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Dynamic Nuclear Magnetic Resonance

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Nuclear magnetic resonance spectroscopy has been widely used in recent years to investigate the kinetics of chemical reactions. Dynamic nuclear magnetic resonance spectroscopy covers the investigation of temperature-dependent n.m.r. spectra and the calculation of rate constants and Arrhenius parameters from these spectra. The present Review describes the principles of d.n.m.r. spectroscopy, methods of recording the spectra, and their processing by exact and approximate methods. The theoretical and experimental foundations are illustrated by many examples of the investigation of hindered rotations, inversions, and rearrangements in various organic and organometallic systems. A list of 81 references is included.

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I. INTRODUCTION

The most diverse physicochemical methods have been used to investigate the kinetics of chemical reactions[1-4]. Recently nuclear magnetic resonance (n.m.r.) spectroscopy has found wide application. Dynamic nuclear magnetic resonance (d.n.m.r.) spectroscopy involves observing the changes with temperature in n.m.r. spectra and hence calculating reaction rate constants and the corresponding Arrhenius parameters. Dynamic effects in n.m.r. spectra were first detected by Gutowsky and his coworkers in 1953.[5,6] Since then various investigations have been made in this field, and several reviews have been published[7-13] on the theory and applications of d.n.m.r. spectroscopy.

At the present stage in the development of the technique and applications of d.n.m.r. spectroscopy several new and original methodological principles have been suggested which broaden significantly the possibilities, and among which carbon-13 n.m.r. spectroscopy may be the most promising approach. Secondly, the abundance of experimental data and the inadequacy of procedures for their analysis demand a critical assessment of the accuracy with which activation parameters are measured. Thirdly, the application of d.n.m.r. has led to the discovery of a completely new class of fluctuating or stereochemically non-rigid molecules, i.e. compounds capable of degenerate intramolecular rearrangements. The present Review discusses these problems as illustrated by various organic and organometallic systems.

II. ELEMENTS OF THE THEORY OF DYNAMIC NUCLEAR MAGNETIC RESONANCE

Dynamic n.m.r. data are usually analysed in terms of the theory of rate processes, clear and detailed accounts of which can be found in monographs[3,4]. Only the main formulae are given below.

The reaction A ⇌ B can be represented most simply by a plot of free energy against the generalised reaction coordinate (Fig. 1), where the state of maximum energy is termed the transition state (Tr). The rate constant of the change from state A to state B is given by the formula

$$k_{AB} = \varkappa \frac{k_{Bol}T}{h} \exp(-\Delta G^{\neq}_{AB}/RT) , \quad (1a)$$

$$\Delta G^{\neq}_{AB} = \Delta H^{\neq}_{AB} - T\Delta S^{\neq}_{AB} , \quad (1b)$$

where $\varkappa$ is the transmission coefficient, $\Delta S^{\neq}$, $\Delta H^{\neq}$, and $\Delta G^{\neq}$ are the entropy, enthalpy, and free energy of activation respectively, T is the temperature, and the remaining symbols represent fundamental constants. In view of the slight temperature dependence of the pre-exponential factor, use is often made of the Arrhenius equation

$$k = A \cdot \exp(-E_a/RT) , \quad (2)$$

where A is the frequency factor and E_a is the activation energy. Comparison of Eqns. (1) and (2) gives

$$\Delta H^{\neq} = E_a - RT ,$$

$$\Delta G^{\neq} = E_a - RT - T\Delta S^{\neq} , \quad (3)$$

$$A = \varkappa \frac{k_{Bol}T}{h} \cdot e \cdot \exp(\Delta S^{\neq}/RT) .$$

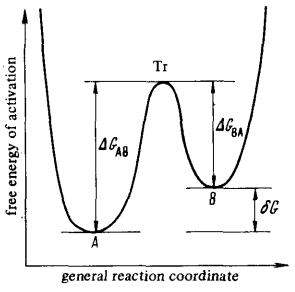


Figure 1. Form of potential-energy surface for exchange between two states.

The activation energy is determined experimentally from the dependence of $\ln k$ on $1/T$ by means of the equation

$$E_a = -R \cdot \frac{\partial(\ln k)}{\partial(1/T)} . \quad (4)$$

Under equilibrium conditions we can determine the equilibrium constant for the reaction A ⇌ B

$$K = p_A/p_B = k_B/k_A = \exp(-\delta G/RT) , \quad (5)$$

where p_A and p_B are the populations (or concentrations) of states A and B, and $\delta G = \Delta G^{\neq}_{AB} - \Delta G^{\neq}_{BA}$.

If the reaction rate constant k_{AB} is considerably smaller than 0.01 s^{-1}, the reaction is slow. The n.m.r. method can then be used to monitor the changes in concentration of the states with time by measuring the integral intensities of the corresponding signals. In spite of the triviality of such measurements, there are an immense number of examples where n.m.r. is used in this way, including extremely complicated coupled reactions in multicomponent systems. Several examples can be found in Ionin and Ershov's book[13].

The concept of the lifetime τ of a state[11-13] is often used in d.n.m.r. spectroscopy. For complex reactions the lifetime τ_{ij} of a state i with respect to transition to state j is defined by the formula

$$\tau_{ij} = 1/k_{ij} . \quad (6)$$

The lifetime may vary within wide limits depending on the temperature (Eqns. 1 and 2). The choice of method for recording a rate process is determined by the ratio of the lifetime of the state to the characteristic time of the method τ_m. The latter quantity is a time constant characterising the processes of energy dissipation (relaxation) in the corresponding frequency range (Table 1). Intermittent processes in a molecular system that are more rapid than the dissipation (relaxation) processes in the corresponding frequency range cannot be recorded, and such a system appears static (averaged over the states involved) when the given method is used.

Table 1. Characteristic times of some physical methods used in chemistry.

Method	Time, s	Method	Time, s
Electron diffraction	10^{-20}	Electron spin resonance	10^{-4}—10^{-8}
X-Ray diffraction	10^{-18}	Nuclear magnetic resonance	10^{-1}—10^{-7}
Ultraviolet (electronic) spectra	10^{-14}—10^{-15}	Molecular beams	10^{-6}
Vibrational spectra	10^{-11}—10^{-13}	Visual methods (separation of isomers)	10^{2}
Ultrasonic absorption	10^{-5}—10^{-9}		

It is interesting that the characteristic time constant of the n.m.r. method covers a very wide range (Table 1). The reason is that various methods are used in n.m.r. spectroscopy, which permit the recording of processes ranging from rapid ($k \simeq 10\ s^{-1}$) to very rapid ($k \simeq 10^7\ s^{-1}$). This range of reaction velocities is usually inaccessible to other methods[12-15]—a fact responsible for the widespread interest in d.n.m.r. spectroscopy.

The discovery of dynamic effects on n.m.r. spectra[5,16] was followed by theoretical descriptions of this phenomenon by Gutowsky and Holm[16], Hahn and Maxwell[17], and McConnell[18] based on Bloch's phenomenological equations for the nuclear magnetisation vector[19]. This work has been analysed in reviews[7,8], so that we shall merely give the equation for the complex magnetisation G in exchange between two positions A ⇌ B

$$G = i\omega_1 M_0 \frac{[(\tau_A + \tau_B) + \tau_A\tau_B(\alpha_A p_A + \alpha_B p_B)]}{(1 + \alpha_A\tau_A)(1 + \alpha_B\tau_B)} \quad (7)$$

where $\omega_1 = \gamma H_1$ (in which γ is the gyromagnetic constant and H_1 the amplitude of the high-frequency field), M_0 is the equilibrium intensity of magnetisation,

$$\alpha_i = \frac{1}{T_2} + i(\omega_i - \omega)$$

τ_A and τ_B are the lifetimes in states A and B,

$$p_A = \frac{\tau_A}{\tau_A + \tau_B} , \qquad p_B = \frac{\tau_B}{\tau_A + \tau_B} , \quad (8a)$$

$$\tau = p_A\tau_B = p_B\tau_A . \quad (8b)$$

T_2 is the spin–spin relaxation time, and ω_i and ω are the resonance and instantaneous frequencies respectively.

The complex magnetisation G is defined as $u + iv$, where in particular the component v perpendicular to the field vector H_1 is termed the absorption signal[7,11,12,19], while the component u is the dispersion signal. The v components are usually recorded. The form of the absorption signal for a two-position exchange can be obtained from the imaginary part of Eqn. (7):

$$v = \omega_1 M_0 \frac{[(1+\tau/T_2)P + QR]}{P^2 + R^2} \qquad (9)$$

where

$$P = \tau\left\{\frac{1}{T_2^2} = \left[\frac{1}{2}(\omega_A + \omega_B) - \omega\right]^2 + \frac{1}{4}(\omega_A - \omega_B)^2\right\} + \frac{1}{T_2} ,$$

$$Q = \tau\left\{\frac{1}{2}(\omega_A + \omega_B) - \omega - \frac{1}{2}(\omega_A - \omega_B)(p_A - p_B)\right\} ,$$

$$R = \left\{\frac{1}{2}(\omega_A + \omega_B) - \omega\right\}(1 + 2\tau/T_2) + \frac{1}{2}(\omega_A - \omega_B)(p_A - p_B).$$

Analysis of Eqn. (9) enables two regions of values of τ to be isolated, for which quite accurate calculations can be made by means of simplified formulae[16,18].

