Systematic Evaluation of the Anomeric Effect in 2-(Arylseleno)-1,3-dithianes. Evidence for Stabilizing Orbital Interactions[1]

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The effects of substitution on the magnitude of the anomeric effect in 2-[(4-substituted-phenyl)seleno]-1,3-dithianes are described. The conformational equilibria were determined by direct measurement of the individual conformer resonances in the ^{77}Se and ^{1}H NMR spectra at the slow-exchange limit. The magnitude of the anomeric effect varies with substituent in the order $NO_2 > CF_3 > Cl > F \approx H > Me > OMe > NMe_2$, providing systematic evidence for $n_S \rightarrow \sigma^*_{C\text{-}Se}$ stabilizing orbital interactions and the existence of the anomeric effect in S–C–Se fragments. Evidence for the mechanism of transmission of the electronic effects is also presented. Thus, analysis of the results by means of a dual substituent parameter approach indicated best correlation with σ_I and σ°_R substituent constants and a slightly greater contribution of the resonance effect than the polar effect. The positive ρ values are interpreted in terms of the accommodation of effective negative charge on the selenium atom in the axial conformer. Further evidence for such increased negative charge is provided by the differences in ^{13}C chemical shifts for the aromatic carbons between the two conformers for a particular substituent and also by the trends in ^{77}Se chemical shifts as a function of substituent for the two conformers. The solvent dependence of the conformational equilibria for selected compounds shows no apparent correlation with dielectric constant although significant anomeric effects and substituent effects are still observed in a polar medium. The results are interpreted in terms of the dominance of the orbital interaction component over the electrostatic component.

Introduction

The anomeric effect[2] continues to be a subject of great interest and of much investigation.[3] Much of the activity has focused on the effects of heteroatom substitution on the nature and magnitude of this conformational effect. Thus, there is an overwhelming body of information on experimental investigations of X–C–Y anomeric interactions involving first-row elements, and the extension of these studies to the corresponding second-row analogues, although more recent a development, is also well documented.[4] The topic has also sparked several theoretical investigations of the nature and origin of first- and second-row anomeric effects.[5] In contrast, accounts on related systems containing lower row elements[6] are relatively scarce. The existence and importance of anomeric interactions in systems containing second-row and lower row elements is not without controversy and has been questioned recently by Schleyer et al.,[5c] on the basis of theoretical calculations of stabilization energies in XCH_2Y molecules, and by Anet and Kopelevich,[7] on the basis of the absence of a conformational deuterium isotope effect in 2-deuterio-5,5-dimethyl-1,3-dithiane. Regarding the origin of the anomeric effect, although several explanations have been advanced,[1,2] that formulated within the framework of molecular orbital theory by Altona[8] and more rigorously in terms of perturbational molecular orbital (PMO) theory[5] seems to have been widely accepted. According to this proposal, favored conformations about X–C–Y fragments resulting in expression of the anomeric effect derive from stabilizing orbital interactions between the p-type nonbonding orbitals on X and Y, n_X and n_Y, with the vacant $\sigma^*_{C\text{-}Y}$ and $\sigma^*_{C\text{-}X}$ orbitals, respectively. Such hyperconjugative interactions have been substantiated by theoretical investigations[5] as well as by X-ray crystallographic studies.[9]

The purpose of the present study[1] is twofold: (1) to evaluate systematically the magnitude of the S–C–Se anomeric effect in a contiguous series of 2-[(4-substituted-phenyl)seleno]-1,3-dithianes 1–8 (Figure 1) and (2) to gain a better understanding of the mechanism of transmission of the electronic effects. Compounds 1–8 were selected as suitable candidates since changes in the nature of the substituent should result in corresponding changes in electronic interactions but only minor changes in geometry. Consequently, changes in steric effects in the above series of compounds should be minimal, permitting evaluation of the electronic component. The second objective of the study is of particular importance in view of the contention of Anet and Kopelevich[7] that π-donation by sulfur is not responsible for the preferred axial orientation of phosphorus and selenium substituents at C-2 of 1,3-dithianes and of electronegative substituents at C-2 of thianes.[3,4b,d,6d] We present herein systematic experimental evidence for the importance of orbital interactions as the

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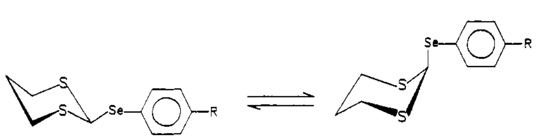

1 R = NMe$_2$
2 R = OMe
3 R = Me
4 R = H
5 R = F
6 R = Cl
7 R = CF$_3$
8 R = NO$_2$

Figure 1. Conformational equlibrium in 2-(arylseleno)-1,3-dithianes 1–8.

