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MOLECULAR DYNAMICS—VI

DEUTERIUM QUADRUPOLAR MICRODYNAMICAL LABELLING*

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Résumé—Après une introduction sur l'étude des propriétés microdynamiques des molécules par relaxation nucléaire, et plus spécialement par relaxation quadrupolaire nucléaire, une méthode d'étude des mouvements locaux est décrite et discutée. L'analyse de la forme de la raie de résonance d'un proton couplé à un noyau de deutérium fournit le temps de relaxation quadrupolaire du deutéron T_q. A partir de T_q on peut calculer le temps de corrélation τ_q des mouvements moléculaires. De cette manière, le *marquage sélectif* de molécules organiques par le deutérium permet l'étude de la *dynamique moléculaire locale*. L'application de cette méthode à des molécules rigides I–III conduit à une description des effets structuraux sur les réorientations moléculaires globales De la même manière les résultats obtenus pour des molécules non rigides IV–XII, permettent l'analyse des effets structuraux sur les mouvements moléculaires *locaux*. Ainsi le temps de corrélation τ_q est un *index de flexibilité* sur la carte microdynamique de la molécule. Divers effets intermoléculaires sur les mouvements moléculaires ont aussi été étudiés.

Abstract—The study of molecular microdynamical properties using nuclear relaxation, and especially nuclear quadrupole relaxation data is introduced. A method for studying local motions in organic molecules is described and discussed. Lineshape analysis of the resonance of a proton coupled to a deuterium nucleus leads to the deuterium quadrupolar relaxation time T_q from which the correlation time τ_q for molecular motions may be calculated. Thus, *selective deuterium labelling* of organic molecules allows studying *local molecular dynamics*. The method is then applied first to rigid polycyclic molecules I–III and structural effects on *overall* molecular reorientation are described. Similarly analysis of data obtained for a series of non-rigid molecules IV–XII leads to a description of structural effects on *local* molecular motions. Thus the quadrupolar correlation time serves as a *motional index* on the microdynamic map of a molecule. Medium effects on molecular motions are also described.

INTRODUCTION

RELAXATION methods, and especially nuclear relaxation in nuclear magnetic resonance (NMR), have in recent years contributed in a very fundamental way to the study of liquid structure, of intra- and inter-molecular motions in the liquid state. Such studies have been mainly confined to molecular chemical physics although many important issues in organic and physical organic chemistry are directly concerned by the dynamical behaviour of molecules in the liquid state or in solution.

Nuclear relaxation effects in NMR are characterized by a time constant, the nuclear relaxation time T_r, which is directly related to the microdynamic behaviour of molecules in liquids,[2–7] described by a *time dependent function* $F(t)$.

$$T_r^{-1} = AF(t) \qquad (1)$$

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The term A represents the interactions leading to relaxation. Depending on the nature of A the relaxation mechanism may be of different types:

(1) *dipole-dipole relaxation*: interaction between the magnetic moments of the nuclei;

(2) *quadrupolar relaxation*: interaction between the electric quadrupole moment of nuclei having a spin $\geqslant 1$ and the molecular electric field gradients;

(3) *paramagnetic relaxation*: interaction between nuclear spins and electron spins of paramagnetic species present in medium;

(4) *scalar relaxation*: indirect interaction between nuclear spins (spin–spin coupling interaction);

(5) *spin-rotation relaxation*: interaction between nuclear magnetic dipoles and the orbital magnetic moments arising from the nuclear and electronic motions;

(6) *relaxation by anisotropic chemical shifts*: interaction between nuclear magnetic moments and anisotropic magnetic fields.

When several mechanisms are operative for a given nucleus, its relaxation time is

$$T_r^{-1} = \sum_i T_r(i)^{-1} \tag{2}$$

These interactions may be intra- or intermolecular or both in some cases. The function $F(t)$ is a complex function of intra- and intermolecular, rotational and translational motions. In the simplest case, that of isotropic motion, $F(t)$ represents the *correlation time* τ_c of the molecular reorientations.

However, in the general case, the molecular motions are anisotropic[8,9] and the form of $F(t)$ depends on the reorientational model used to describe the molecular motions (rotational diffusion[2,10–12] inertial rotation[13–14] conditional rotational diffusion;[15] conditional inertial rotation[16]). Furthermore, *internal motions* in molecules (rotations around bonds, inversions) also contribute to local reorientations and have to be taken into account in the function $F(t)$[17–21].

Dipole–dipole relaxation is dependent both on intra- and on intermolecular motions, necessitating a separation of the two contributions. *Quadrupolar relaxation* has the advantage of depending only on intramolecular motions, molecular rotations, since intermolecular contributions to local electrical field gradients are very weak. Therefore no separation is necessary. In addition, in most cases quadrupolar nuclei relax mainly by the quadrupolar mechanism, the A term in equation (1) being generally much larger for this mechanism than for all others which contribute to the relaxation. Thus the quadrupolar contribution T_q being dominant in the total relaxation time, no separation of the contributions of the other mechanisms is necessary. As a result, quadrupolar relaxation is particularly well suited for studying intramolecular motions.

Nitrogen 14, chlorine 35, and deuterium quadrupolar relaxation have been used for determining the correlation times of various nitrogen,[22] chlorine[23] and deuterium[24–28] containing substances.

A detailed study of motional anisotropy and of internal rotations (determination of the three principal diffusion constants and of rates of internal rotation) requires the simultaneous study of several different quadrupolar nuclei in the same molecule or of specifically labelled molecules.

