A Convenient Procedure for the Preparation of Organic Selenides

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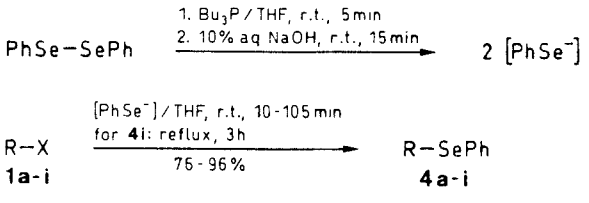
Treatment of diphenyl diselenide with tributylphosphine in an alkaline medium forms phenylselenolate ion which converts alkyl halides, α,β-unsaturated ketones, and epoxides into alkyl selenides, (phenylseleno)alkenones, and β-(phenylseleno)alkanols, respectively, in high yield. Selenation of 3α-bromocholestane gives 3β-(phenylseleno)cholestane with complete inversion of the configuration.

During the course of the preparative study on quinonoid compounds we found[1] that the selenolate ion, generated by treatment of diphenyl diselenide with a phosphine in an alkaline medium, was quite effective in the selenation of halogenated 1,4-naphthoquinones into 2-(phenylseleno)-1,4-naphthoquinones compared to the known methods such as treatment of diphenyl diselenide with sodium borohydride,[2] sodium metal,[3] alkali metal hydroxide,[4] sodium formaldehyde sulfoxylate,[5] or hypophosphoros acid.[6] We also demonstrated the application of this new selenation to the synthesis of naphthopyridoselenazines[7] using bis(3-amino-2-pyridyl) diselenide as a selenating reagent. In order to generalize the present selenation we have further studied the reactivity of the selenolate ion towards various nucleophilic reactions for alkyl halides, α,β-unsaturated ketones, epoxides, and 3α-bromocholestane.

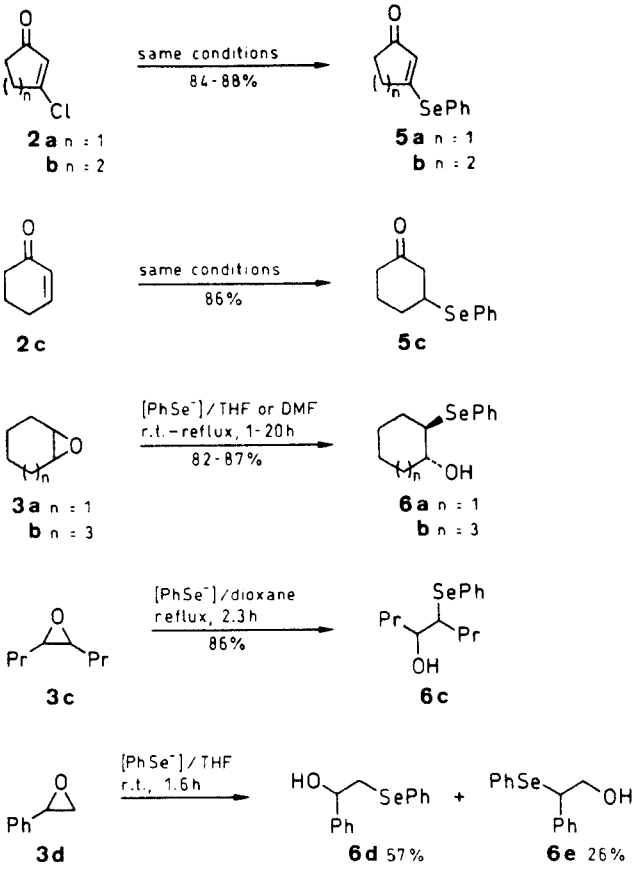
Treatment of various primary and secondary alkyl halides **1a–g** with a mixture containing phenylselenolate ion, generated from diphenyl diselenide (0.55 mole equivalents), tributylphosphine (0.60 mole equivalents), and aqueous sodium hydroxide solution (1.10 mole equivalents), afforded the corresponding alkyl phenyl selenides **4a–g** in high yield. Selenation of the tosylate **1h** also afforded the selenide **4h**.



1,4	R	X	1,4	R	X
a	Bn	Cl	f	Et_2CH	Br
b	Bn	Br	g	EtO_2CCH_2	Br
c	n-C_7H_{15}	Cl	h	Bu	OTs
d	n-$C_{10}H_{21}$	Br	i	cholestan-3-yl[a]	Br
e	n-$C_{10}H_{21}$	I			

[a] For the educt **1**, 3α-, and for the product, **4**, 3β-substitution.

Selenation of 3α-bromocholestane (**1i**) using a twofold excess amount of phenylselenolate ion gave 3β-(phenylseleno)cholestane (**4i**) in 91% yield. The ^1H NMR spectrum of **4i** showed the methine proton at the 3-position as a multiplet centered at $\delta = 3.19$ and no signals were observed at the region ($\delta = 3.81$) which corresponds to the C-3 methine proton of 3α-(phenylseleno)cholestane.[8] This result shows that the selenation proceeds with complete inversion of configuration.



