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**SOLID STATE NMR STUDIES
OF THE
CHIRAL SELECTIVITY, MOLECULAR MOTION
AND REACTIVITY
OF GUEST MOLECULES
IN TRI-*o*-THYMOTIDE CLATHRATES**

by

GLENN ANGUS FACEY

A thesis submitted to
The Faculty of Graduate Studies and Research
in partial fulfilment of
the requirements for the degree of
Doctor of Philosophy

Department of Chemistry
Carleton University
Ottawa, Ontario
September, 1991

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CHIRAL SELECTIVITY, MOLECULAR MOTION
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IN TRI-*o*-THYMOTIDE CLATHRATES

submitted by

GLENN ANGUS FACEY, B.Sc., M.Sc.

in partial fulfilment of the requirements
for the degree of Doctor of Philosophy

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ABSTRACT

Tri-*o*-thymotide (TOT) is a chiral solid host material, forming inclusion compounds with a multitude of guest materials. It has the unusual property of being able to undergo spontaneous optical resolution upon recrystallization from suitable solvents, giving enantiomeric clathrate crystals. If recrystallized from chiral solvents, TOT often enclathrates one enantiomers of the guest in preference to the other. This thesis will show that both solid state ^{13}C and ^2H NMR can be used to evaluate, nondestructively, enantiomeric excesses of chiral guest molecules in *polycrystalline* TOT clathrates. It will also show that the molecular mobility of the favoured and unfavoured enantiomers is quite different and may provide information regarding the mechanism of the selectivity. The solid state NMR methods provide valuable information inaccessible by X-ray crystallographic techniques.

The molecular mobility of several achiral TOT guest molecules has been investigated with solid state NMR. This technique has allowed the mechanism of such motions to be determined. In some cases the information obtained contradicts conclusions made through X-ray diffraction studies.

Chemical reactions of prochiral TOT enclathrated guests with reactive gases have been carried out in the solid state, yielding chiral reaction products. The reactions have been followed with solid state ^{13}C CP/MAS NMR. It will be shown that the chiral host structure has an influence on the chirality of the reaction product.

ACKNOWLEDGEMENTS

Although this thesis bears the name of only one author, it is the result of the efforts of many. To those, I am grateful. I hope you will accept this message as an expression of warmest thanks. Let me begin by mentioning the people whose professional guidance lead me to the completion of this manuscript.

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FOREWORD

The purpose of the work described in this thesis was to learn more about the motion of molecules trapped in solid matrices, the selectivity the solid matrix exhibits and the chemical behaviour of the trapped molecules. The host system chosen for study was tri-*o*-thymotide. This material has been shown to enclathrate many molecules of varying size, shape and functionality. It exhibits chiral selectivity towards many racemic guest molecules and it provides a constrained environment for reactive guest molecules. In order to study such a system one must choose a technique suitable to the study of solids as the clathrates of tri-*o*-thymotide do not exist in solution. Diffraction techniques, although generally very informative, provide insufficient information regarding dynamic processes. Infrared spectroscopy can provide information about unusual conformations and can be used to follow chemical processes, however, it has the disadvantage that contributions due to the guest are often completely masked by the host. Solid state NMR, on the other hand, is sensitive to dynamic processes and problems of spectral overlap due to the host system can often be solved by selective isotopic labelling of the guest species.

Before presenting the experimental work carried out and describing its meaning and significance the fundamental theory of solid state NMR must be presented. The interactions which govern the interpretation of both broadline and high resolution solid state NMR spectra will be described along with the experimental techniques needed to obtain the data. With the theory introduced in chapter one, a general description of inclusion compounds will be given along with a complete literature review of the tri-*o*-thymotide clathrates in chapter 2. Chapter 3 will describe the preparative methods used to obtain the samples as well as the NMR techniques used. The following chapters will investigate specific clathrates or groups of clathrates. At the end a conclusion will be given summing up all of the experimental work and also providing some suggestions for future investigations.

CHAPTER ONE

Introduction to Solid State NMR

I. NMR of Solids

The NMR spectra of solids are dominated by a number of electronic and magnetic interactions. These interactions are present in solutions as well, however the rapid tumbling motion averages them out partially or completely, usually leaving very sharp lines at frequencies determined by the isotropic chemical shift and scalar coupling constant. In general, solids do not possess the same degree of motional freedom and the interactions manifest themselves as very broad resonances which in principle provide much more information than the isotropic lines observed in the NMR spectra of solutions.

The broadline NMR spectrum of a single nucleus in any solid is the result of the following sum of interactions:

$$H_{TOTAL} = H_Z + H_Q + (\sum_{IS} H_D) + H_a + (\sum_{IS} H_J) \quad (1)$$

H_Z is the Zeeman interaction which is responsible for the removal of the degeneracy of the spin energy levels of any non-zero spin nucleus when placed in a magnetic field. It is this fundamental interaction between a spin $I \neq 0$ nucleus and a static magnetic field which makes the NMR experiment possible. H_Q represents the

electric quadrupolar interaction. This interaction is present only for those nuclei with spin $I > \frac{1}{2}$. It is due to the interaction of the nuclear charge with the electric field gradient at the site of the nucleus and often completely dominates the NMR spectrum. H_D is the dipolar interaction. It is a pairwise magnetic interaction which must be summed over all like and unlike spins, I and S, respectively. This interaction normally dominates the NMR spectrum of abundant spin $I = \frac{1}{2}$ nuclei. H_σ is the chemical shielding interaction. It is the result of electronic shielding of a nucleus from the static magnetic field, B_0 . This interaction is most easily observed for dilute spin $I = \frac{1}{2}$ nuclei where the dipolar interaction is either insignificant or has been removed artificially by high power decoupling. H_J is the spin-spin coupling interaction. Like the dipolar coupling term it must also be summed over all like and unlike spins. Also, like the dipolar coupling to protons, heteronuclear J-coupling to protons is usually removed with high power decoupling. Although very important in the interpretation of the NMR spectra of solutions, J-coupling is usually only observed in the solid state NMR spectra of the heavier nuclides when decoupling is not used. For the lighter nuclides the other interactions are normally larger by several orders of magnitude.

1.1 The Quadrupolar Interaction.

The Hamiltonian for the quadrupolar interaction is given by¹:

$$H_Q = \frac{e^2 q Q}{4I(2I-1)} [3I_z^2 - I^2 + \frac{1}{2}\eta(I_+^2 + I_-^2)] \quad (2)$$

where eQ is the quadrupole moment of the nucleus, eq and η are the largest component and asymmetry parameter of the diagonalized electric field gradient tensor, respectively, I is the spin quantum number, I_z is the z component of the spin operator, I , and I_+ and I_- are the raising and lowering operators, respectively. The electric field gradient at the site of the nucleus is rarely spherically symmetric and may therefore be represented by a second rank tensor, V_{ij} , describing its spatial distribution. In its principal axis system it is diagonal with:

$$V_{zz} = eq \quad (3)$$

$$\eta = \frac{|V_{yy}| - |V_{xx}|}{|V_{zz}|} \quad (4)$$

$$0 \leq \eta \leq 1 \quad (5)$$

$$|V_{zz}| \geq |V_{yy}| \geq |V_{xx}| \quad (6)$$

V_{ij} is also traceless such that the relative signs of V_{xx} and V_{yy} are different from that of V_{zz} so that:

$$V_{xx} + V_{yy} + V_{zz} = 0 \quad (7)$$

When a quadrupolar nucleus is placed in a strong magnetic field the total Hamiltonian is that described by equation (1). Very often the quadrupolar interaction is much larger than the dipolar, anisotropic chemical shielding, and spin-spin coupling interactions and the spectrum is entirely governed by the Zeeman and quadrupolar terms. The Hamiltonian is then simplified to:

$$H_{TOTAL} = H_Z + H_Q \quad (8)$$

The Zeeman Hamiltonian is given by²:

$$H_Z = -\frac{\gamma h}{2\pi} \mathbf{B}_0 \cdot \mathbf{I}_Z \quad (9)$$

where γ is the gyromagnetic ratio for the nucleus. There are $(2I+1)$ eigenstates of energy, E_m :

$$E_m = -\frac{\gamma h}{2\pi} m B_0 \quad (10)$$

where m is a quantum number able to take on the $(2I+1)$ values from $-I$ to I in steps of $\Delta m=1$ and B_0 is the magnitude of the magnetic field vector $\mathbf{B}_0$. In the absence of a magnetic field the quadrupolar Hamiltonian for a spin $I=1$ nucleus, such as deuterium with $\eta=0$, has three eigenstates of energy¹:

$$E_m = \frac{e^2 q Q}{4I(2I-1)} [3m^2 - I(I+1)] \quad (11)$$

The $m=1$ and $m=-1$ states are degenerate. If the quadrupolar interaction is treated as a perturbation on the Zeeman interaction (i.e. high field case) we have the following energy levels for a deuterium nucleus with $\eta=0$ (see figure 1):

$$E_{-1} = \frac{\gamma h B_0}{2\pi} + \frac{e^2 q Q}{4} \quad (12)$$

$$E_0 = -\frac{e^2qQ}{2} \quad (13)$$

$$E_{\pm 1} = -\frac{\gamma\hbar B_0}{2\pi} \pm \frac{e^2qQ}{4} \quad (14)$$

These levels give rise to two resonance lines whose frequencies are given by:

$$\nu = \frac{\gamma B_0}{2\pi} \pm \frac{3}{4} \left(\frac{e^2qQ}{h} \right) \quad (15)$$

