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Nuclear Magnetic Resonance Methods for Determining Chemical-Exchange Rates[1]

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Abstract: Factors which affect the accuracy of high-resolution and spin-echo nmr determinations of chemical-exchange rates are analyzed and discussed, including mathematical as well as experimental aspects. Numerical methods show that most of the mathematical approximations commonly used to evaluate exchange rates from high-resolution spectra are subject to systematic error, and circumstances under which the error becomes serious are presented. A line-width equation is derived which gives accurate exchange rates in the vicinity of the coalescence point for an uncoupled AB system, and from which the chemical shift at the coalescence point can be obtained. The effects of saturation broadening are calculated and compared with experiment. In general, it appears desirable to determine exchange rates from high-resolution spectra by using computerized, complete line-shape fitting methods which do not neglect spectral complications unless their effects are demonstrably less than other inaccuracies in the rates. In rate determinations by the spin-echo method which employs a Carr–Purcell train of echoes, it is possible for self-diffusion to cause systematic error. Simple criteria are presented for estimating and minimizing such effects. Other presently known factors peculiar to the spin-echo method, including the effects of finite pulse widths, do not appear to present serious problems.

An impressive variety of nmr methods for studying fast chemical exchange in liquids has evolved during the past decade.[3,4] The putting into practice of these methods involves assumptions and approximations which in many instances were pointed out in early reports. However, only recently has there developed a growing awareness of the possible seriousness of the systematic errors which can occur. The present work is an attempt to analyze in more detail some of these sources of error and to present a few remedies. For convenience in our discussion we classify the problems as mathematical or experimental, even though they are not always entirely separable.

Mathematical problems occur when the theoretical model is an oversimplification of the actual system studied. They also arise when the theoretical model is adequate, but a simplified, approximate equation is used beyond its region of accuracy. For example, the line-shape equations for the semiclassical, two-site model[5–7] are simpler than those for more complicated models which consider internuclear coupling and/or multiple sites.[8–10] Thus, there has been a tendency to apply the simple, two-site line-shape equations to situations where they may fail. Moreover, even when the uncoupled two-site model is appropriate, a practical method must be found for the estimation of the rate of exchange from the line shape.[3,4] If a high-speed computer is unavailable, the comparison between theoretical and experimental line shapes is greatly simplified by using certain characteristic parameters

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[1] This research was supported by the U. S. Office of Naval Research, by the National Science Foundation, and by the National Institutes of Health.

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[3] A. Loewenstein and T. M. Connor, *Ber. Bunsenges. Physik. Chem.*, **67**, 280 (1963).

[4] C. S. Johnson, Jr., in "Advances in Magnetic Resonance," Vol. I, Academic Press Inc., New York, N. Y., 1965, Chapter 2.

[5] H. S. Gutowsky, D. W. McCall, and C. P. Slichter, *J. Chem. Phys.*, **21**, 279 (1953).

[6] H. S. Gutowsky and A. Saika, *ibid.*, **21**, 1688 (1953).

[7] H. S. Gutowsky and C. H. Holm, *ibid.*, **25**, 1228 (1956).

[8] J. Kaplan, *ibid.*, **28**, 278 (1958); **29**, 492 (1958).

[9] S. Alexander, *ibid.*, **37**, 967, 974 (1962).

[10] C. S. Johnson, *ibid.*, **41**, 3277 (1964).

such as peak separation,[7] the ratio of peak (maximum) to central (minimum) intensity,[11-13] or the width of the coalesced lines.[14] Very convenient approximate equations relating these parameters to the rate of exchange have been derived,[7,13,14] but it is important not to apply these equations when the approximations do not hold.

The experimental problems arise in general from instrumental instabilities, calibration errors, and from spectral distortion due to causes other than instabilities. The particular problems and their relative importance vary greatly depending upon which particular nmr technique is used. These techniques include steady-state,[3,4,7] fast-passage,[3,15,16] and double-resonance[17] high-resolution methods and, more recently, spin-echo procedures.[18-22] Our own experience has been limited to the steady-state and spin-echo methods which are in most common use and to which therefore we direct our attention.

The existence and magnitude of the errors in rate determinations by nmr are most evident in the enthalpy and entropy of activation obtained from the temperature dependence of a rate process. This results in part from the fact that several of the methods are applicable over rather limited temperature ranges,[20,21] and in part from systematic errors.[21] One of the exchange processes studied most extensively by nmr is the hindered internal rotation of N,N-dimethylformamide, yet values from 7 to 24 kcal mole^{-1} have been obtained for the barrier, and the true value still is uncertain. Studies of the chair–chair conformational exchange of cyclohexane are more recent and the range of activation enthalpies[23] is smaller, 9 to 11.5 kcal mole^{-1}. Several of the studies cover substantial temperature ranges; nonetheless, the presence of systematic errors in most if not all of the work is indicated by a strong correlation between the activation enthalpies and the corresponding frequency factors.[21] Furthermore, the rate constants themselves and the free energies of activation obtained in different laboratories and/or by different methods agree quite well. So the basic question is that of reducing what are fairly modest systematic errors or of minimizing their effects by extending the rate determinations over larger temperature ranges.[24]

Mathematical Aspects

Theoretical Model. The semiclassical theory[5-7] and, more importantly, density matrix[8-10] and other[25] general formulations enable us in principle to calculate the chemical-exchange effects in any experimentally important case, but it is not surprising that the mathematics get more and more tedious as the experimental system increases in complexity. Neither is it surprising, then, that before high-speed digital computers became more or less widely available, there was a tendency to use the semiclassical equations for exchange between two uncoupled sites in situations where they do not apply. Thus, weakly coupled spin systems have been analyzed as if the components in the multiplet from one set of nuclei originated from chemical shifts between nonequivalent sites. A case of this sort is the methanol CH_3 proton doublet as it coalesces and becomes a singlet with increasing intermolecular exchange of the OH proton. Also, quite strong coupling between nonequivalent sites has been neglected entirely, such as in the analysis of the intramolecular exchange between axial and equatorial hydrogens in cyclohexane, and in consequence only very approximate results are obtained.[21]

Of course, there are limiting situations in which the simple, semiclassical model is *approximately* valid for more complicated systems. But it is dangerous to assume the validity unless it is supported by comparison with the truly applicable equations[25] or established over the appropriate range of parameters by numerical calculations[26] (or the researcher's intuition is high!). For the two examples mentioned above, the semiclassical results are approximately correct for methanol at *low* exchange rates, and for cyclohexane at *high* exchange rates! Moreover, the farther one goes from the region of validity for the approximate expressions, generally the larger will be the error, which thus will usually be systematic in character.

For the relatively simpler systems, serious errors from the above source are best avoided by carrying out a computer calculation with the use of the appropriate equations. The density matrix line-shape equations for the coupled AB system[27] as well as for more complicated situations[28] are now being used increasingly. In some cases, however, a complete analysis may still not be practical, as for the 12-spin cyclohexane case. Even then some other solution may be possible, such as using deuterium decoupling so that the proton high-resolution spectrum of cyclohexane-d_{11} can be treated as an uncoupled AB case.[29] In the spin-echo technique, even the decoupling *may* be unnecessary.[21,25] Such solutions are applicable to many other proton-exchange problems. One replaces mathematical difficulties by problems in chemical synthesis. Of course, the possibility of a deuterium isotope effect on the exchange

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(11) E. Grunwald, A. Loewenstein, and S. Meiboom, *J. Chem. Phys.*, **27**, 630 (1957).

(12) A. Loewenstein and S. Meiboom, *ibid.*, **27**, 1067 (1957).

