mente[17]. Detalhes sobre a base utilizada e os cálculos realizados em nível de π-CI completo, podem ser encontrados em outros trabalhos[18-19]. Na tabela I estão os resultados dos cálculos B_k cumulativos, usando três diferentes valores para o erro de truncamento. Pode-se notar que, exceto para o estado 2^1A_g, as energias de transição diferem de menos de 0,1eV daquelas obtidas com π-CI completo, mesmo para erros de truncamento de 1 mhartree. Para um erro de truncamento de 0,1 mhartree a diferença máxima é de 0,05eV, para os estados Rydberg $4f_{xz^2}$ e $3p_z$.

Quando mais de um estado de mesmo simetria é obtido, é importante assegurar-se a ortogonalidade entre eles. Como cada raiz da mesma simetria é obtida com espaços configuracionais diferentes, não há, em princípio, garantia de ortogonalidade entre eles. Nestes casos, garante-se a ortogonalidade entre os estados, incluindo, entre as configurações de um estado, algumas configurações dominantes do outro estado. Nos cálculos apresentados neste trabalho, a inclusão de uma configuração dominante (a de maior coeficiente) foi suficiente para tornar os estados ortogonais.

Considerando a redução substancial do tamanho da matriz CI, do nível de π-CI completo para o B_k cumulativo, e os valores de energia de transição obtidas em cada caso, podemos concluir que a aproximação B_k cumulativa é bastante eficiente para reproduzir energias de transição obtidas em nível de CI completo. Estes resultados são encorajadores e indicam a possibilidade de se utilizar o método para o tratamento de sistemas mais complexos.

O autor agradece o Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) pelo apoio financeiro.

Referências Bibliográficas

1 H. Shavitt em "Modern Theoretical Chemistty" (Editado por H. F. Schaefer III), Plenum Press, New York, 1977.

2 Existem métodos onde as funções de onda são construídas diretamente dos orbitais moleculares, evitando-se a construção da matriz CI (direct CI). No entanto, eles não são ainda de aplicabilidade geral. Veja, por exemplo: B.O. Ross e P.E.M. Siegbatin, Int. J. Quantum Chem., **16**, 485 (1980).

3 W. Meyer, J. Chem. Phys., **58**, 1017 (1973).

4 S.R. Langhoff e E.R. Davidson, Int. J. Quantum Chem. Symp., **8**, 61 (1974).

5 R.J. Bartlett e D.M. Silver, Int. J. Quantum Chem. Symp., **9**, 183 (1975).

6 R.J. Bartlett e J. Shavitt, Int. J. Quantum Chem. Symp., **11**, 165 (1977).

7 J.A. Pople, R. Seeger e R. Krishnan, Int. J. Quantum Chem. Symp., **11**, 149 (1977).

8 Z. Gershgorn e I. Shavitt, Int. J. Quantum Chem., **2**, 751 (1968).

9 R.J. Buenker e S.D. Peyerimhoff, Theoret. Chem. Acta, **35**, 33 (1974); **39**, 217 (1975).

10 J.J. Eberhard, R. Moecia e M. Zandomeneghi, Chem. Phys. Letters, **24**, 624 (1974).

11 G.A. Segal, R.W. Wetmore e K. Wolf, Chem. Phys., **30**, 269 (1978).

12 T.H. Dunning Jr., Chem. Phys., **42**, 249 (1979).

13 L.E. Nitzche e E.R. Davidson, J. Chem. Phys., **68**, 3103 (1978).

14 E.R. Davidson, L.E. McMurchie e S.J. Day, J. Chem. Phys., **74**, 5491 (1981); L.E. Nitzche e E.R. Davidson, J. Am. Chem. Soc., **100**, 7201 (1978).

15 R.C. Raffaneti, K. Hsu e I. Shavitt, Theoret. Chem. Acta, **45**, 33 (1977).

16 R.E. Brown, Ph. D. Thesis (Indiana University) (1967).

17 W. Haugen e M. Traetteberg em "Selected Topics in Structure Chemistry", (Editado por P. Andersen, O. Bastiansen e S. Eurgerg), Universitet for Laget, Oslo, 1967, p. 113.

18 Marco A.C. Nascimento e W.A. Goddard III, Chem. Phys., **36**, 147 (1979).

19 Marco A.C. Nascimento e W.A. Goddard III, ibid., **53**, 251 (1980).

ARTIGO

MOLECULAR DYNAMICS AND N.M.R. RELAXATION

J.M. Bernassau

Laboratoire de Synthèse Organique, Ecole Polytechnique
91128 PALAISEAU Cedex, França.

