strates, *e.g.*, nitrobenzenesulfonate, chlorobenzene-sulfonate, and particularly *m*-benzenedisulfonate, the desulfonation mechanism predominates. In fact we have found that for *m*-benzenedisulfonate, desulfonation is virtually the sole mechanism of nitration. It is interesting to note that the overall observed rate of acid loss for systems containing *m*-benzenedisulfonate

is nearly the same as that for the corresponding BS⁻ systems at low substrate concentrations, but the leveling off of the rate at higher *m*-BDS concentrations is much more pronounced. We hope that complete studies of the reactions of these substituted benzenesulfonates may help to further elucidate the mechanisms involved in nitration in acidic nitrate melts.

Mechanistic Studies of Chemical Exchange Reactions by Complete Nuclear Magnetic Resonance Line-Shape Fitting. I. General Aspects

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Contribution from the Chemistry Department, University of Waterloo, Waterloo, Ontario, Canada. Received June 17, 1972

Abstract: In any chemical exchange reaction which modifies nuclear magnetic resonance line shapes the spectrum can be computed from a set of pseudo-first-order rate constants arranged in matrix form, provided the line widths in the absence of exchange are accessible experimentally. The spectrum is a sensitive analytical tool in prescribing or eliminating possible reaction mechanisms. The rate matrix formed from the pseudo-first-order rate constants may correspond to a truncated or nontruncated exchange system. In the nontruncated cases all resonances are above the noise level of the spectrometer and in the region where frequency differences are modulated randomly by chemical exchange effects. In truncated systems contributions to line shapes occur also from resonances which are unobservable and which must therefore be included in terms of other measurable parameters in the rate matrix. The information available regarding reaction mechanism is discussed for both cases and the number of pseudo-first-order rate constants which may be independently determined is derived.

The study of chemical-exchange phenomena in modifying line shapes of nuclear magnetic resonance (nmr) spectra is highly developed both from the theoretical and experimental points of view.[2-16] At this point most applications of the technique have been accomplished in the study of hindered-rotation barriers or ring-inversion phenomena, where for the most part the mechanism of the kinetic process is either not in doubt[3,5,7,8,14-17] or resolves itself into simple alternatives.[18-20] In cases where the mechanism of the intra-

molecular process is known emphasis has been placed upon the precision of the measured rate constants and their variation with temperature, solvent, and concentration. The derived kinetic parameters such as energy, entropy, and free energy of activation have provoked a great deal of controversy[5,7,8,14,15] because the measurement of true line shapes is so difficult and different laboratories have not successfully agreed in most cases on the derived kinetic parameters. Very recently, some thorough studies have been made with a full analysis of systematic and random errors encountered in the experiment.[21-23] It is important to include all sites contributing to the exchange, variation of chemical shift and spin coupling with temperature, a careful monitoring of the Lorentzian line shape of an included line-shape standard, and a well defined temperature measurement, and to satisfy all conditions inherent in the slow passage Bloch equations.[24] If sufficient care is exercised in the experiment and the analysis, a full line-shape fit should deviate less than 1.5% over 100 data points in the spectrum, chosen so as to emphasize possible deviations.

Now that the experimental conditions can be reproduced in cases where the mechanism of a chemical process is known the present work seeks to investigate the power of the technique in deciding the mechanism of a chemical reaction in cases where this is unknown. In

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principle the simple first-order multisite exchange theory[10-13] has the power to distinguish which sites are contributing to the overall exchange mechanism and what are the values of the pseudo-first-order rate constants.[21-23] This information can lead to elimination of possible mechanistic schemes as will be shown. Previous studies of chemical reaction mechanisms were accomplished by approximate methods of line-shape analysis. Among other reactions the protolysis kinetics of water and methylammonium ions have been studied by Meiboom, Grunwald, and coworkers[25-27] and halogen exchange reactions by O'Reilly and coworkers.[28] The general theoretical approach to the study of mechanism will be outlined in this paper and a practical example described in a second article to follow.

