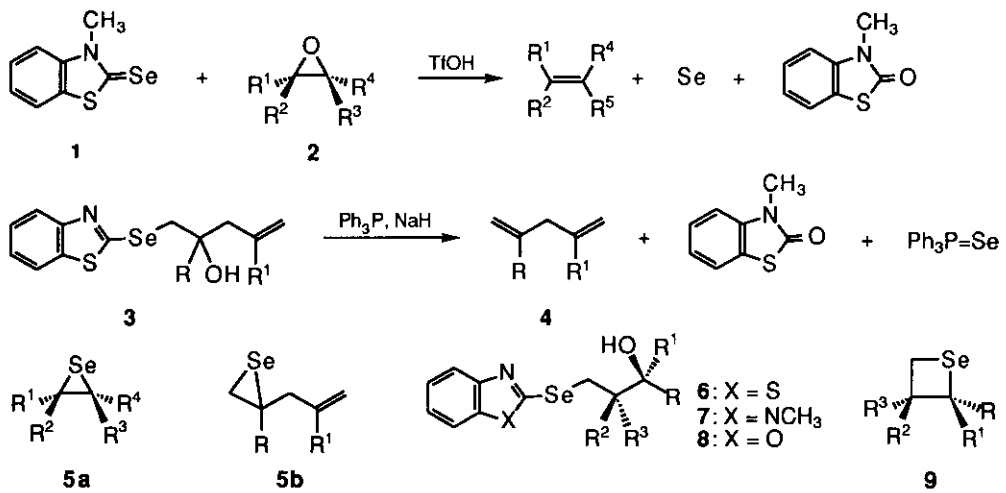
FORMATION OF SELENETANES FROM 2-(3-HYDROXYALKYL-SELENO)BENZOXAZOLES

Kazunori Takemura, Kunihiko Sakano, Ayuko Takahashi, Toshimi Sakamaki, and Oyo Mitsunobu*

Department of Chemistry, College of Science and Engineering, Aoyama Gakuin University.
6-16-1 Chitosedai, Setagayaku, Tokyo 157, Japan

Abstract–The reaction of 2-(3-hydroxyalkylseleno)benzoxazoles with KH afforded the corresponding selenetanes and 2(3*H*)-benzoxazolone.

Aza-aromatic compounds have been attracting much attention as versatile leaving groups in organic functional group transformation[1] and carbon-carbon bond formation.[2] As an interesting example, Calo et al. have demonstrated that the reaction of 3-methyl-2(3*H*)-benzothiazoleselone (**1**) with epoxides (**2**) in the presence of TfOH afforded olefins.[3] Similarly, on treatment with triphenylphosphine and NaH, 2-[(2-alkyl-2-hydroxy-4-pentenyl)seleno]benzothiazoles (**3**) afforded 1,4-dienes (**4**) in good to excellent yields.[4] The formation of olefins could be explained by a sequence of reactions involving seleniranes (**5**) (Scheme 1).



Scheme 1

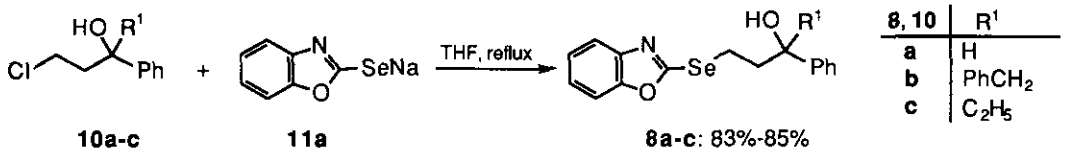
This paper is dedicated to Professor Koji Nakanishi on the occasion of his 75th birthday.

