P-Chiral Phosphinoselenoic Chlorides and Optically Active *P*-Chiral Phosphinoselenoic Amides: Synthesis and Stereospecific Interconversion with Extrusion and Addition Reactions of the Selenium Atom

Tsutomu Kimura and Toshiaki Murai*
Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-1193

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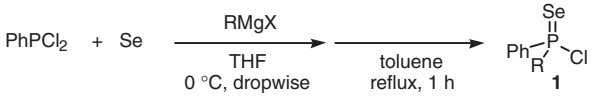
An efficient synthesis of *P*-chiral phosphinoselenoic chlorides and the first optically active *P*-chiral phosphinoselenoic amides was successfully achieved. Stereospecific interconversion with the extrusion of selenium atom from optically active phosphinoselenoic amides and the addition of selenium atom to optically active aminophosphines were also investigated.

P-Chiral organophosphorus compounds[1] are important not only in stereochemical studies of organophosphorus compounds but also as chiral ligands in transition metal-catalyzed asymmetric reactions.[2] Their key precursors, *P*-chiral chlorophosphines,[3] and phosphinic chlorides,[4] have been reported, but these have to be handled carefully because of their sensitivity toward air and water. Alternatively, *P*-chiral phosphinothioic chlorides[3,5] have been reported, although their synthesis involves several steps from readily available materials. The main drawback of phosphine oxides and sulfides is the fact that their reduction to trivalent phosphorus compounds requires strong reducing agents.[1] Moreover, the stereochemical course of the reduction depends on the reducing agents. Very recently, *P*-chiral chlorophosphine boranes have been introduced for use as good precursors of *P*-chiral organophosphorus compounds.[6] Nevertheless, more stable, but still reactive, *P*-chiral chlorophosphine equivalents are needed to conveniently provide optically active *P*-chiral organophosphorus compounds. We recently studied the synthesis and properties of phosphinoselenoic acid derivatives.[7] We report here the synthesis of *P*-chiral phosphinoselenoic chlorides and the first optically active *P*-chiral phosphinoselenoic amides. Stereospecific interconversion with the extrusion of selenium atom from optically active phosphinoselenoic amides and the addition of selenium atom to optically active aminophosphines are also described.

Initially, a one-pot synthetic procedure to give *P*-chiral phenylphosphinoselenoic chlorides[8] **1** was developed. After several disappointing results, the dropwise addition of a THF solution of Grignard reagent to a suspension of $PhPCl_2$ and elemental selenium in THF enabled the highly efficient synthesis of *P*-chiral phosphinoselenoic chlorides **1** (Table 1).[9] Notably, no decomposition of **1** took place during purification by column chromatography on silica gel. Various alkyl Grignard reagents were used to give the chlorides **1a**–**1c** in high to excellent yields (Entries 1–3). In reactions with aryl Grignard reagents, the yields of the products **1d**–**1f** decreased to some extent (Entries 4–6).[10] In all cases, the chlorides obtained were stable under air and in water. This is in marked contrast to the stability of phosphinic chlorides, which are readily hydrolyzed.

The phosphinoselenoic chlorides **1** were characterized spectroscopically. In the ^{31}P NMR spectra, signals of chlorides **1** were observed at 88 ± 23 ppm. Introduction of an aryl group to the phosphorus atom shifted the signals upfield. In the ^{77}Se NMR spectra, signals of chlorides **1** were observed in the range of -219 to -48 ppm, and those of the chlorides bearing two aryl groups **1d**–**1f** were downfield of those of **1a**–**1c**. Typical coupling constants of P=Se bonds (846 ± 8 Hz) were detected, and these were almost independent of the substituents on the phosphorus atom.