(13) M. T. Rogers and J. C. Woodbrey, *J. Phys. Chem.*, **66**, 540 (1962).

(14) L. H. Piette and W. A. Anderson, *J. Chem. Phys.*, 30, 899 (1959).

(15) H. M. McConnell and D. D. Thompson, *ibid.*, **26**, 958 (1957); 31, 85 (1959).

(16) S. Meiboom, *ibid.*, **34**, 375 (1961).

(17) S. Forsén and R. A. Hoffman, *ibid.*, **39**, 2892 (1963).

(18) D. E. Woessner, *ibid.*, **35**, 41 (1961).

(19) S. Meiboom, paper presented at the American Chemical Society Symposium on High Resolution Nuclear Magnetic Resonance, Boulder, Colo., July 1962; Z. Luz and S. Meiboom, *J. Chem. Phys.*, 39, 366 (1963).

(20) A. Allerhand and H. S. Gutowsky, *ibid.*, **41**, 2115 (1964); **42**, 1587 (1965).

(21) A. Allerhand, F. M. Chen, and H. S. Gutowsky, *ibid.*, **42**, 3040 (1965); see also papers cited therein.

(22) M. Bloom, L. W. Reeves, and E. J. Wells, *ibid.*, 42, 1615 (1965).

(23) This range excludes the 5.9 kcal mole^{-1} value given in ref 21 and calculated by us from the peak separation data which cover only a 9° temperature interval as reported by F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Am. Chem. Soc.*, **84**, 386 (1962). The latter article cites a value of 11.5 ± 2 kcal mole^{-1} from line-width measurements above coalescence, but details are not given.

(24) Another, less acceptable, alternative would be to use only the free energy of activation from nmr rate studies; for cyclohexane and cyclohexane-d_{11},the range in ΔF^*_{cb} is only 10.1 to 10.7 kcal mole^{-1} and four of the seven values are 10.3.

(25) H. S. Gutowsky, R. L. Vold, and E. J. Wells, *J. Chem. Phys.*, **43**, 4107 (1965).

(26) A. Allerhand and H. S. Gutowsky, *ibid.*, **42**, 4203 (1965).

(27) See, for example, J. Heidberg, J. A. Weil, G. A. Janusonis, and J. K. Anderson, *ibid.*, **41**, 1033 (1964); J. Jonas, A. Allerhand, and H. S. Gutowsky, *ibid.*, **42**, 3396 (1965).

(28) R. A. Newmark and C. H. Sederholm, *ibid.*, **43**, 602 (1965).

(29) F. A. L. Anet, M. Ahmad, and L. D. Hall, *Proc. Chem. Soc.*, 145 (1964); F. A. Bovey, F. P. Hood, E. W. Anderson, and R. L. Kornegay, *ibid.*, 146 (1964); *J. Chem. Phys.*, **41**, 2041 (1964).

rate has to be considered. However, so long as the exchange involves the motion of heavier atoms, one would expect such effects to be very small, as is borne out by the results for cyclohexane and cyclohexane-d_{11}.[21]

Approximate Equations. Although the model chosen may be appropriate, problems can still arise in applying it to data for the system. Even the line-shape equation for exchange between two uncoupled sites[6,7] is sufficiently complicated that extraction of the exchange rate from the complete line shape requires a computer.[30] So it is useful to have equations which relate some readily measured feature of the spectrum to the exchange rate. But such equations are nearly as complicated as the total line-shape equations unless approximations are made, and the accuracy of such approximations depends upon the relative value for the exchange rate(s) $1/2\tau$,[31] as compared to the chemical shift(s) $\delta\nu$, the coupling constant(s) J, and the natural line width(s) $1/\pi T_2^0$ [33] in the absence of exchange, all assumed here to be in units of sec^{-1} or cps. Neglect of this dependence, as frequently has been the case, leads to appreciable, systematic errors. If an approximate method must be used, the range of its validity should be understood, it should be tested numerically for the case at hand, and it should not be exceeded. And this applies to spin-echo[19,26] as well as to high-resolution methods.

To illustrate, we consider the most widely used approximations: those which relate a single feature of the steady-state spectrum to the exchange rate between two equally populated uncoupled sites, A and B These equations result if

$$1/\tau \text{ and } \delta\nu >> (1/\pi T_2'') \equiv W'' \qquad (1)$$

where

$$(1/T_2'') = (1/T_2^0) + (1/T_2') \qquad (2)$$

and $(1/T_2')$ represents the inhomogeneity, instability, and other instrumental contributions to W'', the effective line width in the absence of exchange; line width here is defined as the *full* width in cps at half-maximum intensity. The condition of eq 1 on the exchange rate can be met for many systems by adjusting the temperature and/or concentrations of reactants. The chemical shift in cps is less adjustable, control being limited to solvent effects and increasing the magnetic field. For very small chemical shifts, the approximate equations are not valid. In such cases graphical methods have been used[7,11,12] but a complete line-shape method seems preferable.[30]

For exchange rates too slow to coalesce the AB doublet to a single line, the experimentally observed peak separation[7] $\delta\nu_e$, in cps, and the maximum to central minimum intensity ratio[11-13] r have been used in the following approximation.

$$(1/2\tau) = (\pi/\sqrt{2})(\delta\nu^2 - \delta\nu_e^2)^{1/2} \qquad (3)$$

$$(1/2\tau) = (\pi\delta\nu/\sqrt{2})[r + (r^2 - r)^{1/2}]^{-1/2} \qquad (4)$$

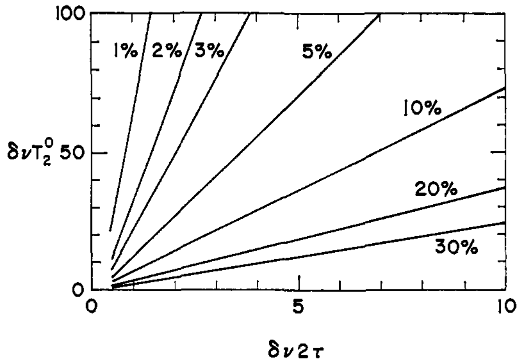

Figure 1. A graphical presentation of the error introduced by using eq 4 to calculate an approximate exchange rate from $\delta\nu$, T_2^0, and the peak to central intensity ratio for an uncoupled AB system undergoing chemical exchange. The apparent rate is always larger than the true rate $1/2\tau$.

The relative sensitivity of the two methods has been discussed.[34] They are applicable, of course, only to rates up to the coalescence limit. We have checked the accuracy of eq 3 and 4 by using them to calculate exchange rates from complete theoretical line shapes computed for a range of the input parameters $1/2\tau$, $\delta\nu$, and T_2^0.

The functional form of eq 3 is such that a general description of the errors associated with its use is difficult. A basic factor is that, as pointed out previously,[7] the major change in peak separation with exchange rate occurs over a rather narrow range, $0.45 \leq \delta\nu 2\tau \lesssim 2$; and $\delta\nu_e$ becomes decreasingly sensitive to rate for slower rates, *i.e.*, for $\delta\nu 2\tau > 2$. At very slow rates, the errors in determining $\delta\nu_e$ exceed the errors involved in using eq 3; both errors then are comparable to the exchange rate itself,[7,13] and the peak separation method should not be used. In our calculations for the faster rates, $1/2\tau$ obtained with eq 3 was always larger than the exact input value used in calculating the line shape and $\delta\nu_e$, provided that the line shape was calculated at points close enough together to give a sufficiently accurate value for $\delta\nu_e$. The values of these *positive* errors depend on all three parameters $\delta\nu$, $1/2\tau$, and T_2^0. Thus, the shorter the relaxation time T_2^0, the larger the per cent error obtained for a particular pair of $\delta\nu$ and $1/2\tau$ values. Also, the effect of T_2^0 on the error is inversely proportional to $\delta\nu$; *i.e.*, the error increases for smaller $\delta\nu$ values. In general, our computer results show that the error introduced by using eq 3 does not exceed $+10\%$ for systems for which $\delta\nu 2\tau \leq 5$.

