# Nuclear Magnetic Resonance Lanthanide-shift Reagents: Conformational Analysis of 1-Methylcyclohexanol

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*Summary* Results of the conformational study of 1-methylcyclohexanol with Eu(dpm)$_3$ are in agreement with a conformational equilibrium shift of the complexed molecule compared to the free one.

LANTHANIDE-SHIFT reagents are used to simplify n.m.r. spectra.[1] Chemically induced shifts measured in the presence of these reagents have allowed configurational assignment of various molecules. Their use in the study of conformationally mobile substrates is more complicated as the induced shift is the sum of the contributions of the various conformations. It is then important to know if the conformational equilibrium of the complexed substrate is different from that of the free one. The results published so far are divergent.[2,3]

We now report the first complete quantitative analysis of the complexation of 1-methylcyclohexanol. It is based on the equilibria shown in the Scheme where $K$ and $K_c$ are the conformational equilibrium constants of the free and complexed molecules, $K_e$ and $K_a$ are the complexation constants where the functional group is equatorial (e) and axial (a) respectively, $K_m$ refers to the mobile compound (I). From this the following relationships can be derived:[4]

$$\begin{tikzcd}
R + S^a \arrow[r, leftrightharpoons, "K"] \arrow[d, leftrightarrows, "K_a"'] & R + S_e \arrow[d, leftrightarrows, "K_e"] \\
RS^a \arrow[r, leftrightharpoons, "K_c"'] & RS_e
\end{tikzcd}$$

SCHEME

$$K = \frac{K_a - K_m}{K_m - K_e} \quad K_c = \frac{K_e}{K_a} \cdot \frac{K_a - K_m}{K_m - K_e} = K \cdot \frac{K_e}{K_a}$$

The complexation constants were investigated by a previously described method,[5] using the induced chemical shift of the methyl protons. The values $K_e$ and $K_a$ were measured for 4-t-butyl-1-methylcyclohexanols assuming that the effect of the 4-t-butyl group was negligible.[6] The results are recorded in the Table.

TABLE

| | | | |
|---|---|---|---|
| Complexation constants/mol$^{-1}$ [a,b] .. .. .. | $K_c = 124$ | $K_m = 95$ | $K_a = 70$ |
| Equilibrium constants/kcal mol$^{-1}$ [c] .. .. .. | $K = 0{\cdot}86$ | $K_c = 1{\cdot}52$ | |
| Free-energy values[d] | $\Delta G^\circ = 0{\cdot}1 \pm 0{\cdot}1$ | $\Delta G^\circ_c = -0{\cdot}3 \pm 0{\cdot}1$ | |

[a] At 313 K in CHCl$_3$ with Eu(dpm)$_3$. [b] Reproducibility is *ca.* 1%. [c] Calculated from experimental data. [d] Estimated errors, 313 K, $\Delta G^\circ$ and $\Delta G^\circ_c$ refer to the free and complexed compounds respectively.

The free-energy difference between the conformations of 1-methyl cyclohexanol is in good agreement with the results obtained by other methods (0·2 kcal $\mathrm{mol}^{-1}$ in aqueous acetic acid[7] at 298 K; 0·24 kcal $\mathrm{mol}^{-1}$ in aqueous dioxan[8]). With regards to the complexed substrate, the data in the Table are in agreement with a change taking place in the conformational equilibrium. The equatorial conformation of the functional group is favoured by complexation. The reasons for this equilibrium shift still remain obscure for other compounds lead to opposite conclusions[3,9] (steric interactions are not solely responsible for conformational changes).

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