Synthesis of New Chiral P,S Hybrid Ligands and Their Use in Asymmetric Hydrosilylation of Ketones[1)]

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Novel chiral P,S-hybrid ligands bearing 1,2-*cis* phosphinomethyl (or thiomethyl) and thio (or phosphino) groups on a cyclopentane skeleton were prepared by using borane as a protecting group for the phosphino group. Asymmetric hydrosilylation of acetophenone with 1 mol% of rhodium complex catalysts prepared *in situ* from $[Rh(COD)Cl]_2$ and P,S ligands, (1*R*,2*R*)-2-(diphenylphosphino)methyl-1-(phenylthio)cyclopentane (TPCP) and (1*R*,2*S*)-1-diphenylphosphino-2-[(phenylthio)methyl]cyclopentane (PTCP) gave the corresponding alcohols. The asymmetric hydrosilylation with the ligand TPCP showed higher enantioselectivity than that with PTCP or a diphosphine ligand (1*R*,2*R*)-1-(diphenylphosphino)-2-[(diphenylphosphino)methyl]cylopentane (PPCP).

Key words sulfide-phosphine ligand; asymmetric hydrosilylation; rhodium(I)-complex; ketone

For more than two decades, various types of C_2-symmetric and non-symmetric chiral ligands mostly bearing phosphine(s) and/or nitrogen(s) have been developed and employed in asymmetric reactions with transition metal catalysts. We have developed several non-symmetric diphosphine ligands, and used them in efficient enantioselective metal-catalyzed hydrogenations[2)] and allylic substitution. However, sulfur-containing ligands have scarcely been used for metal-catalyzed reactions, probably because sulfur compounds are well-known to deactivate metal catalysts. Only a few ligands bearing S-functional groups have been successfully employed in catalytic asymmetric reactions; for example, asymmetric hydrosilylation with a PS-ligands–Rh complex,[3)] asymmetric allylation with SN-ligand–Pd complexes,[4)] and asymmetric Michael addition with SN-ligand–Cu complexes.[5)] Two different functional groups of these non-symmetric ligands were thought to play roles in the relatively high enantioselectivity and catalytic activity on the basis of their electronic effects as well as steric effects, but the ditails have not been clarified.

We describe here the preparation of new P,S-hybrid ligands, (1*R*,2*R*)-2-(diphenylphosphino)methyl-1-(phenylthio)cyclopentane (TPCP, **1**) and (1*R*,2*S*)-1-diphenylphosphino-2-[(phenylthio)methyl]cyclopentane (PTCP, **2**) bearing 1,2-*cis* phosphinomethyl (or thiomethyl) and thio (or phosphiono) groups on a cyclopentane skeleton, and their application to Rh-catalyzed asymmetric hydrosilylation of ketones.

Previously, we reported the design and the synthesis of a 1,3-substituted bisphosphine ligand (1*R*,2*R*)-1-(diphenylphosphino)-2-[(diphenylphosphino)methyl]cyclopentane (PPCP, 4) with a 6-membered chelate ring that selectively adopts a skew conformation.[6)] A new chiral cyclopentane sulfide–phosphine ligand, TPCP bearing a phenylthio group at C_1 and a diphenylphosphinomethyl group at C_2 of the cyclopentane ring was synthesized from the ditosylate (**5**) as shown in Chart 2. Selective mono diphenylphosphination of the primary tosyloxy group of **5** was carried out by reaction with potassium diphenylphosphide in tetrahydrofuran (THF) at −30 °C overnight. Phenylthiolation of the monophosphine compound with sodium thiophenoxide in dimethylformamide (DMF) at room temperature did not give the expected product, but a sulfide-phosphine oxide derivative. Therefore, the phosphino group of the monophosphine compound was protected by reaction with BH_3, and the resulting phosphine–borane (**6**) was allowed to react with sodium thiophenoxide, affording **7** in 51% yield. The free PS ligand TPCP (**1**) was obtained by removal of the BH_3 with diazabicyclooctane (DABCO).

