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MOLECULAR DYNAMICS AND THE RACEMIC MODIFICATION - LACTIC ACIDS AND FLUORO CHLORO ACETONITRILES

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ABSTRACT

Shape differences in the far infra-red have been observed by submillimetre laser spectroscopy between the R enantiomer and racemic mixture of lactic acid at constant temperature (296 ± 2K) in the supercoded liquid and liquid mixture respectively. This observation is interpreted qualitatively to mean that there is a difference in the molecular dynamics attributable in principle to rotation/translation coupling. The theory is illustrated by reference to a computer simulation of the supercooled fluorochloroacetonitriles (enantiomers and racemic mixtures).

INTRODUCTION

Cross-correlation functions of the type:

$$C_{tr} \quad \langle p(t)\, \underset{\sim}{J}^{T}(o) \rangle_{m}$$

exist in moving, molecular frames of reference [1] even in molecules of high symmetry (e.g. linear). In equation (1) $\underset{\sim}{p}$ is the translational momentum of the molecular centre of mass, $\underset{\sim}{J}$ the rotational angular momentum of the same molecule. Both vectors are defined with respect to the moving frame of reference, e.g. that of the principal moments of inertia. In chiral (low symmetry) molecules some elements vanish for all t. The molecular dynamics of two enantiomers (R and S type) are therefore identical in a static, (laboratory) frame of reference but different in a moving frame attached to the molecule. They differ in both frames for the racemic mixture. This

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result is not trivially predictable on the grounds of molecular symmetry because of the use of moving frames [1] and because each off-diagonal element of C_{tr} has characteristics of its own, such as normalised amplitude and time-dependence [1-6]. The analytical theory of molecular diffusion is phenomenological [7-9], not predictive, and is not yet capable of describing C_{tr} in any detail. There is very little available experimental work in the area of chiral molecular dynamics. The exception is camphor [10], in which eleven solid phases have been characterised by the use of hydrostatic pressure.

The correlation of a molecule's rotation with its own centre of mass translation is a factor which has to be taken into account even in a rudimentary description, in molecular dynamical terms,of the physical and spectral differences that exist between an enantiomer and racemic mixture in the condensed states of matter.

In this paper we report some experimental evidence for the r/t effect in the R enantiomer and racemic mixture of lactic acid. Normally the R (or S) enantiomer melts at 326K and the racemic mixture at 291K. By supercooling the R enantiomer it is possible to compare the liquid enantiomer and liquid racemic mixture at the same temperature (296 ± 2K). The R enantiomer normally supercools very easily and can be maintained in this condition at room temperature. It is not yet possible to interpret the far infrared spectra of the lactic acids quantitatively because the molecules are slightly too big for effective computer simulation back-up. Therefore a qualitative interpretation is given and the principles of the r/t effect illustrated by a computer simulation of the fluorochloroacetonitriles in the supercooled liquid state.

EXPERIMENTAL METHOD

The far infra-red spectra of enantiomer and racemic mixture were obtained with an Apollo Instruments tunable submillimetre laser operating at five far infra-red frequencies. The submillimetre radiation was obtained by a CO_2 laser pumping a resonance cavity filled with methanol. The far infra-red signal was detected with a Colay pneumatic cell and measured with an oscilloscope. The far infra-red power absorption coefficient was measured by plotting signal attenuation vs path length difference in a VC-01 variable path length liquid cell. Using this method it is estimated

that power absorption coefficients can be obtained with 5% accuracy even for the most heavily absorbing liquids such as water or acetonitrile. This provides an accurate baseline check for the complementary technique of broad-band interferometry [7], whose limiting uncertainty is often path-length difference in the sample cell. The power of submillimetre laser spectroscopy can be used to reduce this uncertainty considerably because each submillimetre laser can travel through a longer liquid path-length than the diffuse and often uncollimated output beam of the broad-band interferometer [7].

