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Chiral diphenylselenophosphoramides: a new class of chiral ligands for the titanium(IV) alkoxide-promoted addition of diethylzinc to aldehydes

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Abstract

Chiral C_2-symmetric diphenylselenophosphoramides **1** and **2** were prepared from the reaction of diphenylselenophosphinic chloride with (1*R*,2*R*)-(−)-1,2-diaminocyclohexane and (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine, respectively, in high yields. Another novel chiral ligand **3** was prepared from the reaction of diphenylselenophosphinic chloride with (*R*)-(+)-1,1′-binaphthyl-2,2′-diamine using butyllithium as the base. The ligands were used as catalytic chiral ligands in the titanium(IV) alkoxide-promoted enantioselective addition reaction of diethylzinc to aldehydes.

1. Introduction

Previously we reported that chiral C_2-symmetric diphenylphosphoramide and diphenylthiophosphoramide of (1*R*,2*R*)-(−)-1,2-diaminocyclohexane were used as chiral ligands in the catalytic asymmetric addition reaction of diethylzinc to aldehydes in the presence of titanium(IV) isopropoxide to give the corresponding *sec*-alcohols with high ee.[1] This result prompted us to synthesize other such novel chiral ligands for catalytic asymmetric reactions. This time we decided to synthesize diphenylselenophosphoramides **1**, **2** and **3** as novel chiral ligands for the same titanium(IV) alkoxide-promoted addition reaction of diethylzinc to aldehydes. We selected selenophosphoramide as a novel chiral ligand because it is well known that the sulfur-containing compounds such as substituted β-aminothiols[2] and β-hydroxysulfides derived from D-camphor[3] are very effective chiral ligands for the enantioselective addition reaction of aldehydes and reduction of imides. This is largely due to the high coordination ability of sulfur atom to metal center and the bigger Van der Waals radius of the sulfur atom (N: 1.55; O: 1.52; P: 1.80; S: 1.80

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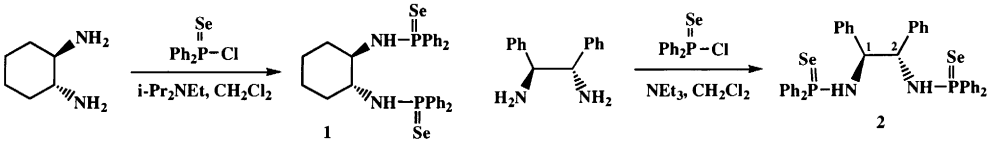
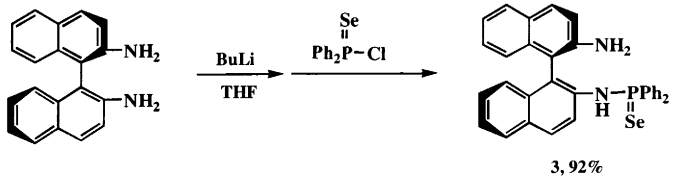
Å). The selenium atom has a similar coordination ability to various metals as sulfur and a slightly bigger Van der Waals radius (Se: 1.90 Å). However, we seldom see reports related to chiral ligands containing selenium.[4] Based on this concept and background, we expect that selenium bound to phosphorus could also have a good coordinative ability to metal centers, and a derived chiral metal complex could achieve chiral induction similar to thiophosphoramide ligands.[1]

2. Results and discussion

Diphenylselenophosphoramides **1** and **2** were synthesized from the reaction of diphenylselenophosphinic chloride with (1*R*,2*R*)-(−)-1,2-diaminocyclohexane and (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine in the presence of diisopropylethylamine or triethylamine in dichloromethane, respectively (Scheme 1). After the usual workup and purification by silica gel column chromatography or recrystallization, compounds **1** and **2** were obtained as colorless solids in over 90% yields. In addition, by utilizing the C_2-symmetric (*R*)-(+)-1,1′-binaphthyl-2,2′-diamine as a chiral scaffold, we prepared another novel chiral ligand **3** (Scheme 2).



Scheme 1.



Scheme 2.