"origin" of the anomeric effect in systems containing second- and third-row atoms. To the best of our knowledge there have been only four independent reports of relevance to the work reported here: the study of the conformational preference in 2-(methylseleno)-1,3-oxathiane,[6a] the estimation of the anomeric effect in 2-(phenylseleno)tetrahydropyran[6b] and studies of the conformational behavior of 2-(phenylseleno)cyclohexanones.[6c,d]

Experimental Section

General Information. Melting points 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 0.11 M solutions in 90:10 mixtures of non-deuteriated:deuteriated solvents at 180 K. Pulses of 9° with a repetition rate of 0.7 s were used. The spectra were obtained without ^{1}H decoupling since NOE effects are negligible in these derivatives.[10] Chemical shifts are given in ppm downfield from Me$_2$Se in CD$_2$Cl$_2$. 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 by using the quadratic equation of Van Geet,[11] scaled to 400 MHz,[12] and a calibration curve for the probe thermocouple was constructed. In the case of ^{1}H and ^{13}C NMR experiments, lower temperatures were required, and the temperatures were obtained from the above curve by extrapolation. Temperatures are believed to be accurate to ±2 K. ^{77}Se T_1 relaxation times were determined by saturation recovery experiments, using the Bruker software for processing of data.

Analytical TLC was performed on precoated 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$_2$SO$_4$ in ethanol, and heated to 100 °C. Medium pressure column chromatography was performed on Kieselgel 60 (230–400 mesh) according to a published procedure.[13]

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′-Disubstituted-diphenyl Diselenides. The diselenides (substituent = OMe, Me, Cl, H, CF$_3$) were prepared as described by Reich et al.[14] and gave physical constants that were in agreement with literature values.[15,16]

4,4′-Difluorodiphenyl diselenide was also prepared by the method of Reich et al.[14] and was obtained as a red liquid, bp 135 °C, 0.1 mm; yield 75%: ^{1}H NMR (CDCl$_3$) δ 6.96 (m, 2 H, H-3, H-5), 7.53 (m, 2 H, H-2, H-6); ^{13}C NMR (CDCl$_3$) δ 116.3 (C-3, $^2J_{CF}$ = 22 Hz), 125.6 (C-1), 134.7 (C-2, $^3J_{CF}$ = 8.9 Hz), 162.9 (C-4, $^1J_{CF}$ = 248.5 Hz). Anal. Calcd for C$_{12}$H$_{18}$FSe$_2$: C, 41.40; H, 2.32. Found: C, 41.54; H, 2.28.

4,4′-Bis(dimethylamino)diphenyl diselenide was prepared as described by Pinto et al.[17]

2-(Arylseleno)-1,3-dithianes. Compounds 1–7 were synthesized by reaction of the respective sodium areneselenolates [generated by treatment of the diselenides with sodium borohydride[6e] or with sodium powder and benzophenone in an ultrasonic bath[18]] with 2-chloro-1,3-dithiane.[6e,19] Similarly, reaction of sodium 4-methoxybenzeneselenolate with 2-chloro-4,6-dimethyl-1,3-dithiane[6e] afforded **9** and **10**. The procedure is illustrated for the case of **6**.

2-[(4-Chlorophenyl)seleno]-1,3-dithiane (6). A solution of 4,4′-dichlorodiphenyl diselenide (2.41 g, 6.33 mmol) in dry THF (20 mL) was treated with Na powder (0.30 g, 13.0 mmol) and benzophenone (30 mg) in an ultrasonic bath for 70 min. The almost colorless selenolate suspension was cooled in an ice bath while a benzene solution (20 mL) of 2-chloro-1,3-dithiane[6e] (12.9 mmol) was added. The mixture was stirred at ambient temperature for 0.5 h and then poured into saturated ammonium chloride solution (75 mL) and extracted with ether. The ether extract was washed with water and saturated NaCl, dried (MgSO$_4$), and concentrated to give an orange semicrystalline residue. Crystallization from ether (75 mL) yielded the title compound **6** as colorless needles (2.06 g, 53%). Purification of the mother liquor by chromatography [hexane–ethyl acetate (20:1)] yielded an additional 0.54 g of **6** after crystallization from ether–hexane (1:1); total yield, 66%.

