PREPARATION OF 2-ALKYLSELENOBENZOTHIAZOLES BY THE REACTION OF ALCOHOLS WITH 2-(2-OXOETHYLSELENO)BENZOTHIAZOLES IN THE PRESENCE OF TERTIARY PHOSPHINES

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Abstract–Reactions of alcohols with 2-(1,2-diphenyl-2-oxoethylseleno)-benzothiazole in the presence of Bu_3P gave the corresponding 2-alkylseleno-benzothiazoles, where inversion of the secondary carbinol center of the alcohols took place. 1,3-Butanediol reacted at the primary hydroxyl group, while 1-phenyl-1,2-ethanediol reacted at the secondary hydroxyl group.

INTRODUCTION

Functionalized 2-alkylseleno aza-aromatic compounds of general formula (**1**) (Figure 1) have a potential for performing highly efficient transformation of the alkyl residues.[1,2]

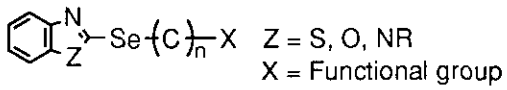

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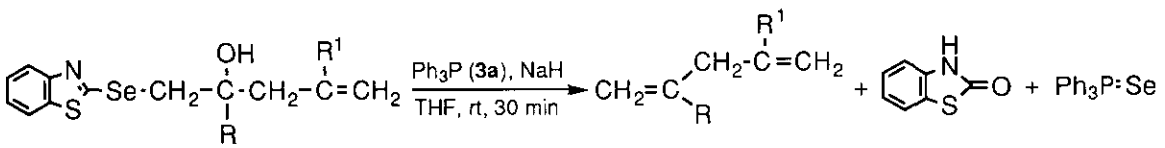
Figure 1

In a previous paper, we reported that the reaction of 2-(2-hydroxyalkylseleno)benzothiazoles (**2**) with NaH in the presence of Ph_3P (**3a**) to afford the corresponding 1,4-dienes (**4**) in good to excellent yields (Scheme 1).[3]



2 **4**

R = Ph, $PhCH_2$, $PhCH_2CH_2$
R^1 = H, Me

Scheme 1

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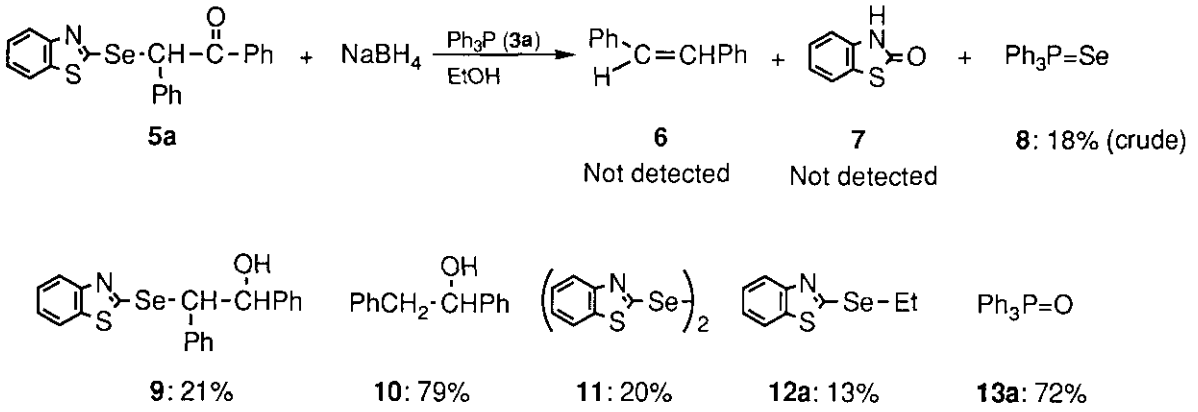
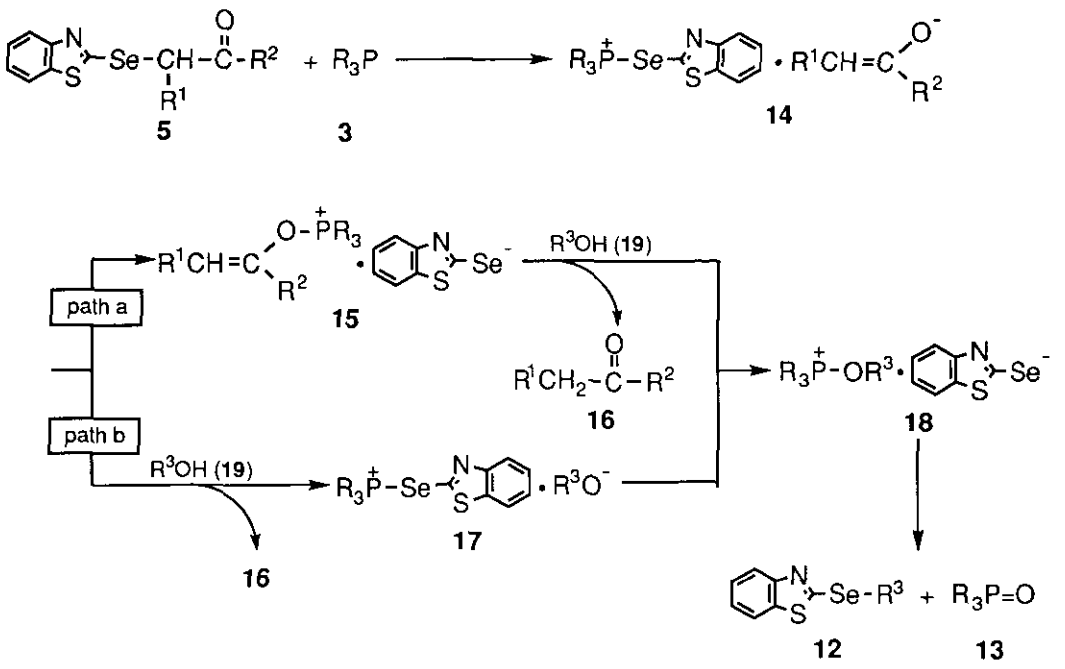
In order to extend this transformation to the synthesis of olefins by one-pot procedure, the reaction of 2-(1,2-diphenyl-2-oxoethylseleno)benzothiazole (**5a**) with $NaBH_4$ in the presence of **3a** was carried out in ethanol. Contrary to our expectation, however, no expected stilbene (**6**) and benzothiazol-2-one (**7**) were obtained but compounds (**8, 9, 10, 11, 12a, 13a**) were isolated in the yields shown in Scheme 2. The predominant formation of 1,2-diphenylethanol (**10**: 79%) suggested that the initially formed 2-(2-hydroxy-1,2-diphenylethylseleno)benzothiazole (**9**: 21%) was reductively cleaved prior to Se→O aza-aromatic ring rearrangement.[3] Of the products isolated, the formation of 2-ethylselenobenzothiazole (**12a**) attracted our attention, because ethanol used as a solvent entered into the reaction and the ethyl residue was directly incorporated into benzothiazolyl group. In the hope to establish a new route for the preparation of a variety of 2-alkylselenobenzothiazoles, we examined the reaction of alcohols with **5a** in the presence of tertiary phosphines.[4]



Scheme 2

RESULTS AND DISCUSSION

Reaction using Ph_3P. The formation of 2-alkylselenobenzothiazole (**12**) could be explained by the assumption that the phosphorus atom of tertiary phosphine (**3**) attacked the selenium atom of α-selenoketone (**5**) to give the phosphonium enolate (**14**) which in turn converted into enol phosphonium salt (**15**) as in the case of Perkow reaction. The enol phosphonium salt (**15**) subsequently reacted with alcohol (**19**) to afford alkoxyphosphonium salt (**18**). Collapse of **18** gave **12** and phosphine oxide (**13**) (Scheme 3, path a).[5-7] Another possible route for the generation of alkoxy phosphonium salt (**18**) is that involving phosphonium alkoxide (**17**) by anion exchange of phosphonium enolate (**14**) (Scheme 3, path b). However, the path b is unlikely because pKa (in DMSO) of 1,2-diphenylethanone (**16a**: $R^1 = R^2 = Ph$) is 17.7 and those of alcohols are 28~29.[8]



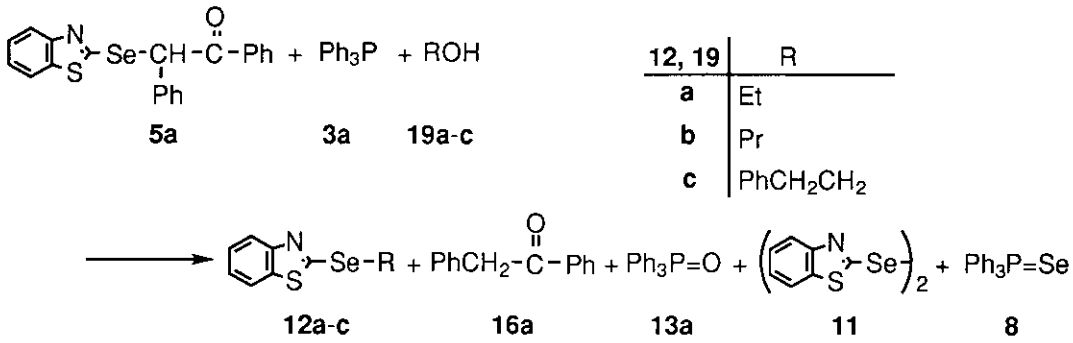
Scheme 3

Whatever the course of the reaction may be, no $NaBH_4$ would be required in the formation of 2-alkylselenobenzothiazoles (**12**). Therefore, the reaction of **5a** with alcohols and **3a** in the absence of $NaBH_4$ was studied.