Such investigations have been performed on CD_3—CN[29–31], ^{14}N, ^{17}O and d_1-N,N,dimethyl formamide,[32] CD_3—C≡CH and CD_3—C≡CD,[33] $CDCl_3$,[34, 35] deuterated isobutylenes,[36] $VOCl_3$, BCl_3 and CCl_3CN,[37] specifically labelled α, β and deuterated pyridine.[1, 38] Methylbenzylcyanides,[39] partially deuterated alkanes[40] and specifically deuterated organic liquids,[28, 41, 42] pure or as aqueous mixtures, have also been studied.

The temperature dependence of the correlation times or diffusion constants obtained leads to the activation parameters of the reorientation process. The experimental data, the quadrupolar relaxation times, have generally been obtained from the resonance of the quadrupolar nucleus. The same information may be obtained by analysing the lineshape of a dipolar nucleus (for instance ^1H, ^{19}F) presenting a spin–spin coupling with a quadrupolar nucleus. In such cases, the spin–spin splittings of the resonance of the nucleus are well resolved when the quadrupolar relaxation time T_q of the quadrupolar nucleus is long; as T_q becomes shorter the splittings disappear progressively and a single line is obtained for short T_q values. Theses effects have been described theoretically.[43–45]

Temperature changes affect the line-shapes[46] by speeding up or slowing down the molecular motions.

Spin–spin coupling to a quadrupolar nucleus and quadrupolar effects on lineshapes have been observed in the ^1H spectra of various nitrogen 14 (isonitriles,[47] ammonium salts,[48–51] nitrogen containing heterocycles,[52] nitro compounds,[53] boron[54] and deuterated[55–56] compounds, and in the ^{19}F spectra of compounds containing a boron[57, 58] chlorine,[57] arsenic,[50] niobium[60] or nitrogen[61] quadrupolar nucleus coupled to the fluorines. In several of these investigations the molecular correlation times have been calculated from quadrupolar relaxation times obtained by analysing the lineshape of the proton or fluorine signals. Recently also it has been possible to use this method for studying the dynamics of π–π complex formation.[62] Following our previous work on nitrogen and deuterium nuclear quadrupolar relaxation and on proton lineshapes,[49, 51, 53, 55, 62] we present here a detailed study of overall and internal molecular motions in a number of derivatives of aromatic molecules* using *selective deuterium quadrupolar labelling* and lineshape analysis of proton resonances in coupled H, D systems; it is in principle possible to derive in this way a *microdynamic map* of the molecules studied.

In the present paper a number of systems will be examined and several structural effects will be illustrated and discussed. In the following paper, attention will be given to a more quantitative separation of local motions into overall and internal molecular reorientations, and the *intramolecular dynamic coupling* of both types of motion will be discussed. The work described here, together with previous studies (see above) may also help defining the scope and limitations of such investigations in problems of molecular dynamics in organic and physical organic chemistry.

METHODS AND RESULTS

Method, general comments

It is first of all necessary to discuss the merits and the drawbacks of the method used in our studies of molecular dynamics. We selected the following method of

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* The dipole–dipole relaxation of the ring and Me protons in toluene and in the xylenes has been studied recently.[63, 64]

investigation: *measurement of deuterium quadrupolar relaxation times by lineshape analysis of the resonance of a proton spin–spin coupled to the deuterium nucleus.* This procedure has numerous advantages:

(1) Since deuterium has a quadrupolar nucleus (spin 1), it has the general advantages of *quadrupolar relaxation*:

quadrupolar relaxation is generally by far the *dominant* relaxation mechanism of a quadrupolar nucleus;

Since the quadrupolar interaction is large (compared to the other interactions) T_q is very sensitive to motional changes in $F(t)$;

It is generally not necessary to degass the samples to remove the dissolved paramagnetic oxygen:

Only *rotational* (but not translational) motions contribute to the relaxation since these motions alone produce fluctuations in the quadrupolar interaction between the nuclear quadrupole and the electric field gradient; in combination with dipole–dipole relaxation studies an easy separation of intra- and intermolecular motions becomes possible.

(2) The choice of the *deuterium nucleus* as quadrupolar nucleus has also advantages:

The electric *field gradient* at the deuterium site is, to a larger extent than for the other quadrupolar nuclei, mainly dependent on the nature of the X—D bond and is remarkably constant in similar molecular environments, especially for C—D bonds; long range effects are negligeable in most cases;

As a corollary *intermolecular* effects on the field gradient at D in >C—D are very small; this is certainly not true for other nuclei, like ^{14}N for instance;[52]

Because of the low quadrupolar coupling constants generally encountered, relaxation rates are in most cases such that lineshape changes may be easily observed (in the case of ^{14}N the relaxation rates are generally much too fast so that only line broadening is observed[52]);

Isotopic substitution of a hydrogen atom by a deuterium atom may in principle be performed at any molecular location; *quadrupolar labelling* by deuterium is thus especially attractive.

(3) Finally the use of *lineshape analysis* of proton resonances has also distinct merits:

Lineshape analysis of the resonances of protons coupled to a deuterium allows the relaxation time of the deuterium to be determined with proton magnetic resonance *sensitivity* (gain: factor of *ca* 100); this advantage is essential for using quadrupolar relaxation in biophysical studies;[65]

The lineshape changes are appreciable and easily detected;

At last, from a *practical* standpoint, regular proton resonance spectrometers, now widely available, may be used to perform the measurements. However, this procedure has also some drawbacks:

Deuterium labelling may not be straightforward, there is therefore a synthetic problem;

The choice of the *substrate* to be studied may become difficult as it must contain locations where appreciable H,D couplings exist (—CHD—, —CH=CD— groups for instance);

The quadrupolar relaxation times may be estimated by comparing visually calculated and experimental lineshapes, but for obtaining accurate data curve fitting by means of a *computer* is essential;

When measurements over extended ranges of temperatures are desired, spin–echo measurements may be preferable, since lineshape changes occur in a comparatively less extended range of temperatures: it is nevertheless commonly found that lineshape analysis may be used over a range of *ca.* 100° or more.

