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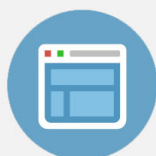
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Study of Moderately Rapid Chemical Exchange Reactions by Means of Nuclear Magnetic Double Resonance

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A nuclear magnetic double-resonance method for the determination of chemical exchange rates has been developed. The method is applicable to systems in which a nuclear spin is reversibly transferred between two nonequivalent sites, *A* and *B*. The lifetime (τ_A) and spin-lattice relaxation time (T_{1A}) in Site *A* are obtained through the study of the decay to a new equilibrium value of Signal *A* upon the sudden saturation of Signal *B*. The converse experiment permits the determination of τ_B and T_{1B} . A number of data for cross checks are furthermore obtained through the study of the recovery of the signals upon the release of various combinations of saturating rf fields.

A simple theory based on the Bloch equations as modified by McConnell to incorporate the effects of chemical exchange is given. Experimental results on the hydroxyl proton exchange in the system salicylaldehyde and 2-hydroxyacetophenone are well described by this simple theory.

The present method, which can readily be extended to systems with several sites, offers a complement to the Gutowsky-Saika single-resonance method and is particularly suited to the study of exchange rates slower than those accessible by the single-resonance method.

1. INTRODUCTION

THE study of rapid and moderately rapid chemical reactions¹ usually requires physical methods to follow the reaction.² Nuclear magnetic resonance spectroscopy is among such methods extensively used for studying rate processes, in particular for the investigation of proton exchange reactions and other rate processes such as restricted rotation.³⁻⁵

With high-resolution nuclear magnetic resonance (NMR) techniques the usual procedure introduced by Gutowsky and Saika⁶ is to deduce the time constants involved from the signal shapes in the NMR spectra³⁻⁵ (cf., however, Refs. 7 and 8). With the presently available techniques it is difficult to extend this method to lifetimes exceeding approximately a second. This is due to the problem of estimating what the true line shapes of the resonances for the nuclei undergoing chemical exchange would have been in the absence of chemical exchange. In addition, the time ranges accessible in a

given system depend on the line separations in the NMR spectra of the exchangeable nuclei. If these separations are large, further limitations are set on the lengths of the lifetimes obtainable with this method.

With the innovation⁹⁻¹² of the homonuclear¹³ double-resonance technique a simple dynamic method for the study of nuclear exchange rates has become feasible. In the present paper a first account of attempts to exploit this possibility is reported.

2. METHOD

Intuitively one expects that when a nuclear species *X* is reversibly transferred between two nonequivalent sites *A* and *B* a disturbance of the magnetization in Site *B* would be detectable at Site *A*, provided that the spin-lattice relaxation time (T_{1A}) in Site *A* is not negligible compared with the lifetime (τ_A) of *X* in Site *A*.

The correctness of this idea may be corroborated by the application to this problem of the modified Bloch equations, as given by McConnell for the systems under going chemical exchange.¹⁴ To be specific, let us

¹ The definition of these terms is somewhat arbitrary. In the following the term moderately rapid is applied to reactions involving lifetimes of the reacting species of the order of 0.1–10 sec.

² M. Eigen and J. S. Johnson, *Ann. Rev. Phys. Chem.* **11**, 307 (1960).

³ J. A. Pople, W. G. Schneider, and H. J. Bernstein, *High Resolution Nuclear Magnetic Resonance* (McGraw-Hill Book Company, Inc., New York, 1959), Chap. 10.

⁴ H. Strehlow, *Magnetische Kernresonanz und chemische Struktur* (D. Steinkopff Verlag, Darmstadt, Germany, 1962), Chap. III.3.

⁵ A. Abragam, *The Principles of Nuclear Magnetism* (Oxford University Press, New York, 1961).

⁶ H. S. Gutowsky and A. Saika, *J. Chem. Phys.* **21**, 1688 (1953).

⁷ H. M. McConnell and D. D. Thompson, *J. Chem. Phys.* **26**, 958 (1957).

⁸ H. M. McConnell and D. D. Thompson, *J. Chem. Phys.* **31**, 85 (1959).

⁹ R. Kaiser, *Rev. Sci. Instr.* **31**, 963 (1960).

¹⁰ D. W. Turner, *J. Chem. Soc.* **1962**, 847.

¹¹ R. Freeman, *Mol. Phys.* **3**, 435 (1960).

¹² L. R. Johnson, *Technical Information Bulletin*, Varian Associates, Palo Alto, California (1962), Vol. III, No. 3.

¹³ W. A. Anderson, *Phys. Rev.* **102**, 151 (1956).

¹⁴ H. M. McConnell, *J. Chem. Phys.* **28**, 430 (1958). In this original paper McConnell indicated the applicability of his equations to "experiments with more than one oscillatory rf field." In the following equations the presence of two rf fields is not explicitly evident in the form of the equations; this is due to the fact that we consider only limiting cases where the rf fields are either sufficiently strong to cause complete saturation or so weak as to cause negligible saturation.

consider an experiment in which the magnetization of X in Site B is destroyed by saturation with strong irradiation at a frequency corresponding to the resonance B while the resonance of X in A is investigated with a weak rf field. (This will be possible only if the lifetimes τ_A and τ_B are sufficiently long to give well-separated resonances for X in A and B , respectively.)

The time dependence of the z magnetization of X in A (M_z^A) is then governed by the differential equation

$$dM_z^A/dt = (M_0^A/T_{1A}) - (M_z^A/\tau_{1A}), \quad (1)$$

where M_0^A is the equilibrium z magnetization of the X nuclei in A and τ_{1A} is given by

$$1/\tau_{1A} = 1/\tau_A + 1/T_{1A}. \quad (2)$$

Equation (1) is identical with Eq. (8) in Ref. 14 except for the omission of the terms M_z^B/τ_B and $\omega_1 v_A$. The former term may be dropped since we assume *complete* saturation of the B signal and the latter may be neglected when the rf field (H_1) centered at A is sufficiently weak to cause *negligible* saturation. In this case the strength of the signal A is proportional to the value of M_z^A provided that the signal is observed under conditions approximating those of slow passage,¹⁵ as discussed below.

The linewidth in the slow passage spectrum is given by $1/\tau_{2A}$, where τ_{2A} is defined by

$$1/\tau_{2A} = 1/T_{2A} + 1/\tau_A, \quad (3)$$

where T_{2A} is the inverse linewidth of Signal A in the absence of the exchange of X between A and B .