1. Approximation of Slow Exchange $\tau \gg (\nu_A - \nu_B)^{-1}$†

Two signals are observed corresponding to the two states with their statistical weights p_A and p_B. The signal from A in particular has a Lorenzian profile, and the line width $\delta\nu_A$ (in c/s) at midheight is given by

$$\delta\nu_A = \frac{1}{\pi T_{2A}} + \frac{1}{\pi\tau_A} \quad . \qquad (10)$$

2. Approximation of Rapid Exchange $\tau \ll (\nu_A - \nu_B)^{-1}$

Only one signal is observed, having the resonance frequency $\nu = p_A\nu_A + p_B\nu_B$. Its width is given approximately by Meiboom's formula[20]

$$\delta\nu = \frac{p_A}{\pi T_{2A}} + \frac{p_B}{\pi T_{2B}} + 4\pi^2 p_A^2 p_B^2 (\nu_A - \nu_B)^2(\tau_A + \tau_B) \quad . \qquad (11)$$

Computers are generally employed to calculate the complete line shape of the signal of the v component for any values of τ_A and τ_B, owing to the cumbersome computations involved, although a few other approximate methods have been suggested (nomograms[12,21], ratio of maxima and minima in the absorption spectrum[22]).

Fig. 2 illustrates the changes undergone by the spectrum in a two-position exchange. When the populations of the states are equal $p_A = p_B = \frac{1}{2}$, the separate stages in the dynamic process are easily detected. When $\tau >$ 100 s, no appreciable broadening of the lines is observed, and exchange cannot be detected. With slow exchange $\tau \simeq 1$ s, each component of the spectrum becomes wider and moves towards the centre (Fig. 2*a*). The signals coalesce at values of $\tau = \sqrt{2}/2\pi(\nu_A - \nu_B)$. On subsequent increase in the rate of exchange the line again narrows. Finally, with $\tau < 10^{-5}$ s (with $\Delta\nu = 100$ Hz—Eqn. 11), the broadening becomes so small ($\sim$ 0.1 c/s) that the exchange process can no longer be reliably recorded. Exchange effects are similar in the case of unequal populations (Fig. 2*b*), the only difference being that they are more significant for the less populated state (B in Fig. 2*b*). It is easily seen that, if the difference in free energies δG exceeds 3 kcal mole^{-1} (Fig. 1), which corresponds to $p_B < 10^{-2}$, the exchange effects become so small that it becomes difficult to record the actual fact of exchange.

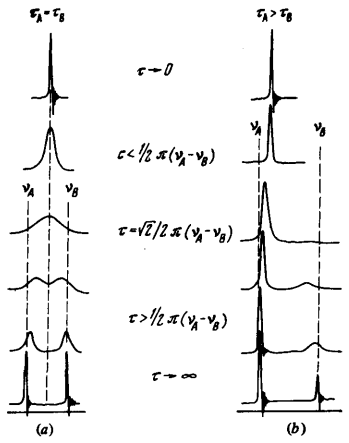


Figure 2. Qualitative shapes of n.m.r. signals for two-position exchange with spectra obtained under the conditions: a) $\tau_A = \tau_B$; b) $\tau_A \neq \tau_B$.

These conditions impose evident limits to the applicability of the d.n.m.r. method to the investigation of rate processes.

III. TECHNIQUE FOR THE ANALYSIS OF DYNAMIC NUCLEAR MAGNETIC RESONANCE SPECTRA

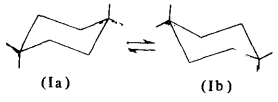
In practice the dynamic effects in n.m.r. spectra described in Section II are always complicated by several additional factors. The greatest difficulties arise from the multiplet structure of the spectra due to indirect spin–spin interaction, in which two cases must be distinguished. (i) The n.m.r. spectra for weakly coupled spin systems ‡ can be regarded as a superposition of d.n.m.r. spectra analogous to those shown in Figs. 2*a* and 2*b* for $p_A = p_B$ and $p_A \neq p_B$ respectively. Simple graphical methods of calculating rate constants have been developed[24,25] to analyse multiplet d.n.m.r. spectra. Relations have also been suggested[26,27] enabling several more complicated situations to be analysed, in which methods of subspectral analysis make it possible to isolate simple subspectra. (ii) With strongly coupled spin systems a complete description of the high-resolution spectra is impossible on the basis of the Bloch equations, and methods of quantum mechanics must be used. A complete description of the effects in systems with strong coupling of the spins was first given by Kaplan[28] using the

† Here and subsequently it is convenient to use angular frequencies $\nu = \omega/2\pi$.

‡ This term is applied to systems[23] in which any pair of nuclei with resonance frequencies ν_A and ν_B and a spin–spin interaction constant J_{AB} conforms to the relation $J_{AB}|\nu_A - \nu_B| \ll 1$.

density matrix. This method was later developed by Alexander[29] for the interchange of spins. Work on these lines was reviewed by Johnson[8] and by Lynden-Bell[9]. In recent years Binsch has put forward a general theory of line shape in high-resolution n.m.r. spectra based on Liouville's theorem[30,31].

The multiplet character of the signals in d.n.m.r. spectra must be taken into account because the most widely used method for analysing dynamic effects is proton magnetic resonance (p.m.r.) spectroscopy[12,13]. The investigation of inversion in cyclohexane



provides a typical example of the procedure for allowing for such multiplets[11-13,32-37]. At room temperature the p.m.r. spectrum is a narrow singlet, so that cyclohexane can be used as a standard of resolution. As the temperature falls the signal begins to broaden, and at −50°C its width is ~ 20 Hz (for a proton resonance frequency of 60 MHz [32]). With further drop in temperature the signal divides into two multiplets separated by 0.5 ppm and having a complicated structure[32]. Below −100°C the width of the lines of the doublet is maintained. The changes observed in the spectrum are interpreted as due to inversion of the ring (Ia ⇌ Ib). With such inversion each proton is sometimes in an axial position and sometimes in an equatorial position: i.e. it is "exchanged" between the two positions.

One of the most important stages in the investigation of dynamic effects is calculation of the spectrum in the absence of exchange. It is easy to see that in the case of cyclohexane such calculation is impracticable, since we need to analyse very complicated n.m.r. spectra (the p.m.r. spectrum of cyclohexane under these conditions can be described as an A_6B_6 system with magnetic nonequivalence).

These difficulties can be avoided to a certain extent by the use of deuteriated compounds[33,34,38]. Isotope effects due to the introduction of heavy hydrogen are assumed to be small and to have no significant effect on the barrier to inversion of the ring. Bovey et al.[33] investigated the proton spectra of undecadeuterocyclohexane. Since $J_{HH}/J_{HD} = \gamma_H/\gamma_D \simeq 7$, the width of the multiplet in the p.m.r. spectra of strongly deuteriated compounds should decrease significantly. Further narrowing of this signal is achieved by the use of $^1H-\{^2D\}$ heteronuclear double resonance. In this case observation of the proton signals at the ^1H frequency (60 MHz) is accompanied by exposure to a second frequency (9.2 MHz), corresponding to ^2D resonance in the same external magnetic field. Use of this technique enabled quite narrow lines (Fig. 3), corresponding to the equatorial and axial positions, to be obtained at low temperatures[34].

The spectra in Fig. 3 already permit approximate methods to be used to calculate rate constants. These methods, based on Eqns. (10) and (11), are often termed *parameter analysis* (Table 2). Many uncertainties generally arise from the use of approximate methods, so that the accuracy of the determination of activation parameters is no better than 10%. Among such uncertainties are the effect of the instrument line width, the temperature dependence of relaxation times and chemical shifts, and the presence of weak spin–spin interactions leading to broadening of the signal. More detailed information on the procedure for correcting for these factors can be found in several published sources[26,27,34,35,40,41].

In some cases it is advisable to simplify the d.n.m.r. spectra by the "fluorine label" method[36] together with the use of deuteriated compounds. The basis of this method is that fluorinated model compounds usually give ^{19}F spectra which are simpler than the proton spectra of the corresponding initial compounds. In particular Roberts[36] suggested that the inversion of cyclohexane (I) should be simulated by that of 1,1-difluorocyclohexane. At +35°C the ^{19}F n.m.r. spectrum of this compound consists of one multiplet (a quintet) due to spin coupling with neighbouring protons. On cooling to −40° the signal broadens, and at −110°C a spectrum of type AB appears, corresponding to two ^{19}F nuclei in a stereochemically rigid structure. The signals of one nucleus are further split into triplets as a result of spin coupling with a pair of neighbouring protons.

