THE THIRD ROW ANOMERIC EFFECT. CONFORMATIONAL ANALYSIS OF 2-PHENYLTHIO- AND 2-PHENYLSELENO-1,3-DISELENANES.#

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Abstract-The conformational behavior of cis- and trans-5-methyl-2-phenylthio- and -2-phenylseleno-1,3-diselenanes has been examined by means of ^{13}C nmr and ^{77}Se nmr spectroscopy. Whereas the cis isomers exhibit highly biased equilibria, the trans isomers display readily measurable equilibria at the slow-exchange limit. Direct integration of the individual conformer resonances in the low temperature spectra of the latter isomers yields ΔG°_{147K} values of -0.33 ± 0.01 (SPh) and -0.08 ± 0.01 (SePh) kcal mol^{-1} in favor of the diaxial conformer. The conformational free energy of the methyl group in 5-methyl-1,3-diselenane (ΔG°_{147K} = +0.87 ± 0.03 kcal mol^{-1}) is then used to derive ΔG°_{147K} values of -1.20 ± 0.04 and -0.96 ± 0.04 kcal mol^{-1} for the equilibrium in 2-phenylthio- and 2-phenylseleno-1,3-diselenane, respectively. Since the conformational free energy, ΔG°_{147K}, of the 2-methyl group in 2-methyl-1,3-diselenane is +1.04 ± 0.01 kcal mol^{-1}, it is argued that there exists a significant Se-C-S and Se-C-Se anomeric effect.

INTRODUCTION

The anomeric effect[1] refers to the torsional preferences about the C-X and C-Y bonds in $RXCH_2YR'$ molecules.[2] The effect has been rationalized both qualitatively[2,3] and quantitatively[4] in terms of stabilizing $n_X \rightarrow \sigma^*_{C-Y}$ and $n_Y \rightarrow \sigma^*_{C-X}$ orbital interactions. The replacement of X and/or Y with the cognate atoms X' and/or Y' can modify the magnitude of the interactions either as a result of differences in orbital energies ($n_X \neq n_{X'}$; $n_Y \neq n_{Y'}$) or as a result of differences in overlap between the interacting orbitals. There is extensive literature on such studies in which X(X') and Y(Y') are first-row atoms and the extension to

#This paper is dedicated, with respect, to Professor Sir D.H.R. Barton on the occasion of his 70th birthday.

systems containing second-row atoms is also now well documented.[2] The major effort has focused on the Group VI atoms, namely O and S. Although a few reports on systems containing the heavier congener, Se, have appeared,[5] our earlier work[2d,e,h] on the solution conformational behavior of the 2-arylseleno-1,3-dithianes provided an example of the systematic extension of studies of this nature to systems in which one of the cognate atoms was a third-row element. In particular, our system displayed a S endo anomeric effect and a Se exo anomeric effect. Furthermore, we have recently reported[6] evidence for the existence of a Se endo anomeric effect based on an unusual solid-state conformation adopted by a selenium coronand. It is also of interest to probe the existence of the latter effect in solution and we report herein the conformational analysis of 2-phenylthio- and 2-phenylseleno-1,3-diselenane which constitutes the first evidence in solution for a third-row anomeric effect. It is noteworthy that the existence of significant anomeric interactions involving second- and lower-row atoms has been questioned recently.[7,8]

EXPERIMENTAL

General Information. Mp's were determined on a Fisher-Johns melting-point apparatus and are uncorrected. ^{1}H Nmr(400.13 MHz), ^{13}C nmr(100.6 MHz), and ^{77}Se nmr(76.3 MHz) spectra were recorded on a Bruker WM-400 NMR spectrometer. For the ^{1}H and ^{13}C nmr spectra, chemical shifts are given in ppm downfield from $SiMe_4$. Chemical shifts and coupling constants were obtained from a first-order analysis of the spectra. ^{77}Se Nmr spectra were measured on 0.1 *M* solutions in $CFCl_3$:CD_2Cl_2 (85:15). Pulses of 15° with a repetition rate of 0.2s were used. The spectra were obtained with ^{1}H decoupling since nOe effects are negligible in these derivatives.[9] Chemical shifts are given in ppm downfield from Me_2Se in CD_2Cl_2. ^{13}C nmr spectra were measured in the same solvent using 14° pulses with a repetition rate of 0.5s. The temperatures were measured in the following manner. Peak separations of the signals from a standard methanol sample within the broadband probe were measured by use of the ^{1}H decoupler coils for observation of the ^{1}H nmr signals. The peak separations were converted into temperature values using the quadratic equation of Van Geet,[10] scaled to 400 MHz,[11] and a calibration curve for the probe thermocouple was constructed. The temperatures were obtained from the above curve by extrapolation. Temperatures are believed to be accurate to ±2K. ^{77}Se T_1 relaxation times were determined by saturation recovery experiments, using the Bruker software for processing of data.

Analytical t.l.c. was performed on pre-coated aluminum plates with Merck silica gel 60F-254 as the absorbent. The developed plates were air dried, exposed to uv light and/or sprayed with 10% H_2SO_4 in ethanol, and heated to 100°C. Flash column chromatography was

performed on Kieselgel 60 (230-400 mesh).[12]
Solvents were distilled before use and were dried, as necessary, by literature procedures. Reactions were performed under nitrogen by use of standard Schlenk-tube techniques. Microanalyses were performed by Mr. M.K. Yang of the Microanalytical Laboratory of Simon Fraser University.

