylsulfonyloxy)propyl]ether **4**

TosCl (1.49 g, 7.80 mmol) was added to a solution of the diol **3** (262 mg, 1.95 mmol) in pyridine (1.5 ml), and stirred overnight at room temperature. Water (10 ml) and  $\text{CH}_2\text{Cl}_2$  (10 ml) were added, and the mixture was stirred for 30 min. The layers were separated, and the aqueous layer was extracted three times with  $\text{CH}_2\text{Cl}_2$  (each 30 ml). The combined organic layers were washed with hydrochloric acid (18%, 50 ml), water (50 ml) and brine (50 ml). The solution was dried over  $\text{MgSO}_4$ , evaporated, and the crude product was chromatographed ( $\text{SiO}_2$ , MTB:hexane 1:1,  $R_f=0.29$ ) to give compound **4** (442 mg, 0.999 mmol, 51%) as a colorless oil.  $[\alpha]_D^{20} -9.9$  (c 11.3,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.19 (6H, d,  $J=6.5$  Hz), 2.44 (6H, s), 3.32 (2H, dd,  $J=4.4$  Hz,  $J=10.8$  Hz), 3.41 (2H, dd,  $J=5.7$  Hz,  $J=10.8$  Hz), 4.53–4.63 (2H, m), 7.30–7.35 (4H, m), 7.74–7.79 (4H, m).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  17.44 (2  $\text{CH}_3$ ), 21.59 (2  $\text{CH}_3$ ), 73.47 (2  $\text{CH}_2$ ), 77.79 (2 CH), 127.73 (4 CH), 129.73 (4 CH), 134.25 (2 C), 144.60 (2 C). IR (ATR): 3066 (w), 2984 (w), 2936 (w), 2874 (w), 1597 (w), 1495 (w), 1451 (w), 1401 (w), 1381 (w), 1348 (s), 1307 (w), 1291 (w), 1211 (w), 1189 (s), 1173 (vs), 1120 (m), 1097 (m), 1045 (w), 1019 (w), 972 (w), 916 (s), 904 (s), 876 (s), 814 (s), 764 (s), 705 (w), 662 (s). MS (EI, 70 eV)  $m/z$  (%)=442

(1), 270 (6), 243 (10), 229 (1), 213 (22), 173 (5), 155 (100), 91 (55), 65 (6). HRMS: Mol. mass calcd 442.1120 (for C<sub>20</sub>H<sub>26</sub>O<sub>7</sub>S<sub>2</sub>), found 442.1121 (M<sup>+</sup>). Anal. calcd for C<sub>20</sub>H<sub>26</sub>O<sub>7</sub>S<sub>2</sub> (442.55): C 54.28, H 5.92, found C 54.00, H 6.00.

#### 5.4. (R,R)-(+)-Bis[2-(diphenylphosphanyl)propyl]ether **1a**

KPPh<sub>2</sub> (5.8 ml of a 0.5 M solution in THF, 2.9 mmol) was added to a degassed (three times) solution of compound **4** (430 mg, 0.972 mmol) in DMF (5 ml) under an atmosphere of Ar at 0°C, stirred for 5 min in the cold, and overnight at room temperature. The mixture was hydrolyzed with water (10 ml), diluted with MTB (75 ml), and washed twice with water (each 50 ml). The organic layer was dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:30, R<sub>f</sub>=0.23) to give compound **1a** (213 mg, 0.453 mmol, 47%) as a colorless oil. [α]<sub>D</sub><sup>20</sup> +34.6 (c 14.8, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.07 (6H, dd, J=6.9 Hz, J=14.6 Hz), 2.54–2.74 (2H, m), 3.17–3.30 (2H, m), 3.30–3.44 (2H, m), 7.22–7.40 (12H, m), 7.40–7.58 (8H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>): δ 14.71 (2 CH<sub>3</sub>, d, J=14.9 Hz), 31.19 (2 CH<sub>3</sub>, d, J=10.9 Hz), 73.54 (2 CH<sub>2</sub>, d, J=23.7 Hz), 128.23 (8 CH, d, J=7.2 Hz), 128.60 (2 CH, s), 128.67 (2 CH, s), 133.27 (4 CH, d, J=19.2 Hz), 133.61 (4 CH, d, J=19.8 Hz), 136.39 (2 C, d, J=13.7 Hz), 136.86 (2 C, d, J=14.1 Hz). <sup>31</sup>P NMR (80 MHz, CDCl<sub>3</sub>): δ -8 (br s). IR (ATR): 3070 (m), 3052 (m), 3015 (w), 3000 (w), 2958 (m), 2924 (m), 2868 (m), 1585 (w), 1570 (w), 1480 (m), 1455 (w), 1433 (s), 1375 (w), 1354 (w), 1307 (w), 1269 (w), 1182 (w), 1157 (w), 1091 (s), 1071 (s), 1027 (m), 999 (m), 916 (w), 880 (w), 741 (s), 696 (vs). MS (EI, 70 eV) *m/z* (%)=470 (3), 285 (100), 262 (4), 227 (4), 185 (38), 183 (29), 109 (15), 108 (13), 77 (2). HRMS: Mol. mass calcd 470.1928 (for C<sub>30</sub>H<sub>32</sub>OP<sub>2</sub>), found 470.1922 (M<sup>+</sup>).