2-[(4-Nitrophenyl)seleno]-1,3-dithiane (8). A solution of 1,3-dithiane (0.545 g, 4.54 mmol) in dry THF (5 mL) at −40 °C under N$_2$ was treated with 2.4 M *n*-BuLi in hexane (2.25 mL). The mixture was stirred at −20 °C for 1 h and then a solution of 4-nitrophenyl selenocyanate[20] (1.03 g, 4.54 mmol) in dry THF (10 mL) at −20 °C was added via cannula. After 15 min the mixture was poured into saturated ammonium chloride solution and, after usual workup procedure, yielded a red-orange solid that was chromatographed on silica gel with dichloromethane–hexane (1:1) as eluant. The title compound 8 was obtained as yellow needles from hexane (0.34 g, 23%).

The physical data for compounds 1–8 are listed in Table S-I and the routine ^{1}H and ^{13}C NMR data are listed in Tables S-II, S-III, and S-IV, (Supplementary material).

Results

Synthesis. Compounds **1–7** were synthesized by reaction of the respective sodium areneselenolates [generated by treatment of the diselenides with sodium borohydride[6e] or with sodium powder and benzophenone in an ultrasonic bath[18]] with 2-chloro-1,3-dithiane.[6e,19] Similarly, reaction of sodium 4-methoxybenzeneselenolate with 2-chloro-4,6-dimethyl-1,3-dithiane[6e] afforded **9** and **10**. Compound **8** was prepared by reaction of 2-lithio-1,3-dithiane with 4-nitrophenyl selenocyanate.

NMR Analysis. The ^{1}H NMR spectra of the conformationally averaged systems, measured in CDCl$_3$ at ambient temperature for all of the derivatives **1–8** show similar characteristics. The salient features of the spectra are (1) the significant chemical-shift differences for the H-4,6 axial and equatorial proton signals, $\Delta\delta_{ax/eq}$, (avg 0.55 ppm),

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Table I. ^{77}Se NMR Chemical Shift Data and Equilibrium Data for 2-(Arylseleno)-1,3-dithianes[a]

compd	chemical shift δ_{avg}[b,d]	δ_{major}[c,d]	δ_{minor}[c,d]	$K_{E\rightarrow A}$ (error)	$-\Delta G°_{180K}$ (error) (kcal mol^{-1})
1	435.5	397.0	479.1	3.8 (0.1)	0.48 (0.02)
2	440.0	403.9	477.9	5.4 (0.1)	0.61 (0.02)
3	446.2	411.2	480.7	6.1 (0.2)	0.65 (0.02)
4	454.7	421.5	486.8	7.6 (0.2)	0.73 (0.03)
5	444.3	412.7	482.4	8.7 (0.2)	0.78 (0.03)
6	447.1	416.7	483.7	9.4 (0.2)	0.81 (0.03)
7	455.0	426.7	484.7	13.4 (0.8)	0.94 (0.07)
8	460.0	438.4	483.8	19.0 (1.2)	1.10 (0.08)
9	455.7				
10	462.7				

[a] In CH_2Cl_2/CD_2Cl_2 (90:10) (0.11 M). [b] At 300 K. [c] At 180 K. [d] ^{77}Se chemical shifts are extremely sensitive to temperature; for example, $\delta(^{77}Se)$ for **9** at 180 K is 436.4 ppm. Consequently, evaluation of K using the average chemical shift method is unreliable.

Table II. ^{1}H NMR Chemical Shift Data and Equilibrium Data for 1–8 at 143 K[a]

compd	chemical shift H-2	H-4a,6a	H-4e,6e	$K_{E\rightarrow A}$ (error)	$-\Delta G°_{143K}$ (error) (kcal mol^{-1})
1a	5.10	3.46	2.59	5.8 (0.3)	0.50 (0.03)
1e	4.85	3.02	2.71		
2a	5.17	3.43	2.60	9.2 (0.2)	0.63 (0.02)
2e	4.90	3.02	2.72		
3a	5.26	3.44	2.60	9.5 (0.1)	0.64 (0.03)
3e	4.94	3.02	2.73		
4a	5.32	3.44	2.60	13.9 (0.1)	0.73 (0.02)
4e	4.97	3.01	2.73		
5a	5.23	3.41	2.61	13.0 (0.3)	0.75 (0.01)
5e	4.94	3.01	2.73		
6a	5.28	3.39	2.60	14.1 (0.1)	0.76 (0.01)
6e	4.96	3.02	2.71		
7a	5.46	3.39	2.62	21.0 (0.7)	0.87 (0.04)
7e	5.07	3.03	2.76		
8a	5.61	3.35	2.62	30.7 (1.2)	0.98 (0.05)
8e	5.22	3.09	2.80		

[a] In $CFCl_3:CD_2Cl_2$ (85:15).