The analysis of the error introduced by using eq 4 is simpler than for eq 3 because the error is relatively insensitive to the relative values of $\delta\nu$ and T_2^0 and of $\delta\nu$ and 2τ. Thus, the results of our computer analysis can be summarized by plotting the per cent error against $\delta\nu T_2^0$ and $\delta\nu 2\tau$. This gives the set of straight lines of constant error shown in Figure 1. For a given $\delta\nu T_2^0$ product, the per cent error increases with decreasing rate, as expected, and decreases with an increasing $\delta\nu T_2^0$ product. The left-hand limit of the

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(30) The best procedure is to use a computer to fit the observed line shape, as described in ref 27b. A more cumbersome, less accurate method is to compare visually the experimental spectra with line shapes computed for a range of exchange rates.

(31) Our definition of 2τ is that given in ref 7 and 20, which corresponds to τ in ref 5, 9, and 32.

(32) M. Takeda and E. O. Stejskal, *J. Am. Chem. Soc.*, **82**, 25 (1960).

(33) For a discussion of the various contributions to the apparent line width, see ref 21.

(34) J. C. Woodbrey, Ph.D. Thesis, Michigan State University, 1960. More recently, these and two other line-shape parameter methods have been treated in detail in connection with a study of N,N-dimethylamides by C. W. Fryer, F. Conti, and C. Franconi, *Ric. Sci.*, [2A] **35**, 3 (1965). Also, errors in the peak separation method have been discussed by K. I. Dahlquist and S. Forsen, *J. Phys. Chem.*, **69**, 4062 (1965).

constant error lines is the coalescence point. Good estimates of the errors in $1/2\tau$ values obtained by using eq 4 with particular sets of $\delta\nu$, $T_2{}^0$, and r values can be found readily from Figure 1 by interpolation. In all cases, eq 4 gives an apparent rate which is larger than the true rate.

In these calculations on the use of eq 3 and 4, the instrumental broadening of the lines has been neglected. However, its effects are not negligible especially for small chemical shifts, for which the overlap of the lines must be taken into account.[7,13] If this is the case, it is best to avoid approximate equations altogether; instead, one can use complete line-shape numerical methods which include the instrumental broadening as a convolution function.

Line Shapes above Coalescence. Another problem associated with the use of eq 3 and 4 for exchange rates below coalescence is that for commonly encountered chemical shifts the range of accessible rates is rather limited.[20] So, if one is seeking activation parameters, the temperature range is correspondingly short, and systematic errors in the rates and/or temperatures can produce quite large errors in the apparent enthalpy and entropy of activation. Because of this, it is desirable to obtain exchange rates above the coalescence temperature T_c, when only a single line is observed. In this event, the obvious spectral parameter is the observed line width, for which we use the full width W^* at half-maximum intensity, given in cps by

$$W^* = (1/\pi T_2{}^*) = (1/\pi T_2)_{ex} + (1/\pi T_2{}'') \qquad (5)$$

where $(1/\pi T_2)_{ex}$ is the exchange contribution to the line width. For two uncoupled sites with fractional populations P_a and P_b, the following simple equation has been derived[14]

$$(1/2\tau) = 2\pi P_a P_b (\delta\nu)^2 (W^* - W'')^{-1} \qquad (6)$$

where W'' is defined by eq 1 and 2, and the equation holds for very fast exchange, that is when

$$(1/\tau) >> 2\pi\delta\nu \qquad (7)$$

Unfortunately, eq 6 for the "residual" exchange broadening has been used close to coalescence, when the very fast exchange condition of eq 7 is not valid. In fact, for $P_a = P_b$, and when eq 1 holds, the exchange rate at T_c is given as[7]

$$(1/2\tau) = (\pi\delta\nu/\sqrt{2}) \qquad (8)$$

which is a long way from being "very fast exchange." Therefore, eq 6 is not expected to be applicable, and this is borne out by our computer line-shape calculations. The latter show that the use of eq 6 leads to large errors in the rate unless the rate is sufficiently above the coalescence value for eq 7 to be true. But then another limitation arises, especially for small $\delta\nu$ values; the exchange contribution to W^* becomes so small that $(W^* - W'')$ approaches the experimental error in W^*, and the error in $1/2\tau$ becomes very large. Because of this, many nmr rate studies have employed eq 6 at the slower rates. The error introduced in this manner is systematic and can have serious effects on ΔH^* and ΔS^*; our computer calculations show that the rates obtained by means of eq 6 are always too low, the error decreasing with increasing rate and thus making ΔH^* too large.

The exchange contribution to the line shape is most significant in the region of coalescence given by eq 8, so it is desirable to have a good method for extracting $1/2\tau$ from the line shape in this region. This has been done in the past by determining T_c as closely as possible and then using eq 8. This method gives a single value of the rate, namely that at T_c. The complete line-shape computer analysis can, of course, be used at any temperature above or below T_c, but, for rapid approximate values and for rate determinations without resorting to computer usage, it is desirable to have a line-width equation valid for $T \geq T_c$. Such a general equation, for $P_a = P_b$, has been derived[32] in connection with the effect of exchange on a spin doublet, and although it is not strictly applicable for the system for which it was derived, it is valid for the case under consideration here. The expression as derived by Takeda and Stejskal[32] is, in our notation[31]

$$(W^*/\delta\nu)^2 = (K + L)[2(2K + L)^{-1} - 8K] + \{(K + L)^2[2(2K + L)^{-1} - 8K]^2 + [4L(2K + L) + 1]^2\}^{1/2} \qquad (9)$$

where

$$K = (4\pi\tau\delta\nu)^{-1} \qquad (10)$$

and

$$L = W''/(2\delta\nu) \qquad (11)$$

Equation 9 was derived without any approximating assumptions, but its complexity makes it of little practical use in determining $1/2\tau$. However, a simpler and more useful result can be derived from eq 9 when eq 1 holds. In this event, $1/2\tau$ is given explicitly by

$$(\pi\delta\nu\tau)^{-1} = \{(W''/\delta\nu) + (W^*/\delta\nu)[1 + 2(W^*/\delta\nu)^2 - (W^*/\delta\nu)^4]^{1/2}\}[(W^*/\delta\nu)^2 - (W''/\delta\nu)^2]^{-1} \qquad (12)$$

If the exchange rate is sufficiently fast so that $(W^*/\delta\nu) << 1$, eq 12 reduces to the Piette–Anderson[14] expression of eq 6, with $P_a = P_b = 0.5$. If $1/2\tau$ is smaller, so that the exchange contribution to the line width is much greater than W'' and we thus have $W^* >> W''$, eq 12 reduces to

$$(\pi\delta\nu\tau)^{-1} = [(\delta\nu/W^*)^2 - (W^*/\delta\nu)^2 + 2]^{1/2} \qquad (13)$$

This result is valid at and above coalescence, when eq 1 holds. We have confirmed its validity from computer-calculated line shapes. It is also valid below coalescence if W^* is defined more generally as the width of the spectrum at the point where it possesses an amplitude one-half of the central intensity.[32]

