Synthesis of 1,1′-Binaphthyl-2,2′-diyl Phosphoroselenoic Amides and Their Conversion to Optically Pure Phosphoramidites

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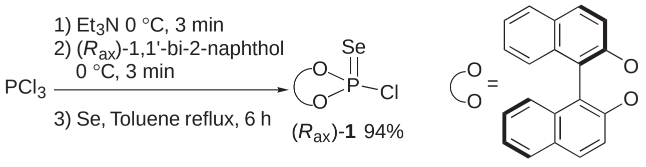
Optically pure phosphoroselenoyl chloride was reacted with racemic amines to give phosphoroselenoic amides as two diastereomeric mixtures in high yields. The diastereomeric mixtures were separated by fractional recrystallization or by chromatography. Extrusion of the selenium atom from the separated amides led to diastereomerically pure phosphoramidites. The ability of the obtained amidites to act as optically active ligands was tested in the hydrogenation of an imine.

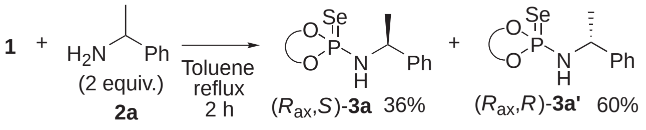
Phosphoramidites bearing a 1,1′-bi-2-naphthoyl group have been recognized as some of the most powerful ligands in catalytic asymmetric reactions[1] since Feringa and co-workers reported the first one bearing a *N*,*N*-dimethylamino group as a chiral discriminating agent in 1994.[2] Their synthesis generally involves the reaction of chlorophosphites with amines.[3] Alternatively, the amino group substitution reaction of *N*,*N*-dimethylamino phosphoramidites with other amines is used.[4] However, only a few phosphoramidites possessing a chiral center at the amino group[5] have been reported except for those with chiral 1-arylalkylamino groups.[6]

We recently found that phosphoroselenoyl chloride **1** can be obtained from PCl_3, elemental selenium and 1,1′-bi-2-naphthol (Scheme 1).[7] The chloride **1** is stable under neutral conditions but reactive under basic conditions. We report here the reaction of **1** with primary and secondary amines leading to phosphoroselenoic amides, separation of their diastereomers, and conversion of the separated diastereomers to optically pure phosphoramidites.



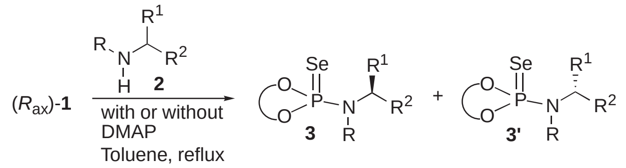
Scheme 1.

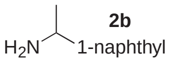
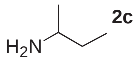
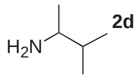
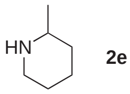
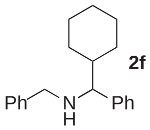
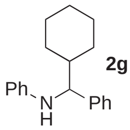
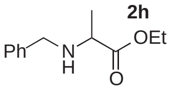
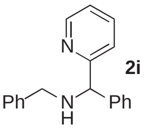
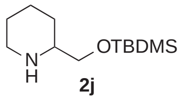
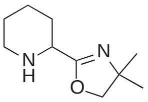
The reaction of chloride **1** with racemic 1-phenylethylamine (**2a**) proceeded smoothly under reflux in toluene (Scheme 2).[8] Two diastereomers of phosphoroselenoic amide (R_{ax},S)-**3a** and (R_{ax},R)-**3a′**[9,10] were obtained in a ratio of 39:61.[11,15] These diastereomers were separated by fractional crystallization to give



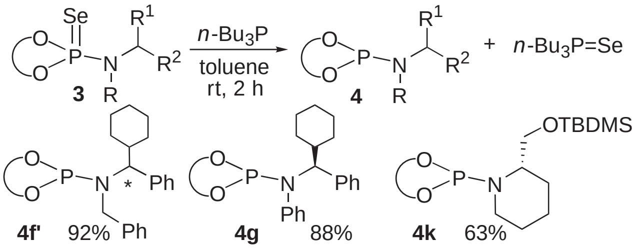
Scheme 2.