Scheme 1

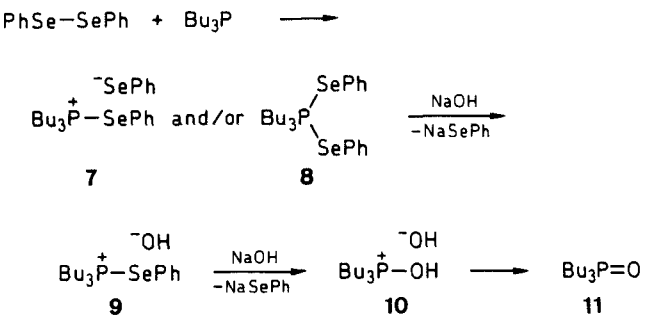
Reaction of 3-chloro-2-cycloalkenones **2a** and **2b** with the phenylselenolate ion afforded 3-(phenylseleno)-2-cycloalkenones **5a** and **5b** in high yield, whereas 2-chloro-2-cyclohexen-1-one[9] remained intact. Successful 1,4-conjugate addition occurred in the selenation of 2-cyclohexen-1-one (**2c**), giving 3-(phenylseleno)cyclohexan-1-one (**5c**). The reaction of epoxides **3a–c** with phenylselenolate ion gave the corresponding β-(phenylseleno)alkanols **6a–c**,[10,11] which were formed via trans opening of the epoxides with the selenolate ion. The reaction of styrene oxide **3d** gave two regioisomers, 1-phenyl-2-(phenylseleno)ethanol (**6d**) and 2-phenyl-2-(phenylseleno)ethanol (**6e**) in 57 and 26% yield, respectively. The regiochemistry of the ring opening of styrene oxide depends on the selenolate ion used: the selenolate ion, generated from diphenyl diselenide and sodium, gives only one regioisomer **6d**,[12] while the selenation with tris(phenylseleno)borane yields only **6e**.[13]

Table. Phenylselenated Compounds Prepared

Substrate	Reaction Conditions	Product	Yield[a] (%)	mp (°C)	IR ν (cm^{-1})	^1H NMR (solvent/TMS) δ, J (Hz)
1a	15 min, r.t., THF	**4a**[16]	96	31.1–31.7 (Lit.[16] 31–32°C)	3000, 2925, 1560, 1440, 1186, 1060, 720, 680[e]	4.00 (s, 2H), 7.00–7.52 (m, 10H)[g]
1b	20 min, r.t., THF	**4a**	85			
1c	45 min, r.t., THF	**4c**[17]	76	oil	2920, 2848, 1576, 1476, 1432, 728, 686[f]	0.87 (t, 3H, J = 5.0), 1.13–1.83 (m, 10H), 2.83 (t, 2H, J = 7.0), 7.03–7.55 (m, 5H)[h]
1d	35 min, r.t., THF	**4d**[16]	87	oil	2900, 2850, 1580, 1460, 720[f]	0.87 (t, 3H, J = 6.0), 1.07–1.98 (m, 16H), 2.83 (t, 2H, J = 6.0), 6.93–7.60 (m, 5H)[h]
1e	20 min, r.t., THF	**4d**	93			
1f	1.75 h, r.t., THF	**4f**[d]	81	oil	2960, 2830, 1574, 1474, 1450, 1432, 730, 684[f]	0.82–1.23 (m, 6H), 1.40–2.93 (m, 4H), 2.75–3.20 (m, 1H), 7.07–7.67 (m, 5H)[h]
1g	20 min, r.t., THF	**4g**[16]	77	oil	2950, 1720, 1250, 1100, 720[f]	1.20 (t, 3H, J = 6.0), 3.43 (br s, 2H), 4.10 (q, 2H, J = 6.0), 7.00–7.75 (m, 5H)[h]
1h	1.75 h, r.t., THF	**4h**[18]	78	oil	3060, 2972, 2880, 1578, 1480, 732, 688[f]	0.88 (t, 3H, J = 6.0), 1.17–1.83 (m, 4H), 2.83 (t, 2H, J = 6.0), 7.05–7.53 (m, 5H)[h]
1i[b]	3 h, reflux, THF[c]	**4i**[19]	91	oil	2930, 2850, 1576, 1458, 1372, 730, 688[e]	0.98–2.04 (m, 46H), 3.10–3.28 (m, 1H), 7.25–7.36 (m, 3H), 7.50–7.64 (m, 2H)[g]
2a[14]	10 min, r.t., THF	**5a**[20]	84	53.8–54.3 (Lit.[20] 51.0–52.0°C)	1670, 1540, 1250, 1163, 735[e]	2.16–2.50 (m, 2H), 2.56–2.85 (m, 2H), 5.76 (br s, 1H), 7.16–7.76 (m, 5H)[h]
2b[15]	10 min, r.t., THF	**5b**[20]	88	45.8–46.5	2930, 1650, 1570, 1280, 1235, 980, 738[e]	1.70–2.65 (m, 6H), 5.62 (br s, 1H), 7.18–7.68 (m, 5H)[g]
2c	40 min, r.t., THF	**5c**[21]	50	oil	2930, 1700, 1212, 730[f]	1.29–2.87 (m, 8H), 3.11–3.70 (m, 1H), 7.07–7.70 (m, 5H)[h]
	10 min, r.t., THF[c]	**5c**	86			
3a	1.25 h, r.t., THF	**6a**[10]	87	oil	3390, 2920, 1580, 1470, 1433, 1060, 730, 685[f]	1.12–1.48 (m, 4H), 1.58–1.84 (m, 2H), 2.08–2.27 (m, 2H), 2.91 (ddd, 1H, J = 12.0, 10.0, 4.0), 3.04 (br s, 1H), 3.35 (dt, 1H, J = 4.0, 10.0), 7.24–7.44 (m, 3H), 7.58–7.72 (m, 2H)[g]
3b	72 h, r.t., THF	**6b**[10]	trace	oil	3450, 2920, 1432, 1038, 732[f]	1.22–2.48 (m, 12H), 2.57 (br s, 1H), 3.20 (ddd, 1H, J = 10.0, 7.4, 3.0), 3.58 (dt, 1H, J = 4.0, 10.0), 7.10–7.23 (m, 3H), 7.24–7.77 (m, 2H)[h]
	20 h, reflux, dioxane	**6b**	35			
	10 h, reflux, DMF	**6b**	82			
3c	24 h, r.t., THF	**6c**[11]	64	oil	3450, 2950, 1460, 1058, 1018, 730, 682[f]	0.84–1.04 (m, 6H), 1.39–1.81 (m, 8H), 2.30 (br s, 1H), 3.26–3.42 (m, 1H), 3.60–3.78 (m, 1H), 7.20–7.42 (m, 3H), 7.55–7.74 (m, 2H)[g]
	2.3 h, reflux, dioxane	**6c**	86			
3d	1.6 h, r.t., THF	**6d**[12]	57	oil	3400, 1570, 1475, 1182, 1040, 730, 690[f]	2.83 (s, 1H), 3.11 (dd, 1H, J = 12.0, 8.4), 3.29 (dd, 1H, J = 12.0, 4.0), 4.74 (dd, 1H, J = 8.4, 4.0), 7.18–7.42 (m, 8H), 7.48–7.64 (m, 2H)[g]
		6e[13]	26	oil	3380, 1574, 1474, 1048, 1016, 736, 684[f]	2.06 (br s, 1H), 3.86 (dd, 1H, J = 11.6, 7.8), 4.03 (dd, 1H, J = 11.6, 7.8), 4.40 (t, 1H, J = 7.8), 7.18–7.40 (m, 8H), 7.46–7.60 (m, 2H)[g]