INTRODUCTION

Organic molecules or biomolecules are usually described by their structures. The simplest form of such description is the connectivity matrix: specification of the various bonds connecting the various atoms of the molecular framework. A somewhat more quantitative description is given by X ray studies which specify the molecular coordinates or, in an equivalent fashion, the bond lenghts, valence and dihedral angles. This is however a static picture of the molecule.

When several conformers are present, each of them can be described by a different set of molecular parameters, in very much the same way we would describe a single rigid molecule. The some extend, dynamic information can be gained, usually through variable temperature studies, on the pathways interconnecting the various conformers.

In the previous kind of studies, the molecules can be considered static, e.g. as if we were looking at them in a frame linked to their center of mass.

The physical reality of molecules in solution is however rather different. Due to intermolecular collisions between

themselves and the solvant, the molecules possess random movements. As usual in classical mecanics these motions can be separated in translational and rotational motions. It is usually easier to probe into the latter process and this paper will be concerned with this aspect of molecular diffusion.

We are usually well acquainted with the geometrical size of molecules. Although the physical meaning of 1 Angstrom = 10^{-10} meter may be a little difficult to grasp, by looking and studying molecular models we have a rather good understanding of the molecular sizes. It is however, more difficult to realize how fast the molecules move in solution. A typical value for a moderate size molecule is around 10^{11} rotations per second. Let us not forget that an electric drill turns at about 60 rotations per second and that the fastest rotations we can impress upon a rigid body in our macroscopic word is c.a. 2000 rotations per second (a dentist drill for instance). It is clear that at the molecular level due to the very small inertial effects much higher rates of rotation can be applied.

These fast motions can be experimentally studied through various spectroscopic techniques and Nuclear Magnetic Resonance can be thought as having the leadership of such studies. The range of molecules that can be studied by such method ranges from very small molecules like methylene chloride to high molecular weight polymers.

In fact all the fast molecular reorientation processes can be studied by N.M.R. Global reorientational motions is one, but the fast internal motion can be studied too. For instance rotation around unhindered sp_3-sp_3 bonds, the activation energy of which ranges from 0 to c.a. 4 kcal/mol is well within the range of relaxation studies. Let us recall that usual variable temperature N.M.R. studies are not able to probe into processes for which the activation energy is less than 7 kcal/mol.

The interest in the reorientational motion of the molecules arises because it can give us a unique vision of the molecular bodies as they really behave in solution. As is often the case for people a dynamic description (a movie) discloses new features of personality or character that a static description (a photograph) would have left unrevealed. The same applies for molecules and we must look through relaxation studies at new microscopic concepts like mobility, flexibility and solvatation. The foregoing discussion will give examples of these various points.

