

Spin Echo Nuclear Magnetic Resonance Studies of Fast Chemical Reactions

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Since the original work of Gutowsky, McCall and Slichter¹ in 1953 high resolution nuclear magnetic resonance has developed into a useful tool for studying fast chemical reactions in liquids. These reactions occur in systems at dynamic equilibrium and involve rapid, reversible transfer of nuclear spins between magnetically non-equivalent environments. For example, intermolecular hydroxyl proton transfer in ethanol,² ring inversion in cyclohexane,³ and hindered internal rotation in N,N-dimethylacetamide⁴ have all been studied by high resolution NMR methods. Useful reviews of such studies have been made by Lowenstein and Connor⁵ and by Johnson.⁶

If the rate at which spins transfer between non-equivalent magnetic environments or "sites" is less than the difference between the resonant frequencies of the sites, separate resonance lines are observed in the spectrum. For faster exchange rates, the spins experience an average resonant frequency, and the resolved lines are collapsed; one or more lines are observed at the average resonant frequencies. By analysis of the details of the lineshape at various temperatures, it is possible to obtain the temperature dependence of the exchange rate constant.

High resolution NMR has been used for many years to measure exchange rates; it is the purpose of this paper to discuss the recently developed spin echo method, which depends on measuring the spin-spin or transverse relaxation rate. The transverse relaxation rate is measured most conveniently by the Carr Purcell method (see Fig. 1). The weak, continuous, oscillating magnetic field of high resolution NMR is replaced by a much stronger oscillating field which is turned on only in short bursts or pulses with duration of a few microseconds. The first pulse, applied at time zero, instantaneously tips the nuclear magnetization into a plane perpendicular to the constant magnetic field (xy plane). The magnetization, as viewed in a coordinate system rotating at the average Larmor frequency, dephases because the constant field is not perfectly homogeneous and spins in different parts of the sample precess at different rates. The rest of the pulses, applied at times τ , 3τ , 5τ , etc., flip the magnetization by 180° , and cause the magnetization to refocus and form spin echoes at times 2τ , 4τ , 6τ etc. The decay of the envelope of echo maxima is independent of magnetic field inhomogeneity, and its time constant defines the transverse relaxation time.

It is reasonable that transfers of spins between different sites should affect the relaxation rate as well as the high resolution lineshape. Spins in magnetically non-equivalent sites precess at different rates around the constant magnetic field, and since individual spin transfers occur at random times, their macroscopic effect is to cause an additional dephasing of the magnetization; a faster relaxation rate. The amount of dephasing which occurs depends on the exchange rate (average time which a spin spends precessing in one site or the other), on the chemical shift between the sites (difference in precessional frequency), and on the spacing of the 180° refocussing pulses. The latter parameter affects the amount of dephasing because it determines the length of time in which the spins can dephase before being refocussed.

The dependence of observed relaxation rate upon rf pulse spacing forms the basis of the spin echo method of determining exchange rates. For exchange rates which are less than the chemical shift, the observed relaxation rate attains a limiting value at long pulse spacings which depends on the rate constant for exchange but not the chemical shift. At short pulse spacings, the observed

relaxation rate approaches another limit which is independent of the chemical exchange rate. At intermediate pulse spacings, the relaxation rate is somewhere between these limiting values. By analysis of the dependence of relaxation rate upon pulse spacing, it is possible to obtain values for the rate constant, chemical shift, and relaxation rate in absence of exchange.

Figure 2 shows some relaxation curves, or graphs of relaxation rate versus inverse pulse spacing, obtained by Allerhand and Gutowsky⁷ for N,N-dimethyltrichloroacetamide. In this molecule the rate process is hindered rotation around the C-N bond, which exchanges the non-equivalent methyl groups. At low temperatures the relaxation rate depends strongly upon pulse spacing, but at higher temperatures the relaxation rate appears to become independent of pulse spacing. This behavior is due to the fact that at higher temperatures the exchange rate is larger, and it is not possible in practice to reduce the pulse spacing sufficiently to prevent dephasing.