Table 1. Synthesis of phosphoroselenoic amides **3** by reacting **1** with amines **2**[a]



Entry	Amine **2**	Time/h		Yield/%[b]
1	 **2b**	2	(R_{ax},S)-**3b** (R_{ax},R)-**3b'**	35[d] 57
2	 **2c**	2	(R_{ax},S)-**3c** (R_{ax},R)-**3c'**	46[e] 49
3	 **2d**	2	(R_{ax},S)-**3d** (R_{ax},R)-**3d'**	44[e] 48
4	 **2e**	2	(R_{ax},S)-**3e** (R_{ax},R)-**3e'**	36[e] 58
5	 **2f**	44	**3f** **3f'** **3f + 3f'**	34[f,g] 34 25
6[c]	 **2g**	18	(R_{ax},S)-**3g** (R_{ax},R)-**3g'** **3g + 3g'**	30[f] 22 36
7	 **2h**	12	**3h** **3h'** **3h + 3h'**	46[f,g] 36 5
8	 **2i**	13	**3i** **3i'** **3i + 3i'**	41[f,g] 40 14
9[c]	 **2j**	2	(R_{ax},S)-**3j** (R_{ax},R)-**3j'** **3j + 3j'**	14[f] 7 54
10[c]	 **2k**	2.5	(R_{ax},S)-**3k** (R_{ax},R)-**3k'** **3k + 3k'**	46[f] 29 14

[a] The chloride **1** was reacted with amine **2** (2 equiv.) under reflux in toluene unless otherwise noted. [b] Isolated yield. [c] Amine **2** (1.2 equiv.) and DMAP (1.2 equiv.) was used. [d] Diastereomers were separated by fractional recrystallization. [e] Diastereomers were separated by HPLC on silica gel. [f] Diastereomers were separated by column chromatography on silica gel. [g] The absolute configuration of diastereomers is not determined.



Scheme 3.

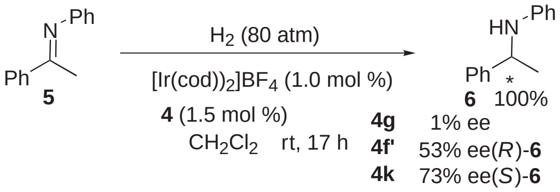
diastereomerically pure **3a** and **3a′** in respective yields of 36 and 60%.

A wide variety of primary and secondary amines are subjected to the amination reaction of **1**. The results are shown in Table 1. The reaction was carried out with either amines **2** (2 equiv.) (Entries 1–5, 7, and 8) or amines **2** (1.2 equiv.) in the presence of 4-dimethylaminopyridine (DMAP, 1.2 equiv.) (Entries 6, 9, and 10). In all cases, the substitution reaction of **1** with amines **2** took place selectively at the phosphorus atom to give phosphoroselenoic amides **3** as a diastereomeric mixture in high yields. The reaction rate depends on the substitution pattern around the nitrogen atom of **2**. The reaction with primary amines **2b**–**2d** was complete within 2 h (Entries 1–3), whereas the reaction with acyclic secondary amines **2f**–**2i** required a longer reaction time (Entries 5–8). The diastereomers **3b** and **3b′** were separated by fractional recrystallization. Other diastereomers **3** were separated either by high performance recycle liquid chromatography on silica gel or by column chromatography on silica gel. The absolute configuration of the diastereomerically pure products **3** was determined by comparison to the ^{31}P NMR spectra of authentic samples derived from optically active amines. Alternatively, stereochemistry was deduced based on X-ray molecular structure analyses of pure **3**.[12,15]

Extrusion of the selenium atom of **3** was then performed (Scheme 3). The reaction of **3** with Bu_3P went to completion within 2 h in toluene at room temperature to give the corresponding phosphoramidites **4** along with $Bu_3P{=}Se$. The complete conversion of **3** to **4** was clearly confirmed by ^{31}P NMR spectra, but the phosphoramidites **4** ($R = H$) derived from primary amines were not isolated, although their synthesis has already been reported.[13] Phosphoramidites **4** ($R = H$) are sensitive toward air to give oxidized products along with several unidentified products. In contrast, phosphoramidites **4** derived from secondary amines were isolated in good yields, as exemplified by **4f′**, **4g**, and **4k**.

Finally, the ability of phosphoramidites **4** to act as optically active ligands was tested in the Ir-catalyzed hydrogenation reaction of imine **5**[14] (Scheme 4). A catalytic amount of $[Ir(cod)_2]BF_4$ efficiently catalyzed the reaction, and the enantiomeric excess was influenced by the substitution pattern in the phosphoramidites **4**. The hydrogenation reaction of **5** in the presence of **4g** gave amine **6** in racemic form. The use of **4f′** effected the asymmetric hydrogenation of **5** to give (*R*)-**6** with 53% ee, whereas the reaction in the presence of **4k** led to (*S*)-**6** with 73% ee.

In summary, we have demonstrated the highly efficient synthesis of optically active phosphoroselenoic amides and their purification in diastereomerically pure form. Extrusion of the selenium atom of phosphoroselenoic amides with Bu_3P provides new types of phosphoramidites, which are not readily accessible by known synthetic procedures, but which may be important as optically active ligands.



Scheme 4.

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