Theory

General line-shape characteristics for chemical exchange are usually concisely described through a square-rate matrix, $\mathbf{K}$.[6,10-13] This matrix appears as a part of $\mathbf{\Lambda}$ in the complex line-shape function $G(x)$ given by

$$G(x) = A\mathbf{I} \cdot \mathbf{S} \cdot [\mathbf{\Lambda} + (R_2 + ix)\mathbf{I}] \cdot {}^{-1}\mathbf{S}^{-1} \cdot \mathbf{P} \qquad (1)$$

through the relation

$$\mathbf{\Lambda} = \mathbf{S}^{-1} \cdot [\mathbf{K} - i\mathbf{\Omega}] \cdot \mathbf{S} \qquad (2)$$

where $\mathbf{\Omega}$ is a diagonal matrix of the spin-site Larmor frequencies, $i = \sqrt{-1}$, $\mathbf{S}$ is the matrix which diagonalizes $[\mathbf{K} - i\mathbf{\Omega}]$ to give $\mathbf{\Lambda}$, $\mathbf{I}$ is a transition intensity row vector, $\mathbf{I}$ is a unit matrix, $\mathbf{P}$ is a spin-site population column vector, R_2 is the transverse relaxation rate including instrumental effects, x is the independent frequency variable, and A is a constant.

The dimension of $\mathbf{K}$ depends on the number of sites[29] involved and being considered in the overall exchange process for a system as will be discussed below.

To investigate an exchange reaction whose mechanism is unknown, an exchange modulated nmr spectrum can always be studied by a complete line-shape fit for the system and the exchange effects be extracted as pseudo-first-order rate constants from the rate matrix $\mathbf{K}$. An acceptable mechanism is then one which will provide a rate law which, in turn, formulates pseudo-first-order rate constants consistent with those derived experimentally. Thus the determination of reaction mechanism is much simplified and generalized through the manipulation of the rate matrix $\mathbf{K}$ of pseudo-first-order rate constants.

Closed or Nontruncated Systems

A closed system here is defined as one in which the exchange modulated resonances of the nuclei under investigation are all included and observable in all possible environments within the domain of the nuclear transfer process. It has been shown[13,23] that such effects of chemical exchange can always be expressed in terms of pseudo-first-order rate constants irrespective

of the mechanism of the exchange reactions. In this case, exchange between n sites can be described completely by not more than $n(n - 1)/2$ pseudo-first-order rate constants. The number $n(n - 1)/2$ is equal to the number of off-diagonal elements in the lower or upper (but not both) triangular part of the $n \times n$ rate matrix $\mathbf{K}$. That the number of pseudo-first-order rate constants required is half the total number $n(n - 1)$ of off-diagonal elements is because of the relations

$$K_{ij} \cdot P_j = K_{ji} \cdot P_i \qquad (3)$$

between one off-diagonal element and its transpose via the site population parameters $\mathbf{P}$'s and that the diagonal elements are given by eq 4 as required by detailed balancing.

$$K_{ii} = -\sum_{j(\neq i) = 1}^{n} K_{ji} \qquad (4)$$

ancing. The number of pseudo-first-order rate constants can, in fact, be further reduced from the maximum by using additional information concerning the exchange process, such as chemically unlikely routes of exchange, multiplet structure, and symmetry.

Truncated Systems

A truncated system in connection with chemical exchange is one in which one or more species, being present in very low relative concentrations, are not observable and have to be neglected in intensity consideration. Such systems essentially fall into one of two categories.

(a) With species of low concentration and short life time. Low concentration and short lifetime of the unobservable species give, in effect, no contribution to the line widths of the observable resonances. The species then passes out of the domain of nmr observation by T_2 effects and must be considered an unstable intermediate in the same sense as a transition complex. Such systems behave similarly to the nontruncated systems.