Furthermore, it follows from eq 8 and 13 that when eq 1 holds, the line width W^* at the coalescence temperature is *equal* to the chemical shift $\delta\nu$, and that $W^* > \delta\nu$ below T_c and $W^* < \delta\nu$ above T_c. These results are evident in Figure 4 of Loewenstein and Meiboom.[12] Also, we have confirmed them by computer line-shape calculations. They have the important practical application that $\delta\nu$ or at least an upper and lower limit to it can be determined without going to the low temperatures where the exchange is "frozen out." We have applied this criterion to the proton chemical shift in N,N-dimethyltrichloroacetamide near T_c. The low-temperature value of $\delta\nu$ is about 0.30 ppm,[13,20a] but spin-echo determinations[20a] indicate a value of 0.35

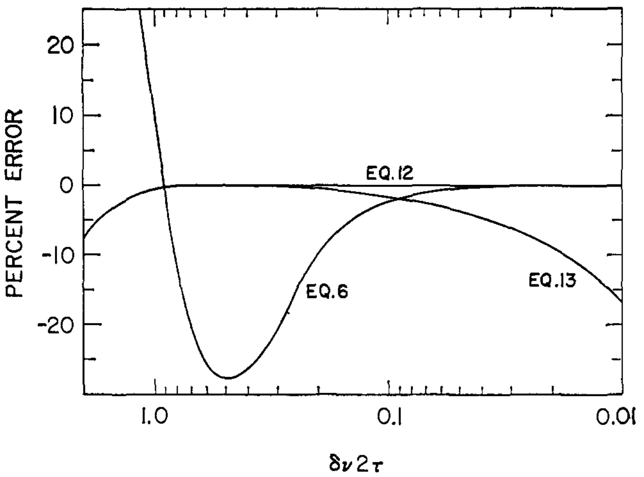

Figure 2. A semilog plot comparing the errors introduced by using eq 6, 12, and 14 to calculate an approximate exchange rate from $\delta\nu$, $T_2{}^0$, and the line width for exchange rates below as well as above coalescence. The line widths are the full widths at half-maximum intensity as obtained from line shapes calculated for an uncoupled AB system with $\delta\nu = 100$ cps and $W'' = W^0 = 1/\pi$ cps. Positive errors correspond to an apparent exchange rate larger than the true rate. For $\delta\nu 2\tau > 1.0$ the error curves for eq 12 and 13 are the same within the accuracy of the graph.

± 0.1 at T_c and values as large as 0.39 ± 0.03 ppm at higher temperatures. The high-resolution line shapes at 60 Mc/sec in the vicinity of T_c indicate an *upper* limit of *at most* 0.33 ppm at T_c (about 18°).

The general nature of our computer results on the accuracy of eq 6, 12, and 13 is shown in Figure 2 where the error for each is plotted against exchange rate for the particular case in which $\delta\nu = 100$ cps and $W'' = W^0 = 1/\pi$ cps. The derivations of both eq 6 and 12 assume fast exchange, and, in fact the equations are the same in the limit of very fast exchange, so it is not surprising that the errors shown for them become negligible for fast rates; but as the rate *decreases* toward the "coalescence" point, eq 6 produces large negative errors, while eq 12 is accurate until $\delta\nu 2\tau \gtrsim 1.0$ which includes *rates* two- to threefold slower than the coalescence rate. Upon changing $T_2{}^0$ over the range 0.1 to 2.0 sec and $\delta\nu$ from 10 to 100 cps, we found some displacements in the error curves for eq 6 at rates near coalescence, but there are virtually no differences at the faster rates. As a general rule, if the approximation errors are to be kept below 5% in magnitude, eq 6 should be used only for rates such that $\delta\nu 2\tau \leq 0.2$.

For fast exchange, a practical limit to the rates which can be determined at all accurately occurs when the exchange broadening is comparable to the experimental error in determining the total line width. With present high-resolution instruments, this limitation for protons is typically of the order $\delta\nu 2\tau \gtrsim 0.05$. A similar effect was found in our calculations in that the accuracy of the "calculated" line width was determined by the spacing of the points used. As the exchange broadening approached this value, usually 0.05 cps, the *apparent* error of eq 6 and 12 became large and random in character.

It is apparent from Figure 2 that both eq 12 and 13 give a good approximation of the exchange rate in the neighborhood of coalescence, but eq 13 is much simpler to use. However, the range of applicability of eq 13

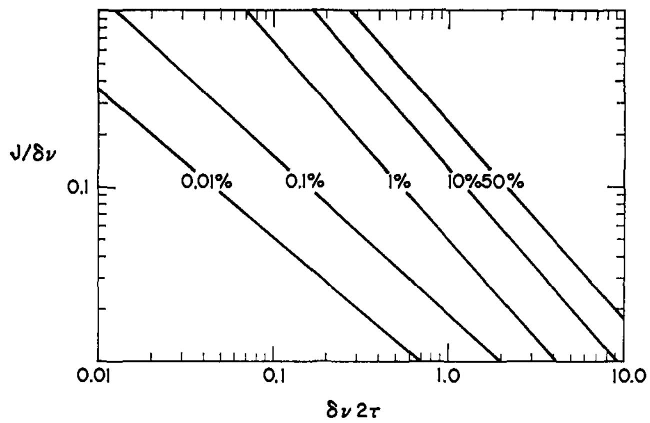

Figure 3. A log–log plot of the error introduced in the apparent exchange rate by neglecting the coupling J in determining the intramolecular exchange rate from the complete line shape of a coupled AB system. Here $1/2\tau$ is the *apparent* rate as obtained from the line shape.

is strongly dependent on both $\delta\nu$ and $T_2{}^0$: the larger the chemical shift, the broader the range of exchange rates within which the equation gives useful results. Also, the magnitude of $T_2{}^0$ has a very pronounced effect upon the shape of the error curves. As $T_2{}^0$ becomes smaller, the curves become narrower and more nearly symmetric about the coalescence point, and for small values of both $T_2{}^0$ and $\delta\nu$, eq 13 is of limited use. The apparent exchange rates obtained with the equation are smaller than the true rates.

Neglect of Coupling. As another example of mathematical approximations, we consider the use of the uncoupled line-shape equations to obtain intramolecular exchange rates for a *coupled* AB system by the complete line-shape fitting process.[35] For spin-echo experiments, it has been shown numerically[26] and analytically[25] that errors less than ~5% are introduced by neglecting the coupling provided that $1/2\tau \gtrsim 20J_{AB}$. For high-resolution spectra, the results of our numerical studies are given in Figure 3 which shows the error as a function of $J/\delta\nu$ and $\delta\nu 2\tau$. The iso-error lines given in the figure correspond to $T_2{}^0 = 0.5$ sec; however, the results are insensitive to $T_2{}^0$ and no marked changes were found for $T_2{}^0$ values ranging from 0.3 to 3 sec. As expected, it follows from Figure 3 that the intramolecular coupling may be neglected at high and intermediate exchange rates without introducing substantial error. In fact, the condition that the error not exceed ~5% is $1/2\tau \gtrsim 15J$, which is about the same as in the spin-echo method. In both instances, neglect of the coupling gives apparent rates larger than the true ones.