The collective term (e^2qQ/h) is referred to as the quadrupolar coupling constant. The resonance lines above apply to a single deuterium atom fixed in a rigid molecule in a strong magnetic field where the largest component of the cylindrically symmetric electric field gradient tensor, eq , at the site of the nucleus is parallel to the magnetic field vector. When eq is not parallel to the magnetic field, H_Q in equation (2) must be rewritten in a reference frame where the magnetic field vector is the principal axis. When this is done an angular dependence between the magnetic field vector and eq arises. The first order perturbations on the Zeeman energy levels are then given by:¹

$$E_m^{(1)} = \frac{3e^2qQ}{8} \left(m^2 - \frac{2}{3} \right) (3 \cos^2\theta - 1) \quad (16)$$

where θ is the angle between eq and B_0 . These perturbations give rise to the two resonance lines:

$$\nu = \frac{\gamma B_0}{2\pi} \pm \left[\frac{3}{8} \left(\frac{e^2 q Q}{h} \right) (3 \cos^2 \theta - 1) \right] \quad (17)$$

with frequency separation:

$$\Delta \nu = \frac{3}{4} \left(\frac{e^2 q Q}{h} \right) (3 \cos^2 \theta - 1) \quad (18)$$

If eq does not have cylindrical symmetry (i.e. $\eta \neq 0$) then the perturbed eigenstates depend on both the polar angles θ and ϕ describing the orientation of the magnetic field in the principal axis system of the electric field gradient tensor (see figure 2). These are given by:¹

$$E_m^{(1)} = \frac{e^2 q Q}{4} (3m^2 - 2) \left(\cos^2 \theta - \frac{1}{2} \sin^2 \theta + \frac{1}{2} \eta \sin^2 \theta \cos 2\phi \right) \quad (19)$$

yielding frequency transitions:

$$\nu = \frac{\gamma B_0}{2\pi} \pm \left[\frac{3}{4} \left(\frac{e^2 q Q}{h} \right) \left(\cos^2 \theta - \frac{1}{2} \sin^2 \theta + \frac{1}{2} \eta \sin^2 \theta \cos 2\phi \right) \right] \quad (20)$$

Since eq for the ^2H nucleus is usually very close to being axially symmetric about C-D bonds in rigid organic compounds, equation (18) shows that the doublet splitting is sensitive to the orientation of the C-D bond in the magnetic field. The study of the changes in the splitting in the spectrum as a function of the crystal orientation in the magnetic field can give the quadrupolar coupling constant and η directly as well as the orientation of eq with respect to the crystal axes. Many such studies have been performed providing a wealth of structural data.³⁻⁶

Often single crystals of a material are not available, or are inconvenient to work with, and one is restricted to working with powdered samples. Unlike single crystals where the C-D bonds have only a limited number of orientations with respect to the magnetic field, powders have all values of θ and ϕ represented. The spectrum then consists of a weighted sum of all possible doublets and is therefore represented by a broad envelope. The lineshape can be described as follows:¹

$$F(\nu) = \int \int f_A(\nu, \theta, \phi) \sin \theta d\theta d\phi + \int \int f_B(\nu, \theta, \phi) \sin \theta d\theta d\phi \quad (21)$$

where the functions f_A and f_B are delta functions representing each of the lines in the doublet. When $\eta=0$ there is no ϕ dependence in the lineshape and the spectrum resembles a Pake doublet.⁷ When $\eta \neq 0$ the powder spectrum is more complicated giving three pairs of discontinuities⁸⁻¹⁰ as opposed to two in the case of an axially symmetric spectrum. In reality the functions f_A and f_B are not well represented by delta functions due to dipolar broadening and other broadening effects. The powder spectrum reflects this in a general broadening or rounding at the singularities. Figure 3 shows a number of powder spectra as a function of the asymmetry parameter. The principal components and the asymmetry parameter of the electric field gradient tensor can be read directly from the frequency separations of the pairs of singularities in the powder spectrum with:

$$\Delta \nu_{xx} \propto |V_{xx}| \quad (22)$$

$$\Delta v_{yy} \propto |V_{yy}| \quad (23)$$

$$\Delta v_{zz} \propto |V_{zz}| \quad (24)$$

$$\Delta v_{xx} \leq \Delta v_{yy} \leq \Delta v_{zz} \quad (25)$$

$$\eta = \frac{\Delta v_{yy} - \Delta v_{xx}}{\Delta v_{zz}} \quad (26)$$

All orientational information present in the spectra of single crystals is lost in powdered samples.

One main application of solid state ^2H NMR is that it is sensitive to molecular motion. The sensitivity arises because the molecular motion gives rise to a time averaged electric field gradient tensor which may or may not have the same orientation as the static tensor. Molecular motions must be divided into three régimes: those that occur at a rate much slower than the reciprocal of the static line width, those that occur at a rate much faster than the reciprocal line width and those of intermediate rates. The conventional quadrupolar echo experiment used routinely to collect ^2H NMR data¹¹ is insensitive to the slow motional régime and the spectra of slow moving molecules are indistinguishable from those of rigidly held molecules. There are however pulse techniques which give spectra sensitive to slow motions.¹²⁻²³ Motions that occur in the fast motional régime average the static electric field gradient tensor and in effect a new averaged tensor, V' , must be used to evaluate the lineshape of the powder spectrum. If both the static and motionally averaged spectra are available it is possible to obtain mechanistic information about

the motion occurring. The fast motional spectrum is, however, insensitive to changes in the rate of the motion responsible for averaging the spectrum. If several fast motions occur simultaneously, the spectrum reflects the overall averaged electric field gradient tensor. Intermediate rate spectra provide information regarding both the mechanism of the motion as well as its rate.²⁴⁻²⁷ The time scale of these motions is of the same order as the time required to obtain an echo and hence pulse spacings in the quadrupolar echo experiment have a drastic effect on the lineshape obtained. A number of authors have dealt with the calculation of intermediate rate spectra²⁸⁻³¹ although such calculations will not be dealt with here.

In order to calculate fast motional limit ^2H NMR spectra one must first determine the time averaged electric field gradient tensor. Once this is determined and diagonalized, if necessary, the spectral lineshape can be determined in a manner exactly analogous to that of calculating the rigid spectrum. Averaged tensors are determined by describing all orientations of the rigid tensor visited over the course of the motion in a common reference frame. The reference frame is usually chosen such that the motion is symmetric about the z axis. This often leads to averaged tensors in their principal axis systems and eliminates the need for diagonalization. For example, in the rotation of a $-\text{CD}_3$ group the principal axis of the rigid tensors along the C-D bonds must be shifted such that the principal axis of the averaged tensor is along the rotation axis of the methyl group. This is done by making use of the Euler angles³², α , β and γ between the two axis systems (see figure 4) and the rotation matrix,³² $R(\alpha, \beta, \gamma)$:

$$R(\alpha, \beta, \gamma) = R_z(\gamma) \cdot R_y(\beta) \cdot R_z(\alpha) \quad (27)$$

$$R_z(\gamma) = \begin{pmatrix} \cos \gamma & \sin \gamma & 0 \\ -\sin \gamma & \cos \gamma & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad R_y(\beta) = \begin{pmatrix} \cos \beta & 0 & -\sin \beta \\ 0 & 1 & 0 \\ \sin \beta & 0 & \cos \beta \end{pmatrix} \quad (28)$$

$$R_z(\alpha) = \begin{pmatrix} \cos \alpha & \sin \alpha & 0 \\ -\sin \alpha & \cos \alpha & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

where the electric field gradient tensor in the new axis system, $V(\alpha, \beta, \gamma)$ is given by:

$$V(\alpha, \beta, \gamma) = R(\alpha, \beta, \gamma) V_{PAS} R^{-1}(\alpha, \beta, \gamma) \quad (30)$$

The tensors, $V_i(\alpha, \beta, \gamma)$ at each of the n sites visited by the deuteron over the course of the motion are obtained from those of the rigid deuteron in its principal axis systems and the time averaged tensor, $V'(\alpha, \beta, \gamma)$ for each deuteron is a simple average of those sampled throughout the entire motion:

$$V'(\alpha, \beta, \gamma) = \left(\frac{1}{n}\right) \sum_{i=1}^n V_i(\alpha, \beta, \gamma) \quad (31)$$

This procedure must be carried out for each deuteron affected by the motion.

Figure 5 shows several ^2H NMR spectra resulting from different types of molecular motion. It is important to note that the appearance of the fast motional lineshape depends on the mechanism of the motion, for example a continuous motion can sometimes be distinguished from a discrete jumping or a flipping motion. For n -fold rotations, where $n \geq 3$, the averaged spectrum is always axial (i.e. $\eta=0$).

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Since the resonance lines in ^2H NMR spectroscopy are very broad, the free induction decay (FID) decays very rapidly and a simple 90° pulse experiment is inadequate in obtaining the data. Pulse breakthrough from the very high power needed to excite the wide frequency range, the dead time of the receiver and the ring down time of the probe circuitry prohibit the collection of the first 20-30 μsec of the transient signal, causing severe distortions in the transformed spectrum. For this reason an echo experiment is used. The $90^\circ_x - \tau_1 - 90^\circ_y - \tau_2 - (\text{acquire})$ pulse sequence, called the quadrupolar echo experiment¹¹ is depicted in figure 6. After the 90°_x pulse the signal is allowed to decay for a time, τ_1 , where τ_1 is shorter than the transverse relaxation time, T_2 . After the 90°_y pulse the signal builds up again until it reaches a maximum after a time, τ_2 . At this point the receiver is switched on and the echo decay is collected. In principle $\tau_1 = \tau_2$ however in practice one makes τ_2 shorter than τ_1 in order to locate the echo maximum more precisely. This pulse sequence has the same qualitative effect on ^2H as the Hahn echo³³ sequence (used to measure T_2 s) has on spin $I = \frac{1}{2}$ systems in solution. However, unlike the Hahn echo sequence, which can be understood with vector diagrams, it requires much more elaborate analysis.³⁴ The quadrupolar echo experiment can provide lineshapes without distortion if the 90° pulses are short enough and any molecular motion occurs at a rate either much faster or much slower than the time scale of the experiment.