Then, if

$$\tau_{2A} \ll \tau_{1A}, \quad (4a)$$

which, in general, will be equivalent to

$$T_{2A} \ll \tau_A, \quad (4b)$$

it will be possible to obtain several slow passage recordings of signal A during a time of approximately τ_{1A} . These latter conditions [Eqs. (4a) and (4b)] can usually be fulfilled by deliberately introducing some extra inhomogeneity in the magnetic field. If Signal A is recorded in a time which is long compared to τ_{2A} and short compared to τ_{1A} then the absorption mode signal will be given by the instantaneous value of v_A where v_A is obtained from the steady-state solutions ($dv_A/dt = du_A/dt = 0$) of the Bloch equations for the transverse magnetization [Eqs. (4) and (6) of Ref. 14]. In the present case

$$(du_A/dt) + \Delta\omega_A v_A = -u_A/\tau_{2A}, \quad (5)$$

and

$$(dv_A/dt) - \Delta\omega_A u_A = -(v_A/\tau_{2A}) - \omega_1 M_z^A. \quad (6)$$

Here u and v are the rotating components of the

transverse magnetization in Site A , $\Delta\omega_A$ is the difference between the Larmor (angular) frequency for X in Site A and the applied observing rf (angular) frequency, and ω_1 is equal to γH_1 .

In Eqs. (5) and (6) the terms¹⁴ u_B/τ_B and v_B/τ_B have again been omitted since Signal B is assumed to be *completely* saturated. They may be omitted even when u_B and v_B are nonvanishing provided that Eq. (4b) is applicable. This latter statement may be inferred from Eqs. (4a) and (4b) and from the condition applicable to any two-component system

$$(q \equiv) \tau_A/\tau_B = M_0^A/M_0^B. \quad (7)$$

So, if the signal B is irradiated,

$$u_B/\tau_B \leq u_A/\tau_A \ll u_A/T_{2A}, \quad (8a)$$

and

$$v_B/\tau_B \leq v_A/\tau_A \ll v_A/T_{2A}. \quad (8b)$$

As is well known, the signal intensity corresponding to the steady-state solution of v_A is proportional to the value of M_z^A . Therefore, when Conditions (4a) and (4b) are fulfilled, the time dependence of M_z^A may be followed by studying successive absorption mode signals of the A resonance.

We consider the time dependence of M_z^A in four different types of experiment (I-IV). Case I, the decay of M_z^A upon the instantaneous saturation of Signal B ; Case II, the recovery of Signal A upon the removal of the saturating field at Resonance B ; Case III, the recovery of Signal A after the release of a prolonged saturation of Signal A ; Case IV, the recovery of Signal A after complete saturation of Signals A and B . Analogous experiments can be performed in which the roles of A and B are interchanged.

It should, however, be pointed out that Eq. (1) is only applicable to Case I in which M_z^B is omitted and that in Cases II-IV, the time dependences of M_z^A and M_z^B are governed by a pair of coupled differential equations. We return to these cases after a discussion of the simple Case I.

Case I. Decay of Signal A upon the Saturation of Signal B

If the saturation of the resonance of X in B can be assumed to occur instantaneously at the time $t=0$, when the z magnetization M_z^A equals M_0^A , the decay of M_z^A is given by the solution of Eq. (1):

$$M_z^A = M_0^A [\tau_{1A}/\tau_A \exp(-t/\tau_{1A}) + (\tau_{1A}/T_{1A})]. \quad (9)$$

From Eq. (9) it follows that the new equilibrium value of M_z^A is

$$M_z^A(t \rightarrow \infty) = M_0^A (\tau_{1A}/T_{1A}), \quad (10)$$

and that M_z^A will attain its new equilibrium value through an exponential decay with the time constant τ_{1A} . The ratio between the initial and final values of

¹⁵ B. A. Jacobson and R. K. Wangsness, Phys. Rev. **73**, 942 (1948).

M_z^A gives the quotient T_{1A}/τ_{1A} and thus by plotting the value of $\log [M_z^A(t) - M_z^A(t \rightarrow \infty)]$ against t , one obtains a straight line, the slope of which gives τ_{1A} . From the known values of T_{1A}/τ_{1A} and τ_{1A} the values of τ_A and T_{1A} are obtained from Eq. (2).

The reverse experiment involving the decay of Signal B upon the sudden saturation of Signal A gives the values of the corresponding parameters τ_B and T_{1B} . The ratio of τ_A and τ_B gives the quantity q defined in Eq. (7). q can also be obtained through integration of Signals A and B in the single-resonance spectrum and may be used as a check of the results in the dynamic experiments. Further checks may be obtained from a study of the recovery after the saturations and thus the parameters are well determined.

Cases II to IV. General Considerations

In these cases the following equations apply:

$$\frac{dM_z^A}{dt} + \frac{M_z^A}{\tau_{1A}} - \frac{M_z^B}{\tau_B} = \frac{M_0^A}{T_{1A}}, \quad (11)$$

$$\frac{dM_z^B}{dt} + \frac{M_z^B}{\tau_{1B}} - \frac{M_z^A}{\tau_A} = \frac{M_0^B}{T_{1B}}. \quad (12)$$

Equations (11) and (12) are the same as Eqs. (8) and (9) of Ref. 14 in the case of negligible saturation.

The complete solutions of Eqs. (11) and (12) are

$$M_z^A = M_0^A + C_1 \exp(-\lambda_1 t) + C_2 \exp(-\lambda_2 t), \quad (13)$$

and

$$M_z^B = M_0^B + C_1 \left[\frac{1}{\tau_{1A}} - \lambda_1 \right] \tau_B \exp(-\lambda_1 t) + C_2 \left[\frac{1}{\tau_{1A}} - \lambda_2 \right] \tau_B \exp(-\lambda_2 t), \quad (14)$$

where C_1 and C_2 are determined by the initial conditions and λ_1 and λ_2 are the roots of the characteristic equation

$$\begin{vmatrix} \left(\frac{1}{\tau_{1A}} - \lambda \right) & -\frac{1}{\tau_B} \\ -\frac{1}{\tau_A} & \left(\frac{1}{\tau_{1B}} - \lambda \right) \end{vmatrix} = 0. \quad (15)$$

From (13) and (14) it follows that the time dependences of M_z^A and M_z^B are not in general, determined by a single time constant. However, if λ_1/λ_2 is appreciably different from unity,¹⁶ one may be able to deduce at least one of the time constants involved.