Table III. Equilibrium Data[a] **at 270 K**

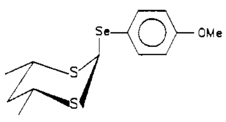
compd	$K_{E\rightarrow A}$	$-\Delta G°_{270K}$ (kcal mol^{-1})
1	2.4	0.47
2	3.0	0.59
3	2.7	0.53
4	2.9	0.57
5	3.3	0.64
6	3.6	0.69
7	4.0	0.74
8	5.3	0.90

[a] Estimated from the ^{13}C NMR spectra of the conformationally averaged systems in $CFCl_3:CD_2Cl_2$ (80:20) by use of the Eliel equation ($K = \delta_E - \delta_{avg}/\delta_{avg} - \delta_A$)[24] and the C-4,6 signals (see text).

(2) the appearance of the H-2 signals as broad singlets (avg $w_{1/2}$ = 2.8 Hz), and (3) the presence of significant long-range $^4J_{2,4e}$ and $^5J_{2,5e}$ couplings (avg 1.0 Hz). These data are consistent only with the preponderance of a conformation in which the arylseleno moiety adopts an axial orientation.[6e] The assignment was corroborated,[6e] for selected compounds, by comparison of the ^{1}H NMR data with those of the anancomeric derivatives, namely, the 2-substituted-4,6-dimethyl-1,3-dithianes, for example **9** and **10**.

Conformational Analysis. Quantitation of the anomeric effect in **1–8** was initially effected by direct examination of the conformational equilibrium by means of low-temperature ^{77}Se NMR spectroscopy. ^{77}Se has a spin of $^1/_2$, a natural abundance of 7.58%, and a receptivity relative to ^{13}C of 2.98.[10] Nuclear Overhauser enhancement is relatively insignificant.[10] The large chemical-shift range of ^{77}Se (≈2000 ppm for organic compounds[10]) and its extreme sensitivity to chemical environment[21] suggested that chemical-shift differences for signals of different conformers might also be relatively large, resulting in higher temperatures of coalescence, and thus permitting observation of individual conformer resonances in the readily accessible temperature range. 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] Measurement of T_1 values of conformationally averaged **1** at 300 K in toluene by the saturation–recovery method revealed a T_1 value of 2.2 s. Interestingly, the T_1 values for both conformers at 180 K were found to be identical (0.64 s) and pose no serious problem in the acquisition of spectra or in obtaining reliable relative intensities. The temperature dependence of the T_1's is inconsistent with a dominance of the spin-rotation mechanism of spin–lattice relaxation most often observed with small molecules.[22] Furthermore, since Se–H distances are relatively long, the dipole–dipole relaxation mechanism (with its inverse 6th-power distance dependence) is probably inefficient, leaving chemical-shift anisotropy as the dominant relaxation mechanism in this class of compounds.

The ^{77}Se NMR spectra of **1–8** in methylene chloride at 180 K showed a major and minor resonance, with the major resonance at higher field, and chemical-shift differences ranging from 45 to 82 ppm (see Table I). The major resonance was assigned to the axial conformer and the minor resonance to the equatorial conformer by comparison of the ^{77}Se NMR data to those of **9** and **10**. In



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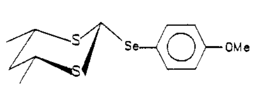

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particular, the selenium atom in the axial isomer **9** is shielded with respect to that in the equatorial isomer **10**, a trend that is also observed[23] with axial and equatorial 2-(phenylseleno)cyclohexane. The equilibrium constants, K, were derived by direct integration of the peaks. The values listed in Table I represent mean values obtained from several spectra as well as from several integrations of each spectrum. The errors in K are the standard deviations of the measurements. The errors in $\Delta G°$ derive from the errors in K and the error in the temperature, T.

Quantitation of the conformational equilibria was also effected by means of ^{1}H NMR spectroscopy. The ^{1}H NMR chemical-shift data for **1–8** in $CFCl_3/CD_2Cl_2$ (85:15) at 143 K that were used for analysis, and the equilibrium data are presented in Table II. The errors in $\Delta G°$ values were derived as already described.

For estimation of the effects of substitution on the equilibria at higher temperatures, an approximate method of analysis was used. Thus, the ^{13}C NMR spectra of the conformationally averaged systems in $CFCl_3/CD_2Cl_2$ (80:20) at 270 K were evaluated by use of the Eliel equation[24] and the C-4,6 signals. The corresponding signals in

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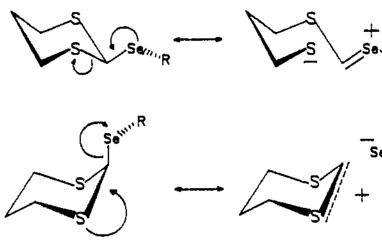

Figure 2. Valence bond representations of the exo (top) and endo (bottom) anomeric effect in 1–8.