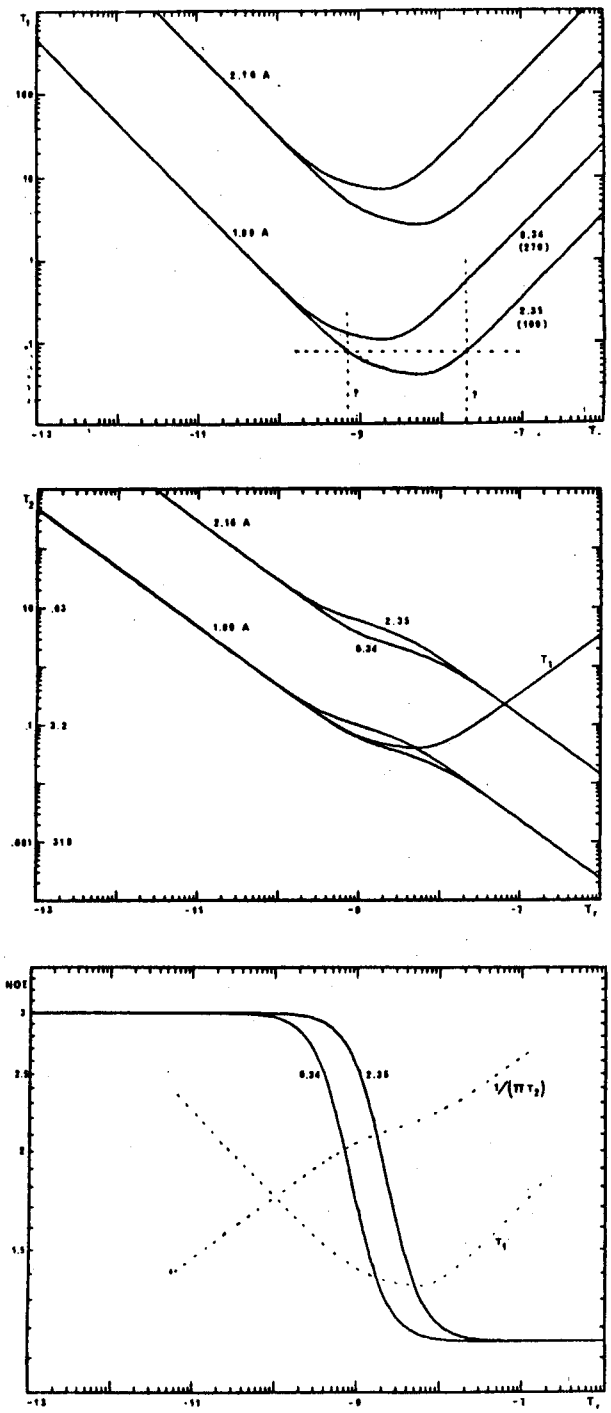

Fig. 1. T_1, T_2 and NOE as a function of the reorientation correlation time τ. T_1 and T_2 are given for two field strengths (2.35 T = 100 MHz proton frequency and 6.34 T = 270 MHz) and two C-H bond legths (1.09 Å = C-H bond length and 2.16 Å = C-C-H average distance).

THEORY

Without going deep in the details, which depending at which level they are looked upon can become very involved it can be said that the longitudinal relaxation rate (T_1) of a carbon-13 nucleus bonded to at least one proton is a direct measure of the mobility of that carbon. A convincing demonstration of the statement is offered by the long chain compounds.

Figure 1 gives the T_1 value of a C-H group as a function of the correlation time τ. This time can be thought as the time it takes for the molecule to rotate of 1 radian. As can be seen on the Figure, T_1 decreases linearly with τ down to a certain point where it goes up again. It can be safely stated that for all organic molecules of molecular weight less than 1000 and not forming associations, the correlation time is such that only the left part of the curve may be considered. This Figure therefore gives numerical values of τ for a given measured T_1.

Care must nevertheless be exercised if motion slows down sufficiently to reach the right side of the T_1 curve. This happens for high molecular weight molecules or molecular associations. In this case it can be seen that for a given T_1 value two values of τ can ben expected. There are however two ways to distinguish between points on the right or left side of the curve: the linewidth and the proton-carbon Nuclear Overhauser Effect (NOE). For points lying on the right side of the curve, the lines are broad (10 Hz and more) and the NOE is null. Let us stress once more that this happens only in special cases and the example provided latter will demonstrate this point.

Carbon-13 relaxation times are usually measured by the inversion recovery method (Fig. 2). This involves inverting the magnetization through a 180° pulse, waiting some time τ and observing the longitudinal component of the magnetization by a 90° pulse. The experiment is repeated for several values of τ judiciously choosen[1] and T_1 is extracted from the exponential recovery curves via a linear or better non linear fitting procedure.

If one looks more closely at the diffusion problem, it is soon realized that a single correlation time cannot describe properly the molecular motions. For instance an elongated molecule (cigar shaped); is going to move much faster around the revolution axis of the cigar. Theories have been devised by which these delicated aspects of the molecular motion can be taken into account.

Finally a word of caution about the physical meaning of the correlation time τ is in order. In solution molecular movements are modeled by Brownian processes. τ is the characteristic time for these processes. Would the process be non Brownian and the correlation time would loose its meaning. This, however, is only the case for very small molecule tumbling very fast. On the other side, the correlation time τ is not the time between two collisions. In fact the shorter the time between collisions the longer the τ.

Depending on the nature of the information one seeks from relaxation studies it is possible to interprete the data in a qualitative, semi-quantitative or quantitative manner. The latter studies are at present confined to very small model molecules whereas the former have been applied to very large biomolecules.