At the outset, **5a** reacted with **3a** (1.2 ma*) in EtOH (**19a**) at room temperature for 8 h. Although 1,2-diphenylethanone (**16a**) was obtained quantitatively, the yield of expected 2-ethylselenobenzothiazole (**12a**) was only 35% (Scheme 4, Table 1, Entry 1). Elongation of the reaction time to 18 h gave practically same result (Entry 2). When the reaction was carried out in propanol (**19b**) for 18 h, the yield of 2-propylselenobenzothiazole (**12b**) was again as low as 23% (Entry 3). In these reactions, **16a** and triphenylphosphine oxide (**13a**) were obtained in good to excellent yields.

Next, **5a** was allowed to react with 2-phenylethanol (**19c**: 1.5 ma) and **3a** (1.1 ma) in benzene where the progress of the reaction was monitored by TLC. The spot of **5a** disappeared after stirring for 4.5 h at room temperature, but that of 2-(2-phenylethylseleno)benzothiazole (**12c**) did not appear at all even after the reaction mixture was stirred overnight. When the mixture was heated under reflux, the spot of **12c** appeared and, after 8 h, the desired product (**12c**) was obtained in 44% yield with 12% (or 42% based on **19c** used) recovery of the starting alcohol (**19c**) (Entry 4). When the reaction was carried out under reflux for 16 h, the yield of **12c** was increased to 72% with 26% (or 51% based on **19c** used) recovery of **19c** (Entry 5).

* ma = Molar amount.



Scheme 4

Table 1. Reaction of alcohol (**19**) with **5a** and **3a**

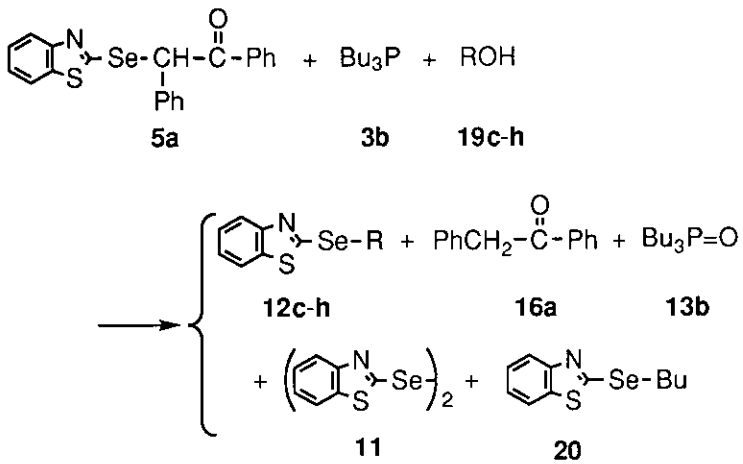
Entry	ROH R	Conditions[a]	Products and Yields/%[b] 12	16a	11	13a	8	Recov./%[b] 19	3a
1	**19a**: Et	A: rt (8 h)	**12a**: 35	>99	29[c]	71	nd	**19a**: nd	nd
2	**19a**: Et	A: rt (18 h)	**12a**: 33	>99	25[c]	71	+	**19a**: nd	6
3	**19b**: Pr	A: rt (18 h)	**12b**: 23	>99	49	68	8	**19b**: nd	nd
4	**19c**: $PhCH_2CH_2$	B: rt (20 h) → reflux (8 h)	**12c**: 44	>99	14	56	15	**19c**: 42[d]	2
5	**19c**: $PhCH_2CH_2$	B: reflux (16 h)	**12c**: 72	92	5[c]	64	6	**19c**: 51[d]	4

a) A: Alcohol was used as a solvent/molar ratio of **5a** : **3a** = 1 : 1.1. B: Benzene was used as a solvent/molar ratio of **5a** : **3a** : **19c** = 1 : 1.1 : 1.5. b) nd = Could not be detected. c) Yield of crude product. d) Recovery based on **19c** used. When the excess was subtracted, the recovery of **19c** was 12% (Entry 4) and 26% (Entry 5), respectively.

In the present reaction, the selenophilicity of phosphines, oxygen-affinity of phosphonio group, and nucleofugacity of 2-oxo-1,2-diphenylethyl residue would play important roles. Since trialkylphosphines are believed to have enhanced selenophilicity and oxygen-affinity than triarylphosphines, a series of reactions were carried out by the use of Bu_3P (**3b**) instead of **3a**.

Reactions using Bu_3P. Reaction of a variety of alcohols with **5a** and Bu_3P (**3b**) was carried out in benzene at room temperature for 2 h (Scheme 5, Table 2). When **19c** reacted with **5a** and **3b** in a molar ratio of 1 : 1 : 1, the expected **12c** was obtained in 78% yield (Entry 1). Secondary alcohol also reacted smoothly to afford the corresponding 2-alkylselenobenzothiazoles (Entries 2 and 4). Functional groups such as chloro, cyano, and alkoxycarbonyl groups were intact in the present reaction system (Entries 3, 4, and 5).

When crotyl alcohol (**19h**) reacted with **5a** and **3b** under the same conditions, 2-(2-butenylseleno)benzothiazole (**12h**) was obtained in 50% yield. Although the yield was moderate, no products arose from allylic rearrangement could be detected (Entry 6).



12, 19	R
c	$PhCH_2CH_2$-
d	PhCH(Me)-
e	$ClCH_2CH_2$-
f	PhCH(COOMe)-
g	$NCCH_2CH_2$-
h	$MeCH=CHCH_2$-

Scheme 5

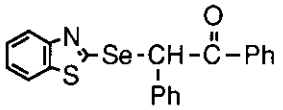
Table 2. Reaction of alcohol (**19**) with **5a** and **3b**

Entry	ROH R	Condi-tions[a]	Products and Yields/% 12	16a	11	20	Recov./%[b] 19	5a
1	**19c**: $PhCH_2CH_2$-	B	**12c**: 78	94	18	1	**19c**: 13	2
2	**19d**: PhCH(Me)-	B	**12d**: 70	>99	16	1[c]	**19d**: 5	3
3	**19e**: $ClCH_2CH_2$-	T	**12e**: 72	91	20[c]	5	**19e**: nd	3
4	**19f**: PhCH(COOMe)-	T	**12f**: 94	96	2[c]	3	**19f**: 6	1
5	**19g**: $NCCH_2CH_2$-	T	**12g**: 65	94	28[c]	5[c]	**19g**: nd	2
6	**19h**: $MeCH=CHCH_2$-	T	**12h**: 50	83	39[c]	3	**19h**: nd	8

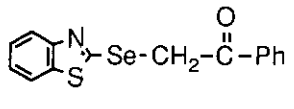
a) B: Reaction was carried out in benzene at room temperature for 2 h. Molar ratio of **19** : **5a** : **3b** = 1.0 : 1.0 : 1.0. T: Reaction was carried out in tetrahydrofuran (THF) at 0 °C for 1 h. Molar ratio of **19** : **5a** : **3b** = 1.0 : 1.1 : 1.2. b) nd = Could not be detected. c) Yield of crude product.

In the present system, the reaction would be initiated by the attack of the phosphorus atom to the selenium atom of **5a**. Therefore, the steric requirement of the reaction site would be expected to be essential for the success of the reaction. Thus, the reactions using α-selenoketones without substituent at the α-position to the carbonyl group were compared with that of **5a**.

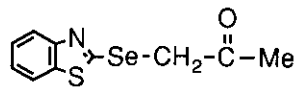
The α-selenoketones (**5a**, **5b**, **5c**) reacted with **19c** and **3b** (molar ratio = 1 : 1 : 1) in benzene at room temperature for 2 h to afford **12c** in 78%, 55% and 41% yields, respectively (Figure 2, Table 3). These results suggested that the steric bulk around the carbon atom neighboring to the seleno group is not crucial in the present reaction.