Table IV. Solvent Dependence of the Conformational Equilibria[a] for 1–3 at 180 K

	$-\Delta G°$ (error) (kcal mol^{-1})		
compd	toluene[b]	methylene chloride[b]	acetone[b]
1	0.64 (0.03)	0.48 (0.02)	0.66 (0.02)
2	0.82 (0.02)	0.61 (0.02)	0.75 (0.02)
3	0.86 (0.03)	0.65 (0.03)	0.80 (0.02)

[a] From direct integration of the individual conformer resonances in the ^{77}Se NMR spectra. [b] 90:10 mixtures of non-deuteriated: deuteriated solvent.

the spectra at 154 K (Table S-V) were used as reference values after correction for temperature effects. This correction was derived from the temperature dependence of the C-4,6 shift in the spectrum of 1,3-dithiane (δ 29.6 at 154 K and δ 30.9 at 270 K). The equilibrium data are listed in Table III.

Finally, the solvent dependence of the conformational equilibria for selected derivatives **1**, **2**, and **3** was investigated by means of ^{77}Se NMR spectroscopy at 180 K. The conformational free energies in toluene, methylene chloride, and acetone are listed in Table IV. Extension of these studies to other suitable solvents was frustrated by problems of solubility.

Discussion

Substituent Effects. The data presented in Table I indicate conformational free energies ranging from −0.48 to −1.10 kcal mol^{-1} at 180 K as a function of substituent, and Table II indicates substituent effects of similar magnitudes at 143 K. The trend in equilibrium constant data within the series of compounds is apparent: *as the electron demand of the substituent increases, so does the proportion of the axial conformer.* This behavior can be rationalized in terms of the orbital-interaction model presented earlier. The relevant interactions are the $n_S \rightarrow \sigma^*_{C\text{-}Se}$ interaction associated with the endo anomeric effect and the $n_{Se} \rightarrow \sigma^*_{C\text{-}S}$ interaction associated with the exo anomeric effect. The valence-bond representations are illustrated in Figure 2. Whereas both these interactions may be expressed in the axial conformer, symmetry considerations dictate that only the exo anomeric effect may be expressed in the equatorial conformer. Since the magnitude of both these interactions is proportional to the square of the overlap between interacting orbitals and inversely proportional to their energy difference, ΔE,[25] and the primary overlap remains the same throughout the series of compounds, it follows that arguments based on differences in ΔE values can be formulated.

In general, increasing the electronegativity of a substituent atom within a related series of compounds results in a lowering of the molecular orbitals associated with that atom.[25,26] It follows that the $n_S \rightarrow \sigma^*_{C\text{-}Se}$ (endo) orbital interaction would be more mportant and the $n_{Se} \rightarrow \sigma^*_{C\text{-}S}$ (exo) interaction less important in **8** than in **1**. Since the magnitude of the anomeric effect reflects a competition between the endo and exo anomeric effects,[27] the foregoing arguments dictate that the relative stabilities of the axial conformer in the series of 2-(arylseleno)-1,3-dithianes should increase as electron withdrawal by the substituent increases.[28] An alternate argument suggests that, since the $n_{Se} \rightarrow \sigma^*_{C\text{-}S}$ interactions (the exo anomeric effect) can be expressed in both coformers and the *sensitivity* of this interaction to the substituent should be of approximately similar magnitude in both conformers,[28] one can focus only on the unique orbital interaction ($n_S \rightarrow \sigma^*_{C\text{-}Se}$) in the axial conformer. Such interaction should increase the negative charge on the Se atom.[30]

Since conformational entropy differences can be significant,[31] it was also of interest to examine the temperature dependence of the conformational equilibria and the effects of substitution at higher temperature. The data in Table III indicate similar magnitudes and a similar range of conformational free energies as a function of substituent at 270 K as observed at 143 K (Table II). Since the former data were obtained by an approximate method of analysis, it is difficult to extract rigorous conclusions. Nevertheless, it is evident that significant substituent effects do exist both at low and high temperatures. Furthermore, since $\ln (K_X/K_Y)_{T1}/\ln (K_X/K_Y)_{T2} = [(\Delta H°_X - \Delta H°_Y)/R][1/T_2 - 1/T_1]$ it is also clear from the data in Tables I, II, and III that $\Delta\Delta H° \neq 0$. The result is of significance since, as indicated recently by Booth et al.,[27b] it is the conformational *enthalpy* differences which are most easily correlated with electronic effects operating in these types of systems.