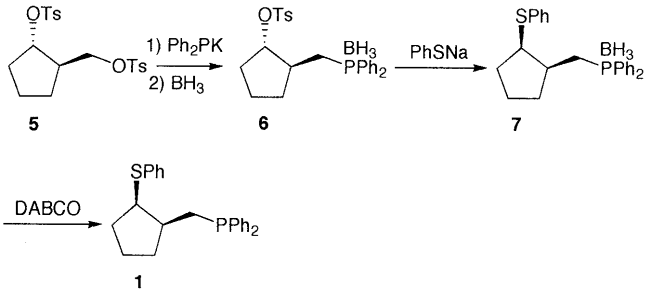

Chart 2

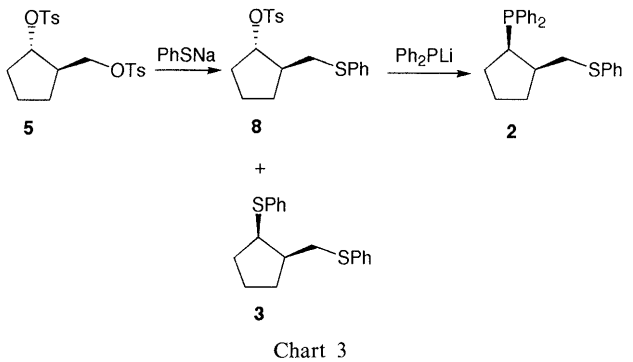

Chart 3

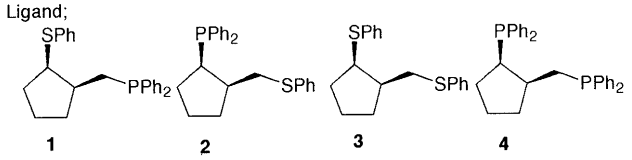

Chart 1

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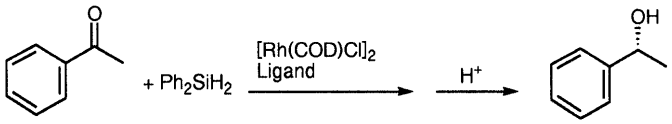

Chart 4

Table 1. Asymmetric Hydrosilylation of Acetophenone

Entry	Ligand	Solv.	Temp. (°C)	Conv. (%)	e.e. (%)[a]
1	PTCP (**1**)	Toluene	20	99	57(*R*)
2	TPCP (**2**)	Toluene	20	56	12(*R*)
3	TTCP (**3**)	Toluene	20	35	2(*R*)
4	PPCP (**4**)	Toluene	20	85	10(*R*)
5	PTCP (**1**)	Et_2O	20	82	47(*R*)
6	PTCP (**1**)	THF	20	22	33(*R*)
7	PTCP (**1**)	Toluene	2	35	45(*R*)

a) Determined by chiral GC analysis (Chirasile DEX CB).

Another P,S ligand, PTCP was synthesized in a similar manner. Selective phenylthiolation of the primary tosyloxy group of **5** was carried out by reaction with sodium thiophenoxide in DMF at 0 °C overnight, yielding **8** (48%) along with a disulfide compound (**3**) (25%) as a by-product. Diphenylphosphinylation of **8** with the lithium salt of diphenylphosphine in THF overnight at −30 °C gave PTCP (**2**).

The asymmetric hydrosilylation of acetophenone was carried out with the substrate (0.4 mmol), [Rh(1,5-cyclooctadiene)Cl]$_2$ (2.0×10^{-3} mmol), ligand (**1**, **2**, **3**, **4**) (4.8×10^{-3} mmol), and diphenylsilane (0.8 mmol) at 20 °C for 18 h in toluene (2 ml) under an argon atmosphere. The results are listed in Table 1.

Ligand **1** showed higher enantioselectivity (57% ee) than the other ligands **2**, **3**, **4** (2—12% ee) (entries 1—4). Hydrosilylation with ligand **3** was slower than with ligands **1**, **2** and **4** (entries 1—4). A solvent effect was observed; more polar solvents showed lower selectivity (entries 5 and 6). A lower temperature did not improve the enantioselectivity (entry 7).