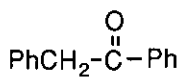
5a



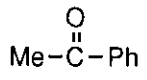
5b



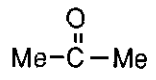
5c



16a
(pKa 17.7)



16b
(pKa 24.7)



16c
(pKa 26.5)

Figure 2

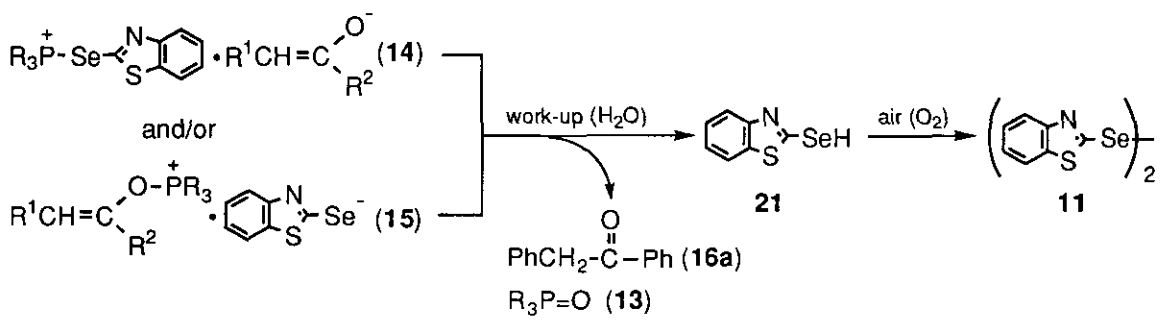
The 2-oxoalkyl residue in α-selenoketones (**5**) functioned as leaving group. The pKa values of **16a**, **16b**, and **16c** were reported to be 17.7, 24.7, and 26.5 (in DMSO), respectively.[8] The correlation observed between the yield of **12c** and pKa value of conjugate acid of leaving enolate is consistent with generality, the weaker the base the better the leaving group. Thus, the yield of **12c** was proportional to acidity of the parent ketone.

Table 3. Reaction of **5** with **19c** and **3b**

Entry	ArSe–CHR^1-C(=O)-R^2 (**5**)[a]			Products and Yields/%				Recov./%	
	No	R^1	R^2	**12c**	**16**	**11**	**20**	**19c**	**5**
1[b]	**5a**	Ph	Ph	78	**16a**: 94	18	1	13	**5a**: 2
2	**5b**	H	Ph	55	**16b**: –[c]	38[d]	3	15	**5b**: 4
3	**5c**	H	Me	41	**16c**: –[c]	53[d]	1	30	**5c**: 5[d]

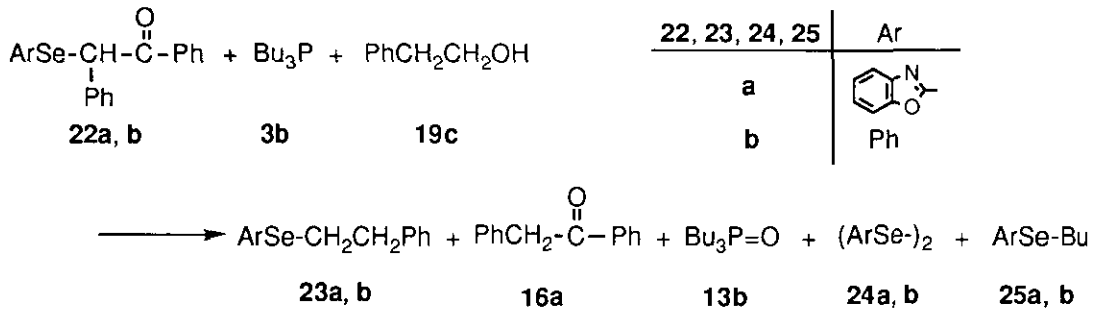
a) Ar = Benzothiazol-2-yl. b) Taken from Table 2, Entry 1. c) Because of low boiling point, the yield could not be determined. d) Yield of crude product.

In these reactions, the yield of diselenide (**11**) increased with decrease of **12c**. Monitoring of the progress of the reaction by TLC revealed that **5** was consumed rapidly in the early stage of reaction irrespective of the substituent pattern at the α-position to the carbonyl group. This observation suggested that the formation of **14** was not rate-determining step. The side product (**11**) would be formed by the hydrolysis of unreacted phosphonium salts (**14**) and/or (**15**) and subsequent oxidation (air) of the resulting benzothiazol-2-selenol (**21**) during manipulation (Scheme 6). Thus, when the transformation of **14** to **15** to **18** is sluggish, the yield of **11** should be increased. If one assume that the rate of conversion of **15** to **18** is proportional to the acidity of the eliminating ketone, the result obtained in the reaction using different kind of α-selenoketones (**5**) (Table 3) could be rationalized. Based on the mechanism proposed above, the formation of varied amount of **11** (Table 3) could be explained in terms of the difference of reactivity of **15** toward alcohol.



Scheme 6

In view of the mechanism shown in Scheme 3, a variety of aromatic group other than benzothiazolyl group could also be directly introduced into alkyl residues of alcohols. Thus, 2-(1,2-diphenyl-2-oxoethylseleno)benzoxazole (**22a**) reacted with **19c** and **3b** in THF at 0 °C for 4 h to give 2-(2-phenylethylseleno)benzoxazole (**23a**) in 68% yield. Similarly, 1,2-diphenyl-1-phenylseleno-2-ethanone (**22b**) reacted with **19c** and **3b** in benzene at room temperature for 2 h to afford the expected (2-phenylethylseleno)benzene (**23b**) in 72% yields (Scheme 7, Table 4).[9]



Scheme 7

Table 4. Reaction of **22** with **19c** and **3b**

Entry	ArSe–CHPh-C(=O)-Ph		Products and Yields/%[a]				Recov./%	
	No	Ar	23	16a	24	25	19c	22
1	**22a**	Benzoxazol-2-yl[b]	**23a**: 68	>99	**24a**: nd	**25a**: 4	28	**22a**: 12
2	**22b**	Ph[c]	**23b**: 72	98	**24b**: 8	**25b**: nd	14	**22b**: 4[d]

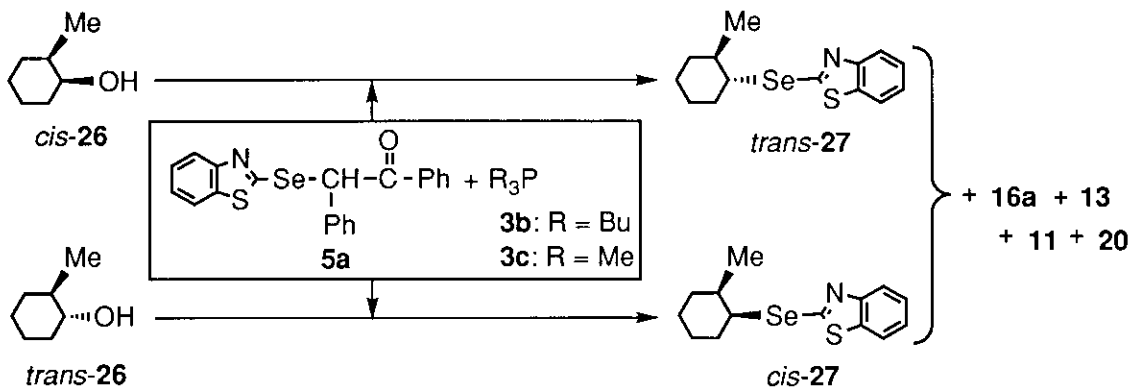
a) nd = Could not be detected. b) Reaction was carried out in THF at 0 °C for 4 h. c) Reaction was carried out in benzene at rt for 2 h. d) Recovery of crude substance.

Stereochemistry. Since the alkylation reaction *via* an alkoxyphosphonium salt generally proceeds in SN2 mode, inversion of configuration at the reaction site of alcoholic component takes place.[10,11]

In order to confirm the stereochemistry of the present reaction system, the reactions of (±)-*cis*- and *trans*-2-methylcyclohexanols (*cis*-**26** and *trans*-**26**) with **5a** and **3b** in THF were investigated (Scheme 8).

When *cis*-**26** was allowed to react with **5a** and **3b** in a molar ratio of 1 : 1.1 : 1.2 at room temperature for 14 h, 1-(benzothiazol-2-ylseleno)-2-methylcyclohexane (**27**) was obtained in 17% yield as a single stereoisomer (Table 5, Entry 1). The structure was confirmed to be *trans* by ^{1}H-NMR study (*vide infra*). Under the similar conditions (room temperature for 24 h), the reaction of *trans*-2-methylcyclohexanol (*trans*-**26**) with **5a** and **3b** afforded *cis*-1-(benzothiazol-2-ylseleno)-2-methylcyclohexane (*cis*-**27**) in 33% yield (Entry 3).

In order to minimize any steric hindrance at the reaction site, Me_3P (**3c**) was used instead of **3b**, where the yields of *trans*-**27** and *cis*-**27** were increased to 26% and 64% , respectively (Entries 2 and 4).



