Preparation of Alkyl or Phenyl Hydroxyaryl Selenides

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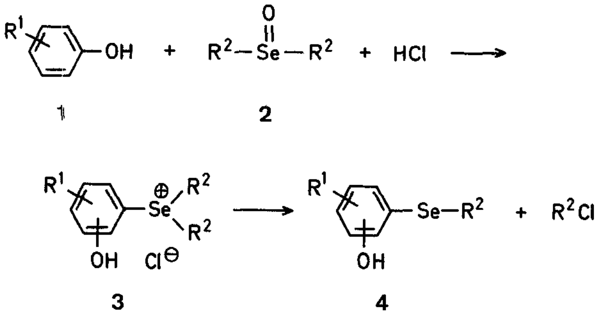
Although much attention has been focused on the synthesis of organoselenium compounds[1], little work has been done on the synthesis of phenols containing selenoalkyl (or aryl) substituents[2,3,4]. The only method of practical interest is a multi-step synthesis reported by Keimatsu[2] in which hydroxyphenyl phenyl selenides have been obtained by the reaction of hydroxyphenyldiazonium chloride with a selenophenolate. Generally, aryl alkyl or dialkyl selenides have been prepared most conveniently from a Grignard reagent, selenium, and alkyl halides[5]. This standard method, however, is not very attractive for the synthesis of alkyl hydroxyaryl selenides from the viewpoint of availability of starting materials and the protection-deprotection problem associated with the hydroxy group.

This paper describes a new route to alkyl hydroxyaryl selenides **4** from phenols **1**, selenoxides **2**, and hydrogen chloride. This paper also reports on the synthesis of dialkyl- (or phenyl-alkyl-) -hydroxyphenylselenonium chlorides **3**.



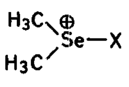
The present method is essentially based on Radzitzky's procedure[6] used for the preparation of sulfur analog of **4**. A large excess of hydrogen chloride was used in Radzitzky's method. In the selenoxide reaction, however, the use of hydrogen chloride in large excess has resulted in poor yields of **3** or undesirable side reactions. We have found that the desired selenonium chlorides **3** can be obtained in good yields by the reaction of dialkyl or alkyl aryl selenoxides with phenols and an equivalent amount of hydrogen chloride using acetonitrile as a solvent. The selenonium chlorides **3** were insoluble in acetonitrile and precipitated as they were formed. Almost pure **3** could be easily isolated by filtration of the reaction mixture. The selenonium chlorides **3** were then transformed to alkyl or aryl hydroxyphenyl selenides by heating at 110° in toluene.

Interestingly, a similar reaction of dimethyl sulfoxide did not take place under the same conditions used for the reaction of dimethyl selenoxide to give **3**. The higher reactivity of dimethyl selenoxide may be attributed to the more polar nature of the selenium-oxygen bond as compared with the sulfur-oxygen bond.

The results of the syntheses of the selenonium chlorides **3** and alkyl or aryl hydroxyaryl selenides **4** are given in Tables 1 and 2, respectively. The structures of **3** and **4** have been determined on the basis of their spectral and analytical data (Table 2).