In view of the facts described above, the reaction of 2-(3-hydroxyalkylseleno)azoles (**6**), (**7**), or (**8**) with a base could be expected to give selenetanes (**9**).[5] In the preliminary experiments, however, thiazole derivatives (**6**) and imidazole derivatives (**7**) hardly gave the corresponding selenetanes (**9**). On the other hand, the reaction of 2-(3-hydroxyalkylseleno)benzoxazoles (**8**) with KH was found to expectedly afford selenetanes (**9**). In this paper, we wish to report preparation of 2-(3-hydroxyalkylseleno)benzoxazoles (**8**) and their conversion into selenetanes (**9**).

1. Preparation of 2-(3-hydroxyalkylseleno)benzoxazoles

The starting materials, 2-(3-hydroxyalkylseleno)benzoxazoles (**8**) were prepared by three different procedures as depicted below. The yields of **8** are summarized in Table 1.

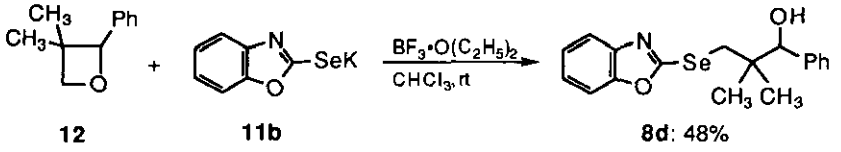
1) The reaction of 3-hydroxyalkyl chlorides (**10a–c**) with sodium 2-benzoxazole selenolate (**11a**) (Method **A**: Scheme 2).



8, 10	R^1
a	H
b	$PhCH_2$
c	C_2H_5

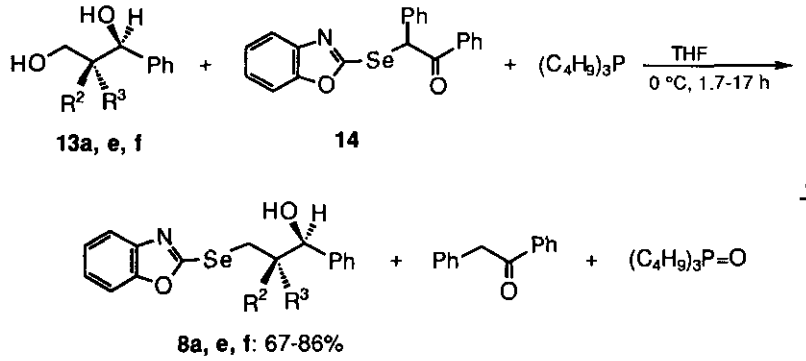
Scheme 2

2) The reaction of oxetane (**12**) with potassium 2-benzoxazole selenolate (**11b**) (Method **B**: Scheme 3).



Scheme 3

3) The reaction of 1,3-diols (**13**) with the reagent formed by the combination of 2-(1,2-diphenyl-2-oxoethylseleno)benzoxazole (**14**) with tributylphosphine (Method **C**: Scheme 4).[6]

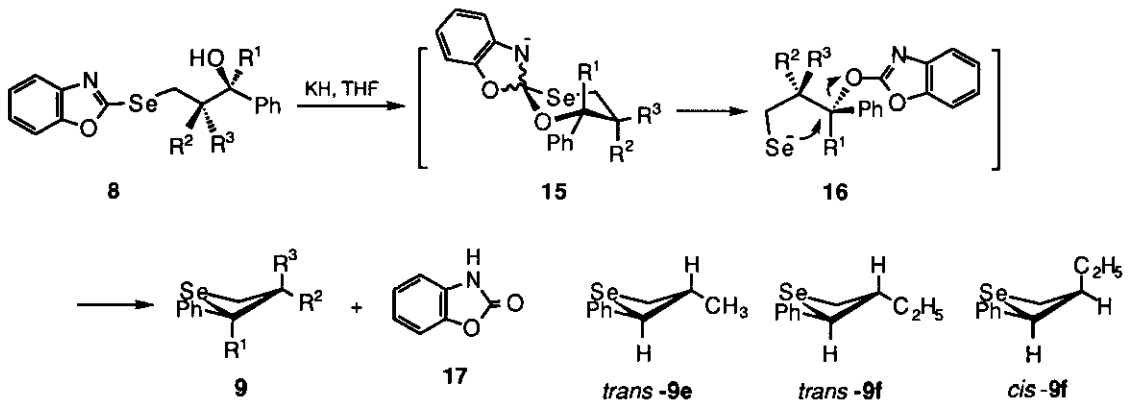


8, 13	R^2	R^3
a	H	H
e	CH_3	H
f	C_2H_5 (H)	H (C_2H_5)

