Generation and Alkylation of α-Lithio-*Se,O*-heteroacetals, and Stereoselective Cyclization of Olefinic *Se,O*-Heteroacetals

Mitsuhiro YOSHIMATSU, Michiyo FUJIMOTO, Hiroshi SHIMIZU, Mikio HORI, and Tadashi KATAOKA*

Gifu Pharmaceutical University, 6–1 Mitahora-higashi 5-chome, Gifu 502, Japan. Received September 25, 1992

Generation of α-lithio-*Se,O*-heteroacetals was accomplished by direct deprotonation of *O*-methoxyethylselenoacetals with lithium 2,2,6,6-tetramethylpiperidide. Alkylation of the α-lithioheteroacetals smoothly proceeded to give the products 6 and 7. Olefinic *Se,O*-heteroacetals 6c and 6d were cyclized *via* α-seleno carbenium ions generated by selective C–O bond cleavage with titanium tetrachloride to provide the cyclohexane derivatives 8a and 8b, respectively.

Keywords *Se,O*-heteroacetal; α-lithio-*Se,O*-heteroacetal; α-seleno carbenium ion; lithium 2,2,6,6-tetramethylpiperidide; selective C–O bond cleavage; cyclization

Dithioacetals have been widely used as acyl anion equivalents with a reverse reactivity compared to that of carbonyl groups[1] and diselenoacetals also play an important role in organic syntheses.[2] Although anions of dithioacetals[1,3] or diselenoacetals[4] can be generated by deprotonation with a strong base, *Se,O*-heteroacetals have not been deprotonated by strong bases such as *n*-butyllithium or lithium diisopropylamide (LDA). Instead, *Se,O*-heteroacetal anions have been generated by elimination of a phenylseleno group from bis(phenyseleno)methoxymethane.[5] This paper describes the first example of the direct deprotonation of *Se,O*-heteroacetals, alkylation of the resulting α-lithioheteroacetals, and stereoselective cyclization of the olefinic heteroacetals thus prepared.

Several *Se,O*-heteroacetals **1**—**5** were lithiated with 1.5 eq of lithium 2,2,6,6-tetramethylpiperidide (LTMP) at −40 or −78 °C and the extent of the lithiation was evaluated by alkylation of the resulting α-lithio-*Se,O*-heteroacetals. The results are listed in Table I. The *O*-methoxyethyl-*Se,O*-heteroacetals **1** and **3** were more cleanly deprotonated than the *O*-methyl derivatives **2** and **4**. The *Se*-benzyl-*Se,O*-heteroacetal **3** was lithiated more smoothly even at lower temperature than the *Se*-phenyl derivatives **1** and **2**. The methoxyethyl group presumably stabilizes the α-lithio-*Se,O*-heteroacetals by chelation of the lithium ion with the oxygen. The superiority of the benzyl group over the phenyl group in deprotonation can be explained by the assumption that the *Se*-benzyl derivative **3** is less sterically congested near the methylene group as compared with the *Se*-phenyl derivative **1**, and consequently the access of the bulky base, LTMP, to **3** is easier than that to **1**. The bulky cyclohexyl and 2-hexenyl groups were introduced to give the products **7d** (90%) and **7e** (85%), respectively.

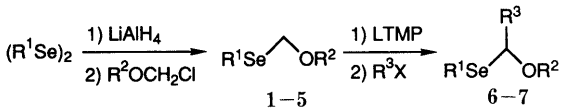
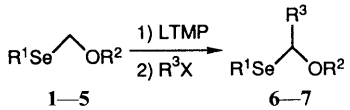


Chart 1

Since we had observed the selective C–O bond cleavage of *O*-methoxyethyl-*Se,O*-heteroacetals with titanium tetrachloride and generation of α-seleno carbenium ions,[6] cyclization of α-seleno carbenium ions generated from the olefinic heteroacetals **6c** and **6d** was next examined in or-

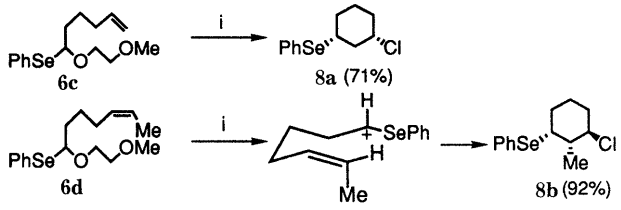
TABLE I. Reactions of α-Lithio-*Se,O*-heteroacetals with Alkyl Halides