(b) With species of low concentration but intermediate lifetime. The exchange effects of the unobservable species in this case are appreciable and can be accounted for fully in terms of the observable species linked together by them. It is systems in the latter category that we shall treat specifically as truncated systems; and we assume such conditions are complied with in the following example.

In a reaction between A and B, collisions between the molecules bring them up to their excited states A* and B* and the activated species then react to give C, namely

$$A + B \underset{a_{-1}}{\overset{a_1}{\rightleftharpoons}} A^* + B^* \underset{a_{-2}}{\overset{a_2}{\rightleftharpoons}} C \qquad (5)$$
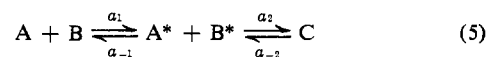
where the a's are the specific rate constants as shown. The rate of formation of A or B is equal to $a_{-1}[A^*][B^*]$ the activity coefficients being assumed to be 1. $[A^*]$ and $[B^*]$ are equilibrium concentrations of the species A* and B*. They are usually very small and cannot be determined by nmr methods. Making use of the dynamic equilibrium nature of the reaction $a_{-1}[A^*][B^*]$ is replaced by $a_1[A][B]$, i.e., rate of formation of A or B equals $a_1[A][B]$ which equals $K_1[C]$, where K_1 is the pseudo-first-order rate constant of formation of A or B indirectly from C and is given by

$$K_1 = a_1[A][B]/[C] \qquad (6)$$

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(29) The term "site" here is synonymous with "individual Larmor frequency" or "spectral line."

where the equilibrium concentrations [A], [B], and [C] are all measurable.

Similarly, the rate of formation of C equals $a_2[A^*][B^*]$ $= a_{-2}[C] = K_2[A] + K_3[B]$, where K_2 and K_3 are pseudo-first-order rate constants given by

$$K_2 = \alpha a_{-2}([C]/[A]) \qquad (7)$$

and

$$K_3 = (1 - \alpha)a_{-2}([C]/[B]) \qquad (8)$$

α is equal to $^1/_2$ if $[A^*]/[A] = [B^*]/[B]$ and is unfortunately indeterminate otherwise for a truncated system. This will be discussed in greater detail in the next section.

Also for a truncated system, detailed balancing no longer applies because of the negligence of the unobservable species in intensity considerations. Consequently eq 3 and 4 of the previous section no longer hold and the diagonal elements of the rate matrix $\mathbf{K}$ are generally given by

$$K_{ii} = -\sum_{j(\neq i)=1}^{n} K_{ij} \times \frac{P_j}{P_i} \qquad (9)$$

Indeed eq 9 is the most general form for the diagonal element K_{ii}. It applies to both truncated or nontruncated systems. In a nontruncated system, eq 9 together with eq 3 gives eq 4 as a special case.

Possibility of Independent Determination of Pseudo-First-Order Rate Constants

It is not always possible to determine independently all the pseudo-first-order rate constants. The criterion for independent determination can, however, be visualized by consideration in the slow exchange region. It is well known[6,10-13] that in the slow exchange limit, the full width at half-maximum of a spectral line $(\Delta \nu_i^{(e)})$ due to exchange is given by the diagonal element of the rate matrix, corresponding to that spectral transition, namely

$$\pi \Delta \nu_i^{(e)} = |K_{ii}| \qquad (10)$$

For a n-site exchange problem the condition for independent determination of all the pseudo-first-order rate constants is

$$n + \beta m \geqslant m \qquad (11)$$

where $\beta = 0$ for truncated and $= ^1/_2$ for nontruncated systems and m is the number of nonzero off-diagonal elements in the rate matrix. Equation 11 simply means that the number of equations $(n + \beta m)$ has to be greater than or equal to m in order to determine all the m unknowns separately in a set of simultaneous equations; and $(n + \beta m)$ is obtained from all the conditions in eq 3 and 10. Thus for a problem with no other simplifying information $m = n^2 - n$. If a system is truncated, $\beta = 0$; therefore

$$n \geqslant n^2 - n$$
$$n^2 \leqslant 2n \qquad (12)$$
$$n \leqslant 2$$

For a nontruncated system, $\beta = ^1/_2$; therefore $n + ^1/_2(n^2 - n) \geqslant n^2 - n$; i.e.