Scheme 8

Table 5. Reaction of 2-methylcyclohexanol (*cis*-**26** and *trans*-**26**) with R_3P (**3**) and **5a**

Entry	Alcohol	3	Conditions Temp (time/h)	Products and Yields/%[a] 27	16a	11	20	Recov. of 5a/%
1	*cis*-**26**	**3b**: Bu_3P	rt (14)[b]	*trans*-**27**: 17	95	63	7	8[c]
2	*cis*-**26**	**3c**: Me_3P	reflux (1.5)	*trans*-**27**: 26	98	44	nd	2
3	*trans*-**26**	**3b**: Bu_3P	rt (24)	*cis*-**27**: 33	88	55[c]	9	14
4	*trans*-**26**	**3c**: Me_3P	rt (1) → reflux (1)	*cis*-**27**: 64	92	29	nd	6

a) nd = Could not be detected. b) Practically same result was obtained when the reaction was carried out at 0 °C for 1.7 h, followed by rt for 1.3 h and then under reflux for 0.5 h. c) Recovery of crude substance.

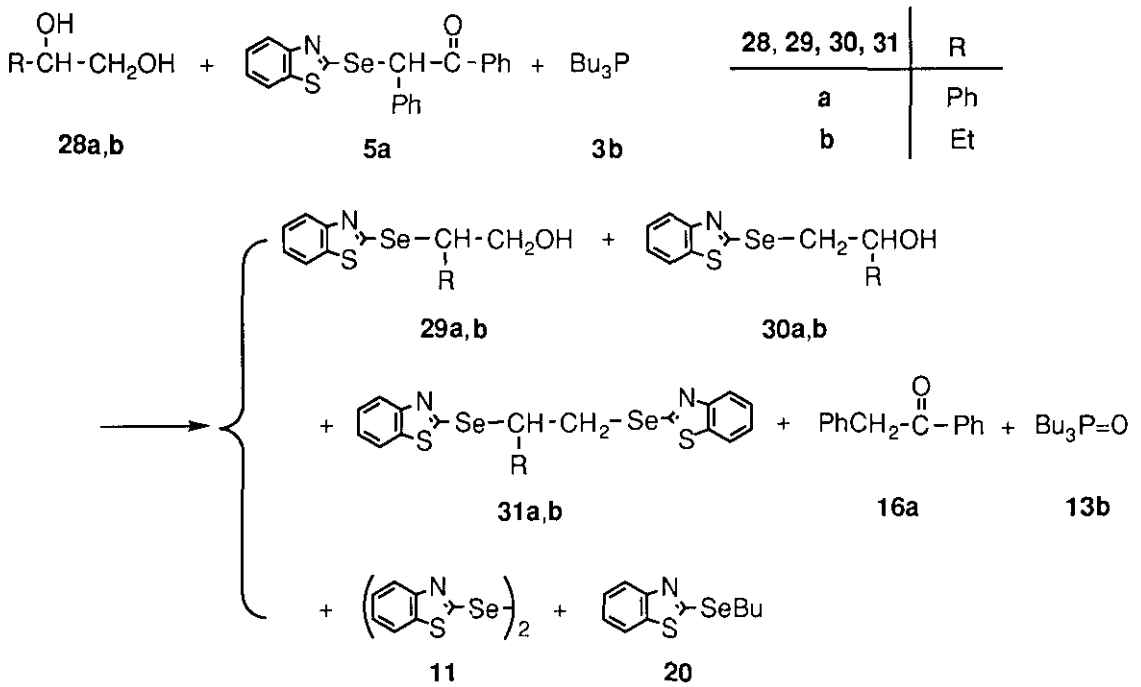
The structures of *trans*-**27** and *cis*-**27** were determined by ^{1}H-NMR. Thus, for **27** arose from *cis*-**26**, the signal of the proton on C-1 showed the splitting of doublet of triplets with $J_{1H,2H}$ = $J_{1H,6Ha}$ = 11.21 Hz and $J_{1H,6Hb}$ = 3.96 Hz, while **27** arose from *trans*-**26** showed a quartet with $J_{1H,2H}$ =

$J_{1H,6Ha} = J_{1H,6Hb} = 3.96$ Hz. These values indicated that the former is *trans*-isomer, while the latter is *cis*-isomer. Since 1-(benzothiazol-2-ylseleno)-2-methylcyclohexane (**27**) was obtained as a single stereoisomer, the complete inversion of the configuration of the secondary carbinol center took place during the collapse of alkoxyphosphonium salt (**18**).[10,11]

Reaction with Diols. a) Optimum Conditions. In general, condensation reactions between polyols and an acidic component mediated by the reagent formed by the combination of a tertiary phosphine with oxidative electrophiles take place at the less hindered site.[10–12]

In order to investigate the regiochemistry of the present system, the reaction of 1-phenyl-1,2-ethanediol (**28a**) with **5a** and **3b** in benzene was examined. Thus, **5a** was allowed to react with **3b** for 10 min, where the phosphonium salt **14** would be expected to be formed. To this solution was added **28a** to afford 2-(2-hydroxy-1-phenylethylseleno)benzothiazole (**29a**) and 2-(2-hydroxy-2-phenylethylseleno)benzothiazole (**30a**) in 39% and 4% yields with 57% recovery of **28a** (Scheme 9, Table 6, Entry 1).

Since the yield of the condensation product was unexpectedly low, several attempts were made to optimize the reaction conditions by changing the order of the addition of the reagents, and solvents as well. When a solution of **5a** was added to a solution of **3b** (2 ma), and, after 5 min, **28a** in benzene was added to the reaction mixture, the yield of **29a** was increased to 51% along with **30a** (1%) and 1,2-bis(benzothiazol-2-ylseleno)-1-phenylethane (**31a**: 13%). However, diselenide (**11**) was again obtained in 20% yield (Table 6, Entry 2).



Scheme 9

When **5a** was added to a mixture of **28a** and an equimolar amount of **3b**, **29a** was formed in 32% yield (Table 6, Entry 3). In this reaction, neither **30a** nor **31a** could be obtained, but the yield of **11** was increased to 30% (Entry 3). However, the formation of undesirable diselenide **11** was suppressed (2% yield) by the use of 2 molar amounts of **3b** under the same conditions where **29a**, **30a**, and **31a** were obtained in 45%, 1%, and 18% yields, respectively (Entry 4). When 2 molar amounts of **3b** was added to a mixture of **5a** and **28a** in benzene, **29a** and **31a** were obtained in 72% and 12% yields (Entry 5).

Table 6. Reaction of 1-phenyl-1,2-ethanediol (**28a**) with **5a** and **3b** in benzene at rt for 2 h

Entry	Molar ratio	Procedure[a]	Products and Yields/%[b]						Recov./%[b]	
	28a : 5a : 3b		**29a**	**30a**	**31a**	**16a**	**11**	**20**	**28a**	**5a**
1	1.0 : 1.0 : 1.0	1) **5a** 2) **3b** 3) **28a**	39	4	0	89	19	5	57	10
2	1.0 : 1.1 : 2.0	1) **3b** 2) **5a** 3) **28a**	51	1	13[d]	96	20	8[d]	17	nd
3	1.0 : 1.0 : 1.0	1) **28a** 2) **3b**[c] 3) **5a**	32	nd	nd	60	30[d]	4[d]	43	26
4	1.0 : 1.1 : 2.0	1) **28a** 2) **3b**[c] 3) **5a**	45	1	18	>99	2	11[d]	12	nd
5	1.0 : 1.1 : 2.0	1) **5a** + **28a** 2) **3b**	72	nd	12	>99	8	nd	6	nd

a) Order of addition of reagents. b) nd = Could not be detected. c) Diol (**28a**) did not dissolved completely. d) Yield of crude product.

Although the yield of **29a** reached up to 72%, the drawback was low solubility of diol **28a** in benzene. The low solvilizing ability and high freezing point of benzene may be, at least in part, responsible for the formation of considerable amount of **31a**. In order to find a suitable solvent, the reaction was carried out in benzene, dichloromethane, THF, or *N*,*N*-dimethylformamide (DMF). Results are summarized in Table 7. As can be seen from the Table, the reaction was optimized when it was carried out in THF at 0 °C to afford **29a** in 74% yield without any detectable formation of **31a** (Table 7, Entry 4).[13]

Table 7. Reaction of **28a** with **5a** and **3b** in different solvents[a]

Entry	Solvent (mL)	Temp	Products and Yields/%[b]						Recov./%	
			29a	**30a**	**31a**	**16a**	**11**	**20**	**28a**	**5a**
1	Benzene (6.5)	rt	57	2	nd	80	41[c]	5	43[c]	9
2	CH_2Cl_2 (1.5)	rt	65	1	1	91	21	6	16	<6
3	THF (1.5)	rt	69	4	5	84	14	5	3[c]	<3
4	THF (1.5)	0 °C	74	2	nd	87	15	5	10	3
5	DMF (2.0)	0 °C	28	2[c]	nd	92	44	5	64	4

a) To a mixture of **28a** (0.5 mmol) and **5a** (0.55 mmol) was added **3b** (0.6 mmol) and the reaction was carried out for 1 h. b) nd = Could not be detected. c) Yield of crude product.