1—5 6—7

Entry	*Se,O*-Heteroacetals	R^3X	Temp. (°C)	Products (% yields)
1	**1** (R^1=Ph, R^2=CH_2CH_2OMe)	Methyl iodide	−40	**6a** (69), **1** (30)
2	**1**	Ethyl iodide	−40	**6b** (73), **1** (3)
3	**1**	5-Bromo-1-pentene	−40	**6c** (44)
4	**1**	6-Iodo-2-hexene	−40	**6d** (60)
5	**1**	*n*-Butyl iodide	−40	**6e** (80)
6	**1**	Benzyl bromide	−40	Complex mixture[a]
7	**2** (R^1=Ph, R^2=Me)	Methyl iodide	−40	Complex mixture[a]
8	**3** (R^1=CH_2Ph, R^2=CH_2CH_2OMe)	Methyl iodide	−78	**7a** (85)
9	**3**	Benzyl bromide	−78	**7b** (98)
10	**3**	Allyl iodide	−78	**7c** (quant.)
11	**3**	Cyclohexyl bromide	−78	**7d** (90)
12	**3**	6-Iodo-2-hexene	−78	**7e** (85)
13	**4** (R^1=CH_2Ph, R^2=Me)	Methyl iodide	−78	Complex mixture[a]
14	**4**	Allyl iodide	−78	Complex mixture[a]
15	**5** (R^1=R^2=CH_2Ph)	Methyl iodide	−78	Complex mixture[a]

a) The structures of the products could not be determined.



i: $TiCl_4$/−80°C

Chart 2

der to utilize the alkylated heteroacetals synthesized above. The selenoacetals **6c** and **6d** were treated with titanium tetrachloride at −80 °C and produced the 1-chloro-3-phenylselenocyclohexanes **8a** and **8b**, respectively, in the 6-*endo*-trig mode of cyclization (Chart 2). The structures of **8a** and **8b** were determined by ^{1}H- and ^{13}C-NMR spectroscopy. From a study of the γ-effect of 1,3-disubstituted cyclohexanes,[7] the axial halogeno group is considered to have a shielding effect on the axial γ-carbons and a deshielding effect on the axial γ-hydrogens. The carbon atom with an axial chloro group appears at lower field than that with an equatorial chloro group. The bulky phenylseleno group lies in the equatorial position rather than in the axial position because of 1,3-diaxial interaction.[8] The ^{1}H-NMR spectrum of the product **8a** showed a multiplet at δ 2.93—3.13 due to the 3-H and a multiplet at δ 3.63—3.83 due to the 1-H. The former chemical shift is very close to that of the axial 1-H (1-H(ax)) of 4-*tert*-butyl-1-(phenylseleno)cyclohexane[8] and therefore the 3-H of **8a** is not affected by the 1-Cl. The chemical shift of the 1-H corresponds to that of the 1-H(ax) of chlorocyclohexane.[9] From these observations, the conformation of **8a** was assigned as 1-Cl(eq) and 3-PhSe(eq).

On the other hand, both the 1-H and the 1-C absorptions of **8b** appeared at lower field (δ 4.03—4.10 and 63.4, respectively) than those of **8a**. These results indicate that the 1-Cl is in the axial position. The 3-H signal was shifted downfield (δ 3.30—3.37) because of the γ-effect of the 1-Cl(ax). The observation of the highfield-shifted methyl signal at δ 2.37—2.43 indicates that the conformation of 2-CH_3(ax) and 2-H(eq) is more probable than the opposite conformation of 2-CH_3(eq) and 2-H(ax). The stereochemistry of **8b** was determined to be 1-Cl(ax), 2-CH_3(ax), and 3-PhSe(eq).