The corresponding thiophosphoramide ligands have been synthesized using the same methods.[5] Their structures were confirmed by spectral data and microanalysis. Moreover, the crystal structure of **3** was disclosed by X-ray analysis (Fig. 1).[6]

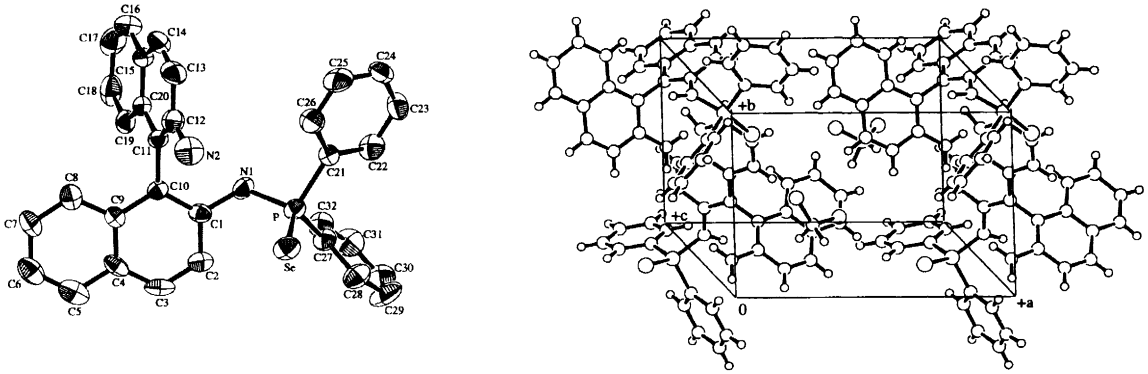
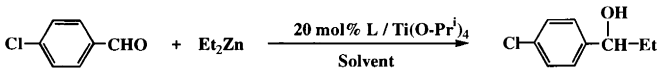


Fig. 1. The crystal structure of **3**

Interestingly, one dichloromethane molecule was included into the crystal lattice of **3** during the recrystallization from dichloromethane. These chiral ligands were used for the titanium(IV) isopropoxide-

promoted enantioselective addition reaction of diethylzinc to *p*-chlorophenylaldehyde in the presence of titanium(IV) isopropoxide [RCHO:Ti(OPr^i)$_4$:Et$_2$Zn=1:1.4:1.8] under various reaction conditions. The ees of the products were determined by HPLC analysis using chiral stationary-phase column (Chiralcel OD and OJ), and the absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation. The results are shown in Table 1.

Table 1
Asymmetric addition reaction of diethylzinc to *p*-chlorobenzaldehyde in the presence of chiral ligands **1**, **2** and **3** under different reaction conditions



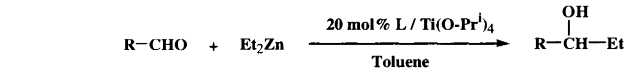
entry	Solvent	Ligand	Ti(O-Pr^i)$_4$ equiv.	Et$_2$Zn equiv.	Temp. [°C]	Time [h]	Yield[a] [%]	ee[b] [%]	Config.
1	Toluene	1	1.4	1.8	-20	24	93	55	R
2	Toluene	1	1.4	1.8	-50	24	92	60	R
3	CH_2Cl_2	1	1.4	1.8	-50	24	86	3	R
4	THF	1	1.4	1.8	-50	24	90	6	R
5	Toluene	2	1.4	1.8	-20	36	87	2	R
6	Toluene	2	1.4	1.8	-50	36	85	3	R
7	CH_2Cl_2	2	1.4	1.8	-50	36	82	3	R
8	Toluene	3	1.4	1.8	-20	36	80	30	R
9	Toluene	3	1.4	1.8	-50	36	82	40	R
10	CH_2Cl_2	3	1.4	1.8	-50	36	94	22	R

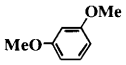
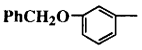
[a] Isolated yields. [b] Determined by chiral HPLC.

For the novel chiral ligand **1**, we found that the solvent drastically affected the enantiomeric excess (ee) of this asymmetric addition reaction as found for the analogous thiophosphoramide.[1] Toluene is a good solvent for achieving higher ee (60%) and the lowest ee of *sec*-alcohol was obtained in tetrahydrofuran (THF) and dichloromethane, although the yields of the reaction products are very similar to toluene. The best reaction conditions were found in toluene at −50°C with 60% ee (Table 1, entry 2). For chiral selenophosphoramides **2** and **3**, we found that the best results were obtained in toluene at −50°C with 3 and 40% ee, respectively (Table 1, entries 6 and 9). Among these three chiral selenophosphoramide ligands, **2** gave the lowest enantioselectivity. This may be due to chiral ligand **2** not having a rigid structure; namely, the two diphenylselenophosphoryl groups can rotate around the C_1 and C_2 bond. Thus it would be difficult to form a rigid chiral titanium(IV) complex to achieve asymmetric induction. By means of this optimized reaction conditions, various aldehydes were used as substrates for this addition reaction and the corresponding *sec*-alcohols could be obtained in 80–95% yield and 53–73, 3–5 and 40–46% ee with *R*-configuration, respectively. Their results are summarized in Table 2. For various aldehydes, **2** also gave the lowest ee. For aliphatic aldehyde using **1** as a chiral ligand, the ee decreased to 53%. It should be emphasized that the chiral selenophosphoramide ligands **1**, **2** and **3** could be recovered from the reaction mixture in 90% after the usual workup and can be used again in the asymmetric reaction without loss of enantioselectivity. Thus, the chiral diphenylselenophosphoramides **1**, **2** and **3** are quite stable chiral ligands in this asymmetric addition reaction. However, these selenophosphoramides are slightly photosensitive and gradually decompose upon sunlight irradiation. For chiral ligands **1** and **2**,

