Optically Pure Haloselenuranes. First Synthesis and Nucleophilic Substitutions†

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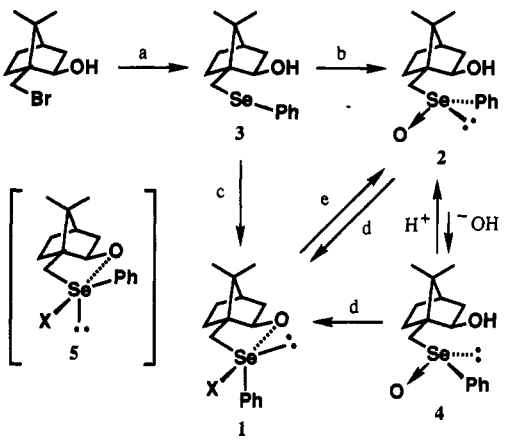
Summary: The first synthesis of optically pure haloselenuranes 1 has been accomplished by utilizing the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand. Complete retention of the configuration has been observed in interconversion reactions between haloselenuranes 1 and selenoxide 2 and in nucleophilic substitution reactions of 1.

In contrast to the many available reports on the synthesis, structural features, and mechanistic aspects of hypervalent 10-S-4[1] organosulfur species (sulfuranes),[2] little is known about the chemistry of hypervalent 10-Se-4 organoselenium species (selenuranes).[3] In particular, the stereochemical aspects of the nucleophilic substitution reactions of these compounds have not been reported due to the lack of a convenient method for the synthesis of optically active selenuranes. We report here the first synthesis of the optically pure haloselenuranes 1. The 2-*exo*-hydroxy-10-bornyl group served as a chiral ligand. We observed complete retention of configuration in the interconversion reactions of haloselenuranes 1 and selenoxide 2 (Scheme 1) and in the nucleophilic substitution reactions of the selenuranes 1 (Scheme 2).

Optically active selenoxide 2 was prepared by a route shown in Scheme 1.[4] Selenide 3 was readily obtained by reaction of (1*S*)-10-bromo-2-*exo*-borneol[5] with sodium phenylselenolate.[6] Oxidation of 3 with 3-chloroperbenzoic acid (*m*-CPBA, −78 °C) afforded a single diastereomeric selenoxide 2[7] (96% yield). On the other hand, use of 30% H_2O_2 or *t*-BuOCl (then $NaHCO_3$–H_2O) for oxidation of the selenide 3 gave a quantitative mixture of two selenoxides, 2 and 4, which were diastereomeric at selenium. Surprisingly, a mixture of the selenoxides 2 and 4 changed into 2 upon silica gel column chromatography of the reaction mixture. Selenoxide 2 was thus the result of this operation. The absolute stereochemistry of the selenium atom in 2 is unequivocally established to be *R* by X-ray crystallography (Figure 1).[7]

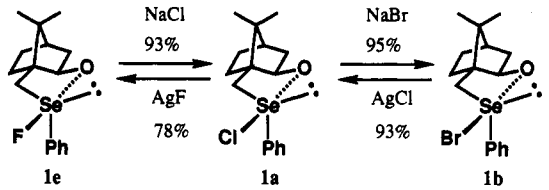
Scheme 1[a]



1a: X = Cl, **1b**: X = Br, **1c**: X = 3,5-dinitrobenzoyloxy, **1d**: X = *p*-TolSO$_3$

[a] Key: (a) $(PhSe)_2/NaBH_4/EtOH/\Delta$; (b) *m*-CPBA/$CH_2Cl_2$/−78 °C; $NaHCO_3/H_2O$; (c) *t*-BuOCl/CH_2Cl_2; (d) HX/MeOH or HX/$MgSO_4$/CH_2Cl_2; (e) $NaHCO_3/H_2O$.

Scheme 2



† This paper is dedicated to Professor Yoshifumi Maki on this occasion of his retirement from Gifu Pharmaceutical University in March 1994.

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(1) Perkins, C. W.; Martin, J. C.; Arduengo, A. J., III; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753–7759.

(2) Hayes, R. A.; Martin, J. C. Sulfurane Chemistry. In *Organic Sulfur Chemistry, Theoretical and Experimental Advances*; Bernardi, F., Csizmadia, I. G., Mangini, A., Eds.; Elsevier: Amsterdam, 1985.

