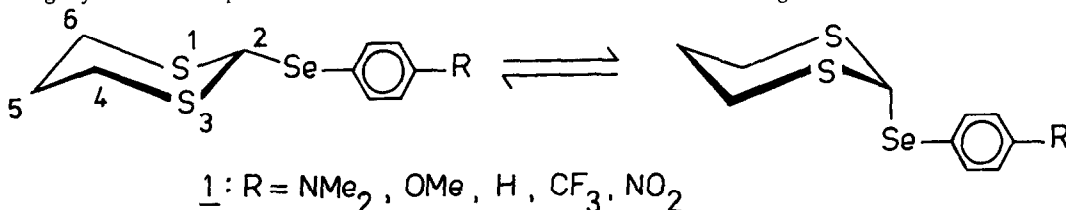


THE ANOMERIC EFFECT IN 2-ARYLSELENO-1,3-DITHIANES¹

B. Mario Pinto*, Jesus Sandoval-Ramirez and R. Dev Sharma
 Department of Chemistry, Simon Fraser University,
 Burnaby, British Columbia, CANADA V5A 1S6

Abstract: The anomeric effect in a series of 2-(4-substituted-phenylseleno)-1,3-dithianes (substituents, R = NO₂, CF₃, H, OMe, NMe₂) decreases in the sequence NO₂ > CF₃ > H > OMe > NMe₂, providing systematic experimental evidence for the role of stabilizing orbital interactions.



The anomeric effect² has been the subject of much investigation in recent years.

Although several explanations have been advanced to account for this conformational effect, that formulated within the framework of perturbational molecular orbital theory has been widely accepted³. According to this proposal, favoured conformations of X-C-Y fragments are those which permit the expression of stabilizing orbital interactions between the p-type orbitals on X and Y, η_X and η_Y , with the vacant σ_{C-Y}^* and σ_{C-X}^* orbitals, respectively. Such hyperconjugative interactions have been substantiated by theoretical investigations^{3,4}. However, apart from crystallographic evidence⁵, there has been little⁶ experimental support for the role of orbital interactions in dictating the conformational preferences in X-C-Y fragments.

As part of a program designed to investigate the nature and origin of conformational effects, we have recently reported⁷ the axial conformational preference of the arylseleno moiety in two 2-arylseleno-1,3-dithianes, both in solution and in the solid state. In order to assess the relative importance of orbital-interaction effects in S-C-Se fragments, we now report the quantitation of the anomeric effect in these and related compounds (1: R = NMe₂, OMe, H, CF₃, NO₂).

Careful analysis of the ¹H nmr spectra (400 MHz) of the conformationally-averaged systems, measured in CDCl₃ at ambient temperature, revealed 1) significant chemical-shift differences for the H-4,6 axial and equatorial proton signals, $\Delta\delta_{ax/eq}$, (avg. 0.55 ppm), 2) the appearance of the H-2 signals as broad singlets (avg. $W_{1/2} = 2.7$ Hz) and 3) the presence of significant long-range ⁴J_{2,4e} and ⁵J_{2,5e} couplings (avg. 1 Hz). These data are consistent only with the preponderance of a conformation in which the arylseleno moiety adopts an axial orientation⁷⁻⁹.

In order to quantitate this conformational effect, we chose to directly examine 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 2.98¹⁰. The large chemical-shift range (≈ 2000 ppm for organic compounds¹⁰) suggested to us that chemical-shift differences for signals of different conformers might also be relatively large, resulting in higher temperatures of coalescence, and thus permitting observations of the individual resonances in the readily accessible temperature range. Indeed, the ^{77}Se nmr spectra of the 2-arylseleno-1,3-dithianes in CD_2Cl_2 at 180.5 K showed a major and minor resonance, assigned¹¹ to the axial and equatorial conformers, respectively, with chemical-shift differences ranging from 45-82 ppm (See Table 1). The equilibrium constants were derived by direct integration of the peaks for the axial and equatorial isomers. The values listed in Table 1 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 ΔG^0 values derive from the errors in K and the error in the temperature, T.