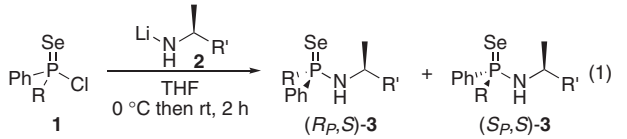
Table 1. Synthesis and selected NMR spectroscopic data of *P*-chiral phosphinoselenoic chlorides **1**[a]



Entry	**1**	R	Yield[b] %	^{31}P NMR ppm	^{77}Se NMR ppm	$^{1}J_{P-Se}$ Hz
1	**1a**	*i*-Pr	91	100.2	−219.7	841.9
2	**1b**	*c*-C_6H_{11}	96	95.8	−196.5	840.4
3	**1c**	*t*-Bu	94	111.0	−171.5	837.3
4	**1d**	*o*-$MeOC_6H_4$	38	66.3	−48.4	840.4
5	**1e**	*p*-MeC_6H_4	72	72.1	−68.4	846.4
6	**1f**	*p*-ClC_6H_4	68	69.9	−67.3	853.9

[a]The reaction was carried out with 8–30 mmol of $PhPCl_2$ and alkyl (1.0 equiv.) or aryl (0.2 equiv.) Grignard reagents in the presence of elemental selenium (1.1 equiv.) in THF under Ar. [b]Yields of isolated products based on the Grignard reagents.

P-Chiral phosphinoselenoic chlorides **1** showed high reactivity toward heteroatom-containing nucleophiles at the phosphorus atom. Among them, the first example of optically active *P*-chiral phosphinoselenoic amides **3** was synthesized by reacting **1** with optically active lithium amides **2** (Eq 1).[11] Two diastereomers of **3** were formed in a nearly equal ratio in high yields, and the two diastereomers were successfully separated by column chromatography on silica gel.



	(R_P,S)-**3**	(S_P,S)-**3**
3a: R = *i*-Pr, R' = *c*-C_6H_{11}	40%	41%
3b: R = *c*-C_6H_{11}, R' = 1-Naphthyl	34%	41%
3c: R = *t*-Bu, R' = Ph	34%	51%

The absolute configuration of phosphinoselenoic amide (R_P,S)-**3c** was determined by X-ray molecular structure analysis (Figure 1).[12] The phosphorus atom adopts a slightly distorted tetrahedral structure.

Finally, interconversion between optically active phosphinoselenoic amides and trivalent aminophosphines[13] was studied

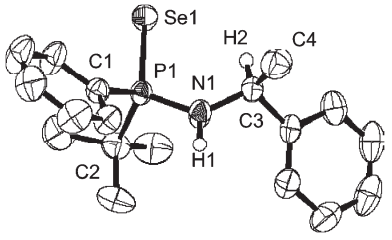
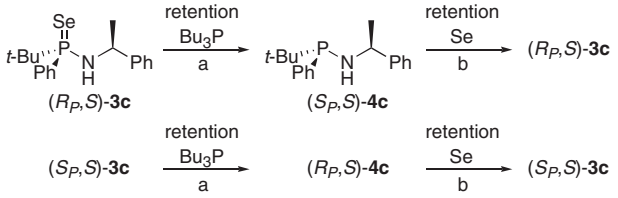


Figure 1. ORTEP drawing of (R_P, S)-**3c** with thermal ellipsoids (non-H atoms) at the 50% probability level. Hydrogen atoms (except for H1 and H2) are omitted for clarity. Selected bond lengths [Å], bond angles [°] and torsion angle [°]: P1–Se1 2.1180(7), P1–N1 1.652(2); Se1–P1–N1 113.00(8), Se1–P1–C1 110.75(9), Se1–P1–C2 112.47(10), N1–P1–C1 105.7(1), N1–P1–C2 106.8(1), P1–N1–C3 126.2(2); Se1–P1–N1–C3 −12.0(3).

because the stereochemical outcome of this type of reaction is of great interest.[1] The selenium atom of **3** was completely extruded at room temperature by reacting with Bu_3P (Scheme 1). Notably, the extrusion reaction of the selenium atom of (R_P, S)-**3c** proceeded with retention of configuration. Furthermore, the addition of a selenium atom to aminophosphine[14] (S_P, S)-**4c** also proceeded with retention of configuration. An identical stereochemical course was observed for a similar reaction of the diastereomer (S_P, S)-**3c**.