For simple systems such as N,N-dimethyltrichloroacetamide the spin echo method appears to be superior to high resolution NMR methods of measuring exchange rates. A larger temperature range is experimentally accessible since exchange contributions comparable to the true "natural linewidth" (without inhomogeneity broadening) can be measured. In addition, analysis of the relaxation curves usually yields values for the chemical shift at each temperature as well as the rate constant. This is important because an undetected and uncorrected temperature dependence of the chemical shift can result in large errors, particularly in the entropy of activation.⁸

These advantages of the spin echo method make its extension to more complicated systems a potentially useful theory. To date, it is possible in principle to calculate spin echo amplitudes for an arbitrarily complicated spin system, including homo- and heteronuclear spin coupling as well as chemical exchange processes.⁹ In practice even large computers require two or three minutes to calculate relaxation curves for systems with about twelve lines in their spectra; this appears to be the current practical limit of complexity.

Ethanes which have been substituted with four or five chlorine or bromine atoms provide a quite stringent test of the spin echo method. There are relatively high barriers to internal rotation about the C-C bond in these molecules,¹⁰ and for unsymmetrically substituted molecules there are three different rotational isomers, each of which may involve spin coupling. The effect of homonuclear spin coupling is to introduce strong modulation of the echo train, and it is then not feasible to define a transverse relaxation rate (see Fig. 3). Heteronuclear spin coupling is usually not observable in Carr Purcell spin echo experiments unless the coupled nuclei are involved in an exchange process. Even in this case the heteronuclear spin coupling does not produce modulations, it contributes to the effective chemical shifts of the exchanging nuclei⁹ (see Fig. 4).

In 1,1-difluoro-1,2-dibromodichloroethane, there are two possible exchange processes: between the rotamer with bromine atoms in a trans conformation and either of the *d,l* pair of "gauche" rotamers, and between the two gauche rotamers. Homonuclear spin coupling between fluorines in the gauche rotamers is observable because the two fluorines are non-equivalent in this case. The low temperature spin echo trains therefore show characteristic modulation patterns¹¹ (see Fig. 3). In agreement with theory, the details of the modulation depend on the rf pulse spacing.