The quadrupolar echo sequence can also be used in conjunction with the inversion recovery method for measuring spin lattice relaxation times. A 180° pulse

is applied to invert the magnetization and a time period τ_R is allowed to pass during which the magnetization is allowed to relax. This is followed by the quadrupolar echo sequence to sample the partially relaxed magnetization. The experiment is repeated as a function of τ_R and the T_1 is calculated in the same manner as in solution NMR.

As stated earlier, fast motional powder lineshapes are often invariant to changes in the correlation time of the motion responsible for the averaging in the spectrum. As a result the study of relaxation processes is often the only way to extract quantitative information from the spectrum. The spin lattice relaxation of ^2H NMR resonances is usually dominated entirely by the quadrupolar relaxation mechanism. This mechanism relies on time dependent fluctuations, $g(t)$, of the electric field gradients at the site of the nuclei. The fluctuations are caused by molecular motion and the relaxation is most efficient when the correlation time of the motion is of the order of the inverse Larmor frequency. A general expression for the rate of spin-lattice relaxation has been given in the literature³⁵:

$$\frac{1}{T_1} = \frac{3}{16} \chi^2 [J_1(\omega_o) + 4J_2(2\omega_o)] \quad (32)$$

In this expression χ is the quadrupolar coupling constant and $J_m(m\omega_o)$ are spectral density functions obtained from a Fourier transform of the autocorrelation functions, $G_m(\tau)$:

$$J_m(\omega_o) = 2 \int_0^{\infty} G_m(\tau) \cos \omega \tau \, d\tau \quad (33)$$

The autocorrelation function can be described as a measure of the "memory" a spin system has about its motional state at a time, $t+\tau$ given that it was known at time, t . This function depends on the motional fluctuations, $g(t)$ which in turn depend on the Euler angles relating the principal axis system of the averaged electric field gradient tensor to the laboratory frame of reference. The Euler angle dependence shows up as anisotropy in the T_1 . In other words the T_1 is not necessarily the same across the width of the powder spectrum. Torchia and Szabo³⁵ have calculated the dependence of the T_1 anisotropy on various motional models including two and three site exchange as well as continuous rotation of a C-D bond on the surface of a cone. The differences in the T_1 anisotropy were found to be useful in identifying the mechanisms of molecular motions. It has been applied to cases where only one type of molecular motion occurs^{28,35-38} and presumably would be much more complicated with the existence of multi-axis rotations.

The temperature dependence of T_1 has been extensively used to calculate the energies of activation of motional processes and their correlation times, τ_c .^{26,39-43} The general dependence of T_1 on the correlation time is shown in figure 7. In calculating activation energies, one generally assumes that the process is thermally activated and that the correlation time of the motion has an Arrhenius temperature dependence:

$$\tau_c = \tau_c^0 e^{(E_a/kT)} \quad (34)$$

where E_a is the activation energy of the process, k is the Boltzman constant and τ_c^0 is a proportionality constant. In the extreme narrowing limit when the product of the correlation time and the Larmor frequency is much less than unity, the relaxation rate at a specific frequency in a powder spectrum is linear in τ_c^{35} therefore the same Arrhenius relationship exists for the reciprocal of T_1 . It is easy to confirm the following relationship:

$$\ln T_1 = C - E_a/kT \quad (35)$$

where C is a constant. A plot of the logarithm of T_1 versus reciprocal temperature will have a slope of $-E_a/k$. All of the relaxation times must be made at the same position in the powder spectrum.

1.2 The Dipolar Interaction

The dipolar interaction can be thought of classically as the direct interaction between a pair of magnetic dipoles. Since the classical picture describes nuclei as microscopic magnetic dipoles, it is not difficult to see how this interaction may prevail. The dipolar hamiltonian for a pair of spins, I_1 and I_2 is given by the following expression⁴⁴:

$$H_D = \left(\frac{h}{2\pi} \right) \left[\left(\frac{\mu_o}{4\pi} \right) \frac{\gamma_1 \gamma_2 h}{2\pi r_{12}^3} \right] (I_1 I_2 - 3 \frac{(I_1 r_{12})(I_2 r_{12})}{r_{12}^2}) \quad (36)$$

where r_{12} is the internuclear vector between the interacting spins and r_{12} is its magnitude. μ_0 is the permeability of free space. It has the value of $4\pi \cdot 10^{-7} \text{ kg} \cdot \text{m} \cdot \text{s}^{-2} \cdot \text{A}^{-2}$ and is used to maintain S.I. units. The term in square brackets is known collectively as the dipolar coupling constant and is often given the symbol, R . If the displacement vector is expressed in polar coordinates with the z direction being parallel to the magnetic field the Hamiltonian becomes⁴⁴:

$$H_D = \left(\frac{h}{2\pi}\right) R (A+B+C+D+E+F) \quad (37)$$

where:

$$A = -I_{1z} I_{2z} (3 \cos^2 \theta - 1) \quad (38)$$

$$B = \frac{1}{4} [I_{1+} I_{2-} + I_{1-} I_{2+}] (3 \cos^2 \theta - 1) \quad (39)$$

$$C = -\frac{3}{2} [I_{1z} I_{2+} + I_{1+} I_{2z}] \sin \theta \cos \theta e^{(-i\phi)} \quad (40)$$

$$D = -\frac{3}{2} [I_{1z} I_{2-} + I_{1-} I_{2z}] \sin \theta \cos \theta e^{(i\phi)} \quad (41)$$

$$E = -\frac{3}{4} I_{1+} I_{2+} \sin^2 \theta e^{(-2i\phi)} \quad (42)$$

$$F = -\frac{3}{4} I_{1-} I_{2-} \sin^2 \theta e^{(2i\phi)} \quad (43)$$

In the high field approximation where the dipolar interaction can be treated as a perturbation on the much stronger Zeeman interaction, only the A and B terms contribute to the spectrum of homonuclear dipolar coupled spins. The total Hamiltonian can then be expressed as:

$$H_T = H_Z + H_D \quad (44)$$

where:

$$H_Z = \frac{-\gamma h B_0}{2\pi} (I_{1z} + I_{2z}) \quad (45)$$

and:

$$H_D = \left(\frac{h}{2\pi}\right) R \left[\frac{(3\cos^2\theta - 1)}{2} (I_{1z}I_{2z} - 3I_{1x}I_{2x}) \right] \quad (46)$$

The unperturbed Zeeman Hamiltonian has four possible energy states; $|++\rangle$, $|+-\rangle$, $| - + \rangle$ and $|--\rangle$ where the + and - represent the spin states of each of the coupled spins. It is more convenient to consider the linear combinations of these states²:

$$|1\rangle^T = |++\rangle \quad |0\rangle^T = \frac{1}{\sqrt{2}}(|+-\rangle + |-+\rangle) \quad (47)$$

$$|-1\rangle^T = |--\rangle \quad |0\rangle^S = \frac{1}{\sqrt{2}}(|+-\rangle - |-+\rangle) \quad (48)$$

where the superscripts ^T and ^S refer to triplet and singlet states, respectively. The singlet state is not coupled to any of the members of the triplet state by either the Zeeman or the dipolar interactions and is therefore ignored. The three components of the triplet state are equally spaced with Zeeman energies:

$$E_{-1} = \frac{\gamma h B_o}{2\pi} \quad E_0 = 0 \quad E_1 = -\frac{\gamma h B_o}{2\pi} \quad (49)$$

This gives rise to a single resonance line. Like the quadrupolar Hamiltonian the dipolar Hamiltonian has three eigenstates which perturb the Zeeman energies. The energies of the perturbed states are⁴⁴:

$$E_{-1} = \frac{\gamma h B_o}{2\pi} - \left(\frac{h}{2\pi}\right) \frac{R}{4} (3\cos^2\theta - 1) \quad (50)$$

$$E_0 = \left(\frac{h}{2\pi}\right) \frac{R}{2} (3\cos^2\theta - 1) \quad (51)$$

$$E_1 = -\frac{\gamma h B_o}{2\pi} - \left(\frac{h}{2\pi}\right) \frac{R}{4} (3\cos^2\theta - 1) \quad (52)$$

and the corresponding transition frequencies are:

$$\nu = \frac{1}{2\pi} (\gamma B_o \mp \left(\frac{3}{4} R(3\cos^2\theta - 1)\right)) \quad (53)$$

Thus for a rigid pair of spin $I=1/2$ nuclei, one would expect to see a doublet with splitting:

$$\Delta\nu = \frac{1}{2\pi} \frac{3}{2} R(3\cos^2\theta - 1) \quad (54)$$

This is exactly analogous to the doublets observed in the ^2H NMR spectra of rigid deuterons, only in this case it is the pair of spins which give rise to the spectrum rather than a single nucleus. It is obvious that the doublet splitting depends on the orientation of the internuclear vector with respect to the magnetic field. Single crystals containing isolated spin pairs have been used in NMR studies where spectra were recorded as a function of crystal orientation in the magnetic field.^{7,45-47} These experiments yield important structural information. Since the frequency separation also depends on R which in turn depends on the inverse cube of the internuclear distance the observed spectra of isolated spin pairs can also be used to explicitly evaluate internuclear distances.