4,4-Dimethyl-1,2-diselenolane **2**

To a solution of 2,2-dimethyl-1,3-propanediol ditosylate **1**,[13] (8.50 g, 20.6 mmol) in HMPA (80 ml) was added potassium selenocyanate (6.00 g, 41.6 mmol). The clear solution was warmed slowly to 170°C over 2 h. Between 130-140°C the solution became viscous and insoluble material appeared. After a further 4 h at 170-180°C, the reaction mixture was a dark-red homogeneous solution. Upon cooling to ambient temperature the mixture was diluted with water (500 ml) and extracted with hexane (3 X 300 ml). The dark-red hexane extracts were washed with water (2 X 200 ml) and filtered through silica gel. The solvent was removed to yield **2** (4.30 g, 92%) mp 33-34°C. Lit.[14] mp 34°C. ^{1}H Nmr (400MHz, $CDCl_3$) δ 1.29 (6H, 2Me, s), 3.11 (4H, $2H_3$,$2H_5$, s, $^2J_{H-Se}$ = 15.7 Hz). ^{13}C Nmr (100 MHz, $CDCl_3$) δ 26.52 (Me), 44.42 (C_2,C_4, $^1J_{C-Se}$ = 68.4 Hz), 49.15 (C_3).

5,5-Dimethyl-1,3-diselenane **3**

A solution of the diselenide **2** (2.26 g, 9.91 mmol) in ether (40 ml) was cooled with an ice bath. Aqueous 48% HBr (25 ml) was added followed by Zn powder (1.5 g, 23 mmol) in small portions over 15 min. After a further 30 min, the reaction mixture was a colorless solution with excess Zn present. Aqueous 37% formaldehyde (1.3 ml, 17 mmol) and concentrated H_2SO_4 (2 ml) were added and the reaction mixture stirred at ambient temperature for 7 h. Further additions of formaldehyde (1.0 ml) and H_2SO_4 (1 ml) were made after 4 h. The reaction mixture was diluted with water (50 ml) and extracted with ether (3 X 50 ml). After washing with water (30 ml), 2N NaOH (30 ml) and saturated NaCl solution (30 ml), the extracts were dried ($MgSO_4$) and concentrated to a light-red syrup. Filtration through silica gel with hexane, concentration, and bulb-to-bulb distillation (80-110°C bath temperature, 0.3 mm Hg) yielded **3** as a light-orange syrup (1.25 g, 52%). An analytical sample (mp = 20°C) was obtained by low temperature crystallization from hexane. ^{1}H Nmr (400MHz, $CDCl_3$) δ 1.27 (6H, 2Me, s), 2.66 (4H, $2H_4$,$2H_6$, s, $^2J_{H-Se}$ = 16 Hz), 3.57 (2H, $2H_2$, s, $^2J_{H-Se}$ = 14 Hz). ^{13}C Nmr (100 MHz, $CDCl_3$) δ 5.40 (C_2, $^1J_{C-Se}$ = 78.3 Hz), 27.80 (Me), 35.01 (C_4,C_6, $^1J_{C-Se}$ = 62.8 Hz). Anal. Calcd for $C_6H_{12}Se$: C, 29.77; H,5.00. Found: C, 29.86 H, 4.97.

5,5-Dimethyl-2-phenylthio-1,3-diselenane **4**

A solution of 4,4-dimethyl-1,2-diselenolane, **2** (1.14 g, 5.00 mmol) in anhydrous ether (50 ml) was cooled with an ice bath while lithium aluminum hydride (0.14g, 3.7 mmol) was added in small portions until the red color disappeared. The reaction mixture was cooled to -78°C and treated with trimethyl orthoformate (0.60 ml, 5.5 mmol) followed by boron tifluoride diethyl etherate (1.5 ml, 12 mmol). After 15 min, benzenethiol (0.60 ml, 5.8 mmol) was added and the reaction mixture was stirred for 45 min before being allowed to warm to ambient temperature. After 1 h the mixture was diluted to 100 ml with ether and poured into 2N aqueous HCl (50 ml). The ether layer was washed with water (30 ml) and 2N NaOH solution (30 ml). Drying ($MgSO_4$) and removal of solvent left a crude orange syrup which was purified by silica gel column chromatography (hexane/ethyl acetate, 100:1) to yield **4** (0.370 g, 21%). mp 45-46°C. ^{1}H Nmr (400MHz, $CDCl_3$) δ 1.25 (3H, Me, s), 1.28 (3H, Me, s), 2.51 (2H,$H_{4eq'}H_{6eq'}$ d, J_{gem} = 13.0 Hz), 3.11 (2H, $H_{4ax'}H_{6ax'}$ d, J_{gem} = 13.0 Hz), 5.27 (1H, H_2, s, $^2J_{H-Se}$ = 24.0 Hz), 7.34 (3H, Ar, m), 7.48 (2H, Ar, m). ^{13}C Nmr (100 MHz, $CDCl_3$) δ 25.68 (C_2, $^1J_{C-Se}$ = 92.78 Hz), 26.23, 26.61, 28.68 (Me,C_5), 35.13 (C_4,C_6, $^1J_{C-Se}$ = 81.8 Hz), 128.09, 128.97, 132.48, 136.50 (Ph). Anal. Calcd for $C_{12}H_{16}SSe_2$: C, 41.15; H,4.60. Found: C, 41.33; H, 4.58.