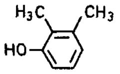
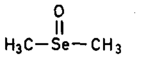
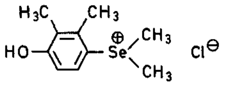
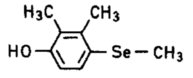
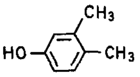
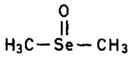
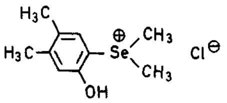
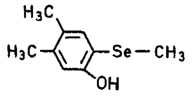
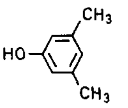
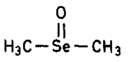
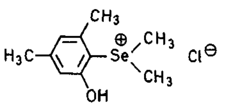
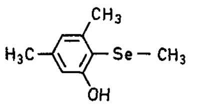
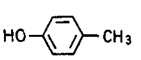
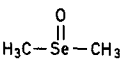
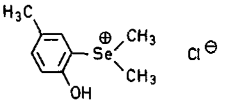
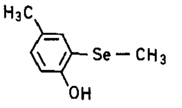
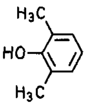
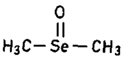
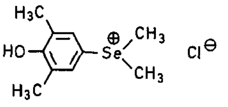
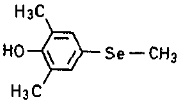
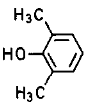
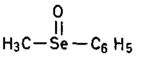
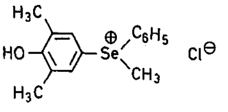
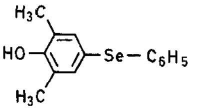
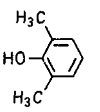
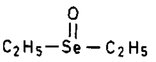
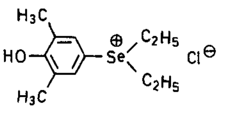
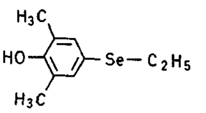
The structures of **4a** and **4c**, in particular, were assigned by comparison of ^{1}H-N.M.R. absorptions of their OH group with those of the other selenides (**4b** and **4d–g**). In the cases of the selenides (**4e–g**) which have OH groups at *para* position to selenoalkyl groups, the OH signals appear in the region between $\delta = 4.42$–4.52 ppm, whereas, in the cases of **4b** and **4d**, the OH signals have been observed at $\delta = 6.10$ and $\delta = 6.20$ ppm, respectively.

Intermediates of the type **5** formed by the reaction of dimethyl selenoxide with hydrogen chloride may be important in the electrophilic aromatic substitution to give **3**[7].


$(H_3C)_2\overset{\oplus}{Se}{-}X$

5 (X = Cl, OH)

Table 1. Preparation of Selenonium Chlorides **3** and Hydroxyaryl Selenides **4**

Entry	Phenol **1**	Selenoxide **2**	Reaction time	Selenonium chloride **3**	Yield [%] of **3**	Hydroxyaryl selenide **4**	Yield [%][a] of **4**
a		 $H_3C-\overset{O}{\overset{\|}{Se}}-CH_3$	24 h		68		68
b		 $H_3C-\overset{O}{\overset{\|}{Se}}-CH_3$	24 h		67		47
c		 $H_3C-\overset{O}{\overset{\|}{Se}}-CH_3$	24 h		64		65
d		 $H_3C-\overset{O}{\overset{\|}{Se}}-CH_3$	20 h		75		65
e		 $H_3C-\overset{O}{\overset{\|}{Se}}-CH_3$	24 h		76		72
f		 $H_3C-\overset{O}{\overset{\|}{Se}}-C_6H_5$	3 h		67		88
g		 $C_2H_5-\overset{O}{\overset{\|}{Se}}-C_2H_5$	9 h		43		75

[a] Thermal decomposition of **3** performed on 2 mmol scale in toluene (10 ml).

