Electronic Effects on Conformational Preferences: A-Values for Aryloxy Groups

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Conformational preferences (A-values) for aryloxycyclohexanes show a modest dependence on the *para*-substituent, as expected for a $\sigma_{C-H}-\sigma^*_{C-OX}$ interaction.

An important contributor to the anomeric effect[1] in tetra-hydropyranyl acetals **1** is the $n_O-\sigma^*_{C-OX}$ interaction between a non-bonded electron-pair on the ring oxygen and the anti-bonding orbital of the C–OX bond. This interaction is strongest when OX is axial, with the orbitals concerned antiperiplanar **1**, and stronger when X is more electronegative.

We needed the A-value[2,3] for PhO (not previously measured) for an accurate estimate of the anomeric effect of this group,[4] and report the necessary measurements. The anomeric effect of OAr (OX) groups is known[1] to increase with increasing electron-withdrawal from oxygen, as the $n_O-\sigma^*_{C-OX}$ interaction increases. It seemed likely that the axial conformation of an aryloxycyclohexane **2** would show a similar, though smaller, effect, based on the (weaker) $\sigma_{C-H}-\sigma^*_{C-OAr}$ interaction. So we have measured[+] conforma-
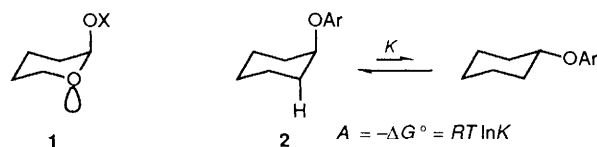
tional preferences for four cyclohexyl 4-substituted-phenyl ethers **2** (Ar = phenyl, *p*-methoxy-, *p*-chloro- and *p*-nitro-phenyl). Amounts of axial isomer fall in the range 11.1–15.5%. Results are summarised in Table 1.

As usual in all but the most careful measurements of this sort, $\Delta S°$ is poorly defined, because of the long extrapolation to $T = 0$, but is close to zero in each case. $\Delta G°$ is available with acceptable accuracy, and is given for 180 K, the midpoint of the temperature range investigated. The equatorial preference (A-value) for the phenoxy group, calculated from the full data set as the intercept of the Hammett plot (weighted least-squares analysis, $r = 0.96$) of $-\Delta G°$ *vs.* σ_p, was 2.750 ± 0.033 kJ mol^{-1} (0.657 ± 0.007 kcal mol^{-1}). It is seen to be reduced by the electron-withdrawing *p*-nitro group and increased by the electron-donating *p*-methoxy group, as predicted.

This conclusion is consistent with other data for certain other cyclohexanol derivatives reviewed by Jensen and
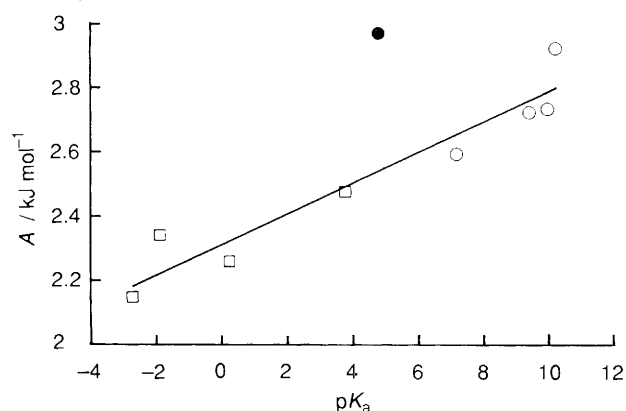

A = -ΔG° = RT lnK

Table 1 Conformational preferences for cyclohexyl substituted-phenyl ethers **2** (Ar = 4-X-phenyl), in 9:1 CFCl$_3$: CD$_2$Cl$_2$

X	$-\Delta G°$ (180 K)/ kJ mol^{-1}	$\Delta H°/$ kJ mol^{-1}	$\Delta S°/$ J mol^{-1} K^{-1}
NO$_2$	2.59 ± 0.01	2.41 ± 0.025	1.00 ± 0.08
Cl	2.72 ± 0.02	2.7 ± 0.3	-0.3 ± 1.7
H	2.73 ± 0.01	2.7 ± 0.2	0.2 ± 0.8
MeO	2.92 ± 0.03	3.0 ± 0.3	-0.4 ± 1.7

[+] By ^{1}H NMR at low temperatures. Spectra were obtained in the slow exchange region on a Bruker AM400 spectrometer (solvent 9:1 CFCl$_3$: CD$_2$Cl$_2$, sample ≈ 0.1 mol dm^{-3}) in 5 mm tubes. Each sample was allowed to equilibrate at 5 K intervals from 200 to 170 and four accumulations collected at each temperature. The methine proton signals for the axial and equatorial isomers between δ 4.0–4.4 were well resolved in each case. Spectra were expanded and plotted over the region of the methine peaks for the two conformers (2 Hz line broadening was used to smooth the baseline). They were then photocopied, and the peaks cut out and weighed accurately.

Fig. 1 Plot of the equatorial preferences for cyclohexanol derivatives *vs.* the pK_a of the conjugate acid (ArOH, XOH) of the leaving group. Data points, in increasing order of pK_a, are for OTs, OMs, OCOCF$_3$ and OCHO (from Jensen and Bushweller[3] Ts = *p*-MeC$_6$H$_4$SO$_2$, Ms = MeSO$_2$), and (○) from Table 1 (OAr). ● Represents Jensen and Bushweller's 'best value' for acetoxy.[‡]

[‡] This apparent positive deviation for the acetoxy group is of interest because of hints[6] that the anomeric effect of the acetoxy group may be smaller than expected, and is being checked under our conditions. The point for acetoxy was omitted from the correlation quoted.

Bushweller.[3] These authors noted a lower A-value for trifluoroacetate compared with acetate, but suggested that increased electron-withdrawal reduces the effective size of the lone pairs on oxygen, and hence the key 1,3-diaxial interactions. Data from their compilation are plotted in Fig. 1 against the pK_a of the OX (OAr) group, together with the data from Table 1 for aryloxy derivatives **2**. The A-value calculated for PhO from the best fit of the extended data set is identical, within experimental error, with that quoted above.

These results complement other evidence for $\sigma_{C-H}-\sigma^*_{C-OX}$ interactions in cyclohexanol derivatives; in particular the C–OX bond length increases with increasing electron-withdrawal from oxygen.[5]

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References

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3 F. R. Jensen and C. H. Bushweller, *Adv. Alicyclic Chem.*, 1971, **3** 140.
4 A. J. Kirby and N. H. Williams, following communication.
5 R. D. Amos, N. C. Handy, P. G. Jones, A. J. Kirby, J. K. Parker, J. M. Percy and M. D. Su, *J. Chem. Soc., Perkin Trans. 2*, 1992, 549. Note that axial and equatorial C–OX bond lengths are not measurably different in crystal structures, even for very electron-deficient groups like methanesulfonate, consistent with closely similar $\sigma_{C-H}-\sigma^*_{C-OX}$ and $\sigma_{C-C}-\sigma^*_{C-OX}$ interactions.
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