Lineshape analysis, deuterium quadrupolar relaxation times and molecular correlation times

Lineshape analysis of the resonances of protons spin–spin coupled to deuterium has been performed using the general lineshape equations [3, 43, 44] and taking into account the "natural" line width at half height in the absence of quadrupolar relaxation Δ (non-quadrupolar line width) as described earlier.[53] By fitting the calculated curves to the experimental ones with a computer, one obtains the deuterium quadrupolar relaxation times T_q.[53, 38, 72]

In two cases the values determined in this way have been checked by spin–echo measurements on the deuterium resonance: excellent agreement of both methods has been found (section 5). For a nucleus of spin 1, the quadrupolar relaxation time T_q is given by:[3]

$$T_q^{-1} = \frac{3}{8}\left(1 + \frac{1}{3}\eta^2\right)\left(\frac{e^2qQ}{\hbar}\right)^2 F(t) \tag{3}$$

with: q electric field gradient at the nucleus of quadrupolar moment Q: η asymmetry parameter of the field gradient. The molecular motions are generally anisotropic in non-symmetric molecules. However, in this first part, we shall make the more or less crude assumption, depending on the system considered, of isotropic reorientation, and replace the correlation function $F(t)$ by a single correlation time τ_q, which will in a sense be used as a motional index on the microdynamic map of molecule. In molecules without internal rotations τ_q is the overall molecular correlation time τ_M: when such rotations are present, τ_q represents local motions which are a combination of overall and internal motions.

As it will be seen, even in this approximation useful data may be gathered for a number of systems, which are generally too complex for a complete anisotropic analysis to be performed (in a reasonable time span!) although such an analysis is possible in principle. As η is very small for C—D bonds,[69, 70] (3) becomes:

$$T_q^{-1} = \frac{3}{8}\left(\frac{e^2qQ}{\hbar}\right)^2 \tau_q \tag{4}$$

The exact deuterium quadrupolar coupling constant (e^2qQ/h) is not known in the compounds studied here. However, as pointed out above, it does not change much if the C—D bond is of similar nature. Thus for sp^3 type C—D bonds the following values have been obtained: 174 kHz in cyclohexane-d_{12},[66] 160 kHz in CD_2Cl_2,[67] 171 kHz in CD_3-Br,[68] 148 kHz in CD_3CN,[68] 165 kHz in toluene —α-d_3[66] 168 kHz in $CD_2(COOH)_2$[69] and in copper acetate —d_3,[70] 176 kHz in $CD_3—C\equiv CH$.[71] For the systems studied here we have then chosen a value of 170 kHz which is probably correct within 5–10% in all cases. Equation (4) then becomes:

$$T_q^{-1} = 0{\cdot}43\ 10^{12}\tau_q \tag{5}$$

For the other relaxation mechanisms of the deuterium nucleus, the numerical factor in (5) is much smaller;[38, 72] it is only 0·7 10^9 for dipole–dipole relaxation of D by a proton at a distance of 1·80 Å (—CHD— groups).

The temperature dependence of T_q leads to the activation parameters for molecular reorientation: the free energy $\Delta G^\ddagger$, the enthalpy $\Delta H^\ddagger$ and the entropy $\Delta S^\ddagger$ of activation. Using the previously derived relations[53] and equation (5) one has:

$$\log(\tau_q T)^{-1} = 10{\cdot}32 + \frac{\Delta S^\ddagger}{4{\cdot}57} - \frac{\Delta H^\ddagger}{4{\cdot}57\,T}$$

$$\log(T_q/T) = \frac{\Delta S^\ddagger}{4{\cdot}57} - 1{\cdot}31 - \frac{\Delta H^\ddagger}{4{\cdot}57\,T} \tag{6}$$

$$\text{since} \qquad \Delta G^\ddagger = 4{\cdot}57\,T\,[10{\cdot}32 + \log(\tau_q T)] \tag{7}$$

Knowing T_q and its temperature dependence, equation (5) and $\log(T_q/T) = f(1/T)$ plots according to equation (6) lead to τ_q and to $\Delta H^\ddagger$ and $\Delta S^\ddagger$. It should be stressed that for solutions, the results obtained describe of course the motions of the solute molecule in a given solvent. Thus it is also possible to study *solvent effects.*

After obtaining correlation times from relaxation times, the second stage in an understanding of molecular motions in liquids is represented by the interpretation and the calculation of τ_q in terms of molecular structure parameters and of solution properties.

This is a very complex task. In the simplest case of a sphere in a viscous medium the Stokes–Einstein relation gives the correlation time τ_c as[2]:

$$\tau_c = \frac{4\pi\eta a^3}{3kT} \tag{8}$$

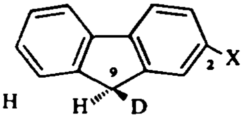
Where η is the viscosity and a is the molecular radius. However, the τ_c values obtained in this way are too large and correction factors have been introduced for solutions of spherical molecules (mutual viscosity;[73] microviscosity factor[74]). A detailed quantitative analysis in terms of liquid structure is only possible when a complete study including anisotropy effects is performed.

Substrates

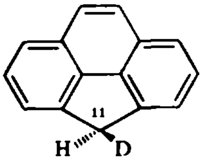
Compounds I–XII have been used as substrates for our studies. Their methods of preparation are described in the experimental section. They have been chosen because they display a variety of interesting structural effects on molecular microdynamical properties, while at the same time presenting appreciable H, D spin–spin coupling and allowing a relatively easy introduction of the deuterium label.