as expected, phosphoryl selenium atoms can coordinate to the titanium(IV) metal center to some extent giving a chiral environment, although the achieved ee is not perfect for **1** and very low for **2**. Meanwhile, for chiral ligand **3**, we believe that it is a bidentate chiral ligand; namely, the nitrogen and phosphoryl selenium atoms can coordinate to the titanium(IV) metal affording the chiral titanium(IV) complex. In order to verify this speculation, we are trying to get a single crystal of the catalyst to confirm their structures.

Table 2
Asymmetric addition reaction of diethylzinc to arylaldehydes in the presence of catalytic amounts of chiral ligands [L:RCHO:Ti(OPr^i)$_4$:Et$_2$Zn=0.2:1:1.4:1.8]



R	Ligand	Temp. [°C]	Time [h]	Yield[a] [%]	ee[b] [%]	Config.[d]
Ph	1	-50	24	93	61	R
p-MePh	1	-50	24	90	63	R
p-MeOPh	1	-50	24	95	64	R
	1	-50	24	90	71	R
	1	-50	24	88	73	R
1-Naphthyl	1	-50	24	90	70	R
Ph-CH=CH−	1	-50	24	94	63	R
n-C_4H_9	1	-50	24	92	53[c]	R
Ph	2	-50	36	86	3	R
p-MePh	2	-50	36	80	5	R
p-MeOPh	2	-50	36	87	5	R
Ph	3	-50	36	82	41	R
p-MePh	3	-50	36	80	46	R
p-MeOPh	3	-50	36	92	44	R

[a] Isolated yield. [b] Determined by chiral HPLC. [c] Determined by chiral GC.
[d] Determined by the sign of the specific rotation.

In conclusion, the chiral C_2-symmetric bidentate selenophosphoramides **1** and **2** prepared from C_2-symmetric (1*R*,2*R*)-(−)-1,2-diaminocyclohexane and (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine and monodiphenylselenophosphoramide **3** derived from (*R*)-(+)-1,1′-binaphthyl-2,2′-diamine were found to be a new class of relatively effective chiral ligands for the titanium(IV) isopropoxide-promoted enantioselective addition reaction of diethylzinc to aldehydes although they are not as effective as ditriflamide.[6] This paper discloses, for the first time, that chiral selenophosphoramides can catalyze the enantioselective ethylation reaction using titanium(IV) alkoxide. Hopefully, these results will open a new way to design and synthesize new chiral ligands for asymmetric reactions. Efforts are underway to

elucidate the mechanistic details of this addition reaction and to disclose the exact structure of the active species. Moreover, we are planning to synthesize other such bidentate chiral phosphoramides embedded into C_2-symmetric chiral scaffolds in order to seek out more effective and stereoselective chiral ligands and to utilize those novel chiral ligands to the other catalytic asymmetric reactions.

3. Experimental

3.1. General

Melting points (mps) were obtained with a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were determined in a solution of $CHCl_3$ at 20°C by using a Perkin–Elmer 241 MC polarimeter; $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; J values are in hertz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. Organic solvents used were dried by standard methods when necessary. All solid compounds reported in this paper gave satisfactory CHN microanalyses with an Italian Carlo Erba 1106 analyzer. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai $60F_{254}$ silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure. All ethylation experiments were performed under argon using standard Schlenk techniques. The optical purities of *sec*-alcohols were determined by HPLC analysis using a chiral stationary phase column (column, Daicel Co. Chiralcel OD and OJ; eluent, 100:0.5–2 hexane:2-propanol mixture; flow rate, 1.0 ml min^{-1}; detection, 254 nm light) and the absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation. Diphenylselenophosphinic chloride was prepared upon heating chlorodiphenylphosphine with selenium at 100°C for 6 h.