2-Methyl-1,3-propane-bis-selenocyanate **7**

A mixture of 2-methyl-1,3-propanediol ditosylate **6**,[15] (16.0 g, 40.2 mmol) and potassium selenocyanate (12.0 g, 83.3 mmol) in DMF (200 ml) was stirred at ambient temperature for 48 h and for 24 h at 50-70°C. The mixture was diluted to 1 l with water and extracted with ether (4 X 100 ml). The combined ether extracts were washed with water and saturated NaCl solution, dried ($MgSO_4$), and concentrated to yield a crystalline residue. Recrystallization from hexane/ethyl acetate, 1:1 (60 ml) yielded **7** (7.63 g, 71%) mp 43-44°C. ^{1}H Nmr (400MHz, $CDCl_3$) δ 1.29 (3H, Me, d, J = 6.7 Hz), 2.48 (1H, H_2, m, J = 6.7, 12.5 Hz), 3.20 (2H,H_1,H_3, dd, J = 13.0, 6.0 Hz), 3.23 (2H, H_1',H_3', dd, J = 13.0, 6.0 Hz). ^{13}C Nmr (100 MHz, $CDCl_3$) δ 19.06 (Me), 34.87 (C_2,C_4, $^1J_{C-Se}$ = 54.2 Hz), 35.21 (C_3), 101.08 (CN); Anal. Calcd for $C_6H_8N_2Se_2$: C, 27.09; H,3.03; N, 10.53. Found: C, 27.23; H, 2.98; N, 10.44.

5-Methyl-1,3-diselenane **8**

To the bis-selenocyanate **7** (1.33 g, 5.00 mmol) in anhydrous THF (30 ml) was added Na powder (0.48 g, 21 mmol) and benzophenone (40 mg).[16] The reaction flask was placed in an ultrasonic bath for 2 h, left 16 h at ambient temperature and sonicated again for 4 h until a

blue color appeared. The heterogeneous mixture was stirred while dibromomethane (0.35 ml, 5.0 mmol) in anhydrous THF (20 ml) was added dropwise over 1.5 h. The reaction mixture was stirred at ambient temperature for 20 h, poured into saturated ammonium chloride solution (150 ml) and extracted with ether (3 X 100 ml). The combined extracts were washed with water and saturated NaCl solution, dried ($MgSO_4$), and concentrated to a red syrup. After storage in the freezer for 2 days most of the crude product mixture was insoluble in ether. The ether soluble material was isolated and recrystallized from hexane/ether to yield **8** as colorless needles, (0.103 g, 9%). mp 37°C. ^{1}H Nmr (400MHz, $CDCl_3$) δ 1.16 (3H, Me, d, J = 6.7 Hz), 2.10 (1H, H_5, m), 2.67 (2H,H_{4ax},H_{6ax}, dd, J = 9.68, 13.0 Hz), 2.75 (2H, H_{4eq},H_{6eq}, ddd, J = 1.0, 2.8, 13.0 Hz), 3.44 (1H, H_{2e}, d, J = 11.68 Hz, $^2J_{H-Se}$ = 23.0 Hz, w½ = 3.0 Hz), 3.85 (1H, H_{2ax}, d, J = 11.71 Hz, $^2J_{H-Se}$ = 5.0 Hz, w½ = 1.2 Hz). ^{13}C Nmr (100 MHz, $CDCl_3$) δ 5.05 (C_2, $^1J_{C-Se}$ = 78.5 Hz), 22.93 (Me), 28.72 (C_4,C_6, $^1J_{C-Se}$ = 61.1 Hz), 30.34 (C_5). Anal. Calcd for $C_5H_{10}Se_2$: C, 26.33; H,4.42. Found: C, 26.43; H, 4.34.

5-Methyl-2-phenylthio-1,3-diselenane **9**

The bis-selenocyanate **7** (1.33 g, 5.00 mmol) was suspended in ether (30 ml) and cooled to 0°C. Lithium aluminum hydride (0.270 g, 7.10 mmol) was added in small portions over 15 min. A colorless precipitate formed and the selenocyanate went into solution. A temporary red color was noticed between LAH additions. After stirring for 30 min at ambient temperature, the suspension was cooled to -78°C and trimethyl orthoformate (0.60 ml, 5.5 mmol) and boron trifluoride etherate (1.2 ml, 9.8 mmol) were added. After 45 min, benzenethiol (0.55 ml, 5.3 mmol) and additional boron trifluoride etherate (0.6 ml, 5 mmol) were added. The cooling bath was removed and the reaction mixture was stirred at ambient temperature for 1.5 h. The mixture was diluted with ether (100 ml) and washed with cold 2N HCl solution (50 ml), water (50 ml), saturated $NaHCO_3$ (50 ml), and saturated NaCl solution (50 ml). Drying ($MgSO_4$) and solvent removal yielded a red syrup which was kept under high vacuum for 2 h to remove unreacted benzenethiol. Purification by silica gel chromatography (hexane/ethyl acetate, 98:2) and recrystallization from hexane/ether, 1:1 (10 ml) yielded **9** (0.235 g, 14%) as a white powder (mixture of *cis - trans* isomers). Analysis by capillary GC (15 m DB-1 capillary column, 170°C isothermal) indicated a 58:42 isomer mixture. Attempts at fractional crystallization gave different ratios of the two isomers but did not result in their separation. ^{1}H Nmr (400MHz, $CDCl_3$) major isomer, cis δ 1.20 (3H, Me, d, J = 6.76 Hz), 2.19 (1H, H_5, m, w½ = 28.6 Hz), 2.64 (2H,H_{4eq},H_{6eq}, ddd, J = 13.0, 3.0, 1.0 Hz), 3.17 (2H, H_{4ax},H_{6ax}, dd, J = 13.0, 10.6 Hz), 5.19 (1H, H_2, br s, w½ = 2 Hz, $^2J_{H-Se}$ = 27.4 Hz). Minor isomer, trans δ 1.197 (3H, Me, d, J = 6.68