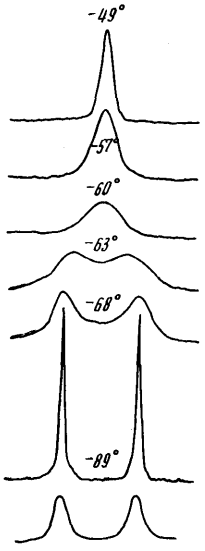


Figure 3. Proton magnetic resonance spectra of C_6HD_{11} with uncoupling from deuterons[34]; the bottom spectrum has been recorded at low temperatures without such uncoupling.

In the temperature range between −100° and +40°C quite complicated changes are observed in the ^{19}F spectrum, owing to mixing of A and B states both as a result of exchange and because of strong coupling between the spins[41]. Nevertheless, the fluorine-19 spectra permit quite accurate analysis of activation parameters by $^{19}F-\{^1H\}$ double resonance.

Dynamic processes can be investigated also by means of non-stationary n.m.r. techniques[35,37,40], for which purpose spectra can be recorded under conditions of rapid flow or pulse methods can be used[42]. Information on rate constants can also be obtained from measurements of relaxation times T_1 (or T_2). In the Carr–Purcell method[37,42], which is most convenient for measuring times T_2, the magnetisation vector M is first subjected to a 90° pulse, i.e. a pulse which turns the vector through 90° and brings it into the xy plane. This is followed by

a series of 180° pulses at intervals of time t_p, $3t_p$, $5t_p$, etc.; as a result of the action of each such pulse the "warmed up" magnetisation vector begins to "run down" and will give spin echo signals at times $2t_p$, $4t_p$, $6t_p$, etc.

Table 2. Approximate methods of calculating rate constants in d.n.m.r. spectroscopy.

Type of method	Basic information	Ref.
Approximation of slow exchange	line width of components $\Delta\nu_{1/2}$ and distance between them $\Delta\nu$ used	7, 18, 34
Approximation of rapid exchange	line width of signal after merging $\Delta\nu_{1/2}$ used	7, 20, 34
Temperature of collapse T_c	temp. determined at which signals merge	7, 34
Temperature of stereochemical rigidity T_r	temp. determined at which appreciable broadening of lines observed at stage of slow exchange	7.39

Because of the occurrence of transverse relaxation processes with time T_2, however, a successive weakening of these signals is observed, which enables T_2 to be measured. If we choose $t_p \ll \tau$, the system will be perceived as static, and damping will correspond solely to dipole–dipole relaxation. If, however, $t_p > \tau$, damping will include a contribution by the exchange process. Equation (10) shows that the contribution by the dynamic process will shorten the effective relaxation time.

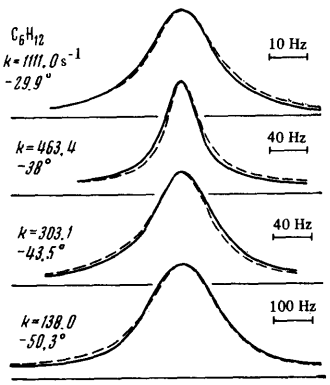


Figure 4. Line-shape analysis in p.m.r. spectra of cyclohexane (100 MHz) at various temperatures[21]: full curves obtained experimentally; broken curves theoretically.

The spin echo method is convenient for investigating rapid dynamic processes. It has been used in particular to measure the time T_2 in cyclohexane (C_6HD_{11}) in the high-temperature range (up to 312°K)[35,37], where continuous n.m.r. methods are ineffective.

It is interesting that spin–spin multiplicity in the region of high-temperature narrowing can be allowed for classically in terms of the Bloch equations[8], which enables methods of *complete line shape analysis* to be applied on the basis of an equation of type (7)§. Calculations by this method are made on an electronic computer[45–48], and sometimes include a stage in which experimental and theoretical spectra are matched by means of special iterative procedures[26,27,49]. The method has been applied to cyclohexane by Inglefield et al.[35] Fig. 4 shows the theoretical spectra having the smallest standard deviation from the corresponding experimental spectra for cyclohexane C_6H_{12}. Satisfactory agreement between the line shapes is evident. Such comparison enables a derived parameter—the rate constant k—to be correlated with an experimental parameter—the temperature.

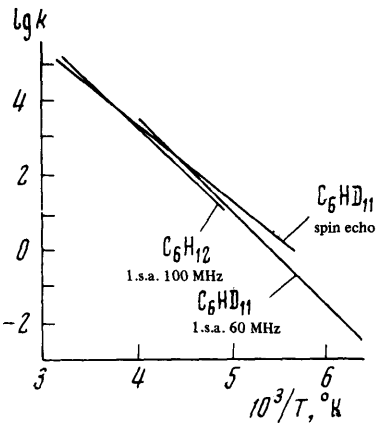


Figure 5. Comparison of various results for the dependence of $\lg k$ on $1/T$ for cyclohexane[35].

Fig. 5 illustrates the variation in $\lg k$ (the rate constant of the inversion of cyclohexane) for three different methods—(a) spin echo[37] and complete line shape analysis at (b) 100 MHz (Fig. 4)[35] and (c) 60 MHz [34] for C_6HD_{11}.

Table 3. Activation parameters for the inversion of cyclohexane and related compounds*.

Compound	Method	Temp. range, °C	E_a, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	$\Delta G^{\neq}$, kcal mole^{-1}	Ref.
C_6H_{12}	l.s.a., 100 MHz	223—263	10.8±0.2	—3.6	10.8	35
C_6HD_4	spin echo	178—312	9.5	—5.8	10.6	37
$C_6D_{11}H$	l.s.a., 60 MHz	156—256	11.24	+2.8	9.8	35
$C_6D_{11}H$	p.a., 60 MHz	198—226	10.9+0.5	+1.4	10.0	12, 33
$C_6H_{10}F_2$	l.s.a., 56 MHz	200—320	9.5	—3.3	0.0	41
C_6H_{12}	p.a., 60 MHz	168—218	12.0	+4.9	9.9	32

* l.s.a. = line-shape analysis; p.a. = parameter analysis.

The results of the various investigations of the inversion of cyclohexane (Table 3) enable certain comments to be made on the accuracy of the measurements of activation parameters. Interest in this question has arisen from

§ Dynamic n.m.r. spectra under conditions of multiposition exchange have been considered in Refs. 43 and 44.

the fact that, despite the wide application of d.n.m.r. spectroscopy in various kinetic investigations, the accuracy of the measurement of activation parameters is small. As a consequence, the analysis of dynamic effects is restricted in many cases to a qualitative picture (establishment of the actual fact of exchange, determination of the approximate temperature range, estimation of the free energy of activation). Recent detailed analyses of the errors involved in the use of various forms of d.n.m.r. [21,26,27,35,39,40,49] lead to certain conclusions.

Approximate methods of analysis (Table 2) yield activation parameters with an accuracy of at best 10%. In principle an accuracy of 2–3% can be achieved by line shape analysis, provided that several conditions are observed, primarily careful experimental recording of the spectra. Important factors are slow passage, absence of phase distortions and amplitude non-linearities, control of resolution throughout the temperature range, and accurate measurement of temperature [39]. Experimental data can be compared only if conditions (solvent, concentration) are fully adequate [11,26]. On the other hand, methods of line shape analysis should be adequate in allowing for relaxation, the temperature dependence of the resonance frequencies, and the character of the iteration procedures [27,49].

In the analysis of complicated spectral systems (e.g. cyclohexane) it is possible to use simpler model systems. It must always be borne in mind that the model may not be adequate to the system. In particular, when strongly deuteriated models are used (C_6HD_{11} in the case of cyclohexane), the total secondary isotope effect may exceed the error of measurement [4]. Fluorinated models (systems with a fluorine label), while being attractive experimentally, must be all the more inadequate models.

Investigations of the activation parameters for inversion in cyclohexane show that the possibility of making measurements over a wide temperature range is an important factor.

It is interesting that, in spite of the poor accuracy with which the activation functions E_a and $\Delta S^{\neq}$ are determined (especially by approximate methods), the free energy of activation can be determined very accurately [10,11,39,49] (Table 3). The reason is that the value of $\Delta G_T^{\neq}$ is obtained directly from data on rate constants (Eqn. 1), whereas E_a is evaluated as the difference between two sometimes closely similar values of $\lg k$ (Eqn. 4). Kessler [10] gave a curious graph for the activation functions of rotation in dimethylformamide: a plot of E_a against $\Delta S^{\neq}$ showed that values of E_a obtained experimentally in various studies cover a range of 8–28 kcal mole^{-1}. [1] However this variation is almost linear, so that values of $\Delta G_T^{\neq}$ differ by at most ±1 with a mean value of 21.5 kcal mole^{-1}.

Summarising, we can say that d.n.m.r. spectroscopy at present has diverse ways of recording spectra and techniques for analysing the data, which permits both the rapid and straightforward estimation of free energy of activation and also the accurate determination of activation parameters.

IV. CLASSIFICATION ACCORDING TO TYPE OF SPECTRA OF THE EXCHANGEABLE SPIN SYSTEMS

Where spin multiplicity is present the d.n.m.r. spectra can be classified in conformity with the type of n.m.r. spectra (according to Pople's nomenclature [12,13,23] characteristic of the separate instantaneous structures.

