Molecular Dynamics: Quadrupolar Microdynamical Labelling

By CH. BREVARD, J. P. KINTZINGER, and J. M. LEHN*
(*Institut de Chimie, 1 rue Blaise Pascal, Strasbourg-67, France*)

Summary Deuterium quadrupolar relaxation is used to study local molecular motions and dynamic coupling between overall molecular reorientations and intramolecular rotations in substituted aromatic molecules.

LINE-SHAPE analysis of n.m.r. spectra has been extensively used in recent years for studying very varied types of intra- and inter-molecular rate processes. Such processes lie in the 1—10^4 sec.$^{-1}$ frequency range.[1,2] However, much faster molecular processes, in the 10^8—10^{12} sec.$^{-1}$ frequency range, may be investigated through the determination of nuclear relaxation times.[3-6] The relaxation of quadrupolar nuclei (spin $\geqslant 1$) is generally dominated by the quadrupolar mechanism, which only depends on rotational molecular motions.[7]

For a nucleus of spin 1, one has:[7]

$$T_q^{-1} = \tfrac{3}{8}\,(e^2qQ/\hbar)^2\tau_q \qquad (1)$$

(T_q: quadrupolar relaxation time; e^2qQ/h: quadrupolar coupling constant; τ_q: correlation time of the molecular motions leading to relaxation).†

Both overall molecular reorientations and intramolecular motions influence T_q and may therefore be studied.[9-11]

The present preliminary report is principally aimed at illustrating through some specific example (compounds **1**—**10**)‡ how *selective "quadrupolar labelling"* may lead to establishing a microdynamic map of molecular behaviour. Any proton in a molecule may in principle be replaced by a deuteron (spin 1). Measuring T_q of a given deuteron then leads to the local correlation time τ_q at the site of the deuteron, if (e^2qQ/h) is known [equation (1)].

Furthermore, the line-shape of the n.m.r. signal of a proton spin–spin coupled to a deuteron is determined by T_q of that deuteron, being a triplet for long T_q and a singlet for short T_q.[7,12,13] We have used conventional ^{1}H n.m.r. and line-shape analysis[14] of the proton signal to determine the quadrupolar relaxation time of the coupled deuteron.§ The correlation times τ_q are obtained from T_q using equation (1).¶

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† In this preliminary report the motions are assumed to be isotropic, τ_q being a characteristic of a given motion. This approximation should not affect our present mainly qualitative conclusions, although in the general case the reorientations of the molecules described here should be considered as anisotropic.[8]

‡ The labelled compounds (**1**—**10**) were prepared in high isotropic purity by conventional methods.

§ Only the up-field half of the proton resonance signal has been analysed. The low-field portion is somewhat distorted by the presence of a small signal ($\leqslant 1\%$) of the undeuteriated compound, thus leading to the slight dissymmetry observed for the peak (see Figures 1 and 2). Independent determinations of T_q(D) by spin-echo measurements on [$^2H_2$]fluorene lead to the same values as those obtained by line-shape analysis on (**1**).

¶ The quadrupolar coupling constants for the deuteron in compounds of the type studied here fall in a narrow range. A value of 170 kHz. has been used.[10] All results reported are for molar solutions in $CDCl_3$. The correlation times τ_q are given in picoseconds (1 psec. = 10^{-12} sec.) units and are characteristic of the solute–solvent system used.

The activation parameters of the local motions at the deuteron site may be obtained from an Arrhenius plot of log (T_q/T) as a function of $1/T$.

In *rigid* molecules like [$^2H_1$]fluorene (**1**) and [$^2H_1$]methylenephenanthrene (**4**), the correlation time τ_q of the deuteron describes the overall molecular motions. The temperature dependence of the 9-H resonance of (**1**) is shown in Figure 1, together with the computed line-shapes. A triplet ($^2J_{HD}$ 3·5 Hz.) is observed at high temperature. The triplet fine structure disappears progressively as the temperature is lowered. A similar temperature-dependence is observed for compound **4**. The corresponding values of T_q and of τ_q have been obtained. At a given temperature, (**4**) leads to a slightly longer value of τ_q (13·0 psec. at 35°) than (**1**) (10·6 psec. at 35°) indicating that its rate of reorientation is slower than that of (**1**). Arrhenius plots[14] yield the activation parameters for the reorientation process:

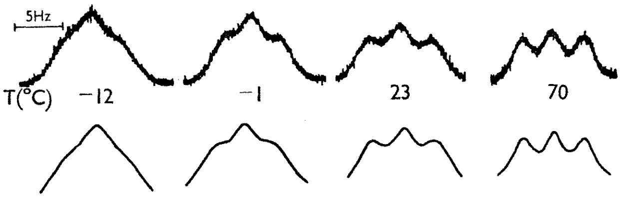


FIGURE 1. *Line-shape analysis and temperature-dependence of the* 9-H *proton resonance of* [$^2H_1$]fluorene (**1**) (*molar solution in* $CDCl_3$). *Experimental* (*above*) *and calculated* (*below*) *curves.*

$\Delta H^\ddagger = 3{\cdot}4$ kcal./mole, $\Delta S^\ddagger = 2{\cdot}8$ eu for (**1**) and
$\Delta H^\ddagger = 2{\cdot}65$ kcal./mole, $\Delta S^\ddagger = 0{\cdot}3$ eu for (**4**).