In certain special cases rather simple expressions may be obtained for the roots λ_1 and λ_2 .

Thus, in the limit of very long lifetime in one of the sites, say A , i.e., $\tau_A \gg T_{1A}$, one obtains

$$\lambda_1 = 1/\tau_{1B}, \quad (16a)$$

$$\lambda_2 = 1/T_{1A}. \quad (16b)$$

¹⁶ It is readily seen that both λ_1 and λ_2 are always positive.

In the limit of very slow exchange when in addition $\tau_B \gg T_{1B}$, they go

$$\lambda_1 = 1/T_{1B} \quad (17a)$$

$$\lambda_2 = 1/T_{1A} \quad (17b)$$

as might be expected for physical reasons.

In the limit of very fast exchange, $\tau_A \ll T_{1A}$ and $\tau_B \ll T_{1B}$, one obtains

$$\lambda_1 = 1/\tau_A + 1/\tau_B, \quad (18a)$$

$$\lambda_2 = (P_A/T_{1A}) + (P_B/T_{1B}), \quad (18b)$$

where

$$P_A = \tau_A/(\tau_A + \tau_B) \quad \text{and} \quad P_B = \tau_B/(\tau_A + \tau_B).$$

Case II. Recovery of Signal A upon the Removal of the Saturating Field at B

The initial conditions are $M_z^B = 0$ and according to Eq. (10) $M_z^A = M_0^A (\tau_{1A}/T_{1A})$ at $t = 0$.

The coefficients C_1 and C_2 in Eqs. (13) and (14) are then given by

$$C_1 = M_0^A [\lambda_2 (T_{1A} - \tau_{1A}) / (\lambda_1 - \lambda_2) T_{1A}] \quad (19)$$

and

$$C_2 = M_0^A [\lambda_1 (T_{1A} - \tau_{1A}) / (\lambda_2 - \lambda_1) T_{1A}]. \quad (20)$$

Since in this case $C_1/C_2 = -\lambda_2/\lambda_1$, one may infer that the recovery of signal A will be virtually exponential if λ_2/λ_1 differs appreciably from unity [cf. Eq. (13)].

Case III. Recovery of Signal A after Prolonged Saturation of Signal A

The initial conditions are $M_z^A = 0$ and $M_z^B = M_0^B (\tau_{1B}/T_{1B})$ in symmetry with the Case II. It should be noted that Eqs. (8a) and (8b) are not strictly applicable in the initial stage of the recovery since u_A and v_A are both zero at $t = 0$. Therefore the intensity of signal A is not accurately represented by Eq. (13) in the *initial* stage.

The coefficients C_1 and C_2 in the present case are given by

$$C_1 = M_0^A \frac{1 - \lambda_2 T_{1A} + (\tau_B/\tau_A) [T_{1A}/(\tau_B + T_{1B})]}{(\lambda_2 - \lambda_1) T_{1A}}, \quad (21)$$

$$C_2 = M_0^A \frac{1 - \lambda_1 T_{1A} + (\tau_B/\tau_A) [T_{1A}/(\tau_B + T_{1B})]}{(\lambda_1 - \lambda_2) T_{1A}}. \quad (22)$$

From symmetry considerations it follows that $(1/\tau_{1A} - \lambda_1)\tau_B C_1$ should give the coefficient C_1 of Case II except for the interchange of the indices A for B . In the same way, $(1/\tau_{1A} - \lambda_2)\tau_B C_2$ should give the coefficient C_2 of Case II with the roles of A and B interchanged. This may also be shown with some straightforward but tedious algebra.

In the present case the conditions for a virtually

exponential recovery of Signal *A* are not so readily seen as in Case II.

Case IV. Recovery of Signal *A* after Saturation of both Signals *A* and *B*

The initial conditions are very simple, $M_z^A=0$ and $M_z^B=0$ at $t=0$, the coefficients C_1 and C_2 of Eqs. (13) and (14) then read as

$$C_1 = M_0^A(1 - \lambda_2 T_{1A}) / (\lambda_2 - \lambda_1) T_{1A}, \quad (23)$$

and

$$C_2 = M_0^A(1 - \lambda_1 T_{1A}) / (\lambda_1 - \lambda_2) T_{1A}. \quad (24)$$

Since

$$C_1/C_2 = -(1 - \lambda_2 T_{1A}) / (1 - \lambda_1 T_{1A}),$$

it follows that the recovery will be virtually exponential provided that λ_1/λ_2 differs appreciably from unity and λ_1 or λ_2 is large compared to $1/T_{1A}$.

The recovery will also be virtually exponential if $\tau_A \gg T_{1A}$ since it follows from Eq. (16) that C_1 will be negligibly small and the recovery of signal *A* will be dependent only on T_{1A} as might be expected for physical reasons.

On comparison of Eqs. (21) and (22) with Eqs. (23) and (24) one finds that Case III is equivalent to the present case if $\tau_B \ll \tau_A$ or $T_{1B} \gg T_{1A}$.

3. EXPERIMENTAL PROCEDURE

The chemical shifts and the relative intensities of the pertinent signals in the samples used were measured on a Varian Associates A 60 spectrometer.

The double-resonance experiments were performed with a Varian Associates Model V 4300 B (DP 60) spectrometer operating at a radio frequency of 60.336 Mc/sec. The signals were recorded employing phase sensitive detection by operating the Varian V 3521 integrator in the lower sideband mode.¹² The strong rf field was obtained by af modulation of the magnetic field (H_0) using a Philips model GM 2505 B audio oscillator. The modulation amplitude was chosen sufficiently large to ensure complete saturation but small enough not to reduce the amplitude of the weak (observing) rf field.

The modulation frequency was measured with a Hewlett-Packard Model 5512 A electronic counter; however the frequency settings were not very critical owing to the extent of the sweep widths used.

The spectra were studied by repeated scanning of the magnetic field with the phantastron sweep of the spectrometer. A high repetition rate (at least one run per second) was used and the sweep width was about twice the width of the signal.