Scheme 1. Stereochemistry of interconversion between **3c** and **4c**. (a) THF, rt, 1 h; (b) THF, rt, 15 min.

In summary, we have reported the synthesis of *P*-chiral phosphinoselenoic chlorides and the first optically active *P*-chiral phosphinoselenoic amides. We described the stereospecific interconversion between the amides and aminophosphines. The broad applicability of chlorides has promoted synthetic studies on a series of *P*-chiral phosphinoselenoic acid derivatives.[15] The application of optically active *P*-chiral phosphinoselenoic amides and aminophosphines as chiral ligands[13,16] is also under investigation.

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9 Typical experimental procedure for the synthesis of the chlorides **1**: To a suspension of elemental selenium (33.0 mmol) in THF (150 mL) was added $PhPCl_2$ (30.0 mmol) at room temperature under an Ar atmosphere. To this mixture was added *t*-BuMgCl (1.0 M solution in THF, 30.0 mmol) in THF (120 mL) dropwise over a period of 1 h at 0 °C with vigorous stirring. After the solvent was removed, toluene (80 mL) was added to the residue, the mixture was stirred under reflux in toluene for 1 h, and the insoluble parts were filtered off. After the solvent was removed, the resulting oil was purified by column chromatography on silica gel (hexane:CH_2Cl_2 = 1:1) to give **1c** (94%) as a colorless solid.
10 It is very important to control the ratio of the reagents. Otherwise, products in which two equivalents of the Grignard reagent are introduced to the phosphorus atom of $PhPCl_2$ are formed.
11 Typical experimental procedure for the synthesis of the amides **3**: To a solution of (*S*)-1-phenylethylamine (2.2 mmol) in THF (5 mL) was added butyllithium (1.6 M solution in hexane, 2.0 mmol) at 0 °C, and the reaction mixture was stirred at that temperature for 10 min. To a solution of **1c** (2.0 mmol) in THF (5 mL) was added the reaction mixture at 0 °C, and the mixture was stirred at room temperature for 2 h. The mixture was extracted with CH_2Cl_2 (50 mL), and the organic layer was washed with water (50 mL × 2), dried over $MgSO_4$ and filtered off. After the solvent was removed, the resulting oil was purified by column chromatography on silica gel (hexane:CH_2Cl_2 = 1:1) to give (R_P, S)-**3c** (Rf = 0.4, 34%) as a colorless solid and (S_P, S)-**3c** (Rf = 0.3, 51%) as a colorless solid. The optical purity of **3** was determined by ^{31}P NMR spectra. $[\alpha]_D^{20}$ (c = 1.0, CH_2Cl_2): (R_P, S)-**3a**, −33°; (S_P, S)-**3a**, +25°; (R_P, S)-**3b**, −13°; (S_P, S)-**3b**, +27°; (R_P, S)-**3c**, −40°; (S_P, S)-**3c**, −62°.
12 Crystallographic data for (R_P, S)-**3c**: $C_{18}H_{24}NPSe$, fw = 364.33, orthorhombic, space group $P2_12_12_1$, a = 7.223(2), b = 13.269(4), c = 19.121(6) Å, V = 1832(1) Å^3, Z = 4, D_{calcd} = 1.320 g cm^{-3}, T = 296 K, R = 0.045 R_w = 0.059, Flack parameter = 0.006(9), 3474 reflections ($I > 2\sigma(I)$). Crystallographic data reported in this paper have been deposited with the Cambridge Crystallographic Data Center (CCDC) as supplementary publication no. CCDC-235151. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-003; e-mail: deposit@ccdc.cam.ac.uk).
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