Computer Simulation

The simulation algorithm has been described fully elsewhere [2-10]. The input temperature used for the fluorochloroacetonitrile was 133K, i.e. a supercooled liquid condition with zero Verlet parameter on average but with a Kirkwood factor about 10% different from unity - indicating natural dipole-dipole alignment at equilibrium. The principal Cartesian co-ordinates of the atoms and site-site parameters for R and S fluorochloroacetonitrile are given in Table 1. The intermolecular pair potential was modelled roughly with a 6 x 6 atom-atom potential, with Lennard-Jones and partial charge terms as in the table. There is no attempt to "adjust" the Lennard-Jones parameters because we are interested only in using the computer simulation as a gedankexperiment intended to illustrate the fundamental principle of the r/t effect. It is difficult to see in what other way computer simulation can be used in practice in complex liquid systems in the often complete absence of basic thermodynamical and physical data, and in the continued absence of a reliable method for inverting, for example, virial,data to give inter-molecular potential parameters.

Our literature checks have revealed [e.g. 2-10] that even the most basic data such as melting points have often not been recorded for simple chiral liquids, and the thermodynamic data needed for adjusting the intermolecular pair potential are not available. On the other hand, a careful computer-based study of the dynamics of chiral molecules has proven [2-10] to be useful. We therefore use "unadjusted" Lennard-Jones parameters in our simulations of chiral symmetries of interest. We note that even the "crudest" atom-atom representation is much more useful than the obscure (e.g. cosine) potentials often used in the analytical theory, powerful though this can be for the construction of generally valid

TABLE 1

Site-Site Potential for fluorochloroacetonitrile:Lennard-Jones and Partial Charge Terms

Atom	Principal Cartesian Co-ordinates/Å				Lennard-Jones Terms		Partial Charges
	$x(e_2)$	$y(e_1)$	$z(e_2)$ (R)	$z(e_2)$ (S)	ε/k	σ/Å	$q/\|e\|$
N	0.75	-2.28	0.35	-0.35	47.8	3.0	-0.16
C_1	0.27	-1.29	-0.03	0.03	35.8	3.4	-0.02
C_2	-0.34	-0.05	-0.51	0.51	35.8	3.4	0.03
H	-0.34	-0.34	-1.59	1.59	10.0	2.8	0.51
Cl	0.61	1.33	0.07	-0.07	127.9	3.6	-0.16
F	-1.64	0.06	0.02	-0.02	54.9	2.7	-0.20

Input Temperature = 133 K

Input Molar Volume = 91.4 cm^3

theorems of the liquid state. The computer simulation method, irrespective of the accuracy of its pair-potential, is capable of predicting new explanations and new phenomena [9]. Kramers equations of the analytical theory [7-9] have not yet reached this level of sophistication.

RESULTS

The far infra-red power absorption coefficients ($\alpha(\bar{\nu})$/neper cm^{-1}) or R and RS lactic acid liquids are illustrated in figure (1) as a function of wavenumber ($\bar{\nu}$/cm^{-1}). The racemic mixture absorbs more strongly than the R(L(+)) enantiomer but there is also a difference in the shape of the two spectra. This implies [7] that the rotational velocity correlation function is different at the same temperature for the enantiomer and racemic mixture. It seems that the broad-band absorption of the racemic mixture peaks at slightly the higher frequency in fig (1), so that the oscillatory rotational velocity correlation function would cut the time axis earlier [7] for the racemic mixture.

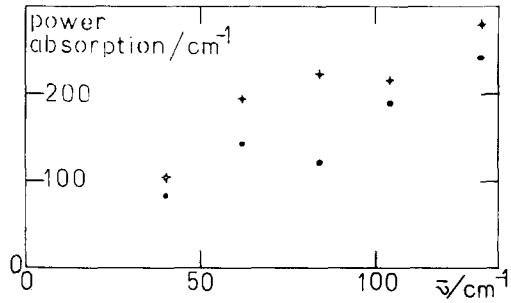

Fig. 1. Power absorption coefficient ($\alpha(\bar{\nu})$/neper cm^{-1}) of RS lactic acid (-◇-) and R lactic acid (o) in the far infra-red.
Submillimetre laser spectroscopy.
Abscissa: $\bar{\nu}$/cm^{-1}
Ordinate: $\alpha(\bar{\nu})$/neper cm^{-1}.