1. The ^{19}F spectrum of 1,1-difluorocyclohexane, under conditions of uncoupling from the protons [41] at sufficiently low temperatures, is of type AX, where A is a ^{19}F nucleus in an axial position, and X a ^{19}F nucleus in an equatorial position, which can be denoted as the A(1)X(2) type. As a result of inversion of the ring the fluorine atoms exchange positions. Thus the whole spectrum under conditions of exchange is described by the relation

$$\begin{array}{c} A(1)\,X(2) \rightleftarrows X(1)\,A(2), \\ \text{or}\quad AX \rightleftarrows XA\ . \end{array} \qquad (12)$$

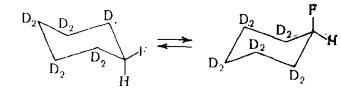
In principle this case of exchange is described more rigorously by the equation

$$AB \rightleftarrows BA \qquad (13)$$

which takes into account the mixing of the eigenfunctions of nuclei A and B due to strong spin coupling. In the limit of rapid exchange (i.e. as $\tau \to 0$) the spectrum is a singlet in both cases (12) and (13). In systems with strong mixing of the spin functions of the nuclei the lifetime of a state at the instant of collapse of the signals in the spectrum can be estimated [50] by means of the formula

$$\tau_c = \frac{2}{\pi}[(\nu_A - \nu_B)^2 + 6J^2]^{-1/2}\ . \qquad (14)$$

2. In contrast to the exchange described by Eqns. (12) and (13), corresponding to so called interchange [11,31], cases are theoretically possible in which the individual structures are not identical. Let us examine in particular the d.n.m.r. spectra of decadeuterofluorocyclohexane (II) under conditions of conformational mobility [51]



$$\text{or}\quad F_{eq}\,H_{ax} \underset{k_2}{\overset{k_1}{\rightleftarrows}} F_{ax}\,H_{eq} \qquad (15)$$

$$A_1X_1 \underset{k_2}{\overset{k_1}{\rightleftarrows}} A_2X_2\ .$$

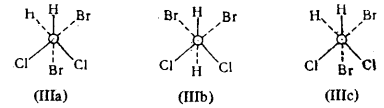
The different subscripts for AX systems in this case show that the spectral parameters of the systems are different. Processes of type (15) are in general non-degenerate ($k_1 \neq k_2$). In the case of rapid exchange the spectrum corresponds to a system of type AX with the average parameters

$$\begin{aligned} \langle\delta_A\rangle &= p_1\delta_{A_1} + p_2\delta_{A_2}\ , \\ \langle\delta_X\rangle &= p_1\delta_{X_1} + p_2\delta_{X_2}\ , \\ \langle J_{AX}\rangle &= p_1J_{A_1X_1} + p_2J_{A_2X_2}\ , \end{aligned} \qquad (16)$$

where

$$p_1 = \frac{k_2}{k_1 + k_2};\quad p_2 = \frac{k_1}{k_1 + k_2}\ .$$

3. A system of two nuclei with slightly non-equivalent instantaneous structures is illustrated by 1,1,2,2-tetra-substituted ethanes, e.g. HCl_2C-CBr_2H. [51] Rapid rotation about the carbon–carbon bond usually occurs in these molecules, which is clearly depicted by Newman projections as the three structures



(IIIa) (IIIb) (IIIc)

Two of them (a and c) are gauche (or skew) forms, and one a *trans*-form. In the absence of exchange the spectra of structures (IIIa), (IIIb), and (IIIc) are of types A*B*, A**B**, and A*B* respectively, where it is implied that the gauche isomers are spectrally indistinguishable.

Rotation about the carbon–carbon bond is described by the equations

$$A^*B^* \underset{k_2}{\overset{k_1}{\rightleftarrows}} A^{**}B^{**} \underset{k_1}{\overset{k_2}{\rightleftarrows}} A^*B^* \qquad (17)$$

where in general $k_1 \neq k_2$, since the statistical weights of forms (a) and (b) may differ.

A more complicated situation was examined by Newmark and Sederholm[52,53] for the case of completely non-degenerate exchange (rotation about the carbon–carbon bond in fluorinated ethanes)

$$A_1B_1 \rightleftarrows A_2B_2 \rightleftarrows A_3B_3 . \qquad (18)$$

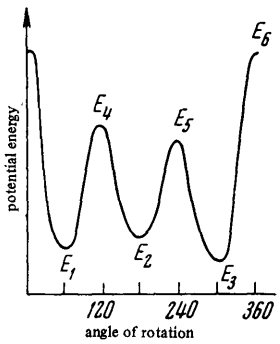


Figure 6. Form of the potential-energy surface for rotation about carbon–carbon bond in unsymmetrically fluorinated ethanes.

The potential-energy curve for such a process is characterised by three maxima E_4, E_5, E_6 and three minima E_1, E_2, E_3 corresponding to three stable rotamers (Fig. 6). Analysis of the stereochemically rigid case will give the populations of the states, i.e. the values of E_1, E_2, and E_3. Determination of the activation barriers E_4, E_5, and E_6 involves analysis of the complete kinetic scheme[52].

4. The most complicated type of system comprising three nuclei with interchange[30] involves exchange among six possible states—ABC, ACB, BAC, CBA, BCA, and CAB—in particular the cyclic exchange

$$ABC \rightleftarrows BCA \rightleftarrows CAB \qquad (19)$$

or exchange between two positions

$$ABC \underset{k_{21}}{\overset{k_{12}}{\rightleftarrows}} BAC . \qquad (20)$$

The latter type of exchange process can be illustrated by the spectra calculated by Binsch[30] (Fig. 7). With very slow exchange the spectrum is described by the parameters (all in Hz) $\nu_A = 19.6$, $\nu_B = 22.9$, $\nu_C = 52.7$, $J_{AB} = 12.3$, $J_{BC} = 7.3$, and $J_{AC} = -17.7$. The spectrum is quite complex, and combination transitions are observed. Increase in the rate k is accompanied by complicated changes in the spectrum, not susceptible to simple analysis. When sufficiently high rates are reached the system passes into an effective A_2B type (the spectrum at k = 10 000 s^{-1} in Fig. 7). Results of an analysis of d.n.m.r. spectra have been published for complete interchange in a system of three spins[31].

5. A system of four spins is represented by the spectrum of formamide $H_2{}^{15}NCHO$,[54] described in general as an ABCX system (where X is the ^{15}N nucleus and C the formyl proton). Here rotation about the partly double carbon–nitrogen bond leads to an exchange process of the type

$$ABCX \rightleftarrows BACX . \qquad (21)$$

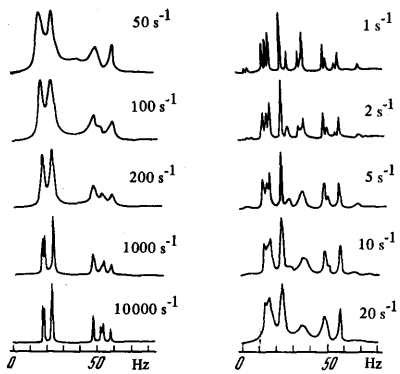


Figure 7. Theoretical spectra[30] calculated for various rate constants by means of a d.n.m.r. programme for exchange of the type ABC ⇌ BAC.

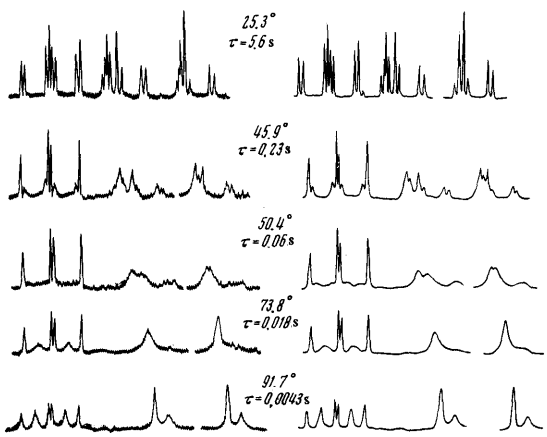


Figure 8. Experimental (on left) and theoretical spectra in formamide $H_2{}^{15}NCOH$ (exchange of type ABCX ⇌ BACX) at various temperatures and rate constants[54].

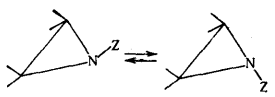
Experimental investigations of this spectrum made at various temperatures by Drakenberg and Forsen[54] are illustrated in Fig. 8. Rate constants were calculated by line shape analysis. A necessary first stage in the calculation was to analyse the ABCX spectrum in the absence of exchange. This gave values of chemical shifts and bond constants (δ_H, J_{HH}, J_{NH}), which were then used in calculating the spectra during exchange by means of a DENSMAT programme[54,55]. A theoretical spectrum characterised by a definite value of k was then selected

by comparison with the experimental spectrum (Fig. 8), after which the activation parameters were calculated (Table 4). This rigorous approach permitted a significant improvement in the accuracy of determination of the activation parameters in comparison with previously published values.