A somewhat different approximation occurs when the nuclei in a coupled AB system are coupled differently to a third set of nuclei and the latter is neglected. A case of this sort is 1,1-difluorocyclohexane for which a complete line-shape analysis was made of the ^{19}F resonance, treating it as a coupled AB system but neglecting the H–F coupling to the α-CH$_2$ group protons.[27b] The results of this approximation were investigated by means of theoretical line shapes

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(35) If computing facilities were available for the complete line-shape method, the coupling would ordinarily be included in the analysis. It is more likely that the coupling would be neglected in studies using single line-shape parameter approximations. Our approach is designed to separate the error due to neglect of the coupling from the errors of the single parameter methods.

calculated as a function of the chair–chair conversion rate with the H–F coupling included.[36] The exchange rates obtained by treating these line shapes as a "simple" coupled AB system are increasingly too high for slow exchange and increasingly too small for very fast exchange, and give an apparent activation energy which is 5 to 10% low. Of course, such errors can be reduced or avoided, at the expense of increased programming and computer time, by including all of the couplings in the complete line-shape method used to fit the observed spectra; or the effects can be handled experimentally by using decoupling techniques.[29] Spin-echo determinations appear to be less susceptible to such effects.[21,26] Nonetheless, recent theoretical work indicates that coupling to nonexchanging nuclei can affect a spin-echo train;[25] it does not seem safe to neglect such effects without first establishing their magnitude.

Experimental Aspects

In the introduction we classified experimental problems as arising from instrumental instabilities, calibration errors, or other inaccuracies in the measurements, and spectral distortions. Examples of instabilities in steady-state work are temperature drifts, frequency changes, magnetic-field drifts, and variations in sample spinning rate. Instabilities in spin-echo instruments can be numerous. Unlike high-resolution instrumentation, there is little uniformity among different spin-echo spectrometers. Commercial equipment is just now coming into fairly general use. In our early model, "homemade" instrument[37] we have encountered instabilities in the pulse separations, in addition to those in temperature, frequency, and field, which are held in common with high-resolution equipment. Spectral distortion can result from the electronic filtering network, too high a radiofrequency level, radiation damping, or a mismatch of sweep speed and recorder response in high-resolution experiments. In the case of spin echoes, the finite pulse widths, molecular diffusion in the sample, and receiver nonlinearity can lead to distortions. In both methods, errors can arise in determining the temperature of the sample. Also, care must be taken in the choice of chemical shift(s) used to determine the exchange rates by either method, especially if there is any reason to suspect solvent and/or temperature effects. In addition, field sweep and oscilloscope sweep calibration errors are possible, but readily avoided, in high-resolution and spin-echo techniques, respectively. In this section, we treat several of these problems in some detail.

High-Resolution Methods. The problems discussed here are those that have been encountered with the Varian A-60 and HR-60 spectrometers. However, they are general in character. First, we consider those associated with temperature fluctuations and changes. In the usual gas flow, variable temperature probe,[38] these result from variations in heater current or the flow rate of the gas. The magnitude of the errors which result from temperature fluctuations depend upon both the heat capacity and amount of sample present. For example, the original system gave excellent results with liquid samples, but the spectra of gas phase samples exhibited temperature variations which were observed indirectly as a scattering of chemical-shift values; these were corrected by the use of a better temperature-regulating system. The temperature of the sample depends also upon its spinning rate; with our spectrometer a 1° difference was found between a spinning and nonspinning sample.

Probably the most important temperature effect is the loss in resolution produced by changing the temperature of the sample. Several factors contribute including the changes in sample position produced by thermal expansion, and the perturbations in field distribution produced by changes in bulk magnetic susceptibility. Such loss in resolution has generally less effect upon peak separations than upon line shapes. In the intensity ratio method, it causes the ratio of peak maximum to central minimum to be too small. The area under a peak is independent of the inhomogeneity broadening, so as the line width increases, the peak height decreases, the minimum increases, and the apparent exchange rate is too high. Thus, the resolution must be "peaked up" at each temperature; moreover, if errors are to be avoided, the resolution should be the same at each temperature. This requires considerable care because, in addition to the relatively reversible resolution changes produced by short-term changes in sample temperature, and in spite of numerous precautions,[39,40] there is a gradual deterioration in resolution, on the time scale of a day or so, caused by fluctuations in room temperature, magnet cooling water, and line voltage.

Instabilities commonly occur in the sweep rate, in the frequency, and in the static magnetic field. Their effects can be reduced by averaging several spectra. Also, instrumental improvements such as the single-sample, lock-on stabilization schemes are reducing the magnitude and importance of the instabilities. Nonetheless, a spectrometer must be maintained in first-rate operating condition if one is to obtain accurate rates with it. For example, the crystal which was the basic radiofrequency source on one of our spectrometers had to be replaced after 4 years of use because its "aging" led to intolerable frequency drifts.

In calibrating spectra by the side-band method, an inaccurate measurement can be obtained by using side-band frequencies of less than 25 cps and not correcting for the resultant change[41,42] in resonance frequency, which may be as much as several cycles per second in special cases. The separation of side bands produced by audiofrequency modulation of the magnetic field H_0 or of the radiofrequency ν_0 depends not only upon the angular frequency ω_m of the audiomodulation but also upon the amplitude H_1 of the radiofrequency field, as given by the equation[43]

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[36] We wish to thank Professor J. D. Roberts for providing us with the theoretical line shapes used in the analysis.

[37] J. Buchta, H. S. Gutowsky, and D. E. Woessner, *Rev. Sci. Instr.*, 29, 55 (1958).

[38] J. N. Shoolery and J. D. Roberts, *ibid.*, **28**, 61 (1957).

[39] J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance, McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 69.

[40] Varian Associates, "NMR and EPR Spectroscopy," Pergamon Press, Oxford, 1960.

[41] L. G. Alexakos and C. D. Cornwell, *Rev. Sci. Instr.*, **34**, 790 (1963).

[42] N. Boden, Ph.D. Thesis, University of Liverpool, Liverpool, England, 1964.

[43] W. A. Anderson, *Phys. Rev.*, **151**, 102 (1956).

$$H_0 = (\omega_1/\gamma) \pm [(\omega_m/\gamma)^2 - H_1^2]^{1/2} \qquad (14)$$

in which γ is the nuclear magnetogyric ratio and ω_1 is the angular radiofrequency. Equation 14 has two solutions corresponding to the values of the magnetic field for the first two side bands. For example, a side band nominally at 10 cps with an H_1 of 0.2 mgauss will be in error by 1%. Also, if a spectrum is calibrated by modulating ν_0, errors can be produced by switching side bands on and off while the spectrum is being recorded, so it seems best to adjust the amplitude of the audiofrequency so that the side band and "fundamental" resonances are of similar magnitude, and the entire spectrum can be recorded without further adjustment.

A common source of experimental error is the measurement of sample temperature, because spinning of the sample discourages a direct reading. In practice, three methods are commonly used. A thermocouple can be inserted into the probe so that it measures the temperature at the coil or it may be placed somewhere in the flow of gas used to regulate the temperature of the sample. The main difficulty with these methods is that they must be calibrated in order to give the actual temperature of the sample; moreover, the constancy of the calibration is poor and must be repeated at least whenever there is any change in probe geometry or the sample temperature regulation system. The third method requires a secondary standard with a highly temperature-dependent shift, such as the hydroxyl proton in methanol, and uses the shift to deduce the temperature. In principle the method is capable of accurate temperatures, particularly if a coaxial sample assembly is used; but it does have the difficulty that any errors in sweep calibration affect not only the apparent line shape but also the apparent temperature. Moreover, interference between absorption by the standard and by the sample can be troublesome.

The main sources of spectral distortion are inhomogeneities in H_0, improper adjustment of sweep rate and instrumental response times, and saturation effects of too large radiofrequency field. In the first of these, when two inhomogeneously broadened peaks start to overlap, their real separation is no longer equal to their apparent separation. Theoretical calculations have shown that such effects become important when the full line width at half-amplitude of a peak equals the apparent peak separation.[7] Then, the apparent rates are too large by an amount depending on the ratio of inhomogeneity broadening to total width, and the error increases as coalescence is approached. Similar errors result with the intensity ratio method as mentioned in connection with the effects of resolution instabilities. The complete line-shape method is less sensitive to such errors; moreover, they can be allowed for by incorporating in the line-shape calculations a broadening function derived from a TMS or other reference line in the sample.