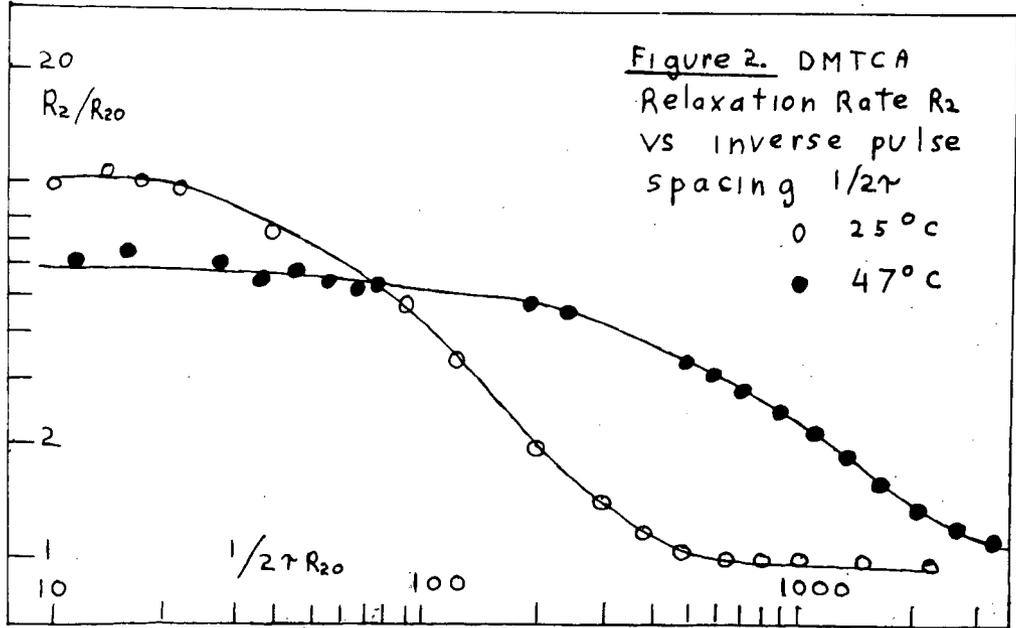
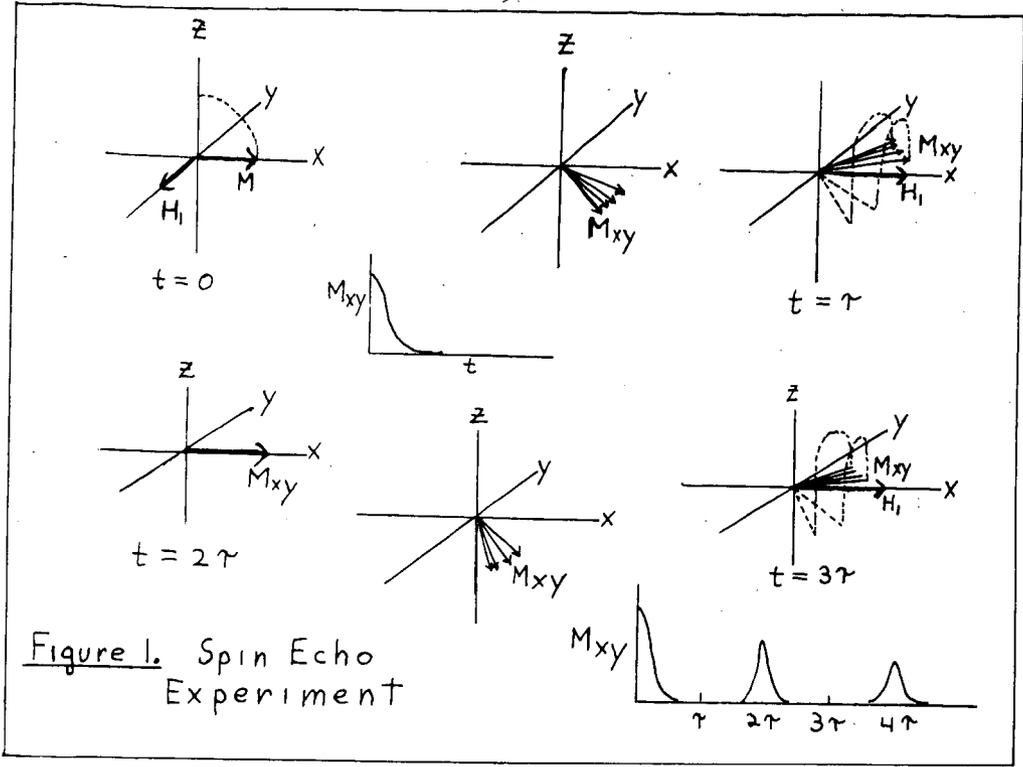
At temperatures above about -60°C the modulation disappears and the echo trains become exponential. This is because the chemical exchange is sufficiently rapid to "average out" effects of coupling. A high resolution NMR spectrum at this temperature would show a single, broad featureless line. The apparent relaxation rate depends upon rf pulse spacing up to about -20°C, and the dependence can be

analysed to yield values of the free energy barrier for *gauche*-*trans* internal rotation (11.0 kcal/mole) and for *gauche-gauche* internal rotation (12.0 kcal/mole).

For 1-fluoro-1,1,2,2-tetrachloroethane, only one exchange process is observable by magnetic resonance: the interchange of the rotamer with hydrogen and fluorine in a *trans* conformation with either of the magnetically equivalent "*gauche* rotamers". It is easy to show that for spin echo experiments, the observed echo trains should be a sum of two contributions, each corresponding to a two site exchange process.¹² The two processes occur at the same rate but with different effective chemical shifts, given by the true proton chemical shift between *gauche* and *trans* rotamers, plus or minus one half the difference of the heteronuclear coupling constants for each rotamer. At the field strengths used (corresponding to proton resonance at 26.8 and 17.7 MHz) the chemical shift is small, and the two effective chemical shifts are equal, and independent of field strength (see Fig. 4). In this compound the free energy barrier for interconversion of the *gauche* and *trans* rotamers was found to be about 8.7 kcal/mole. It is less than the barriers found in $\text{CF}_2\text{BrCCl}_2\text{Br}$ because in the former compound the activated complex involves eclipse of smaller atoms than in the latter.