When *intramolecular motions* are present local correlation times have to be considered. For instance, in a molecule like (**6**) triple labelling allows the local motions at the $C\text{–}CH_2D$, –CHD–O–, and $\text{–CO–}CH_2D$ sites to be studied. Figure 2 illustrates the temperature-dependence of the resonances of the protons in the $C\text{–}CH_2D$ and –CHD–O– groups. In the former case (as well as for the $\text{–CO–}CH_2D$ signal) the shape of the signal is only slightly changed when the temperature is lowered. By contrast, a very marked temperature-dependence is observed in the case of the –CHD–O– signal. It is clear that the local motions are very different: the τ_q values for the CH_2D groups are much shorter and much less temperature-dependent (lower activation free energy) than for the –CHD–O– group. It is also possible to investigate how the overall molecular reorientation and the various intramolecular processes make up the local motion at various sites in the molecule. Such *intramolecular dynamic coupling* of local intramolecular processes (*e.g.* internal rotations, inversions, *etc.*) to the overall molecular motions may be illustrated by studying the mono- and di-labelled systems (**2**), (**3**), (**5**), (**7**), and (**8**) in which two processes are expected to be operating: overall reorientation and internal rotation. In compounds (**2**) and (**3**) the deuterons at C-9 and in the X group may be considered as describing respectively the motions of the rigid molecular framework and the motions within the X groups.†

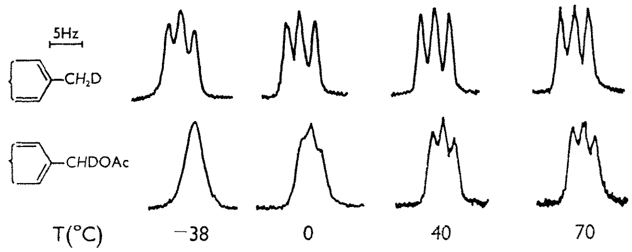


FIGURE 2. *Temperature-dependence of the* $\text{–}CH_2D$ and –*CH*DOAc *proton resonance signals in compound* (**6**) (*molar solution in* $CDCl_3$).

Intramolecular motions are expected to increase T_q and to shorten τ_q[9,10] with respect to a rigid system, the effect being stronger the faster the internal motion. In other words, the actual motions within the X group (characterized by the correlation time $\tau_q(X)$ obtained from T_q of the deuteron in the X group) in (**2**) and (**3**) depend both on the reorientation of the molecular framework and on the internal reorientations (correlation times τ_m and τ_i, respectively).

For (**2**) at 0°: $\tau_m = 35{\cdot}5$, $\tau_q(CH_2D) = 3{\cdot}0$ psec. while for (**3**) at 0° $\tau_m = 61{\cdot}5$ and $\tau_q(\text{CHDOAc}) = 27{\cdot}5$ psec. The effect of internal rotation about the C–X bond reduces $\tau_q(X)$ with respect to τ_m by a factor of 10 in (**2**) and only by a factor of 2 in (**3**). This is in agreement with the much lower barrier to internal rotation expected for $C\text{–}CH_2D$ as compared with C–CHDOAc, leading to much faster internal rotation (smaller τ_q) in (**2**) than in (**3**).**

Thus the amount of coupling between the motions τ_m and τ_i determines $\tau_q(X)$. When τ_m/τ_i is large, maximum decoupling of the two types of motions occurs, whereas $\tau_m/\tau_i \ll 1$ leads to maximum coupling [*i.e.* $\tau_q(X)$ tends towards τ_m]. The "coupling coefficient" τ_m/τ_i is expected to be related to the height of the barrier to internal rotation; thus, if it is possible to determine τ_i, its temperature-dependence may lead to the barrier to internal rotation. This may be shown for compound (**3**).

Assuming that τ_m describes the motions of the C–X axis one may write:[10]

$$\tau_q(X) = 0{\cdot}11\tau_m + 0{\cdot}89\,(\tau_m^{-1} + \tau_i^{-1})^{-1} \qquad (2)$$

Thus, τ_m being obtained from T_q of D at C-9 at each temperature, the temperature-dependence of τ_q may be obtained. An Arrhenius plot leads to the activation parameters for reorientation about the C–CHDOAc bond: $\Delta H^\ddagger = 2{\cdot}5$ kcal./mole; $\Delta S^\ddagger = -1{\cdot}4$ eu.†† The –*C*HDOAc proton signal of (**3**) is much more temperature-dependent than the $\text{–}CH_2D$ resonance of (**2**), indicating that the activation energy is much lower in the second case (Figures 3 and 4).