It is more difficult to correct for spectral distortions associated with the passage conditions under which the spectrum is recorded, and the best procedure is to avoid them by proper adjustment of the spectrometer. A common error is to use a small filter band width, to improve signal-to-noise and obtain a smooth curve for analysis, without decreasing the sweep rate accordingly. The dampened response gives distortions such as those in Table I, where the apparent intensity ratio is given for two equal peaks separated by 2 cps as observed on a Varian A-60 spectrometer with various filter band widths and sweep rates. As expected, the ratio comes smaller for smaller band widths and faster sweep rates, the errors being as large as 30%. Similar distortions arise from having a sweep rate too fast for the pen response time of the recorder, which is easy to do with the A-60.

Table I. Effects of Filter Band Width and Sweep Rate upon the Apparent Intensity Ratio for Two Equal Peaks Separated by 2 Cps

Band width, sec	Sweep rate, cps/sec	Intensity ratio
2.0	0.2	3.02
0.4	0.2	2.91
0.2	0.2	2.64
0.2	0.1	2.66
0.1	0.2	1.94
0.1	0.1	2.34

Theoretical line shapes, and also the single parameter equations, are calculated ordinarily for steady-state passage conditions and no saturation, but neither of these conditions is met in an actual experiment. Nonsteady-state passage tends to reduce the saturation effects at the expense of line-shape distortion by relaxation transients. The complexity of the combined effects leads us to believe that it is better to avoid or minimize them than to try to correct for them.[44a] Nonetheless, we have made some theoretical calculations of the saturation effects and compared the results with experimental measurements of the internal rotation rate about the central C–N band in N,N-dimethyltrichloroacetamide (DMTCA).[13,20]

The theoretical calculations were made with the modified Bloch equations[44b,c] in the uncoupled two-site case. As given in eq 4 to 9 of ref 44b, these equations become a system of six linear equations under steady-state conditions with an appreciable radiofrequency field. The system is solved most readily by numerical, computer methods to give the line-shape point by point. This was done for various values of the radiofrequency field, $H_1 = \omega_1/\gamma$, for equal populations using $\delta\nu = 18$ cps and values of $T_1 = T_2^0$ and $1/2\tau$ corresponding to those found experimentally[13,20] for DMTCA at 0 and 14°. As H_1 is increased, the lines are of course broadened, and the ratio of peak-to-valley amplitudes decreases and the apparent exchange rate increases. The peak separation is affected appreciably only for extremely large radiofrequency fields ($H_1 \gtrsim 1$ mgauss) which are unlikely to be used, so in Table II we give details only for the intensity ratio r. It is seen that even a rather small H_1 increases the calculated apparent rate by $\gtrsim 10\%$, the increase being greater for the lower exchange rate. However, the experimental effect as measured with a Varian A-60 is much smaller, and a 20-fold larger H_1 is required to produce a 10% increase in the apparent exchange rate.

The experimental values for H_1 are not very accurate, but the uncertainty in them is insufficient to account for

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(44) (a) A treatment of line shapes under intermediate passage conditions has just been given by R. R. Ernst and W. A. Anderson, *Rev. Sci. Instr.*, **36**, 1696 (1965); (b) H. M. McConnell, *J. Chem. Phys.*, **28**, 430 (1958); (c) E. L. Hahn and D. E. Maxwell, *Phys. Rev.*, **88**, 1070 (1952).

Table II. Calculated and Observed Effects of H_1 upon the Intensity Ratio and Apparent Exchange Rate for Two Equally Populated Uncoupled Sites at Exchange Rates below Coalescence[a]

Theoretical[b]			Experimental		
H_1, mgauss	r	$1/2\tau$,[c] sec^{-1}	H_1, mgauss	r	$1/2\tau$,[c] sec^{-1}
			0.02	17.5	6.76
0.047	12.1	8.60	0.04	17.5	6.76
0.117	10.0	9.42	0.1	18.2	6.62
0.235	6.35	11.78	0.2	16.3	7.00
0.352	4.16	14.61	1.0	10.4	8.89
			0.02	1.83	22.8
0.047	1.74	23.8	0.04	1.98	21.7
0.117	1.62	24.9	0.1	1.99	21.7
0.235	1.39	27.6	0.2	1.98	21.7
0.352	1.24	30.1	1.0	1.74	23.6

[a] Experimental results were obtained at 60 Mc/sec for DMTCA at 0 and 14°. The upper set of results is for 0° and the lower for 14°. [b] For 0° the true $1/2\tau$ was taken to be 6.35 sec^{-1} and $T_1 = T_2^0$ = 0.43 sec, while for 14°, $1/2\,\tau$ = 22.65 sec^{-1}, $T_1 = T_2°$ = 0.90 sec. An instrumental broadening function of 0.63 cps was included in the calculations. [c] The values of $1/2\tau$ were obtained from r by means of eq 4.

the difference between experimental and theoretical results. Also, the inhomogeneous broadening of the lines does not account for the difference. It has only a modest effect (~5 to 10%) upon r, because the exchange broadening is much larger, and the change it produces in the H_1 effects is even less. This was checked by including in the line-shape calculations a static line-broadening function of 0.63 cps as determined from a TMS reference line. The most likely explanation of the difference in theoretical and experimental results lies in the passage conditions which are not at all close to the steady state assumed. In any event, our experimental results are consistent with those of Grunwald, Loewenstein, and Meiboom who investigated the effects of sweep rate and H_1 experimentally in proton-exchange studies of aqueous methylammonium salts and found r to be essentially constant over 100-fold changes in H_1 and sixfold changes in sweep rate.[11] It is apparent, nonetheless, that care must be taken on this point, and theoretical studies of the combined effects of H_1 and nonsteady-state passage conditions are desirable.

Spin-Echo Methods. Some of the areas of experimental concern in spin-echo studies of exchange rates are similar to those found in other nmr methods. Sample temperature is one of these. In spin-echo experiments the sample is not spun, so its temperature can be measured by inserting a thermocouple in the sample itself, or by affixing it to the exterior of the sample tube. This is more direct than in high-resolution work, but there is a larger probability of thermal gradients in the sample. Also, when the decay of the Carr-Purcell train of echoes[45] is measured for a wide range of pulse separations, as described previously,[20] the total time spent on a single temperature may be considerably longer than in a high-resolution experiment, especially if T_1 is 10 sec or longer! Because of this, better temperature stability is required. Fortunately, a highly homogeneous H_0 is not needed, so larger gaps, probes, and samples can be used and good temperature stability can be achieved more readily. In our measurements[20] we have maintained the temperature with ±0.5° over periods of several hours at temperatures above room temperature, though our probe design made this more difficult at low temperatures, especially below −60°.

Instabilities in H_0 and ν_0 have little or no effect on the spin-echo results even at magnitudes up to 10^3 times as large as the usual tolerances in high-resolution nmr. However, new instabilities and maladjustments are possible and must be considered. Incorrect settings of the pulse widths and also instabilities in the gating circuits, and thereby in the widths and spacings, can cause the echo train in the Carr-Purcell experiment to decay faster than the true rate.[46] The effects of using pulse widths differing from the requisite 90 and 180° can be reduced to a negligible extent by a 90° phase shift in the radiofrequency between the 90 and 180° pulse,[46] and this feature is a must for rate studies. The phase shift serves also to avoid the effects of inhomogeneity in H_1, which correspond to having a distribution of pulse widths over the sample volume. Instabilities in the widths and spacings can be reduced to an acceptable level by careful design such as digital control of the time base.[47] Stability in amplitude of the radiofrequency pulses requires well-regulated power supplies of capacity commensurate with the duty cycle.