In the sample studied, the relaxation times were considerably longer than one second. With shorter relaxation times a higher sweep repetition rate would be required in order to prevent recovery of the mag-

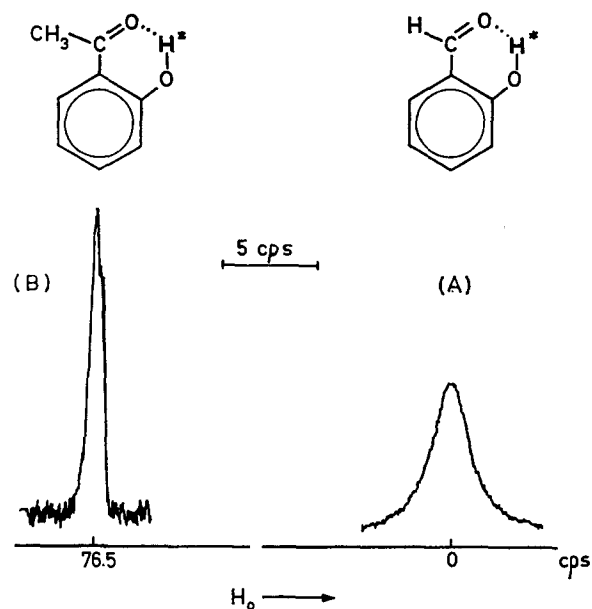


FIG. 1. The hydroxyl proton signals in the 60-Mc/sec NMR spectrum for a mixture (5.65:1) of salicylaldehyde (*A*) and 2-hydroxyacetophenone (*B*) containing a small amount of acetic acid. Signal *B* is recorded with a gain 3.15 times that of Signal *A*.

netization due to relaxation between the successive sweeps.

In order to approximate slow passage conditions at these high sweep rates the resolution was deliberately reduced by using nonspinning samples and mis-adjusting the field homogeneity until wiggles did not distort the spectra. Since a good signal-to-noise ratio is desirable, it is fortunate that one may avoid the microphonic noise that usually accompanies sample spinning. The filter bandwidth of the phase-sensitive detector was usually set at 5 cps.

The intensities of the signals in these double-resonance experiments were obtained as peak heights on a Sanborn Model 151 recorder.

4. MATERIALS

In this first exploratory study we have investigated a two-component system in which the proton exchange is known to be moderately rapid.¹⁷ Thus, in the hydroxyl band of 2-hydroxyacetophenone, a splitting of less than 0.5 cps caused by the coupling between the hydroxyl proton and the ring proton in the 4 position is found (cf., the analogous hydroxyl coupling observed in methyl salicylate).¹⁸ This splitting is also discernible in mixtures of 2-hydroxyacetophenone in various alcohols. Thus the average time that a proton remains attached to the phenolic oxygen cannot be appreciably smaller than $(0.5 \cdot 2\pi)^{-1} = 0.3$ sec.

In a mixture of 2-hydroxyacetophenone and salicyl-

¹⁷ S. Forsén and B. Åkermark (unpublished results).

¹⁸ R. Freeman, N. S. Bhacca, and C. A. Reilly, *J. Chem. Phys.* **38**, 293 (1963).