Previous attempts at substituent effect studies in analogous systems containing oxygen have not yielded effects which are as pronounced as those obtained in the present study. Thus, Ouedraogo and Lessard,[32] in their investigation of the conformational equilibria of 2-(4-substituted-phenoxy)tetrahydropyrans, have measured $\Delta G°_{E\rightarrow A\,156K}$ values ranging from −0.7 (4-NO$_2$) to −0.4 (4-OMe) kcal mol^{-1} in CF$_2$Br$_2$ solvent and −0.5 (4-NO$_2$) to −0.3 (4-OMe) kcal mol^{-1} in CHFCl$_2$ solvent. Similarly, Pericas et al.[33] have reported no significant electronic effect of the substituent on the conformational equilibria of *trans*-2,3-bis(4-substituted-phenoxy)-1,4-dioxanes, although this conclusion was based on estimation of highly biased equilibria by an approximate method of analysis. It is noteworthy, however, the Cantacuzene and Tordeux[34] have observed $-\Delta G°_{E\rightarrow A\,298K}$ values for the conformational equilibria of 2-(4-substituted-phenoxy)cyclohexanones ranging from 0.93 (4-NO$_2$) to −0.10 (4-NEt$_2$) kcal mol^{-1} in CCl$_4$ solvent.

Mechanism of Transmission of the Electronic Effects. (a) Dual Substituent Parameter Analysis. The equilibrium data in Tables I and II were analyzed by

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[26] Pross, A.; Radom, L.; Taft, R. W. *J. Org. Chem.* **1980**, *45*, 818.

[27] (a) Praly, J.-P.; Lemieux, R. U. *Can. J. Chem.* **1987**, *65*, 213. (b) Booth, H.; Khedhair, K. A.; Readshaw, S. A. *Tetrahedron* **1987**, *43*, 4699.

[28] It is recognized that the exo anomeric effect differs in magnitude in the axial vs equatorial conformers.[27a,29]

[29] Thogersen, H.; Lemieux, R. U.; Bock, K.; Meyer, B. *Can. J. Chem.* **1982**, *60*, 44.

[30] Lehn, J.-M.; Wipff, G.; Demuynck, J. *Helv. Chim. Acta* **1977**, *60*, 1239.

[31] For example: ref 27b.

[32] Ouedraogo, A. Ph.D. Thesis, Université de Sherbrooke, Québec, Canada, 1984: Ouedraogo, A.; Lessard, J. manuscript in preparation.

[33] Pericas, M. A.; Riera, A.; Giralt, E. *Tetrahedron* **1985**, *41*, 3785.

[34] Cantacuzene, D.; Tordeux, M. *Can. J. Chem.* **1976**, *54*, 2759.

means of a dual substituent parameter approach[35] using algorithms from Draper and Smith.[36] A two-parameter model was judged to be significant by means of an f-test.[36] Of the resonance substituent constants, σ^-_R, σ^0_R, σ^{BA}_R, and σ^+_R, best correlation was obtained with σ^0_R, as judged by the lowest sum of squares of the residuals and the best percent variation explained by the model. The probability that the result is random with σ^0_R was zero. Thus, correlations of the type $\log (K_X/K_H) = \rho_I\sigma_I + \rho^0_R\sigma^0_R$ gave, for the equilibrium data in Table I, $\rho_I = 0.52 \pm 0.02$; $\rho^0_R = 0.57 \pm 0.02$, and for the equilibrium data in Table II, $\rho_I = 0.52 \pm 0.02$; $\rho^0_R = 0.58 \pm 0.02$, that is a slightly greater sensitivity of the equilibria to resonance effects than polar effects exerted by the substituent. The positive ρ values are consistent with a mechanism involving greater negative charge on the Se atom resulting from a dominance of $n_S \rightarrow \sigma^*_{C-Se}$ orbital interactions in the axial conformation or, alternatively, a greater positive charge on the Se atom in the equatorial conformer owing to greater $n_{Se} \rightarrow \sigma^*_{C-S}$ interactions. The results auger well for the existence of charge-transfer interactions associated with the endo and exo anomeric effect.