DISCUSSION

The results of figure (1) indicate that there is a difference in the molecular dynamics of liquid R and RS lactic acid at the same temperature which requires a detailed explanation.

The conventional infra-red spectra of R and S enantiomers are identical. In the laboratory frame, the molecular dynamics of both enantiomers also appear to be identical in all respects. We know, however, that the R enantiomer is the mirror image of the S enantiomer. The theory of molecular diffusion has not addressed itself to the problem of explaining this difference in dynamical terms (the language of time correlation functions). In fact, the conventional purely rotational theory of molecular diffusion [7], first proposed by P. Debye does not produce a difference between enantiomer and racemic mixture. This is because both enantiomers must be ascribed the same Debye relaxation time, for example, and cannot be told apart in any way by the theory. Without fore-knowledge it would not be possible to say to which enantiomer the Debye relaxation time referred. The same reasoning applies to a theory of molecular diffusion that is purely translational [7]. The translational diffusion coefficients of both R and S enantiomers are exactly the same. Similarly, "rotational" NMR relaxation times (spin-rotation, spin-spin etc) and other types of relaxation times normally used to study molecular diffusion would be identical for both enantiomers.

There would be no dynamical evidence or reason to suspect that sample A would be different in any way from sample B. Therefore we could not reasonably expect any change if A were mixed with B on the basis of classical molecular diffusion theory. The racemic modification, observable in figure (1) for example, would be inexplicable in a purely rotational, or purely translational, description.

There must therefore be stereospecific properties, normally invisible to the observer, that cause the physical and spectral properties of enantiomer and racemic mixture to differ, and are therefore indirectly measurable through this difference. In a static (i.e. non-dynamical) context the most obvious (and visible) stereospecific property is the fact that one enantiomer is the other's mirror image. This has been known since the work of Pasteur and van't Hoff. In a dynamical context we are dealing with chiral molecules that can rotate and translate in a very complicated way. The net results of this movement appear identical to spectral probes for R and S liquids in the laboratory frame of reference. What recent computer simulations have revealed [2-10] is that the properties of cross-correlation functions such as C_{tr} are different in a frame of reference attached to the moving chiral molecule. This is, therefore, a stereospecific dynamical property - the first

of its kind that has been detected since the discovery of enantiomers by Pasteur. There are probably others to be found.

This stereospecific dynamical property must be a cross-correlation function.

This is the new theorem at the basis of the molecular dynamical explanation for the racemic modification of physical and spectral properties.

Therefore, a comparison such as that in figure (1) produces, in principle, information about cross-correlation functions between, for example, rotation and translation on the most fundamental, single molecule, level. This information would be extracted from figure (1) by building up the observables (in this case rotational velocity correlation functions, i.e. far infra-red spectra) by computer simulation. After completing this exercise, i.e. after the experimental data has been described satisfactorily by molecular dynamics simulation, the moving frame C_{tr} elements can then be computed entirely self consistently from the same pair potential. These C_{tr} elements would then have been extracted from the experimental data using computer simulation as a means of self-consistent interpretation. The C_{tr} elements are therefore obtainable from experimental data through the medium of computer simulation.

The Fluorochloro Acetonitriles: An Illustration

Normally, there is a large, 35K, difference between the melting points of R and RS lactic acid. In the whole of this range the molecular dynamics of R lactic acid are normally those of a solid and the RS those of a liquid mixture, i.e. wholly different and easily distinguishable. Figure (1) shows that this difference is not lost by supercooling the enantiomer, i.e. maintaining it as a liquid. A computer simulation must be realistic enough to reproduce these observables in detail. Such an algorithm is not yet available for the lactic acids because the molecules are slightly too large needing too much computer time. (There is no difficulty, in principle, in taking into account the hydrogen-bonding in the computer simulation.)

Therefore we end this paper by illustrating some relevant elements of C_{tr} for the supercooled fluorochloroacetonitriles. The elements illustrated are those that change sign for the R and S liquids and vanish in the racemic mixture (figure (2)). In the laboratory frame, the same

computer simulation runs self-consistently produce the small laboratory frame difference between enantiomer and racemic mixture illustrated in figure (3).