Hz), 2.01 (1H, H_5, m, w½ = 22.4 Hz), 2.65 (2H,H_{4ax},H_{6ax}, dd, J = 13.0, 7.4 Hz), 3.19 (2H, H_{4eq},H_{6eq}, dd, J = 13.0, 3.2 Hz), 5.25 (1H, H_2, br s, w½ = 2 Hz, $^2J_{H-Se}$ = 17.0 Hz), 7.35, 7.45, 7.52 (5H, Ph, 3m's, both isomers). ^{13}C Nmr (100 MHz, $CDCl_3$) major isomer, cis δ 22.92 (Me), 23.19 (C_2, $^1J_{C2-H2}$ = 163.6 Hz, $^1J_{C-Se}$ = 92.2 Hz), 27.18 (C_4,C_6, $^1J_{C-Se}$ = 64.3 Hz), 30.41 (C_5), 128.05 (C_{para}), 128.99 (C_{ortho}), 132.48 (C_{meta}), 137.23 (C_{ipso}). Minor isomer, trans δ 20.71 (Me), 25.50 (C_2, $^1J_{C2-H2}$ = 166.2 Hz), 27.12 (C_5), 30.53 (C_4,C_6, $^1J_{C-Se}$ = 64.8 Hz), 128.21 (C_{para}), 128.96 (C_{ortho}), 132.62 (C_{meta}), 135.59 (C_{ipso}). Anal. Calcd for $C_{11}H_{14}SSe_2$: C, 39.30; H,4.20. Found: C, 39.59; H, 4.11.

5-Methyl-2-phenylseleno-1,3-diselenane **10**

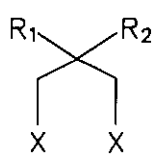
The bis-selenocyanate **7** (1.33 g, 5.00 mmol) and diphenyl diselenide (0.780 g, 2.50 mmol) in dry ether (30 ml) were reduced with lithium aluminum hydride (0.455 g, 12.0 mmol). The selenolate mixture was treated at -78°C with trimethyl orthoformate (0.60 ml, 5.5 mmol) and boron trifluoride etherate (2.0 ml, 16 mmol). Processing as described for the phenylthio derivative, followed by purification by silica gel chromatography (hexane/ethyl acetate, 98:2), and recrystallization from hexane/ether yielded **10** (0.272 g, 28%) as a white powder (mixture of *cis* - *trans* isomers). The isomers were inseparable by capillary GC. ^{1}H Nmr (400MHz, $CDCl_3$) major isomer, cis δ 1.21 (3H, Me, d, J = 6.6 Hz), 2.18 (1H, H_5, m), 2.67 (2H,H_{4eq},H_{6eq}, ddd, J = 13.4, 3.0, 1.0 Hz), 3.14 (2H, H_{4ax},H_{6ax}, dd, J = 13.2, 10.4 Hz), 5.30 (1H, H_2, br s, w½ = 2.4 Hz, $^2J_{H-Se}$ = 27 Hz), 7.34 (3H, Ph, m) 7.61 (2H, Ph, m). Minor isomer, trans δ 1.18 (3H, Me, d, J = 6.7 Hz), 2.03 (1H, H_5, m), 2.68 (2H,H_{4ax},H_{6ax}, dd, J = 13.0, 8.4 Hz), 3.08 (2H, H_{4eq},H_{6eq}, dd, J = 13.0, 3.0 Hz), 5.23 (1H, H_2, s, $^1J_{H2-Se}$ = 14.4 Hz), 7.33 (3H, Ph, m) 7.65 (2H, Ph, m). ^{13}C Nmr (100 MHz, $CDCl_3$) major isomer, cis δ 12.31 (C_2, $^1J_{C2-H2}$ = 157.3 Hz, $^1J_{C-Se}$ = 97.7 Hz), 23.03 (Me), 27.66 (C_4,C_6, $^1J_{C-Se}$ = 67.7 Hz), 30.33 (C_5), 128.33, 129.05, 134.71, 134.84 (Ph). Minor isomer, trans δ 13.96 (C_2, $^1J_{C2-H2}$ = 167 Hz), $^1J_{C-Se}$ = 96.6 Hz), 21.17 (Me), 27.13 (C_5), 31.35 (C_4,C_6, $^1J_{C-Se}$ = 64.8 Hz). Anal. Calcd for $C_{11}H_{14}Se_3$: C, 34.99; H,3.68. Found: C, 34.60; H, 3.66.