(b) Low-Temperature ^{13}C NMR Chemical-Shift Data. The presence of increased negative charge on the Se atom in the axial conformer is also substantiated by the trends in ^{13}C NMR data for the aromatic carbons (Table S-V).[37,39] The observed chemical-shift differences for a particular carbon between the two conformers, $\Delta\delta_{C_a-C_e}$ are 7.7 to 5.2 ppm for C_{ipso}, −1.0 to −1.6 for C_{ortho}, 0.1 to 0.2 for C_{meta}, and −0.4 to −1.0 for C_{para}. The deshielding of C_{ipso} in the axial conformer is attributable to the polarization of the phenyl ring which reduces π-electron density at that carbon[40] whereas the shielding of C_{ortho} and C_{para} in the axial conformer is consistent with π-resonance effects, leading to increased π-electron density at these carbons. The data correlate with previous data on phenylamines, -phosphines, and -arsines and their anions,[41] as well as phenol, thiophenol, and toluene and their anions.[42] Furthermore, the trends are consistent with π-electron populations, calculated by ab initio MO methods, for phenol vs phenoxide ion and aniline vs aniline anion.[43]

(c) Low-Temperature ^{77}Se NMR Chemical-Shift Data. Further evidence for increased negative charge on the Se atom in the axial conformers is provided by the trends in ^{77}Se NMR data (Table I). Whereas the ^{77}Se shifts for the equatorial conformers span a range of only 9 ppm, those for the axial conformers span a range of 41 ppm. The more pronounced differences in the latter case are consistent with greater negative charge on Se since Lewis et al.[44] have demonstrated that ^{77}Se NMR chemical shifts of phenylselenide anions are more sensitive to the effect of substituents ($\Delta\delta$ = 112 ppm for 4-CF_3 vs 4-OMe) than the corresponding methyl phenyl selenides ($\Delta\delta$ = 24 ppm).

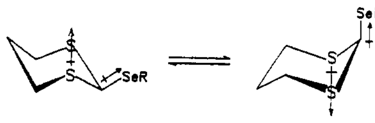

Figure 3. Proposed dipolar interactions in the axial and equatorial conformers of 1–8.

The results presented in the preceding sections constitute, therefore, systematic experimental evidence for stabilizing orbital interactions operating in S–C–Se fragments.

Anet and Kopelevich[7] have recently proposed that π-donation by sulfur may not be responsible for the axial orientation of C-2 substituents such as SePh in 1,3-dithianes. The proposal is based on the absence of a conformational deuterium isotope effect in 2-deuterio-5,5-dimethyl-1,3-dithiane (**11**), which suggests that $n_S \rightarrow \sigma^*_{C-H(D)}$ hyperconjugative interactions are not important. We attribute the latter result to a decrease in overlap between the fragment orbitals, relative to the corresponding oxygen analogues, as a result of the longer C–S bonds.[45] Since the magnitude of the stabilizing orbital interaction is proportional to the square of the overlap between interacting orbitals and inversely proportional to their energy difference,[25] it is possible that the $n_S \rightarrow \sigma^*_{C-H(D)}$ interaction in **11** is "overlap-dominant" and the $n_S \rightarrow \sigma^*_{C-Se}$ interaction in the 2-(arylseleno)-1,3-dithianes **1–8** is "energy-gap dominant", the σ^*_{C-Se} orbital being of lower energy than the $\sigma^*_{C-H(D)}$ orbital.

Solvent Effects. An explanation for the anomeric effect based on minimization of dipolar repulsion has been advanced.[2a] The proposed dipolar interactions of possible consequence in the present systems are shown in Figure 3. The interaction derives from the ring dipole of the 1,3-dithiane ring[46] coupled with the dipole associated with the C–Se bond. Since carbon and selenium have similar electronegativities,[47] one might not have expected a significant C–Se dipole. However, dipole moment measurements of **9** and **10** indicate values of 2.1 and 3.2 D, respectively.[48] In order to evaluate the relative importance of electrostatic effects on the conformational equilibria of **1**–**8**, the solvent effects on the equilibria at low temperature were investigated for selected compounds (Table IV). Increasing the polarity of the solvent is predicted[49] to minimize dipolar interactions and to maximize the proportion of the more polar compound, i.e., the equatorial conformer. Whereas the data in toluene (ϵ = 2.4)[50] as compared to those in methylene chloride (ϵ = 8.9)[50] are in accord with the postulate of significant dipolar interactions, those in acetone (ϵ = 20.5)[50] are not. Juaristi et al.[4c] have observed a similar increase in the proportion of the less polar axial conformer of 2-carbomethoxy-1,3-dithiane with

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(39) It is of interest that Juaristi et al.[4c] have observed apparent chemical shift degeneracy for the aromatic carbons in the axial and equatorial conformers of 2-(phenylthio)-1,3-dithiane in spite of a substantial anomeric effect. This contrasts with the present work and also with previous work[4b] by the same group on 2-(diphenylphosphinoyl)-1,3-dithianes.