RESULTS

Quadrupolar effects on the lineshape of the —CHD— proton resonances have been observed for all compounds I–XII. The lineshapes depend on the type of molecule and of —CHD— group studied; they change with temperature from a more or less well resolved triplet at high temperature (fast molecular motions; short τ_q; long T_q)



Ia X = H
Ib X = CH_2D
Ic X = Cl
Id X = Br
Ie X = I



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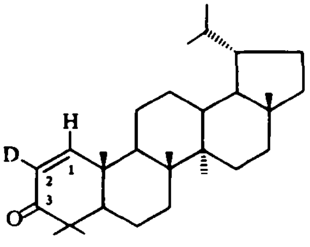

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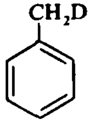

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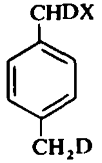
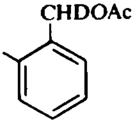


Va X = OH
NbX = O—CO—CH_2D



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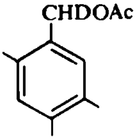

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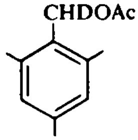

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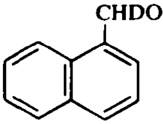

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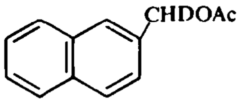

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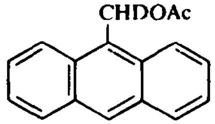

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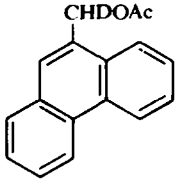

XII

to a more or less broad single line at low temperatures (slow molecular motions: long τ_q; short T_q).

Fig 1 illustrates the spectral modifications obtained for the three different deuterium labels in compound Vb. The —CO—CH_3 impurity present may serve as an indicator for the onset of quadrupolar broadening in the —CO—CH_2D resonance. The results obtained for compounds I-XII are listed in the Table. The values of the H, D couplings have been measured at high temperature (at about 110°) where the signals are much better resolved because of increased T_q. The non-quadrupolar linewidth parameter Δ includes broadening caused by unresolved long range spin-spin coupling. During lineshape analysis, variations in $J_{H,D}$ and Δ have been allowed in order to optimize line-fitting as a function of T_q.

The values listed for these parameters are those leading to the best fit. As expected the Δ values obtained for —CHD— proton resonances are somewhat smaller (some tenths of a Hz) than the linewidths measured in similar conditions on the corresponding —CH_2— signal.

Fig 2 shows an example of lineshape analysis performed on d_1-fluorene, Ia. The correlation times τ_q and the free energies of activation $\Delta G^{\ddagger}_{306}$ at 306°K have been obtained using equations (5) and (7). The enthalpies and entropies of activation, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ have been obtained from $\log(T_q/T) = f(1/T)$ plots according to equation (6). The plots for compounds Ia and II are shown in Fig 3.

The accuracy and the interpretation of the low $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values obtained leaves however much to be desired. This is a general problem and especially the meaning of $\Delta S^{\ddagger}$ is far from being clear.[75] Thus, it is much preferable to discuss τ_q and $\Delta G^{\ddagger}$ values

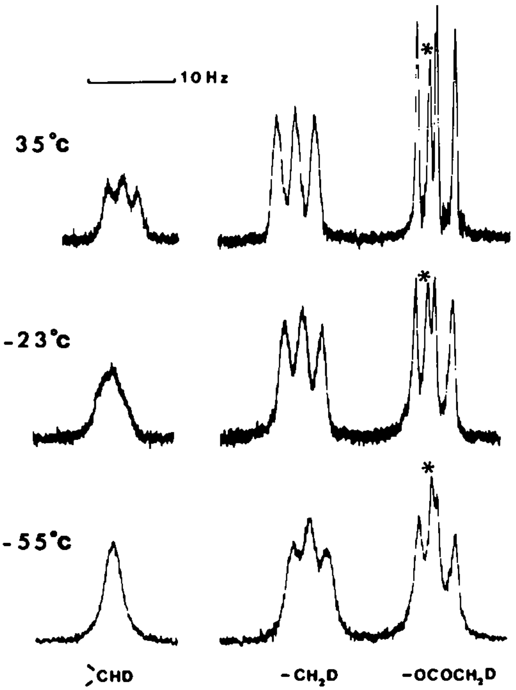

FIG 1. Temperature dependence of the PMR spectrum of the deuterium labelled compound Vb (60 MHz; $CDCl_3$ solution). Undeuterated acetyl peak (*).

at the same temperature in a series of related compounds which probably have very similar $\Delta S^{\ddagger}$ values. This is especially to be preferred when assuming isotropic motions as is done here. In cases where the quadrupolar contribution to the lineshapes is too small (as in the —CO—CH_2D group of Vb) only a lower limit to T_q may be determined.

DISCUSSION

Overall molecular reorientation

Although none of the molecules studied here presents isotropic motions, the correlation times for overall molecular reorientation obtained by assuming isotropy, are a valuable index of molecular dynamical behaviour (see also above). In fluorene Ia and its 2-substituted derivatives Ib–Ie, in methylene phenantrene II, and in Δ^1-lupenone III, the deuterium label is rigidly attached to the molecular framework and thus describes overall molecular motions. These compounds cover a range of molecular sizes.

From tricyclic (I) to tetracyclic (II) and to pentacyclic (III) systems, the reorientation time increases with molecular size. It increases also when larger substituents are attached to the fluorene skeleton. The correlation time is related to the molecular volume (equation 8).