3.2. Preparation of chiral selenophosphoramide ***1***

To a solution of (1*R*,2*R*)-(−)-1,2-diaminocyclohexane (325 mg, 2.85 mmol) and diisopropylethylamine (1.10 g, 8.55 mmol, 1.5 ml) in dichloromethane (20 ml) was added diphenylselenophosphinic chloride (1.71 g, 5.70 mmol) at −30°C. After stirring the mixture for 6 h, the reaction mixture was washed with 3% aq. HCl, water, 10% Na_2CO_3 and brine, and the product was extracted with ether. The extract was dried over $MgSO_4$, and then evaporated under reduced pressure. The residue was purified by silica gel column chromatography to give the compound **1** (1.74 g, 95%) as a colorless solid. Mp 53–54°C; $[\alpha]_D$ +7.8 (*c* 3.6, $CHCl_3$); δ_H ($CDCl_3$) 1.0–1.20 (2H, m, CH_2), 1.22–1.42 (4H, m, CH_2), 1.43–1.60 (2H, m, CH_2), 1.70–1.90 (2H, m), 3.30–3.51 (2H, m), 3.90–4.02 (2H, m), 7.30–7.40 (4H, m, Ar), 7.40–7.60 (8H, m, Ar), 7.70–7.90 (4H, m, Ar), 7.95–8.12 (4H, m, Ar); MS (FAB) *m/z* (%): 640 (M^+, 40), 561 (30), 297 (40), 265 (100), 183 (80) [found: C, 55.89; H, 4.91; N, 4.07%. HRMS (FAB) *m/z*: 642.0368 (M^+); $C_{30}H_{32}N_2Se_2P_2$ requires: C, 56.26; H, 5.04; N, 4.37%; M, 642.0371].

3.3. Preparation of chiral selenophosphoramide ***2***

To a solution of (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (214 mg, 1.0 mmol) and triethylamine (300 mg, 3.0 mmol, 0.42 ml) in dichloromethane (20 ml) was added diphenylselenophosphinic chloride (598 mg, 2.0 mmol) at 0°C. After stirring the reaction mixture for 10 h, the solvent was removed under reduced

pressure. The crude product was extracted with ether and washed with water (3×50 ml), 10% Na_2CO_3 (50 ml) and brine. The organic layer was dried over anhydrous Na_2SO_4 and then evaporated under reduced pressure. The residue was recrystallized from dichloromethane and hexane (4:1) to give **2** as a colorless crystal (673 mg, 91%). Mp 170–172°C (dec.); $[\alpha]_D$ −56.2 (*c* 1.9, $CHCl_3$); δ_H ($CDCl_3$) 4.50–4.65 (2H, m, CH), 5.56–5.78 (2H, m, NH), 6.80–6.95 (4H, dd, *J*=7.4, 1.3 Hz, Ar), 7.0–7.20 (8H, m, Ar), 7.24–7.50 (10H, m, Ar), 7.55–7.75 (4H, m, Ar), 7.75–8.0 (4H, m, Ar); MS (EI) *m/z* (%): 738 (M^+, 10), 370 (70), 290 (30), 265 (100), 183 (90) [found: C, 61.77; H, 4.70; N, 3.80%. HRMS (EI) *m/z*: 740.0517 (M^+); $C_{38}H_{34}N_2Se_2P_2$ requires: C, 61.80; H, 4.64; N, 3.79%; M, 740.0528].

*3.4. Preparation of chiral selenophosphoramide **3***

To a solution of (*R*)-(+)-1,1′-binaphthyl-2,2′-diamine (244 mg, 0.84 mmol) in THF (20 ml) was added dropwise 2.0 M *n*-butyllithium in cyclohexane (1.20 ml, 2.4 mmol) at −40°C over 40 min and the reaction mixture was stirred for 1 h. Then diphenylselenophosphinic chloride (720 mg, 2.4 mmol) was added dropwise and the reaction solution was stirred for a further 10 h at −40°C to room temperature. The mixture was filtered to remove the solid and the THF was removed under reduced pressure. The organic product was extracted with ether and the organic layer was washed with water, 10% Na_2CO_3 and brine. The extract was dried over $MgSO_4$ and then evaporated under reduced pressure. The residue was purified by alumina (Al_2O_3) column chromatography to give the compound **3** as colorless solid (428 mg, 92%). Mp 110–115°C (dec.); $[\alpha]_D$ −9.0 (*c* 1.10, $CHCl_3$); δ_H ($CDCl_3$) 3.40 (2H, s, br, NH_2), 5.02 (1H, d, *J*=6.4 Hz), 7.0–7.50 (10H, m, Ar), 7.50–7.70 (4H, m, Ar), 7.70–8.0 (8H, m, Ar); MS (EI) *m/z* (%): 548 (M^+, 70), 467 (20), 391 (20), 283 (16), 267 (100) [found: C, 62.60; H, 4.22; N, 4.32%. HRMS (EI) *m/z*: 548.0918 (M^+); $C_{32}H_{25}N_2PSe{\cdot}CH_2Cl_2$ requires: C, 62.67; H, 4.30; N, 4.43%; M, 548.0921].

