

# 1,1'-Binaphthyl-2,2'-diyl Phosphoroselenoyl Chloride as a Chiral Molecular Tool for the Preparation of Enantiomerically Pure Alcohols and Amines

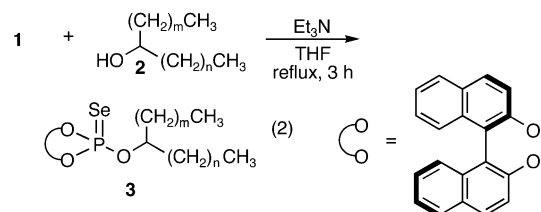
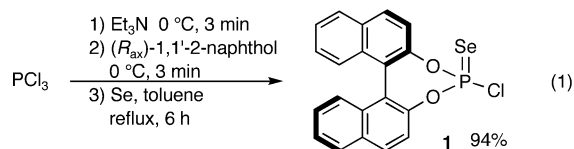
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The development of new tools, which can be used to determine the enantiomeric purities of a chiral substance, resolve chiral molecules, and promote asymmetric catalytic reactions, is of great importance in modern organic chemistry. Although various types of chiral discriminating agents have been developed,<sup>1</sup> the analysis, resolution, and preparation of simple optically active secondary alcohols, found in a wide variety of biologically active natural compounds, such as insect pheromones,<sup>2</sup> represent a continuing challenge in organic chemistry. As a result, new chiral molecular tools, which can be used not only as chiral derivatizing agents but also as chiral resolving agents, remain in high demand. Below, we report the preparation of 1,1'-binaphthyl-2,2'-diyl phosphoroselenoyl chloride and describe its utility as a new chiral molecular tool to promote chiral discrimination and enantiomer resolution, as well as to mediate stereocontrolled amination reactions of simple secondary alcohols.

Preparation of (*R*<sub>ax</sub>)-1,1'-binaphthyl-2,2'-diyl phosphoroselenoyl chloride (**1**) was achieved through efficient reaction of PCl<sub>3</sub> with elemental selenium and (*R*<sub>ax</sub>)-1,1'-2-binaphthol in the presence of Et<sub>3</sub>N (eq 1). Chloride (**1**) is purified by column chromatography on silica gel, and unlike the corresponding phosphoryl chloride which vigorously reacts with water,<sup>3</sup> (**1**) is stable in water under neutral conditions even at elevated temperatures.



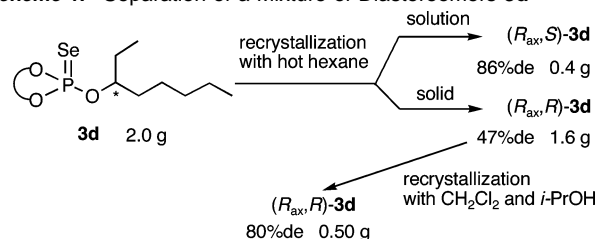
The ability of (*R*<sub>ax</sub>)-**1** to serve as a chiral derivatizing agent for alcohols was probed. Reactions of (*R*<sub>ax</sub>)-**1** with alcohols **2** in the presence of Et<sub>3</sub>N proceed to completion in 3 h and yield the corresponding phosphoroselenoic acid esters **3** in high yields (eq 2, Table 1).<sup>4</sup> The high reactivity of (*R*<sub>ax</sub>)-**1** is in a marked contrast to that of the corresponding phosphoryl chlorides,<sup>5</sup> which do not react with alcohols **2** under identical conditions. Mixtures of diastereomeric esters **3** are formed in these processes in ratios that are not dependent on the alcohol used. Interestingly, kinetic resolution of the alcohols does not occur except in the case of **2h**. In the <sup>31</sup>P NMR spectra of the esters,<sup>6,7</sup> separate signals due to each diastereomer are observed. This is the case even in the spectrum of **3f**, which contains *n*-butyl and *n*-hexyl substituents on the chiral

**Table 1.** Synthesis and <sup>31</sup>P and <sup>77</sup>Se Chemical Shift Differences of Phosphoroselenoic Acid O-Esters **3**

entry	alcohol	product <b>3</b> <sup>a</sup> yield, %	<sup>31</sup> P NMR Δδ (ppm)	<sup>77</sup> Se NMR Δδ (ppm)
1	2-heptanol <b>2a</b>	 <b>3a</b> 99%	0.20	2.33
2	2-butanol <b>2b</b>	 <b>3b</b> 82%	0.15	0.84
3	2-hexanol <b>2c</b>	 <b>3c</b> 86%	0.13	1.72
4	3-octanol <b>2d</b>	 <b>3d</b> 92%	0.10	1.32
5	3-heptanol <b>2e</b>	 <b>3e</b> 83%	0.04	0.97
6	5-undecanol <b>2f</b>	 <b>3f</b> 65%	0.07	0.48
7	 <b>2g</b> Ph	 <b>3g</b> Ph 88%	0.18	1.88
8	 <b>2h</b>	 <b>3h</b> <sup>b</sup> 85%	0.55	2.68

<sup>a</sup> All reactions were carried out with chloride **1**, Et<sub>3</sub>N (2.0 equiv), and alcohol (1.1 equiv) in THF. <sup>b</sup> Two diastereomers were formed in a ratio of 9:10.

