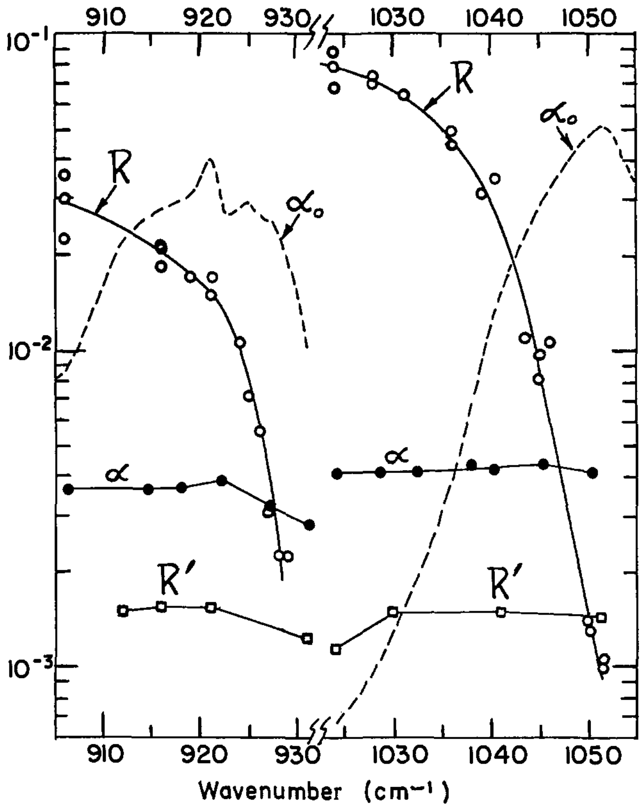

Figure 1. Data for various frequencies through two bands of CF_2ClCF_2Cl. Curves α_0 are the "ground-state" optical absorption coefficients (in units of cm^{-1} Torr^{-1}). Curves α are absorption coefficients (cm^{-1} Torr^{-1}) induced by a 4-W, 1-mm-diameter laser beam in 200 Torr of CF_2ClCF_2Cl. Curves R are the reaction rates (arbitrary units) of 200 Torr of CF_2ClCF_2Cl for a 4-W, 1-mm-diameter laser beam. Curves R′ are the reaction rates (arbitrary units) of the "temperature probe" gas PFB.

measurements show that α varies only weakly with intensity for incident powers exceeding 1 W, so that Beer's law is approximately satisfied over the path length.

Figure 1 shows that α is essentially *independent* of laser frequency in both bands. Similar results are obtained for pressures at least as low as 20 Torr. According to standard equations for steady-state heat flow, temperatures in the beam region are determined (all other factors equal) by the power absorbed per unit volume, which is proportional to αI, where I is the intensity. Since α does not change with frequency, neither should the temperature.

Reaction rates, on the other hand, increase sharply with decreasing frequency. We consider the contrast of rate with absorption as strong evidence for a nonthermal, vibrationally enhanced reaction route. The results are consistent with the above-mentioned interpretation of the red shift, where frequencies below band centers are favored for excitation to higher vibrational states.

Very little of the absorbed power is drained by the reaction, since the rates are sufficiently low for 4-W radiation. Nearly all absorbed power is carried to the cell walls. Accordingly, the frequency behavior of α is essentially unaffected by that of the reaction rate.

Since the magnitude of α is nearly the same for both bands while the maximal rates differ by a factor of three, a *small* difference in mode energy content may be indicated.

To corroborate the results, we introduced a small amount (2.44%) of a "temperature probe" gas,[5] perfluorobutadiene (PFB), which converts thermally to perfluorocyclobutene (PFCB) according to known kinetics.[6,7] The PFB does not absorb at the frequencies used here[8] and alone reacts negligibly under radiation at these frequencies. Therefore, PFB should serve as a temperature probe in the mixture, since most but not all of the input energy is expected to lie in modes of CF_2ClCF_2Cl that are already equilibrated at the translational temperature.

Curves R′ in Figure 1 show the rates of cyclization of PFB, obtained by monitoring absorption at the 1416-cm^{-1} band of PFCB. These rates are nearly independent of frequency. If indeed the probe is measuring mainly translational temperature, then the results are entirely consistent with those for absorption α of CF_2ClCF_2Cl, namely, constant translational temperature over the frequency ranges.