#### 5.5. (R,R)-(+)-Bis[2-(ethylsulfanyl)propyl]ether **1b**

A solution of compound **4** (1.64 g, 3.71 mmol) in DMF (7.5 ml) was added to a solution of NaSEt (1.25 g, 14.8 mmol) in DMF (7.5 ml), stirred overnight at room temperature in a tightly closed reaction flask, and diluted with MTB (50 ml). The mixture was washed three times with water (each 35 ml), dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:10, R<sub>f</sub>=0.50) to give compound **1b** (656 mg, 2.95 mmol, 80%) as a colorless oil. [α]<sub>D</sub><sup>20</sup> +59 (c 7.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 1.25 (6H, t, J=7.4 Hz), 1.28 (6H, d, J=7.0 Hz), 2.60 (2H, q, J=7.4 Hz), 2.61 (2H, q, J=7.4 Hz), 2.91–3.02 (2H, m), 3.40 (2H, dd, J=7.8 Hz, J=9.6 Hz), 3.54 (2H, dd, J=5.5 Hz, J=9.6 Hz). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>): δ 15.04 (2 CH<sub>3</sub>), 18.44 (2 CH<sub>3</sub>), 24.83 (2 CH<sub>2</sub>), 39.04 (2 CH), 76.12 (2 CH<sub>2</sub>). IR (ATR): 2964 (vs), 2927 (vs), 2869 (s), 2792 (w), 1728 (w), 1451 (s), 1375 (m), 1355 (w), 1295 (w), 1265 (m), 1210 (w), 1086 (vs), 1011 (w), 971 (w), 926 (w), 785 (w), 763 (w), 723 (w), 664 (w). MS (EI, 70 eV) *m/z* (%)=222 (1), 193 (1), 133 (6), 103 (100), 102 (79), 89 (75), 74 (23), 61 (26). HRMS: Mol. mass calcd 222.1112 (for C<sub>10</sub>H<sub>22</sub>OS<sub>2</sub>), found 222.1117 (M<sup>+</sup>). Anal. calcd for C<sub>10</sub>H<sub>22</sub>OS<sub>2</sub> (222.42): C 54.01, H 9.97, found C 54.01, H 10.02.

#### 5.6. (R,R)-(+)-Bis[2-(phenylsulfanyl)propyl]ether **1c**

A solution of compound **4** (453 mg, 1.02 mmol) in DMF (3 ml) was added to NaSPh (404 mg, 3.06 mmol), stirred overnight at room temperature in a tightly closed reaction flask, and diluted with MTB (30 ml). The mixture was washed twice with water (each 20 ml), dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:50, R<sub>f</sub>=0.11) to give compound **1c** (213 mg, 0.669 mmol, 66%) as a colorless oil. [α]<sub>D</sub><sup>20</sup> +50 (c 6.4, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz,