b) Regiochemistry. As described above, the reaction of **28a** with **5a** and **3b** took place at the more hindered site irrespective of the reaction conditions. This result could be explained by assuming phosphorane intermediate (**32a**) rather than phosphonium salt (**33a** or **34a**) as demonstrated by Evans, Jr. (Figure 3).[14]

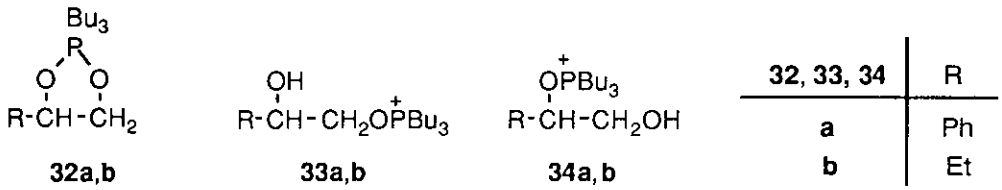


Figure 3

Contrary to the clean regioselectivity observed in **28a**, the reaction of 1,2-butanediol (**28b**) with **5a** (1.1 ma) and **3b** (1.2 ma) in THF at 0 °C for 1 h by the same procedure described above gave both 2-(1-hydroxymethylpropylseleno)benzothiazole (**29b**) and 2-(2-hydroxybutylseleno)benzothiazole (**30b**) in 8% and 8% yields, respectively (Scheme 9, Table 8, Entry 1). Although the yields of **29b** and **30b** were increased under forced conditions, the product ratio was practically unchanged (ca 1 : 1) (Table 8, Entries 2 and 3).

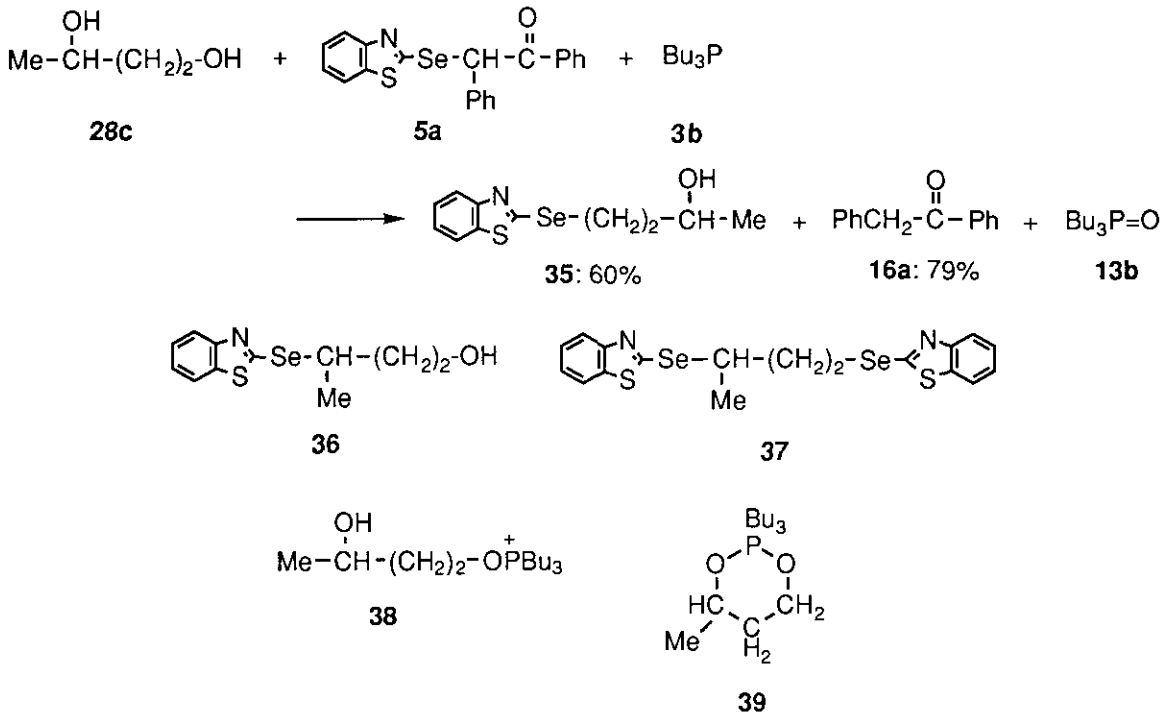
Table 8. Reaction of 1,2-butanediol (**28b**) with **5a** and **3b**

Entry	Conditions	Products and Yields/%					Recov./%	
	Temp (time/h)	**29b**	**30b**	**16a**	**11**	**20**	**28b**	**5a**
1	0 °C (1)	8	8	93	65[a]	7	42	2
2	0 °C (2) → rt (15)	30	28	88	35[a]	5	36	4
3	reflux (2)	38	39	91	12	5	9	4

a) Yield of crude product.

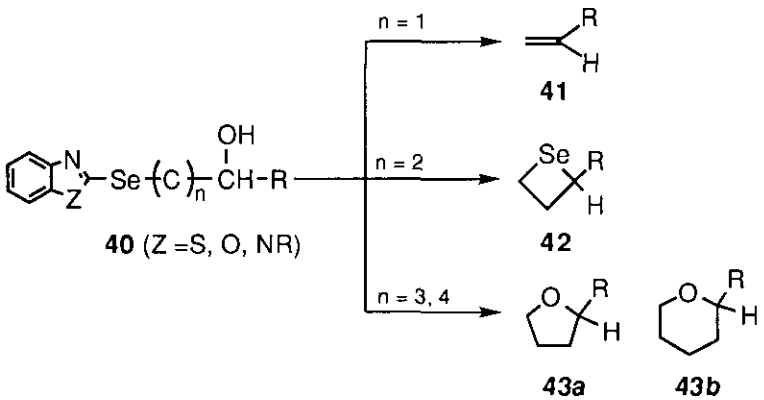
Similar to the reaction using **28a**, phosphorane **32b** rather than alkoxyphosphonium salt **33b** or **34b** would be reasonable to assume as the key intermediate of the present transformation (Figure 3), The difference of the selectivity observed in the transformation of **28a** and **28b** suggested that developed cationic character at the reaction site are major controlling factors for exhibiting regioselectivity.

When 1,3-butanediol (**28c**) reacted with **5a** and **3b** under the same conditions as above, 2-(3-hydroxybutylseleno)benzothiazole (**35**) was obtained in 60% yield without formation of 2-(3-hydroxy-1-methylpropylseleno)benzothiazole (**36**) and 1,3-bis[(benzothiazol-2-yl)seleno]butane (**37**) (Scheme 10). Diselenide (**11**) and **20** were isolated in 25% and 7% yields. The formation of **35** could be explained by assuming phosphonium salt (**38**) rather than phosphorane (**39**).



Scheme 10

By the procedure described in this paper, a variety of alcohols could be directly converted into the corresponding 2-alkylselenobenzothiazoles by the reaction with **5a** and tertiary phosphines. The resulting 2-alkylselenobenzothiazoles could be considered to be activated alcohols. The present reaction system could be readily extended to the preparation of a variety of 2-(hydroxyalkylseleno)azoles (**40**), which were converted into olefins (**41**),[3] selenetanes (**42**),[15] and cyclic ethers (**43**)[16] (Scheme 11).



Scheme 11

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

EXPERIMENTAL

General. All the melting points were obtained on Yanagimoto melting point apparatus and uncorrected. IR spectra were recorded on a JASCO Model A-302 spectrophotometer. ^{1}H NMR spectra were obtained on a JEOL JNM GX-270 (270 MHz) spectrometer in deuteriochloroform solution using tetramethylsilane as an internal standard. MS spectra were obtained on a JEOL JMS-SX-102 mass spectrometer operating under EI or FAB conditions. The reactions using selenium compounds were carried out in a well-ventilated hood with caution. All reactions were monitored by TLC (silica gel). Preparative TLC was performed on 20 cm x 30 cm silica gel plates (Merck silica gel 60 PF_{254} Art. 7734) using UV light for detection and acetonitrile (distilled from P_2O_5) was used for extraction. All solvents used for the reactions were purified by ordinary methods. Elemental analyses were performed by RIKEN Institute (Institute of Physical and Chemical Research), Wako, Saitama.

1-Bromo-1,2-diphenyl-2-ethanone. This compound was prepared by modifying a literature procedure,[17] and was used for the preparation of **5a**. To a solution of 1,2-diphenylethanone (9.80 g, 50 mmol) in benzene (44 mL) was added bromine (2.58 mL, 50 mmol) over a period of 3 min at 0 °C and the mixture was stirred for 1 h at the same temperature. After N_2 was passed through the resulting solution for 5 min, aqueous 10% sodium hydrogen sulfite solution (20 mL) was added. The mixture was filtered through Hyfro Super-Cel. The organic layer was separated, the aqueous layer was extracted with benzene, and the combined organic layer was dried over magnesium sulfate. The solvent was evaporated and 13.9 g of crude product was obtained (syrup, 101%). To the residue were added hexane and a small amount of ethanol to crystallize and filtered. The crude crystals were washed with the combined solvent of hexane and a small amount of ethanol to afford 11.9 g (87%) of 1-bromo-1,2-diphenyl-2-ethanone as white crystals (mp 51-53 °C; lit.,[17] mp 50 °C). ^{1}H NMR δ = 6.39 (1H, s), 7.96-8.00 (2H, m), 7.23-7.58 (8H, m).