It should be noted that for frequencies in the range 1024–1036 cm^{-1}, the high intensity absorption α exceeds the low intensity absorption α_0. This induced absorption can be ascribed to anharmonicity and the onset of excited-state transitions, in concurrence with the explanation of the red shift of reaction rates. Induced absorption has been observed in SF_6 and other compounds.[9] The lack of a corresponding effect for the 921-cm^{-1} band may be due to the onset of absorption by another band at 883 cm^{-1}.

More extensive data and the results of continued studies of this compound will appear later.

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References and Notes

(1) R. N. Zitter and D. F. Koster, *J. Am. Chem. Soc.*, **98**, 1614 (1976).
(2) Self-focussing is produced by refractive index variations across the beam profile.
(3) R. Rinck, R. Bachmann, H. Noth, and K. L. Kompa, in a talk presented by K. L. Kompa at the Ninth International Conference on Quantum Electronics (Digest), Amsterdam, Netherlands, June 14–18, 1976.
(4) The factor 160 given in ref 1 for the ratio of 921–1051-cm^{-1} (band centers) reaction rates must be amended to a more correct number, 25, resulting from a more careful analysis of the shape of time-decay curves in the experiment.
(5) The use of a probe gas for temperature has been reported by H. R. Bachmann, H. Noth, R. Rinck, and K. L. Kompa, *Chem. Phys. Lett.*, **33**, 261 (1975).
(6) M. Prober and W. T. Miller, Jr., *J. Am. Chem. Soc.*, 71 598 (1949).
(7) The reverse reaction induced by a TEA CO_2 laser has been reported by A. Yogev and R. M. J. Benmair, *Chem. Phys. Lett.*, **46**, 290 (1977).
(8) PFB has an absorption band at 969 cm^{-1}.
(9) U. P. Oppenheim and P. Melman, *IEEE J. Quant. Elect.*, **QE-7**, 426 (1971); A. V. Nowak and J. L. Lyman, *J. Quant. Spectrosc. Radiat. Transfer*, **15**, 945 (1975); A. B. Peterson, J. Tiee, and C. Wittig, *Opt. Commun.*, **17**, 259 (1976).

Robert N. Zitter*
Department of Physics and Astronomy
Southern Illinois University
Carbondale, Illinois 62901

David F. Koster*
Department of Chemistry and Biochemistry
Southern Illinois University
Carbondale, Illinois 62901

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Multiple Frequency (Field) Carbon-13 Spin-Lattice Relaxation Studies. Probe to Cooperativity of Complex Molecular Motions

Sir:

Variable frequency (and hence, variable field) ^1H spin-lattice relaxation time (T_1) measurements contain dynamics information that is not available from single frequency T_1 experiments.[1] ^1H T_1 data obtained at only one spectrometer frequency may only give information about one or more individual correlation times, τs, which are assumed to follow from a simple description of exponential decay of the autocorrelation function,[2] $G(\tau)$. By contrast, ^1H T_1 data obtained at more than

Table I. ^{13}C Spin-Lattice Relaxation Data for 1,2-Decanediol, 1-Decanol, and Molecules Used for Comparison

Compd[a]	Temp, °C[b]	Freq, MHz	^{13}C T_1, s[c]									
			C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
1,2-Decanediol	54	22.6	0.27	0.41	0.30	0.37	0.3[d]	0.4	0.5	0.95	1.5	3.4
	54	67.9	0.5	0.7	0.5	0.6	0.6	0.7	1.0	1.8	2.7	5.3
1-Decanol	36	22.6	0.7	0.7	0.7		~1.0[e]			1.5	2.4	3.9
	36	67.9	0.6	0.6	0.7		~1.0			1.4	2.3	3.8
n-Heptane	28	22.6	12.1	10.6	11.3	10.9						
	28	67.9	12.5	11.8	12.9	10.8						
n-Eicosane	49	22.6	6.0	4.0	2.8	~1.4[e]						
	49	67.9	5.9	4.3	3.0	~1.4						

[a] Samples neat unless noted. [b] Temperature ±1 °C, measured directly before and after data collection. [c] Maximum probable error ±5–10%. Decanediol and decanol data, average of two to four runs. [d] When only one significant figure is given, T_1 is considered accurate to only 10–15%. [e] The given T_1 is a composite number as resolution is insufficient to obtain accurate, individual values.

one frequency probe which describes the effect of molecular (and internal group) motions on intramolecular dipolar spin-lattice relaxation.