A similar analysis may be applied to the labelled methylenephenanthrene derivative (**5**). At 35°, $\tau_m = 58{\cdot}0$, $\tau_q(\text{CHDOAc}) = 25{\cdot}0$, and $\tau_i = 35{\cdot}0$ psec. for (**5**), as compared to 23·5, 11·5, and 18·0 psec., respectively, for (**2**).

The attachment of X groups on the fluorene molecule

** Microwave spectra indicate barriers of *ca.* 14 cal/mole for rotation about the $C\text{–}CH_3$ bond in toluene and related compounds.[15]

†† This example is mainly illustrative. The quantitative significance of the numbers obtained (τ_i, $\Delta H\ddagger$, $\Delta S\ddagger$) has still to be analysed in detail.

slows down the molecular motions. The 9-H signal of (**2**) at 0° has a shape similar to that of the 9-H signal of (**3**) at *ca.* 40° (Figures 3 and 4). τ_m at 0° is equal to 25 psec. for (**1**), 35·5 psec. for (**2**), and 61·5 psec. for (**3**).

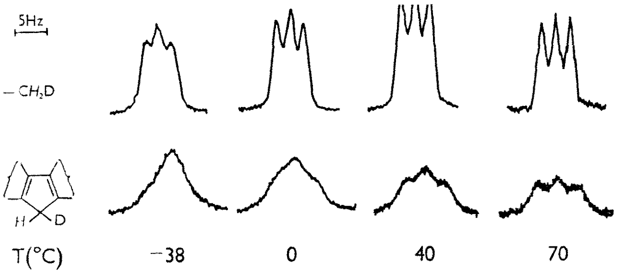


FIGURE 3. *Temperature-dependence of the methylene and* –CH_2D *proton resonance signals in compound* (**2**) (*molar solution in* $CDCl_3$).

Coupling of the overall to the internal motions may also be shown by the effect of increasing molecular size. Thus, the –CHDOAc group occupies similar sites (*i.e.* internal correlation times τ_i should be the same) in (**3**) and in (**7**), in (**5**) and in (**8**). However, the molecules (**7**) and (**8**) are smaller than (**3**) and (**5**), respectively. Increasing molecular size slows down the overall reorientation rate and this effect is transmitted to the CHDOAc group with an atenuation factor depending on the barrier to rotation about the C–CHDOAc bond. Thus at 35° τ_q(CHDOAc) = 8·5, 11·5, 11·7, and 20·2 psec. for (**7**) and (**3**), (**8**) and (**5**), respectively, displaying the expected trend.

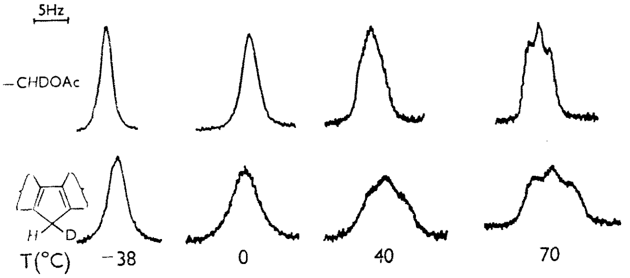
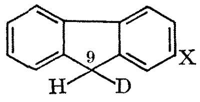
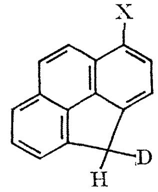


FIGURE 4. *Temperature-dependence of the methylene and* –CHDOAc *proton resonance signals in compound* (**3**) (*molar solution in* $CDCl_3$).

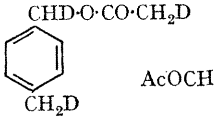
Steric effects are also expected to be of importance in determining molecular dynamical properties. A much longer correlation time is obtained for D in the –CHDOAc group of compound (**10**) (τ_q = 13·7 psec. at 35°) as compared with (**9**) (τ_q = 9·4 psec. at 35°). This may be due in part to the change in inertial properties of the substituted phenyl group, but a major contribution to motional slowing down is expected to arise from steric hindrance to rotation about the C-CHDOAc bond by the two *ortho*-methyl groups in the mesityl derivative (**10**).



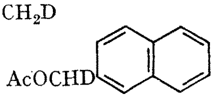
(**1**) X=H
(**2**) X=CH_2D
(**3**) X=CHDOAc



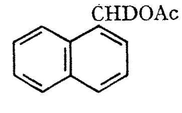
(**4**) X=H
(**5**) X=CHDOAc



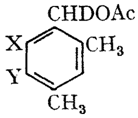
(**6**)



(**7**)



(**8**)



(**9**) X=H; Y=CH_3
(**10**) X=CH_3, Y=H

Selective quadrupolar labelling of complex molecules allows a detailed study of molecular dynamics: overall motions, local intramolecular motions, and effects of molecular size and of steric hindrance. The influence of intermolecular interactions, like solvent effects or complex formation, may also be investigated and, in particular answers to the interesting question of how these interactions perturb local molecular motions may be sought.[16]

A detailed analysis may not always be feasible; however the variations and trends in the number (T_q, τ_q) obtained lead to semi-empirical information which may be of much chemical significance.

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