[a] Isolated yield.
[b] $[\alpha]_D$ +28.6° (c = 1.0, $CHCl_3$), mp 102.5–103.8°C (Lit.[22] $[\alpha]_D$ +28.67° in $CHCl_3$, mp 103–104°C).
[c] Reactions were carried out using 1.10 mole equiv of $(PhSe)_2$, 1.20 mole equiv of Bu_3P, and 2.20 mole equiv of aq NaOH.
[d] $C_{11}H_{16}Se$ (227.2) calc. C 58.15 H 7.11; found C 58.39 H 7.20.
[e] Measured on KBr discs.
[f] Measured in film.
[g] Measured in $CDCl_3$.
[h] Measured in CCl_4.

In the present selenation, two moles of the selenolate ion become available from 1 mole of the diselenide in accord with the postulated mechanism as shown in Scheme 2. A selenophosphonium ion **7** and/or a pentavalent phosphorus species **8** are initially formed in the reaction of diphenyl diselenide and a phosphine, and then the addition of sodium hydroxide liberates phenylselenolate ion and the phosphonium ion **9**, from the latter of which is generated more selenolate ion together with phosphine oxide **11** by the action of sodium hydroxide. The present reaction provides a convenient and efficient method for selenation.



Scheme 2

Melting points were measured with a Yanaco micro-melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO A-102 spectrophotometer. ^1H NMR spectra were obtained on either a JEOL JNM-PMX 60SI or a Varian XL 200 spectrometers.

Benzyl Phenyl Selenide (4a); Typical Procedure:
A solution of diphenyl diselenide (1.72 g, 5.5 mmol) and Bu_3P (1.50 mL, 6.0 mmol) in THF (10 mL) was vigorously stirred vibrationally or ultrasonically under Ar atmosphere at r.t. for 5 min. To

this was added 10% NaOH (3.96 mL, 11 mmol), and the mixture was stirred for further 15 min, during which time the two-phase mixture became homogeneous and the yellow solution turned to colorless. Then, the mixture was added dropwise to a solution of benzyl chloride (1.15 mL, 10 mmol) in THF (5 mL) at r. t. under Ar atmosphere and stirred for 15 min. The mixture was poured into a mixture of brine (30 mL) and Et_2O (10 mL), and the aqueous layer was extracted with Et_2O (4 × 10 mL). The combined extracts were washed with brine (5 mL), dried ($MgSO_4$), and evaporated. Column chromatography on silica gel with hexane as eluent yielded benzyl phenyl selenide (**4a**); yield: 2.36 g (96%).

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