For powdered or polycrystalline samples, all orientations of the internuclear vector, r_{12} with respect to the magnetic field are possible, just as all orientations of the electric field gradient tensor were possible when considering solid state ^2H NMR spectra. Similarly the powder spectrum consists of a weighted superposition of all possible doublets and the result is again a Pake doublet.⁷ The inner singularities are the 90° orientations separated by $3R/4\pi$ and the outer shoulders are the 0° or 180° orientations separated by $3R/2\pi$. Although all of the orientational information is lost in the powder spectrum it is still possible to determine the internuclear distance directly from the spectrum.

The dipolar powder spectrum of spin systems is sensitive to molecular motion, and this is especially true of isolated spin pairs. In this case the internuclear vector

can be treated in exactly the same manner as the largest component of the electric field gradient tensor in spin $I=1$ systems to calculate an averaged spectrum.

Most often the spin system under consideration does not consist of isolated spin pairs. Spectra have been calculated for spin systems containing up to six isolated spins and they are much more complicated than that of the two spin case^{48,49} (figure 8). When many abundant spins are present the rigid lattice spectrum appears as one broad Gaussian peak. Such spectra can often be used to study motional processes and solid-solid phase transitions by way of a moment analysis⁵⁰ or relaxation studies.^{51,52}

For abundant homonuclear many-spin systems in the solid state the T_1 relaxation time is common to all of the spins. Thus, for example, the protons in an organic solid which may give rise to a single gaussian resonance, relax at the same rate. This phenomenon is usually explained with a thermodynamic analogy.⁵³ The individual protons, if initially prepared so as to have different spin temperatures, rapidly exchange energy with each other due to strong dipole-dipole coupling and establish a common spin temperature. These then interact more slowly with the lattice and therefore all protons have common spin lattice relaxation times. The common T_1 is sensitive to motion and has been used in many studies.⁵⁴ Another relaxation time exploited for abundant spin $I=1/2$ systems is the relaxation time in the rotating frame, $T_{1\rho}$. This relaxation time is analogous to T_1 relaxation. In the case of T_1 relaxation, the time constant is characteristic of spins returning to their equilibrium state under the influence of the static magnetic field, B_0 . $T_{1\rho}$ relaxation

is characteristic of the spins returning to their equilibrium state under the influence of a magnetic field applied to them in the rotating frame in the form of an r.f. spin locking pulse, H_1 . Since relaxation is most efficient when molecular motions occur at the Larmor frequency, $T_{1\rho}$ relaxation is sensitive to motions of lower frequency than T_1 relaxation because $\gamma H_1 < \gamma H_0$.

So far the discussion has only been applied to homonuclear dipolar interactions. The same interactions can occur between unlike spins.⁵⁵⁻⁶⁰ This interaction has been exploited to extract information about bond lengths and molecular motion and has been used indirectly in the study of chemical shielding tensors.⁵⁹⁻⁶⁰ Often heteronuclear dipolar interactions between dilute nuclei and protons are removed with high power proton decoupling in the interest of obtaining high resolution spectra of the dilute nuclei.

1.3 The Chemical Shielding Interaction

Unlike the multiplet states which arise as a result of the dipolar interaction between spins, the chemical shielding interaction for spin $I = \frac{1}{2}$ nuclei involves only one nuclear spin and, therefore, only two energy states and one transition. The frequency of the transition depends not only on the Zeeman interaction and B_0 but also on the electronic environment around the nucleus. The mobile electrons surrounding the nucleus generate their own magnetic fields which shield or deshield the nucleus from B_0 . The position of the resonance line in the frequency spectrum therefore depends on the chemical environment of the nucleus. Since the electronic orbitals surrounding a nucleus are not normally spherically symmetric but are usually

spatially anisotropic, the chemical shielding interaction must therefore be a tensorial property. The degree of shielding around a nucleus and hence the position of its resonance line, will depend on the orientation of the molecules with respect to the magnetic field. The chemical shielding Hamiltonian can be represented as follows:

$$H_s = \frac{\gamma h}{2\pi} I_z \sigma B_0 \quad (55)$$

where σ is the chemical shielding tensor. Unlike the electric field gradient tensor for the electric quadrupolar interaction which is traceless and symmetric, the chemical shielding tensor is not traceless and not necessarily symmetric. It can however be separated into a symmetric tensor, σ_s , and an antisymmetric tensor, σ_a ⁶¹:

$$\sigma_s = \frac{1}{2}(\sigma + \sigma^T) \quad (56)$$

$$\sigma_a = \frac{1}{2}(\sigma - \sigma^T) \quad (57)$$

where σ^T is the transpose of σ . The antisymmetric component contributes negligibly to the NMR spectrum and will be ignored leaving only σ_s .

In the absence of quadrupolar and dipolar effects the total Hamiltonian for a spin $I = \frac{1}{2}$ nucleus is given by:

$$H_{TOTAL} = H_z + H \quad (58)$$

$$H_{TOTAL} = -\frac{\gamma h}{2\pi} I_z B_o (E - \sigma) \quad (59)$$

where E is a second rank unit matrix. The corresponding energy levels, E_m are:

$$E_{1/2} = -\frac{\gamma h}{4\pi} B_o (1 - \sigma_{zz}) \quad E_{-1/2} = \frac{\gamma h}{4\pi} B_o (1 - \sigma_{zz}) \quad (60)$$

where σ_{zz} is the largest principal component of the chemical shielding tensor assumed to be parallel to the magnetic field. These levels give rise to a single resonance line at:

$$\nu = \frac{\gamma}{2\pi} B_o (1 - \sigma_{zz}) \quad (61)$$

If σ_{zz} is not parallel to the magnetic field then the shielding tensor must be described in an axis system where the magnetic field vector is the principal axis. In this case the line has an orientationally dependent position given by:

$$\nu = \frac{\gamma}{2\pi} [1 - (\sigma_{xx} \cos^2 \theta_{xx} + \sigma_{yy} \cos^2 \theta_{yy} + \sigma_{zz} \cos^2 \theta_{zz})] \quad (62)$$

Where σ_{ii} are the principal components of the shielding tensor and θ_{ii} are the angles between these components and the magnetic field vector. For a single crystal, this means that the resonances of each crystallographically unique nucleus will depend on the orientation of the crystal in the magnetic field. The situation is similar to that in ^2H NMR spectra except that in this case there is only one resonance line rather than two. Experiments where the orientation of a crystal is varied with

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respect to the magnetic field are used to find the principal components of shielding tensors as well as their orientation with respect to the crystallographic axes.⁶²⁻⁶⁷

In powders where all values of θ_{ij} are represented the spectrum is a superposition of all possible orientationally dependent lines. The lineshape is identical to that expected for a single transition in a ^2H NMR powder spectrum (figure 9). The shielding parameters can be read directly from the discontinuities in the spectrum. A mathematical description of a general lineshape is given by Bloembergen and Rowland.^{8,9} This description is used to simulate lineshapes given the frequencies of the discontinuities in the powder spectrum. It is used to describe powder spectra resulting from the chemical shielding anisotropy interaction as well as the quadrupolar interaction. The mathematical details of the lineshapes and a computer program used to calculate them is given in appendix 1.

In solution, where rapid isotropic molecular motion occurs, the terms $\cos^2\theta_{ij}$ take on their isotropic average value of 1/3 and a single line is observed with frequency:

$$\nu = \frac{\gamma}{2\pi} B_0 (1 - \sigma_i) \quad (63)$$

where σ_i is (1/3) of the trace of σ . It is this shielding parameter which gives rise to the chemical shift observed in solution.

Often one would like to observe a solution-like spectrum for a solid material. In the case of ^{13}C a number of difficulties must first be overcome. The heteronuclear dipolar interaction between ^{13}C and protons must be removed. This

can be accomplished by applying a high power r.f. field at the resonance frequency of the protons. Homonuclear interactions are not a problem since ^{13}C is isotopically dilute and the nuclei are far enough apart to render the interaction insignificant. The anisotropic chemical shielding interaction must also be removed. This is done with a technique known as magic angle spinning.^{61,68-74} A rigid array of nuclei is spun at angular velocity ω_r about an axis at an angle, β to the magnetic field and at angles χ_{ii} ($i=1,2,3$) to the principal components of σ (see figure 10). The angles θ_{ii} become time dependant and can be expressed in terms of other angles in the system:

$$\cos \theta_{ii} = \cos \beta \cos \chi_{ii} + \sin \beta \sin \chi_{ii} \cos(\omega_r t + \psi_{ii}) \quad (64)$$

where ψ_{ii} are the azimuth angles of the principal components of σ at time $t=0$. If equation (64) is substituted into equation (62) and the time average taken the time averaged resonance frequency becomes:

$$\nu = \frac{\gamma}{2\pi} B_0 \left[1 - \left(\frac{3}{2} \sigma_{zz} \sin^2 \beta + \frac{1}{2} (3 \cos^2 \beta - 1) \sum_{ii} \sigma_{ii} \cos^2 \chi_{ii} \right) \right] \quad (65)$$

If β is chosen such that the term $(3 \cos^2 \beta - 1) = 0$ (i.e. $\beta = 54.7^\circ$) then equation (65) reduces to equation (63) which means that a solution-like spectrum will be obtained for the solid. The angle 54.7° is referred to as the "magic angle". The time dependent terms of $\cos \theta_{ii}$ which are periodic in ω_r manifest themselves as rotational echoes in the free induction decay and sidebands in the frequency spectrum separated from the isotropic peak by $\pm n\omega_r$, where n is an integer. The spinning sidebands extend over a frequency range comparable to the static line width. In the limit of $\omega_r \rightarrow 0$, the sideband envelope mimics the lineshape of the static spectrum.