The formation of **8b** from the *cis*-olefinic *Se,O*-heteroacetal **6d** implies that this cyclization proceeded in a stereospecific manner. The difference in the conformations of 1-Cl of **8a** and **8b** can be explained as follows. The chloride ion would approach the intermediary cyclohexenium ion, which is formed by the attack of the α-seleno carbenium ion from **6d** at the olefinic moiety, from the opposite side to the methyl group, and consequently the *trans*-1-chloro-2-methyl product **8b** is produced. In the case of **6c**, the chloride ion attacks the cyclohexenium ion intermediate from the less congested side and the 1-Cl(eq) product is formed. Recently, we have reported *endo*-selective cyclization from diselenoacetals,[4b] but the present work is more practical from the viewpoints of yield and stereoselectivity. The details of the α-seleno carbenium ion cyclization reaction will be described in another paper.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra of solids (KBr) and liquids (film) were recorded on a JASCO IRA-100 spectrophotometer. ^{1}H-NMR spectra were obtained for solutions in $CDCl_3$ on Hitachi R-20B (60 MHz) and JEOL GX-270 (270 MHz) spectrometers with tetramethylsilane as an internal standard, unless otherwise indicated. ^{13}C-Spectra were run on a JEOL GX-270 spectrometer. Mass spectra were recorded by a JEOL JMS-D300 spectrometer with a direct-insertion probe at 70 eV. Exact mass determination was done with a JMA 2000 on-line system.

2-Methoxyethoxymethyl Phenyl Selenide (1) (Typical Procedure for Syntheses of *Se,O*-Heteroacetals) Diphenyl diselenide (5.0 g, 16.0 mmol) in dry ether (25 ml) was added dropwise to an ether (63 ml) suspension of $LiAlH_4$ (0.35 g, 9.1 mmol) at −78 °C under an Ar atmosphere. The mixture was stirred for 30 min and β-methoxyethoxymethyl chloride (6.0 g, 48.1 mmol) was added dropwise to it. The whole was warmed to room temperature and poured into ice-cold water (200 ml). The organic layer was separated and the aqueous layer was extracted with ether. The organic layer and extracts were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2–hexane (1 : 10). 2-Methoxyethoxymethyl phenyl selenide (**1**) (3.51 g, 45%) was obtained as a yellow oil. IR (film) cm^{-1}: 3060, 2990, 2930—2875, 2825, 1740, 1580, 1480, 1440, 1270—1240, 1200, 1080, 1070, 1020, 835, 690, 665. ^{1}H NMR (60 MHz, $CDCl_3$) δ: 3.33 (3H, s, OMe), 3.40—3.83 (4H, m, CH_2CH_2O), 5.28 (2H, s, OCH_2Se), 7.10—7.38 (3H, m, ArH), 7.38—7.73 (2H, m, ArH). High-resolution MS *m/z*: Calcd for $C_{10}H_{14}O_2Se$: 246.0159. Found: 246.0163.

Methoxymethyl Phenyl Selenide (2) The title compound **2** was synthesized by the method of Reich *et al.*[5]

2-Methoxyethoxymethyl Benzyl Selenide (3) The title compound **3** was prepared from dibenzyl diselenide (4.0 g, 11.8 mmol), $LiAlH_4$ (0.25 g, 6.7 mmol) and 2-methoxyethoxymethyl chloride (4.41 g, 35.4 mmol) by the procedure given above for **1**. Yield was 5.74 g (quant.) as a yellow oil. IR ν (film) cm^{-1}: 3640—3300, 3100—2800, 1600, 1500, 1450, 1360, 1280—1240, 1200, 1130, 1080, 1020, 840, 760, 700. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 3.35 (3H, s, OMe), 3.43—3.75 (4H, m, OCH_2CH_2O), 3.83 (2H, s, $SeCH_2Ph$), 4.93 (2H, s, OCH_2Se), 7.25 (5H, br s, ArH). High-resolution MS *m/z*: Calcd for $C_{11}H_{16}O_2Se$: 260.0315. Found: 260. 0322.

Methoxymethyl Benzyl Selenide (4) The title compound **4** was prepared from dibenzyl diselenide (3.4 g, 10 mmol), $LiAlH_4$ (0.22 g, 5.7 mmol) and methoxymethyl chloride (2.42 g, 30 mmol) by the procedure given for **1**. Yield was 3.7 g (87%) as a yellow oil. IR (film) cm^{-1}: 3120—2750, 1600, 1490, 1450, 1420, 1265, 1170, 1090, 1020. ^{1}H NMR (60 MHz, $CDCl_3$) δ: 3.29 (3H, s, Me), 3.81 (2H, s, $SeCH_2Ph$), 4.82 (2H, s, $SeCH_2O$), 7.21—7.50 (5H, m, ArH). High-resolution MS *m/z*: Calcd for $C_9H_{12}OSe$: 216.0053. Found: 216.0056.