(3) We use the name "selenurane" for tetrasubstituted selenium(IV) compounds.[3a] For the synthesis of racemic selenuranes see ref 3b–g. For the synthesis and separation of racemic diastereomers of a dialkoxyselenurane see ref 3a. For the synthesis and partial separation of a bis(acyloxy)selenurane see ref 3h. (a) Reich, H. J. C. *J. Am. Chem. Soc.* **1973**, *95*, 964–966. (b) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986. (c) Back, T. G. *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1987; Vol. 2. (d) McCullough, J. D.; Hamburgar, G. *J. Am. Chem. Soc.* **1941**, *63*, 803–807; **1942**, *64*, 508–513. (e) Fujihara, H.; Mima, H.; Ikemori, M.; Furukawa, N. *J. Am. Chem. Soc.* **1991**, *113*, 6337–6338. (f) Fujihara, H.; Mima, H.; Erata, T.; Furukawa, N. *J. Am. Chem. Soc.* **1992**, *114*, 3117–3118. (g) Fujihara, H.; Mima, H.; Erata, T.; Furukawa, N. *J. Am. Chem. Soc.* **1993**, *115*, 9826–9827. (h) Lindgren, B. *Acta Chem. Scand.* **1972**, *26*, 2560–2561.

(4) Little work has been reported on configurationally stable selenoxides with high optical purity except for studies on the systems having bulky substituents[4a–c] and an intramolecular hydrogen bond:[4d] (a) Zylber, N.; Zylber, J. *J. Chem. Soc., Chem. Commun.* **1978**, 1084–1085. (b) Shimizu, T.; Kikuchi, K.; Ishikawa, Y.; Ikemoto, I.; Kobayashi, M.; Kamigata, N. *J. Chem. Soc., Perkin Trans. 1* **1989**, 597–602. (c) Davis, F. A.; Reddy, T. *J. Org. Chem.* **1992**, *57*, 2599–2606. (d) Back, T. G.; Iburahim, N.; McPhee, D. J. *J. Org. Chem.* **1982**, *47*, 3283–3289. In addition to the phenyl selenoxide 2, we obtained the corresponding methyl and ethyl derivatives by using the 2-*exo*-hydroxy-10-bornyl group as a chiral ligand.

(5) Poth, N. *Rev. Tech. Luxemb.* **1976**, *68*, 195–199; *Chem. Abstr.* **1977**, *87*, 135965k.

(6) Sodium selenolate anion was prepared *in situ* from $(PhSe)_2$ and $NaBH_4$: Scaborough, R. M., Jr.; Toder, B. H.; Smith, A. B., III. *J. Am. Chem. Soc.* **1980**, *102*, 3904–3913. 3 (100% yield): $[\alpha]^{24}_D$ −19.0° (*c* 2.67, $CHCl_3$).

(7) Crystallographic data for 2: orthorhombic, space group $P2_12_12_1$, with a = 11.455(3) Å, b = 13.535(3) Å, c = 9.879(3) Å, V = 1531.7(5) Å^3, and $Z = 4$ (d_{calcd} = 1.411 g cm^{-3}), μ (CuK$_\alpha$) = 33.46 cm^{-1} absorption corrected by ω scans; 1336 unique reflections; 1224 with $I > 3.00\sigma(I)$ were used in refinement; R = 3.3%, R_w = 4.4%. The authors have deposited atomic coordinates for 2, 1a, and 1b with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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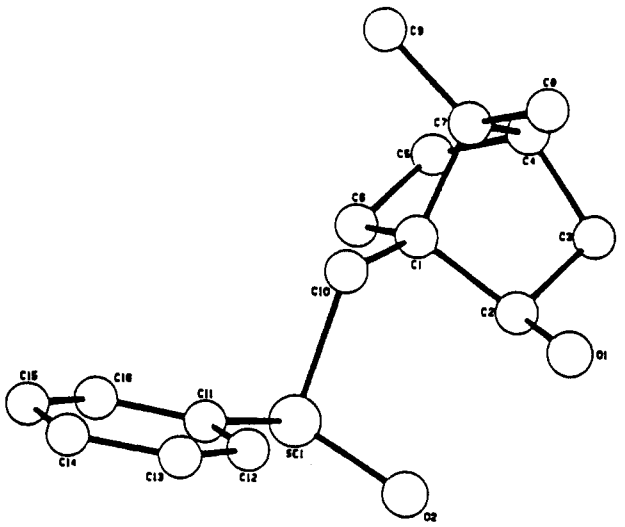


Figure 1. Perspective structure of **2**.