2-(1,2-Diphenyl-2-oxoethylseleno)benzothiazole (5a). Sodium borohydride (0.84 g, 22 mmol) was added portionwise to a suspension of **11** (4.26 g, 10 mmol) in ethanol (43 mL) and the mixture was refluxed for 15 min After the mixture was cool to rt, 1-bromo-1,2-diphenyl-2-ethanone (5.52 g, 20 mmol) in ethanol (20 mL) was added, and then the mixture was refluxed for 40 min. After the solvent had been evaporated under reduced pressure, dichloromethane and water were added to the residue and the mixture was filtered through Hyfro Super-Cel. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The combined organic layer was dried over magnesium sulfate and evaporated under reduced pressure. The residue was recrystallized from ethanol to give 7.03 g (86%) of **5a** as yellow crystals (mp 97-99 °C). ^{1}H NMR δ = 6.98 (1H, s), 7.17-7.57 (10H, m), 7.74 (1H, ddd, J = 8.25, 1.32, and 0.66 Hz), 7.90 (^{1}H, ddd, J = 7.92, 1.32, and 0.66 Hz), 8.02-8.11 (2H, m). MS *m/z* 409 (M^+), 354, 304, 268, 224, 215, 196, 167, 152, 135, 106, 91, and 77. HRMS Found: *m/z* 409.0056. Calcd for $C_{21}H_{15}NOSSe$: M,

409.0040. Anal. Calcd for $C_{21}H_{15}NOSSe$: C, 61.76; H, 3.70; N, 3.43. Found: C, 61.55; H, 3.70; N, 3.44.

2-(2-Phenyl-2-oxoethylseleno)benzothiaole (5b) and 2-(Acetonylseleno)benzothiazole (5c). These compounds were prepared as described in a previous paper.[3]

1,2-Diphenyl-1-phenylseleno-2-ethanone (22b). Diphenyl diselenide (**24b**)[18] was used instead of **11**, and **22b** was prepared by the same method as **5a**. The crude product was recrystallized from hexane-ethanol (1 : 1) to give **22b** (56%) as yellow crystals (mp 83-86 °C). ^{1}H NMR δ = 5.84 (1H, s), 7.88-7.91 (2H, m), and 7.16-7.53 (13H, m). MS *m/z* 352 (M^+), 247, 165, 157, 105, and 77. Anal. Calcd for $C_{20}H_{16}OSe$: C, 68.38; H, 4.59. Found: C, 68.62; H, 4.53.

Reaction of 5a with Ph_3P (3a) and an alcohol (19) (Table 1).

A. Reaction using alcohol as a solvent (Entries 1-3). A typical procedure. A solution of **5a** (0.204 g, 0.5 mmol) and **3a** (0.144 g, 0.55 mmol) in ethanol (2 mL) was stirred at rt under argon for 8 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 10 : 1) to give **11**, **12a**, **13a**, and **16a** (Table 1; Entry 1).

Triphenylphosphine selenide (8). White crystals (mp 184-185 °C, lit.,[19] mp 184-185 °C). ^{1}H NMR δ = 7.41-7.64 (9H, m) and 7.66-7.77 (6H, m).

Bis(2-benzothiazolyl)diselenide (11). Yellow crystals (mp 173-174 °C, lit.,[2] 173-174 °C). ^{1}H NMR δ = 7.33 (2H, dt, J = 7.58 and 0.66 Hz), 7.81 (2H, dd, J = 7.58 and 0.66 Hz), and 7.98 (2H, dd, J = 7.58 and 0.99 Hz). MS *m/z* 428 (M^+), 294, 214, and 134.

2-Ethylselenobenzothiazole (12a). A syrup. ^{1}H NMR δ = 1.63 (3H, t, J = 7.58 Hz), 3.36 (2H, q, J = 7.58 Hz), 7.31 (1H, td, J = 7.26 and 1.32 Hz), 7.42 (1H, td, J = 7.26 and 1.32 Hz), 7.80 (1H, dd, J = 7.26 and 1.32 Hz), and 7.93 (1H, dd, J = 7.26 and , 1.32 Hz). MS *m/z* 243 (M^+), 215, 163, 135, and 108.

2-Propylselenobenzothiazole (12b). A syrup. ^{1}H NMR δ = 1.08 (3H, t, J = 7.26 Hz), 1.93 (2H, sextet, J = 7.26 Hz), 3.34 (2H, t, J = 7.26 Hz), 7.30 (1H, ddd, J = 8.74, 7.42, and 1.32 Hz), 7.41 (1H, td, J = 8.74 and 1.32 Hz), 7.79 (1H, dd, J = 7.42 and 0.66 Hz), and 7.92 (1H, ddd, J = 8.74, 1.32, and 0.66 Hz). MS *m/z* 257 (M^+), 215, 176, 135, and 108. HRMS Found: *m/z* 256.9795. Calcd for $C_{10}H_{11}NSSe$: M, 256.9777.

B. Reactions with 19c in benzene (Entries 4 and 5). A typical procedure. To a mixture of **5a** (0.204 g, 0.5 mmol) and **3a** (0.144 g, 0.55 mmol) was added a solution of **19c** (0.092 g, 0.75 mmol) in benzene (2 mL) at rt under argon. The reaction mixture was stirred at the same temperature for 20 h and then refluxed for 8 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 10 : 1) to give **8**, **11**, **12c**, **13a**, and **16a** as summarized in Table 1 (Entry 4).

2-(2-Phenylethylseleno)benzothiazole (12c). A syrup. ^{1}H NMR δ = 3.19 (2H, t, J = 7.75 Hz), 3.57 (2H, t, J = 7.75 Hz), 7.16-7.36 Hz (6H, m), 7.41 (1H, ddt, J = 7.91, 6.92, and, 0.99 Hz), 7.78 (1H, dd, J = 7.91 and 0.99 Hz), and 7.94 (1H, dd, J = 7.91 and 0.66 Hz). MS *m/z* 319 (M^+), 228,

214, 135, 105, 91, and 77.

Reactions of various alcohols (19) with 5a and 3b (Table 2).

A. Reactions of 2- and 1-phenylethanol (Entries 1 and 2). A typical procedure. To a solution of **5a** (0.204 g, 0.5 mmol) and **19c** (0.016g, 0.5 mmol) in benzene (1 mL) was added a solution of **3b** (0.101 g, 0.5 mmol) in benzene (1 mL) at rt and the mixture was stirred at the same temperature under argon for 2 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 10 : 1) to give **11**, **12c**, **16a**, and **20** as summarized in Table 2 (Entry 1).

2-(1-Phenylethylseleno)benzothiazole (12d). A syrup. ^{1}H NMR δ = 1.98 (3H, d, J = 6.93 Hz), 5.21 (1H, q, J = 6.93 Hz), 7.19-7.45 (7H, m), 7.75 (1H, d, J = 7.26 Hz), and 7.98 (1H, d, J = 8.25 Hz). MS *m/z* 319 (M^+), 215, 135, 105, and 77. HRMS (FAB Glycerol matrix) Found: 319.9989. Calcd For $C_{15}H_{14}NSSe$: M+H, 320.0012.

2-Butylselenobenzothiazole (20). A syrup. ^{1}H NMR δ = 0.96 (3H, t, J = 7.26 Hz), 1.50 (2H, sextet, J = 7.59 Hz), 1.88 (2H, quint, J = 7.26 Hz), 3.36 (2H, t, J = 7.26 Hz), 7.30 (1H, ddd, J = 7.92, 7.25, and 1.32 Hz), 7.41 (1H, ddd, J = 8.24, 7.25, and 1.32 Hz), 7.79 (1H, ddd, J = 7.92, 1.32 and 0.66 Hz), and 7.92 (1H, ddd, J = 8.24, 1.32, and 0.66 Hz). MS *m/z* 271 (M^+), 215, and 135. HRMS Found: 270.9927. Calcd for $C_{11}H_{13}NSSe$: M, 270.9934.

B. Reactions of alcohols having various functional groups (19e-h; Entries 3-6). A typical procedure. To a solution of **5a** (0.224 g, 0.55 mmol) and **19e** (0.040 g, 0.5 mmol) in THF (0.5 mL) was added a solution of **3b** (0.121 g, 0.5 mL) in THF (0.5 mL) at 0 °C and the mixture was stirred at the same temperature under argon for 2 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 10 : 1) to give **11**, **12e**, **16a**, and **20** as summarized in Table 2 (Entry 3).