2-Methyl-1,3-diselenane **12**

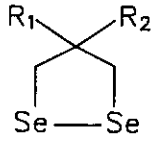
A suspension of 1,3-propane-bis-selenocyanate **11**[17] (1.26 g, 5.00 mmol) in dry ether (30 ml) was stirred with ice-bath cooling while lithium aluminum hydride (0.230 g, 6.10 mmol) was added in small portions over 0.5 h. The reaction mixture became red-brown at first and then finally colorless with a white insoluble precipitate after all of the LAH had been added. The cooling bath was removed for 0.5 h and later replaced while acetaldehyde diethylacetal (0.80 ml, 5.6

mmol) was added, followed by boron trifluoride etherate (1.30 ml, 10.6 mmol). After 24 h at ambient temperature, the reaction mixture was poured into saturated $NaHCO_3$ solution (125 ml) and stirred for 15 min. Ether extraction (2 X 75 ml), drying ($MgSO_4$), and solvent removal yielded a crude red oil which was purified by silica gel chromatography (hexane/ethyl acetate, 98:2) and bulb-to-bulb distillation (bp 75-80°C, 0.1 mm Hg) to yield **12** as a light red oil (0.306 g, 27%). ^1H Nmr (400MHz, $CDCl_3$) δ 1.73 (3H, Me, d, J = 7.0 Hz), 1.97 (1H, H_{5ax}, dtt, $^2J_{5ax,5eq}$ = -14.5 Hz, $^3J_{4ax,5ax}$ = 11.5 Hz, $^3J_{4eq,5ax}$ = 3.0 Hz), 2.17 (1H, H_{5eq}, dtt, $^2J_{5ax,5eq}$ = -14.5 Hz, $^3J_{4eq,5eq}$ = 5.5 Hz, $^3J_{4ax,5eq}$ = 2.5 Hz), 2.86 (2H, H_{4eq},H_{6eq}, ddd, $^2J_{4ax,4eq}$ = -13.5 Hz, $^3J_{4eq,5eq}$ = 5.5 Hz, $^3J_{4eq,5eq}$ = 3.0 Hz), 2.97 (2H, H_{4ax},H_{6ax}, ddd, $^2J_{4ax,4eq}$ = -13.5 Hz, $^3J_{4ax,5ax}$ = 11.5 Hz, $^3J_{4ax,5eq}$ = 3.0 Hz). ^{13}C Nmr (100 MHz, $CFCl_3$:CD_2Cl_2(85:15), 270K) δ 21.88 (C_2, $^1J_{C-Se}$ = 75.6 Hz), 23.99 (Me), 24.22 (C_4,C_6, $^1J_{C-Se}$ = 61.0 Hz), 26.65 (C_5). Anal. Calcd for $C_5H_{10}Se_2$: C, 26.33; H, 4.42. Found: C, 26.62; H, 4.48.

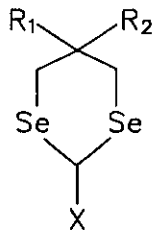
RESULTS



1 $R_1 = R_2 = Me$; X = OTs
5 $R_1 = H$, $R_2 = Me$; X = OH
6 $R_1 = H$, $R_2 = Me$; X = OTs
7 $R_1 = H$, $R_2 = Me$; X = SeCN
11 $R_1 = R_2 = H$; X = SeCN



2 $R_1 = R_2 = Me$



3 $R_1 = R_2 = Me$; X = H
4 $R_1 = R_2 = Me$; X = SPh
8 $R_1 = H$, $R_2 = Me$; X = H
9 cis/trans $R_1 = H$, $R_2 = Me$; X = SPh
10 cis/trans $R_1 = H$, $R_2 = Me$; X = SePh
12 $R_1 = R_2 = H$; X = Me
13 $R_1 = R_2 = H$; X = SPh
14 $R_1 = R_2 = H$; X = SePh

NMR Analysis

Assignment of the ^1H, ^{13}C and ^{77}Se nmr spectra of the conformationally averaged systems, at ambient temperature, was unexceptional. A noteworthy feature, however, is the high-field chemical shift of C-2 in the ^{13}C nmr spectra of compounds **3**, **8**, and **10**. It is assumed here, as in the case of the 4,6-dimethyl-1,3-diselenanes,[18] that the 1,3-diselenane ring adopts a chair-like conformation.

Assignment of the low-temperature ^{13}C and ^{77}Se nmr spectra was somewhat more interesting and is based to a large extent on the γ-gauche effect.[2d,e,h,19] The ^{77}Se and ^{13}C nmr data are summarized in Tables I and II, respectively.

Table I ^{77}Se Nmr Chemical-shift Data[a] for **8**, **9**, **10** and **12**

Compound	Se-1, Se-3	Se-2′
8ax	144	—
8eq	276	—
9A	395	—
9B	397	—
9C	264	—
9cis[b]	397	—
9trans[b,c]	328	—
10A	396	440
10B	391	456
10C	265	428
10cis[b]	397	463
10trans[b,c]	336	454
12ax	361	—
12eq	348	—
Avg.[b,c]	361	—

[a] In $CFCl_3$:CD_2Cl_2 (85:15) at 147°K unless otherwise indicated. [b] Refers to the time-averaged-spectra at 270°K. [c] ^{77}Se chemical shifts are sensitive to temperature.[2h] Consequently, evaluation of K using the average chemical shift method is unreliable.