Selenoxide **2** is stable at room temperature in the solid state. The configurational stability of **2** seems to reflect stabilization by an intramolecular hydrogen bond between the seleninyl oxygen and the secondary hydroxy group. The presence of an intramolecular hydrogen bond is supported by a 3299 cm^{-1} absorption in the FT-IR spectrum of a highly dilute (0.005 M) CCl_4 solution of **2**. Treatment of (R_{Se})-selenoxide **2** with 1 N aqueous NaOH in MeOH gave an equilibrium mixture of (R_{Se})- and (S_{Se})-selenoxides, **2** and **4**, in a ratio of 2:1. Interestingly, the ratio of **2**/**4** changed from 2:1 to 96:4 upon exposure of the mixture to 70% aqueous $HClO_4$ in MeOH. Under similar conditions, pure selenoxide **2** changed into a mixture of **2** and **4** (98:2).

To gain some insight into the steric course of the epimerization of the selenoxide and to isolate optically active selenuranes, we examined the following reactions. Treatment of the selenoxide **2** with HCl[8] gave the chloroselenurane **1a**[9] as an exclusive product (100% yield) (Scheme 1). When a mixture of the selenoxide **2** and **4** (2:1) was treated with HCl, the chloroselenurane **1a** was obtained as a single diastereomer (96% yield). Chloroselenurane **1a** was also isolated from the reaction of selenide **3** with *t*-BuOCl (100% yield). In a similar manner, bromoselenurane **1b** was obtained by treatment of **2** with HBr (95% yield). The [(3,5-dinitrobenzoyl)oxy]- and [(*p*-toluenesulfonyl)oxy]selenuranes (**1c** and **1d**) were prepared by the reaction of the selenoxide **2** with 3,5-dinitrobenzoic acid (88% yield) and *p*-toluenesulfonic acid (91% yield) in the presence of $MgSO_4$, respectively. No selenuranes **5a–d**, epimeric at selenium, were detected in these reactions. Formation of the selenuranes **5** might be unfavorable because of steric repulsion between the 7-methyl group of the bornyl moiety and the phenyl group. It has been established that the chloroselenurane **1a** has

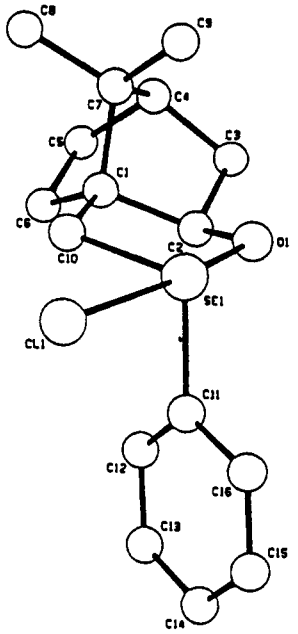


Figure 2. Perspective structure of **1a**.

a trigonal-bipyramidal (TBP) structure (*R* configuration[11] at the selenium center) by X-ray analysis (Figure 2).[9] The apical-bond distances of Se–Cl [2.587(2) Å] and Se–O [1.838(5) Å] are shorter than each of the sums of van der Waals radii (3.80 and 3.40 Å, respectively), thus ruling out a linear charge-transfer complex structure.[12] The Cl–Se–O angle [174.1(2)°] is consistent with those (Cl–Se–C or Cl–Se–N) of racemic selenuranes reported previously.[3d,e] X-ray analysis of the bromoselenurane **1b** gave similar results.[13] In analogy with **1a** and **1b**, the stereochemistry of the selenuranes **1c** and **1d** can be assigned the *R* configuration, as depicted in Scheme 1. Addition of aqueous $NaHCO_3$ to a CH_2Cl_2 solution of **1a** resulted in complete hydrolysis, leading to the selenoxide **2**, exclusively.[14]