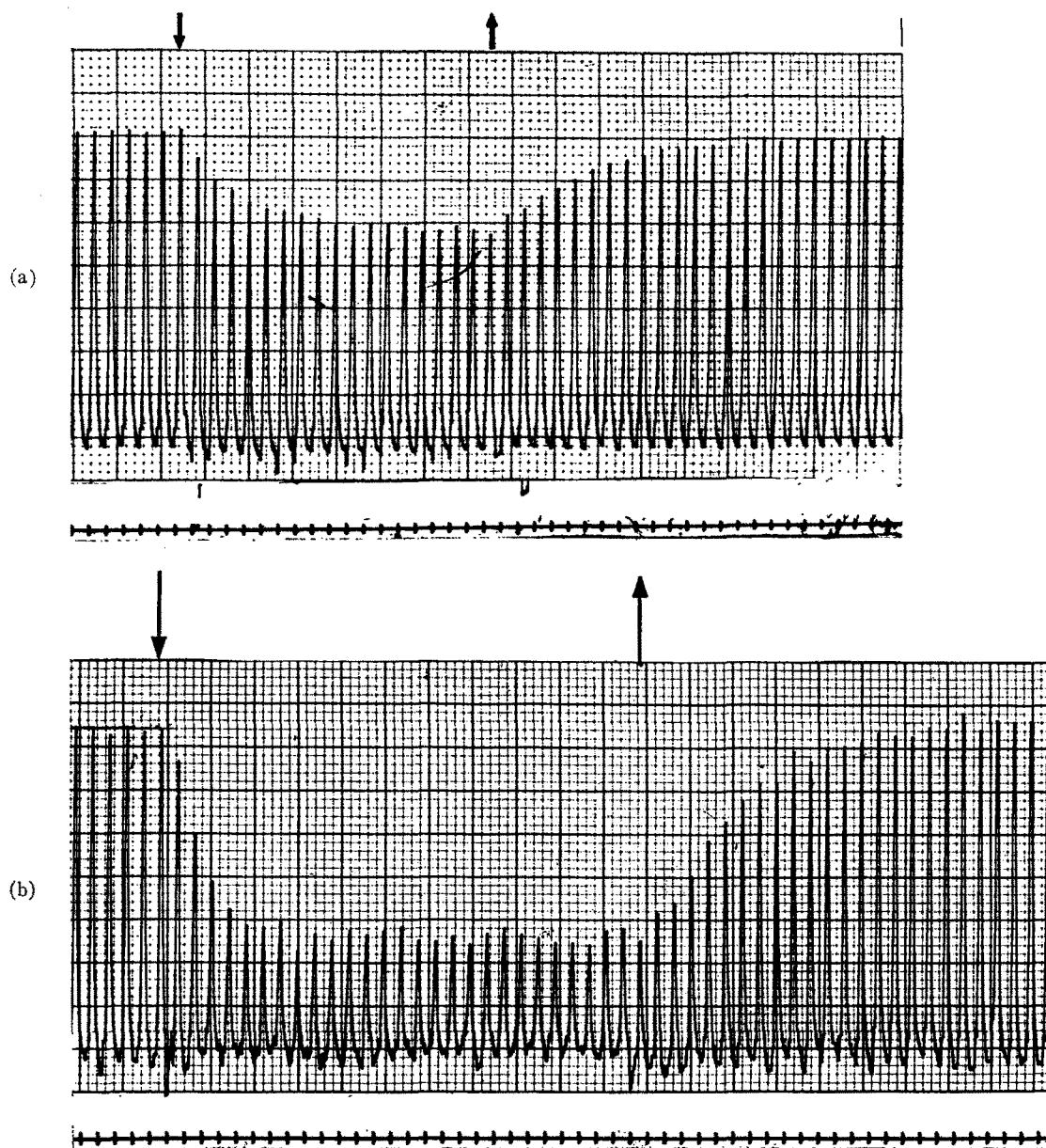


FIG. 2. The decay and recovery of the NMR signal intensities (Cases I and II). The arrows pointing downward (\downarrow) indicate the moment when the saturating rf field is turned on and the arrows pointing upward (\uparrow) indicate the moment when the saturating rf field is turned off. The markers in the lower part of the figures are second intervals. (a) The decay to a new equilibrium value of the hydroxyl signal *A* upon the sudden saturation of the hydroxyl signal *B* and its progressive recovery upon the instantaneous removal of the saturating rf field at *B*, (b) the analogous decay and recovery of the hydroxyl signal *B*.

aldehyde the exchange rate appears to be even slower as judged from the well resolved splitting of the hydroxyl band in 2-hydroxyacetophenone. In order to obtain a sample with different lifetimes τ_A and τ_B and with an exchange rate well suited for our experimental setup we prepared a mixture of salicylaldehyde and 2-hydroxyacetophenone in the (molar) ratio 6:1. To this were added a trace of acetic acid to catalyze the

proton exchange, and about 30% (by volume) of CS_2 in order to lower the viscosity of the sample and increase the spin-lattice relaxation times. The sample was degassed before use. The appearance of the two hydroxyl bands in this sample is shown in Fig. 1. The hydroxyl band in salicylaldehyde is seen to be considerably broader than that in 2-hydroxyacetophenone. This broadening of the salicylaldehyde hydroxyl band

has been also observed in samples of different chemical composition and may possibly be related to the somewhat weaker intramolecular hydrogen bond in salicylaldehyde compared to that in 2-hydroxyacetophenone.¹⁹

TABLE I. Time constants observed in the system salicylaldehyde (A) and 2-hydroxyacetophenone (B).

	τ_{1A} (sec)	τ_{1A}/T_{1A}	τ_{1B} (sec)	τ_{1B}/T_{1B}
	3.67	0.69	1.33	0.38
	3.46	0.67	1.38	0.37
	3.54	0.67	1.41	0.36
	3.75	0.67		
	4.00	0.69		
Mean value:	3.69	0.68	1.37	0.37

5. RESULTS AND DISCUSSION

System Salicylaldehyde (A) and 2-Hydroxyacetophenone (B)

The absolute values of the exchange rates reported in the present section should be treated with reserve, since they are sensitive to the amounts of catalyzing agents added. These amounts were not accurately determined since the prime purpose of the present investigation was to illustrate the principles of the method and to check the validity of the theory developed in Sec. 2.

From the integrals of five single-resonance spectra the intensity ratio of the two hydroxyl signals, i.e., M_0^A/M_0^B , was found to have the value of 5.65 ± 0.15 . The values of the parameters τ_{1A} , T_{1A} , τ_A , and τ_{1B} , T_{1B} , and τ_B were obtained from the decay of the appropriate hydroxyl signal upon the sudden irradiation of the other hydroxyl signal as elaborated in Sec. 2 (Case I).

Spectra illustrating these two experiments are shown in Figs. 2(a) and 2(b) in which the recovery of the signals upon the removal of the irradiation field (Case II) is also seen.

Figures 3(a) and 3(b) illustrate the growth of the signals when saturating fields centered at these *same* signals were removed (Case III). Figures 4(a) and 4(b) display the progressive recovery of the signals after saturation of *both* signals (Case IV).

Case I

Eight decays were followed, five for Signal A and three for Signal B. The results are summarized in Table I. The time constants τ_{1A} and τ_{1B} were evaluated from the slopes of logarithmic plots of the decay curves and the ratios τ_1/T_1 were obtained directly from the ratio of minimum to maximum peak heights. Logarithmic plots of the decays in Figs. 2(a) and 2(b) are shown in Figs. 5(a) and 5(b), respectively.

It is seen from Table I that the ratios τ_1/T_1 can be determined quite accurately but that the time constant τ_{1A} shows a spread²⁰ of the order of 10%. However, we use them in the following with a somewhat higher

