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EQUILIBRIA AND ^{13}CMR SHIFTS OF CYCLOHEXANE CONFORMERS$^{1)}$

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Low temperature cmr spectra can be used to determine energy differences between equatorial (e) and axial (a) substituted cyclohexanes$^{2)}$ and at the same time to investigate substituent effects on cmr shifts in single conformers, which are possibly masked in conformationally **inhomogeneous mixtures.**$^{3)}$

We have obtained conformer ratios by line intensity comparison in the proton noise decoupled PFT spectra, using small pulse angles for faster relaxation. The ratios yielded ΔG^{o} values with a standard error of $\pm$ 5-40 cal/mole, based on several independent signal pairs. The observed energy differences are essentially consistent with those obtained by other techniques$^{4)}$, as far as these are available. The effective sizes of the OH and NH_2 groups are enhanced by dimerization$^{5)}$ so that at the higher concentrations used for cmr measurements the corresponding axial conformers were not detected.

In the compounds C_6H_{11}-X-Y with Y=H the α carbon shifts decrease linearly with increasing electronegativity of X (Pauling parameters x, correlation coefficient r=0.986), as has been observed with other functionalized alkyl compounds.$^{6a)}$ The compounds with Y≠H also fit into the correlation, if one subtracts the effects of Y on Cα which can be taken from the literature$^{6)}$ values. There is no significant difference between the correlation for e and a substituents: $\alpha\text{-}\nu_e=(43.3x-106.05) \pm 3.3$ ppm; $\alpha\text{-}\nu_a=(40.3x-98.7) \pm 2.8$ ppm (relative to cyclohexane). These results strongly suggest (a) a dominant inductive effect on the α-carbon shifts and (b) not to rely upon shifts of the atom closest to the substituent for the differentiation of stereoisomers, which is common practice in pmr spectroscopy and appeared to be an attractive feature of cmr with some special cyclohexanes.6b)

Equatorial substituents exert a downfield shift on the ß-carbon which is consistently greater than that of axial groups. The ß-carbon deshielding (not the stereoselectivity) can be associated with the square electric field component from the Cα-X bond7) ($\delta_{\beta} \approx 5 \cdot 10^{12} \cdot E^2$ + const., for X=H, Hal). The ß-carbon of the cyclohexanes bearing halogens (e or a) are shielded with increasing substituent electronegativity (r=0.996). This could be expected on the basis of charge alternation effects8), but the results with the combined substituents are easier to rationalize with dominant electric field effects.

The observation of upfield *and* downfield anti-γ-shifts (δ_{γ} with e-substituents, relative to the hydrocarbon) places the more flexible cyclohexane between the strained 2-norbornane9a) (upfield anti-γ-shift) and the rigid 1-adamantane9b) or 1-bicyclo-(2.2.2)-octane9c) (downfield shifts) derivatives. A linear function between γ-C-shielding and electronegativity exists with e-substituents, particularly with X=Hal (r=0.992). Axial substituents invariably shield the positions to a higher degree, but the shielding does *not* increase with the effective size of the substituent for which the ΔG^{o} values are considered to be an approximate measure. Hence the often cited shielding mechanism through sterically induced charge polarization cannot be a dominant factor for the observed 1.3-diaxial shielding effects.10)

The δ ring carbons undergo a small upfield shift, which is rather independent of the substituent, and may be due to a general ring distortion. It is noteworthy that fluorine, being the "smallest" substituent, exerts a very similar shielding in both stereoisomeric positions. Thus, for the more remote positions δ and, to a lesser degree, γ, electronic substituent effects are difficult to separate from those of steric origin.

Table 1. ^{13}C Shifts[a] and Free Energy Differences of Cyclohexane Conformers

X		α	β	γ	δ	Substituent[b]				ΔG^o (cal/Mol)	Temp [°K]
F	e	64.54	5.56	-3.37	-2.51					360 ± 25	180
	a	61.10	3.11	-7.17	-2.02						
Cl	e	32.32	10.51	-0.57	-2.19					620 ± 40	200
	a	32.32	6.74	-7.10	-1.44						
Br	e	24.59	11.20	0.34	-2.45					585 ± 25	200
	a	27.51	7.23	-6.48	-1.54						
I	e	2.03[c]	13.73	2.03	-2.06					455 ± 25	180
	a	9.12[c]	9.12	-4.59	-1.26						
OH	e	42.57	7.95	-2.70	-2.05					> 1.400	180
	a										
OCH_3	e	51.80	4.49	-2.80	-1.76	CH_3	55.05			750 ± 35	180
	a	47.05	1.75	-7.23	-1.37		55.05				
$OOCCH_3$	e	45.79	5.03	-2.38	-1.73	CO	169.77	CH_3	21.32	885 ± 30	180
	a	42.08	2.76	-6.34			169.77		21.32		
NH_2	e	23.81	9.86	-1.64	-1.02					> 1.400	180
	a										
-NC	e	24.86	6.67	-2.64	-1.82[c]	NC	153.78			182 ± 15	180
	a	23.29	3.52	-6.87	-1.82[c]		155.34				
CH_3	e	5.85	8.15	-0.65	-0.72	CH_3	27.73			> 1.400	180
	a										
-CN	e	1.38	2.81	-1.93	-1.93[c]		--			152 ± 5	190
	a	0.09	-0.93	-4.53	-1.41		--				

a) 20 ± 5% in CF_2Cl_2 with 5% TMS as standard; in ppm relative to cyclohexane (δ_{TMS}=27.66 ppm), except b) relative to TMS. c) Overlapping with other signals.

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References and Footnotes:

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