Table 4. Activation parameters in formamide.

Solvent	E_a, kcal mole^{-1}	lg$A$	$\Delta H^{\neq}$, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	$\Delta G^{\neq}_{300°}$, kcal mole^{-1}	Ref.
Pentan-2-one	19.2±0.2	13.2	18.2±0.2	2.7±0.6	17.55±0.2	54
Acetone	13±8	—	—	—	—	56

Another example is provided by inversion in substituted aziridines[57,58]



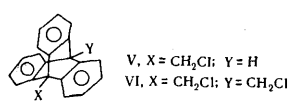
(IVa) (IVb)

The p.m.r. spectrum of the four protons in this compound is described as the AA'BB' system. As a result of rapid inversion at the nitrogen atom, represented by the equation

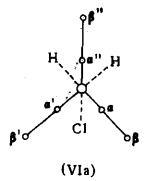
$$AA'BB' \rightleftarrows BB'AA', \qquad (22)$$

the spectrum is converted into a singlet.

6. Rather complicated spin systems have been examined theoretically by Binsch and Kleier[31] (including $A_3B_3 \rightleftharpoons C_3D_3$, $A_3B_3 \rightleftharpoons B_3A_3$, and $AA'BB' \rightleftharpoons CC'DD'$) using symmetry properties. These systems correspond to the upper limit of the possibilities of the best modern electronic computers[30,31]. The investigation of dynamic effects in complicated spin systems is therefore usually based on a series of simplifying assumptions. A very instructive example is the study of hindered rotation about $C_{(9)}$–CH_2Cl bonds in chloromethyltriptycenes[59] substituted at positions 9 and 10 (V, VI)



V, X = CH_2Cl; Y = H
VI, X = CH_2Cl; Y = CH_2Cl



(VIa)

The spectrum of the initial compound (triptycene) consists of two groups of signals with their centres at 5.50 (bridge protons) and at 7.50 and 7.00 ppm (aromatic protons). The spectrum of the latter is quite simple and of type AA'BB' owing to the high symmetry ($C_{(9)}$–$C_{(10)}$ is a threefold symmetry axis). Replacement of the 9- and 10-protons by chloromethyl groups produces significant changes in the spectrum: both parts become notably broader (part A to a greater extent) in the spectrum measured at room temperature. The symmetry of the system may be assumed to be diminished by the hindered rotation of the chloromethyl group; the individual structure is shown as a Newman projection (VIa). On heating, the spectrum becomes narrower, and passes into type AA'BB' at 100°C (Fig. 9). Estimates of the barrier to rotation in this system yielded the value $\Delta G^{\neq}_{300°} = 16$ kcal mole^{-1}.

Similar changes are observed with the monosubstituted 9-chloromethyltriptycene[60], where rapid rotation transforms an extremely complicated superposition of ABCD spectra characteristic of each ring into a comparatively simple spectrum of ABCD type. In this latter case the exchange process is degenerate, and can be represented by a scheme involving all twelve [aromatic] protons in the molecule:

$$A_1B_1C_1D_1A_2B_2C_2D_2A_1B_1C_1D_1 \rightleftarrows A_1B_1C_1D_1A_1B_1C_1D_1A_2B_2C_2D_2 \rightleftarrows \rightleftarrows A_2B_2C_2D_2A_1B_1C_1D_1A_1B_1C_1D_1 . \qquad (23)$$

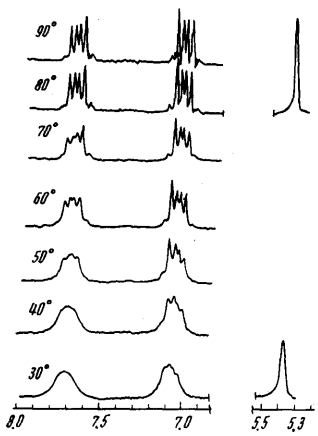
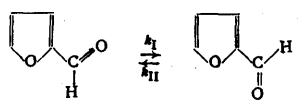


Figure 9. Proton magnetic resonance spectra of 9,10-bischloromethyltriptycene at various temperatures[59].

The exchange scheme for the disubstituted compound will be still more complicated owing to interaction of the chloromethyl groups lowering the symmetry of the system. It is significant that in these examples the spectra are almost incapable of analysis under conditions of stereochemical rigidity.

V. COMBINATION WITH OTHER METHODS OF INVESTIGATION OF THE KINETICS OF CHEMICAL REACTIONS

In several cases the accuracy of the measurement of activation parameters can be significantly improved by combining d.n.m.r. with other methods of determining rate constants[15]. An instructive example is provided by hindered rotation in 2-furaldehyde



(VIIa) (VIIb)

In the p.m.r. spectrum of this compound at room temperature the aldehydic proton is observed as a doublet of doublets with constants $J_{CHO(H_{(4)})}$ and $J_{CHO(H_{(3)})}$ of 0.3 and 0.77 Hz. When the temperature is lowered to −115°C two signals are observed in the region of aldehydic protons, the intensity ratio being 1 : 10. These signals are doublets with separations of 0.85 and 1.10 Hz (low- and high-field signals). The chemical shifts showed that the

isomer (VIIa) is present in higher concentration: i.e. $k_{II} > k_I$ and $\delta G = \Delta G_I^{\neq} - \Delta G_2^{\neq} > 0$. The activation parameters for processes k_I and k_{II} were calculated from the temperature-dependent p.m.r. spectra by means of McConnell's modification of Bloch's equation for unequal p_A and p_B.[61]

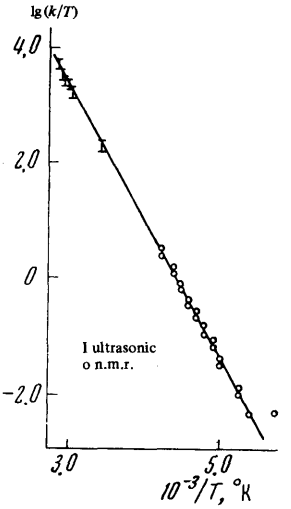
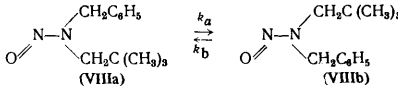


Figure 10. Dependence of lg (k/T) on $1/T$ for rotation in 2-furaldehyde from n.m.r. and ultrasonic relaxation data[62].

The same system has since been investigated by means of ultrasonic relaxation[15], which permits study of equilibria established with rates of 10^5–10^6 s^{-1}. Fig. 10 illustrates the dependence of $\lg k_A/T$ on $1/T$ based on the combined results of n.m.r. and ultrasonic relaxation[62]. Use of an extended temperature range (from −100° to +90°C) enables extremely reliable values to be obtained: E_a = 11.5 ± 0.5 kcal mole^{-1} and the frequency factor $A = 2 \times 10^{13}$ s^{-1}.

In many cases d.n.m.r. can be combined with "visual" kinetic methods (Table 1). Only the isotopic labelling version of these methods is applicable to degenerate exchange processes[1]. The usual methods for measuring concentrations of states (including n.m.r. with integration of the signals) can be applied to non-degenerate exchange processes. We shall examine an investigation of a dynamic process using both n.m.r. methods (in the corresponding temperature range, of course).

Jaeschke et al.[63] have examined equilibrium and exchange in benzylneopentylnitrosamine and detected rotation about the partly double bond:



In the temperature range 0–50°C the rates of both processes are small ($< 10^{-4}$ s^{-1}), so that the slow establishment of equilibrium in the system can be investigated by integration in the n.m.r. spectra, for which purpose a pure rotamer is isolated and appearance of the second rotamer is observed. Above +100°C a gradual broadening of the signals in the nitrosamine spectrum is observed, which enables d.n.m.r. spectroscopy to be used in this range.

These workers[63] concluded from a complete survey of various methods for calculating rate constants from n.m.r. spectra that closely similar results are obtained by parameter analysis and by line shape analysis. In view of the diversity of initial line shapes and the uncertainties in the procedure for matching experimental and theoretical spectral curves, parameter-analysis methods (line widths, distance between signals) were mostly used.

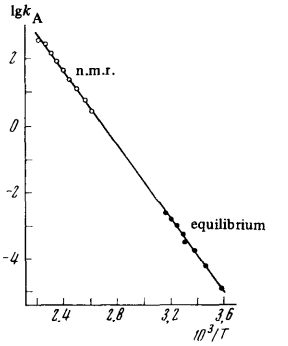


Figure 11. Dependence of $\lg k$ on $1/T$ for the isomerisation of benzylneopentylnitrosamine[63].