Scheme 4

2. Preparation of selenetanes

When 2-(3-hydroxy-3-phenylpropylseleno)benzoxazole (**8a**) was treated with 1.5 molar amount of KH in THF at room temperature for 30 min, selenetane (**9a**) was obtained in 84% yield (Table 1, Entry 1). The structure of the selenetane was determined by mass spectrometry including HRMS and ^{1}H-NMR spectroscopy.[7] Under the same conditions, however, *tert.*-alcohols (**8b**) and (**8c**) gave complex mixtures of products and no expected selenetane (**9b**) and (**9c**) could be obtained (Table 1, Entries 2 and 3). These results would be attributed to the steric hindrance at the reaction site. Seleno alcohol (**8d**) could be converted into selenetane (**9d**) when the reaction was carried out at room temperature for 24 h in the presence of 18-crown-6 (Table 1, Entry 4).
The formation of a selenetane would be explained by assuming a spiro intermediate (**15**) which in turn converted into a selenolate anion (**16**). Intramolecular displacement of **16** gave rise to the selenetane (**9**) (Scheme 5).



Scheme 5 (For R^1, R^2, and R^3, see Table 1)

Table 1. Preparation of **8** and their conversion into selenetane (**9**)[a)]

Entry	**8** and **9**			Method[b)] and yield of **8**/%				Starting	Yields of **9** and **17**/%	
	R^1	R^2	R^3		A	B	C	material	**9**	**17**
1	H	H	H	**8a**	85		69	**8a**	**9a**: 84	71
2	$PhCH_2$	H	H	**8b**	83			**8b**	**9b**: nd[c)]	95
3	C_2H_5	H	H	**8c**	84			**8c**	**9c**: nd[c)]	80
4	H	CH_3	CH_3	**8d**		48	nd[c)]	**8d**	**9d**: 70[d)]	>99
5	H	CH_3	H	*syn*-**8e**	86			*syn*-**8e**	*trans*-**9e**: 30[d)]	80
6	H	C_2H_5	H	*syn*-**8f**	81			*syn*-**8f**	*trans*-**9f**: 78	>99
7	H	H	C_2H_5	*anti*-**8f**			73	*anti*-**8f**	**9f**: 30[d, e)]	67

a) For R^1, R^2, R^3, see Scheme 5. b) For methods **A**, **B**, and **C**, see Schemes 2, 3, and 4. c) nd = Not detected. d) The reaction was carried out in the presence of 18-crown-6 (1 equiv). e) See text.

The reaction of *syn*-**8e** with KH at room temperature resulted in the formation of an unidentified product as indicated by thin layer chromatography. When the reaction was carried out in the presence of an equimolar amount of 18-crown-6, however, the expected selenetane (**9e**) was isolated in 30% yield as a single isomer. Although the configuration of the product has not yet been determined, the structure was tentatively assigned to be trans (*trans*-**9e**) (Table 1, Entry 5). In contrast, the reaction of *syn*-**8f** with KH proceeded smoothly even in the absence of the crown ether to afford selenetane (**9f**) in 78% yield as a single isomer which was again tentatively assigned to be *trans*-isomer (*trans*-**9f**; Table 1, Entry 6). On the other hand, the reaction of *anti*-**8f** with KH was sluggish to give a mixture of two selenetanes, one of which could be assigned to be *trans*-**9f** by comparison of NMR spectrum with that of the product obtained in the reaction of *syn*-**8f**. Another selenetane was therefore assigned to be *cis*-**9f** (combined yield 5%; the ratio of *trans*-**9f** to *cis*-**9f** = 1 : 2.8). When the reaction was carried out in the presence of 18-crown-6, the yield of **9f** was increased to 30% with *trans*-isomer : *cis*-isomer = 1 : 4.6 (Table 1, Entry 7).