Nucleophilic substitution of **1a** with 3–5 equiv of NaBr gave the bromoselenurane **1b**, exclusively (95% yield) (Scheme 2). Although treatment of **1b** with NaCl gave not **1a** but the unreacted starting material (95% yield), similar reaction of **1b** with AgCl afforded **1a** (93% yield). No mixtures of **1a** and **1b** were obtained from these reactions. Moreover, substitution of **1a** by AgF gave the fluoroselenurane **1e** (78% yield), which reverted to the parent chloroselenurane **1a** (93% yield) upon treatment with NaCl.[15]

To sum up, (i) a base treatment of the selenoxide **2** afforded an equilibrium mixture of **2** and **4** (2:1), (ii) an acid treatment ($HClO_4$) of the selenoxide **2** or a mixture of the selenoxides **2** and **4** gave **2** predominantly, (iii) the selenuranes **1** were formed both from **2** and a mixture of

(8) Martin, J. C.; Balthazor, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 152–162.

(9) ^{77}Se NMR[10] ($CDCl_3$) δ 901.06. Crystallographic data for **1a**: orthorhombic, space group $P2_12_12_1$, with a = 9.573(2) Å, b = 20.975(4) Å, c = 7.796(3) Å, V = 1561.2(6) Å^3, and Z = 4 (d_{calcd} = 1.462 g cm^{-3}), μ (CuK_α) = 48.55 cm^{-1} absorption corrected by ω scans; 1552 unique reflections; 1379 with $I > 3.00\sigma(I)$ were used in refinement; R = 3.8%, R_w = 6.6%.

(10) ^{77}Se NMR spectra were measured for solutions in $CDCl_3$ with $(MeSe)_2$ as an external standard. The chemical shifts relative to Me_2Se were calculated based on $(MeSe)_2$: Odom, J. D.; Dawson, W. H.; Ellis, P. D. *J. Am. Chem. Soc.* **1979**, *101*, 5815–5822.

(11) Designation of absolute configuration at tetracoordinate selenium-(IV) was followed by an extension of the Cahn, Ingold, Prelog (CIP) *R–S* nomenclature proposed by Martin and Balthazor (ref 8).

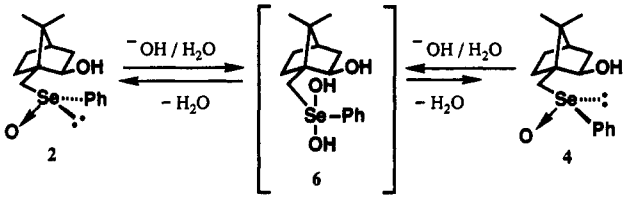
(12) Rømming, C. *Acta Chem. Scand.* **1960**, *14*, 2145–2151.

(13) Crystallographic data for **1b**: monoclinic, space group *C*2, with a = 20.870(5) Å, b = 6.916(6) Å, c = 13.117(8) Å, V = 1574(1) Å^3, and Z = 4 (d_{calcd} = 1.638 g cm^{-3}), μ (CuK_α) = 61.13 cm^{-1} absorption corrected by ω scans; 1348 unique reflections; 1232 with $I > 3.00\sigma(I)$ were used in refinement; R = 3.8%, R_w = 5.7%.

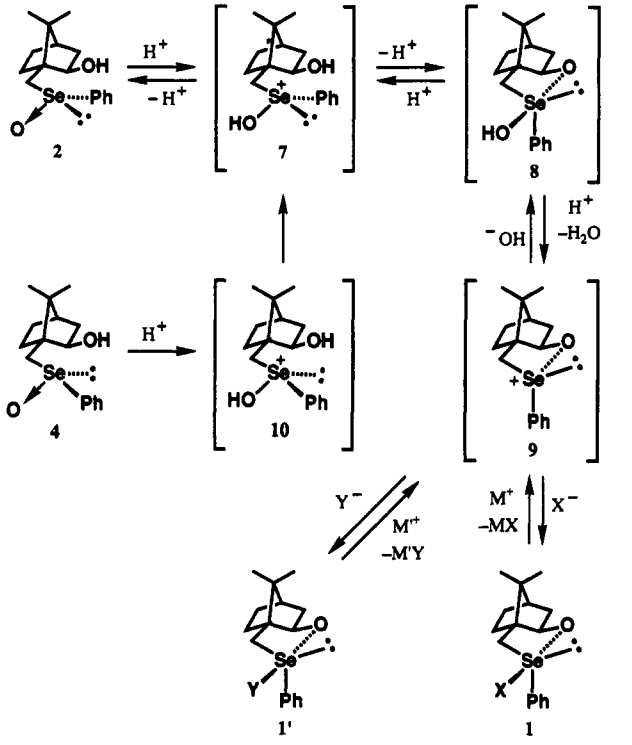
(14) A mixture of the selenoxides **2** and **4** was obtained by a prolonged treatment of **1a** with alkaline solution.