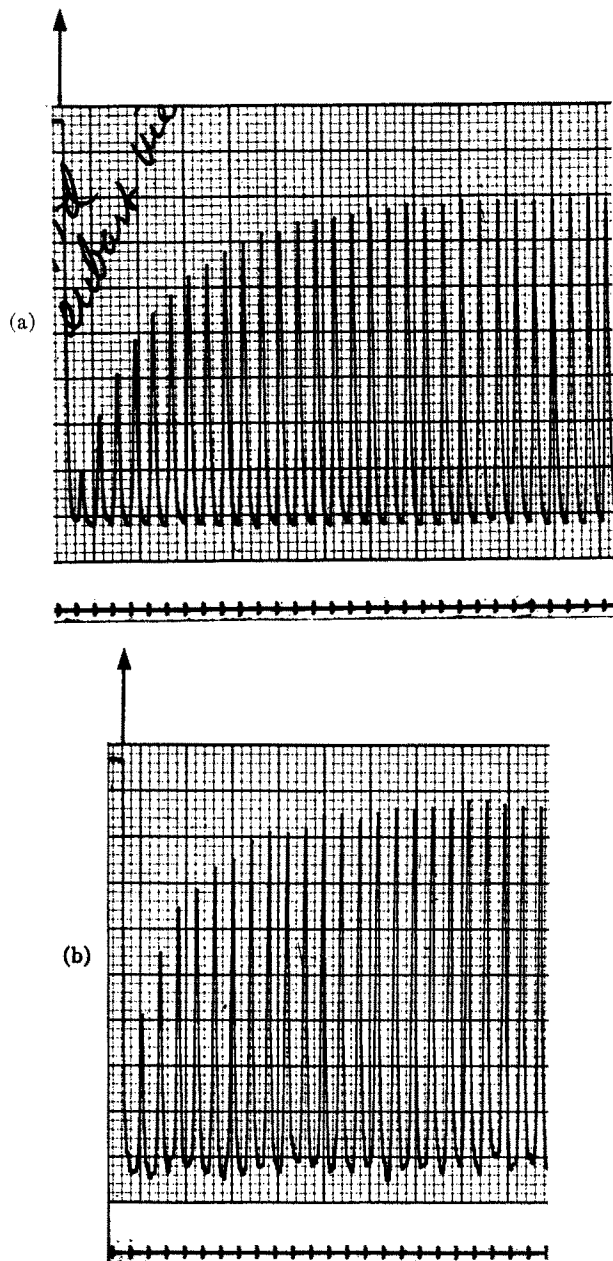


FIG. 3. The recovery of the NMR signal intensities upon the removal of the saturating rf fields at these same signals (Case III). The arrows (\uparrow) indicate the moment when the saturating rf field is removed. The markers in the lower part of the figures are second intervals. (a) The recovery of the hydroxyl signal A. (b) The recovery of the hydroxyl signal B.

¹⁹ S. Forsén and B. Åkermark, Acta Chem. Scand. (to be published).

²⁰ Actually the accurate evaluation of the time constants from the decay curves requires a high precision in the asymptotic values.

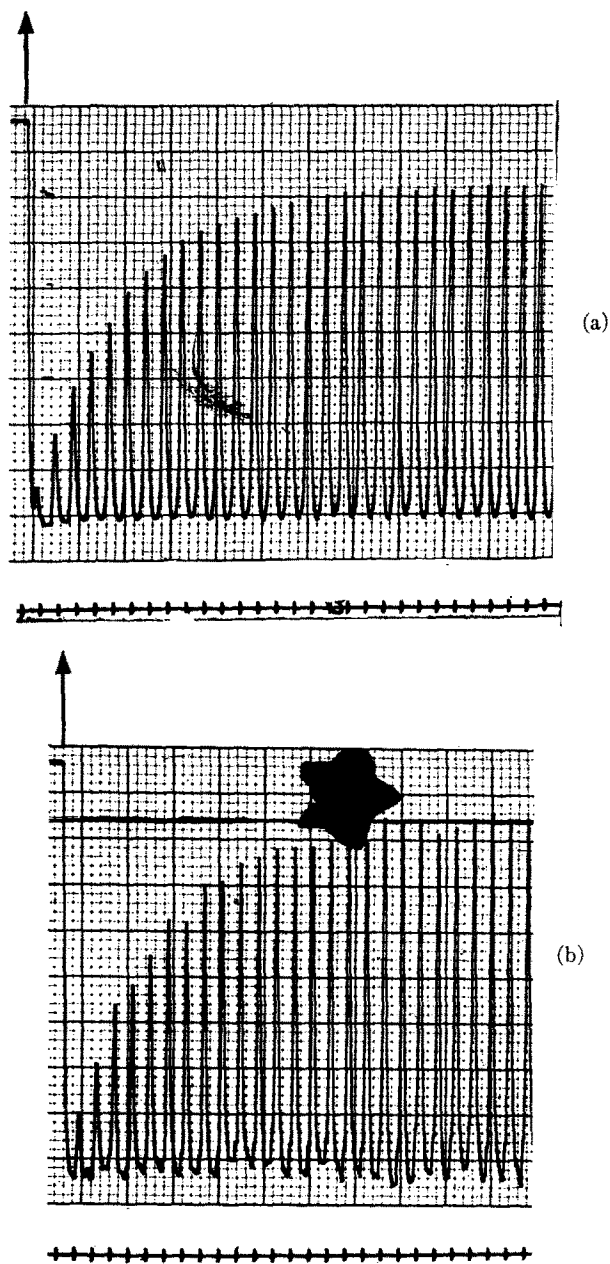


FIG. 4. The recovery of the NMR signal intensities upon the removal of saturating rf fields at *both* signals (Case IV). The arrows indicate the moment when the saturating rf fields are removed. The markers in the lower part of the figures are second intervals. (a) The recovery of the hydroxyl signal A. (b) The recovery of the hydroxyl signal B.

precision than is warranted, so that the reader may more easily reproduce our calculations.

From the values of Table I we obtained, using Eq. (2), the values of $\tau_A=11.53$ sec, $T_{1A}=5.43$ sec, $\tau_B=2.17$ sec, and $T_{1B}=3.70$ sec.

The ratio $\tau_A/\tau_B=5.31$ compares favorably with the ratio $M_0^A/M_0^B=5.65$ obtained from the single-resonance spectra.

From the known values of the time constants, the characteristic roots λ_1 and λ_2 of Eq. (15) are calculated to be

$$\lambda_1=0.805 \text{ sec}^{-1},$$

and

$$\lambda_2=0.196 \text{ sec}^{-1}.$$

These values approximate to within 10% those given by Eq. (16) which seems reasonable since $\tau_A > 2T_{1A}$.

Case II

According to Eqs. (13), (19), and (20), the recovery of Signal A follows the relation

$$M_0^A - M_z^A = M_0^A (0.423e^{-0.196t} - 0.103e^{-0.805t}). \quad (25)$$

In the present case the recovery of the signals becomes virtually exponential since $C_2/C_1=\lambda_1/\lambda_2=4.11$. In Fig. 6(a) the full curve represents the above function (25) and the circles represent the experimental

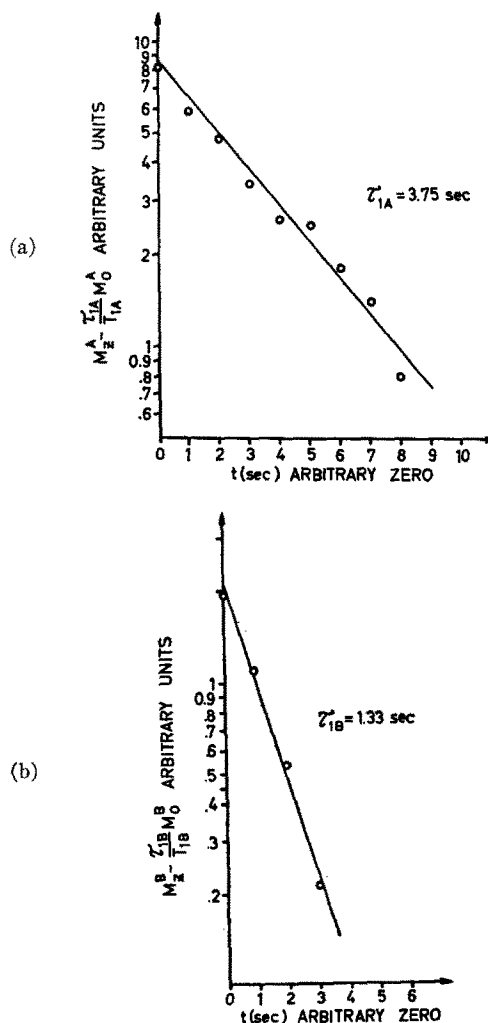


FIG. 5. Logarithmic plots of (a) the decay in Fig. 2(a) and (b) the decay in Fig. 2(b) (Case I).