Although, at the present stage of the investigation, the structure-reactivity relationship is not elucidated, the reaction described in this paper makes several selenetanes readily available and suggests a number of interesting possibilities for the further work.

General procedure for the preparation of selenetanes: To a suspension of KH (1.3-3.5 molar amounts. Aldrich; 35 wt %, washed with hexane) in THF was added dropwise under N_2 at room temperature a solution of 2-(3-hydroxyalkylseleno)benzoxazole (**8**) in THF. The resulting mixture was stirred at room temperature until **8** was consumed (0.5-24 h). The reaction was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with CH_2Cl_2 and the organic layer was dried with $MgSO_4$ and filtered. After evaporation, the residue was separated by silica gel layer chromatography. When the reaction was sluggish, the reaction was carried out in the presence of 18-crown-6. The results are summarized in Table 1.

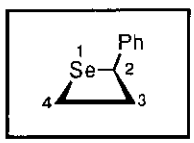
This work was supported in part by a Grant-in-Aid for Scientific Research from Ministry of Education, Science, Sports and Culture, Japan.

REFERENCES AND NOTES

1. See for example, a) T. Mukaiyama, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 707. b) A. R. Katritzky, S. Rachwal, and G. J. Hitchings, *Tetrahedron*, 1991, **47**, 2683. c) T. Mukaiyama, M. Imaoka, and T. Izawa, *Chem. Lett.*, 1977, 1257. d) T. Mukaiyama, M. Yamaguchi, and K. Narasaka, *Chem. Lett.*, 1978, 689. e) S. Valverde, M. Bernabé, S. Garcia-Ochoa, and A. M. Gómez, *J. Org. Chem.*, 1990, **55**, 2294, and refs therein. f) A. R. Katritzky, W.-Q. Fan, and Q.-H. Long, *Synthesis*, 1993, 229.
2. See for example, H. Takei, H. Sugiura, M. Miura, and H. Okamura, *Chem. Lett.*, 1980, 1209. b) H. Sugimura, H. Okamura, M. Miura, M. Yoshida, and H. Takei, *Nippon Kagaku Kaishi*, 1985, 416.
3. V. Calo, L. Lopez, L. Marchese, and G. Pesce, *Synthesis*, 1976, 621. See also V. Calo, L. Lopez, L. Marchese, and G. Pesce, *J. Chem.* Soc.. *Chem. Commun.*, 1975, 621.

4. K. Shibata and O. Mitsunobu, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 3163.
5. For the preparation and reactions of selenetanes, see for example, a) B. Lindren, *Chemica Scripta.*, 1980, **16**, 24. b) G. Polson, and D. C. Dittmer, *J. Org. Chem.*, 1988, **53**, 791. c) M. R. Detty, 'Comprehensive Heterocyclic Chemistry II: Four-membered Ring with One Selenium or Tellurium Atom, ' ed. by A. R. Katrtzky, C. W. Rees, and E. F. V. Scriven, Volume ed., A. Padwa, Pergamon, Oxford, 1996, pp. 823-831. For the properties and reactions of organoselenium compounds, see for example, C. Paulmier, 'Selenium Reagents and Intermediates in Organic Synthesis,' Pergamon Press, Oxford, 1986.
6. The alkyl group of an alcohol was incorporated into 2-selenobenzothiazole residue in the reaction with 2-(1,2-diphenyl-2-oxoethylseleno)benzothiazole and tributylphosphine. K. Shibata and O. Mitsunobu, *Chem. Lett.*, 1993, 549.
7. Spectroscopic data; NMR spectra (270 MHz) were taken in $CDCl_3$ using TMS as internal standard (δ, ppm).