CDCl<sub>3</sub>):  $\delta$  1.24–1.30 (6H, m), 3.28–3.47 (4H, m), 3.47–3.59 (2H, m), 7.19–7.37 (6H, m), 7.37–7.49 (4H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  18.01 (2 CH<sub>3</sub>), 42.21 (2 CH<sub>3</sub>), 74.86 (2 CH<sub>2</sub>), 126.84 (2 CH), 128.76 (4 CH), 131.87 (4 CH), 134.46 (2 C). IR (ATR): 3073 (w), 3056 (w), 2966 (w), 2925 (w), 2864 (w), 2791 (w), 1583 (w), 1572 (w), 1474 (m), 1438 (m), 1374 (w), 1354 (w), 1291 (w), 1268 (w), 1208 (w), 1088 (s), 1067 (s), 1024 (m), 1014 (m), 911 (w), 737 (vs), 689 (vs). MS (EI, 70 eV)  $m/z$  (%)=318 (12), 181 (5), 168 (39), 151 (100), 137 (86), 123 (28), 109 (69), 77 (13). HRMS: Mol. mass calcd 318.1112 (for C<sub>18</sub>H<sub>22</sub>OS<sub>2</sub>), found 318.1113 (M<sup>+</sup>). Anal. calcd for C<sub>18</sub>H<sub>22</sub>OS<sub>2</sub> (318.50): C 67.88, H 6.96, found C 68.03, H 7.21.

### 5.7. (S)-(+)-(2-Hydroxy-1-propyl)-diphenylphosphane **2a**

KPPh<sub>2</sub> (3.0 ml of a 0.5 M solution in THF, 1.5 mmol) was added to a degassed (three times) solution of tosylate **5a** (230 mg, 1.00 mmol) in DMF (2 ml) under an atmosphere of Ar at 0°C, stirred for 5 min in the cold, and overnight at room temperature. The mixture was hydrolyzed with water (10 ml), diluted with MTB (75 ml), and washed twice with water (each 50 ml). The organic layer was dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:1,  $R_f$ =0.40) to give **2a** (93.0 mg, 0.381 mmol, 38%) as a colorless oil.  $[\alpha]_D^{20}$  +21.5 (c 12.1, CHCl<sub>3</sub>),  $[\alpha]_D^{20}$  -3.8 (c 8.6, AcOEt; lit.<sup>5</sup> -7.2, c 2, AcOEt). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.32 (3H, d, J=6.1 Hz), 2.02 (1H, br s), 2.27–2.43 (2H, m), 3.87–3.97 (1H, m), 7.28–7.60 (10H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  24.51 (CH<sub>3</sub>, d, J=6.3 Hz), 39.17 (CH<sub>2</sub>, d, J=12.1 Hz), 65.67 (CH, d, J=16.5 Hz), 128.1–128.7 (6 CH, m), 132.49 (2 CH, d, J=18.4 Hz), 132.72 (2 CH, d, J=18.6 Hz), 137.6–138.4 (2 C, m). <sup>31</sup>P NMR (80 MHz, CDCl<sub>3</sub>):  $\delta$  -24 (br s). IR (ATR): 3383 (s), 3070 (w), 3053 (w), 2966 (m), 2928 (w), 2898 (w), 1585 (w), 1481 (m), 1454 (w), 1433 (s), 1405 (w), 1375 (w), 1306 (w), 1273 (w), 1213 (w), 1183 (w), 1157 (w), 1118 (m), 1098 (m), 1063 (m), 1018 (m), 1000 (w), 936 (m), 861 (w), 810 (w), 738 (s), 696 (vs). MS (EI, 70 eV)  $m/z$  (%)=244 (89), 227 (8), 202 (26), 199 (100), 186 (54), 183 (57), 121 (95), 108 (57), 91 (18), 77 (9). HRMS: Mol. mass calcd 244.1017 (for C<sub>15</sub>H<sub>17</sub>OP), found 244.1019 (M<sup>+</sup>). Anal. calcd for C<sub>15</sub>H<sub>17</sub>OP (244.27): C 73.76, H 7.01, found C 73.19, H 7.04.