Table II Low Temperature ^{13}C Nmr Chemical-shift Data[a] for **8**, **9**, **10** and **12**

Compound	C-2	C-4,6	C-5	Me
8ax	7.0	30.2	23.2	17.3
8eq	5.8	28.5	32.4	25.1
9A	21.6	25.5	32.3	24.7
9B	26.4	32.9	30.5	24.0
9C	22.0	27.1	22.8	17.3
10A	12.5	26.3	32.3	24.9
10B	13.9	33.8	30.2	23.1
10C	13.3	27.9	24.6	17.6
12eq	22.2	24.1	25.3	22.7

[a] In $CFCl_3$:CD_2Cl_2 (85:15) at 147°K.

The ^{77}Se nmr spectrum of 5-methyl-1,3-diselenane **8** showed a major and a minor resonance, with the minor resonance at higher field. The assignment of the latter resonance to the axial conformer is consistent with expectations based on the γ-gauche effect. The chemical-shift difference, 132 ppm, can be taken as the difference between the γ-gauche and γ-anti effects of

a methyl group on the Se atom. As expected, the 5-Me and C-5 resonances of the axial conformer in the ^{13}C nmr spectrum are also shifted upfield relative to their equatorial counterparts ($\Delta\delta$ = 7.8 and 5.3 ppm, respectively) owing to the γ-gauche effect.

The ^{77}Se nmr spectrum of a cis/trans mixture of 5-methyl-2-phenylthio-1,3-diselenane **9** showed one peak (δ 395) whose chemical shift was essentially temperature invariant and two others (δ 397(min) and δ 264(maj)) that underwent mutual exchange at higher temperatures. The signal at δ 395 is assigned to the cis isomer in which the phenylthio group is axial and the methyl group is equatorial (isomer A in Figure 1); this conformer is the only observable one in

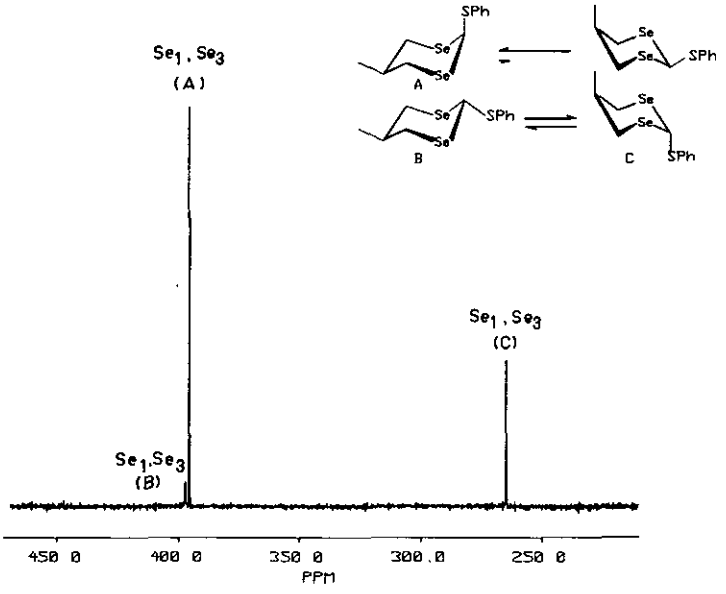


Figure 1. ^{77}Se nmr spectrum of a mixture of cis and trans-5-methyl-2-phenylthio-1,3-diselenane **9** in $CFCl_3$:CD_2Cl_2 (85:15) at 147°K.

a highly biased equilibrium. The peaks at δ 397 and δ 264 are assigned to conformers B and C, respectively, of the trans isomer (Figure 1). The latter assignment is based on the γ-gauche effect established above in the case of **8**. The ^{13}C nmr spectrum of **9** displayed one set of peaks whose chemical shifts were essentially temperature invariant and two other sets, each of which underwent mutual exchange as the temperature was raised. The assignment of peaks to isomers A, B and C was made by means of coupled experiments and on the basis of known

substituent effects (*inter alia*). Thus, for example, C-2, C-4, C-5 and 5-Me in **9C** are shielded relative to the corresponding carbons in **9B** ($\Delta\delta$ = 4.4, 5.8, 7.7 and 6.7 ppm, respectively) owing to the γ-gauche effects of the 5-Me and 2-SPh groups. Similarly, comparison of the data for **9A** and **9C** reveals that 5-Me in **9C** is shielded (7.4 ppm) relative to that in **9A**, and C-4 in **9C** is only slightly deshielded (1.6 ppm) relative to that in **9A**. The latter difference compares favorably with the effect of an axial *vs.* equatorial 5-Me group on the C-4 chemical shift ($\Delta\delta$ = 1.7 ppm) in 5-methyl-1,3-diselenane **8**.