Benzyloxylmethyl Benzyl Selenide (5) The title compound **5** was prepared from dibenzyl diselenide (3.4 g, 10 mmol), $LiAlH_4$ (0.22 g, 5.7 mmol) and benzyl chloromethyl ether (3.13 g, 20 mmol) by the procedure given for **1**. Yield was 3.05 g (52%) as a yellow oil. IR (film) cm^{-1}: 3150—2800, 1600, 1500, 1460, 1430, 1380, 1300—1140, 1140—1020. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 3.84 (2H, s, $SeCH_2O$), 4.55 (2H, s, OCH_2Ph), 4.91 (2H, s, $PhCH_2Se$), 7.00—7.42 (10H, m, ArH). High-resolution MS *m/z*: Calcd for $C_{15}H_{16}OSe$: 292.0366. Found: 292.0379.

Methylation of α-Lithio-*Se,O*-heteroacetal of 1 with Methyl Iodide (Typical Procedure for Alkylation of *Se,O*-Heteroacetals) A hexane solution of *n*-BuLi (1.0 ml, 1.5 mmol) was added to a THF (5 ml) solution of 2,2,6,6-tetramethylpyperidine (0.28 g, 2.0 mmol) at −78 °C under an Ar atmosphere. The reaction mixture was warmed to 0 °C and stirred for 20 min. A solution of 2-methoxyethoxymethyl phenyl selenide (**1**) (0.25 g, 1.0 mmol) in THF (2 ml) was added dropwise at −78 °C to the solution of LTMP thus prepared. After the mixture had been warmed to −40 °C over 30 min, a solution of methyl iodide (0.21 g, 1.5 mmol) in THF (2 ml) was added dropwise to the mixture at −78 °C. The resulting solution was allowed to warm to room temperature overnight and poured into water. The organic layer was separated and the aqueous layer was extracted with ether. The organic layer and the extracts were combined and dried over $MgSO_4$. The solvent was evaporated off under reduced pressure. The residue was purified by preparative layer chromatography (PLC) on silica gel with CH_2Cl_2–hexane (1 : 5). 1-(2-Methoxyethoxy)-1-phenylselenoethane (**6a**) (0.18 g, 69%) was obtained as a yellow oil accompanied with **1** (0.08 g, 30%). **6a**: IR (film) cm^{-1}: 3020—2800, 1580, 1480, 1440, 1370, 1320, 1240, 1200, 1100, 1080, 1020, 940, 850, 740, 690. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.68 (3H, d, J=6 Hz, Me), 3.33 (3H, s, OMe), 3.38—3.50 (3H,

m, CH_2CH_2O), 3.80—4.10 (1H, m, CH_2O), 5.15 (1H, q, J=6 Hz, CHMe), 7.25—7.33 (3H, m, ArH), 7.48—7.63 (2H, m, ArH). *Anal.* Calcd for $C_{11}H_{16}O_2Se$: C, 50.97; H, 6.22. Found: C, 50.73; H, 6.15.

Alkylation of 1 with Ethyl Iodide The heteroacetal **1** (0.13 g, 0.5 mmol) was treated with LTMP and ethyl iodide (78 mg, 0.8 mmol) by a procedure similar to that used in the case of methyl iodide. 1-(2-Methoxyethoxy)-1-phenylselenopropane (**6b**) (0.1 g, 73%) was obtained as a yellow oil accompanied with **1** (4 mg, 3%). **6b**: IR (film) cm^{-1}: 3020—2800, 1580, 1470—1440, 1360, 1260, 1200, 1140—1060, 1020, 980, 900, 740, 680. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.00 (3H, t, J=8 Hz, Me), 1.68—2.15 (2H, m, CH_2), 3.33 (3H, s, OMe), 3.43—3.63 (3H, m, CH_2CH_2O), 3.83—4.13 (1H, m, CH_2O), 4.90 (1H, t, J=8 Hz, SeCH), 7.15—7.33 (3H, m, ArH), 7.50—7.65 (2H, m, ArH). *Anal.* Calcd for $C_{12}H_{18}O_2Se$: C, 52.75; H, 6.64. Found: C, 52.50; H, 6.58.