### 5.8. (S)-(+)-(2-Hydroxy-2-phenyl-1-ethyl)-diphenylphosphane **2b**

KPPh<sub>2</sub> (3.0 ml of a 0.5 M solution in THF, 1.5 mmol) was added to a degassed (three times) solution of tosylate **5b** (292 mg, 1.00 mmol) in DMF (2 ml) under an atmosphere of Ar at 0°C, stirred for 5 min in the cold, and overnight at room temperature. The mixture was hydrolyzed with water (10 ml), diluted with MTB (75 ml), and washed twice with water (each 50 ml). The organic layer was dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:3,  $R_f$ =0.26) to give compound **2b** (134 mg, 0.437 mmol, 44%) as a colorless oil.  $[\alpha]_D^{20}$  +43.8 [c 10.7, CHCl<sub>3</sub>; lit.<sup>6</sup> -36 for (R)-**2b**, no concentration and solvent given]. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  2.33 (1H, br s), 2.57 (1H, ddd, J=1.6 Hz, J=4.9 Hz, J=13.9 Hz), 2.63 (1H, ddd, J=1.5 Hz, J=8.8 Hz, J=13.9 Hz), 4.79 (1H, ddd, J=4.9 Hz, J=7.1 Hz, J=8.8 Hz), 7.22–7.58 (15H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  39.63 (CH<sub>2</sub>, d, J=13.9 Hz), 71.90 (CH, d, J=16.9 Hz), 125.63 (2 CH), 127.54 (CH), 128.1–128.6 (7 CH, m), 128.71 (CH), 132.49 (2 CH, d, J=18.5 Hz), 132.94 (2 CH, d, J=19.2 Hz), 137.79 (C, d, J=12.3 Hz), 138.26 (C, d, J=11.5 Hz), 144.44 (C, d, J=6.1 Hz). <sup>31</sup>P NMR (80 MHz, CDCl<sub>3</sub>):  $\delta$  -23 (br s). IR (ATR): 3559 (m), 3385 (vs), 3068 (m), 3053 (m), 3029 (w), 3001 (w), 2938 (w), 2901 (w), 1953 (w), 1884 (w), 1812 (w), 1601 (w), 1585 (w), 1571 (w), 1492 (w), 1481 (m), 1454 (m), 1433 (s), 1406 (w), 1329 (w), 1306 (w), 1273 (w), 1183 (w), 1157 (w), 1095 (w), 1046 (m), 1026 (s), 1000 (m), 969 (w), 914 (w), 878 (w), 846 (w), 807 (w), 770 (m), 739 (s), 723 (s), 696 (vs). MS (EI, 70 eV)  $m/z$  (%)=306 (17), 262 (63), 199

(100), 186 (13), 183 (26), 121 (77), 108 (15), 91 (13), 77 (22). HRMS: Mol. mass calcd 306.1174 (for C<sub>20</sub>H<sub>19</sub>OP), found 306.1174 (M<sup>+</sup>). Anal. calcd for C<sub>20</sub>H<sub>19</sub>OP (306.34): C 78.42, H 6.25, found C 78.08, H 6.20.

### 5.9. (S)-(+)-Ethyl-(2-hydroxy-1-propyl)thioether **2c**

Attention: Due to the high volatility of the product **2c** all evaporation processes should be done carefully. A solution of the tosylate **5a** (461 mg, 2.00 mmol) in DMF (3 ml) was added to NaSEt (336 mg, 4.00 mmol), and stirred overnight at room temperature in a tightly closed reaction flask, and diluted with MTB (75 ml). The mixture was washed twice with water (each 50 ml), dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:1, R<sub>f</sub>=0.31) to give compound **2c** (194 mg, 1.61 mmol, 81%) as a yellowish oil. [ $\alpha$ ]<sub>D</sub><sup>20</sup> +78.7 (c 13.8, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.25 (3H, d, J=6.2 Hz), 1.27 (3H, t, J=7.4 Hz), 2.44 (1H, dd, J=9.0 Hz, J=13.7 Hz), 2.56 (2H, q, J=7.4 Hz), 2.57 (1H, br s), 2.74 (1H, dd, J=3.5 Hz, J=13.7 Hz), 3.78–3.88 (1H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  14.59 (CH<sub>3</sub>), 21.77 (CH<sub>3</sub>), 25.89 (CH<sub>2</sub>), 40.82 (CH<sub>2</sub>), 65.39 (CH). IR (ATR): 3396 (s), 2970 (s), 2926 (vs), 2875 (m), 2855 (m), 1733 (m), 1496 (w), 1454 (m), 1375 (m), 1355 (w), 1266 (m), 1205 (w), 1177 (m), 1129 (m), 1079 (s), 1059 (s), 1029 (m), 938 (w), 730 (w), 702 (w). MS (EI, 70 eV) *m/z* (%)=120 (100), 105 (11), 77 (13), 76 (81), 75 (41), 61 (57), 59 (17). HRMS: Mol. mass calcd 120.0609 (for C<sub>5</sub>H<sub>12</sub>OS), found 120.0610 (M<sup>+</sup>).

