Conformational Free Energies of CH_2OR Groups as determined by ^{13}C Nuclear Magnetic Resonance

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EXTENDING our investigations[1] of the applications of ^{13}C n.m.r. spectroscopy to conformational analysis, we have begun an examination of ^{13}C nuclear shieldings of carbon atoms in axial and equatorial substituent groups of cyclohexane systems. Measurements of the conformational free energies $(-\Delta G_x^0)$ for many such groups are difficult using the more established techniques because differences in suitable parameters are small. The ^{13}C shieldings of axially and equatorially oriented carbons, however, are found to differ appreciably and determination of the equilibrium constants for mobile systems are possible. We report results for some CH_2OR (R=H, Me, Ac) groups to illustrate the approach and to record the observed $-\Delta G^0$ values, which have not been available.

The natural abundance 15·1 Mc./sec. ^{13}C spectra of *cis*- and *trans*-4-t-butylcyclohexylmethanols (I and II, respectively), their methyl ethers and acetates were obtained using the "proton-decoupling" technique of Paul and Grant.[2] For each pair of isomers, a shielding difference of *ca.* 5 p.p.m. is found for the carbinol (CH_2OR) carbons, the axial appearing at the higher field. (This may be compared with the 0·2 p.p.m. difference observed for the corresponding methylene proton shieldings.) Assuming these values to be characteristic of the two "fixed" chair conformations, estimates of K_e, the conformational equilibrium constant, for the CH_2OR (R=H, Me, Ac) groups are given by

$$K_e = (\delta_{cis} - \delta)/(\delta - \delta_{trans})$$

where δ is the observed shielding of the mobile systems, cyclohexylmethanol (III), its methyl ether or acetate, *i.e.*,
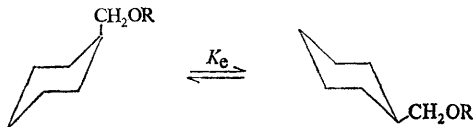
For example, (I), (II), and (III) (5M in CS_2) exhibit carbinol absorption at $128·3_8$, $123·7_4$, and $124·1_7$ p.p.m. from CS_2, respectively. Thus, $K_e = 9·8$ or $-\Delta G^0(CH_2OH) = 1·4_1 \pm 0·2_5$ kcal./mole. In a similar way, the values, $1·4_4$ and $1·8_8$ kcal./mole, were obtained for the CH_2OMe and CH_2OAc groups, respectively, using the neat liquids.

The only available figures for related systems are 1·7—1·8 kcal./mole for the tosyloxymethyl group, CH_2OTs,[3] and 1·56 kcal./mole for CH_3 in 4-substituted cyclohexanes.[4] The latter value is felt to be the most reliable for the methyl group although a number of previous estimates are larger.[5] The present data are in reasonable agreement with these, as may be expected since the atom bonded directly to the ring generally governs the magnitude of $-\Delta G^0$. There is an indication that the acetoxyl moiety tends to destabilize the axial form relative to OH or OMe.

We suggest that the conformational shielding differences arise from nonbonded interactions between the axial substituents and the C-3 and C-5 axial protons, interactions which are absent in the equatorial forms. Support for this is given by the fact that isobutyl alcohol exhibits carbinol absorption at $123·3_8$ p.p.m., *i.e.*, very close to that of (II). Inspection of models reveals that the most probable conformation of (II) is very similar to that for isobutyl alcohol. Thus, a large part of the shielding found for the carbinol carbon in (I) may be due to nonbonded interactions. Analogous trends have been found for hydrocarbons.[6] To aid a more detailed assessment of the importance of these steric effects we are examining an extensive series of related systems of known geometry.

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