can be accomplished by applying a high power r.f. field at the resonance frequency of the protons. Homonuclear interactions are not a problem since ^{13}C is isotopically dilute and the nuclei are far enough apart to render the interaction insignificant. The anisotropic chemical shielding interaction must also be removed. This is done with a technique known as magic angle spinning.^{61,68-74} A rigid array of nuclei is spun at angular velocity ω_r about an axis at an angle, β to the magnetic field and at angles χ_{ii} ($i=1,2,3$) to the principal components of σ (see figure 10). The angles θ_{ii} become time dependant and can be expressed in terms of other angles in the system:

$$\cos \theta_{ii} = \cos \beta \cos \chi_{ii} + \sin \beta \sin \chi_{ii} \cos(\omega_r t + \psi_{ii}) \quad (64)$$

where ψ_{ii} are the azimuth angles of the principal components of σ at time $t=0$. If equation (64) is substituted into equation (62) and the time average taken the time averaged resonance frequency becomes:

$$\nu = \frac{\gamma}{2\pi} B_0 \left[1 - \left(\frac{3}{2} \sigma_{zz} \sin^2 \beta + \frac{1}{2} (3 \cos^2 \beta - 1) \sum_{ii} \sigma_{ii} \cos^2 \chi_{ii} \right) \right] \quad (65)$$

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When this condition is not met the envelope of the sidebands does not mimic the static lineshape however, it still contains enough information to determine the principal components of the shielding tensor. Two methods based on slow spinning experiments^{75,76} have been used to extract this information as well as others using pulse methods synchronized to the rotational period of the spinner.⁷⁷⁻⁷⁹ Most often one is not interested in the information provided by the sidebands and in fact they are often considered a nuisance. If the rate of the spinning is not sufficient to remove the sidebands completely from the spectrum they can often obscure other isotropic peaks. For this reason pulse sequences designed to partially^{80,81} or fully⁸²⁻⁸⁴ suppress spinning sidebands have been developed and are frequently used.

The high resolution magic angle spinning (MAS) spectra of solids often give chemical shifts different than those observed in solution. This is a result of crystallographic effects or distortions not present in solution. In principle every crystallographically nonequivalent atom will give rise to its own resonance. It is the crystallographic symmetry rather than the molecular symmetry that determines the equivalence or nonequivalence of any group of atoms. Chemical shift values for the nuclei in solids can sometimes be used to study solid-solid phase transitions as the spectrum for each phase may be different. For noncrystalline or amorphous solids the spectral peaks may be broadened as the result of the nuclei having a distribution of electronic environments.

Even with the heteronuclear dipolar interaction removed by high power decoupling and the chemical shielding anisotropy removed through magic angle

spinning, solid state ^{13}C NMR is still faced with the problem that ^{13}C is not a very receptive nucleus since it often has long T_1 s. This problem has been solved with the development of a double resonance technique first introduced as proton enhanced nuclear induction spectroscopy (PENIS)⁸⁵⁻⁸⁷ but now known as cross polarization (CP). This pulse technique transfers magnetization from the abundant protons to the dilute ^{13}C and is illustrated in figure 11. A 90° pulse is first given at the resonance frequency of the protons in the x channel and then they are spin-locked with the application of a contact pulse, $B_{1\text{H}}$ phase shifted from the first pulse by 90° . While the protons are spin-locked, a pulse, $B_{1\text{C}}$ is applied at the resonance frequency of ^{13}C such that the Hartman - Hahn condition⁹¹ is met:

$$\gamma_{\text{H}}B_{1\text{H}} = \gamma_{\text{C}}B_{1\text{C}} \quad (66)$$

Since the gyromagnetic ratio for protons is approximately four times that of ^{13}C , $B_{1\text{C}}$ must be four times the power of $B_{1\text{H}}$. When this condition is satisfied the protons and ^{13}C nuclei have equal energies and precess at the same rate in their respective rotating frames of reference. Under these circumstances, magnetization can be transferred from the protons to the ^{13}C by way of the B term in the heteronuclear dipolar Hamiltonian (see equations 37-43). The magnetization depleted from the proton reservoir is small since the protons are so much more abundant than the ^{13}C . Once the ^{13}C nuclei have been magnetized they can be observed by switching off the $B_{1\text{C}}$ pulse and switching on the receiver. The spin-locking ^1H pulse is left on during data acquisition to remove the heteronuclear dipolar interaction. The result is a signal enhancement of the ^{13}C resonances by a factor equal to the ratio of the

gyromagnetic ratios (~ 4). In principle, the ^{13}C magnetization can be allowed to build up more than once for a given $B_{1\text{H}}$ pulse, being limited only by the $T_{1\rho}$ of the protons and ^{13}C . Usually however, only one transient is collected per $B_{1\text{H}}$ pulse. It should be noted that the repetition rate of the experiment depends on the T_1 of the protons rather than that of the ^{13}C . This is a considerable advantage since T_1 s for ^{13}C are typically an order of magnitude greater than those of protons.

The ^{13}C CP/MAS experiment removes the dipolar coupling between ^{13}C and protons efficiently through both magic angle spinning and high power proton decoupling. The removal of dipolar coupling between ^{13}C and other nuclei relies only on magic angle spinning which is often not enough to fully remove the interaction. This is especially true of the dipole-dipole interactions between ^{13}C and quadrupolar nuclei. Mixing between the quadrupolar and Zeeman Hamiltonians gives rise to new angular terms in the dipolar Hamiltonian which are not removed by magic angle spinning.^{93a} As a result the CP/MAS resonances of ^{13}C atoms attached to quadrupolar nuclei such as ^{14}N , ^{35}Cl , ^{37}Cl and ^2H are often quite broad. In some cases however, the relaxation between the eigenstates of the quadrupolar nucleus is so fast that the dipolar interaction to the ^{13}C is effectively averaged to zero.^{93b} This phenomenon has been referred to as "self decoupling"^{93b} and is responsible for the sharp ^{13}C CP/MAS resonances often observed for ^{79}Br , ^{81}Br or ^{127}I bearing carbons.

In order to obtain quantitative results with the cross polarization experiment, the duration of the contact pulse must be carefully chosen. Figure 12 shows the

relationship between the observed ^{13}C magnetization and the contact time. It is important to notice that carbon atoms in different chemical environments have different dipolar coupling strengths and therefore cross polarize at different rates, however, they loose magnetization at the same rate characterized by the common $T_{1\rho}$ of the proton reservoir. If the contact time is chosen too short then the peak intensities will not quantitatively reflect the number of carbon atoms. It must be chosen long enough such that all the ^{13}C atoms in the sample reach their equilibrium magnetization but short compared to $T_{1\rho}$ so as not to loose a significant amount of signal intensity. To ensure quantitative results a series of spectra collected as a function of contact time must be obtained. For heterogeneous samples which may not share a common proton magnetization reservoir and hence not have a common T_1 or $T_{1\rho}$, the problems of quantitative reliability are much more severe.⁸⁸ Also in cases where spinning sidebands have significant intensity, quantitative interpretation relies on the intensity of the entire signal (including the sidebands).

Since its first implementation, the CP/MAS experiment has been used in conjunction with other techniques to investigate many systems.⁸⁹ One of the simplest modifications to the CP/MAS experiment is the non-quaternary carbon suppression or dipolar dephasing technique. This experiment is identical to the standard CP/MAS experiment except that a delay just prior to data acquisition is inserted where the high power decoupling is switched off. It is switched on again during the collection of data. While the decoupler is off, the ^{13}C nuclei evolve

under the influence of the heteronuclear dipolar Hamiltonian. For rigid systems, this interaction is strongest for those carbon atoms directly attached to protons. The dipolar broadening causes the signals of the proton-bearing carbon atoms to decay completely during an inserted delay period of the correct length and when the data are collected these resonances do not appear in the spectrum. Quaternary carbon atoms such as carbonyl carbons are not influenced by such strong dipolar interactions and their signals do not decay substantially during the delay period although they are slightly attenuated in the spectrum. Mobile proton-bearing carbon atoms, for example rotating methyl groups, may also appear in the dipolar dephased spectrum as the heteronuclear dipolar interaction is averaged by the motion and the signal does not completely decay during the delay period.

CP/MAS experiments have been used to investigate molecular motions, as the line widths (or the T_2 s) have been found to depend on the correlation time of the molecular motion, τ_c .⁹² For carbon atoms with strong heteronuclear dipolar interactions the transverse relaxation rate ($1/T_2$) is proportional to the spectral density function, $J(\omega_1, \tau_c)$:

$$J(\omega_1, \tau_c) = \frac{\tau_c}{1 + \omega_1^2 \tau_c^2} \quad (67)$$

where ω_1 represents the strength of the decoupling field. When the decoupling field is of the same order as the reciprocal correlation time of the motion, the linewidth is a maximum, and often the line is too broad to be observed in the CP/MAS spectrum. In the regions where the product of the decoupler field strength and the

correlation time of the motion are either much greater or much less than unity, the line width obeys an Arrhenius relationship with temperature, and activation energies have been measured.⁹²

From the above discussion it is clear that solid state NMR is a very powerful technique for the investigation of the structure and mobility of solid materials. It will be shown in further chapters that some of the information obtained with these methods is indeed unique to the technique.

Figure 1: Energy level diagram for a spin $I=1$ nucleus in a magnetic field showing the perturbation of the Zeeman levels due to the quadrupolar interaction.

Figure 2: Diagram showing the polar angles θ and ϕ made by the magnetic field vector in the principal axis system of the electric field gradient tensor.