### 5.10. (S)-(+)-(2-Hydroxy-1-propyl)-phenyl thioether **2d**

A solution of the tosylate **5a** (461 mg, 2.00 mmol) in DMF (3 ml) was added to NaSPh (529 mg, 4.00 mmol), stirred overnight at room temperature in a tightly closed reaction flask, and diluted with MTB (75 ml). The mixture was washed twice with water (each 50 ml), dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:1, R<sub>f</sub>=0.40) to give compound **2d** (302 mg, 1.79 mmol, 90%) as a yellowish oil. [ $\alpha$ ]<sub>D</sub><sup>20</sup> +60.1 [c 12.2, CHCl<sub>3</sub>; lit.<sup>9</sup> +54.7, c 1, CHCl<sub>3</sub>]. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.27 (3H, d, J=6.2 Hz), 2.33 (1H, br s), 2.84 (1H, dd, J=8.6 Hz, J=13.7 Hz), 3.12 (1H, dd, J=3.6 Hz, J=13.7 Hz), 3.80–3.89 (1H, m), 7.18–7.41 (5H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  21.83 (CH<sub>3</sub>), 43.28 (CH<sub>2</sub>), 65.54 (CH), 126.39 (CH), 128.90 (2 CH), 129.81 (2 CH), 135.26 (C). IR (ATR): 3378 (s), 3075 (w), 3058 (w), 2970 (m), 2918 (w), 1584 (m), 1480 (m), 1438 (m), 1409 (w), 1372 (w), 1302 (w), 1264 (w), 1239 (w), 1186 (w), 1123 (m), 1068 (m), 1036 (m), 1025 (s), 934 (m), 874 (w), 816 (w), 736 (vs), 689 (vs). MS (EI, 70 eV) *m/z* (%)=168 (72), 135 (4), 124 (100), 123 (36), 110 (15), 109 (20), 91 (31), 78 (26), 65 (10), 51 (14). HRMS: Mol. mass calcd 168.0609 (for C<sub>9</sub>H<sub>12</sub>OS), found 168.0612 (M<sup>+</sup>).

### 5.11. (S)-(+)-Ethyl-(2-hydroxy-2-phenyl-1-ethyl)thioether **2e**

A solution of the tosylate **5b** (585 mg, 2.00 mmol) in DMF (3 ml) was added to NaSEt (336 mg, 4.00 mmol), stirred overnight at room temperature in a tightly closed reaction flask, and diluted with MTB (75 ml). The mixture was washed twice with water (each 50 ml), dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:2, R<sub>f</sub>=0.38) to give compound **2e** (313 mg, 1.72 mmol, 86%) as a yellowish oil. [ $\alpha$ ]<sub>D</sub><sup>20</sup> +81 [c 6.4, CHCl<sub>3</sub>; lit.<sup>10</sup> -75.8 for (*R*)-**2e**, c 2.19, CHCl<sub>3</sub>]. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.28 (3H, t, J=7.4 Hz), 2.58 (2H, q, J=7.4 Hz), 2.73 (1H, dd, J=9.6 Hz, J=13.8 Hz), 2.95 (1H, dd, J=3.6 Hz, J=13.8 Hz), 3.03 (1H, br s), 4.71–4.77 (1H, m), 7.25–7.41 (5H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  14.51 (CH<sub>3</sub>), 25.81 (CH<sub>2</sub>), 41.12 (CH<sub>2</sub>), 71.65 (CH), 125.56 (2

