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ENDO SELECTIVE CYCLIZATIONS OF SELENONIUM ION INTERMEDIATE: EFFICIENT FORMATION OF 1-HALO-3-SELENO-CYCLOHEXANES

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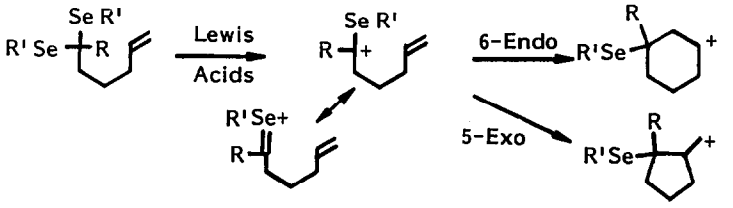
Abstract: Selenoacetal **1** was cyclized with tin(IV) chloride in the 6-Endo-Trig mode to give 1-chloro-3-methylselenocyclohexanes (**2a,b**) regio- and stereoselectively. Bromo- or iodocyclohexane derivatives were afforded by use of tin(IV) bromide or titanium(IV) iodide, respectively.

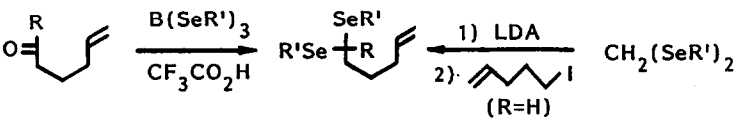
In recent years, cyclizations via radical, anionic and cationic species have attracted considerable interest.[1] Ionic cyclizations can control regio- and stereoselectivity more easily than the radical cyclizations.[2] Iminium[3] and thionium ions[4] are the useful cationic sources and cyclize with double bonds in the Exo-Trig fashion.

We recently investigated the synthetically useful radical reactions using tris-(phenylseleno)- and tris(methylseleno)boranes,[5] which are used for synthesis of selenoacetals from ketones, and reported that these selenoboranes cleaved the C-O bonds of 5- and 6-membered cyclic ethers in the presence of zinc iodide.[6] This paper describes the cationic cyclizations by way of a selenonium ion generated from a selenoacetal (Scheme 1).



Scheme 1

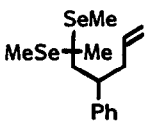
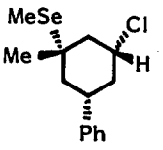
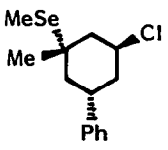
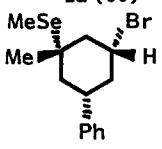
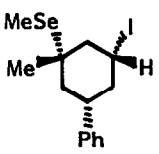
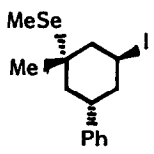
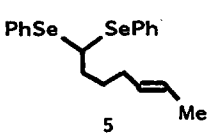
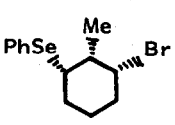
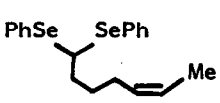
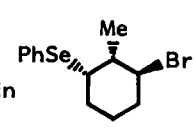
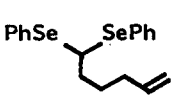
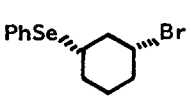
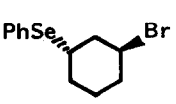
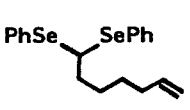
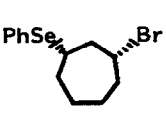
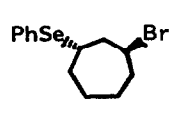
Selenoacetals were synthesized in satisfactory yields by two methods as shown in Scheme 2: one is selenoacetalization of aldehydes or ketones using tris(methylseleno)-borane and a catalytic amount of CF_3CO_2H,[7] and the other is alkylation of bis(phenylseleno)methane.