Figure 3: Deuterium NMR powder lineshapes as a function of asymmetry parameter. (a) $\eta=0$, (b) $\eta=0.2$, (c) $\eta=0.5$ (d) $\eta=0.8$ (e) $\eta=1$. The integrated intensity and full width of all spectra are the same.

Figure 4: Diagram showing the three rotations through the Euler angles α , β and γ . Taken from reference 32.

Figure 5: The effect of molecular motion on ^2H NMR line shapes. (A) rigid C-D bond, (B) Two-fold flipping of a para- di-substituted deuterated aromatic ring about its long axis, (C) The in plane rotation of a deuterated benzene ring, (D) Rotation of a deuterated methyl group about its three-fold axis.

Figure 6: Depiction of the quadrupolar echo sequence. For description see text.

Figure 7: The dependence of the spin lattice relaxation time on the correlation time of a molecular motion. The same dependence is exhibited for $\ln T_1$ vs. $1/T$.

Figure 8: The theoretical ^1H NMR lineshape for three protons at the corners of a rigid equilateral triangle. Taken from reference 1.

Spin $I=1/2$ Chemical Shielding Tensor

Figure 9: The general powder NMR lineshape for a proton decoupled dilute spin $I=1/2$ nucleus.

Figure 10: A depiction of the motion of the principal components of a chemical shielding tensor as the sample is rotated macroscopically about an axis inclined at angle β to the magnetic field vector.

Figure 11: A diagram showing the pulse sequence used to acquire CP/MAS ^{13}C NMR spectra. For description see text.

Figure 12: The dependence of the intensity of a ^{13}C NMR line in a CP/MAS spectrum as a function of contact time. (A) $-\text{CH}_2-$ carbon, (B) carbonyl or quaternary carbon. The curves have been displaced from one another for clarity.

CHAPTER TWO

Introduction to Tri-*o*-thymotide Clathrates

The purpose of this chapter is to define clathrate compounds with a brief description of their uses, and to describe, in a comprehensive manner, the work previously done for a particular group of clathrates - the tri-*ortho*-thymotides. After presenting a complete literature review on these systems, the problems to be investigated throughout this thesis will be introduced.

I. Introduction.

The word *clathrate* comes from the Latin *clathratus* meaning "enclosed or protected by crossbars or grating".⁹⁴ Clathrate compounds are combinations of two or more independent substances joined without formal chemical bonds. The components are normally referred to as the *host* and the *guest*. The host structure is an open network with void spaces able to accommodate the guest material. As the Latin word suggests, the guest is enclosed or protected by the host. The host component of clathrate compounds forms a molecular cage around the fully self contained guest. Clathrates belong to a more general group of substances, called inclusion compounds. The most common void spaces in these materials are either channels or cages. A few examples of channel inclusion compounds are urea and

thiourea adducts,⁹⁵ zeolites,⁹⁶ choleic acids⁹⁷ and cyclophosphazine inclusion compounds.⁹⁸ Some cage clathrates include: clathrate hydrates,⁹⁹ Dianin's compound,¹⁰⁰ and β -quinol clathrates.¹⁰⁰ Tri-*o*-thymotide forms both cage clathrates and channel inclusion compounds.

Aside from the chemical and physical interest in studying clathrate inclusion compounds, there are practical reasons as well. Clathrates can be selective in their ability to trap molecules and have therefore been used in separating the components of mixtures.¹⁰¹ Zeolites have been used widely as catalysts in the chemical and petroleum industries. Although not well understood, the catalytic role of these materials is undoubtedly related to their ability to absorb guest molecules. Inclusion compounds have been used as traps for volatile molecules. Such materials often have very low vapour pressures compared to the pure guest, and can therefore be used in the safe transport and handling of dangerous volatile materials. Other uses of inclusion compounds are found in the pharmaceutical industry, where they are used in the production of solid tablets from liquid or gaseous drugs, and in the agricultural industry, where they are used as a medium for the slow release of volatile pesticides and fertilizers. Many potential uses of clathrate compounds have not been exploited and in order to do so, a greater understanding of the inclusion process is called for.

II. Literature Review.

Tri-*o*-thymotide, (TOT) is the trimeric lactone of *o*-thymotic acid. Its molecular structure is shown in figure 13. An examination of a molecular model of

this material reveals that it is quite flexible, having a large number of possible conformations. The most stable of these are the so called propeller conformations, in which all of the carbonyl groups are directed towards one side of the macrocycle, and the helical conformations, where only two of the three carbonyl groups are so directed. All of these conformations have *trans* ester linkages. There are two possible propeller conformations each with perfect C_3 symmetry: one, where the aromatic rings resemble the blades of a right handed (P)¹³¹ propeller and its enantiomer where the rings form a left handed (M)¹³¹ propeller. The helical conformations also form an enantiomeric pair but lack C_3 symmetry. It has been shown^{102,103} that the propeller and helical conformations both exist in solution and that the propeller conformations are more stable than the helical ones. It has also been shown^{102,103} that in order for a given propeller to be converted into its enantiomer it must first go through each of the helical conformations as follows:

The activation energy for racemization of the propeller conformations was measured as 22.2 kcal/mol by NMR methods^{102,103} and 21.2 kcal/mol by polarimetric methods.¹⁰⁴

Early crystallographic experiments¹⁰⁴⁻¹⁰⁶ revealed that TOT clathrates were composed of only the propeller conformations. The propellers, however, were distorted by the crystal packing forces and the perfect C_3 molecular symmetry was

therefore removed. Furthermore, for the majority of TOT clathrates, it was observed that each clathrate crystal contained only one TOT molecule in the asymmetric unit and hence only one of the two possible enantiomeric propellers. Thus, most recrystallizations of TOT clathrates are examples of spontaneous optical resolutions. Dissolved single crystals of TOT clathrates therefore give optically active solutions which, upon standing, yield the optically inactive equilibrium mixture of conformers. Polarimetric experiments on these solutions gave the first energy of racemization for TOT.¹⁰⁴ The early X-ray measurements also showed that there were two main types of TOT clathrates: channel and cage types.¹⁰⁵ Since these early measurements many crystal structures of TOT inclusion compounds have been studied. Table 1 lists those substances for which a complete structural determination has been made. It should be noted that the space groups and lattice constants of many more TOT inclusion compounds than those listed in table 1 have been determined and compiled in the literature.¹⁰⁵

All of the cage clathrates are isostructural and belong to the space group $P3_121$. The majority of the channel inclusion compounds belong to the space groups $P3_1$, $P6_1$ and $P6_2$, however, some have been found to belong to $P1$, $P1$, $P2_1$, $P2_1/c$, $P2/c$, P/bca , and $Pbcn$. The members of the latter group appear to be far less common.¹¹⁹ All clathrates in the same space group have very similar cell dimensions. The deviations in TOT molecules from C_3 molecular symmetry have been documented^{113,119,120} for a number of different crystal environments and account for the chemical shift inequivalence observed in the ^{13}C CP/MAS NMR

Table 1

Published Crystal Structures of Tri-o-thymotide Clathrates		
Clathrate	Space Group	Reference
TOT / (R)(S)-2-Bromobutane	$P3_121$	108
TOT / (S)-2-Bromobutane	"	109,110
TOT / (R)-2-Butanol	"	111
TOT / Chlorocyclohexane	"	112
TOT / (RR)-trans-2,3-Epoxybutane	"	110
TOT / (RR)(SS)-2,3-Dimethylthiirane	"	110
TOT / (RR)-2,3-Dimethylthiirane	"	109
TOT / (SS)-2,3-Dimethylthiirane	"	110
TOT / Ethanol	"	113
TOT / (R)(S)-Ethyl methyl sulfoxide	"	114
TOT / 3-Buten-2-ol	"	115
TOT / Pyridine	"	116
TOT / n-Cetyl alcohol	$P6_1$	113
TOT / Benzene ^a	$P1$	117
TOT / cis-Stilbene	"	118
TOT / trans- Stilbene	"	118
Unsolvated TOT	$Pna2_1$	113
a: TOT / Benzene is also known to exist in the $P3_121$ space group ¹⁰⁴ however a complete crystal structure determination has not been carried out.		

resonances for the host structure in the NMR spectra of solid TOT clathrates.¹²¹

Presently, more than 100 TOT clathrates have been found, in fact it is difficult to find a small molecule that will not form a TOT clathrate. The structure of the clathrates depends on the nature of the guest material. Chain-like molecules whose length exceeds $\sim 9.5 \text{ \AA}$ form exclusively channel type clathrates while smaller molecules (overall length $< 9.5 \text{ \AA}$) usually form cage type clathrates. There are, however, a few examples of channel type inclusion compounds with guest molecules whose overall length is less than $9.5 \text{ \AA}$.^{117,118} These cases are the exceptions rather than the rule.