9a: ^{1}H-NMR; 2.80-2.90 (m, 1H, H_a-4), 3.37-3.67 (m, 3H, H_b-4, H_a-3, H_b-3), 5.12 (dd, 1H, H-2, $J_{2,\,3a}$ = 7.75 Hz, $J_{2,\,3b}$ = 9.07 Hz), 7.19-7.54 (m, 5H, aromatic-H). HRMS; Found: m/z = 197.9967 (M^+), Calcd for $C_9H_{10}Se$: 197.9948.



9d: ^{1}H-NMR; 0.95 (s, 3H, $C\underline{H}_3$), 1.20 (s, 3H, $C\underline{H}_3$), 2.47 (d, 1H, H_a-4, $J_{4a,\,4b}$ = 7.58 Hz), 3.15 (d, 1H, H_b-4), 4.82 (s, 1H, H-2), 7.20- 7.34 (m, 5H, aromatic-H). MS; m/z = 225 (M^+-1), 148, 77.

trans-**9e**: ^{1}H-NMR; 1.00 (d, 3H, CH_3 , J_{vic} = 6.6 Hz), 2.90 (dd, 1H, H_a-4, $J_{3,\,4a}$ = 7.92-8.24 Hz), 3.07 (dd, 1H, H_b-4, $J_{4a,4b}$ = 7.91 Hz, $J_{3,\,4b}$ = 9.89 Hz), 3.51-3.70 (m, 1H, H-3), 4.63 (d, 1H, H-2, $J_{2,\,3}$ = 9.57 Hz), 7.16-7.52 (m, 5H, aromatic-H). HRMS; Found: m/z = 212.0073 (M^+), Calcd for $C_{10}H_{12}Se$: 212.0104.

trans-**9f**: ^{1}H-NMR; 0.73 (t, 3H, $C\underline{H}_3CH_2$, J_{vic} = 7.25 Hz), 1.42 (dq, 2H, $CH_3C\underline{H}_2$, $J_{vic} \approx J_{3,\,CH_2}$ = 7.25 Hz), 2.90 (dd, 1H, H_a-4, $J_{3,\,4a}$ = 8.24 Hz, $J_{4a,\,4b}$ = 7.92 Hz), 3.05 (dd, 1H, H_b-4, $J_{3,\,4b}$ = 9.73 Hz), 3.38-3.54 (m, 1H, H-3), 4.69 (d, 1H, H-2, $J_{2,\,3}$ = 9.56 Hz), 7.18-7.52 (m, 5H, aromatic-H). HRMS; Found: m/z = 226.0251 (M^+), Calcd for $C_{11}H_{14}Se$: 226.0261.

cis-**9f**: ^{1}H-NMR; 0.61 (t, 1H, $C\underline{H}_3CH_aH_b$, J_{vic} = 7.25 Hz), 1.05 (ddq, 1H, $CH_3C\underline{H}_aH_b$, $J_{Ha,\,Hb}$ = 13.9 Hz, $J_{3,\,CHa}$ = 6.59-7.25 Hz), 1.23-1.34 (m, 1H, $CH_3CH_aC\underline{H}_b$), 3.02 (dd, 1H, H_a-4, $J_{4a,\,4b} \approx J_{3,\,4a}$ = 7.91-8.24 Hz), 3.20 (dd, 1H, H_b-4, $J_{4a,\,4b} = J_{3,\,4b}$ = 8.24 Hz), 3.61-3.76 (m, 1H, H-3), 4.85 (d, 1H, H-2, $J_{2,\,3}$ = 8.90 Hz), 7.14-7.54 (m, 5H, aromatic-H).

Received, 30th April, 1997