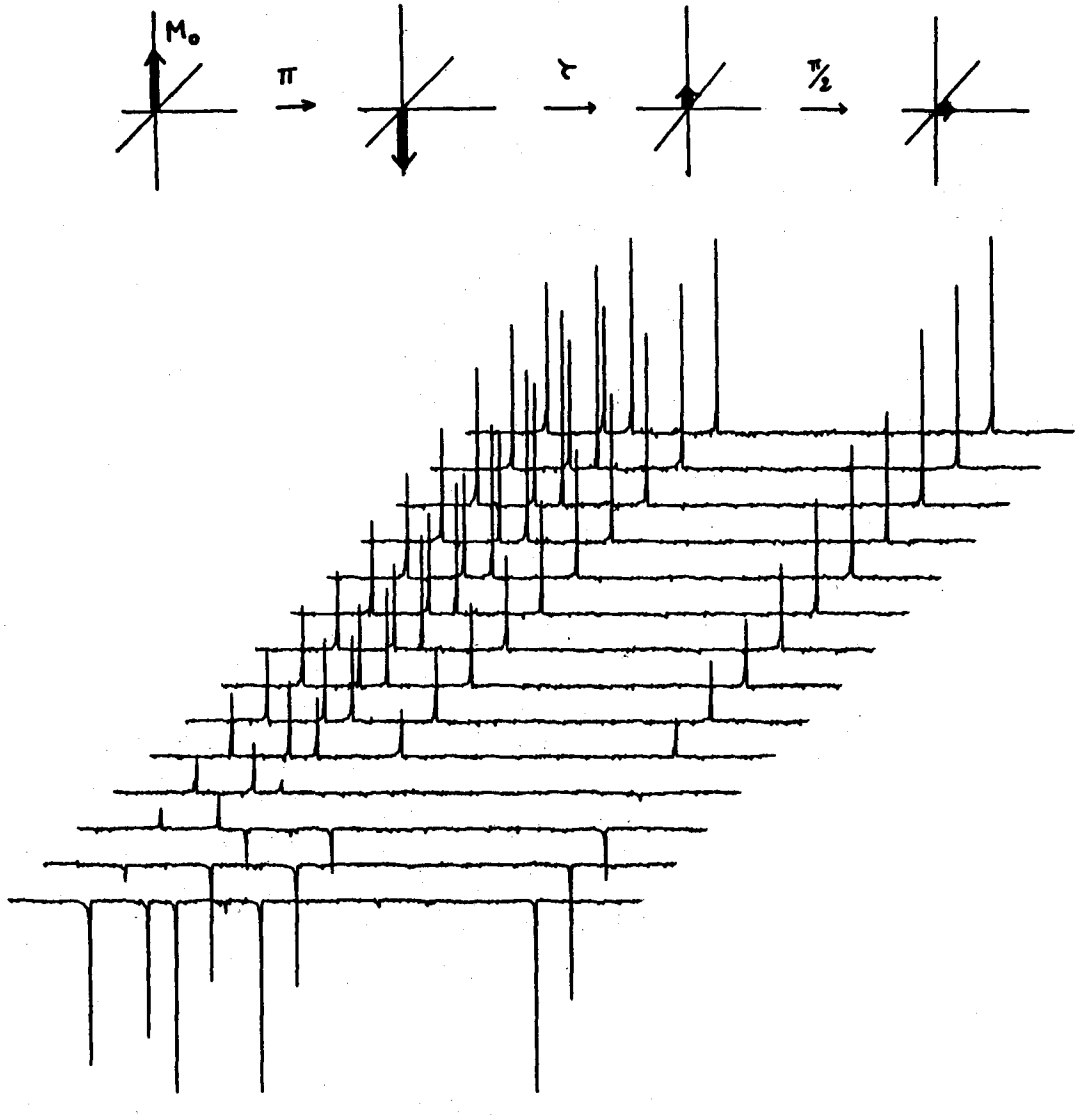

Fig. 2. Inversion recovery pulse sequence and a typical set of spectra.

DISCUSSION

On the lower part of Fig. 3, the spectrum of a molar solution of Virescenoside A in $CDCl_3$ is diplayed[2]. As can ben seen, only a few peaks have a reasonable width, most of the other resonances being broadened out. Addition of 10 drops of Methanol yields the spectrum of the higher part of the Figure. This spectrum possess the usual features of carbon-13 N.M.R.: sharp and well resolved lines. Comparison of this spectrum with published data reveals that the resolved lines of the spectrum is deuteriochloroform were those belonging to quaternary carbons or methyl groups.