Alkylation of 1 with 5-Bromo-1-pentene Compound **1** (1.0 g, 4.1 mmol) was treated with LTMP and 5-bromo-1-pentene (1.22 g, 8.2 mmol). 6-(2-Methoxyethoxy)-6-phenylseleno-1-hexene (**6c**) (0.57 g, 44%) was obtained as a pale yellow oil. IR (film) cm^{-1}: 3020, 3000—2800, 1640, 1580, 1480, 1440, 1120—1060, 900, 850, 740, 690. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.38—2.13 (6H, m, $CH_2\times3$), 3.33 (3H, s, OMe), 3.43—3.63 (3H, m, CH_2CH_2O), 3.80—4.20 (1H, m, CH_2O), 4.75—5.23 (2H, m, olefinic H), 5.00 (1H, t, J=6 Hz, SeCH), 5.45—6.00 (1H, m, olefinic H), 7.18—7.33 (3H, m, ArH), 7.50—7.65 (2H, m, ArH). *Anal.* Calcd for $C_{15}H_{22}O_2Se$: C, 57.51; H, 7.08. Found: C, 57.66; H, 7.12.

Alkylation of 1 with 6-Iodo-2-hexene Treatment of **1** (1.0 g, 4.1 mmol) with LTMP and 6-iodo-2-hexene (1.3 g, 6.2 mmol) afforded 7-(2-methoxyethoxy)-7-phenylseleno-2-heptene (**6d**) (0.81 g, 60%) as a yellow oil. IR (film) cm^{-1}: 3030—2800, 1740, 1580, 1480, 1440, 1370, 1240, 1200, 1160—1060, 850, 740, 700. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.25—2.20 (6H, m, $CH_2\times3$), 1.58 (3H, br d, J=6 Hz, Me), 3.35 (3H, s, OMe), 3.43—3.63 (3H, m, CH_2), 3.83—4.20 (1H, m, OCH_2), 5.00 (1H, t, J=6 Hz, SeCH), 5.25—5.45 (2H, m, olefinic H), 7.20—7.35 (3H, m, ArH), 7.50—7.70 (2H, m, ArH). *Anal.* Calcd for $C_{16}H_{24}O_2Se$: C, 58.71; H, 7.39. Found: C, 58.53; H, 7.41.

Alkylation of 1 with *n*-Butyl Iodide Treatment of **1** (2.0 g, 8.2 mmol) with LTMP and *n*-butyl iodide (2.3 g, 12.3 mmol) afforded 1-(2-methoxyethoxy)-1-phenylselenopentane (**6e**) (1.98 g, 80%) as a yellow oil. IR (film) cm^{-1}: 3100—2800, 1650, 1580, 1480, 1440, 1380, 1200, 1120, 1080, 1020, 850, 740, 680. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 0.75—2.03 (6H, m, $CH_2\times3$), 0.83 (3H, t, J=6 Hz, Me), 3.33 (3H, s, OMe), 3.48—4.10 (4H, m, OCH_2CH_2), 5.00 (1H, t, J=8 Hz, CHSe), 7.13—7.65 (5H, m, ArH). *Anal.* Calcd for $C_{14}H_{22}O_2Se$: C, 55.81; H, 7.36. Found: C, 55.73; H, 7.29.

Alkylation of 3 with Methyl Iodide The heteroacetal **3** (0.13 g, 0.5 mmol) was treated with LTMP and methyl iodide (0.14 g, 1.0 mmol) by the procedure given for **1** and methyl iodide. 1-Benzylseleno-1-(2-methoxyethoxy)ethane (**7a**) (0.15 g, 85%) was obtained as a yellow oil. IR (film) cm^{-1}: 3100—2800, 1600, 1500, 1450, 1360, 1280, 1260, 1200, 1130, 1080, 1020, 980, 840, 760, 700. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.73 (3H, d, J=8 Hz, Me), 3.33 (3H, s, OMe), 3.43—3.70 (4H, m, OCH_2CH_2), 4.28 (1H, q, J=8 Hz, SeCH), 4.88 (2H, br s, CH_2Ph), 7.10—7.38 (5H, m, ArH). MS m/z: 353 (small M^+).

