Conformational Free Energy of the Formyl Group as determined by ¹H Nuclear Magnetic Resonance

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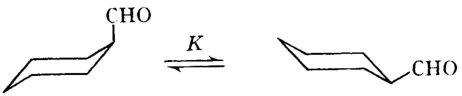
ALTHOUGH the estimation of conformational free energies ($-\Delta G_x^0$) by high-resolution n.m.r. spectroscopy has been reported for a wide assortment of substituents in cyclohexyl systems,[1] a determination for the formyl (CHO) group has not appeared. As part of an extensive study of the n.m.r. spectral characteristics of aldehydes[2] we have prepared and examined the *cis*- and *trans*-4-t-butylcyclohexanecarboxaldehydes (I) to obtain the necessary data for calculating $-\Delta G_{\text{CHO}}^0$ for cyclohexanecarboxaldehyde(II). We report the results of these measurements.

From the proton spectra of various natural products having an aldehyde function it is well known that axial and equatorial formyl groups exhibit significantly different proton chemical shifts.[3] In otherwise similar environments, the differences range up to 0·6 p.p.m. with the axial formyl proton at lower field. To investigate the origin of this difference we have been examining some simpler systems, one of which is (I). Unlike the more complex cases, the formyl proton shift between *cis*-(I) and *trans*-(I) is *ca.* 0·1 p.p.m. in a variety of solvents. Careful chemical-shift



(IIa) (IIe)

measurements by the "wiggle-beat" method,[4] however, have permitted us to determine the relative populations of the two conformations (IIa) and (IIe) with reasonable precision. The observed formyl shift, ν^0, for (II) is equal to $(N_a\nu_{\text{IIa}} + N_e\nu_{\text{IIe}})$ where N_a and N_e are the mole fractions of each conformer. Assuming the formyl shift for *cis*-(I) to be equal to ν_{IIa} and $\nu_{trans\text{-I}} = \nu_{\text{IIe}}$, as is usual, the equilibrium constant is given by

$$K = (\nu_{cis\text{-I}} - \nu_{\text{II}})/(\nu_{\text{II}} - \nu_{trans\text{-I}})$$

for which all shift measurements are determined under exactly similar conditions and solute concentrations. The $-\Delta G_{\text{CHO}}{}^0$ parameters were calculated from these data at two concentrations for each of four solvents and the results are collected in the Table. An alternative method for the estimation of $-\Delta G_{\text{CHO}}{}^0$ employing the vicinal coupling constant data yields comparable results.

From the Table it is clear that the equatorial form, (IIe), is strongly favoured, to the extent of *ca.* 90%, and there is no pronounced solvent effect on the conformational equilibrium, (IIa)$\rightleftharpoons$(IIe). The slightly larger $-\Delta G^\circ$ for the more dilute solution in chloroform may be due to hydrogen-bonding with the solvent since an equatorial grouping is less hindered. The $-\Delta G^0$-values of 1·35 ± 0·1 kcal./mole are comparable to those generally accepted for the carboxyl and methoxycarbonyl groups, 1·1—1·2 kcal./mole,[5] indicating that the major factor tending to destabilize the axial CHO, CO_2H, and CO_2Me groupings is the interaction of the carbonyl function with the axial 3- and 5-protons. Further comparisons of the conformational preferences of these functional groups in related systems are under active investigation.

TABLE

$-\Delta G^\circ$-*Values for the* CHO *group*
(±0·1 *kcal./mole*)

Solvent	Concentration (mole %)	
	10	50
CCl_4	1·33	1·40
C_6H_6	1·34	1·41
CH_3CN	1·38	1·33
$CHCl_3$	1·45	1·32

The model compounds, *cis*-(I) and *trans*-(I), were obtained by oxidation of the corresponding carbinols[6] with CrO_3 in 90% acetic acid. Separation of the mixture of alcohol, aldehyde, and acid was accomplished by chromatography on silica gel. The isomeric aldehydes (I) were characterized by proton n.m.r. and i.r. spectra and as their semicarbazone derivatives.

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