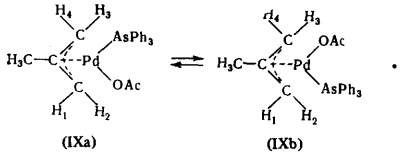
Fig. 11 illustrates the dependence of $\lg k_a$ on $1/T$ based on both equilibrium (integration at low temperatures) and d.n.m.r. (at high temperatures) data. The linearity of this relation enables the two methods to be compared (Table 5), with the following significant conclusions: (*a*) the accuracy of the determination of activation energy from d.n.m.r. spectra is ±10%; (*b*) this is substantially inferior to the accuracy obtained by the equilibrium method (±1.5%); (*c*) use of data from both methods yields an improvement to 0.5%; and (*d*) in all cases the determination of $\Delta G^{\neq}$ is more accurate than that of E_a.

Table 5. Comparison of activation parameters for the process (VIIIa) → (VIIIb) in benzylneopentylnitrosamine obtained by equilibrium method and from n.m.r. spectra[63].

Method	E_a, kcal mole^{-1}	lg A	$\Delta G^{\neq}$, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	Temp., range, °C
Dynamic n.m.r.	25.3±2.2	14.8±1.2	22.0	+6.7	112—182
Equilibrium (integration)	24.2±0.3	14.1±0.2	22.1	+3.5	0—50
Mean	24.7±0.1	14.5±0.1	22.0	+5.2	0—182

Furthermore, the temperature range of the measurement of rate constants can be extended by applying various modifications of d.n.m.r. Mention has already been made

of spin echo methods, useful in the investigation of rapid dynamic processes. Double magnetic resonance (saturation transfer effect) has recently been used to investigate exchange processes where rates of exchange are not too high[64]. An example is the study of pseudorotation in a π-allylpalladium complex[65], sometimes termed *π-rotation*[65]



(IXa) (IXb)

As a consequence of such rotation the spectrum, originally consisting of individual signals $H_1H_2H_3H_4$ somewhat broadened by spin–spin interactions, is averaged out on heating, with the proton H_1 exchanging with H_4, and the proton H_2 with H_3. The occurrence of exchange in the slow stages was proved in this case by the use of double resonance methods, the most detailed description of which has been given by Hoffman and Forsen[64] in a survey of various applications of double resonance.

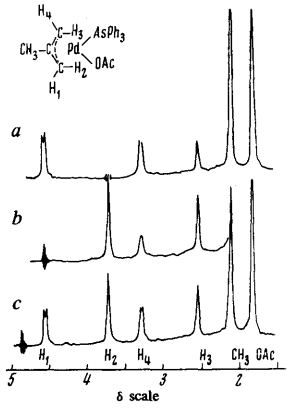


Figure 12. Proton magnetic resonance spectra of π-allylpalladium complex: a) single resonance; b) exposure of signal of proton H_1; c) exposure of signal of proton H_2.[65]

If we imagine a system in which a nucleus can occupy positions A and X, application of the Bloch–McConnell equations gives for the longitudinal magnetisation of nucleus A the formula

$$\frac{dM_z}{dt} = \frac{M_0^A - M_z^A}{T_{1A}} - \frac{M_z^A}{\tau_A} + \frac{M_z^B}{\tau_B} \qquad (24)$$

where M_0 is the equilibrium magnetisation and τ_A the lifetime of state A. If the signal of nucleus B is saturated by means of a second high-frequency field (i.e. $M_z^B \to 0$), we obtain

$$\frac{dM_z}{dt} = \frac{M_0^A}{T_{1A}} - \frac{M_z^A}{\tau_{1A}} \qquad (25)$$

where

$$\frac{1}{T_{1A}} = \frac{1}{\tau_A} + \frac{1}{T_{1A_0}} \quad .$$

The solution of this equation for the equilibrium case is given by

$$M_z^A(t \to \infty) = M_0^A \frac{\tau_{1A}}{T_{1A}} \quad . \qquad (26)$$

Thus the magnetisation in state A falls with increase in the rate of exchange ($\tau/T_{1A} \to 0$). This has been termed the saturation transfer effect. If the signal of the proton H_1 is now exposed to the second high-frequency field, the signal intensity of the proton H_4, bound to H_1 by exchange, becomes weaker. Similarly, exposure of the signal of proton H_2 produces a fall in signal intensity of the proton H_3 (Fig. 12). Thus proof of the occurrence of a dynamic process has not required the measurement of a temperature dependence.

Equation (26) can in principle be used to measure the lifetime τ (from the relative fall in intensity of the signal of state A). However, such measurements encounter certain difficulties (incomplete saturation of signal of state B, allowing for the relaxation time T_{1A}). Use of the saturation transfer effect makes it possible in principle to measure slower processes than in the case of single resonance, since as a rule $T_1 > T_2$, so that the effect can be expected to be appreciable at earlier stages of exchange than can the line-broadening effect (τ/T_2).

The temperature range over which rate constants can be measured can be extended also by the use of carbon magnetic resonance (c.m.r.) spectroscopy. Such spectra are usually recorded under conditions of uncoupling from protons, with a consequent significant improvement in the signal/noise ratio both as a result of collapse of the multiplet structure and because of the Overhauser effect. This is responsible for the first advantage of c.m.r. over p.m.r. spectroscopy, since there is no need to correct for the multiplet character of the spectra. Furthermore, the range of chemical shifts of carbon nuclei is about thirty-fold the range for protons. Equation (11) shows that, for the line width in the case of rapid exchange, it becomes possible to measure faster processes. We have in fact, for rate constants measured at the upper limit of rapid exchange, the ratio

$$k_C/k_H = (\Delta\nu_C)^2/(\Delta\nu_H)^2 \simeq (30)^2\gamma_C^2/\gamma_H^2 \simeq 45$$

where $\Delta\nu_C$ and $\Delta\nu_H$ (Hz) are the ranges of chemical shifts for ^{13}C and ^{1}H spectra respectively. This usually enables rate constants to be measured from c.m.r. spectra at temperatures 50–60 deg higher than in the case of p.m.r. spectra. An example of the use of carbon magnetic resonance for this purpose will be given in Section VI.

VI. FLUCTUATING OR STEREOCHEMICALLY NON-RIGID SYSTEMS

Two main groups—intermolecular and intramolecular processes—can easily be distinguished from the range of dynamic phenomena studied by d.n.m.r. spectroscopy. Intermolecular processes are not discussed in the present Review: references are merely given to sufficiently comprehensive and competent reviews on general[7,8] and special aspects (proton exchange in alcohols, acids, etc.[66], dissociation–recombination processes in organometallic compounds[67]). Several examples of intramolecular processes have been given in Sections III–V. A number of up-to-date reviews have been published on rotations about various types of partly double or sterically hindered bonds[10] and on inversions of various cyclic organic molecules[68].

Recent years have seen a widening use of d.n.m.r. spectroscopy for the investigation of various rearrangements, i.e. processes in which, in contrast to rotations and inversions, some bonds are broken and new bonds are formed. Degenerate intramolecular rearrangements, during which the molecule passes "into itself", are of especial theoretical interest. The individual structures formed during such rearrangements are termed instantaneous structures. In contrast to the classical method of examining rearrangements—isotopic labelling—d.n.m.r. spectroscopy involves considerably fewer technical difficulties and also enables rapid processes to be examined (Table 1). Examples of degenerate rearrangements are extraordinarily varied and are encountered in organic [69], inorganic [70], and organometallic [71] systems. Several terms have been suggested to denote systems capable of degenerate processes—stereochemically non-rigid systems (Muettertis [70]), fluctuating molecules (Doering and Roth [69], Cotton [71]).

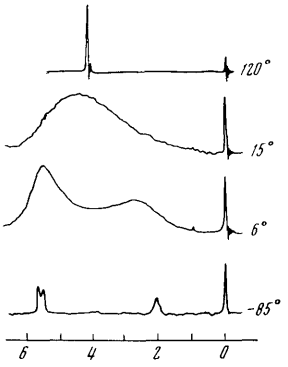
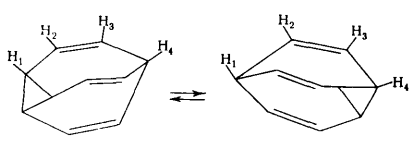


Figure 13. Proton magnetic resonance spectrum of bullvalene measured at various temperatures.

Perhaps the most impressive fluctuating molecule is that of bullvalene, whose existence was predicted by Doering and Roth [69]. The compound itself was prepared and described by Schröder [72]. At sufficiently low temperatures its spectrum consists of two poorly resolved multiplets (Fig. 13): the signal at 5.65 ppm corresponds to the six olefinic protons, and that at 2.08 ppm to the remaining four protons. It is interesting that the proton attached to the tertiary carbon atom gives resonance in the same region as those of the three-membered ring, probably as a result of the magnetically anisotropic effect of this ring. Broadening of both groups of signals is detected on heating above 0°C, the change occurring more rapidly in the high-field signal. On further heating (to 100°C) a singlet appears for all the protons (Fig. 13) with a shift of 4.42 ppm.