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increasing solvent polarity at low temperature and have suggested an explanation based on a solvent compression effect[51] to explain this anomaly. According to this proposal,[51] the population of the conformer with the smaller molar volume (the axial conformer) should increase with the more polar solvent owing to higher internal pressure exerted by the solvent. An alternate explanation advanced by Fuchs et al.[52] suggests that when the molecular dipoles of the axial and equatorial conformers are of similar magnitudes, the more polar double-bond no-bond structure,[53] resulting from hyperconjugative interactions in the axial conformer, will be stabilized in the more polar solvent.

Regardless of the exact explanation for the anomalous solvent dependence of the equilibria of **1**–**8**, it is clear from the data in Table IV that similar substituent effects are observed in nonpolar and polar solvents. If dipolar interactions were important, then a marked substituent effect on $\Delta G°$ would not be observed in a polar solvent. The data suggest, therefore, that dipole/dipole interactions do not have a dominating influence. In fact, the appearance of a large proportion of the axial conformers even in a polar medium suggests that other electronic factors are important. It is noteworthy that Cantacuzene and Tordeux[34] have observed no substituent effect on the conformational equilibria of 2-(4-substituted-phenoxy)cyclohexanones in the polar solvent CD_3CN and Ouedraogo and Lessard[32] have noted a lesser sensitivity of the conformational equilibria in 2-(4-substituted-phenoxy)tetrahydropyrans to the effect of the substituent in a polar medium.

The solvent and *temperature* dependence of the equilibria in 2-(arylseleno)-1,3-dithianes is being studied in greater detail in order to evaluate the enthalpic and entropic contributions to the conformational free energies, and the results will be reported in a separate study.

Conclusions

Conformational analysis of 2-[(4-substituted-phenyl)seleno]-1,3-dithianes in solution by means of ^1H and ^{77}Se NMR spectroscopy indicates that the magnitude of the anomeric effect varies with substituent in the order $NO_2 > CF_3 > Cl > F \approx H > Me > OMe > NMe_2$, providing systematic evidence for the role of stabilizing orbital interactions operating in S–C–Se fragments. The postulate is reinforced by analysis of the data by means of a dual substituent parameter approach which suggests that increased electron density is present on selenium in the axial conformers. The latter conclusion is also substantiated by trends in ^{13}C NMR and ^{77}Se NMR shifts for the axial and equatorial conformers. The solvent dependence of the conformational equilibria for selected compounds shows no apparent correlation with dielectric constant although significant anomeric effects and substituent effects are still observed in a polar medium. The results are interpreted in terms of the dominance of the orbital interaction component over the electrostatic component.

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Supplementary Material Available: Tables S-I, S-II, S-III, S-IV, and S-V (8 pages). Ordering information is given on any current masthead page.

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Selective Syntheses of Mono- and Bis(2-fluoro-2,2-dinitroethoxy)alkanes: Scope of the Utility of Triflate Intermediates[1]

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While displacement of bromide in 1-bromo-2-(2-fluoro-2,2-dinitroethoxy)propane (**1**) cannot be effected by silver trifluoromethanesulfonate because of the electronegative vicinal alkoxide's deactivating inductive effect on the primary bromine, substituents in the secondary position are more labile with respect to nucleophilic displacement. The scope of the utility for conducting nucleophilic substituents using homologous α,ψ-dibromoalkanes [1,(n − 1)-dibromoalkanes] and a vicinal dibromoalkane, 2,3-dibromoalkane, is reported. This approach produced a variety of new fluorodinitroethyl ethers (**3**–**9**), including the novel 2,3-bis(2-fluoro-2,2-dinitroethoxy)butane (**3**)—which possesses two electronegative alkoxy substituents in a vicinal arrangement—from the fortuitous intermediate 2-bromo-1-(2-fluoro-2,2-dinitroethoxy)propane (**2**) by way of anchimeric assistance in the reaction of 1,2-dibromopropane, also yielding **1**, the regioisomer of **2**. Typically, α,ψ- and α,ω-dibromoalkanes are distinctly stepwise in their two possible S_N1Ag^+ displacements of bromide by silver triflate, a characteristic which allows selective incorporation of relatively nonnucleophilic alkoxy substituents via displacements of triflate intermediates.

Trifluoromethanesulfonate esters have come to be recognized as especially useful intermediates for effecting functionalizations of certain organic substrates,[3] even for allowing classical nucleophilic substitutions by notoriously nonnucleophilic species such as polynitroaliphatic alcohols.[4] In a previous report,[5] we showed that α,ω-dibromoalkanes can be readily converted to corresponding ω-bromoalkyl triflates or α,ω-alkanediyl ditriflates with silver triflate salt under appropriate conditions; the me-

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