Table 1. ^{77}Se nmr chemical-shift data^a and equilibrium data for 2-arylseleno-1,3-dithianes

Substituent	Chemical Shift		K (error)	$-\Delta G^0_{180.5 \text{ K}}$ (error) k cal-mol ⁻¹
	δ major	δ minor		
NMe ₂ (<u>1a</u>)	397.0	479.1	3.8 (0.1)	0.48 (0.02)
OMe (<u>1b</u>)	403.9	477.5	5.4 (0.1)	0.61 (0.02)
H (<u>1c</u>)	421.5	486.8	7.6 (0.2)	0.73 (0.03)
CF ₃ (<u>1d</u>)	426.7	484.7	13.4 (0.8)	0.94 (0.07)
NO ₂ (<u>1e</u>)	438.4	483.8	19.0 (1.2)	1.10 (0.08)

^a In CD_2Cl_2 (0.11 M), relative to Me_2Se in CD_2Cl_2 at 180.5 K.

Conformational free energies ranging from -0.48 to -1.10 kcal-mol⁻¹ are obtained. The trend in equilibrium constant data within the series of compounds is apparent: **as the electron demand of the substituent increases, the proportion of the axial conformer also increases.** This behaviour can be rationalized in terms of the orbital-interaction model presented earlier. Consider first the effect of increasing electron demand of the substituent on the $\sigma_{\text{C-Se}}^*$ orbital energy. In general, increasing electronegativity of a substituent atom leads to a lowering of the energies of molecular orbitals associated with that atom¹². Thus, the $\sigma_{\text{C-Se}}^*$ orbital will be of lower energy in the p-nitro derivative than in the corresponding p-dimethylamino compound. Since the magnitude of the orbital interaction is proportional to the square of the overlap and inversely proportional to the energy difference between interacting orbitals¹³ and the primary overlap remains the same for the series of compounds, it follows that the $\eta_{\text{S}}-\sigma_{\text{C-Se}}^*$ orbital interaction would be more important in the former compound. Consequently, the relative stabilities of the axial conformer (in which the $\eta_{\text{S}}-\sigma_{\text{C-Se}}^*$ interaction is expressed) in the series of 2-arylseleno-1,3-dithianes should decrease in the sequence $\text{NO}_2 > \text{CF}_3 > \text{H} > \text{OMe} > \text{NMe}_2$. Alternatively, consideration of the effects of substitution on the orbital interactions associated with the exo-anomeric effect¹⁴, namely the $\eta_{\text{Se}}-\sigma_{\text{C-S}}^*$ interactions, suggests that increasing electron withdrawal would lead to a

progressive lowering of the η_{Se} orbital energy and a less important $\eta_{\text{Se}}-\sigma_{\text{C-S}}^*$ interaction. However, since the latter interaction can be expressed in both conformers and the sensitivity of this interaction to the substituent effect should be of approximately similar magnitude in both conformers, one can focus only on the unique orbital interaction ($\eta_{\text{S}}-\sigma_{\text{C-Se}}^*$) in the axial conformation. The data presented herein constitute, therefore, systematic experimental evidence for the role of stabilizing orbital interactions in the anomeric effect.

As a final point of interest, we comment on the magnitudes of the anomeric effect in the 2-arylseleno-1,3-dithianes la-le. Since the A value for phenylseleno cyclohexane is reported¹⁵ to be $1.1 \text{ kcal}\cdot\text{mol}^{-1}$ and the conformational free energy of methyl in 2-methyl-1,3-dithiane is of approximately the same magnitude as that in methylcyclohexane (1.7 ¹⁶ vs. 1.74 ¹⁷ $\text{kcal}\cdot\text{mol}^{-1}$), one may estimate anomeric effects of 1.6, 1.7, 1.8, 2.0 and 2.2 $\text{kcal}\cdot\text{mol}^{-1}$ in la, lb, lc, ld and le, respectively.

Experimental

The 2-arylseleno-1,3-dithianes la-ld were synthesized by reaction of 2-chloro-1,3-dithiane with the corresponding sodium arylselenolates⁷. le was prepared by reaction of 2-lithio-1,3-dithiane with 4-nitrophenyl selenocyanate. All compounds were crystalline and gave satisfactory elemental analysis and spectroscopic data.

⁷⁷Se nmr spectra were measured at 76.3 MHz on a Brüker WM 400 spectrometer. Since ⁷⁷Se nuclei can have long relaxation times¹⁰, only 9° pulses were used with a repetition rate of 0.7 s¹⁸. The spectra were obtained without ¹H decoupling since nOe effects are negligible in these derivatives¹⁰. 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 ¹H decoupler coil for observation of the ¹H nmr signals. The peak separations were converted into temperature values using the quadratic equation²⁰ of Van Geet, scaled to 400 MHz²¹. Temperatures are believed to be accurate to ± 2 K.

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