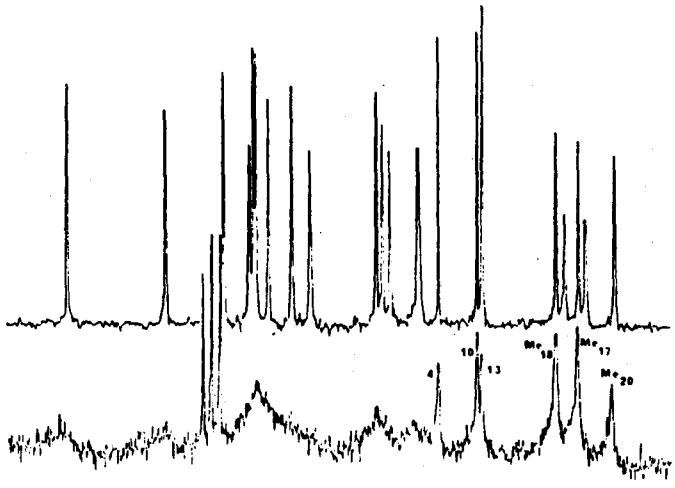

Fig. 3. Carbon-13 spectrum of virescenoside A in $CDCl_3$ (lower) and in $CDCl_3$-MeOH (upper).

The previous phenomenon can be explained by molecular dynamics alone. In pure $CDCl_3$ the molecules, which posses several OH groups, gather in high molecular weight associations of limited mobility. Adding methanol breaks the hydrogen bonds and restore the usual mobility to the molecule. A plot of T_1 versus the methanol concentration is very informative in this respect. As can be seen on Figure 4, the T_1 values follow the theoretical U shaped curve. The transverse relaxation time T_2 ($1/\pi$ linewidth) is also plotted on that Figure. As predicted by the theory, at the bottom of the T_1 curve $T_1 = T_2$.

Another example of slowly diffusing molecular entities is given by polymers. Fig. 5 displays the spectrum of a sample of poly-L-lysyne formed by linkage of 250 lysyne units.

Circular dichroism studies have shown that in methanol solutions the polymer exists in two exchanging conformations: helix and random coil. As can be seen on the Figure, most of the carbons appear as doublets, distance between the two resonance decreasing as one goes onway from the backbone. These two sets of resonances can be assigned by dilution studies to the coil and helix conformations.

Molecular dynamics provide here an interesting corroboration of these findings. T_1 measurements of the various resonances indicate that the peaks of the helix conformer invariably posses longitudinal relaxation times shorter than those of the random coil. This is simply because the latter

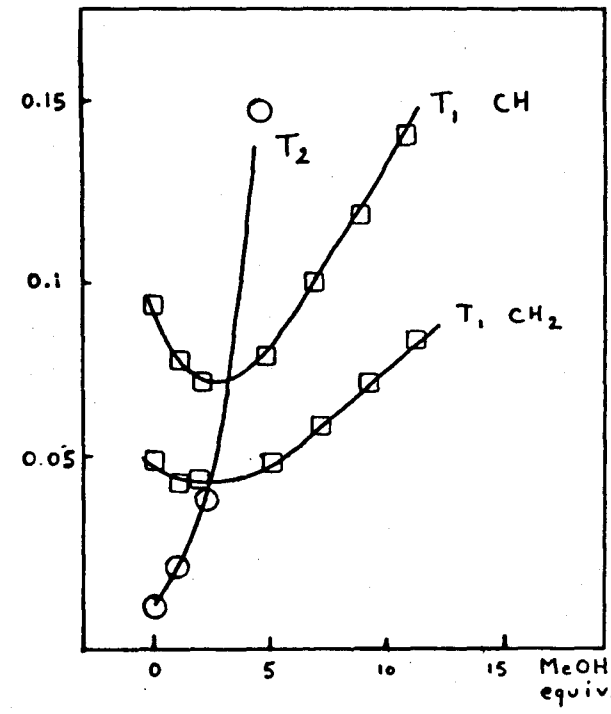

Fig. 4. Plot of T_1 and T_2 for some carbons of virescenoside A as a function of methanol concentration.

conformer has an increased mobility with respect to the helix conformer. Moreover it can be showh that the T_1 values increase is the order $C_\alpha < C_\beta < C_\gamma < C_\delta < C_\epsilon$ in each of the two conformations. This is due to increased mobility along the side chain.