Anisotropic reorientation of a rigid ellipsoidal body has been treated by Shimizu.[76] A crude estimate of the relative effect of molecular volume in our systems may be obtained by replacing the volume of a sphere by that of an ellipsoid in equation (8)

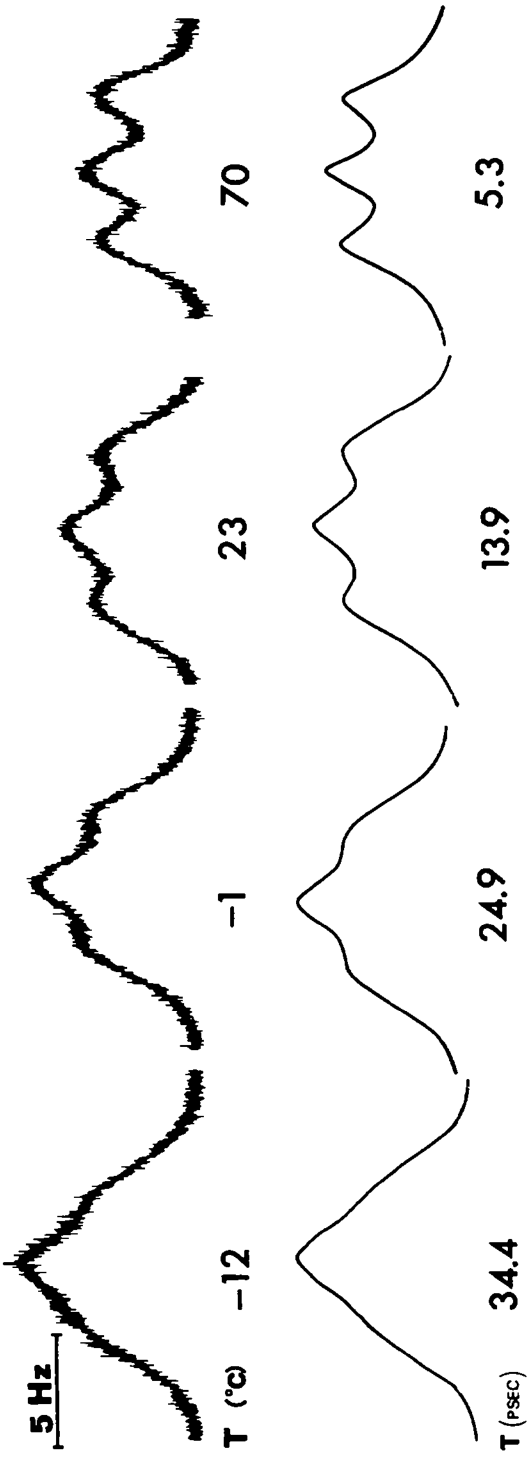

FIG 2. Lineshape analysis of the —CHD— proton resonance of 9-*d*-fluorene, Ia. Temperature dependence of the signal and of the deuterium quadrupolar correlation time.

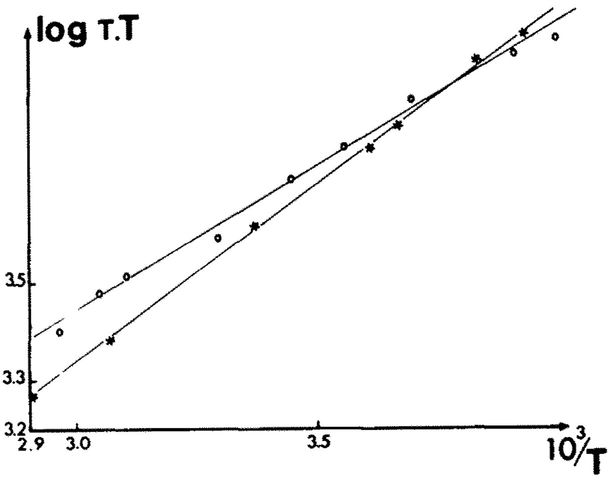

FIG 3. Activation plots log ($\tau_q T$) = $f(1/T)$ for compounds Ia (*) and II(0)

and comparing ratios of correlation times τ'_q/τ_q to ratios of semiaxes products $a'b'c'/abc$.

$$\tau = \frac{4\pi\eta abc}{3kT} \tag{8'}$$

Measuring a, b and c on molecular models and taking Ia as reference one has:

Compound i	Ia	Ib	Ic	Id	Ie	II	III
$\tau_q(i)/\tau_q(Ia)$	1	1·5	2·0	2·25	2·45	1·3	2·3
$(abc)_i/(abc)_{Ia}$	1	1·05	1·1	1·15	1·35	1·55	4·0
$(MW)_i/(MW)_{Ia}$	1	1·12	1·25	1·53	1·82	1·18	2·58

It is seen that the correlation between the two ratios leaves much to be desired. The trend along the Ib–Ic series is found, however compounds Ib–Ic behave quite differently from Ia; especially sharp inconsistencies are found for II and III. Thus, a simple formula such as (8') cannot be used to predict dynamic behaviour of complex molecules. In addition to the theoretical limitations of the model, strongly anisotropic motions of the substrates and the very different nature of the solvent molecules are for an important part at the origin of these discrepancies.

Only the actual experimental result allows the molecular behaviour to be described. It is seen that even in rigid molecules, the notion of "overall" motions has a *local* sense. The knowledge of the motions of a given site in a molecular framework may be of interest in the study of molecular reactivity, especially in the case of very fast processes. In the inertial model[13–14] of the reorientation process, the correlation time depends on the square root of the moments of inertia of the molecule which itself is a function of the molecular mass.