Another possible source of error is decay in the transversal nuclear magnetization associated with its induction of the radiofrequency signal in the sample coil. The effect of such "radiation damping" has been discussed by Abragam,[48] who points out that in steady-state experiments it adds the following term to $1/T_1$

$$(1/T_1)_i = 4\pi^2 Q\chi_0\nu_0 \qquad (15)$$

where $(1/T_1)_i$ is the decay constant describing the damping effect of the nuclear induction, Q is the "Q" of the sample circuit, and χ_0 is the nuclear magnetic susceptibility for the line in question. Substitution of typical values for the parameters in eq 15 shows that the effect can be appreciable. If the exchange involves lines of equal intensity, the damping should not be a source of error because it is constant and simply increases the apparent values of $1/T_1$ and $1/T_2^0$. However, lines of unequal χ_0 are damped at correspondingly different rates, and in high-resolution experiments this leads to apparent rates lower than the true rates. In a spin-echo experiment, "radiation damping" occurs during the Bloch decay and when an echo is induced. However, as pointed out by Abragam[48] the effects are reversed by the 180° pulses, and thus the echo train is unaffected (with or without a 90° phase shift between 90 and 180° pulses).

A mathematical approximation which can lead to difficulty because of experimental limitations is neglect of the finite pulse widths. This approximation makes it possible to derive the various analytical expressions used to describe the echo train, but it is not surprising that the approximation leads to error when the pulse width t_w becomes comparable to or larger than the half-life of the exchange reaction and is an appreciable fraction of the pulse separation.[49] The magnitude of such effects has been investigated by numerical

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(45) H. Y. Carr and E. M. Purcell, *Phys. Rev.*, 94, 630 (1954).

(46) S. Meiboom and D. Gill, *Rev. Sci. Instr.*, 29, 688 (1958).

(47) I. J. Lowe and R. L. Howard, *ibid.*, 33, 96 (1962).

(48) A. Abragam, "The Principles of Nuclear Magnetism," Oxford University Press, Oxford, 1961, p 73.

(49) C. S. Johnson, Jr., and M. Saunders, *J. Chem. Phys.*, 43, 4170 (1965).

integration of the modified Bloch equations including the intervals in which the radiofrequency pulses are applied[49] as well as the time between pulses.[20a] The results indicate that the errors can be as much as 10% for high pulse repetition rates when $t_w \gtrsim \tau$. Thus, with pulse widths of 10 μsec, which are not too difficult to obtain, the exchange rate would need to exceed about 10^5 sec^{-1} before the finite pulse width would need consideration. This does not seem to be a very serious limitation at present and, in any case, it appears to be an error which is correctable. Neglect of the finite pulse widths gives T_2's which are too short and tends to give apparent exchange rates which are too large. An inexact "correction" can be made by including t_w as part of the pulse separation but otherwise neglecting it.

Another effect which may be of more concern in the spin-echo experiment is the contribution to T_2 of self-diffusion. The formation of nonoverlapping spin echoes requires a field inhomogeneity ΔH_0 over the sample such that the induction decay after a 90° pulse is over before the 180° pulse is applied, *i.e.*, $\gamma\Delta H_0 \gtrsim 2/t_{cp}$ where t_{cp} is the time between 180° pulses in the Carr–Purcell train. However, diffusion from one precessional frequency ω_0 to another causes an irreversible dephasing of the nuclei, which contributes an exponential term to the decay of the Carr–Purcell train and reduces the apparent value of T_2. This diffusional contribution to $1/T_2$ is given by[45]

$$(1/T_2)_d = (^1/_{12})D(\Delta\omega_0)^2 t_{cp}^{\,2} \qquad (16)$$

Here, D is the diffusion coefficient in cm^2 sec^{-1} and $\Delta\omega_0$, in radians sec^{-1} cm^{-1}, is defined by

$$\Delta\omega_0 = \gamma G \qquad (17)$$

with G the field gradient in gauss cm^{-1}. The diffusional contribution to $1/T_2$ decreases with pulse spacing, and it increases with temperature because D is temperature dependent. Thus, it can affect the apparent exchange rate; whether or not it does can be checked experimentally simply by changing the field inhomogeneity over the sample. Also, the functional form of the diffusional term lends itself to a graphical comparison of its magnitude with the $1/T_2$ predicted for an exchanging system without diffusion.

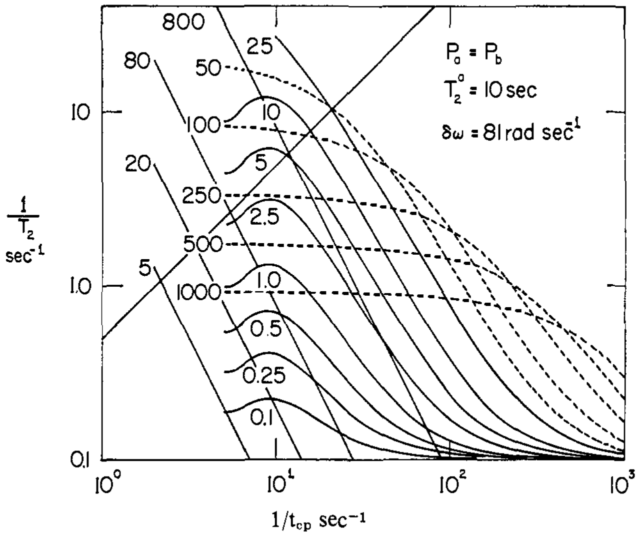

Figure 4. A log–log plot of the diffusional and exchange contributions to $1/T_2$, as a function of the pulse repetition rate $1/t_{cp}$ in the Carr–Purcell train of echoes for an uncoupled AB system. The dashed and solid curves were computed for the fast and slow exchange rates, respectively, listed near their end. The straight lines are plots of the diffusional contribution for the values of $\epsilon(1/T_2)_d$ at their left, as discussed in connection with eq 16 and 18. Experimental $1/T_2$ values above and to the left of the straight line of positive slope are difficult to obtain because too few echoes are observable.

We wish to ensure that $(1/T_2)_d$ does not exceed a given fraction of the total $1/T_2$, which we shall call ϵ. We take this maximum fractional contribution to be the experimental error in $1/T_2$, which is typically 0.05 to 0.1. Then, on log-log curves of $1/T_2$ *vs.* $1/t_{cp}$ for different exchange rates,[20,21,26] we plot the quantity $\epsilon(1/T_2)_d$ for appropriate values of D, $\Delta\omega_0$, and ϵ. Such plots of $(1/T_2)_d$ *vs.* $1/t_{cp}$ appear as straight lines of slope -2, as shown in Figure 4. Rates with curves to the right of and above the appropriate $(1/T_2)_d$ line should not be in error by more than about approximately ϵ through neglect of diffusional effects. It is apparent in Figure 4 that the latter are most important for rates which are very slow or very fast compared to the coalescence rate. This is to be expected because these are the rates for which the exchange broadening is smallest. In the uncoupled AB case shown in the figure, a range of about 10^5 in the exchange rate would be unaffected in practice provided that

$$\epsilon(^1/_{12})D(\Delta\omega_0)^2 \lesssim 20 \qquad (18)$$

For $\epsilon \lesssim 0.1$ and $D \cong 5 \times 10^{-5}$ cm^2 sec^{-1}, which is representative of nonviscous liquids,[50] the resultant modest requirement on the field inhomogeneity is $\Delta\omega_0 \lesssim 600$ radians sec^{-1} cm^{-1}, a value commensurate with ordinary operating conditions. Inspection of the curves in Figure 4 shows that the diffusional contribution tends to make the fast rates, with respect to the coalescence rate, appear slower, and the slow rates appear faster, which would tend to decrease the apparent activation energy.

