

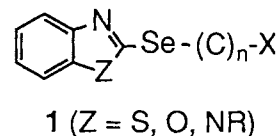
Preparation of 2-(Alkylseleno)benzothiazoles. Direct Incorporation of
the Alkyl Group of Alcohols into Benzothiazolylseleno Residue

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Reaction of alcohols with 2-(1,2-diphenyl-2-oxoethylseleno)benzothiazole in the presence of tributylphosphine gave the corresponding 2-alkylselenobenzothiazoles, 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.

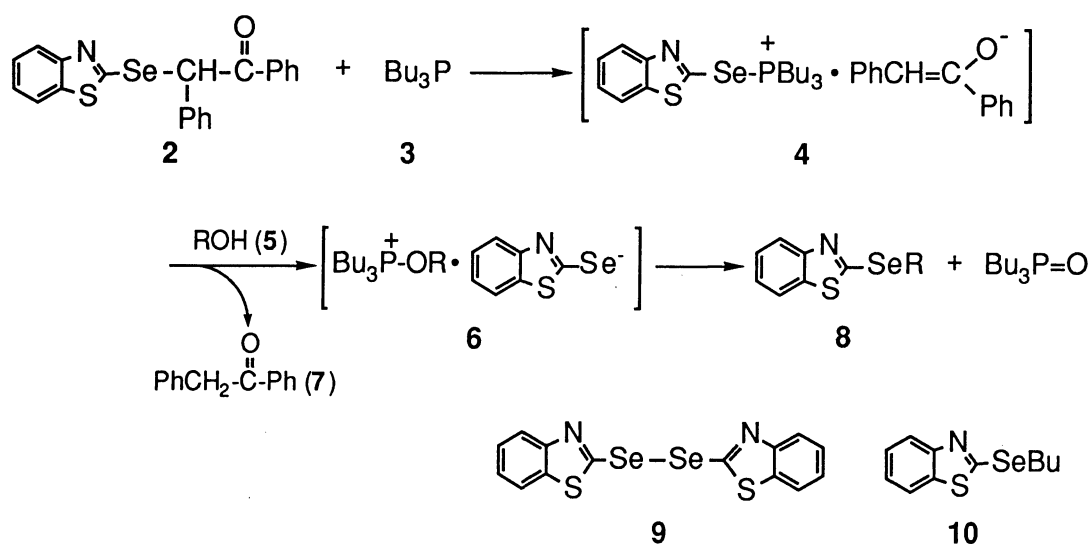
Functionalized 2-alkylseleno azaaromatic compounds of general formula **1** (X = functional groups) have a potential for performing highly efficient transformation of a variety of organic compounds.^{1,2)} In order to materialize this possibility, there is a need to develop an efficient general procedure for the preparation of **1**. In this communication, we wish to report tributylphosphine promoted direct incorporation of the alkyl group of alcohols into 2-benzothiazolylseleno residue.



When 2-(1,2-diphenyl-2-oxoethylseleno)benzothiazole (**2**) was allowed to react with tributylphosphine (**3**) and 2-phenylethanol (**5a**) in benzene at room temperature for 2 h, 2-(2-phenylethylseleno)benzothiazole (**8a**) and benzyl phenyl ketone (**7**) were obtained in 78% and 94% yields, respectively, along with small amounts of bis(2-benzothiazolyl)diselenide (**9**) and 2-butylselenobenzothiazole (**10**) (Scheme 1, Table 1; entry 1).³⁾ The reaction could be explained by the assumption that **3** attacked the selenium atom of **2** to give phosphonium salt **4**. The **4** thus formed reacted in turn with **5a** to give 2-phenylethyloxyphosphonium salt (**6a**) which collapsed to **8a** and tributylphosphine oxide (Scheme 1).^{4,5)}

The reactions of secondary alcohols (**5b**, **5c**) and functionalized alcohols (**5d**, **5e**, **5f**) also gave corresponding selenides (**8b-f**) in moderate to good yields (Table 1; entries 2-6). No allylic rearrangement was observed (Table 1; entry 7). As illustrated in Table 1, the present system is compatible with halogen, alkoxy carbonyl, and cyano groups.