Finally, inspection of the spectrum of Fig. 5 shows that the two resonances of the α carbon have very different line widths. Measurement of the proton-carbon NOE shows that the broad peak has a null NOE whereas the sharp one presents an enhancement close to 3. One therefore concludes that the T_1 value of the broad peak lies on the right side of the T_1 curve whereas the sharp peak lies on the left.

Relaxation studies can also be applied very fruitfully to long chain compounds. In such molecules, if one end bears an hydrogen bonding group (COOH, OH), this group is sort of anchored in the solvent. Motion therefore increases from this end to the other, due to the internal rotation around the C-C bonds. If no end bears an hydrogen bonding group then minimum motion occurs in the center of the chain.

Figure 6 shows the T_1 values for a C_{22} fatty acid and two esters. In these compounds, a few resonances can be immediately assigned: the chain ends and the two carbons adjacent to the double bond. All the other resonances cannot be identified, and in particular the position of the double bond cannot be inferred from the carbon-13 spectrum. Relaxation measurement however provide an immediate answer[3]: as we know that the motion increase along the chain, T_1 should also increase. By simply counting how many carbons have T_1 greater than and less than those of the two carbons adjacent to the double bond the unsaturation can be located.

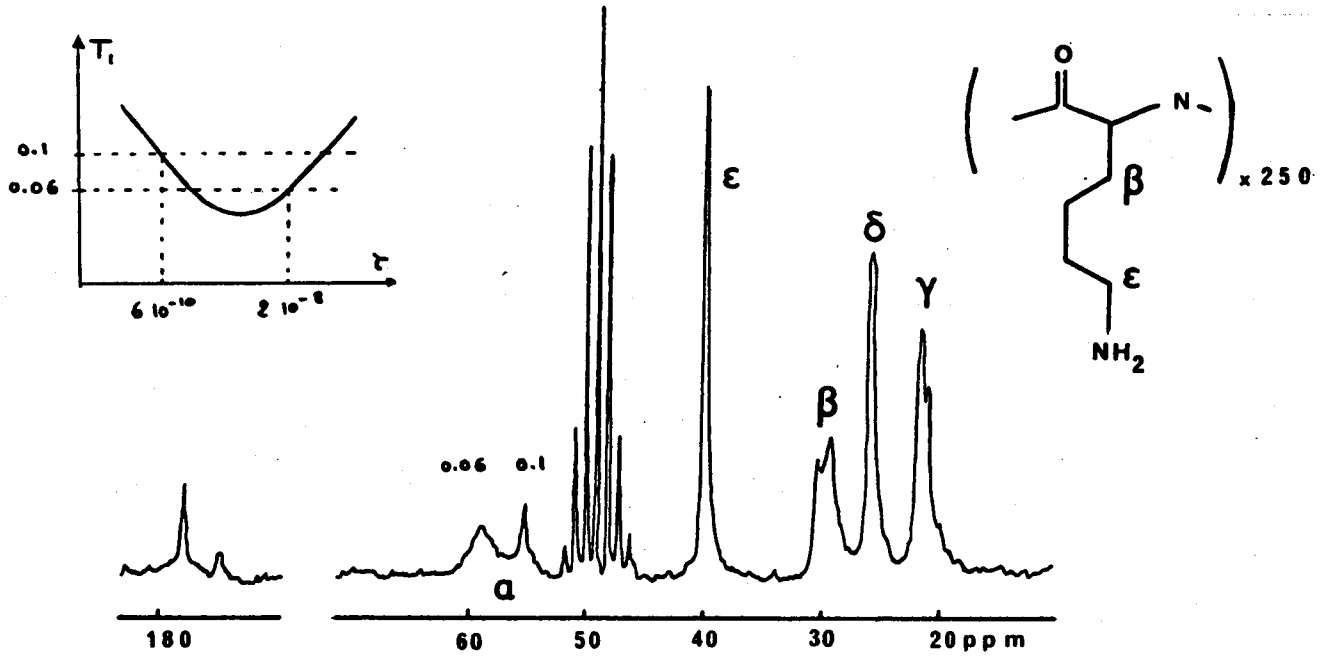

Fig. 5. Spectrum of poly-L-lysine in water-methanol. Inset shows the computation of τ for the αcarbon.

The two other spectra of the Figure 6 show that similar remarks can be made for ester groups and/or compounds possessing several double bonds.