values from Fig. 2(a). The curve gives an excellent fit to the experimental values if one assumes a time lag of 0.5 sec between the removal of the saturation and the first observation. This delay time seems to be reasonable with the present experimental procedure.

The recovery of Signal *B* calculated in the same way is

$$M_0^B - M_z^B = M_0^B(0.833e^{-0.196t} - 0.203e^{-0.805t}). \quad (26)$$

As is evident from the form of Eqs. (10), (19), and (20), the coefficients multiplying the exponentials in Eq. (26) are proportional to the coefficients of Eq. (25) with the constant of proportionality given by

$$(1 - \tau_{1B}/T_{1B}) / (1 - \tau_{1A}/T_{1A}) = 0.63/0.32 = 1.97.$$

Thus the curve representing the recovery of Signal *B* is congruent with that representing the recovery of Signal *A* [cf. Figs. 6(a) and 6(b)].

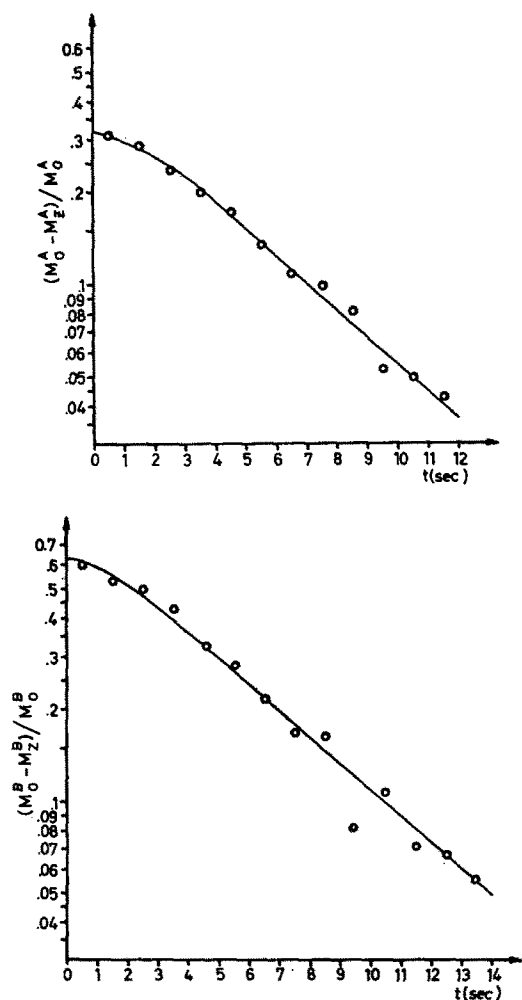


FIG. 6. Logarithmic plots of (a) the recovery in Fig. 2(a) and (b) the recovery in Fig. 2(b) (Case II). The full curves represent the theoretically predicted recoveries (see text).

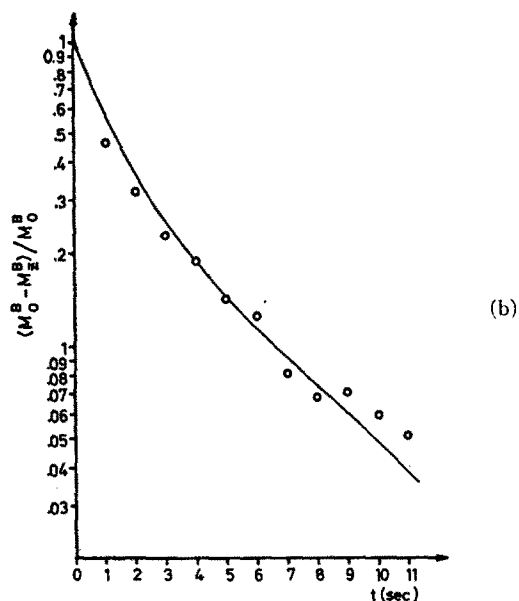
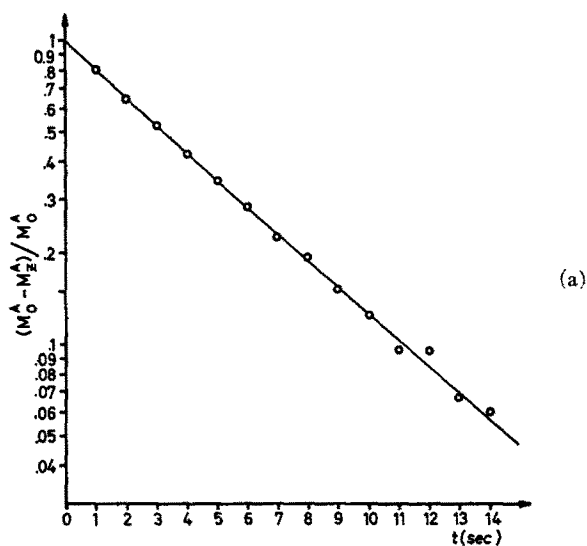


FIG. 7. Logarithmic plots of (a) the recovery in Fig. 3(a) and (b) the recovery in Fig. 3(b) (Case III). The full curves represent the theoretically predicted recoveries (see text).

Case III

The recovery of the hydroxyl Signal *A* after its saturation is given according to Eqs. (3), (21), and (22) by

$$M_0^A - M_z^A = M_0^A(0.967e^{-0.196t} + 0.033e^{-0.805t}).$$

Within the precision of our measurements this recovery cannot be distinguished from a genuine exponential [cf. Fig. 7(a)].