The ^{77}Se nmr spectrum of a cis/trans mixture of 5-methyl-2-phenylseleno-1,3-diselenane **10** displayed three pairs of peaks. One of these pairs (δ 396, 440), attributable to the major isomer, showed the following temperature dependent behavior. Whereas the Se-2′ signal at δ 440 showed no line broadening as the temperature was raised, the Se-1 (Se-3) signal at δ 396 broadened at about 200°K and sharpened again at about 250°K, the maximum broadening occurring at about 220°K. The chemical shift of the latter signal at the slow- and fast-exchange limits was

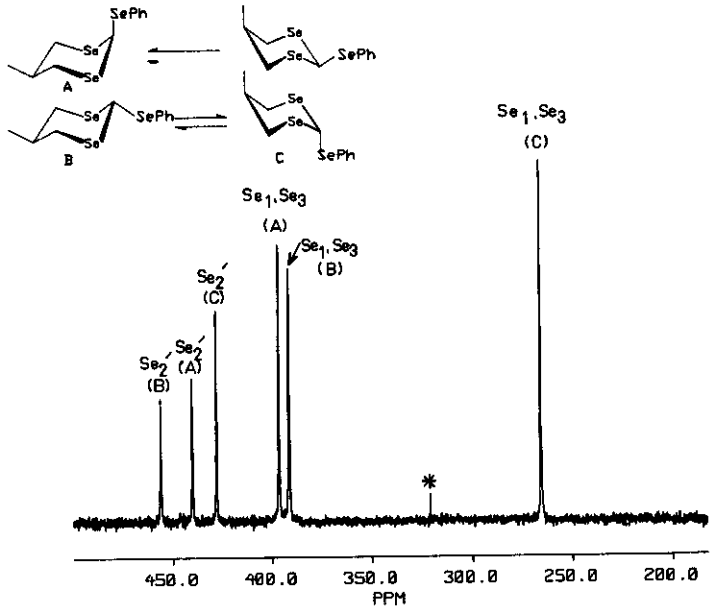


Figure 2. ^{77}Se Nmr spectrum of a mixture of cis and trans-5-methyl-2-phenylseleno-1,3-diselenane **10** in $CFCl_3$:CD_2Cl_2 (85:15) at 147°K. The peak marked with an asterisk is due to an impurity.

virtually identical. This behavior is consistent with the presence of a highly-biased equilibrium in which detection of the signals of the minor conformer is beyond the limit of the experimental technique, and this pair of signals is attributed to conformer **10A** of the cis-isomer (Figure 2). That the Se-1 (Se-3) signal should exhibit significant line broadening is expected because of the large chemical-shift difference between the individual conformer resonances predicted on the basis of the γ-gauche effect of the 5-Me substituent. The other pairs of peaks (δ 391, 456 and δ 265, 428) showed normal line-broadening and coalescence behavior and are assigned to conformers **10B** and **10C**, respectively, of the trans isomer (Figure 2). The peak assignments are based on careful observation of the coalescence behavior of the pairs. The assignment of peaks to the endocyclic selenium atoms in **10B** and **10C** is in accord with expectations based on the γ-gauche effect and arguments presented earlier for the cases of **8** and **9**, while the assignment of peaks to the exocyclic selenium atoms in **10B** and **10C** is consistent with our previous work[2d,e,h] on 2-arylseleno-1,3-dithianes and with the trend observed[20] for the ^{77}Se nmr shifts in axial and equatorial phenylselenocyclohexane. The assignment of ^{13}C nmr signals to **10A**, **10B**, and **10C** (Figure 3) followed a procedure that is

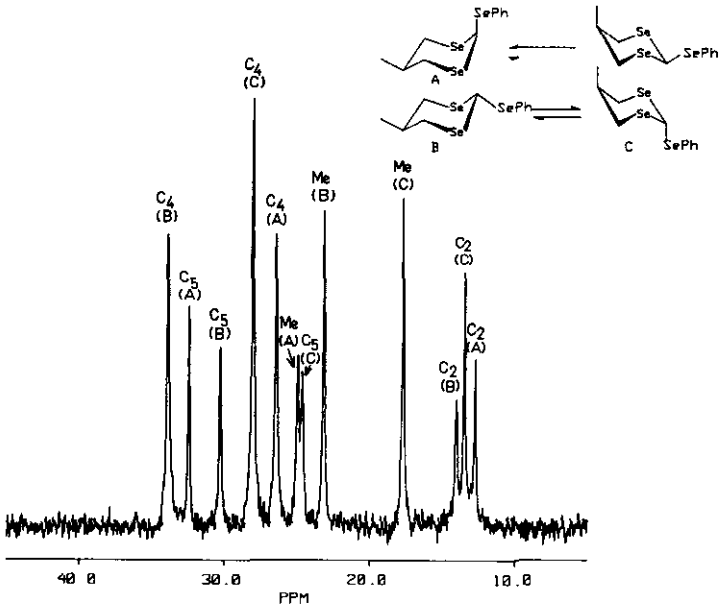


Figure 3. ^{13}C Nmr spectrum of a mixture of cis and trans-5-methyl-2-phenylseleno-1,3-diselenane **10** in $CFCl_3$:CD_2Cl_2 (85:15) at 147°K.

entirely analogous to that used for the cases of **9A**, **9B**, and **9C**.

The assignment of the ^{77}Se nmr shifts in the spectrum of 2-methyl-1,3-diselenane **12** was straightforward. However, owing to the low abundance of the axial conformer, its resonances in the ^{13}C nmr spectrum could not be unambiguously assigned.