Scheme 2

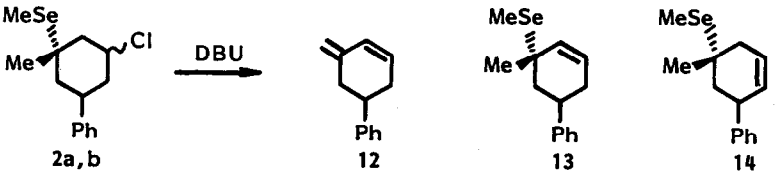
We examined some procedures for generation of a selenonium ion intermediate and used the Hevesi's method[8] in which selenonium ions were generated by the reaction of selenoacetals with $SnCl_4$. Eneselenoacetal **1** (1.0 mmol) was added to a solution of $SnCl_4$ (2.0 mmol) in CH_2Cl_2 at -40 °C. The reaction mixture was gradually warmed to room temperature, stirred for 10 min and then worked up as usual. The product was purified by

Table I Cyclization Reactions of Selenoacetals with Lewis Acids

Entry No.	Selenoacetals	Lewis Acids (molar ratio)	Conditions	Products (% yields) [a]
1	 1	$SnCl_4$ (2)	-40°→rt, 10min	 2a (60)  2b (7)
2	1	$SnBr_4$ (2)	-40°→rt, 10min	 3a (90)
3	1	$TiCl_4$ (2)	-40°→rt, 10min	2a (55)
4	1	TiI_4 (2)	-40°→rt, 12h	 4a (56)  4b (5)
5	 5	$SnBr_4$ (2)	-40°→rt, 2h	 6a (44)
6	 7	$SnBr_4$ (2)	-40°→rt, 10min	 6b (46)
7	 8	$SnBr_4$ (2)	-40°→rt, 1h	 9a (39)  9b (13)
8	 10	$SnBr_4$ (2)	-40°→rt, 5h	 11a (31)  11b (8)

a) The cis- and trans-isomer ratios were determined by comparison of the intensities of 1-H in the ^1H NMR spectra.

preparative TLC on silica gel (hexane) to give a stereoisomeric mixture of 1-chloro-3-methylselenocyclohexane derivatives[9] **2a** and **2b** (Table I, Entry 1). When one molar equivalent of $SnCl_4$ was used, a complex mixture was afforded. Bromo- **3a** and iodocyclohexanes[9] **4a** and **4b** were similarly provided by use of $SnBr_4$ and TiI_4, respectively. Trans-olefin **5** afforded (1R*, 2S*, 3S*)-1-bromo-2-methyl-3-phenylselenocyclohexane **6a** and cis-isomer **7** yielded (1S*, 2S*, 3S*)-1-bromo-2-methyl-3-phenylselenocyclohexane **6b**. These findings indicate that the selenonium ions cause stereospecific cyclization. Reactions of the phenylselenoacetals (Entries 5-8) were slow, because the C-Se bond of phenylselenoacetals is more difficult to be cleaved by Lewis acids than that of methylselenoacetals.



2a,b **12** **13** **14**

Scheme 3

We treated a mixture of products **2a,b** with 1,5-diazabicyclo[5,4,0]undec-7-ene (DBU) in order to determine the structure of the products. The result giving a mixture of dehydrochlorinated products[10] **13** and **14** (25%) together with a diene [10,11] **12** indicated that compounds **2a,b** have a 1-chloro-3-methylseleno moiety.

Conformations of the cyclized products shown in Table I were determined by reference to Schneider's reports on the γ-substituent-induced shielding in 1,3-disubstituted cyclohexanes.[12] The axial halogeno group shields the γ-carbons and deshields the axial γ-hydrogens, and the carbon with the axial bromo group appears in the lower field than that with the equatorial bromo group.[12] The bulkiest group, methylseleno or phenylseleno group occupies the equatorial position rather than the axial one.[13] The stereoisomer **8a** exhibiting absorptions at δ_H 2.24-2.29 (m, 2-Hax), 2.60-2.69 (m, 2-Heq), 3.01-3.13 (m, 3-H), 3.85-3.97 (m, 1-H), and δ_C 40.98 (d, 3-C), 50.03 (d, 1-C) was assigned to be cis-1-bromo-3-(phenylseleno)cyclohexane. The other isomer **8b** showing absorptions at δ_H 2.33-2.41 (m, 2-Heq), 3.67-3.76 (m, 3-H), 4.56-4.60 (m, 1-H) and δ_C 38.88 (d, 3-C), 52.77 (d, 1-C) was determined to be the trans-isomer. Conformations of other products **2**, **3**, **4**, **6**, **11** were similarly determined.[14]

This reaction offers a convenient route through a selenonium ion intermediate for preparing cyclohexane or cycloheptane derivatives under mild conditions and in high yield. In particular, it can simultaneously introduce 1-halo and 3-seleno groups as useful functionalities for further synthetic studies.