The time dependence of the function $G(\tau)$ is indeed closely described in many liquid systems by an exponential decay. However, this is not necessarily the case. Molecular motions in complicated structures or with simple associated molecules may require a more complex description, including various degrees of cooperativity for overall and internal motional components. Some descriptions have invoked more complex formulation of $G(\tau)$ with resultant distributions of correlation times to describe motion in synthetic and biopolymers[3] and strongly associated liquids.[3d,4]

Thus far, variable field (or frequency) T_1 measurements have not been used to probe complex group segmental motions at individual sites.[5] In this communication we report an initial study of ^{13}C T_1s obtained on several molecular systems at two widely different magnetic fields. The results indicate that such measurements are capable of greatly increasing our knowledge of complex molecular motions.

Several types of systems are under investigation: straight-chain associated alcohols and polyols, carboxylic acids, alkyl and aromatic ions, and synthetic high polymers having pendant alkyl chains. In this communication we will discuss primarily the results of 22.6-MHz and 67.9-MHz ^{13}C T_1 and NOE measurements on 1,2-decanediol. Table I summarizes the experimental data for decanediol and several other molecules, used for test and comparison purposes.

The important and unexpected thing to note in Table I is the large difference between the low and high field ^{13}C T_1s of decanediol. By contrast, the ^{13}C T_1 values of *n*-heptane and *n*-eicosane show no field dependence, in accord with standard theories for molecules undergoing rapid reorientation in solution. In *n*-eicosane rapid segmental (internal) motions near the ends of the 20-carbon chain give rise to increasing ^{13}C T_1s, as observed previously.[6]

In 1,2-decanediol the strongly associated glycol function results in a large degree of observed segmental motion, clearly seen from the increasing T_1 values for carbons successively removed from the hydroxyl groups. This observation of segmental motion is not unexpected, since the situation is quite close to that observed for 1-decanol in 1971 by Doddrell and Allerhand.[7] However, *new* information may be derived from the fact that all 10 carbons of 1,2-decanediol exhibit a significant dependence on magnetic field, despite the fact that according to its observed T_1 even the motionally restricted C-1 CH_2 carbon does not significantly violate the condition of "extreme spectral narrowing." (At 67.9 MHz a methylene carbon dipolar T_1 shorter than 200 ms (corresponding to $\tau_c \gtrsim 10^{-10}$ s) increasingly deviates from T_1 obtained for the same carbon at a lower field.[8])

The large dependence of the longer decanediol T_1s on the experimental Larmor frequency ν_L can be explained only if molecular motion in decanediol is not describable in terms of one, two, or three discrete effective reorientational correlation times. A qualitative rationalization of the data can be made in terms of the presence of a distribution of correlation times[9-11] (or its mathematically indistinguishable equivalent, a nonexponential correlation function $G(\tau)$), the evidence for which is the field-dependent relaxation time behavior for correlation times which are apparently within extreme narrowing according to the single correlation time approximation.[8] An exact analysis should also explicitly account for the effects of bond rotation about each of the carbon–carbon single bonds. However, the data indicate that the motion of the end methyl and methylenes is not effectively decoupled from the "anchored" end of the molecule. The segmental motions are coupled to the overall molecular tumbling (which retains some of the characteristics of a distribution of correlation times).

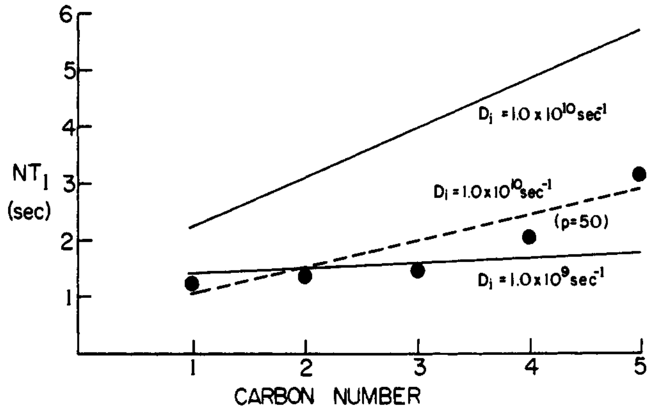

Figure 1. NT_1 as a function of carbon number at 67.9 MHz for the first five carbons of an alkyl chain whose effective center of mass in carbon 0. The solid lines ($D_i = 1.0 \times 10^{10}$ s^{-1} and 1.0×10^{9} s^{-1}, i = 1, 5), assume a single correlation time, describes the overall molecular motion. The dashed line ($D_i = 1.0 \times 10^{10}$ s^{-1}) is calculated for a log $-\chi^2$ distribution characterized by a width p = 50 superimposed on the multiple internal rotations. Experimental data points for 1,2-decanediol at 67.9 MHz are denoted by ●.