When 1,3-butanediol (**11a**) reacted with **2** (1.1 molar amount) and **3** (1.2 molar amount) in THF at room temperature for 1 h, 2-(3-hydroxybutylseleno)benzothiazole (**12a**) was obtained



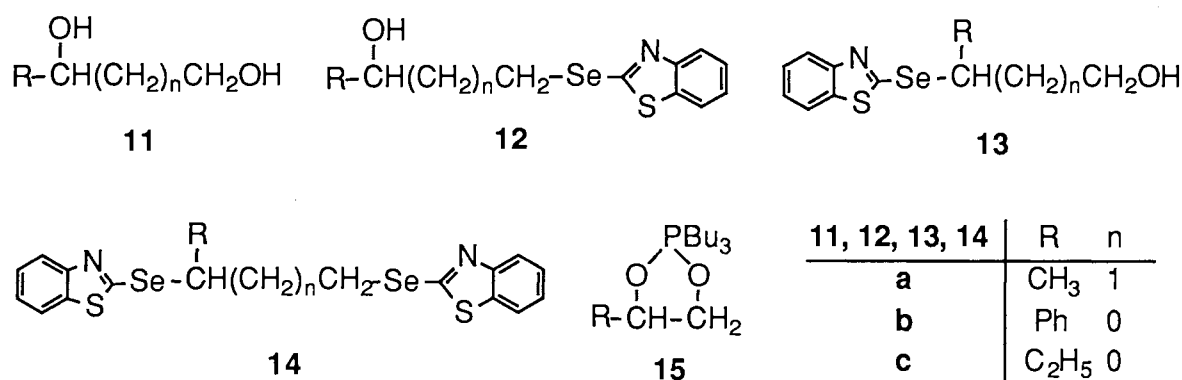
Scheme 1.

Table 1. Reaction of 5 with 2 (1.0-1.1 molar amount) and 3 (1.0-1.2 molar amount)

Entry	ROH R	Solvent	Temp °C	Time h	Products and yields/% ^{a)}				Recov./% ^{a)}	
					8	7	9	10	2	5
1	5a: PhCH ₂ CH ₂ -	Benzene	rt	2	8a: 78	94	18	1	2	13
2	5b: PhCH(CH ₃)-	Benzene	rt	2	8b: 70	>99	16	1 ^{b)}	3	5
3	5c: C ₂ H ₅ CH(CH ₃)-	THF	rt	1	8c: 70	>99	30	nd	nd	
4	5d: ClCH ₂ CH ₂ -	THF	0	1	8d: 72	91	20 ^{b)}	5	3	nd
5	5e: PhCH(COOCH ₃)-	THF	0	1	8e: 94	96	2 ^{b)}	3	1	6
6	5f: NCCH ₂ CH ₂ -	THF	0	1	8f: 65	94	28 ^{b)}	5 ^{b)}	2	nd
7	5g: CH ₃ CH=CHCH ₂ -	THF	0	1	8g: 50	83	39 ^{b)}	3	7	nd

a) nd = Not detected. b) Yield of crude product.

without any detectable formation of regioisomer, 2-(3-hydroxy-1-methylpropylseleno)benzothiazole (**13a**) (Scheme 2, Table 2; entry 1). Contrary to the reaction of **11a**, opposite regioselectivity was observed in the reaction of 1,2-diols. Thus, the reaction of 1-phenyl-1,2-ethanediol (**11b**) with **2** and **3** in THF at room temperature for 1 h, 2-(2-hydroxy-2-phenylethylseleno)benzothiazole (**12b**), 2-(2-hydroxy-1-phenylethylseleno)benzothiazole (**13b**), and 1,2-bis(benzothiazolylseleno)ethylbenzene (**14b**) were obtained in 4%, 69%, and 5% yields, respectively (Table 2; entry 2). The formation of **14b** could be suppressed when the reaction was carried out at 0 °C (Table 2; entry 3). The reaction of 1,2-butanediol (**11c**) was less regioselective than that of **11b**, and **12c** and **13c** were obtained in a ratio of 1 : 1 (Table 2; entries 4 and 5).



Scheme 2.

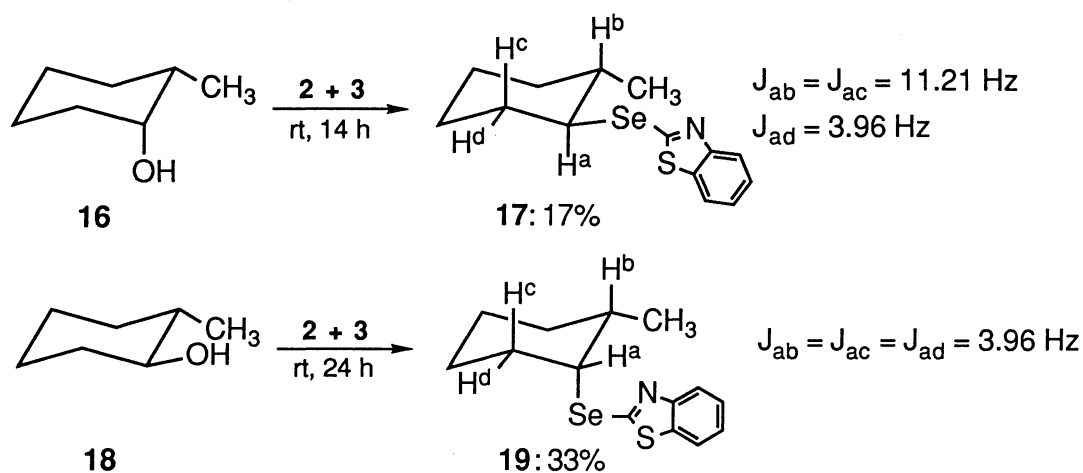
The formation of *sec*-alkylseleno derivatives **13** could be explained by assuming an intermediacy of phosphorane **15** as proposed by Pautard and Evans, Jr. in the reaction of **11b** with benzoic acid, diethyl azodicarboxylate, and triphenylphosphine.⁶⁾ The fact that **7** was obtained in good yields irrespective of the yields of **12** and/or **13** suggests that the attack of selenolate ion to phosphorane is the rate determining step and that the reactivity of phosphorane was influenced by the nature of the substituents (Table 2).