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9 All new compounds gave satisfactory mass specta and/or elemental analyses. Structures were established by ^{1}H and ^{13}C NMR.

10 The data of compounds **12-14**. **12**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.23-2.36 (2H, m, CH_2), 2.47-2.52 (2H, m, CH_2), 2.81-2.89(1H, m, CH), 4.74(1H, brs, olefinic H), 4.81 (1H, brs, olefinic H), 5.23-5.85(1H, m, olefinic H), 6.16(1H, brd, J=10 Hz, olefinic H), 7.12-7.34 (5H, m, ArH). High resolution mass m/z calcd. for $C_{13}H_{14}$: 170.1096. Found: 170.1105. **13** and **14**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.55 (s, Me), 1.56 (s, Me), 1.58-2.27 (m, CH_2), 2.53-2.72 (m, CH_2), 2.82-2.90 (m, CH), 3.40-3.48 (m, CH), 5.76-5.83 (m, olefinic H), 7.19-7.35 (m, ArH). High resolution mass m/z calcd. for $C_{14}H_{18}Se$: 266.0574. Found: 266.0587.

11 As far as we know, deselenylation of a selenide with DBU has not been reported. No explanation for formation of **12** can be offered at the present time.

12 Schneider, H.-J.; Hoppen, V. J. Org. Chem., **43**, 3866 (1978). Schneider, H.-J.; Buchheit, U.; Hoppen, V.; Schmidt, G. Chem. Ber., **122**, 321 (1989).

13 Krief, A.; Dumont, W.; Clarembeau, M.; Bernard, G.; and Badaoui, E. Tetrahedron, **45**, 2005 (1989).

14 **6a**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.43 (3H, d, J=7 Hz, Me), 1.46-1.91 (4H, m, CH_2), 2.05-2.11 (2H, m, CH_2), 2.28-2.34 (1H, m, 2-H), 2.74-2.84 (1H, m, 3-H), 3.68-3.78 (1H, m, 1-H), 7.23-7.33 (3H, m, ArH), 7.53-7.57 (2H, m, ArH). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 21.65 (q), 28.19 (t), 34.94 (t), 38.55 (t), 46.41 (d), 49.17 (d), 59.78 (d), 128.89 (d), 128.92 (d), 135.79 (d). **6b**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.25 (3H, d, J=7 Hz, Me), 1.34-2.00 (6H, m, CH_2), 2.38-2.46 (1H, m, 2-H), 3.34-3.41 (1H, m, 3-H), 4.21-4.28 (1H, m, 1-H), 7.24-7.29 (3H, m, ArH), 7.52-7.58 (2H, m, ArH). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 11.00 (q), 27.07 (t x 2), 31.16 (t), 40.73 (d), 47.92 (d), 56.76 (d), 127.53 (d), 129.07 (d), 134.39 (d). **11a**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.45-1.81 (5H, m, CH_2), 1.94-2.37 (4H, m, CH_2), 2.72-2.80 (1H, m, CH_2), 3.19-3.30 (1H, m, 3-H), 4.04-4.14 (1H, m, 1-H), 7.24-7.31 (3H, m, ArH), 7.49-7.59 (2H, m, ArH). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 24.86 (t), 26.36 (t), 35.14 (t), 39.85 (t), 40.77 (d), 47.37 (t), 52.75 (d), 127.69 (d), 129.06 (d), 129.37 (s), 134.68 (d). **11b**: Methylene and aromatic protons were overlapped with **11a**. ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.46-2.56 (1H, m, CH_2), 3.64-3.70 (1H, m, 3-H), 4.46-4.53 (1H, m, 1-H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 25.17 (t), 26.85 (t), 34.76 (t), 39.04 (t), 40.27 (d), 45.08 (t), 53.99 (d).

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