$$n \leqslant 3 \qquad (13)$$

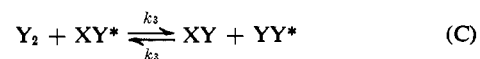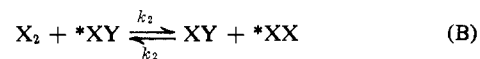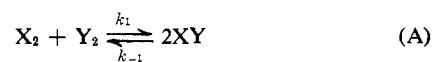For exchange problems involving more sites than two

or three other information has to be known in order to determine some or all of the pseudo-first-order rate constants separately; otherwise only sums of two or more of such rate constants can be obtained.

Relation between Pseudo-First-Order Rates and a Specific Kinetic Process

The rate law of a kinetic process depends on the actual mechanism involved in the process. For a proposed mechanism a rate law can be formulated from the rate-determining steps and, in turn, pseudo-first-order rate constants can be expressed as functions of specific rate constants of the rate-determining steps, concentrations of reacting species, and activity coefficients if they are appreciably different from 1. In the following an example is shown to formulate pseudo-first-order rate constants from a proposed mechanism for a hypothetical process

$$X_2 + Y_2 \rightleftharpoons 2XY$$
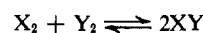
For simplicity of expression, all activity coefficients are assumed to be 1. Let us simply assume the mechanism to be a number of bimolecular reactions and formulate a rate law on that basis. First, we write down all the rate-determining reactions that will affect the nmr spectrum. They are

$$X_2 + Y_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2XY \qquad (A)$$

$$X_2 + {}^*XY \underset{k_2}{\overset{k_2}{\rightleftharpoons}} XY + {}^*XX \qquad (B)$$

$$Y_2 + XY^* \underset{k_3}{\overset{k_3}{\rightleftharpoons}} XY + YY^* \qquad (C)$$

Reactions B and C do not change the equilibrium concentrations but affect the nmr spectrum because X_2 or Y_2 becomes XY and XY becomes X_2 or Y_2 in the exchange process. The * labels are added for clarity. In this system there are three exchanging species and they are all observable. The rate matrix $\mathbf{K}$ will be a 3×3 one with a maximum of three pseudo-first-order rate constants (K_1, K_2, and K_3), namely

$$\mathbf{K} = \begin{bmatrix} D_1 & -K_1' & -K_3' \\ -K_1 & D_2 & -K_2' \\ -K_3 & -K_2 & D_3 \end{bmatrix} \qquad (14)$$

in the representation of X_2, XY, and Y_2. The K's are related to the K''s by eq 3.

Then considering the rate of formation of the XY species we have

$$d[X_2]/dt = k_{-1}[XY]^2 + 2k_2[X_2][XY] =$$
$$(k_{-1}[XY] + 2k_2[X_2])[XY] =$$
$$K_1'[XY] + K_3'[Y_2] \qquad (15)$$

$$d[XY]/dt = 2k_1[X_2][Y_2] + 2k_2[X_2][XY] +$$
$$2k_3[Y_2][XY] = (k_1[Y_2] + 2k_2[XY])[X_2] +$$
$$(k_1[X_2] + 2k_3[XY])[Y_2] = K_1[X_2] + K_2'[Y_2] \qquad (16)$$

$$d[Y_2]/dt = k_{-1}[XY]^2 + 2k_3[XY][Y_2] =$$
$$(k_{-1}[XY] + 2k_3[Y_2])[XY] = K_2[XY] + K_3[X_2] \qquad (17)$$

From eq 15-17

$$K_1 = K_1'([XY]/[X_2]) = k_1[Y_2] + 2k_2[XY] \qquad (18)$$

$$K_2 = K_2'([Y_2]/[XY]) = k_{-1}[XY] + 2k_3[Y_2] \quad (19)$$

$$K_3 = K_3' = 0 \quad (20)$$

In this case all the pseudo-first-order rate constants can be individually determined, condition 11 being of course satisfied. The specific rate constants k_1, k_{-1}, k_2, and k_3 can in turn be solved for by varying the relative concentrations of the reactants.