Conformational Analysis

Quantitation of the conformational equilibria in **8**, **9**, and **10** was effected by direct examination using low temperature ^{77}Se and ^{13}C nmr spectroscopy. In the case of **12**, only ^{77}Se nmr spectroscopy was used. ^{77}Se has a spin of ½, a natural abundance of 7.58% and a receptivity relative to ^{13}C of 2.98.[9] Nuclear Overhauser enhancement is relatively insignificant.[9] The large chemical-shift range of ^{77}Se (≈2000 ppm for organic compounds)[9] and its extreme sensitivity to chemical environment[21] result in relatively large chemical-shift differences for signals of different conformers and thus, in higher temperatures of coalescence. Before proceeding , however, it was necessary to determine the ^{77}Se spin-lattice relaxation (T_1) times in compounds of this type in order to insure that parameters be chosen that give reliable intensities. ^{77}Se nuclei in small molecules can have fairly long relaxation times.[21] Compound **10** was chosen as a representative candidate. Thus, measurement of T_1 values for all selenium atoms in **10A**, **10B**, and **10C** in the spectrum at 152°K by the saturation recovery method revealed T_1 values of about 0.1 s. The T_1 values therefore pose no serious problem in the acquisition of spectra or in obtaining reliable intensities.

Table III Equilibrium Data[a] for Substituted 1,3-Diselenanes

Compound	K_{E-A} (error)	$\Delta G^{\ddagger}_{147°K}$ (error) (kcal-mol^{-1})
8	0.050 (0.002)	0.87 (0.03)
9-trans	3.07 (0.10)	-0.33 (0.01)
10-trans	1.32 (0.06)	-0.08 (0.01)
12	0.030 (0.001)	1.04 (0.01)

[a] In $CFCl_3$:CD_2Cl_2 (85:15) at 147°K.

The equilibrium constants, K, were derived by direct integration of the appropriate pairs

of peaks in both the ^{77}Se and ^{13}C nmr spectra. In the latter case, only those signals that were well isolated were used for purposes of analysis. The relative intensities obtained from both types of spectra were in good agreement with each other. The values listed in Table III represent mean values obtained from all signals used as well as from several integrations of each set of signals. The errors in K are the standard deviations of the measurements. The errors in ΔG° derive from the errors in K and the error in the temperature, T.

DISCUSSION

Our initial plan to use the 5,5-dimethyl-1,3-diselenanes as candidates for the conformational analysis was thwarted owing to the highly-biased equilibria of the 2-substituted derivatives. For example, the low temperature ^{77}Se or ^{13}C nmr spectra of 5,5-dimethyl-2-phenylthio-1,3-diselenane **4** indicated only peaks attributable to one conformer. We therefore turned our attention to the 5-methyl derivatives **9** and **10** in which the methyl group serves as a counterpoise to give a more balanced conformational equilibrium for one of the configurational isomers (the trans isomer). Thus, $\Delta G^{\circ}_{147K} = -0.33 \pm 0.01$ and -0.08 ± 0.01 kcal mol^{-1} (Table III) for the equilibria in trans-5-methyl-2-phenylthio-1,3-diselenane and trans-5-methyl-2-phenylseleno-1,3-diselenane, respectively, in favor of the diaxial conformers. Since the conformational free energy of the methyl group in 5-methyl-1,3-diselenane **8** is $+0.87 \pm 0.03$ kcal mol^{-1} (Table III) in favor of the equatorial isomer, one derives $\Delta G^{\circ}_{147K\ E-A}$ values of -1.20 ± 0.04 and -0.96 ± 0.04 kcal mol^{-1} for the equilibria in 2-phenylthio- and 2-phenylseleno-1,3-diselenane, **13** and **14**, respectively. That "normal" behavior based on a consideration of non-bonded interactions is to be expected in this series of compounds is indicated by the conformational free energy, $\Delta G^{\circ}_{147K\ E-A} = 1.04 \pm 0.01$ kcal mol^{-1}, for the equilibrium in 2-methyl-1,3-diselenane **12**. The steric effect here is 60% less than that (1.74 kcal mol^{-1})[22] in methylcyclohexane. To a first approximation, the steric effect of a 2-SPh or a 2-SePh group in 1,3-diselenane will be correspondingly reduced relative to the analogously substituted cyclohexanes. Since the A values of SPh[21] and SePh[20] are about the same (1.1 kcal mol^{-1}), a conformational free energy of 0.7 kcal mol^{-1} for the 2-SPh and 2-SePh groups in 1,3-diselenane can be estimated, on steric grounds alone. The axial preference of the SPh and SePh groups in **13** and **14**, respectively, constitutes, therefore, strong evidence for the existence of the selenium endo-anomeric effect operating in Se-C-S and Se-C-Se fragments.

The present work represents the first extension of the study of the endo-anomeric effect in solution to the third-row. The evidence corroborates that reported[6] recently for the Se endo-anomeric effect in the solid state. On the basis of our previous work[2d,2h] regarding the role of $n_S \rightarrow \sigma^*_{C-Se}$ and $n_{Se} \rightarrow \sigma^*_{C-S}$ orbital interactions in controlling the conformational

preferences in 2-arylseleno-1,3-dithianes, we attribute the conformational behavior in **13** and **14** to the dominance of stabilizing $n_{Se} \rightarrow \sigma^*_{C-S}$ and $n_{Se} \rightarrow \sigma^*_{C-Se}$ orbital interactions, respectively.

CONCLUSIONS

Examination of the conformational equilibria in trans-5-methyl-2-phenylthio-1,3-diselenane and trans-5-methyl-2-phenylseleno-1,3-diselenane, together with those in 5-methyl- and 2-methyl-1,3-diselenane, provides evidence for the existence of significant Se-C-S and Se-C-Se anomeric interactions. This work is the first study of the solution endo-anomeric effect involving third-row elements.

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