The Anomeric Effects of Aryloxy Groups

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Newly available A-values for aryloxy groups allow estimates of their anomeric effects to be made; their sensitivity to electronic effects is reported.

Ouedraogo and Lessard[1] recently measured conformational equilibria for a series of 2-(4-substituted-phenoxy)tetra-hydropyrans 1, and showed that the axial preference of the OAr group (resulting from the anomeric effect) increases with increasing electron-withdrawal by the *para*-substituent. These data do not define the absolute magnitudes of the anomeric effect[2] for these groups, because their steric preference (A-value) has not, until now, been accurately known; and they define the relative magnitudes only if A-values are constant across the series. We have measured A-values for a series of aryloxy groups,[3] and shown that they do in fact include an electronic component. We report here the corrected anomeric effect for PhO, and an estimate of the electronic effects of substituents.
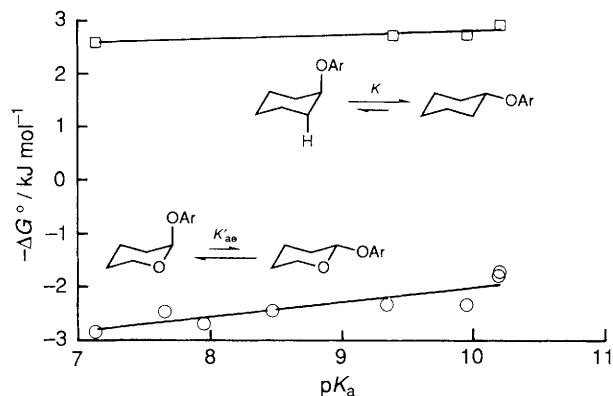

Fig. 1 Axial preferences of 2-aryloxytetrahydropyrans (data taken from Ouedraogo & Lessard[1]) compared with equatorial preferences (A-values) for the same groups in aryl cyclohexyl ethers§

The anomeric effect of an electronegative group is usually defined[2] as its preference for the axial configuration at the anomeric centre of pyranoses. In practice it is most often, and most accurately, measured, in 2-substituted tetrahydro-pyrans 1, and the magnitude of the effect is known[2] not to be very different in these simpler systems. A quantitative measure of the effect must take into account the steric preference of a group larger than H for the equatorial position. This is assumed to be of the same magnitude as in a substituted cyclohexane; an assumption which does not lead to serious inconsistency in most cases. The anomeric effect is thus defined as the sum of the free energy difference $-\Delta G°$ for the anomeric equilibrium and the A-value for the same substituent in cyclohexane.

Our A-values[3] for aryloxy groups, in four aryl cyclohexyl ethers 2, are compared† in Fig. 1 with the axial preferences reported by Ouedraogo and Lessard[1] for a more extensive series of 2-(4-substituted-phenoxy)tetrahydropyrans 1 in sol-

$$1 \qquad -\Delta G° = RT \ln K'_{ae}$$

$$2 \qquad A = RT \ln K$$
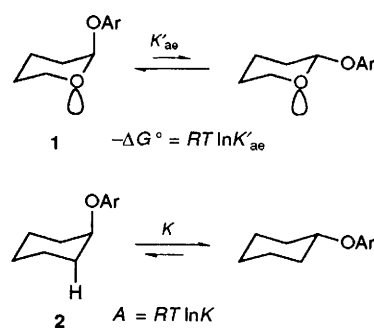
† As pointed out by a referee, it is not formally valid to compare directly A-values, which are temperature independent ($\Delta G° ≈ \Delta H°$), with the axial preferences reported by Ouedraogo and Lessard,[1] for which the temperature dependence has not been demonstrated. In practice it is likely that ring inversion involves only a very small entropy change, and that any resulting uncertainty is smaller than the experimental error in these not particularly precise measurements.

ution in CF_2Br_2 (containing 8% CD_2Cl_2) at 156 K.‡ The vertical distance between the two lines at the pK_a of a group gives its anomeric effect. The anomeric effect is thus expressed

as a function of the pK_a of the ArOH group by the difference between the equations§ for the two lines: anomeric effect/kJ $mol^{-1} = 7.1 \pm 0.8 - (0.22 \pm 0.08)\ pK_a$.

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‡ Our A-values were measured at 180 K (A-values show little sensitivity to temperature variation) in 9:1 $CFCl_3$:CD_2Cl_2, a non-hydrogen bonding solvent of similar polarity. Ouedraogo and Lessard[1] also report data in $CHFCl_2$ (containing 8% CD_2Cl_2), which show that axial preferences are smaller, as expected,[2] in this more polar, hydrogen-bonding solvent. The solvent dependence of the anomeric effect is not well-defined, but it seems clear that it is greater than that of A-values, which mostly show only small effects. (A predictable exception[4] is the OH group, which gives larger A-values in solvents that can form hydrogen bonds.)

References

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