Alkylation of 3 with Benzyl Bromide Treatment of **3** (0.13 g, 0.5 mmol) with LTMP and benzyl bromide (0.17 g, 1.0 mmol) afforded 1-benzylseleno-1-(2-methoxyethoxy)-2-phenylethane (**7b**) (0.17 g, 98%) as a yellow oil. IR (film) cm^{-1}: 3080—2800, 1600, 1500, 1460, 1360, 1300—1240, 1130, 1080, 1030, 840, 760, 700. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 3.25—3.63 (4H, m, OCH_2CH_2O), 3.30 (3H, s, OMe), 3.43 (2H, d, J=8 Hz, CH_2Ph), 4.33 (1H, t, J=8 Hz, SeCHO), 4.75 (2H, br s, $SeCH_2$), 7.10 (5H, br s, ArH), 7.20 (5H, br s, ArH). High-resolution MS m/z: Calcd for $C_{18}H_{22}O_2Se$: 350.0784. Found: 350.0804.

Alkylation of 3 with Allyl Iodide Treatment of **3** (0.13 g, 0.5 mmol) with LTMP and allyl iodide (0.17 g, 1.0 mmol) afforded 4-benzylseleno-4-(2-methoxyethoxy)-1-butene (**7c**) (0.19 g, quant.) as a yellow oil. IR (film) cm^{-1}: 3080—2800, 1640, 1500, 1450, 1360, 1250, 1200, 1130, 1070, 1020, 990, 850, 750. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 2.75 (2H, br t, J=8 Hz, $CH_2C=C$), 3.30 (3H, s, OMe), 3.38—3.58 (4H, m, OCH_2CH_2), 4.13 (1H, t, J=8 Hz, SeCHO), 4.80 (2H, br s, $PhCH_2$), 4.95—5.18 (2H, m, olefinic H), 5.38—6.05 (1H, m, olefinic H), 7.23 (5H, br s, ArH). High-resolution MS m/z: Calcd for $C_{14}H_{20}O_2Se$: 300.0628. Found: 300.0631.

Alkylation of 3 with Cyclohexyl Bromide Treatment of **3** (0.13 g, 0.5 mmol) with LTMP and cyclohexyl bromide (0.16 g, 1.0 mmol) afforded 1-benzylseleno-1-cyclohexyl-1-(2-methoxyethoxy)methane (**7d**) (0.15 g, 90%) as a yellow oil. IR (film) cm^{-1}: 3050—2850, 1600, 1500, 1450, 1360, 1270, 1200, 1130, 1080, 980, 910, 850, 840, 760, 730, 700. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 0.75—2.38 (11H, m, cyclohexyl H), 3.33 (3H, s, OMe), 3.35—3.70 (4H, m, OCH_2CH_2), 3.90 (1H, d, J=9 Hz, SeCH), 4.68 (1H, d, J=11 Hz, benzyl H), 4.83 (1H, d, J=11 Hz, benzyl H), 7.25 (5H, br s, ArH). High-resolution MS m/z: Calcd for $C_{17}H_{26}O_2Se$: 342.1098. Found: 342.1123.

Alkylation of 3 with 6-Iodo-2-hexene Treatment of **3** (0.52 g, 2.0 mmol) with LTMP and 6-iodo-2-hexene (0.84 g, 4.0 mmol) afforded 7-benzylseleno-7-(2-methoxyethoxy)-2-heptene (**7e**) (0.58 g, 85%) as a yellow oil. IR (film) cm^{-1}. 3100—2800, 1500, 1450, 1400, 1360, 1280, 1250, 1200, 1130, 1080, 1020, 980, 860, 830, 760, 700. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.18—1.68 (2H, m, CH_2), 1.58 (3H, br d, J=6 Hz, Me), 1.88—2.25 (4H, m, $CH_2\times2$), 3.33 (3H, s, OMe), 3.53 (4H, br s, OCH_2CH_2), 4.08 (1H, t, J=8 Hz, SeCHO), 4.83 (2H, br s, $PhCH_2$), 5.25—5.51 (2H, m, olefinic H), 7.25 (5H, br s, ArH). High-resolution MS m/z: Calcd for $C_{17}H_{26}O_2Se$: 342.1097. Found: 342.1072.