## Scheme 1. Separation of a Mixture of Diastereomers **3d**

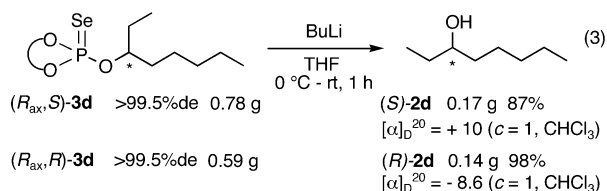


carbon atom. More highly resolved peak separations are present in the <sup>77</sup>Se NMR spectra<sup>8</sup> of the esters.

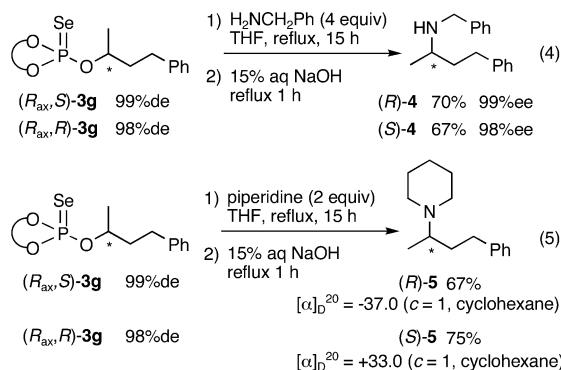
Separation of the diastereomeric esters **3** can be effectively performed by ordinary recrystallization and/or trituration with organic solvents.<sup>9</sup> For example, when the ester **3d** is recrystallized with hot hexane, the solid derived from the hexane solution contains predominantly (*R*<sub>ax</sub>,*S*)-**3d** (86% de) and the precipitate contains (*R*<sub>ax</sub>,*R*)-**3d** (47% de) (Scheme 1).

Recrystallization of the precipitate from  $\text{CH}_2\text{Cl}_2$  and *i*-PrOH gives ( $R_{ax},R$ )-**3d** with 80% de.

Reactions of diastereomerically pure esters **3** with a variety of nucleophiles were explored. Butyllithium was found to react with ( $R_{ax},S$ )-**3d**<sup>10</sup> selectively at phosphorus to give enantiomerically pure (*S*)-3-octanol ((*S*)-**2d**)<sup>11–13</sup> in 87% yield (eq 3). A similar reaction of ( $R_{ax},R$ )-**3d**<sup>9</sup> provides (*R*)-3-octanol ((*R*)-**2d**).<sup>12,13</sup>



In contrast, reactions of ester **3g** with amines take place selectively at the chiral carbon (eqs 4 and 5). For example, benzylamine participates in a stereospecific substitution reaction with **3g** to produce the amine **4** with a high enantiomeric excess.<sup>14</sup> In a similar manner, piperidine reacts with **3g** to form enantiomerically pure tertiary amine **5**. The specific rotations of the products **4** and **5**<sup>15</sup> demonstrate that the substitution reactions of **3g** with amines proceed with inversion of configuration at the chiral carbon atom.



The observations described above show that enantiomerically pure 1,1'-binaphthyl-2,2'-diyl phosphoroselenoyl chloride (**1**), readily prepared from  $\text{PCl}_3$ , elemental selenium, and 1,1'-bi-2-naphthol, is a new, multifunctioning chiral molecular tool. This chloride can be used to resolve simple secondary alcohols. In addition, selective cleavage of either the phosphorus–oxygen and oxygen–carbon bonds in the esters **3**, formed by reaction of **1** with simple alcohols, can be accomplished without loss of enantiomeric purity. Importantly, these cleavage reactions provide access to a variety of optically active alcohols and amines with high enantiomeric purities. The results of continuing studies in this area that focus on the preparation of biologically important optically active compounds and optically active ligands will be reported in due course.

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nation of the enantiomeric excess of amines. This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Area (No. 16033224, “Reaction Control of Dynamic Complexes”) from the Ministry of Education, Culture, Sports, Science and Technology of Japan, and Nagase Science and Technology Foundation.

**Supporting Information Available:** Experimental procedures and characterization of new compounds, including spectral data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (9) See Supporting Information for details of the separation of esters **3a**, **3c**, **3d**, and **3g**.
- (10) The esters **3d** with high diastereomeric excess were obtained by HPLC purification of the esters obtained in Scheme 1.
- (11) Since optically active 3-octanol is a known pheromone, its synthesis and isolation in enantiomerically pure form are important: (a) Cho, B. T.; Kim, D. J. *Tetrahedron* **2003**, *59*, 2457–2462. (b) Ichikawa, A.; Ono, H. *Tetrahedron: Asymmetry* **2005**, *16*, 2559–2568.
- (12) Specific rotation of enantiomerically pure (*S*)- and (*R*)-**2d** is reported to be  $[\alpha]_D^{20} = +10$  ( $c = 0.14$ ,  $\text{CHCl}_3$ ) and  $[\alpha]_D^{20} = -8$  ( $c = 0.16$ ,  $\text{CHCl}_3$ ), respectively.<sup>11b</sup>
- (13) The  $^{31}\text{P}$  NMR spectra of esters **3d**, formed by reactions of alcohols (*S*)- and (*R*)-**2d** with **1**, each contain only a single signal.
- (14) Enantiomeric excess of amine **4** is determined by HPLC (chiralcel AD-H).
- (15) The absolute configurations of the amines **4** and **5** are assigned by comparison of their specific rotations with those reported. (a) For **4**: Cannata, V.; Samori, B.; Tramontini, M. *Tetrahedron* **1971**, *27*, 5247–5254. (b) For **5**: Pyne, S. G.; Griffith, R.; Edwards, M. *Tetrahedron Lett.* **1988**, *29*, 2089–2092.

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