In the first step, the hydrosilane should approach the metal from the direction parallel to the P–Rh(I) bond , which has higher electron density than the S–Rh(I) bond because an S-atom is a stronger π-acceptor than a P-atom. Then the ketone will coordinate cis to the S-atom under the influence of the silyl group. These ideas[7] are supported by the above results that the ligand **1**–Rh(I) complex in which ketone coordinates cis to the S-atom on C_1 showed higher enantioselectivity than the ligand **2**–Rh(I) complex. Since the phenylthio group at C_1 of ligand **1** plays an important role in the enantioselecting step, development of more efficient P,S ligands should be possible by introduction of a more chiral environment around the S-functional groups.

Experimental

All melting points were determined with a micromelting point apparatus (Yanagimoto) and are uncorrected. Optical rotations were measured on a JASCO DIP-140 digital polarimeter. ^{1}H-NMR spectra were recorded on a JEOL JNM-GX spectrometer using tetramethylsilane (TMS) as an internal standard; the abbreviations of signal pattern are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Column chromatography was carried out on silica gel (Kiesel gel 60, 70—230 mesh, Merck).

(1*S*,2*S*)-2-[(Boranatodiphenylphosphino)methyl]-1-[(4-methylphenyl)-sulfonyloxy]cyclopentane (6) Compound **5** (255 mg, 0.6 mmol) was stirred in THF under an argon atmosphere and a solution of 0.5 M potassium diphenylphosphide (1.44 ml, 0.72 mmol) in THF was added dropwise. The reaction solution was stirred for 17 h at −30 °C, then a solution of borane (1.1 ml, 1.1 mmol) in THF was added dropwise to it at 0 °C, and the whole was stirred for 3 h at room temperature. The reaction mixture was washed with degassed H_2O, dried over $MgSO_4$ with ice cooling under an argon atmosphere for 20 min and then evaporated. The residue was chromatographed on silica gel with degassed *n*-hexane–toluene as the eluent to provide white crystals, and recrystallization from degassed ethanol gave **6** (135 mg, 50%). mp 115 °C, $[\alpha]_D^{29}$ −2.77 (c=1.0, toluene). ^{1}H-NMR ($CDCl_3$) δ: 1.20—2.19 (m, 7H, $CH_2CH_2CH_2CH$), 2.41 (m, 3H, *p*–CH_3), 2.45—2.51 (m, 2H, P–CH_2), 4.65 (m, 1H, O–CH), 7.18—7.82 (m, 14H, Ar-H). *Anal.* Calcd for $C_{25}H_{30}BO_3PS$: C, 66.38; H, 6.68. Found: C, 66.18; H, 7.01.

(1*R*,2*R*)-2-[(Boranatodiphenylphosphino)methyl]-1-(phenylthio)cyclopentane (7) A solution of thiophenol (0.035 ml, 0.34 mmol) and 70% sodium hydride (11.7 mg, 0.34 mmol) in DMF (2 ml) was stirred for 1 h at room temperature under an argon atmosphere. This solution was added to a solution of **6** (76 mg, 0.17 mmol) in DMF (3 ml). The reaction solution was stirred for 16 h at room temperature, then washed with degassed H_2O, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with degassed toluene–AcOEt as the eluent to give **7** (34 mg, 51%). ^{1}H-NMR ($CDCl_3$) δ: 1.05—2.02 (m, 7H, $CH_2CH_2CH_2CH$), 2.20—2.88 (m, 2H, P–CH_2), 3.53—3.62 (m, 1H, S–CH), 7.13—7.80 (m, 15H, Ph). *Anal.* Calcd for $C_{24}H_{28}BPS$: C, 73.85; H, 7.23. Found: C, 73.35; H, 7.37.

(1*R*,2*R*)-2-(Diphenylphosphino)methyl-1-(phenylthio)cyclopentane (1) Compound **7** (34 mg, 0.087 mmol) was stirred in toluene under an argon atmosphere and a solution of DABCO (9.8 mg, 0.087 mmol) in toluene was added. The reaction mixture was stirred for 4 h at 40 °C, then evaporated and the residue was chromatographed on silica gel with degassed toluene as the eluent to give **1** (26 mg, 80%), as a viscous oil. FAB-MS: (M+H)] 377. $[\alpha]_D^{23}$ +20.8° (c=0.39, toluene). ^{1}H-NMR ($CDCl_3$) δ: 1.14—2.84 (m, 9H, $CH_2CH_2CH_2CH$–CH_2), 3.51—3.64 (m, 1H, S–CH), 7.04—7.89 (m, 15H, Ph). *Anal.* Calcd for $C_{24}H_{25}PS$: C, 76.56; H, 6.69. Found: C, 76.82; H, 6.41.

