Enthalpic and Entropic Contributions to the B-C-P(O) Anomeric Effect.¹

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<u>Abstract</u>. The conformational bahavior of the 2-(diphenylphosphinoyl)-1,3-dithiane was studied in the 258-323 K temperature range. Plots of ln K versus 1/T are linear, permitting evaluation of the enthalpic and entropic contributions of the S-C-P(O) anomeric effect. Comparison with the corresponding thermodynamic data in the cyclohexyl analogue allows estimation of the enthalpic anomeric effect in this system: ca. 3.4 kcal/mol.

Introduction.

1-ax

Several years ago the discovery of an important anomeric interaction in 2-(diphenylphosphinoyl)-1,3-dithiane (1, eq 1) was reported.² Incorporation of the coupling constants of H(2) to phosphorus in 1 and in appropriate anancomeric models into Eliel's equation³ allowed quantitative determination of the conformational free energy in 1, $\Delta G_{39}^{2} \cdot c = + 1.0$ kcal/mol in solvent chloroform.²



By constrast, the conformational energy value for the diphenylphosphinoyl substituent in cyclohexane is a substantial $\Delta G^{\circ}[P(0)(C_{6}H_{5})_{2}] = -2.74$ kcal/mol at ambient temperature in solvent chloroform (eq.2).⁴

1-eq

Consideration of the relative size of the diphenylphosphinoyl group in 1,3-dithiane and in cyclohexane (60% in the former)⁵



permitted evaluation of the anomeric effect in $1: 1.0 + (0.60 \times 2.74) = 2.64 \text{ kcal/mol.}^{6}$

In this respect, however, Booth, et al.⁷ have stressed that in studies of the anomeric effect it is the ΔH° values (rather than the $T\Delta S^\circ$ dependent ΔG° values) that correlate with the steric, polar and stereoelectronic interactions of interest. We therefore deemed it necessary to evaluate the enthalpic and entropic contributions to the anomeric interactions involved in <u>1</u>.

Results and Discussion.

2-(Diphenylphosphinoyl)-1,3-dithiane ($\underline{1}$) and its conformationally fixed models ($\underline{3}$ and $\underline{4}$) were prepared according to the procedure of Juaristi, et al.^{2,8}



As previously reported,² comparison of the proton NMR of 3 and 4 with that of 1 (all three in CDCl₃) revealed a most interesting variation in the coupling constants of H(2) to phosphorus: 4.2, 15.0 and 6 Hz, respectively. While ${}^{2}J_{H(2)/P}$ for the anancomeric models remains unchanged at various temperatures, that for the mobile compound (1) shows a systematic change (table I). On the assumption that ${}^{2}J_{H(2)/P}$ in the mobile dithiane is the weighted average of those for the model diastereomers 3 and 4,⁹ then $K = (J_{eq} - J)/(J - J_{ax})$, which yields the free energy differences at the temperatures of measurement.

This temperature-dependent behavior clearly reflects a substantial entropy effect. Indeed, a plot of ln K versus 1/T was linear (r=0.978) and allowed for the derivation of ΔH° and ΔS° .¹⁰ The resulting values are ΔH° = +2.21 ± 0.17 kcal/mol, and ΔS° = +4.27 ± 0.59 cal/K mol (eq 1).

Temperature (K)	² J _{H(2)/P}	K	$\Delta G^{O}(\text{kcal/mol})$	
323	6.60	0.29	0,80	
300	5.94	0.19	0.98	
273	5.71	0.16	0,99	
258	5,28	0.11	1.33	

Table I. Temperature-dependent Variation in the Coupling Constant of H(2) to Phosphorus in 1, and Estimated Free Energy Differences (Eq 1)

By comparison, $\Delta H^{\circ}(POPh_2)$ in cyclohexane is -1.96 kcal/mol, and ΔS° = + 2.6 cal/K mol (eq 2).⁴ Therefore, the present results confirm the existence of a large *enthalpic* S-C-P(O) anomeric effect in <u>1</u>: 2.21 + (0.6 x 1.96)= 3.39 kcal/mol. In fact, this favorable enthalpy term overcomes the entropic contribution, the equatorial conformer being of higher entropy.¹¹

Essentially identical ΔH° and ΔS° values for equilibrium <u>3</u>-ax \pm <u>4</u>-eq were derived from a ln K versus 1/T plot (r=0.964) obtained by chemical equilibration (EtO⁻Na⁺/EtOH) of these diastereomers at various temperatures (Table II). The equilibrium data were derived by direct integration of the ³¹P NMR signals after equilibration from both sides. The resulting values are $\Delta H^{\circ} = +2.29 \pm 0.26$ kcal/mol, and $\Delta S^{\circ} = +4.59 \pm 0.9$ cal/K mol.

Temperature (K)	$K(\frac{4}{3})$	$\Delta G^{\circ}(\text{kcal/mol})$
323	0.31	0.75
313	0.26	0.84
303	0.22	0.91
298	0.19	0.98
283	0.17	1,00
273	0.16	0,99

Table II. Chemical Equilibration of Anancomeric <u>3</u> and <u>4</u> with Ethanolic Sodium Ethoxide at Various Temperatures (Eq 3).

The similarity of the thermodynamic data obtained in ethanol and chloroform is striking, but is in agreement with previous observations,² which suggested that less polar media do not necessarily give rise to a stronger S-C-P(0) anomeric effect. In summary, evaluation of the conformational behavior of 2-(diphenylphosphinoyl)-1,3-dithiane (1) at various temperatures permitted evaluation of the enthalpic and entropic contributions to ΔG° . Comparison with the corresponding $\Delta H^{\circ}(\text{POPh}_2)$ and $\Delta S^{\circ}(\text{POPh}_2)$ in the cyclohexyl analogue allows estimation of the enthalpic anomeric effect in 1, worth ca. 3.4 kcal/mol. In contrast, the entropy term favors equatorial 1, so that this conformer is anticipated to predominate at temperature highers than 508 K.

<u>Acknowledgment</u>. We are grateful to G. Uribe for recording the FT NMR spectra, and to CONACYT (México) for partial financial support.

References and Notes.

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- (11) Observation of Dreiding models suggests that an axial diphenylphosphinoyl group is conformationally constrained to rotamers with the P=O bond above the cyclohexane ring, whereas an equatorial diphenylphosphinoyl substituent is apparently free to fully rotate around the C-P bond.

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