Asymmetric [2,3]Sigmatropic Rearrangement of Chiral Allylic Selenimides

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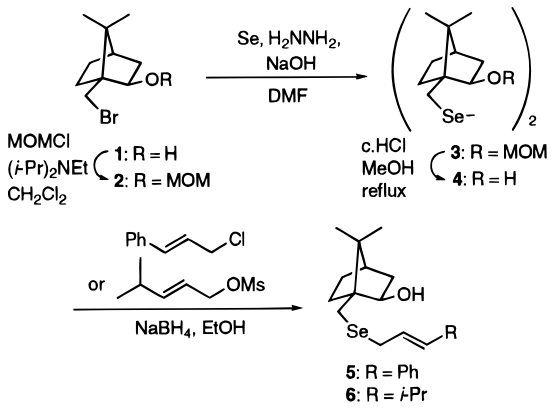
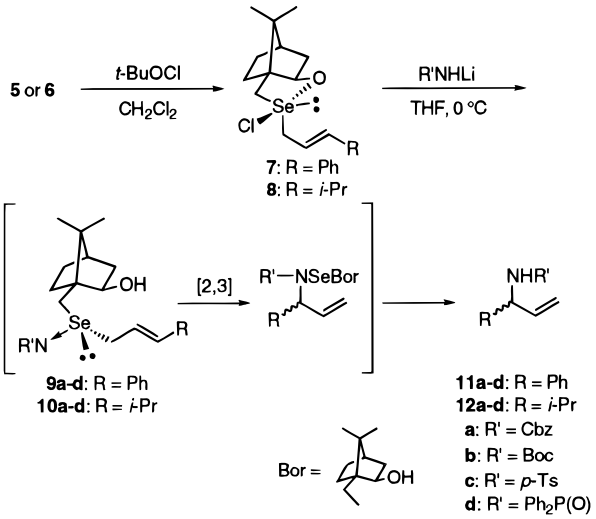
In contrast to the many reports on asymmetric reactions using chiral sulfinyl compounds, few applications of chiral seleninyl compounds to asymmetric synthesis have been described.[1] Recently, some groups have reported the asymmetric [2,3]sigmatropic rearrangement of chiral selenoxides.[1] Uemura and co-workers have succeeded in the asymmetric [2,3]sigmatropic rearrangement of chiral selenimides giving the chiral sulfonamide with up to 87% enantiomeric excess.[2] However, the stereochemical course of the reaction was not described. The key steps of these asymmetric reactions are enantio- or diastereoselective oxidation or imination of the selenides and transfer of the chirality of the selenium atom to C-3 of the resulting allylic alcohols or amines. We recently reported the first synthesis of optically pure haloselenuranes using the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand.[3] Alkaline hydrolysis of the (R_{Se})-chloroselenurane proceeds with retention of configuration to give (R_{Se})-selenoxide as the sole product.[3,4] This selenoxide is stable at room temperature due to the bulkiness of the bornyl group as well as in intramolecular hydrogen bond between the seleninyl oxygen and the secondary hydroxy group.[5] Nucleophilic reaction of the corresponding chiral allylic chloroselenurane with an *N*-protected amine should also occur with complete retention of configuration. If [2,3]sigmatropic rearrangement of the resulting allylic selenimide proceeded stereoselectively, a chiral *N*-protected allylic amine would be obtained with high enantioselectivity. We report here that the nucleophilic reaction of the allylic chloroselenuranes with *N*-protected amines followed by the [2,3]sigmatropic rearrangement of the resulting chiral allylic selenimides proceeds in a highly stereoselective manner to afford chiral *N*-protected allylic amines. [2,3]-Sigmatropic rearrangement of the allylic selenimides was evidenced to progress selectively *via* an *endo* transition state.