The recovery of Signal *B* in this case is more complicated:

$$M_0^B - M_z^B = M_0^B(0.365e^{-0.196t} + 0.635e^{-0.805t}).$$

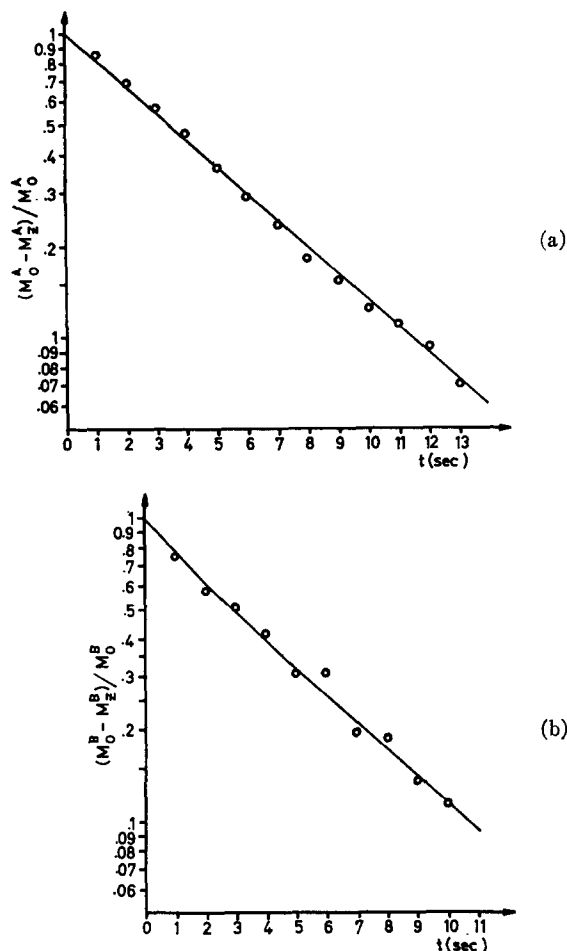


FIG. 8. Logarithmic plots of (a) the recovery in Fig. 4(a) and (b) the recovery in Fig. 4(b) (Case IV). The full curves represent the theoretically predicted recoveries (see text).

The curve representing this function [Fig. 7(b)] departs observably from a straight line even 10 sec after the removal of the saturating field, i.e., as long as we are able to follow the recovery.

It appears from Figs. 7(a) and 7(b) that the neglect of the transverse magnetization (u and v) exchange discussed in Sec. 2 is reasonably well justified. However, the somewhat low experimental values evident in the first three points in Fig. 7(b) might possibly be attributed to effects neglected in our treatment. If exchange of transverse magnetization increases the intensity of the initial experimental signals, the effects would be in the direction observed. (It should be noted that the sense of increasing signal intensity is *downward* in the logarithmic plots of the recovery curves, Figs. 6–8.)

The type of experiment performed here (Case III) could be used for the determination of the relaxation times T_{1A} and T_{1B} had there been no chemical exchange. Actually the recovery of Signal A does give an accept-

able estimate of T_{1A} owing in part to the fact that $\tau_A > 2T_{1A}$. However, the recovery of Signal B is far from exponential and the asymptotic slope is determined by T_{1A} rather than by T_{1B} .

Case IV

It follows from the discussion in Sec. 2 that the recovery of the hydroxyl Signal A , in the present case, depends mainly on T_{1A} since $\tau_A > 2T_{1A}$, and therefore Eq. (16a) is approximately valid. The recovery is given by

$$M_0^A - M_z^A = M_0^A (1.020e^{-0.196t} - 0.020e^{-0.805t}).$$

The logarithmic plot of this case [Fig. 8(a)] is practically identical with the plot shown in Fig. 7(a).

The recovery of the hydroxyl Signal B is determined mainly by $\lambda_2 \approx 1/T_{1A}$, although the contribution from the exponential involving λ_1 is discernible as a small curvature in the plot in Fig. 8(b). The time dependence of the recovery is given by

$$M_0^B - M_z^B = M_0^B (0.879e^{-0.196t} + 0.121e^{-0.805t}).$$

6. CONCLUSION

The nuclear magnetic double-resonance technique appears to be a powerful method for the study of moderately rapid chemical exchange reactions.

The simple theory presented in Sec. 2 provides an adequate description of the time dependence of the signal intensities in the four different types of experiments reported in Sec. 5.

A particularly attractive feature of the method is the simplicity of the experiments. Two time constants—the spin-lattice relaxation time T_1 and the lifetime τ of the spins at any one site—can be determined in a single experiment, in which the decay to the new equilibrium value of the magnetization at this particular site following upon the sudden saturation of the signal from the other site, is studied. For a given two-component system only three time constants—the two spin-lattice relaxation times and one exchange rate parameter—are independent.

In Sec. 2 we have considered four simple types of experiment in which the time dependence of the signal intensity at any one site is studied. Thus, three independent parameters have to comply with a total of eight different observations. The parameters are thus well determined.

The present method requires only a moderate resolution and the chemical shifts between the two signals of the exchangeable spins need only be known to within, say, 1 cps. However, high demands are placed on the signal/noise ratio and on the linearity of the detecting system (amplifiers, detectors, and recorders). A fast (preferably direct-writing) recorder is also required.

The technique presented here should be suitable for the study of a variety of problems. Longer lifetimes than those encountered in the present investigation could be handled if samples with longer relaxation times can be prepared. In this connection it should be remembered that in mixtures in which the concentrations of the two components are very different the lifetime in one site may possibly be determined with the present technique even when the lifetime in the other site is outside the range accessible with the method. The other lifetime is then determined by the relative amounts of the two components in the sample.

The measurement of short lifetimes requires samples with short relaxation times. In general, this requirement should not present any difficulties since the relaxation times can be shortened by the addition of small amounts of paramagnetics. The experimental technique may have to be modified in order to ensure fast detection and instantaneous saturation. The experimental setup used in our experiments is commercially available and in general use; however, different modes of observation might offer some interesting

alternatives. Thus one should consider the utilization of a method in which the saturating and observing rf fields remain continuously at resonance. Spin-echo and other pulse techniques might also be used.

In the foregoing we have discussed the applicability of the double-resonance method for the determination of chemical exchange rates; however, the method should also apply to problems of hindered rotation.

Finally, the present method may readily be extended to the more general case of exchange between several sites. Work in progress indicates that such experiments may provide information on the mechanism of exchange in complex chemical systems.

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