Exchange involving all positions is obviously occurring in this system. One step in such exchange is



in which the proton H_1 "rearranges" into H_4, proton H_3 into H_2, proton H_4 into H_1, and H_2 into H_3. At the next stage in the rearrangement the olefinic protons H_2 and H_3 may change positions with those attached to the extreme carbon atoms, and so on. The multiplicity of paths in such a dynamic process and of individual instantaneous structures (computed [69] as 1 209 600) led Doering [69] to introduce the term "fluctuating" molecules. Saunders and Hagen [46] used a programme for multipositional exchange to calculate the activation energy of degenerate rearrangement in bullvalene as $E_a = 11.8$ kcal mole^{-1}, while the entropy of activation is close to zero.

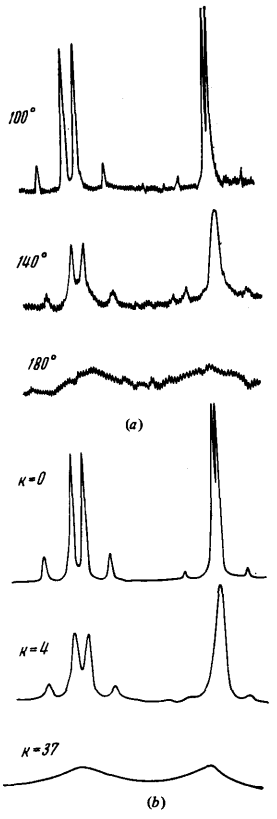
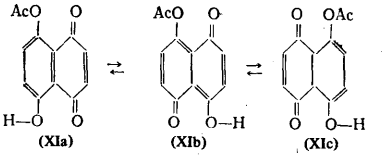


Figure 14. Experimental (a) and theoretical (b) p.m.r. spectra of monoacetatonaphthazarin at various temperatures [73].

An interesting rearrangement has been discovered by Calder et al. [73] in an investigation of the temperature-dependent spectra of acetatonaphthazarin (XI)

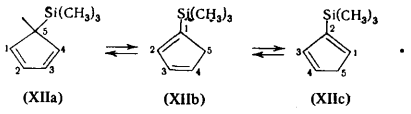


The p.m.r. (100 MHz) spectrum of this compound measured at 100°C (Fig. 14) exhibits two groups of signals

giving spectra of type AB—at 6.70 and 6.67 ppm with a constant J_{HH} = 10 Hz, and at 7.20 and 7.10 ppm with J_{HH} = 8.1 Hz—from which the high-field signals can be assigned to protons of the quinonoid ring. On heating above 140°C the signals begin to broaden, which indicates the occurrence of a dynamic process on the pattern $A_1 \rightleftharpoons A_2$, $B_1 \rightleftharpoons B_2$. The dynamic process may be assumed to involve formation of the product (XIb), which is intermediate (but not transitional) and corresponds to a "jump" by the proton in the hydrogen bond. However, the p.m.r. spectra do not reveal the presence of (XIb), and hence the acetyl rearrangement and the proton shift take place synchronously.

In order to estimate the parameters of the rearrangement theoretical spectra were calculated by the use of a d.n.m.r. programme. The free energy of activation of this process proved to be 22.5 kcal mole^{-1}. Conditions of rapid exchange could not be attained even at 180°C, but available data suggest that the acetyl exchange occurs intramolecularly. It may be supposed that a single spectrum of type AB should be observed at high temperatures.

An example of a fluctuating organometallic molecule is the cyclopentadienylsilicon compound $C_5H_5Si(CH_3)_3$.[39,74] As a consequence of prototropic rearrangement—characteristic also of cyclopentadiene itself[75] and of its alkyl derivatives[76]—this compound may be present in one of the forms (XII):



(XIIa) (XIIb) (XIIc)

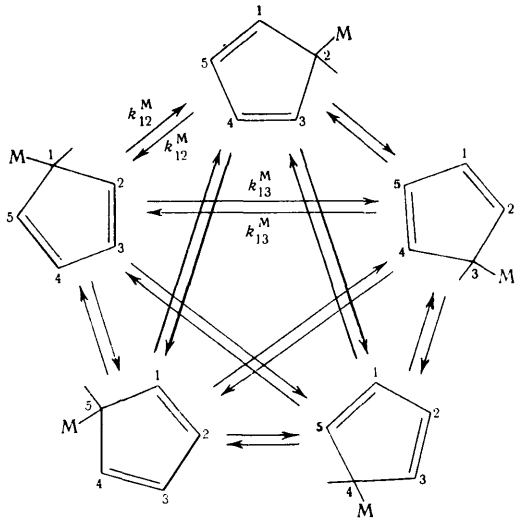


Figure 15. Scheme of degenerate metallotropic rearrangement in cyclopentadienyl derivatives of metals C_5H_5M.

This process is non-degenerate, and is characterised in general by complicated kinetic and equilibrium parameters. Up to temperatures of 100°C, however, the rate constants of prototropic rearrangement are small, so that the process remains slow on the n.m.r. time scale.

The p.m.r. spectrum at room temperature exhibits signals from all three isomers (XII) (a solution of the compound in benzene gives three signals due to the methyl groups with the intensity ratio A : B : C = 90 : 9 : 1). Integral measurements indicate that equilibrium in the compound is displaced towards the isomer (XIIa). Furthermore, a second dynamic process—metallotropic rearrangement, shown diagrammatically in Fig. 15—has been noted with this isomer. The p.m.r. spectrum at −20°C and below includes the AA'BB'X type (Fig. 16) corresponding to the isomer (XIIa), where X is a methine proton (at 3.00 ppm). The following stages of the dynamic process are observed on heating—broadening of the multiplet structure, coalescence of the signals in the AA'BB' part, collapse of all signals, and the appearance of one signal (a singlet) at 5.87 ppm¶.

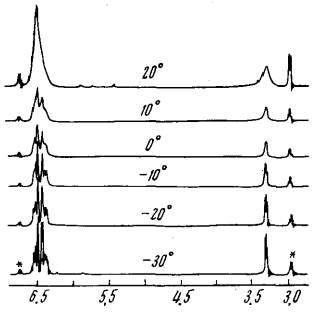
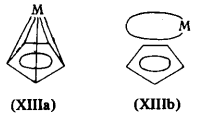


Figure 16. Proton magnetic resonance spectra (100 MHz) of $C_5H_5Si(CH_3)_3$ at various temperatures[39]. Signals marked with an asterisk (*) correspond to contamination with vinyl isomers.

Slow migration of the heavier metals (tin, mercury, gold) in cyclopentadienyl compounds can be achieved only at very low temperatures (around −150°C), and it becomes difficult to choose between alternative structures—true (XIIIa) and effective (XIIIb) centrosymmetric complex



(XIIIa) (XIIIb)

In such cases ^{13}C n.m.r. is useful (Section V), which can be illustrated by a specific example. Migration of the metal across the ring in cyclopentadienyltrimethylstannane $C_5H_5Sn(CH_3)_3$ has such a low activation energy (~ 6 kcal mole^{-1} [77]) that the line width in the proton spectra remains < 1 Hz right down to around −80°C (the most practicable temperatures when carbon disulphide is used as solvent). In the carbon spectra[78] (Fig. 17) significant broadening is already observed at −45°C.

In certain cases accurate line-shape analysis in the n.m.r. spectrum during exchange enables the mechanism of the process to be determined. In cyclopentadienyl

¶ The latter stages of the dynamic process are not shown in Fig. 16, since at high temperatures cyclopentadienyl compounds of silicon dimerise quite rapidly.

derivatives of metals, in particular, it is theoretically possible to choose one of the mechanisms[79] (Fig. 18)—(*a*) 1,2-migration of the metal, (*b*) 1,3-migration, and migration to any position in the ring equally probable, either via a centrosymmetric transition state (*c*) or by intermolecular exchange (*d*). Until quite recently it was both experimentally and theoretically problematical to separate these mechanisms. Experimental determination of the predominant migration was first achieved by Cotton et al.[79] from the unsymmetrical collapse in the d.n.m.r. spectra. This idea has since been used in many studies[39,48,77,78] of the fluctuating behaviour of the cyclopentadienyls of various metals.

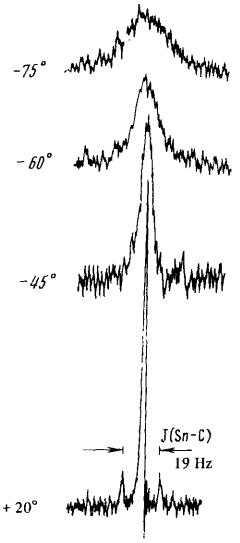


Figure 17. Carbon-13 n.m.r. spectra of trimethylstannylcyclopentadiene at various temperatures[78].

It can be postulated[79,78] that the assignment of the lines in the scheme illustrated by Fig. 15 is such that the low-field signal in the general spectrum AA'BB'X is due to the 1,4-protons of the isomer (XIIa). In a single act of migration the frequencies of the protons will then undergo different changes for the different mechanisms of migration (Table 6). Thus in the case of 1,2-migration the signal A merges with B and X, while signal B merges with A and with the other B (null exchange) (Table 6). The signals of protons A will therefore undergo greater broadening than those of protons B. Thus unsymmetrical broadening of the signals in the olefinic region may be observed at the stage of exchange at which the migration rate constant is comparable with the shift $\Delta\nu_{AB}$ (expressed in frequency units Hz). In the case of the alternative assignment $\delta_A = \delta_{2,3}$ and $\delta_B = \delta_{1,4}$ the signal B will obviously undergo greater broadening.