(1*S*,2*S*)-2-[(Phenylthio)methyl]-1-[(4-methylphenyl)-sulfonyloxy]-cyclopentane (8) A solution of thiophenol (0.72 ml, 7.0 mmol) and 70% sodium hydride (240 mg, 7.0 mmol) in DMF (5 ml) was stirred for 1 h at room temperature under an argon atmosphere. This solution was added to a solution of **5** (2.97 g, 7.0 mmol) in DMF (5 ml). The reaction mixture was stirred for 16 h at room temperature, washed with degassed H_2O, dried over $MgSO_4$ and then evaporated. The residue was chromatographed on silica gel with degassed toluene–AcOEt as the eluent to give **3** (504 mg, 24%) from the a first fraction and **8** (1.31 g, 51%) from the last fraction.

3: viscous oil. ^{1}H-NMR ($CDCl_3$) δ: 1.15—2.01 (m, 7H, CH_2CH_2-CH_2CH), 2.72—2.98 (m, 2H, S–CH_2), 3.52—3.61 (m, 1H, S–CH), 7.11—7.75 (m, 10H, Ph).

8: mp 71 °C $[\alpha]_D^{26}$ −3.22° (c=1.0, toluene). ^{1}H-NMR ($CDCl_3$) δ: 1.21—2.04 (m, 7H, $CH_2CH_2CH_2CH$), 2.42 (s, 3H, *p*–CH_3), 2.60—2.69, 2.90—2.99 (m, 2H, S–CH_2), 4.65—4.72 (m, 1H, O–CH), 7.11—7.81 (m, 9H, Ar-H). *Anal.* Calcd for $C_{19}H_{22}O_3S_2$: C, 62.95; H, 6.12. Found: C,62.75; H, 6.44.

(1*R*,2*S*)-1-Diphenylphosphino-2-[(phenylthio)methyl]cyclopentane (2) A solution of diphenylphosphine (0.83 ml, 4.8 mmol) and *n*-butyllithium (3.18 ml, 5.0 mmol) in THF/hexane was stirred for 30 min at −30 °C under an argon atmosphere. The mixture was added to a solution of **8** (181 mg, 0.5 mmol) in THF under an argon atmosphere and the whole was stirred for 17 h at room temperature. The mixture was filtered through Celite, which was then washed with degassed toluene. The filtrate and washing were combined, washed with degassed H_2O, dried over $MgSO_4$ with ice cooling under an argon atmosphere for 20 min and then evaporated. The residue was chromatographed on silica gel with degassed toluene as the eluent to give **2** (57 mg, 30%) as a viscous oil. FAB-MS: $(M+H)^+$ 377. *Anal.* Calcd for $C_{24}H_{25}PS$: C, 76.56; H, 6.69. Found: C,77.36; H, 6.85.

Asymmetric Hydrosilylation of Acetophenone (General Procedure) The catalysts were prepared *in situ* by reaction of 2.0×10^{-3} mmol of a [Rh(cod)Cl]$_2$ (chloro (1,5-cyclooctadiene) rhodium (I) dimer) with

4.8×10^{-3} mmol chiral ligand in 2 ml of degassed toluene under an argon atmosphere. The mixture was stirred for 10 min and then diphenylsilane (0.8 mmol) was added. Stirring was contined for a further 10 min, then acetophenone was added and the whole was stirred at 20 °C or 0 °C for 18 h. The reaction mixture was treated with 10% hydrochloric acid in MeOH. The hydrolyzed mixture was stirred for 30 min before further work-up. The organic compounds were then extracted with toluene, dried over magnesium sulfate, and evaporated to give α-methylbenzyl alcohol as a colorless oil. Optical yield was determinded by GC analysis using Chirasil DEX CB.

References and Notes

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