The moments of inertia of the present molecules are not known. We thought that there might be some interest in comparing the ratios of the correlation times to those of the molecular weights of compound i and Ia: $(MW)_i/(MW)_{Ia}$. These ratios are also given above. It is seen that the agreement is somewhat better than in the case of the molar volumes, especially the trends between systems I, II and III are better reproduced. The values themselves remain quite different, but a better agreement is not expected in such a grossly approximate comparison. In addition, the same remarks apply as for the molar volume dependent model (see above). It is also worth comparing our results to those obtained from dielectric relaxation studies of fluorenone and of phenantrenequinone.[77] The relation between dielectric and NMR correlation times is[3, 7] (see also the following paper):

$$\tau_{\text{diel}} = 3\tau_{\text{NMR}} \tag{9}$$

The dielectric relaxation data lead to the following results:[77]

	τ_{diel} (psec)	$\Delta G^{\ddagger}_{306}$ (kcal/mole)	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (eu)
Fluorenone	14·9	2·8	2·0	2·6
Phenantrenequinone	22·2	3·1	2·6	1·6

In similar conditions (benzene at + 40°)*, we obtain:

τ_q = 9·7 psec for I*a* and 12·6 psec for II.

The agreement between the dielectric and the present values (equation (9)) is reasonable considering the differences in molecular structure and in experimental conditions. Dielectric relaxation studies[80] of Δ^4-cholestenone and of $\Delta^{20(30)}$-lupenone in benzene and decalin lead to relaxation times (>200 psec) which seem much too long when compared to the results obtained for fluorenone or phenantrenequinone by the same method (see above). The deuterium at C(2) and the carbonyl group at C(3) in III should reorient in a very similar fashion: thus one would expect a dielectric relaxation time of *ca.* 75 ± 25 psec. in similar experimental conditions.

Intramolecular motions

When the deuterium label is borne by a group undergoing internal rotation its local motion is dependent on the *dynamic coupling* between the overall reorientation and the internal motion. Separation of both components is possible and will be attempted in the following paper. We shall here discuss primarily the structural effects on the resultant *local* motions. The temperature dependence of —CHD— resonances of the triply labelled compound *V*b (Fig. 1) clearly shows that local motions and their changes with temperature are very different. Fast internal motion efficiently decouples the local motions from the overall reorientation. This is the case for the —CH_2D groups in IV and V. When the barrier to internal rotation increases, both motions are coupled. Thus, structural features hindering internal motions greatly affect local motions and render them more sensitive to changes in other parts of the molecules.

The barrier to internal rotation in toluene is very low (14 cal/mole[78]): as a consequence —CH_2D proton resonances are only slightly temperature dependent and display well resolved triplets at low temperatures. As shown in Fig 1 the —CO—CH_2D signal is even less temperature dependent. This is due to the presence of several internal

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* The concentration is not given in ref. 77. We used 0·8M solutions: on dilution τ_q is expected to decrease.

motions between the —CH_2D group and the part of the molecule with largest inertia, the aromatic ring. Internal rotation about the C—CHDOAC bond is certainly much slower, so that several structural effects may be observed. Making the reasonable assumption that the contribution of internal rotations is similar in similar environments one finds a clear effect of an increase of *molecular size* on local motions. Indeed, τ_q, $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ are appreciably larger in VII, X, XII than in VI, Vb and IX respectively because of the addition of new groups to the molecular framework (addition of two —Me groups in VII, of an extra aromatic ring in X and XII). Conversely, keeping the molecular size nearly constant, *steric effects* which hinder internal motions lead to a stronger coupling of the —CHDOAC reorientation with overall motions. Thus, larger τ_q, $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ values are found in VIII and IX than in VII and X respectively. In VIII internal rotation is hindered by the presence of an extra *ortho*-CH_3 group; in IX it is probably the steric effect due to the *peri* C—H bond which is operative. No change is observed from Vb to VI although one goes from *para* to *ortho* substitution; this might arise from the fact that in VI librational motion is probably much less hindered, than complete rotation. The anthracene derivative XI displays the largest —CHD—OAC correlation time of all compounds studied: comparison with XII indicates that this arises probably from increased hindrance to internal rotation by two *peri* interactions.

Intermolecular and medium effects

The motion of a molecule in a solution is of course strongly influenced by the nature of the solvent and the concentration of the solution; this results from equation (8) where τ_c is proportional to the viscosity of the medium. Furthermore, intermolecular interactions also show up in the dynamic properties of a molecule. Activation parameters for the reorientation process of a solute molecule depend both on the behaviour of solute and solvent molecules.

The Arrhenius activation energy E_a for the reorientation of the chloroform molecule is *ca.* 1·5 kcal/mole from nuclear relaxation measurements; the activation energy of the viscosity is 1·8 kcal/mole.[23, 34] Since

$$\Delta H^{\ddagger} = E_a - RT \tag{10}$$

the corresponding activation enthalpies are respectively ($RT \sim 0{\cdot}6$ kcal/mole at 25°C): *ca.* 0·9 and 1·2 kcal/mole. These values are much lower than those measured for the present compounds which are generally above 2 kcal/mole some of them attaining 3 kcal/mole. From this one may conclude that the solute molecule retains much of its identity in the solution. Nevertheless, changing from CH_2Cl_2, to $CDCl_3$ to $CHBr_3$ solutions of Ia, the reorientation of the fluorene molecule slows down and the free energy of the activation increases as the solvent molecules become larger (see Table 1). According to equations (8) and (8′), the ratios of the τ_q values should be comparable to the ratios of the viscosities of the solvents. This is grossly verified: with:

$$\eta(CH_2Cl_2) = 0{\cdot}38,\ \eta(CHCl_3) = 0{\cdot}49 \text{ and } \eta(CHBr_3) = 1{\cdot}65 \text{ cp}$$