Cyclization of *Se,O*-Heteroacetal 6c (Typical Procedure for Cyclization of *Se,O*-Heteroacetals) A solution of *Se,O*-heteroacetal **6c** (0.15 g, 0.5 mmol) in CH_2Cl_2 (1 ml) was added dropwise to a CH_2Cl_2 (2 ml) solution of $TiCl_4$ (0.14 ml, 1.0 mmol) at −80 °C under an Ar atmosphere. The reaction mixture was stirred for 10 min and poured into a saturated $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with ether. The organic layer and the extracts were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by PLC on silica gel with hexane. 1-Chloro-3-phenylselenocyclohexane (**8a**) (0.10 g, 71%) was obtained as a yellow oil. IR (film) cm^{-1}: 3040, 2855, 1720, 1580, 1480, 1440, 1330, 1280, 1220, 1210. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.06—2.22 (7H, m, alkyl H), 2.44—2.59 (1H, m, 2-H), 2.93—3.13 (1H, m, 3-H), 3.63—3.83 (1H, m, 1-H), 7.22—7.35 (3H, m, ArH), 7.49—8.00 (2H, m, ArH). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ 26.6 (t), 32.6 (t), 36.3 (t), 40.1 (d), 44.6 (t), 58.5 (d), 127.9 (d), 129.0 (d), 135.4 (d). High-resolution MS m/z: Calcd for $C_{12}H_{15}ClSe$: 274.0027. Found: 274.0039.

Cyclization of 6d with $TiCl_4$ Treatment of the *Se,O*-heteroacetal **6d** (0.18 g, 0.5 mmol) with $TiCl_4$ (0.14 ml, 1.0 mmol) gave 1-chloro-2-methyl-3-phenylselenocyclohexane (**8b**) (0.13 g, 92%) as a yellow oil. IR (film) cm^{-1}: 3055, 2950, 2855, 1720, 1575, 1470, 1440, 1380, 1280. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.19 (3H, d, J=7 Hz, Me), 1.26—1.41 (1H, m, alkyl H), 1.71—1.90 (5H, m, alkyl H), 2.37—2.43 (1H, m, 2-H), 3.30—3.37 (1H, m, 3-H), 4.03—4.10 (1H, m, 1-H), 7.25—7.30 (3H, m, ArH), 7.53—7.56 (2H, m, ArH). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 10.0 (q), 27.4 (t×2), 30.5 (t), 40.4 (d), 47.9 (d), 63.4 (d), 127.5 (d), 129.1 (d), 134.4 (d). High-resolution MS m/z: Calcd for $C_{13}H_{17}ClSe$: 288.0182. Found: 288.0168.

References

1) B. T. Greobel and D. Seebach, *Synthesis*, **1977**, 357; P. C. B. Page, M. B. van Niel, and J. C. Prodger, *Tetrahedron*, **45**, 7643 (1989).
2) D. V. Ende, A. Cravador, and A. Krief, *J. Organometal. Chem.*, **177**, 1 (1989); S. Halazy, J. Lucchetti and A. Krief, *Tetrahedron Lett.*, **1978**, 3971; B. Hermans and L. Hevesi, *ibid.*, **31**, 4363 (1991).
3) E. J. Corey and D. Seebach, *Angew. Chem.*, **77**, 1134, 1135 (1965).
4) *a*) D. Seebach and N. Peletie, *Chem. Ber.*, **105**, 511 (1972); *b*) T. Kataoka, M. Yoshimatsu, H. Shimizu, and M. Hori, *Tetrahedron Lett.*, **32**, 105 (1991).
5) H. J. Reich, F. Chow, and S. K. Shah, *J. Am. Chem. Soc.*, **101**, 6638 (1979).
6) Methoxy-substituted acetals did not suffer C–O bond fission but underwent C–Se bond cleavage to give diselenides.
7) H.-J. Schneider and V. Hoppen, *J. Org. Chem.*, **43**, 3866 (1978); H.-J. Schneider, U. Buchheit, V. Hoppen, and G. Schmidt, *Chem. Ber.*, **122**, 321 (1989).
8) A. Krief, W. Dumont, M. Clarembeau, G. Bernard, and E. Badaoui, *Tetrahedron*, **45**, 2005 (1989).
9) J. Seibl and T. Clerc, "Tables of Spectral Data for Structure Determination of Organic Compounds," 2nd ed., translated by K. Biemann, Springer-Verlag, Berlin, 1985, p. H195.