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COUPLING CONSTANTS AND FREE-ENERGY DIFFERENCES IN INVERTING SYSTEMS

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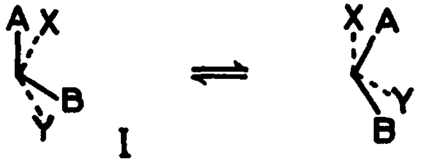
Consider two adjacent methylene groups in a system undergoing conformational inversion between two arrangements in each of which the methylene protons form an *ABXY* spin-group as follows:



I

II

We assume that vicinal coupling constants in each conformation are given by a Karplus-type relation (1,2)

$$J_{ij} = J^{o}\cos^{2}\phi_{ij} - c$$

where ϕ_{ij} is the dihedral angle subtended by protons *i* and *j*, J^{o} is the value of the coupling constant for $\phi_{ij} = 0$ if $0 \leqslant \phi_{ij} \leqslant \pi/2$ and is to be replaced by $J^{\pi} = J^{o}(1+\varepsilon)$ where ε is a constant if $\pi/2 \leqslant \phi_{ij} \leqslant \pi$, and *c* is a small constant which for present purposes will be neglected. Provided the rate of inversion is large compared with the difference of resonance frequencies for the two sites available to each proton, the observed spectrum will be time-averaged. Let $(1-\alpha)$ be the mole fraction of I and α that of II at equilibrium (*i.e.* the system has no appreciable residence time in any other conformation) where $K = \alpha/(1-\alpha)$.

If ϕ_{AX} has the same value $>\pi/6$ in both conformations and all projected geminal angles are $2\pi/3$, three independent equations connect the observed coupling constants and the four unknowns, J^{0}, ϕ, α, and ε, *viz*

$$J_{AX} = J_{BY} = J^{0}\cos^{2}\phi$$

$$J_{AY} = J^{0}[(1-\alpha)(1+\varepsilon)\cos^{2}(2\pi/3+\phi) + \cos^{2}(2\pi/3-\phi)]$$

$$J_{BX} = J^{0}[(1-\alpha)\cos^{2}(2\pi/3-\phi) + \alpha(1+\varepsilon)\cos^{2}(2\pi/3+\phi)]$$

Individual coupling constants often cannot be readily extracted from the *ABXY* analysis (3), but values of $(N-R)$ and $(N+R)$ where

$$2N = J_{AX} + J_{AY} \qquad 2R = J_{BX} + J_{BY}$$

usually can be from the *AB* part alone. Insertion of the above expressions and expansion give

$$2(N-R) = J^{0}(1-2\alpha)[2\varepsilon - \varepsilon\cos 2\phi + \sqrt{3}(2+\varepsilon)\sin 2\phi]/4$$

$$2(N+R) = J^{0}[(8+2\varepsilon)+(2-\varepsilon)\cos 2\phi + \varepsilon\sqrt{3}\sin 2\phi]/4$$

For $0 < \varepsilon < 0.6$, $(N-R)$ passes through a flattish maximum in the range, $45^{\circ} < \phi < 49^{\circ}$, given by $\cot 2\phi = -\varepsilon/\sqrt{3}(2+\varepsilon)$, and depends directly on $J^{0}(1-2\alpha)$. The sum of the coupling constants, $2(N+R)$, depends on J^{0}, but is independent of α. Dependence on J^{0} may be eliminated by taking the ratio

$$r = (N-R)/(N+R) = (1-2\alpha)F(\phi,\varepsilon)$$

The function F passes through a flattish maximum given by

$$\sin 2\phi = [-\varepsilon\sqrt{3} \pm \sqrt{240+744\varepsilon+903\varepsilon^{2}+504\varepsilon^{3}+108\varepsilon^{4}}]/4(4+6\varepsilon+3\varepsilon^{2})$$

which, for $0 \ll \varepsilon \ll 0.6$, lies in the range, $52^{\circ} < \phi < 55^{\circ}$.

A value of ϕ near 50° is expected for several inverting ring systems such as cyclohexenes (4) or δ-lactones (5), but not including ideal chair-rings. The range of values of ε quoted cover the arbitrary situation, $J^{0} = J^{\pi}$, through that (0.12) corresponding to Karplus's original equations (1) up to that (0.6) suggested for some systems by Johnson and Williamson (2). Expressions for α and K are not very sensitive to exact values of ϕ in the range 40-55° or of ε. We therefore take $\phi = 50^\circ$, $\varepsilon = 0.25$ as reasonable average values, and obtain

$$\alpha = 0.5 - 0.98\,r$$

$$K = (1-1.97\,r)/(1+1.97\,r)$$

These expressions may not of course be used without other evidence that the system satisfies the stated conditions; there are an infinity of solutions (α and ϕ) of the basic equations. Where they are applicable, the value of ΔG° given by $|RT \ln K|$ may be taken as an approximation to the free-energy difference of the two rapidly inverting conformations represented by I and II. It does not directly tell which is the more stable conformation, for the sign of $(N-R)$ is arbitrary; further, X and Y may be interchanged without affecting calculated values of $(N-R)$ and $(N+R)$ although $(N-R)$ is then equal to $|J_{AX} - J_{BX}|$. This is also the value of $(L+T)$ extracted along with $(N+R)$ from the *XY* part alone of the *ABXY* spectrum; the sub-group labels, *AB* and *XY*, are of course arbitrary. If the observed spectrum is better described as *ABCD* and is able to be analyzed, the same expressions for α and K apply with $2(N+R)$ replaced by the sum of the four vicinal coupling constants, and $2(N-R)$ replaced by the difference of the two *trans* coupling constants. For an *ABX* system there are no convenient functions of the coupling constants having stationary properties of the above kind and comparable approximations cannot be made.

By this method we have obtained reasonable values of ΔG° in a series of substituted valerolactones (5). As an example, the *ABXY* spectrum of the 4- and 5- methylene protons of 2,2-dimethyl-3-phenylvalerolactone in deuterochloroform at 30° gives

$$N-R = 2.8 \qquad N+R = 11.5$$

Then $K = 0.32$ and ΔG° (30°) = 680 cal/mole. This value may not be very accurate (it changes by 20 cal/mole for 0.1 c/s change in $N-R$), but it seems reasonable that a half-chair conformation with the phenyl group axial should be less stable than that with the phenyl group equatorial by a quantity of this order.

The spectrum was measured by Mr. R.N. Johnson on a Varian HA-60-IL spectrometer purchases with a grant from the Australian Research Grants Committee.

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