TABLE 1. DEUTERIUM QUADRUPOLAR RELAXATION TIMES (T_q) CORRELATION TIMES (τ_q) AND ACTIVATION PARAMETERS ($\Delta G^\ddagger$, $\Delta H^\ddagger$, $\Delta S^\ddagger$) OBTAINED BY PROTON LINESHAPE ANALYSIS FOR COMPOUNDS I–XII[a]

	Compound (solvent: $CDCl_3$ concentration: 1·0M)	J_{HD} Hz ± 0·1	Δ^b Hz ± 0·1	T_q msec ± 5%	τ_q psec	$\Delta G^\ddagger_{306}$ kcal/mole ± 0·1	$\Delta H^\ddagger$ kcal/mole ± 0·5	$\Delta S^\ddagger$ e.u. ± 2	Temperature range (°C) for $\Delta H^\ddagger$ and $\Delta S^\ddagger$ determination
Ia		3·5	1·9	220	10·6 ± 0·5	2·5	3·3	2·6	−18, +70
Ia	($CHBr_3$, 1·0M)	3·5	1·9	83	28 + 1	3·10	3·0	−0·4	+30, +82
Ia	(CH_2Cl_2, 1·0M)	3·5	1·9	260	90 ± 0·5	2·40	1·9	−1·8	−3, +33
Ib	—$C\underline{H}D$—	3·5	1·9	140	16 ± 1	2·8	2·4	−1	−56, +72
	—$C\underline{H}_2D$	2·2	1·1	>900	<2	—	—	—	—
Ic		3·5	1·9	110	21 ± 1	2·9			
Id		3·5	1·9	98	24 ± 1	3·0			
Ie		3·5	1·9	88	26 ± 2	3·1			
II		3·4	1·6	180	13·6 ± 0·6	2·7	2·6	0	−23, +63
III		1·6	0·7	93	25·1 ± 2	3·1			
IV		2·2	1·0	⩾1500	⩽1				
Va		1·9	0·9	458	5·1 ± 0·2	2·1	4·3	7·1	−34, +55
Vb	—$C\underline{H}_2D$	2·2		360 (−43·5)					
	—$C\underline{H}D$—O—	1·9	0·8	78 (−43·5) 380	6·1 ± 0·3	2·2	1·7	−1·8	−32, +33
	—O—$COCH_2D$	2·2		297 (−43·5)					
VI		1·9	0·7	380	6·1 ± 0·3	2·2			
VII		1·9	0·7	250	9·4 ± 0·5	2·5	2·0	1·9	−6, +72
VIII		1·9	0·7	170	13·7 ± 0·7	2·7	2·3	−1·5	−15, +71
IX		1·9	0·7	222	10·5 ± 0·5	2·5	2·7	0·6	−4, +70
X		1·9	0·9	275	8·5 ± 0·4	2·4	2·5	0·6	−37, +47
XI		1·9	0·9	90	26 ± 2	3·1	2·8	−0·4	+10, +70
XII		1·9	1·0	110	20 ± 1	2·9			

[a] T_q, τ_q and $\Delta G^\ddagger$ values are for 33° ± 2°C

[b] Δ is the "natural" linewidth at half height due to other processes than quadrupolar relaxation. It is obtained from the computer fitting of calculated to experimental curves

[c] psec: picosecond (10^{-12} sec)

one has:

$$\eta(CH_2Cl_2)/\eta(CHCl_3) = 0{\cdot}77;\ \eta(CHBr_3)/\eta(CHCl_3) = 3{\cdot}37$$

$$\tau_q(CH_2Cl_2)/\tau_q(CHCl_3) = 0{\cdot}85;\ \tau_q(CHBr_3)/\tau_q(CHCl_3) = 2{\cdot}73$$

Thus as pointed out above, the motions of the molecule result both from its intrinsic dynamic properties and from those of the solvent lattice. A further result of interest is obtained for the hydroxymethyl compound Va. The $\Delta H^‡$ and $\Delta S^‡$ values are much larger than for the other compounds, whereas the $\Delta G^‡$ value is comparable to others. Such a marked difference is certainly significant and is due to the presence of hydrogen bonding.[79]

CONCLUSION

Although the results described here are quite crude in comparison to the detailed analyses performed on simpler molecules, they clearly demonstrate that quadrupolar relaxation studies (using in the present case proton lineshape analysis) allow describing the *local molecular motions* and the structural (and medium) effects on such motions in relatively complex organic systems. The deuterium nucleus was used here as a label on the microdynamic ways of the molecule. No separation of local motions into their components has been attempted. Such an analysis will be performed in the following paper.

EXPERIMENTAL

NMR spectra and lineshape analysis

The PMR spectra have been measured on a Varian A-60 spectrometer as already described. Lineshape analysis has also been described earlier.[38, 53, 72] A small amount of undeuterated compound is present in all samples (*ca* – 0·5%) and leads to a slight deformation of the downfield half of the —CHD— resonances. The —CH_2— resonance is isotopically shifted downfield (*ca.* 1 Hz) from the center of the —CHD— resonance. Thus only the upfield half of the —CHD— resonance has been used for lineshape analysis. The scatter of the T_q values obtained is *ca.* ± 5%. It was not necessary to degas the samples; a degassed sample of Ia (1·0 M in $CDCl_3$ at 33°) gave T_q = 210 ± 10 msec identical within experimental error to the value listed in the Table.