Consideration should be given also to the temperature dependence of D. The activation energies for self-diffusion are quite low for nonviscous liquids so D can be estimated readily for different temperatures from the activation energies reported for typical liquids.[50] When D is not known, a value of the order of 10^{-5} cm^2 sec^{-1} is a good, approximate upper limit for ordinary liquids at room temperature.

The curves in Figure 4 are for a chemical shift of 81 radians sec^{-1}, which corresponds to the axial–equatorial proton shift in cyclohexane and cyclohexane-d_{11} at 25.85 Mc/sec, the frequency we used in our spin-echo studies of the chair–chair conformational exchange in these compounds.[21] Thus, it appears that the diffusional effects were unimportant in those studies, particularly as the highest temperature for which we determined the exchange rate is 25°. For larger chemical shifts, or for a given shift at a higher resonance frequency, the curves in Figure 4 for the various exchange rates are displaced upward and to the right. In this event, for given values of D and of $\Delta\omega_0$, the exchange

(50) D. W. McCall, D. C. Douglass, and E. W. Anderson, *Ber. Bunsenges. Physik. Chem.*, **67**, 336 (1963).

rate can be determined over a wider range without appreciable error from the diffusional contribution to T_2.

Acknowledgment. We wish to thank Mr. Fu-ming Chen for his assistance with a number of the calculations.

The Thermochemistry of the Gas Phase Equilibrium $I_2 + C_3H_6 \rightleftarrows C_3H_5I + HI$[1]

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Abstract: A Cary spectrophotometer, modified for use with high-temperature gas systems, has made it possible to obtain the equilibrium constant for the reaction $C_3H_6 + I_2 \rightleftarrows C_3H_5I + HI$ over the temperature range 208–300°. Taking the bond additivity[2] value $S°_{298}$(allyl iodide, g) = 77.8 ± 1 gibbs/mole, the best "third-law" fit to all the temperatures is: $\Delta H_f°_{298}$(allyl iodide, g) = 22.99 ± 0.6 kcal/mole (using $\Delta \bar{C}_p° = 1.6 \pm 1$ gibbs/mole). From a Van't Hoff plot of log K against $1/T$(°K), the following thermodynamic quantities were calculated: $\Delta H°_{527} = 8.33 \pm 0.23$ kcal/mole and $\Delta S°_{527} = -1.00 \pm 0.46$ gibbs/mole. When corrected to room temperature, these become $\Delta H°_{298} = 7.96 \pm 0.33$ kcal/mole and $\Delta S°_{298} = -1.91 \pm 0.80$ gibbs/mole. This yields "second-law" values of $\Delta H_f°_{298}$(allyl iodide, g) = 21.46 ± 0.25 kcal/mole and $S°_{298}$(allyl iodide, g) = 74.81 ± 0.80 gibbs/mole when combined with known values[3] for C_3H_6, HI, and I_2. The above values of the heat of formation both compare well with a previously measured value[4] of $\Delta H_f°_{298}$(allyl iodide, g) = 22.0 ± 3 kcal/mole and the bond additivity[2] value of $\Delta H_f°_{298} = 22.7 \pm 3$ kcal/mole, but calculation of the entropy yields agreement with the higher bond additivity figure and supports the third-law values.

By use of a spectrophotometric technique, it has been shown[5,6] that the kinetic parameters and equilibrium constants of reactions of the type $RH + I_2 \rightleftarrows RI + HI$ may be conveniently and accurately determined in the temperature range 200–400°, even though the extent of reaction is small and the equilibria are well to the left. The work presented here concerns the equilibrium constant for the case where R is the allyl radical and thus yields values for the heat of formation and entropy of allyl iodide. The following paper[7] is concerned with the kinetic parameters and mechanism of the reaction and thus the heat of formation of the allyl radical itself. In order to reduce the rate data meaningfully, it is necessary to know the equilibrium constant data presented here.

Experimental Section

1. Materials. Phillips research grade propylene and reagent grade resublimed iodine were used for the reaction studied. Matheson anhydrous hydrogen iodide and Eastman allyl iodide and isopropyl iodide, all further purified under vacuum, were used for calibration purposes (Dow Corning silicone grease was used on all stopcocks).

2. Apparatus. The apparatus has been described in detail previously.[5] The spectrophotometric sensitivity toward allyl iodide was found to be such as to permit detection of ~1 × 10^{-3} torr, *i.e.*, 5 × 10^{-8} mole/l. at the temperatures employed.

3. Procedure. The experiments were performed in a manner essentially analogous to the procedure described previously for the reaction of methane and iodine.[5] Convenient monitoring wavelengths were 500, 350, 270, 245, and 235 mμ, the 350-mμ wavelength being used once again as an optical window. The attainment of equilibrium was signified by a lack of change in absorbance after several half-lives. Since the reaction of interest is always followed by the slower reaction of propylene and hydrogen iodide to produce isopropyl iodide, in long duration equilibrium studies it was necessary to make allowances for slight absorption changes due to small concentrations of isopropyl iodide. (Since, as can be seen in the following paper,[7] the rate of reaction was always followed, it was relatively easy to determine when equilibrium had been attained.)

A further complication arises from the essentially instantaneous formation of small amounts of 1:1 adducts of iodine and propylene over the entire temperature range employed. These adducts turn out to be propylene diiodide and a molecular complex and will be called PI_2, jointly. They contribute a large absorbance at all the monitoring wavelengths, and this absorbance must be subtracted from the total absorbance in order to determine the absorbance due to allyl iodide and hydrogen iodide. The absorbance due to PI_2 could be determined at any wavelength by observing the initial instantaneous increase in absorbance at that wavelength when propylene was added to the iodine already in the vessel. Plots of this absorbance divided by the product of I_2 and propylene pressures were shown to be linear for several wavelengths and temperatures. The slopes of such plots yield a value for the product of the absorption coefficient and the equilibrium constant for the formation of PI_2 from propylene and iodine.[8] Thus, the absorbance due to PI_2 can be calculated at any pressure of I_2 and propylene.

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(1) This investigation was supported in part by a research grant (AP-00353-01) from the Air Pollution Division, Public Health Service, U. S. Department of Health, Education, and Welfare.

(2) S. W. Benson and J. H. Buss, *J. Chem. Phys.*, **29**, 546 (1958).

(3) (a) "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," American Petroleum Institute, Carnegie Press, Pittsburgh, Pa., 1953; (b) "JANAF Interim Thermochemical Tables," D. R. Stull, Ed., Dow Chemical Co., Midland, Mich., 1963.

(4) O. H. Gellner and H. A. Skinner, *J. Chem. Soc.*, 1145 (1949).

(5) D. M. Golden, R. Walsh, and S. W. Benson, *J. Am. Chem. Soc.*, **87**, 4053 (1965).

(6) R. Walsh, D. M. Golden, and S. W. Benson, *ibid.*, **88**, 650 (1966).

(7) D. M. Golden, A. S. Rodgers, and S. W. Benson, *ibid.*, **88**, 3196 (1966).

(8) At 108° where propylene diiodide is formed slowly, the spectra of the complex and the diiodide were separated. From the known value of the equilibrium constant for the diiodide,[9] values of the absorption coefficients at various wavelengths could be obtained, assuming these (in concentration units) to be independent of temperature. This permits the calculation of the contribution of the diiodide to the observed PI_2 absorbance. Such a procedure leads to the conclusion that most of the