3.5. Typical reaction procedure

To a solution of selenophosphoramide **1** (104 mg, 0.16 mmol) in dichloromethane (5 ml) was added titanium(IV) isopropoxide (320 mg, 1.12 mmol, 0.33 ml) at room temperature. After stirring the mixture for 0.5 h, *p*-chlorobenzaldehyde (112 mg, 0.8 mmol) was added to the reaction solution and the reaction mixture was cooled to −50°C. Then diethylzinc (1.44 ml, 1.44 mmol, 1 M solution in hexane) was added to the solution and the reaction mixture was stirred for 48 h at −50°C. The reaction was quenched by 5% aq. HCl and the product was extracted with ether. The organic layer was washed with brine and dried over $MgSO_4$, and then evaporated under reduced pressure. The residue was purified by silica gel TLC to give the optically active 1-(*p*-chlorophenyl)propan-1-ol (125 mg, 92%).

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References

1. (a) Shi, M.; Sui, W.-S. *Tetrahedron: Asymmetry* **1999**, *10*, 3319, and references cited therein. For reviews and other references on catalytic enantioselective alkylation using dialkylzincs, see: (b) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49. (c) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833. (d) Schmidt, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.*

1991, *30*, 99. (e) Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, 2171. (f) Zhang, F.-Y.; Yip, C.-W.; Cao, R.; Chan, S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 585.

2. (a) Kang, J.; Lee, J. W.; Kim, J. I. *J. Chem. Soc., Chem. Commun*. **1994**, 2009; (b) Hof, R. P.; Poelert, M. A.; Peper, N. C. M. W.; Kellog, R. M. *Tetrahedron*: *Asymmetry* **1994**, *5*, 31; (c) Kang, J.; Lee, J. W.; Kim, J. I.; Pyum, C. *Tetrahedron Lett*. **1995**, *36*, 4265. (d) Rijnberg, E.; Jastrzebski, J. T. B. H.; Janssen, M. D.; Boersma, J.; Koten, G. v. *Tetrahedron Lett*. **1994**, *35*, 6521; (e) Carreno, M. C.; Ruano, J. L.; Maestro, M. C.; Cabrejas, L. M. M. *Tetrahedron*: *Asymmetry* **1993**, *4*, 727; (f) Masaki, Y.; Satoh, Y.; Makihara, T.; Shi, M. *Chem. Pharm. Bull*. **1996**, *44*, 454.
3. Arai, Y.; Nagata, N.; Masaki, Y. *Chem. Pharm. Bull*. **1995**, *43*, 2243.
4. For a few papers related to selenium ligands, see: (a) Kataoka, T.; Iwama, T.; Tsujiyama, S.-I.; Kanematsu, K.; Iwamura, T.; Watanabe, S.-I., *Chem. Lett*. **1999**, 257. (b) Kataoka, T.; Iwama, T.; Tsujiyama, S.-I. *J. Chem. Soc., Chem. Commun*. **1998**, 197. (c) Wirth, T. *Tetrahedron Lett*. **1995**, *36*, 7849.
5. Shi, M.; Sui, W.-S. *Tetrahedron: Asymmetry* **2000**, *11*, 773–779.
6. The crystal data of **3**. Empirical formula: $C_{33}H_{27}N_2SePCl_2$; formula weight: 632.43; crystal color, habit: colorless, prismatic; crystal dimensions: 0.20×0.20×0.30 mm; crystal system: monoclinic; lattice type: primitive; lattice parameters: a=11.950(3) Å, b=8.164(3) Å, c=16.127(3) Å, β=107.56(2) Å, V=1500.1(7) Å^3; space group: $P2_1$ (#4); Z value=2; D_{calc}=1.400 g/cm^3; F_{000}=644.00; μ(MoKα)=15.08 cm^{-1}; diffractometer: Rigaku AFC7R; temperature: 20°C; scan type: ω-2θ.