It is interesting to note, finally, that cross-correlations such as C_{tr} become directly observable in the laboratory frame with the use of a

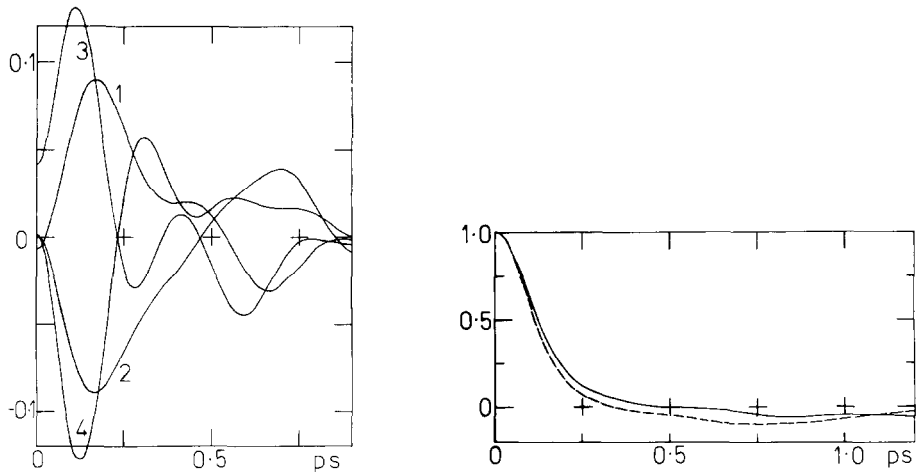

Fig. 2. Moving frame (1,2,3) cross-correlation functions for chloro fluoro acetonitrile. (Principal molecular moment of inertia frame).

$$(1)(1,3) \equiv \frac{\langle p_1(t) J_3(o) \rangle}{\langle p_1^2 \rangle^{\frac{1}{2}} \langle J_3^2 \rangle^{\frac{1}{2}}} \qquad \text{S enantiomer}$$

(2) As for (1), R enantiomer; (3) (3,1), R; (4) (3,1) S
This function for the racemic mixture vanishes for all t. For definition of frame (1,2,3), see Table 1.
Abscissa: time/ps
Ordinate: Normalised cross-correlation function.

Fig. 3. Laboratory frame rotational velocity a.c.f. Note the racemic mixture a.c.f. cuts the time axis earlier (cf. text and fig (1)).
———— S enantiomer.
- - - - - Racemic Mixture
Abscissa: time/ps;
Ordinate Normalised a.c.f.

symmetry breaking external variable - in the case of figure (4), by the use of a strong external, electric field of force [11]. The amplitude of the laboratory frame cross-correlations is proportional to the strength of the electric field. Again, this new phenomenon cannot be explained satisfactorily with Kramers equation theory at its current state of development [7-9].

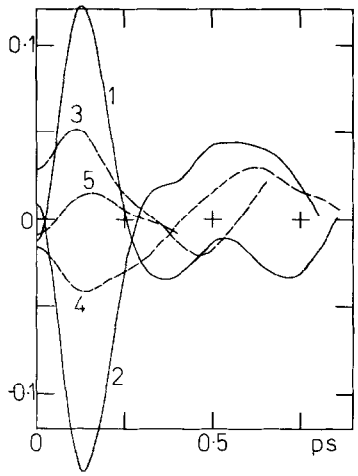

Fig. 4. Laboratory frame (x,y,z) cross-correlation functions for S chlorofluoroacetonitrile, induced by the application of an external electric field, in the z axis.

(1) $\dfrac{\langle p_y(t)J_x(o)\rangle}{\langle p_y^2\rangle^{\frac{1}{2}}\langle J_x^2\rangle^{\frac{1}{2}}}$ (2) $\dfrac{\langle p_x(t)J_y(o)\rangle}{\langle p_x^2\rangle^{\frac{1}{2}}\langle J_y^2\rangle^{\frac{1}{2}}}$

Energy of electric field = 20.0 kT;
(3) As for (1), μE = 2.0kT; (4) As for (2) μE = 2.0kT; (5) as for (1), $\mu E/kT$ = 0.0
Abscissa: time/ps;
Ordinate: Normalised cross-correlation function.

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