Tetrahedron Letters No. 51/52, pp 4533 - 4536, 1974. Pergamon Press. Printed in Great Britain.

A SIMPLE METHOD FOR THE DETERMINATION OF RATE CONSTANTS AT COALESCENCE OF EXCHANGING AB SYSTEMS IN DYNAMIC NMR

Daniel Kost* and Arie Zeichner
Department of Chemistry,
Ben Gurion University of the Negev,
Beersheva, Israel

(Received in UK 1 November 1974; accepted for publication 13 November 1974)

Dynamic NMR measurements[1] are most useful for the determination of energy barriers to conformational changes, such as pyramidal inversions[1a,d-g], rotations about formal single bonds,[1a,g-h] and ring inversions.[1a] A number of methods have been used to calculate activation parameters from the temperature dependent NMR spectra of exchanging diastereotopic groups. These methods include the complete line shape analysis (CLSA), that yields both enthalpies and entropies of activation, and coalescence measurements, in which a single rate constant (k_c) is evaluated at the temperature of highest line shape sensitivity, to yield a value for the free energy of activation ($\Delta G^{\neq}$) at this temperature. The coalescence rate constant can either be determined by line shape analysis, or by the use of approximate equations that relate it to certain spectral parameters.[1,2] Although the use of such equations has been criticized as an unreliable procedure,[1a] it has been shown experimentally,[3] and by a systematic comparison,[4] that $\Delta G^{\neq}$ values obtained using these equations are in good agreement with the results obtained by CLSA. This is true mainly in the case of uncoupled equally populated exchanging singlets, for which many of the approximate equations have been derived. For the exchange of coupled nuclei in an AB spectrum, the equation $k_c=(\pi/\sqrt{2})\sqrt{(\Delta\nu^2+6J^2)}$ has been employed.[5] Its usefulness was shown to be restricted within certain limits,[4] and hence it should be used with care.

We wish to propose a method for the determination of rate constants at the coalescence of an AB spin system to a singlet. A single parameter, the width at half height ($W_{\frac{1}{2}}$), is obtained from the spectrum at the coalescence point. This is used to evaluate k_c from a plot of k_c against $W_{\frac{1}{2}}$ (Figure 1), that has been calculated for various values of the coupling constant J_{AB} by means of a line shape program.[6] The only other parameter that is needed is J_{AB}, which must be measured at the slow exchange limit. The use, at the coalescence temperature, of a J_{AB} value that has been measured at lower temperature causes no difficulty, however, as spin spin couplings of individual conformations are known to be temperature independent.[8]

The chemical shift difference ($\Delta\nu_{AB}$) is also obtained from the same parameters by interpolation from the calculated plot (Figure 2). In all the approximate methods $\Delta\nu_{AB}$ is a necessary parameter, and its value at the coalescence point must be extrapolated from low temperature measurements. Since $\Delta\nu_{AB}$ is sometimes strongly temperature dependent, and since the exact nature of this dependence is unknown, a possible error in k_c is introduced by using $\Delta\nu_{AB}$ as an experimental parameter. This source of error is eliminated in the present method.

It is noteworthy to point out that in Figure 2 the curve for J = 2 Hz approaches a straight line with unit slope, as is predicted for the case of uncoupled singlets; likewise, the lowest curve on Figure 1 approaches the line $k_c=2.2\ W_{\frac{1}{2}}$. This reconfirms the validity of the equations $\Delta\nu_c=W_{\frac{1}{2}}$ and $k_c=\pi\ \Delta\nu/\sqrt{2}$ for the coalescence of uncoupled (or, in this case, weakly coupled) singlets.

The main source of error in this method, as well as in CLSA upon which it is based, and in all other methods, remains the inaccuracy of temperature measurements. In view of this fact, and it being generally accepted that the most accurate parameter obtainable from DNMR is $\Delta G^{\neq}$, we believe that the present method can be used successfully for all simple AB systems and yield results in very good agreement with those obtained from the more laborious CLSA.

References

1. For leading references on DNMR see: (a) G. Binsch, *Topics in Stereochem.*, 3, 97 (1968); (b) R. Lynden-Bell, in "Progress in Nuclear Magnetic Resonance Spectroscopy," Vol. 2, eds. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon Press, Oxford, 1967, ch. 4; (c) C. S. Johnson, jr., in "Advances in Magnetic Resonance," Vol. 1, ed. J. S. Waugh, Academic Press, New York, 1965, ch.2; (d) A. Rauk, L. C. Allen and K. Mislow, *Angew. Chem. Internat. Edn.*, 9, 400 (1970); (e) J. B. Lambert, *Topics in Stereochem.*, 6, 19 (1971); (f) J.-M. Lehn, *Fortschr. Chem. Forsch.*, 15, 311 (1970); (g) H. Kessler, *Angew. Chem. Internat. Edn.*, 9, 219 (1970); (h) W. E. Stewart and T. H. Siddal, III, *Chem. Rev.*, 70, 715 (1970).