(15) From these results, softness of the alkoxy selenonium ion **6** is suggested to be between Ag^+ and Na^+: Ho, T.-L. *Hard and Soft Acids and Bases Principle in Organic Chemistry*; Academic Press: New York, 1977.

Scheme 3



Scheme 4



2 and 4 by the action of HX, (iv) quick treatment of the selenuranes 1 with aqueous base gave the selenoxide 2, and (v) nucleophilic displacement reactions of the haloselenuranes 1 with metal halides proceeded with retention of configuration. Moreover, the progress of the nucleophilic substitution depended on the countercation.

These results (i–v) can be most reasonably explained as shown in Schemes 3 and 4, which presume two intermediates, acyclic 6 and cyclic 8 or 9. In the case of epimerization of 2 under basic conditions (i), attack of hydroxide ion on the selenium center of 2, followed by protonation, gives the hydrate 6 (Scheme 3). Dehydration of 6 affords the selenoxides 2 and 4 in a thermodynamically-determined ratio. Under acidic conditions (ii), initial protonation of the seleninyl oxygen of 2 gives the selenonium ion 7 (Scheme 4). As for the selenoxide 4, protonation on the seleninyl oxygen affords the selenonium ion 10 under similar conditions. Inversion of configuration occurs at the selenium atom of the ion 10 to give the ion 7. Intramolecular attack by the hydroxyl group of 7 proceeds stereoselectively, leading to the hydroxyselenurane 8. With weakly nucleophilic perchlorate anion (ClO_4^-), the selenurane 8 reverts to the parent selenoxide 2 by successive protonation on the ring oxygen, cleavage of the oxaselenane ring, and deprotonation of the ion 7. In the presence of halogen ions, carboxylate ion, or arylsulfonate ion (iii), the selenurane 8 is converted to the corresponding selenuranes 1 by dissociation of the Se–OH bond, followed by stereoselective association of the resulting alkoxyselenonium ion 9 with X^-. Hydrolysis of the selenuranes 1 (iv) proceeds by the reverse pathway, *via* the ion 9, the hydroxyselenurane 8, and the ion 7, to give the selenoxide 2 stereoselectively. In the nucleophilic substitution reactions of the selenuranes 1 (v),[16] X-selenurane 1 becomes the ion 9, by the action of M^+ followed by elimination of MX. Halogen anion (Y^-) attacks 9 to give Y-selenurane 1′, whose reaction with M′X affords the parent selenurane 1 by the reverse pathway.

We are now investigating the substitution reactions of the selenuranes 1 in detail to gather further evidence of the formation of the selenonium ion 9 during these reactions.

Acknowledgment. This work was supported in part by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture, Japan (No. 04217104).

Supplementary Material Available: Experimental procedures, characterization data, and ^1H and ^{13}C NMR spectra of new compounds (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version on the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) One of the reviewers commented on the stereoselective substitution reactions of the selenuranes 1 as follows: The apparent retention is probably simply the result of a high thermodynamic preference for one isomer. It is possible that both isomers are in rapid equilibrium as the reaction proceeds. However, we have proposed Schemes 3 and 4 as the most reasonable mechanisms to elucidate the whole results that we obtained in this paper (i–v). The presence of the ion 9 could be suggested by no formations of mixtures of 1 and 1′ as well as by the dependence of these reactions on a countercation (M^+ or M'^+).