Assuming no distribution for the overall motion and employing the appropriate theory of multiple internal rotations,[12-14] one can calculate the T_1 values for a constant rotational diffusion coefficient about each single bond. Figure 1 illustrates the effects of the various parameters on the calculated T_1 values of the first five carbons in an alkyl chain. For the sake of simplicity (and a considerable decrease in computational expenses) the first carbon–carbon bond is taken to be that between C-3 and C-4; i.e., we are considering the anchored diol end of the molecule to be C-0 for the purposes of this qualitative explanation. C-0 should represent the center of mass of the molecule, an obviously difficult choice for a molecule in the presence of a highly variable phenomenon such as hydrogen bonding. With the given parameters the $D_i = 1 \times$

10^{10} s^{-1} line obviously overestimates the T_1 values of 1,2-decanediol while the $D_i = 1 \times 10^9$ s^{-1} line gives a much closer fit, *although no frequency dependent T_1 values are predicted.* However, the presence of a relatively narrow distribution ($p = 50$)[15] with $D_i = 1 \times 10^{10}$ s^{-1} provides a much better fit at 67.9 MHz and also *predicts the requisite field dependence,* albeit only qualitatively.

The value of the correlation time required to describe the overall molecular motion is consistent with the fact that the molecule is extensively hydrogen bonded, the correlation time being about an order of magnitude greater than that observed for decane.[14a] Significantly, the diffusion coefficients along the chain in 1,2-decanediol are in close agreement with the values obtained by Levine et al.[14a] for decane.

The qualitative agreement between calculated and observed T_1s at the two fields using both the distribution and multiple internal rotation cannot be improved upon without introducing additional factors. The observed field dependence is too great for the longer relaxation times to be quantitatively predicted. Apparently, the assumption of independent rotation by a diffusional process about the carbon–carbon bonds is inadequate. The calculated field dependence could be increased by taking into account the interdependence of the conformational changes possible along the chain.[14b] (The motions would necessarily be more correlated.) It is apparent that the published theory[13,14] which finds that five successive methylene carbons are sufficient to decouple effectively chain segments is *not* valid for decanediol.

1-Decanol is also extensively hydrogen bonded in neat solution.[7] The ^{13}C T_1s of 1-decanol given also in Table I do not show a significant field dependence. The two field T_1 data for decanol at 36 °C thus do not require invocation of a complex cooperative motional description as in 1,2-decanediol.

The nuclear Overhauser enhancement factors (NOEF) were $\sim$1.90 for all carbons of 1,2-decanediol, the theoretical limit being 1.988. The predicted NOEFs for the carbons using the distribution modified by the multiple internal rotations are also in this region. This parameter is not a sensitive indication of the motional model under these circumstances. Decanol also exhibits maximum nuclear Overhauser enhancements but no T_1 field dependence.

Conclusions. All of the T_1 field dependences for 1,2-decanediol can be explained with a model of at least partially cooperative segmental motions superimposed on an overall molecular reorientation having some slow ($\gtrsim 10^{-9}$ s) components. The slower motions are incompletely decoupled from the segmental motions of the chain carbons, including the C-10 CH_3 group.

The implications of this preliminary study may be far reaching. One of the strengths of ^{13}C T_1 measurements is an ability to probe molecular motion at individual carbon sites. A weakness has been the inability to generally probe cooperativity or couplings of group internal motions. The variable field approach can probe motions as in the segmental chain motion of 1,2-decanediol. We are now investigating further this situation and its application to the study of segmental motions in model membrane structures.

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References and Notes

(1) H. B. Coates, K. A. McLaughlan, I. D. Campbell, and C. E. McColl, *Biochem. Biophys. Acta*, **310**, 1 (1973); S. H. Koenig and R. D. Brown, *Ann. N.Y. Acad. Sci.*, **222**, 752 (1973).

(2) A. Abragam, "The Principles of Nuclear Magnetism", Oxford Press, Oxford, 1961, p 299 ff.

(3) (a) J. Schaefer, *Macromolecules*, **6**, 882 (1973); (b) F. Heatley and A. Begum, *Polymer*, **17**, 399 (1976); (c) J. R. Lyerla and D. A. Torchia, *Biochemistry*, **14**, 5175 (1975); (d) R. Lenk, *Adv. Mol. Relaxation Processes*, **3**, 3 (1972).

(4) (a) T. M. Connor, *Trans. Faraday Soc.*, **60**, 1574 (1964); (b) J. P. Kintzinger and M. D. Zeidler, *Ber. Bunsenges. Phys. Chem.*, **77**, 98 (1973).