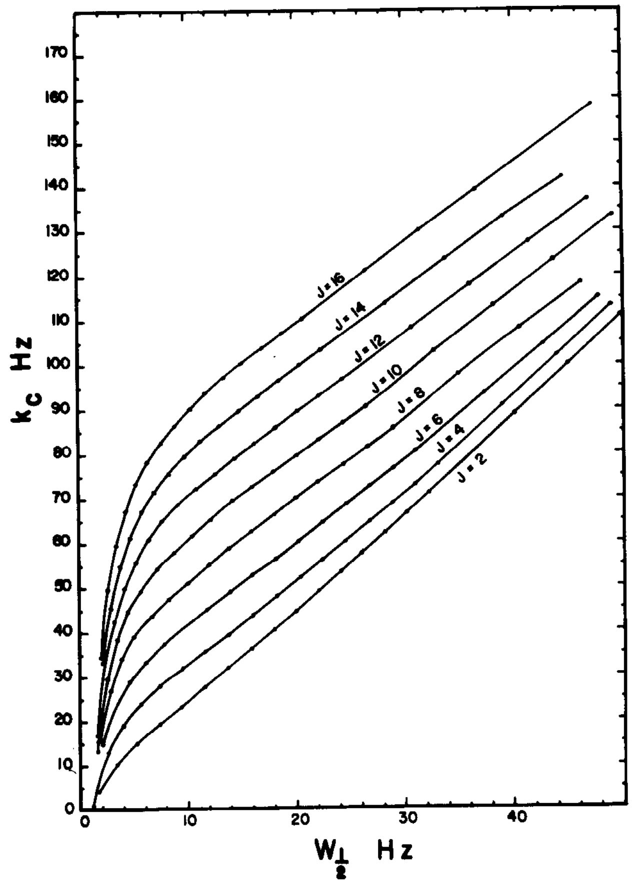

Figure 1: A plot of rate constants *vs*. line widths at half height at the coalescence of an AB quartet with various J_{AB} values (J_{AB} given in Hz).

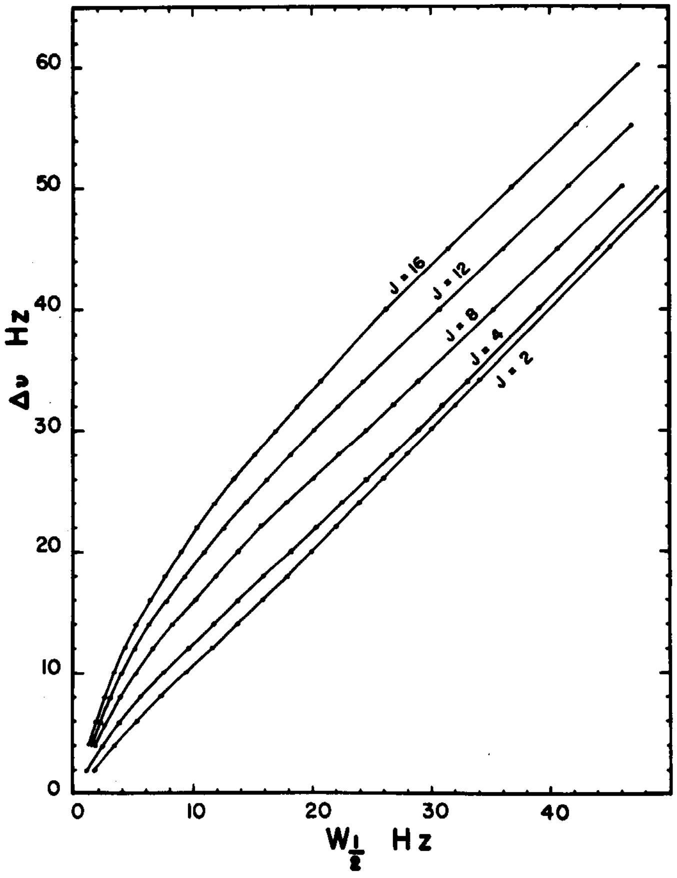

Figure 2: A plot of chemical shift differences *vs*. line widths at half height at the coalescence of an AB quartet with various J_{AB} values (J_{AB} given in Hz).

2. V. S. Dimitrov, *Org. Mag. Resonance*, 6, 16 (1974).

3. (a) K.-I. Dahlqvist, S. Forsen and T. Alm, *Acta Chem. Scand.*, 24, 651 (1970); (b) E. H. Carlson, F. B. Jones, jr., and M. Raban, *Chem. Comm.*,1235 (1969); (c) M. Raban, F. B. Jones, jr., E. H. Carlson, E. Banucci, and N. A. LeBel, *J. Org. Chem.*, 35, 1496 (1970); (d) W. Egan, R. Tang, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, 93, 6205 (1971); (e) R. C. Neuman, jr., and V. Jonas, *J. Org. Chem.*, 39, 925 (1974).

4. D. Kost, E. H. Carlson and M. Raban, *Chem. Comm.*, 656 (1971).

5. R. J. Kurland, M. B. Rubin and M. B. Wise, *J. Chem. Phys.*, 40, 2426 (1964).

6. We have used a modification of program Quabex from reference 1a, p. 180. A reasonable value of $T_2 = 0.4$ s has been used throughout the calculations. It has been noted[7] that the line shape near coalescence is insensitive to small changes in T_2. The usual definition of coalescence has been used, as in reference 4.

7. T. Drakenberg, K.-I. Dahlqvist and S. Forsen, *Acta Chem. Scand.*, 24, 694 (1970).

8. J. W. Emsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy", Vol. 1, Pergamon Press, Oxford, 1965, p. 63.