2-(2-Chloroetylseleno)benzothiazole (12e). A syrup. ^{1}H NMR δ = 3.67 (2H, t, J = 7.83 Hz), 3.98 (2H, t, J = 7.83 Hz), 7.33 (1H, ddd, J = 7.92, 7.26, and 0.99 Hz), 7.44 (1H, ddd, J = 7.92, 7.26, and 0.99 Hz), 7.80 (1H, ddd, J = 7.92, 0.99, and 0.33 Hz), and 7.94 (1H, ddd, J = 7.92, 0.99, and, 0.33 Hz). MS *m/z* 277 (M^+), 215, 135, and 102. HRMS Found: 276.9255. Calcd for $C_9H_8NSSeCl$: M, 276.9228.

2-[Phenyl(methoxycarbonyl)methylseleno]benzothiazole (12f). A syrup. ^{1}H NMR δ = 3.75 (3H, s), 5.79 (1H, s), 7.24-7.34 (4H, m), 7.42 (1H, ddd, J = 8.25, 7.26, and 1.32 Hz), 7.52-7.58 (2H, m), 7.76 (1H, ddd, J = 7.92, 1.32, and 0.66 Hz), and 7.96 (1H, ddd, J = 8.25, 1.32, and 0.66 Hz). MS *m/z* 363 (M^+), 304, 283, 251, 223, 214, 149, 135, 121, 105, 91, and 77. HRMS Found: 362.9871. Calcd for $C_{16}H_{13}NO_2SSe$: M, 362.9832.

2-(2-Cyanoetylseleno)benzothiazole (12g). A syrup. ^{1}H NMR δ = 3.10 (2H, t, J = 7.09 Hz), 3.54 (2H, t, J = 7.09 Hz), 7.33 (1H, td, J = 7.59 and 0.66 Hz), 7.43 (1H, ddd, J = 7.92, 7.59, and 1.32 Hz), 7.80 (1H, ddd, J = 7.59, 1.32, and 0.66 Hz), and 7.92 (1H, dt, J = 7.92 and 0.66 Hz). MS *m/z* 268 (M^+), 228, 215, 187, 135, 108, and 102. HRMS Found: 267.9598. Calcd for $C_{10}H_8N_2SSe$: M, 267.9573.

(*E*)-2-(2-Butenylseleno)benzothiazole (12h). A syrup. ^{1}H NMR δ = 1.68 (3H, ddd, J = 3.96, 1.65, and 0.99 Hz), 3.94-3.97 (2H, m), 5.70-5.76 (2H, m), 7.29 (1H, ddd, J = 7.92, 7.26, and 1.32 Hz), 7.40 (1H, ddd, J = 8.58, 7.26, and 1.32 Hz), 7.78 (1H, ddd, J = 7.92, 1.32, and 0.66 Hz), and 7.93 (1H, ddd, J = 8.58, 1.32, and 0.66 Hz). MS *m/z* 269 (M^+), 214, 188, 135, 108, and 102. HRMS (FAB Glycerol matrix) Found: 269.9837. Calcd for $C_{11}H_{12}NSSe$: M+H, 269.9855. IR (neat) 660, 705, 725, 755, 850, 920, 690, 1010, 1070, 1120, 1190, 1235, 1270, 1310, 1380, 1420, 1455, 1560, 1660, 1690, and 2950 cm^{-1}.

Reaction of 5b or 5c with 19c and 3b (Table 3). α-Selenoketones (**5b**) or (**5c**) reacted with **19c** and **3b** in the same manner as described for **5a**.

Reaction of 22 with 3b and 19c (Table 4).

A. Reaction using 22a. To a solution of **22a** (0.216 g, 0.55 mmol) and **19c** (0.061 g, 0.5 mmol) in THF (1 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in THF (0.5 mL) at 0 °C and the mixture was stirred at the same temperature under argon for 4 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **16a** and **23a** as summarized in Table 4 (Entry 1).

2-(2-Phenylethylseleno)benzoxazole (23a). A syrup. ^{1}H NMR δ = 3.22 (2H, t, J = 7.59 Hz), 3.57 (2H, t, J = 7.59 Hz), 7.19-7.34 Hz (7H, m), 7.43-7.46 (1H, m), and 7.62-7.65 (1H, m). MS *m/z* 303 (M^+), 199, 170, 105, 91, and 77. HRMS Found: 303.0113. Calcd for $C_{15}H_{13}NOSe$: M, 303.0162.

2-Butylselenobenzoxazole (25a). A syrup. ^{1}H NMR δ = 0.97 (3H, t, J = 7.42 Hz), 1.47-1.57 (2H, m), 1.83-1.94 (2H, m), 3.36 (2H, t, J = 7.42 Hz), 7.20-7.31 (2H, m), and 7.44-7.67 (2H, m). MS *m/z* 255 (M^+), 199, and 119. HRMS (FAB *m*-Nitrobenzylalcohol matrix) Found: 256.0212. Calcd for $C_{11}H_{14}NOSe$: M+H, 256.0241.

B. Reaction using 22b. To a solution of **22b** (0.716 g, 0.5 mmol) and **19c** (0.061 g, 0.5 mmol) in benzene (1 mL) was added a solution of **3b** (0.101 g, 0.5 mmol) in benzene (1 mL) at rt and the mixture was stirred at the same temperature under argon for 4 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 10 : 1) to give **16a**, **23b**, and **24b** as summarized in Table 4 (Entry 2).

2-(Phenylethylseleno)benzene (23b). A syrup. ^{1}H NMR δ = 2.86-3.15 (4H, m) and 7.13-7.50 (10H, m).

Reaction of 11 with 3b and 19c (ref 9). To a mixture of **11** (0.123 g, 0.5 mmol) and **19c** (0.061g, 0.5 mmol) in THF (1 mL; diselenide **11** was not dissolved completely) was added a solution of **3b** (0.121 g, 0.6 mmol) in THF (1 mL) at rt and the mixture was stirred at the same temperature under argon for 17.4 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **12c** and **20** in 65% and 1% yields, respectively.

Reaction of 26 with 5a and 3. A typical procedure. To a solution of **5a** (0.224 g, 0.55 mmol) and

(±)-*cis*-**26** (0.057 g, 0.5 mmol) in THF (1 mL) was added a solution of **3b** (0.121g, 0.6 mmol) in THF (0.5 mL) at rt and the mixture was stirred at the same temperature under argon for 14 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **20**, and *trans*-**27** as summarized in Table 5 (Entry 1).

***trans*-1-(Benzothiazol-2-ylseleno)-2-methylcyclohexane (*trans*-27).** A syrup. ^{1}H NMR δ = 1.21-1.90 (8H, m), 1.44 (1H, d, J = 6.60 Hz), 2.36-2.44 (1H, m), 3.60 (1H, td, J = 11.21 and 3.96 Hz), 7.31 (1H, td, J = 7.92 and 1.32 Hz), 7.42 (1H, ddd, J = 8.58, 7.92, and 1.32 Hz), 7.80 (1H, ddd, J = 7.92, 1.32, and 0.66 Hz), and 7.95 (1H, ddd, J = 8.58, 1.32, and 0.66 Hz). MS *m/z* 311 (M^+), 230, 215, and 135. HRMS Found: 311.0245. Calcd for $C_{14}H_{17}NSSe$: M, 311.0247.

***cis*-1-(Benzothiazol-2-ylseleno)-2-methylcyclohexane (*cis*-27).** A syrup. ^{1}H NMR δ = 1.07 (3H, d, J = 6.59 Hz), 1.19-1.39 (2H, m), 1.48-1.72 (4H, m), 1.91-2.06 (2H, m), 2.23 (1H, dq, J = 13.86 and 3.96 Hz), 4.44 (1H, q, J = 3.96 Hz), 7.29 (1H, td, J = 7.58 and 0.99 Hz), 7.40 (1H, td, J = 7.58 and 0.66Hz), 7.77 (1H, dd, J = 7.58 and 0.66 Hz), and 7.91 (1H, dd, J = 7.58 and 0.99 Hz). MS *m/z* 311 (M^+), 230, 215, and 135. HRMS Found: 311.0242. Calcd for $C_{14}H_{17}NSSe$: M, 311.0247.

Reaction of 28a with 5a and 3b (Table 6).

A. Reaction of Entry 1. To a solution of **5a** (0.204 g, 0.5 mmol) in benzene (1 mL) was added a solution of **3b** (0.101 g, 0.5 mmol) in benzene (0.5 mL) at rt and the mixture was stirred for 10 min, and then was added a solution of **28a** (0.069 g, 0.5 mmol) in benzene (6 mL) and the mixture was stirred at the same temperature for 2 h under argon. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **20**, **29a**, and **30a** as summarized in Table 6 (Entry 1).