The TOT cage type clathrates provide an interesting chemical system for the study of enclathrated molecules. The differences in the physical and chemical behaviour between the free and enclathrated guest can provide valuable information about host-guest interactions. X-ray crystallography has provided a very detailed picture of the TOT host system. The unit cell constants for the $P3_121$ cage clathrates are typically: $a=b \sim 13 \text{ \AA}$, $c \sim 30 \text{ \AA}$ with 6 host molecules and 3 guest molecules per unit cell. The cages are bordered by 8 TOT molecules whose centres are separated by $\sim 13 \text{ \AA}$. Each cage contains only one guest molecule. The Van der Waals shape of the void space in TOT cage type clathrates has been described as a distorted ellipsoid with C_2 crystallographic symmetry.^{119,120} The short axis of the ellipsoid is typically $5.2 \text{ \AA}$ in length and lies parallel to the crystallographic c axis. The middle axis, typically $\sim 6.1 \text{ \AA}$ in length, is parallel to the crystallographic a axis and the long axis, $\sim 7.0 \text{ \AA}$, is in the a - b crystallographic plane. The inner cage

walls are lined mainly with the protons of the methyl and isopropyl groups of the TOT molecules. There are, however, two carbonyl oxygens at one end of the cage. Figure 14 shows representations of TOT cages. Without strong polar substituents lining the cage the forces holding the guest molecules inside must therefore be largely of the Van der Waals type with little if any hydrogen bonding effects. An exact crystallographic description of the guest molecules in the cages poses a serious problem as the guests are often disordered. The type of disorder can be either static, dynamic or a combination of both. Static disorder implies that the crystallographic coordinates of the guest molecules are dissimilar for guests in different cages, while dynamic disorder implies that the crystallographic coordinates of the guest molecule in each cage are functions of time. Since X-ray diffraction methods measure long-time averages and long-range order they sometimes fail to locate the guest entirely.^{108,122} In the absence of firm crystallographic data crystallographers often assume specific rigid guest conformations for use in crystal structure refinements.^{108,111,115} Without an adequate description of the guest molecules inside the cages from crystallography, one is forced to find alternative methods.

Infrared spectroscopy has been used in conjunction with X-ray diffraction measurements to study the TOT / chlorocyclohexane *P3₁21* cage clathrate. Chlorocyclohexane and similar molecules have been observed to exist in unusual disordered conformations in their TOT cage clathrates.¹¹² In solution, at room temperature, the axial and equatorial chair conformations of chlorocyclohexane are

in rapid equilibrium,¹²³ whereas, inside the TOT cage it is believed to take on both the axial chair and axial boat conformations in a 2:1 ratio. The authors suggested that the disorder exhibited by the chlorocyclohexane was static rather than dynamic. With the possibility of guest molecules adopting unusual conformations, one is led to wonder if this is a more general phenomenon.

Since each crystal of the cage clathrates is composed of only one of the two types of enantiomeric TOT propellers, the void spaces themselves must have the property of dissymmetry, i.e. the cages in each single crystal must have only one of the two possible enantiomeric shapes. With dissymmetric cages present, it is not surprising that the TOT cage clathrates exhibit chiral selectivity towards racemic guests. That is, a single crystal of a TOT clathrate, recrystallized from a racemic solvent, often contains more of one of the guest enantiomers than the other.^{105,106} This has been a subject of great interest.^{108-111,114,115,119,121,124-129} In such cases, if the TOT is recrystallized from the optically enriched chiral solvent, one of the two possible crystal types is formed in preference to the other.¹¹⁹ In the extreme case, where the clathrate is recrystallized from optically pure guest, the process affords optically pure TOT.^{110,119,121} Chiral selectivity has also been observed for some of the channel inclusion compounds,^{110,120,124} however, this occurs to a much lesser extent. The degree of chiral selectivity is usually expressed in terms of the enantiomeric excess (ee) where:

$$\% ee = 2(\% \text{ MAJOR ENANTIOMER}) - 100 \%$$

The magnitude of the enantiomeric excess has been observed to take on a range of values, from 83% to < 1%. It has been argued that chiral guest molecules with two-fold molecular symmetry axes exhibit higher enantiomeric excesses as they "fit better" into the two-fold symmetric chiral TOT cavities.^{110,119,124} Indeed such molecules seem to have high enantiomeric excesses but, molecules like the chiral 2-substituted butanes or methyl ethyl sulfoxide, which also exhibit large enantiomeric excesses, lack this symmetry and remain an anomaly. Table 2 gives a list of guest molecules with their measured enantiomeric excesses. Invertible chiral guest molecules with low thermal barriers to racemization have also been included as guests in TOT clathrates with significant enantiomeric excesses.^{110,120} It was found that the temperature required for racemization to occur was higher for the enclathrated guest compared to that of the free molecule. It was thought that the mobility of the TOT cage molecules at higher temperatures must lessen the extent of chiral recognition, supporting a "goodness of fit" model as the mechanism for chiral specificity.

The absolute configuration for each of the propellers of TOT was first assigned both in solution and in the solid state by circular dichroism measurements.¹⁰⁷ The *P* conformation was believed to represent the (-) enantiomer and the *M* configuration, the (+) enantiomer. These results were later disputed when both X-ray diffraction techniques and polarimetry were used in conjunction

TABLE 2

Enantiomeric Excesses of Guest Molecules in <i>P</i> (+) TOT Crystals			
Guest	Type	ee (%)	References
(<i>S</i>)-2-chlorobutane	cage	32,45,47	110,126,121,120
(<i>S</i>)-2-bromobutane	cage	34,35,37	110,121,124
2-iodobutane ^a	cage	<1	110,120,121
2-aminobutane ^a	cage	<2	126
(<i>S</i>)-2-butanol	cage	<5	120,126
(<i>SS</i>)- <i>trans</i> -2,3-epoxybutane	cage	47	110,120
(<i>SS</i>)- <i>trans</i> -2,3-dimethylthiirane	cage	30	110,120,124
<i>trans</i> -2,4-dimethyloxetane ^a	cage	38	110,120
<i>trans</i> -2,4-dimethylthietane ^a	cage	9	110,120
(<i>R</i>)-epoxypropane	cage	5	110,120,124
(<i>S</i>)-2-methyltetrahydrofuran	cage	2	110,120,124
(<i>R</i>)-methyl methanesulfinate	cage	14,15	110,120,124
1,2-dibromopropane ^a	cage	<2	119
2,3,3-trimethyloxaziridine ^a	cage	7	110,120
(<i>R</i>)-ethyl methyl sulfoxide	cage	83,40-50	114,126
(<i>R</i>)-3-buten-2-ol	cage	5	115,130
(<i>S</i>)-2-chlorooctane	channel	4	110,120,124
(<i>S</i>)-2-bromooctane	channel	4	110,120,124
(<i>S</i>)-2-bromononane	channel	5	110,120,124
(<i>S</i>)-2-bromododecane	channel	5	110,120,124
(<i>S</i>)-3-bromooctane	channel	4	110,120
a: Absolute configuration not established.			

to study the TOT / (*R*)-2-butanol clathrate.^{132,111} The diffraction results established the *M* conformation while the polarimetry experiment on the same crystal established it to be the (-) enantiomer. The latter assignment of absolute configuration has been supported by subsequent studies.^{109,110,120} The question, as to which of the TOT crystal forms (P-(+) or M-(-)) favours which of the guest enantiomers (*R* or *S*), has been addressed.^{110,119,120,124} The data show that there is a correlation of configuration for guests of similar shape. For example, for the 2-substituted butanes, the P-(+)-TOT / *S*-guest and M-(-)-TOT / *R*-guest combinations are the most favoured. This property can be used to assign the absolute configuration of guest molecules in a homologous series.

Although the "lock and key" or "goodness of fit" model is an attractive one, it would be an oversimplification to approach the problem of identifying the mechanism of chiral selectivity on the basis of molecular shape alone. A semi-empirical approach to this problem was undertaken.^{119,125,126} The energy of a system composed of a conformationally rigid chiral guest molecule, placed in a TOT cage of given handedness, was minimized with the use of a computer. The program¹³³⁻¹³⁵ allowed both the rigid guest and host molecules to undergo translations and rotations in order to minimize the overall crystal packing energy. This procedure was carried out for both enantiomers of the guest and the energies of each were compared. The calculations gave energy differences, ΔRS , between the two diastereomeric combinations of guest and host, which seemed qualitatively to support the experimental measurements of enantiomeric excesses.^{119,126} The

magnitude of the calculated energy differences, however, was an order of magnitude larger than that expected on the basis of thermodynamic considerations alone.

Solid state NMR has recently been demonstrated to be a useful tool to study chiral selectivity in TOT clathrates.^{121,127} The ^{13}C CP/MAS chemical shifts for some atoms of chiral guests were found to be different for the pairs of diastereomeric combinations of guest and host. In some cases the chemical shifts of the enclathrated guests were also considerably different than those of the free guest. The intensities of the guest resonances were used to evaluate the enantiomeric excesses for the 2-substituted butanes directly from high resolution spectra of polycrystalline samples. This was the first time that enantiomeric excesses for such materials could be evaluated for powdered samples containing both *P*(+) and *M*(-) crystals. These experiments also revealed that the favoured and unfavoured enantiomers had different degrees of molecular mobility. It was postulated that the differences in mobility may contribute to the degree of chiral selectivity. A broadline ^{19}F solid state NMR study was conducted on the TOT / halothane ($\text{CF}_3\text{-CHBrCl}$) clathrate.¹³⁶ The authors concluded that the $-\text{CF}_3$ groups of the halothane guest molecules were rapidly rotating at temperatures as low as 108 K and that additional molecular motion occurred at higher temperatures. This study did not permit any conclusions to be drawn regarding the effects of molecular motion on chiral discrimination.

Changes in chemical behaviour have been observed for some guest molecules inside TOT inclusion compounds compared to those of the free guests. The *PI*

channel inclusion compounds of stilbene and methyl cinnamate were used to study the effects of inclusion on photoisomerism.^{119,120} In solution equilibrium mixtures of the *cis* and *trans* isomers are easily established under the proper photochemical conditions. In the pure solid state neither of the conversions *cis*→*trans* nor *trans*→*cis* occurs for stilbene and only the *cis*→*trans* conversion occurs for methyl cinnamate. For the TOT/stilbene inclusion compounds, it was found that the *cis*→*trans* conversion but not the *trans*→*cis* conversion occurred and for the TOT/methyl cinnamate inclusion compounds both conversions occurred. The authors believe that the photo-conversions are controlled by the crystallographic symmetry of the system. In the case of the stilbene inclusion compounds the *trans* isomer is preferred because its symmetry matches that of the centrosymmetric crystallographic site. For the methyl cinnamate clathrates, the guests are disordered and both photo-conversions are able to occur easily.