Comparison with *spin-echo* determinations of T_q gave the following results (T_q in msec):

Spin-echo:	Lineshape analysis:
9·9—Dideuterofluorene: 160 ± 30	9—Deuterofluorene: 150 ± 10
C_6H_5—CD_2—OAc: 360 ± 10	C_6H_5—CHD—OAc: 370 ± 10

(all samples in CCl_4 at 25°; fluorenes: 1·28 molar; benzyl acetates: 2·82 molar)

Substrates

9-d-Monodeuterofluorene, Ia. 9 *d*-fluorene was obtained by treating (under N_2) an anhyd. ether soln of fluorene by a 1·7 fold excess of BuLi. The soln was stirred (12 hr) and the salt formed destroyed with heavy water (99·5%D). After drying (Na_2SO_4), the ether was evaporated and Ia purified by chromatography on an alumina column (petroleum ether as eluant). m.p. 86°.

2-Deuteromethyl-9d-fluorene, (Ib). 9 *d*-fluorene-2-carboxaldehyde was prepared according to the literature;[81] reduction with LAD gives the corresponding *d* hydroxymethyl compound,[82] which on treatment with $SOCl_2$ in toluene at reflux temperature leads to 2-chloromethyl *d*-9 *d*-fluorene.[83] The reduction of this compound by LAH in ether (48 hr) gave Ib in a quantitative yield. This general method was employed for preparing all the —CH_2D substituted compounds.

2-Aldehyde-9d-fluorene: m.p. 86°. Litt: 86°[81] PMR ($CDCl_3$: $C\underline{H}D$: 3·9 p.m; Aromatic: 6·8–8·1 p.p.m; CHO: 10·0 p.p.m.

2-Hydroxymethyl-9d-fluorene: m.p. 133°. Litt: 131°.[82] PMR ($CDCl_3$): —O$\underline{H}$: 2·75 p.p.m: —C$\underline{H}$D: 3·6 p.p.m; —C$\underline{H}$DOH: 4·5 p.p.m; aromatic: 7–7·8 ppm.

2-Methyl-9d-fluorene: m.p.: 104°. Lit: 104.[83]

2-Chloro, 2-bromo, 2-iodo 9d-fluorene (Ic, Id, Ie). Compounds Ic and Id were prepared by diazotation of 2-amino-9*d*-fluorene,[84] followed by destruction of the diazo compound with CuBr or CuCl in HBr or HCl.[85] Ie was prepared by direct reaction of Ia with I_2 in AcOH containing a drop of H_2SO_4.[86] Ic: m.p.: 94°; Id: m.p.: 111·5°; Ie: m.p. 121°. All three compounds show PMR signals at 3·8 ppm (—C$\underline{H}$D) and at 7–7·9 p.p.m (aromatic protons), ($CDCl_3$ solution).

11-*d*-4,5-*Methylene-phenantrene* (II). II was prepared using the procedure described for Ia, m.p.: 116°.

2-*d*-3 *Oxo-lupene* (III). (2α + 2β) *bromo 3-lupanone*. 2·3 g of 3-lupanone in CH_2Cl_2 were treated with 25·12 g of a solution containing 2·70 g of Br_2 per 75·82 g of $CHCl_3$. After 10 min, evaporation to dryness and recrystallization in cold CH_2Cl_2-EtOH affords the mixture of the bromo-ketone epimers.

3-Oxo 1-lupene. The mixture of epimeric bromo 3-lupanones was dissolved in 70 ml of anhyd. DMF and heated at reflux with 1 g of LiCl (under N_2, 24 h). After cooling, water was added and the precipitate recrystallized in CH_2Cl_2—EtOH. 3-oxo 1-lupene was obtained by chromatography on a silica column (petroleum ether-benzene 6·5/3·5) followed by recrystallization in CH_2Cl_2—EtOH. m.p.: 182°–183°. PMR($CDCl_3$): two doublets centered at 5·78 p.p.m and 7·1 p.p.m (J = 10·5 cps). The enone dissolved in dioxane was treated (under N_2) with heavy water and BaO at reflux for 4 days. After extraction, one obtains 2-*d*-3 oxo-1-lupene (III). PMR ($CDCl_3$) broad singlet at 7·1 p.p.m.

para *d-Hydroxymethyl α-d-toluene* (Va). A solution of 2·8 g of 4-bromomethyl-benzaldehyde in 30 ml of THF was slowly added to a slurry of 600 mg of LAD in 20 ml of THF under N_2. The mixture was heated under reflux for 2 hr. After cooling, excess LAD was destroyed, the resulting solution filtered and dried (K_2CO_3). Removal of solvent gave 1·5 (85%) of Va.

d-Acetate of para-*d-hydroxymethyl-α-d-toluene* (Vb). *d-acetyl chloride*. The mixture resulting from the reaction of $SOCl_2$ with monobromoacetic acid was esterified by BzOH. The esters heated 14 hr at 105° with heavy water and Zn gave the monodeutero benzyl acetate, 4 g of this ester hydrogenolysed with 5% Pd/charcoal in hexane at atmospheric pressure, give monodeutero acetic acid. The anhydrous acetate treated with oxalyl chloride in ether gave an ethereal solution of *d*-acetyl chloride which was used directly for the esterification of Va in the usual manner.

d Labelled acetates (VI–XII). All acetates were obtained by treating the corresponding alcohol with Ac_2O in py. Their physical and spectral properties are in accordance with structure and literature data. The starting alcohols were prepared by reducing the corresponding aldehyde with LAD in ether; the aromatic aldehydes were commercial products (the aldehydes corresponding to IX, X, XII) or have been prepared according to the literature procedure (the aldehydes corresponding to VII[81] and XI[87]).

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