Table 2. Physical Data for Selenonium Chlorides **3** and Selenides **4**

Product	m.p. or b.p./torr	Molecular formula[a]	I.R. (KBr)[b] [cm^{-1}]	^{1}H-N.M.R. (D$_2$O for **3**[c]; CCl$_4$ for **4**) δ [ppm]	Mass spectra m/e
3a	127.5–127.9°	$C_{10}H_{15}ClOSe$ (265.6)	805	1.95 (s, 3H); 2.33 (s, 3H); 2.83 (s, 6H); 6.73–7.63 (m, 2H)	—
3b	119.8–120°	$C_{10}H_{15}ClOSe$ (265.6)	858	2.26 (s, 6H); 3.10 (s, 6H); 6.97 (s, 1H); 7.38 (s, 1H)	—
3c	131.3–133.2°	$C_{10}H_{15}ClOSe$ (265.6)	840	2.32 (s, 3H); 2.57 (s, 6H); 3.20 (s, 6H); 6.79 (s, 2H)	—
3d	105.2–106.2°	$C_9H_{13}ClOSe$ (251.6)	3400; 824	2.37 (s, 3H); 3.06 (s, 6H); 6.97–7.56 (m, 3H)	—
3e	119.4–119.8°	$C_{10}H_{15}ClOSe$ (265.6)	3175; 885	2.30 (s, 6H); 3.04 (s, 6H); 7.55 (s, 2H)	—
3f	89.6–90.6°	$C_{15}H_{17}ClOSe$ (327.7)	3400; 862	2.16 (s, 3H); 3.21 (s, 6H); 7.20 (s, 2H); 7.44 (s, 5H)	—
3g	120.8–122.3°	$C_{12}H_{19}ClOSe$ (293.7)	3300; 860	1.42 (t, 6H, J=7 Hz); 2.32 (s, 6H); 3.61 (q, 4H, J=7 Hz); 7.48 (s, 2H)	—
4a	119.8–122.7°	$C_9H_{12}OSe$ (215.2)	3200; 900	2.15 (s, 6H); 2.37 (s, 3H); 4.03 (s, 1H, OH); 6.40–7.09 (m, 2H)	216 (M$^+$); 201 (M$^+$–CH$_3$)
4b	97–98°/0.2	$C_9H_{12}OSe$ (215.2)	3375; 845	2.00 (s, 3H); 2.22 (s, 3H); 2.44 (s, 3H); 6.50 (s, 1H, OH); 6.60 (s, 2H)	216 (M$^+$); 201 (M$^+$–CH$_3$)
4c	78–82°/0.3	$C_9H_{12}OSe$ (215.2)	3350; 838	2.08 (s, 3H); 2.10 (s, 3H); 2.16 (s, 3H); 6.10 (s, 1H, OH); 6.68 (s, 1H); 7.20 (s, 1H)	216 (M$^+$); 201 (M$^+$–CH$_3$); 121 (M$^+$–SeCH$_3$)
4d	64–66°/0.5	$C_8H_{10}OSe$ (201.1)	3380; 813	2.10 (s, 3H); 2.22 (s, 3H); 6.20 (s, 1H, OH); 6.82–7.20 (m, 2H); 7.43 (s, 1H)	202 (M$^+$); 187 (M$^+$–CH$_3$)

Table 2. (Continued)

Product	m.p. or b.p./torr	Molecular formula[a]	I.R. (KBr)[b] [cm^{-1}]	^{1}H-N.M.R. (D_2O for **3**[c]; CCl_4 for **4**) δ [ppm]	Mass spectra *m/e*
4e	50.6–51.6°	$C_9H_{12}OSe$ (215.2)	3250; 840	2.10–2.20 (s, 9H); 4.44 (s, 1H, OH); 6.98 (s, 2H)	216 (M^+); 201 ($M^+ - CH_3$); 121 ($M^+ - SeCH_3$)
4f	147–148°/0.7	$C_{14}H_{14}OSe$ (277.2)	3550; 864	2.13 (s, 6H); 4.42 (s, 1H, OH); 7.10 (s, 7H)	278 (M^+); 198 ($M^+ - Se^{80}$)
4g	111–112°/0.7	$C_{10}H_{14}OSe$ (229.2)	3450; 862	1.34 (t, 3H, $J=7$ Hz); 2.15 (s, 6H); 2.69 (q, 2H, $J=7$ Hz); 4.25 (broad, 1H, OH); 7.00 (s, 2H)	230 (M^+); 201 ($M^+ - C_2H_5$) 121 ($M^+ - SeC_2H_5$)

[a] All products gave satisfactory microanalyses (C $\pm 0.4\%$; H $\pm 0.26\%$).

[b] Infrared spectra were obtained on a Hitachi IR-400 spectrophotometer; **4b–d** and **4f–g** as thin films.

[c] Measured with respect to acetonitrile; converted to TMS reference by the expression $\delta_{TMS} - \delta_{CH_3CN} = 2.11$.

Preparation of Selenonium Chlorides (3):

To a stirred solution of selenoxide **1**[8] (10 mmol) and phenol **2** (10 mmol) in acetonitrile (30 ml) is added an acetonitrile solution (20 ml) of hydrogen chloride (10 mmol) at 0–20° within 30 minutes. After the addition is completed, stirring is continued for 3–24 h (Table 1) at room temperature. The precipitates are isolated by filtration, washed with acetonitrile, and dried in vacuo to give the corresponding selenonium chloride **3** as a colorless solid, which is sufficiently pure for use in further reactions.

Preparation of Selenides 4 by Thermal Decomposition of Selenonium Chloride 3:

The selenonium chloride **3** (2 mmol) is heated in dry toluene (10 ml) under reflux for 6 h. The cooled solution is filtered, the solvent is evaporated in vacuo, and the residue is recrystallized from *n*-hexane for **4a** and **4e**, or distilled under reduced pressure for **4b–d** and **4f–g**.

Received: July 22, 1976

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