Allylic selenides were prepared by a route shown in Scheme 1. (1*S*)-10-Bromo-2-*exo*-borneol (**1**)[6] was converted to the corresponding MOM ether **2**. Reaction of **2** with sodium selenolate[7] followed by hydrolysis of the resulting diselenide **3** gave the deprotected diselenide **4**. Allylic selenides **5** and **6** were obtained by reaction of cinnamyl chloride or allylic mesylate with selenolate anion which was prepared *in situ* from **4** and sodium borohydride.[8] Treatment of the allylic selenides **5** and **6** with *t*-BuOCl gave allylic chloroselenuranes **7** and **8** as an exclusive product.[9] We selected benzyl carbamate, *tert*-butyl carbamate, *p*-tosylamide, and diphenylphosphinamide as an *N*-protected amine for selenimide formation (Scheme 2 and Table 1). Nucleophilic reaction of **7** and **8** with lithium *N*-protected amides afforded chiral allylic selenimides, **9a**−**d** and **10a**−**d**, *in situ*, with retention of configuration. [2,3]Sigmatropic rearrangement of **9a**−**d** and **10a**−**d** gave chiral *N*-protected allylic amines **11a**−**d** and **12a**−**d**. These results are shown in Table 1. The ee values of allylic amines **11** and **12** were determined by HPLC using a Daicel Chiralcel OJ or a Chiralpak AS column. Determination of the absolute configuration of **11** and **12** is summarized in the footnote of Table 1.

Scheme 1



Scheme 2



(1) For asymmetric [2,3]sigmatropic rearrangement of chiral selenoxides: (a) Nishibayashi, Y.; Singh, J. D.; Fukuzawa, S.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 4114. (b) Komatsu, N.; Nishibayashi, Y.; Uemura, S. *Tetrahedron Lett.* **1993**, *34*, 2339. (c) Davis, F. A.; Reddy, R. T. *J. Org. Chem.* **1992**, *57*, 2599. (d) Reich, H. J.; Yelm, K. E. *J. Org. Chem.* **1991**, *56*, 5672. For asymmetric β-elimination of chiral selenoxides: ref 1a and references cited therein.

(2) Nishibayashi, Y.; Chiba, T.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, *59*, 3262.

(3) Takahashi, T.; Kurose, N.; Kawanami, S.; Arai, Y.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1994**, *59*, 3262.

(4) Nucleophilic reaction of the (R_{Se})-chloroselenurane with active methylene compounds also proceeds with retention of configuration to afford (S_{Se})-selenonium ylides exclusively: Takahashi, T.; Kurose, N.; Kawanami, S.; Nojiri, A.; Arai, Y.; Koizumi, T.; Shiro, M. *Chem. Lett.* **1995**, 379.

(5) We have applied this selenoxide to an asymmetric protonation reaction: Takahashi, T.; Nakao, N.; Koizumi, T. *Chem. Lett.* **1996**, 207.

(6) Poth, N. *Rev. Tech. Luxemb.* **1976**, *68*, 195; *Chem. Abstr.* **1977**, *87*, 135965k.

(7) Syper, L.; Młochowski, J. *Synthesis* **1984**, 439.

(8) Scaborough, R. M., Jr.; Toder, B. H.; Smith, A. B., III. *J. Am. Chem. Soc.* **1980**, *102*, 3904.

(9) The structure of chloroselenuranes was confirmed by comparison of their ^{1}H-NMR spectra with that of (1*S*,R_{Se})-5-chloro-10,10-dimethyl-5-phenyl-5λ^4-selena-4-oxatricyclo[5.2.1.0^{3,7}]decane (ref 3).

(10) Moriwake, T.; Hamano, S.; Saito, S.; Torii, S.; Kashino, S. *J. Org. Chem.* **1989**, *54*, 4114.

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Table 1. Asymmetric [2,3]Sigmatropic Rearrangement of Selenimides 9a−d and 10a−d

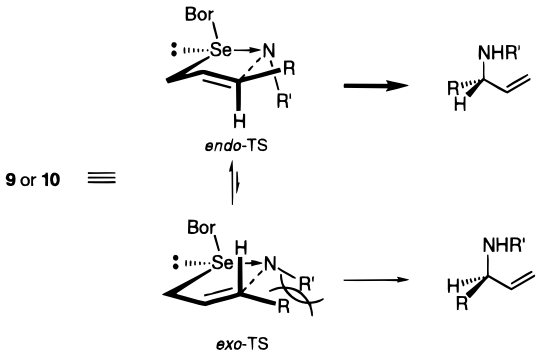
entry	R	R'	product	time (h)	yield (%)	ee[a] (%)	$[\alpha]_D$	confign
1	Ph	Cbz	**11a**	3	67	24	−14.1	
2	*i*-Pr	Cbz	**12a**	3	57	67	+19.6	*S*[e]
3	Ph	Boc	**11b**	3	74	7[c]	−0.7	
4	*i*-Pr	Boc	**12b**	3	63	73[d]	+22.0	*S*[f]
5	Ph	*p*-Ts	**11c**	3	57	90	+49.2	*R*[g]
6[b]	Ph	*p*-Ts	**11c**	3	74	93	−50.2	*S*[g]
7	*i*-Pr	*p*-Ts	**12c**	3	86	93	+22.7	*S*[f]
8	Ph	$Ph_2P(O)$	**11d**	5	53	92	+25.7	*R*[g]
9	*i*-Pr	$Ph_2P(O)$	**12d**	5	69	93	+17.7	*S*[h]