Table 2. Reaction of **11** with **2** (1.1 molar amount) and **3** (1.2 molar amount)

Entry	Diol (11)	Temp °C	Time h	Products and yields/% ^{a)}						Recov./%	
				12	13	14	7	9	10	2	11
1	11a	rt	1	12a : 60	13a : nd	14a : nd	79	21	7	10	24
2	11b	rt	1	12b : 4	13b : 69	14b : 5	84	14	5	<3	3
3		0	1	12b : 2	13b : 74	14b : nd	87	15	5	3	10
4	11c	0	1	12c : 8	13c : 8	14c : nd	93	65	nd	2	42
5		reflux	2	12c : 39	13c : 38	14c : nd	91	12	5	4	9

a) nd = Not detected.

The reaction involving an alkoxy phosphonium salt generally proceeds in S_N2 mode. In order to examine the stereochemical outcome of the present reaction, *cis*- and *trans*-2-methylcyclohexanols were used as the alcoholic components. When (±)-*cis*-2-methylcyclohexanol (**16**) were allowed to react with **2** and **3**, the cyclohexylselenobenzothiazole **17** obtained as a single isomer was determined to have *trans* configuration by NMR spectroscopy. On the other hand, (±)-*trans*-2-methylcyclohexanol (**18**) reacted with **2** and **3** to give a single isomer **19** with *cis* configuration (Scheme 3). Although the yields were low (17% and 33%), the results clearly indicated that the reaction proceeds with inversion of configuration at secondary carbinol center.



Scheme 3.

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References

- 1) For a review of organoselenium compounds, see for example; C. Paulmier, "Selenium Reagents and Intermediates in Organic Synthesis," Pergamon Press, Oxford (1986).
- 2) K. Shibata and O. Mitsunobu, *Bull. Chem. Soc. Jpn.*, **65**, 3163 (1992).
- 3) The structural assignments reported herein were confirmed by proton magnetic resonance (270 MHz) and, in part, mass spectral data.
- 4) In the reaction of α -halo ketones with P(III)-compounds, the phosphorous compounds initially attacks the halogen atom. See for example, I. J. Borowitz and L. I. Grossman, *Tetrahedron Lett.*, **1962**, 471; I. J. Borowitz, K. C. Kirby, P. E. Rusek, and E. W. R. Casper, *J. Org. Chem.*, **36**, 88 (1971).
- 5) Grieco et al. have reported the reaction of *o*-nitrophenyl selenocyanate with alcohols and **3** to give alkyl aryl selenides, where selenophosphonium salts are proposed as a key intermediate. P. A. Grieco, S. Gilman, and M. Nishizawa, *J. Org. Chem.*, **41**, 1485 (1976). See also, M. Sevrin and A. Krief, *J. Chem. Soc., Chem. Commun.*, **1980**, 656; P. A. Grieco, J. Y. Jaw, D. A. Claremon, and K. C. Nicolaou, *J. Org. Chem.*, **46**, 1215 (1981). Arylselenophosphonium salts are also formed by the reaction of diaryl diselenides with phosphines. See for example, M. Sakakibara, K. Katsumata, Y. Watanabe, T. Toru, and Y. Ueno, *Synthesis*, **1992**, 377, and references therein.
- 6) A. M. Pautard and S. A. Evans, Jr., *J. Org. Chem.*, **53**, 2300 (1988). Although the reaction of **11b** with benzoic acid, diethyl azodicarboxylate, and triphenylphosphine has been demonstrated to take place with complete inversion of the secondary carbinol center, the stereochemical outcome of the present reaction involving *vic*-diols has not yet been elucidated.

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