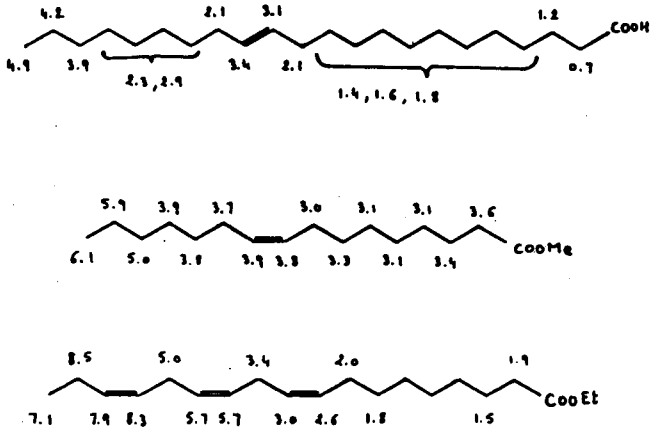

Fig. 6. $T_{1,S}$ of various long chain compounds.

Another way to restrict motion at one end of long aliphatic chain is attaching on heavy weight to it. The upper part of Fig. 7 shows the T_1 values of decyne. As previously noted they increase from the center of the chain to the ends. In the lower part of the Figure, the $T_{1,S}$ of the complex of decyne and dicobalt octocarbonyl are shown. They are now nicely ordered.

Of course introduction of cobalt atoms in the molecule displaces the resonances and the method as such cannot be used for assignment purposes. In the case shown assignments were done from labelled compounds.

Silver complexation is a better tool for these studies. Addition of 1 equivalent of Ag FOD to a solution of heptene yield a spectrum whose resonances possess the $T_{1,S}$

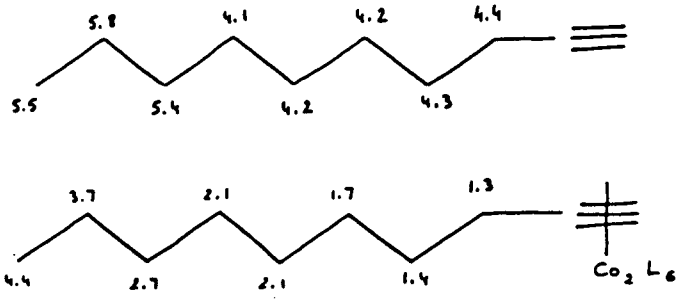

Fig. 7. $T_{1,S}$ of decyne and its cobalt complex.

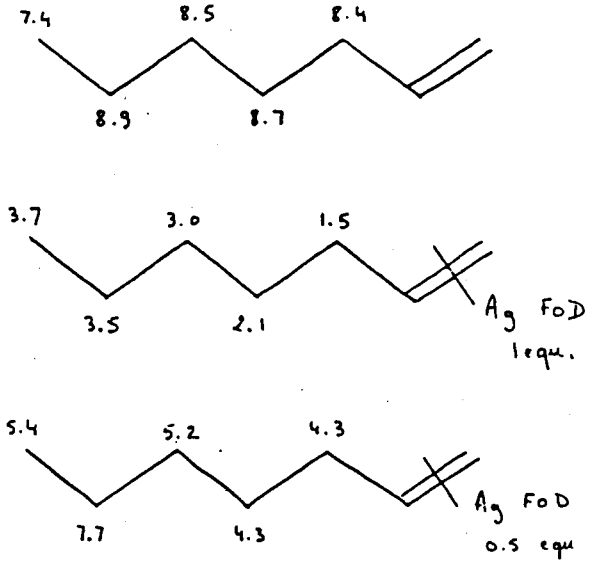

Fig. 8. $T_{1,S}$ of heptene in $CDCl_3$ and with various amounts of Ag(FOD).

displayed in the lower part of Fig. 8. The higher part of that Figure shows the $T_{1,S}$ of heptene alone. As can be seen by comparing these two sets of numbers complexation with silver has ordered the $T_{1,S}$ along the chain. Chemical shifts are only slightly modified in this case.

As previously noted, relaxation studies can provide information about the fast internal motions of molecules. Such is the case of methyl group, which usually possess rotational barriers in the range 0 - 3 kcal/mol. We recently conducted such a study on several methyl perhydrophenanthrenes. In these compounds the rotational barrier of the CH_3 groups can independently computed by the force field method. Fig. 9 shows the results thus obtained. As can be seen the theoretical results (left side) are in very good agreement with the experimental results (right side). Although an intuitive interpretation of these results is difficult, the detailed information provided by the force field calculations show that the delicate interactions between the methyl groups of the molecule is responsible for the observed energy variations.