CH), 127.46 (CH), 128.14 (2 CH), 142.48 (C). IR (ATR): 3423 (vs), 3085 (w), 3062 (w), 3029 (w), 2925 (m), 2871 (w), 1952 (w), 1882 (w), 1809 (w), 1756 (w), 1602 (w), 1585 (w), 1493 (m), 1453 (s), 1409 (m), 1376 (m), 1332 (w), 1266 (m), 1231 (w), 1194 (m), 1081 (w), 1058 (s), 1028 (s), 1002 (w), 980 (m), 915 (w), 860 (w), 769 (m), 758 (m), 730 (s), 699 (vs). MS (EI, 70 eV)  $m/z$  (%)=182 (4), 107 (58), 91 (6), 79 (44), 77 (31), 76 (100), 61 (11). HRMS: Mol. mass calcd 182.0765 (for C<sub>10</sub>H<sub>14</sub>OS), found 182.0761 (M<sup>+</sup>). Anal. calcd for C<sub>10</sub>H<sub>14</sub>OS (182.29): C 65.89, H 7.74, found C 65.58, H 7.90.

### 5.12. (S)-(-)-(2-Hydroxy-2-phenyl-1-ethyl)-phenyl thioether **2f**

A solution of the tosylate **5b** (585 mg, 2.00 mmol) in DMF (3 ml) was added to NaSPh (529 mg, 4.00 mmol), stirred overnight at room temperature in a tightly closed reaction flask, and diluted with MTB (75 ml). The mixture was washed twice with water (each 50 ml), dried over MgSO<sub>4</sub>, and evaporated to dryness. The crude product was chromatographed (SiO<sub>2</sub>, MTB:hexane 1:3, R<sub>f</sub>=0.35) to give compound **2f** (420 mg, 1.82 mmol, 91%) as a yellowish oil. [ $\alpha$ ]<sub>D</sub><sup>20</sup> -12.5 [c 13.9, CHCl<sub>3</sub>; lit.<sup>10</sup> +8.6 for (R)-**2f**, c 1.07, CHCl<sub>3</sub>]. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  2.85 (1H, br s), 3.10 (1H, dd, J=9.5 Hz, J=13.8 Hz), 3.34 (1H, dd, J=3.4 Hz, J=13.8 Hz), 4.73 (1H, dd, J=3.4 Hz, J=9.5 Hz), 7.21–7.46 (10H, m). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  43.75 (CH<sub>2</sub>), 71.61 (CH), 125.76 (2 CH), 126.59 (CH), 127.85 (CH), 128.42 (2 CH), 129.00 (2 CH), 130.00 (2 CH), 134.93 (C), 142.09 (C). IR (ATR): 3394 (s), 3059 (w), 3029 (w), 3003 (w), 2919 (w), 2886 (w), 1601 (w), 1582 (m), 1493 (w), 1480 (m), 1453 (m), 1438 (m), 1408 (w), 1332 (w), 1302 (w), 1230 (w), 1192 (w), 1156 (w), 1086 (w), 1053 (m), 1025 (s), 1001 (w), 989 (w), 914 (w), 858 (w), 768 (w), 737 (vs), 698 (vs), 689 (vs). MS (EI, 70 eV)  $m/z$  (%)=230 (9), 124 (100), 107 (29), 91 (8), 79 (21), 77 (15), 65 (3), 51 (7). HRMS: Mol. mass calcd 230.0765 (for C<sub>14</sub>H<sub>14</sub>OS), found 230.0763 (M<sup>+</sup>). Anal. calcd for C<sub>14</sub>H<sub>14</sub>OS (230.33): C 73.01, H 6.13, found C 73.12, H 6.25.

### 5.13. Asymmetric catalysis: ethyl 2-(3-oxobutyl)cyclopentanone-2-carboxylate **8**

Metal compound (0.05 mmol, 5 mol%), chiral ligand **1** (0.075 mmol, 7.5 mol%) or **2** (0.1 mmol, 10 mol%) and oxoester **6** (156 mg, 1.0 mmol) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1 ml). After stirring for 1 h at room temperature methyl vinyl ketone **7** (84 mg, 1.2 mmol) was added and the mixture was stirred overnight at room temperature. Subsequently, all volatile materials were removed in vacuo and the residue was filtered through SiO<sub>2</sub> (MTB:hexane 1:1, R<sub>f</sub>=0.25). The product mixture was analyzed by chiral GC, isothermal elution (130°C).

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