References

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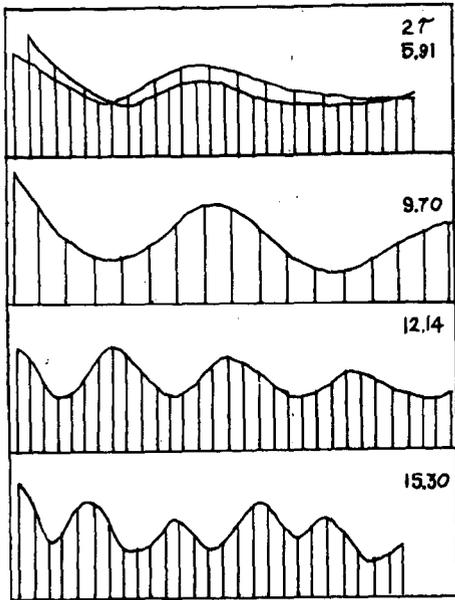


Figure 3. Fluorine spin echoes from $\text{CF}_2\text{BrCCl}_2\text{Br}$ at -100°C and 25.27 MHz. The vertical lines represent echo amplitudes plotted on an arbitrary scale, and for each echo train the spacing between the lines is the rf pulse spacing, given in milliseconds above each echo train. The solid curves define characteristic modulation patterns for each pulse spacing.

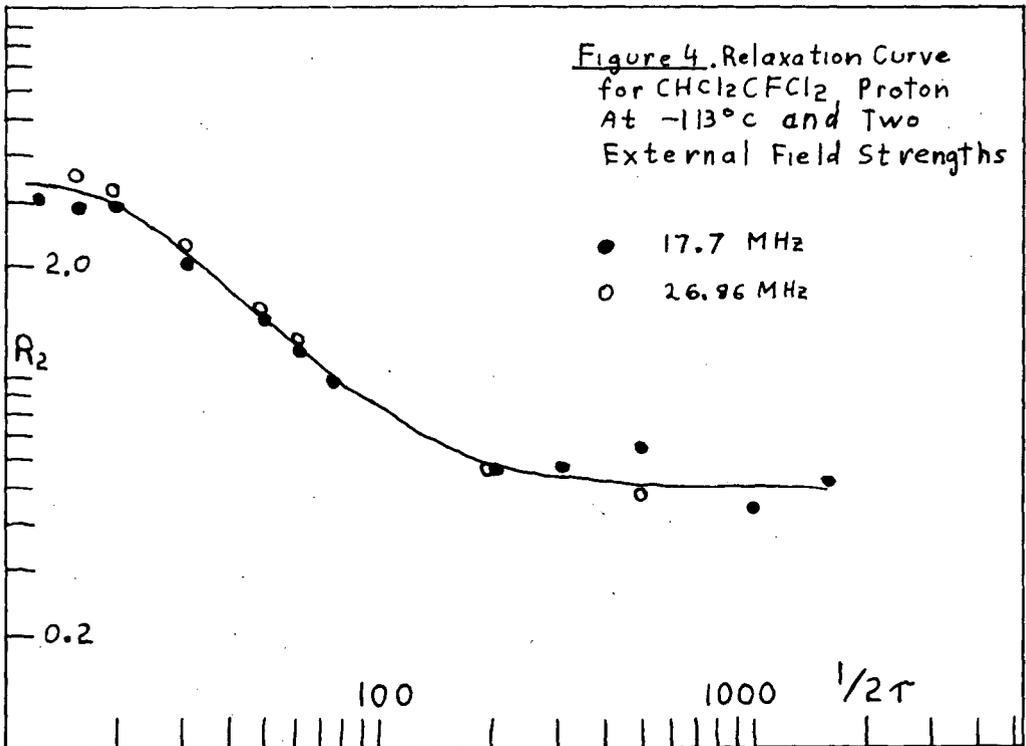


Figure 4. Relaxation Curve for $\text{CHCl}_2\text{CFCl}_2$ Proton At -113°C and Two External Field Strengths

- 17.7 MHz
- 26.96 MHz