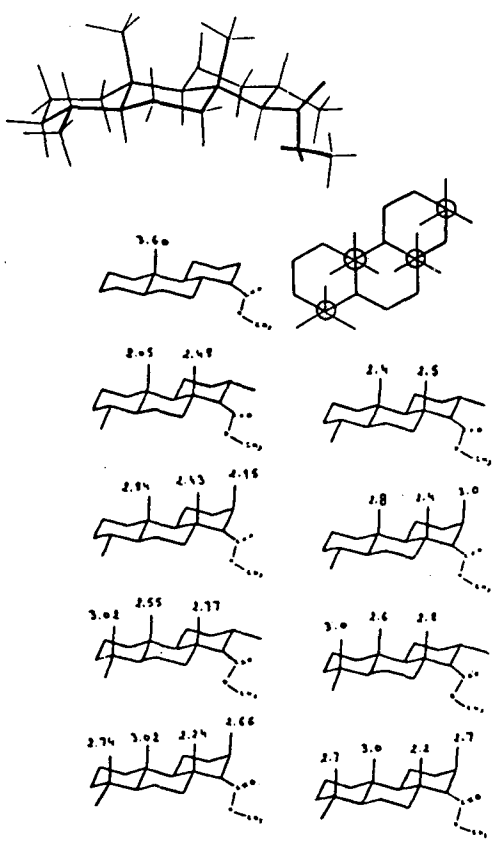

Fig. 9. Methyl rotational barriers of various diterpenes from force field (left) and NMR (right) studies.

When it comes to smaller molecules, carbon-13 enriched, much more detailed information can be obtained from relaxation studies. Fig. 10 for instance shows the 3 correlation times for diffusion of methylene chloride in CS_2 and deuterio-acetone[5]. In CS_2 motion is much faster around the Cl-Cl axis. The molecule moves so as to displace the bulky chlorines as little as possible. Although the motion seems related to the inertia moments of the molecule it is not inertia controlled. It is rather the number of solvant molecules displaced by CH_2Cl_2 during its movement that decides the value of the diffusion constants. When the dichloromethane is dissolved in acetone it can be seen that motion around the y and z axes slows down but not motion around x. This is because there is now a specific solute-solvant interaction along the x axis which therefore slows down motion around y and z.

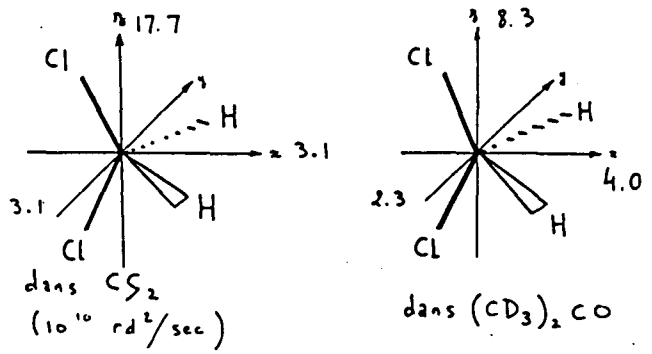

Fig. 10. Correlation times of methylene chloride in CS_2 and deuteroacetone.

CONCLUSION

We have provided here several examples from our own research work which show the information attainable through N.M.R. relaxation studies. As can be seen the scope of application of the method extends from very large to very small molecules. This provides the chemist with a new kind of information about the behaviour of molecules in solution.

Acknowledgement I thank Mr G. de MAGALHÃES for bringing the matter to my attention.

Referências Bibliográficas

1 J.M. Bernassau and F. Hyafil, J. Magn. Res., **40**, 245 (1980)
2 N. Bellavita, J.M. Bernassau, P. Ceccherelli and E. Wenkert, J. Amer. Chem. Soc., **102**, 17 (1980)
3 J.M. Bernassau and M. Fetizon, Tetrahedron, **37**, 2105 (1981)
4 J.M. Bernassau, M. Bertranne, C. Collongues and M. Fetizon, in press
5 M.T. Chenon, J.M. Bernassau, C.L. Mayne and D.M. Grant, J. Phys. Chem., **86**, 2733 (1982)