[a] Determined by HPLC. [b] *ent*-**7** was used for the reaction. [c] Determined after conversion of **11b** into **11c**. The ee of **11c** was consistent with that of **11b** which was determined by ^{1}H-NMR spectrum using Eu(hfc)$_3$. [d] Determined after conversion of **12b** into **12a**. The ee of **12a** was consistent with that of **12b** which was determined by HPLC. [e] Determined by comparison with the authentic sample by HPLC. [f] Determined by comparison of the sign of optical rotation with the reported one.[10] [g] The absolute configuration of **11c,d** was determined from the steric course of the reaction. [h] Determined after conversion of **12d** into **12c**.

Treatment of **7** and **8** with 3 equiv of CbzNHLi (prepared from $CbzNH_2$ and *n*-BuLi) gave the allylic Cbz-amines **11a** (24% ee) and (*S*)-**12a** (67% ee), respectively (Table 1, entries 1 and 2). Reaction of **7** and **8** with BocNHLi afforded the allylic Boc-amines **11b** (7% ee) and (*S*)-**12b** (73% ee), respectively (Table 1, entries 3 and 4). Treatment of **7** and **8** with *p*-TsNHLi yielded the corresponding allylic *p*-tosylamides (*R*)-**11c**[11] (90% ee) and (*S*)-**12c** (93% ee) (Table 1, entries 5 and 7). When *ent*-**7**[12] and *p*-TsNHLi were used for this reaction, the preferred configuration of **11c** changed to *S* (93% ee) (Table 1, entry 6). The ee of allylic phosphinamides, (*R*)-**11d** and (*S*)-**12d**, went up to 92% and 93%, respectively, when **7** and **8** were treated with $Ph_2P(O)NHLi$ (Table 1, entries 8 and 9). Thus, we obtained (*S*)-**12c** with the highest ee (93%) and chemical yield (86%) in the rearrangement of selenimide **10c**.

From the absolute configuration of the resulting *N*-protected allylic amines as well as their high ee, we propose the stereochemical course of the asymmetric [2,3]-sigmatropic rearrangement of the allylic selenimides as shown in Scheme 3. Nucleophilic reaction of the chloroselenuranes **7** and **8** with *N*-protected amines will form the selenimides **9** and **10** exclusively. In the [2,3]-sigmatropic rearrangement of the allylic selenimides, the *endo* transition state will be more stable than the *exo* transition state similar to that of allylic selenoxides.[1] In the formation of *N*-*p*-tosylamides **11c** and **12c** as well as *N*-diphenylphosphinamides **11d** and **12d** the steric interaction would be increased between the alkyl group and the *p*-Ts or $Ph_2P(O)$ group in the *exo* transition state, leading to high stereoselectivity.

Scheme 3



In conclusion, the [2,3]sigmatropic rearrangement of the allylic selenimides (1) proceeds predominantly *via* the *endo* transition state and (2) is available for practical preparation of various chiral allylic amines.

We are now investigating mechanistic studies on the [2,3]sigmatropic rearrangement reaction of the selenimides in more detail.

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Supporting Information Available: Experimental procedures, characterization data, and ^{1}H and ^{13}C NMR spectra for new compounds (40 pages).

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(11) Uemura *et al.* have obtained **11c** in 87% ee. Its absolute configuration has not been reported (ref 2).

(12) *ent*-**7** was prepared from (1*R*)-10-camphorsulphonic acid according to the method for the synthesis of **7** in 29% overall yield.