(5) A recent paper observes that a field dependence for the ^{13}C T_1s of several proteins is not accounted for by current models of isotropic or anisotropic motion: D. J. Wilbur, R. S. Norton, A. O. Clouse, R. Addleman, and A. Allerhand, *J. Am. Chem. Soc.*, **98**, 8250 (1976).

(6) J. R. Lyerla, H. M. McIntyre, and D. A. Torchia, *Macromolecules*, **7**, 11 (1974).

(7) D. Doddrell and A. Allerhand, *J. Am. Chem. Soc.*, **93**, 1558 (1971).

(8) J. R. Lyerla and G. C. Levy in *Top. Carbon-13 NMR Spectrosc.*, **1**, Chapter 3 (1974).

(9) T. M. Connor, *Trans. Faraday Soc.*, **60**, 1574 (1964).

(10) F. Heatley and A. Begum, *Polymer*, **17**, 399 (1976).

(11) J. Schaefer, *Macromolecules*, **6**, 882 (1973).

(12) R. E. London and J. Avitabile, *J. Chem. Phys.*, **65**, 2443 (1976).

(13) Y. K. Levine, P. Partington, and G. C. K. Roberts, *Mol. Phys.*, **25**, 497 (1973).

(14) (a) Y. K. Levine, N. J. M. Birdsall, A. G. Lee, J. C. Metcalfe, P. Partington, and G. C. K. Roberts, *J. Chem. Phys.*, **60**, 2890 (1974). (b) Y. K. Levine, *J. Magn. Reson.*, **11**, 421 (1973).

(15) A log $-\chi^2$ distribution was used: J. Schaefer, *Macromolecules*, **6**, 882 (1973). A detailed description of the theory of multiple internal rotations in conjunction with a distribution of correlation times to describe overall molecular motion has been submitted for publication.

(16) Alfred P. Sloan Fellow, 1975–1977; Camille and Henry Dreyfus Teacher-Scholar, 1976–1981.

George C. Levy,*[16] Mary Pat Cordes
John S. Lewis, David E. Axelson
Department of Chemistry
The Florida State University
Tallahassee, Florida 32306

Received February 18, 1977

14α-Ethyl-5α-cholest-7-ene-3β,15α-diol, an Extraordinarily Potent Inhibitor of Sterol Biosynthesis in Animal Cells[1]

Sir:

A number of oxygenated derivatives of cholesterol have been shown to act as potent inhibitors of sterol biosynthesis in animal cells in culture.[2-4] The site of the inhibitory action of these compounds appears to be at the level of 3-hydroxy-3-methylglutaryl coenzyme A reductase, a key enzyme in the regulation of sterol biosynthesis which is responsible for the formation of mevalonic acid.[2-4] The most potent inhibitor of this type reported to date is 25-hydroxycholesterol which caused a 50% reduction of sterol synthesis in L cells and in primary cultures of liver cells at concentrations of 7.0×10^{-8} M and 1.0×10^{-6} M, respectively. Recently we have found that a number of 15-oxygenated sterols also act as inhibitors of sterol synthesis in the same cell culture systems.[5] We have also found that subcutaneous administration to rats of one of these compounds, 5α-cholest-8(14)-en-3β-ol-15-one, results in a reduction in serum cholesterol levels and an inhibition of hepatic sterol synthesis.[6]

The purpose of this communication is to describe the chemical syntheses of 14α-ethyl-5α-cholest-7-ene-3β,15β-diol and 14α-ethyl-5α-cholest-7-ene-3β,15α-diol and to report that the latter compound is an extraordinarily potent inhibitor of sterol biosynthesis in both L cells and in primary cultures of fetal mouse liver cells.

5α-Cholest-8(14)-en-3β-ol-15-one, prepared as described previously,[6] was alkylated with ethyl iodide in the presence of potassium *tert*-butoxide in *tert*-butyl alcohol to give, after purification by medium pressure silica gel column chromatography and crystallization from acetone–water, 14α-ethyl-5α-cholest-7-en-3β-ol-15-one (I)[7] in 42% yield. Reduction of I with lithium aluminum hydride in ether gave a 70:30 mixture of 14α-ethyl-5α-cholest-7-ene-3β,15α-diol and 14α-ethyl-5α-cholest-7-ene-3β,15β-diol (89% yield) which could not be resolved by TLC on silica gel G or on GLC on OV-1 or OV-17 columns but which could be separated, in the form of the bis-