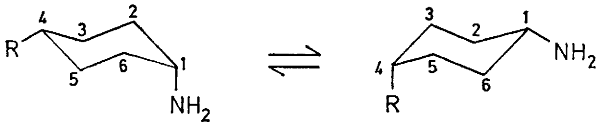
Conformational Free Energy (ΔG Value) of the Amino-group in Cyclohexylamine from Low Temperature Carbon-13 Nuclear Magnetic Resonance Spectroscopy

By HAROLD BOOTH

(*Department of Chemistry, University of Nottingham, Nottingham* NG7 2RD)

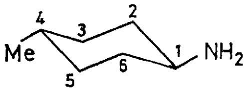
Summary The carbon-13 n.m.r. spectrum of *cis*-4-methylcyclohexylamine, measured at −75 °C, reveals signals for both possible chair conformations, and the measured ratio of 1·95 to 1 leads to a value of 6·05 ± 0·17 kJ mol^{-1} for $\Delta G(NH_2)$.

THE most direct method of determining conformational free energies (ΔG or A values) of substituents uses low-temperature n.m.r. spectroscopy of substituted cyclohexanes. Using ^1H resonance, the method has been applied to cyclohexanes substituted by most common groups,[1,2] a notable exception being the amino-group. Using ^{13}C resonance, we have hitherto failed to observe signals from the axial conformation (**1a**) of cyclohexylamine (expected proportion *ca.* 2%) when recording the noise-decoupled spectrum in the Fourier transform (F.T.) mode at −75 °C. The amine, dissolved in $CFCl_3$ containing 9% (v/v) $CDCl_3$, was examined over 4000 Hz with a pulse width of 4 μs (30° tip) and a 1·2 s repetition time, the free induction decay being sampled using 8k data points.



(1)
a ; R=H
b ; R=Me

(2)
a ; R=H
b ; R=Me



(3)

However, when the same conditions were applied to *cis*-4-methylcyclohexylamine (**1b**) ⇌ (**2b**) (the low-temperature ^{1}H spectrum of which is complicated by overlapping signals), the ^{13}C spectrum showed broadening effects at reduced temperatures and exhibited signals for both (**1b**) and (**2b**) at −75 °C. Assignment of lines to individual carbon atoms (see Table) made use of the known parameters for equatorial and axial methyl groups,[3] and the carbon-13 shifts in cyclohexylamine and *trans*-4-methylcyclohexylamine (**3**). The spectrum of (**3**) was unaffected by cooling the sample to −80 °C, confirming that the rate process being observed for the *cis*-amine was one of ring inversion (**1b**) ⇌ (**2b**).

Proportions of (**1b**) and (**2b**) were estimated by integration and comparison of (i) integrals for C-1 [giving (**1b**)/(**2b**) = 2·04]; (ii) integrals for the methyl carbon [**1b**)/(**2b**) = 1·92]; and (iii) total integrals for (**1b**) and (**2b**) [**1b**)/(**2b**) = 1·88]. Differences in spin–lattice relaxation times (T_1) of structurally identical (but stereochemically different) carbon atoms could lead to distortions in observed intensities. However, T_1 experiments (involving a 180°–τ–90° pulse sequence) at rooom temperature (solvent $CDCl_3$) showed that each carbon in (**1b**) ⇌ (**2b**) had an almost identical T_1 value to that of the corresponding carbon in the *trans*-amine (**3**). Measured values were 8·6 s (C-1), 5·7 s (C-4), 4·3 s (C-2, C-3, C-5, C-6), and 4·3 s (CH_3). It follows that structurally identical carbon atoms in (**1b**) and (**2b**) almost certainly possess identical T_1 values.[5]

TABLE

Carbon-13 shifts (p.p.m. from Me_4Si) in cyclohexylamines ($CFCl_3$–$CDCl_3$)

Carbon	(**1a**)⇌(**2a**) −72 °C	(**1b**)⇌(**2b**) −10 °C	(**1b**) −75 °C	(**2b**) −75 °C	(**3**) −75 °C
1	50·9	47·4	44·9	51·4	50·6
2,6	37·1	29·7	28·5	30·7	36·5
3,5	25·6	32·9	33·0	30·7	34·0
4	25·8	31·1	33·0	26·2	32·1
Me	—	21·2	23·1	17·4	22·6

The ratio (**1b**):(**2b**) of 1·95:1 leads to a conformational free-energy difference (at −75 °C) of 1·09 kJ mol^{-1}. Taking ΔG(Me) as 7·14 kJ mol^{-1} gives $\Delta G(NH_2)$ as 6·05 ± 0·17 kJ mol^{-1}; for comparison, Hirsch[1] quotes a 'best value' of 5·04 kJ mol^{-1} for NH_2 in aprotic solvents.

The shifts in the Table yield the following additive chemical shift parameters (see refs. 3, 4 for nomenclature) for the NH_2 group in cyclohexanes, in p.p.m.:

α_e 24·7, β_e 9·8, γ_e −1·2, δ_e −0·7
α_a 18·7, β_a 2·0, γ_a −2·4, δ_a 0·9.

Of additional interest are the small but significant shift differences between the methyl carbon of (**1b**) and (**3**) and between C-1 of (**2b**) and (**3**).

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