Examination of the p.m.r. spectra of cyclopentadienyltrimethylsilicon at temperatures near 0°C (Fig. 16) reveals greater broadening of the up-field signal in the AA'BB' part. Unfortunately, *a priori* assignment of the signal in the olefinic part of the spectrum is not possible. Detailed analysis of the spectrum by double resonance under conditions of stereochemical rigidity[39] shows that $\delta_A = \delta_{2,3}$ and $\delta_B = \delta_{1,4}$. Thus silicon undergoes 1,2-migration in its cyclopentadienyl compounds. Correct assignment of the signals is of decisive importance in selecting the predominant mechanism of migration.

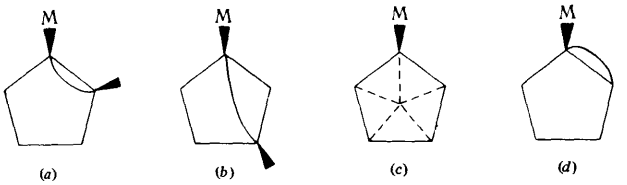


Figure 18. Possible modes of migration of metal in cyclopentadienyl compounds (intramolecular): a) 1,2-displacement; b) 1,3-displacement; c) through a centrosymmetric transition state; d) intermolecular migration.

There is usually no difficulty in eliminating the remaining mechanisms of migration. Unsymmetrical broadening is not observed when migration takes place through a centrosymmetric state or by intermolecular exchange. These two mechanisms can be distinguished by the use of additional data, in particular on the dependence of the rate of migration on the solvent and on the concentration of the solution.

Table 6. Transpositions of nuclei in exchanges involving 1,2- and 1,3-migration.

Position of proton	Position of signals in spectrum ($\delta_A > \delta_B$)		
	initial	final	
		1,2-shift	1,3-shift
5	X	A	B
1	A	B	B
2	B	B	A
3	B	A	X
4	A	X	A

In calculating the activation parameters of metallotropic rearrangement we encounter difficulties that are sufficiently common not to receive special mention. These difficulties arise primarily from the presence of strong spin coupling, which is apparent in the complicated multiplet structure of the signals in the absence of exchange (spectra of type AA'BB'X). Certain technical difficulties connected with the great size of the computations derive from the multipositional character of the exchange (five-position exchange allowing for magnetic non-equivalence—Section IV). In the limit of slow exchange the line width of the methine proton can be used to calculate the rate

constants. On the assumption of a mechanism of 1,2-migration we can write for the line widths of signals A, B, and X[39]

$$\pi\delta\nu_A = \left(\frac{1}{T_2}\right)_A + \frac{1}{\tau}\ ,$$
$$\pi\delta\nu_B = \left(\frac{1}{T_2}\right)_B + \frac{1}{2\tau}\ , \qquad (28)$$
$$\pi\delta\nu_X = \left(\frac{1}{T_2}\right)_X + \frac{1}{\tau}\ .$$

In the region of rapid exchange we can start from the approximations $\delta_A = \delta_B$, $p_A = 4/5$, $p_X = 1/5$. From Eqn. (11) we can obtain

$$k_{eff} \approx \frac{1.61 \cdot (\Delta\nu)^2}{\Delta\nu_{1/2} - (\Delta\nu_{1/2})^0} \qquad (29)$$

where $\Delta\nu$ (in Hz) is the distance between the AB and the X parts of the spectrum, and $\Delta\nu_{\frac{1}{2}}$ is the line width with infinitely rapid exchange.

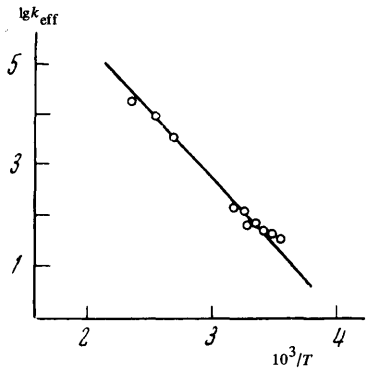
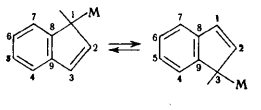


Figure 19. Dependence of lg$k$ on $1/T$ for metallotropic rearrangement in $C_5H_5Si(CH_3)_3$.[39]

Fig. 19 illustrates the dependence of lgk_{eff} on $1/T$ for migration in cyclopentadienyltrimethylsilicon. At low temperatures values of k_{eff} somewhat exceed k_{true}, since initial dipole–dipole relaxation and the multiplet structure make a contribution to the line width. At high temperatures, on the other hand, values of k_{eff} are rather lower than k_{true} owing to neglect of the relaxation term $(1/T_2)$ in Eqn. (28). Extrapolation from each section thus leads to underestimates of the activation energy E_a. A linear approximation to the dependence of lg$k$ on $1/T$ yields for the activation energy E_a and the entropy of activation $\Delta S^{\neq}$ values of 13 kcal mole^{-1} and −9.2 e.u. respectively[39].

Migration of the metal is detected also in indenyl derivatives of Group IVb elements[80,81]:



(XIVa) (XIVb)

The p.m.r. spectra of these compounds show complicated temperature relations, from which it is difficult to calculate rate constants. These difficulties are due primarily to overlapping between the signals from protons of aromatic and five-membered rings. At low temperatures (−30°C with M = $Sn(CH_3)_3$) the spectrum of the protons divides into two parts—ABCD (aromatic protons 4–7) and ABX (protons 3–1). Heating produces a gradual broadening of the signals due to the exchangeable protons H_1 and H_3 in the ^1H spectrum: the spectrum of the aromatic protons passes into that of the AA′BB′ system, while the spectrum of protons 1–3 is transformed into the A_2B system. Because migration is intramolecular the multiplet character of the spectra does not disappear but is averaged out: e.g. the constant J_{AB} for the mean spectrum of type A_2B (protons 1–3) is $\frac{1}{2}(J_{12} + J_{23})$, where J_{12} and J_{23} are coupling constants for the instantaneous structure (XIVa).

The difficulties of calculating rate constants in strongly coupled spin systems with overlapping signals in the p.m.r. spectra can be avoided by using carbon-13 spectra. Under conditions of uncoupling from protons, splitting due to spin coupling with protons is absent from these spectra. It thus becomes possible to apply the Bloch–McConnell equations (Section II).

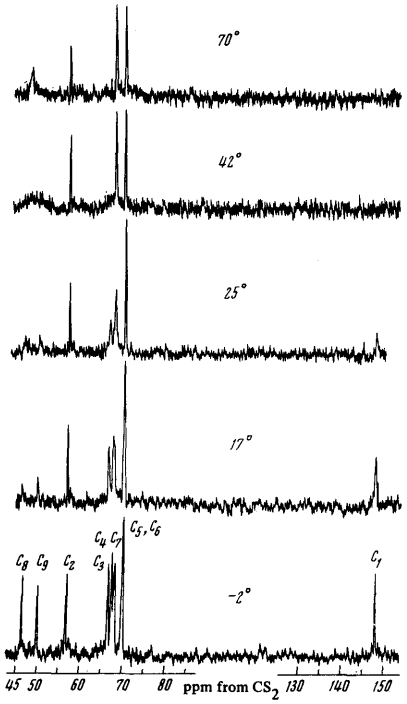


Figure 20. Carbon-13 n.m.r. spectra of trimethylstannylindene with uncoupling from protons at various temperatures[81].

Fig. 20 shows $^{13}C-\{^1H\}$ spectra (25.1 MHz) for trimethylstannylindene $C_9H_7Sn(CH_3)_3$ measured over a range of temperatures[81]. At room temperature (and below) the ^{13}C spectrum corresponds to the stereochemically rigid structure (XIVa). The assignment of the signals to individual carbon atoms is indicated on the spectrum (Fig. 20). Thanks to the absence of spin–spin interaction the exchange can at once be investigated for several pairs of

merging signals, viz. $C_{(1)}$–$C_{(3)}$, $C_{(4)}$–$C_{(7)}$, and $C_{(8)}$–$C_{(9)}$ (the signals from atoms $C_{(5)}$ and $C_{(6)}$ coincide in the limit of slow exchange). Comparison of experimental and theoretical spectral curves by line-shape analysis gives estimates of the activation functions for this process of $E_a = 13.8$ and $\Delta G^{\neq}_{300} = 15.3$ kcal mole^{-1}.

Fluctuating behaviour is of considerable theoretical interest, since it enables structural and kinetic features of certain molecular systems to be described from a single point of view. It may be supposed that d.n.m.r. spectroscopy will lead to the discovery of new classes of molecules of this type, and will enable quantitative aspects to be introduced into the construction of a theory of fluctuating behaviour.

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