Spin-Multiplet Structures

Questions always arise in chemical exchange problems involving spin coupled systems whether each component of a spin multiplet can be considered as an independent site. Usually when spin coupling is modulated by exchange without being interrupted by breaking of bonds between scalar coupled spins, the multiplet structures can always be considered as independent sites and if such bonds are broken whether spin multiplets can be considered as independent sites depends on whether there is spin coherence during the exchange or not. If spin orientation is conserved, multiplets then behave as independent sites. In fact if the multiplet independent site situation is established, the number of pseudo-first-order rate constants can be considerably reduced by the uniformity of the multiplet structure.

Discussion and Conclusion

The nuclear magnetic resonance (nmr) spectrum of a reacting mixture of compounds contains much more information of a quantitative analytical nature than the more classical methods of studying chemical kinetics. The measurement and analysis, for example, of a gas pressure or the record of the intensity of an ultraviolet absorption with time are very selective pieces of information and tell us very little about the reaction except the rate of growth or decay of one individual component with time. It is well known that nmr methods measure reaction rates at equilibrium and can also be used to follow the progress of reactions in nonequilibrium situations. The limitation of the method is the time window of the inverse frequency differences which are modulated by the exchange in the case where reactions are taking place at equilibrium. We have shown in this paper, the total information that can be derived from a complete line-shape fit approach to first-order spectra,[30] before an appeal to the chemical situation must be invoked to solve a reaction mechanism. An example of the application to a specific reaction is given in the following article.

(30) Second order effects present no additional complication to this general analytical method though a spectrum with such effects will be more complex.

Mechanistic Studies of Chemical Exchange Reactions by Complete Nuclear Magnetic Resonance Line-Shape Fitting. II. 15-Site Halogen Exchange in Binary Mixtures of Dimethyltin Dihalides

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Abstract: The unsymmetric halogen exchange reactions of mixed dimethyltin dihalides in toluene solutions have velocities suitable for study by complete line-shape fit methods of exchange-broadened proton magnetic resonance spectra. The problem of modulation of 15 Larmor frequencies can be reduced to five equivalent sets of three, with no exchange between these five groups. In the 3 × 3 site rate matrix, tolerable line-shape fits can be obtained at several concentrations with only two independent pseudo-first-order rate constants but the linear relationship to proposed chemical rate constants is not consistent for a nontruncated system. Use of three independent pseudo-first-order rate constants does not improve the fit to experimental data and always renders the third pseudo-first-order rate constant near zero in magnitude. An optimum fit to experimental line shapes, at all relative concentrations, to within 1% deviation over at least 70 data points is obtained by the use of four independent pseudo-first-order rate constants in a truncated system. The reactions are inhibited by molecular iodine and accelerated by halide ions and a reaction mechanism involving ionization steps and unsymmetric reassociation and exchange of halogen ions with molecules is proposed. The concentration of ions is extremely low but their rate-determining control is properly demonstrated by adding iodine and halide ions in the order of 10^{-3}–10^{-2} M concentrations. The influence of iodine on the pseudo-first-order rate constants can be accounted for in terms of rate expressions derived from the proposed mechanism and the changes can be shown to be approximately proportional to the inverse square root of the concentration of molecular iodine which removes halide ions to form the trihalide complex ions.

Previous applications of nmr in chemical-exchange studies have mostly been directed to determination of rates in kinetic processes in which the mechanism is either known[2-8] or resolves into simple alternatives.[9-11] The few studies made to date on chemical reaction

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