2-(2-Hydroxy-1-phenylethylseleno)benzothiazole (29a). A syrup. ^{1}H NMR δ = 4.29 (2H, dd, J = 6.60 and 5.28 Hz), 4.46 (1H, t, J = 5.28 Hz), 5.11 (1H, t, J = 6.60 Hz), 7.15-7.44 (7H, m), 7.70 (1H, ddd, J = 7.59, 0.66, and 0.33 Hz), and 7.89 (1H, ddd, J = 7.92, 0.66, and 0.33 Hz). MS *m/z* 335 (M^+), 317, 305, 215, 187, 136, 120, and 109. HRMS Found: 334.9854. Calcd for $C_{15}H_{13}NOSSe$: M, 334.9883.

2-(2-Hydroxy-2-phenylethylseleno)benzothiazole (30a). A syrup. ^{1}H NMR δ = 3.55 (1H, dd, J = 13.19 and 7.91 Hz), 3.71 (1H, dd, J = 13.19 and 3.30 Hz), 5.05 (1H, d, J = 3.30 Hz), 5.22 (1H, dt, J = 7.91 and 3.30 Hz), 7.16-7.46 (7H, m), 7.76 (1H, ddd, J = 7.92, 0.99, and 0.33 Hz), and 7.92 (1H, ddd, J = 7.92, 0.66, and 0.33 Hz). MS *m/z* 335 (M^+), 227, 216, 150, 136, 116, and 109.

B. Reaction of Entry 2. To a solution of **3b** (0.202g, 1.0 mmol) in benzene (0.5 mL) was added dropwise a solution of **5a** (0.224g, 0.55 mmol) in benzene (2 mL) over a period of 1 min at rt under argon. The reaction mixture was stirred for 5 min and then was added a solution of **28a** (0.069 g, 0.5 mmol) in benzene (5 mL), and the mixture was stirred at the same temperature for 2 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **20**, **29a**, **30a**, and **31a** as summarized in Table 6 (Entry 2).

1,2-Bis(benzothiazol-2-ylseleno)-1-phenylethane (31a). A syrup. ^{1}H NMR δ = 4.17 (1H, t, J = 12.20 Hz), 4.51 (1H, dd, J = 12.20 and 4.62 Hz), 5.46 (1H, dd, J = 12.20 and 4.62 Hz), 7.21-7.48 (9H, m), and 7.70-7.90 (4H, m). MS *m/z* 428 (M^+), 348, 318, 268, 214, 135, 108, and 104.

C. Reaction of Entry 3. To a suspension of **28a** (0.069 g, 0.5 mmol) in benzene (2 mL) was added a solution of **3b** (0.101 g, 0.5 mmol) in benzene (1 mL) at rt and then a solution of **5a** (0.204 g, 0.5 mmol) in benzene (2.5 mL) over a period of 8 min, and the mixture was stirred at the same temperature under argon for 2 h . The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11, 16a, 20,** and **29a** as summarized in Table 6 (Entry 3).

D. Reaction of Entry 4. To a suspension of **28a** (0.069 g, 0.5 mmol) in benzene (0.5 mL) was added a solution of **3b** (0.202 g, 1.0 mmol) in benzene (1 mL) at rt under argon. Since **28a** was not dissolved, 3.5 mL of benzene was added to dissolve completely. To the resulting solution was added dropwise a solution of **5a** (0.224 g, 0.55 mmol) in benzene (2 mL) at rt over a period of 4 min and the mixture was stirred at the same temperature for 2 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 10 : 1) to give **11, 16a, 20, 29a, 30a,** and **31a** as summarized in Table 6 (Entry 4).

E. Reaction of Entry 5. To a solution of **28a** (0.069 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in benzene (6 mL) was added a solution of **3b** (0.202 g, 1.0 mmol) in benzene (1 mL) at rt and the mixture was stirred at the same temperature under argon for 2 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (chloroform) to give **11, 16a, 29a,** and **31a** as summarized in Table 6 (Entry 5).

Reactions of 28a with 5a and 3b in several solvents (Table 7).

A. Reaction in benzene (Entry 1). To a solution of **28a** (0.069 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in benzene (6 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in benzene (0.5 mL) at rt and the mixture was stirred at the same temperature under argon for 1 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11, 16a, 20, 29a,** and **30a** (Table 7; Entry 1).

B. Reaction in dichloromethane (Entry 2). To a solution of **28a** (0.069 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in dichloromethane (1 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in dichloromethane (0.5 mL) at rt and the mixture was stirred at the same temperature under argon for 1 h . The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11, 16a, 20, 29a, 30a,** and **31a** as summarized in Table 7 (Entry 2).

C. Reaction in THF at rt (Entry 3). To a solution of **28a** (0.069 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in THF (1 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in THF (0.5 mL) at rt and the mixture was stirred at the same temperature under argon for 1 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11, 16a, 20, 29a, 30a,** and **31a** as summarized in Table 7 (Entry 3).

D. Reaction in THF at 0 °C (Entry 4). To a solution of **28a** (0.069 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in THF (1 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in THF (0.5 mL) at 0 °C and the mixture was stirred at the same temperature under argon for 1 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **20**, **29a**, and **30a** as summarized in Table 7 (Entry 4).

E. Reaction in DMF (Entry 5). To a solution of **28a** (0.069 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in DMF (1.5 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in DMF (0.5 mL) at 0 °C and the mixture was stirred at the same temperature under argon for 1 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **29a**, and **30a** as summarized in Table 7 (Entry 5).

Reactions of 28b with 5a and 3b (Table 8). A typical procedure. To a solution of **28b** (0.045 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in THF (1 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in THF (0.5 mL) at rt and the mixture was refluxed for 2 h under argon. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **20**, **29b**, and **30b** as summarized in Table 8 (Entry 3).

2-(1-Hydroxymethylpropylseleno)benzothiazole (29b). A syrup. ^{1}H NMR δ = 1.11 (3H, t, J = 7.25 Hz), 1.80-1.97 (2H, m), 3.85-4.00 (1H, m), 4.03-4.16 (2H, m), 7.34 (1H, td, J = 7.92 and 1.32 Hz), 7.43 (1H, td, J = 7.92 and 1.32 Hz), 7.80 (1H, ddd, J = 7.92, 1.32, and 0.66 Hz), and 7.92 (1H, ddd, J = 7.92, 1.32, and 0.66 Hz). MS *m/z* 287 (M^+), 257, 215, and 135.

2-(2-Hydroxybutylseleno)benzothiazole (30b). A syrup. ^{1}H NMR δ = 1.03 (3H, t, J = 7.26 Hz), 1.58-1.76 (2H, m), 3.37 (1H, dd, J = 13.19 and 7.26 Hz), 3.58 (1H, dd, J = 13.19 and 2.97 Hz), 3.98-4.04 (1H, m), 4.25 (1H, d, J = 3.96 Hz), 7.32 (1H, td, J = 7.91 and 0.99 Hz), 7.42 (1H, td, J = 7.91 and 0.99 Hz), 7.78 (1H, ddd, J = 7.91, 0.99, and 0.33 Hz), and 7.90 (1H, ddd, J = 7.91, 0.99, and 0.33 Hz). MS *m/z* 287 (M^+), 258, 229, 215, and 135.

Reactions of 28c with 5a and 3b. To a solution of **28c** (0.045 g, 0.5 mmol) and **5a** (0.224 g, 0.55 mmol) in THF (1 mL) was added a solution of **3b** (0.121 g, 0.6 mmol) in THF (0.5 mL) at rt and the mixture was stirred at the same temperature under argon for 1 h. The resulting mixture was evaporated under reduced pressure, and the products were separated by TLC (hexane - ethyl acetate = 5 : 1) to give **11**, **16a**, **20**, and **35** as summarized in Scheme 10.

2- (3-Hydroxybutylseleno)benzothiazole (35). A syrup. ^{1}H NMR δ = 1.25 (3H, s), 1.92 (1H, dddd, J = 14.85, 9.90, 5.61, and 4.28 Hz), 2.06 (1H, dq, J = 14.85 and 4.95 Hz), 3.38 (1H, ddd, J = 13.19, 5.61, and 4.95 Hz), 3.71 (1H, ddd, J = 13.19, 9.90, and 4.95 Hz), 3.99 (1H, qdd, J = 6.26, 4.95, and 4.28 Hz), 4.47 (1H, broad-s), 7.30 (1H, ddd, J = 7.92, 6.92, and 1.32 Hz), 7.41 (1H, ddd, J = 7.91, 6.92, and 0.99 Hz), 7.76 (1H, dd, J = 7.92 and 0.99 Hz), and 7.89 (1H, dd, J = 7.91 and 1.32 Hz). MS *m/z* 287 (M^+) and 135. HRMS Found: 286.9862. Calcd for $C_{11}H_{13}NOSSe$: M, 286.9883.

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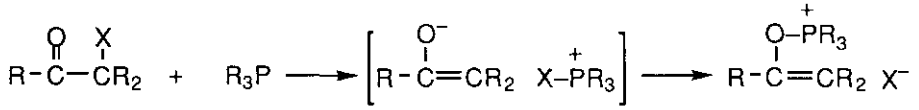

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Received, 31st August, 1998