The dissymmetric cages of the TOT clathrates provide an interesting environment in which chemical reactions may be carried out, with the possibility of chirality being transferred from the host cavities to the reaction products. This notion was adopted for the study of the photo reaction of *trans*-2-methoxy-2-butene with singlet oxygen ($^1\text{O}_2$).¹³⁷ In solution this reaction gives the racemic hydroperoxide, $\text{CH}_2=\text{CH}-\text{C}(\text{CH}_3)(\text{OCH}_3)(\text{OOH})$. The crystals of the $P3_121$ TOT / *trans*-2-methoxy-2-butene clathrate were hand sorted into P(+) and M(-). Each crystal was exposed to singlet oxygen separately, under the proper conditions, and it was found that the chirality of the host crystal had an influence on the reaction

product. The P(+) crystal gave more of the *R* product whereas the M(-) crystal gave more of the *S* product. Thus, it was demonstrated that the chirality of the clathrate cavity had an influence on which side of the SP_2 plane of the guest was attacked by the 1O_2 .

Along similar lines, reactions of TOT enclathrated epoxides with HCl and HBr have been investigated.^{115,127,130,138} In these cases, as with the previous example, the reactive gas can attack the guest molecule from either side of the molecular plane resulting in a chiral product whose configuration is dependant on the side of the molecule attacked. In solution, under acidic conditions, the product of the reaction between an epoxide and HX (X=Cl,Br) is a halohydrin. In some cases this product is also observed for the reaction of epoxides in their $P3_121$ TOT clathrates.^{130,138} A notable exception to this is the reaction of TOT / *cis*-2,3-epoxybutane with HBr gas. The reaction gives the TOT clathrate of chiral 3-buten-2-ol as the product, with an enantiomeric excess of ~ 5%. This again demonstrates that the chirality of the cavity can influence the chirality of the reaction product.

III. Problems to be Investigated.

The TOT clathrate systems are by no means well understood. Crystallographic data show that guest molecules are often disordered in the $P3_121$ TOT cages yet the disorder has not been identified as static or dynamic. The work presented in this thesis will establish that the type of disorder present for a variety of guest molecules is indeed dynamic. The molecular motions will be studied as a function of temperature and the mechanisms will be established where possible.

This work represents the first detailed study of the mobility of guest molecules inside TOT cage clathrates.

The chiral selectivity of the TOT cage clathrates has been studied extensively since the 1950's, but still it is not well understood. This problem will be addressed for the TOT cage clathrates of 2-bromobutane and 2-butanol. The molecular motion of both chiral and achiral guest molecules will be studied as a function of temperature. A novel NMR method for evaluating enantiomeric excesses in the solid state will be presented and used to help understand the processes responsible for the observed chiral selectivity.

The ability of solution NMR to distinguish between diastereomers has long been known. Chiral chemical shift reagents have been used to identify the enantiomers of a racemic pair and also to distinguish between the enantiotopic chemical groups on the same prochiral molecule.¹³⁹ The ability of TOT to behave as a "solid state chiral chemical shift reagent" will be investigated along with its ability to distinguish between the enantiotopic methyl groups of 2-propanol, 2-bromopropane, 2-chloropropane, *cis*-2,3-epoxybutane and dimethylsulfoxide.

The chemical reactions of TOT enclathrated guest molecules have provided intriguing examples of the ability of a host system to alter the chemical behaviour of its guest. Such chemical reactions will be followed for the first time in the solid state using ¹³C CP/MAS NMR. Specifically, the reactions of TOT enclathrated prochiral epoxides with HBr gas will be investigated. The ability of the host system to impart its chirality on the reaction products will be examined.

The conformationally flexible molecules which have been found to adopt unusual conformations in TOT cages show directly the effects of the constrained environment on the guest molecule. The TOT chlorocyclohexane clathrate was examined using ^{13}C CP/MAS NMR as a function of temperature. The chemical shift of the carbon atoms of the guest will be compared to those of the free molecule. These observations will be used with hopes of gaining more information regarding the conformation and dynamic state of the guest molecule.

It is hoped that the experiments presented herein will help improve the state of knowledge regarding the behaviour of guest molecules in clathrate systems as well as provide a link between the dynamic state of molecules and molecular recognition.

Enantiomeric Molecules

Figure 13: Molecular structure of tri-*o*-thymotide showing both the *P* and *M* propeller conformations.

Enantiomeric Cages

Figure 14: Representation of the enantiomeric $P3_121$ TOT clathrate cages. Each cage is composed of eight TOT molecules of the same absolute configuration.

CHAPTER THREE

Synthesis, Sample Preparation and NMR Experiments

The purpose of this chapter is to describe the preparation of the materials used throughout this work and also to describe the NMR experiments conducted.

I. Syntheses

I.1. Preparation of *o*-Thymotic Acid

o-Thymotic acid was prepared from thymol as described by Spallino and Provenzal.¹⁴⁰

Thymol (50 g, 0.33 mol) was dissolved in 300 mL of xylenes contained in a 1 L, three necked round bottom flask, initially equipped with a reflux condenser and two stoppers. The mixture was heated to reflux in order to dissolve all of the thymol. One of the stoppers was replaced by a gas inlet tube which allowed a continuous flow of $\text{CO}_2(\text{g})$ to be introduced into the solution over the course of the reaction. The CO_2 was generated by the evaporation of dry ice. Sodium metal (15 g, 0.65

mol.) was added into the third neck of the flask, over a five hour period. This gave an abundant white precipitate, presumed to be the sodium salt of *o*-thymotic acid. A constant reflux and a continuous flow of $\text{CO}_2(\text{g})$ were maintained over the course of the reaction and were allowed to continue for three hours after the addition of the sodium metal was complete. The refluxing was stopped and the mixture allowed to cool under a atmosphere of CO_2 . Cautiously, water was added dropwise to the mixture to react with any remaining sodium. When this was complete, enough water was added to dissolve the sodium salt giving a mixture consisting of two layers. The mixture was separated in a separating funnel and the aqueous layer was added to 500 mL of 1 M HCl giving *o*-thymotic acid as an abundant white precipitate. The yield was 34 g (53 %). During the course of this work, *o*-thymotic acid became commercially available from the Aldrich Chemical Company and was purchased thereafter.

1.2. Preparation of Tri-*o*-thymotide (TOT)

Tri-*o*-thymotide was prepared from *o*-thymotic acid as described by Baker, Gilbert and Ollis.¹⁴¹

o-Thymotic acid (20 g, 0.10 mol) was dissolved in 110 mL of xylenes in a round bottom flask. Phosphorus oxychloride, POCl_3 (9.5 mL, 0.10 mol) was then added. The flask was fitted with a reflux condenser topped with a CaCl_2 drying tube. The mixture was heated for 20 hours at 95-105°C then allowed to cool. Water (~100 mL) was added and the mixture was again allowed to cool. The xylene layer was separated from the aqueous layer and allowed to stand for two days, after which a white solid began to crystallize from the solution. The mixture was cooled in an ice bath and suction filtered. The crude solid was recrystallized twice from acetone yielding 1.4 g of the TOT / acetone 2:1 clathrate (7.5 % yield). The purity of this product was tested by ^{13}C CP/MAS NMR (figure 15). The spectrum showed no impurities. Guest free TOT was obtained by heating the acetone clathrate in an oven at 150°C for 48 hours. The ^{13}C CP/MAS NMR spectrum was obtained for this material (figure 16) to ensure that all of the acetone was removed.

1.3. Preparation of (*R*)(*S*)-2-Butanol-(1,1,1- d_3)

Racemic 2-butanol-(1,1,1- d_3) was prepared via Grignard reaction from propanal and deuterium labelled methyl magnesium iodide.

A 1 L, three necked round bottom flask was thoroughly dried in an oven and equipped with a septum, an addition funnel and a reflux condenser topped with a CaCl_2 drying tube. A commercially available ethereal solution of $\text{CD}_3\text{-MgI}$ (Aldrich, 300 mL, 1.0 M) was introduced into the flask through the septum via a flexible stainless steel transfer line (see figure 17). The flask was cooled in an ice bath. Redistilled propanal (17.5 mL, 0.24 mol) was added slowly to the Grignard reagent through the dropping funnel over a one hour period producing a grey precipitate. The mixture was allowed to reflux from the heat generated by the reaction. The rate of reflux was controlled with the ice bath. After the addition was complete the mixture was allowed to stand for two hours. Sufficient 10 % H_2SO_4 (~150 mL) was added very slowly over a thirty minute period dissolving all of the precipitate. The resulting ethereal and aqueous layers were separated. The aqueous layer was washed several times with ether and all of the ethereal extracts were combined and dried with Na_2SO_4 . The ether was removed by flash distillation leaving ~10 mL of a red coloured liquid. This liquid was distilled giving a colourless liquid, b.p. 90-100°C (8 mL, 35 % yield) and leaving a high boiling sticky brown-black residue. The colourless liquid was examined with high resolution ^1H and ^{13}C NMR. These spectra were compared to those of pure 2-butanol. The NMR analysis confirmed

that the sample was very pure and labelled, quantitatively, with ^2H on the C1 position.

I.4. Preparation of (*R*)(*S*)-2-Bromobutane-(1,1,1- d_3)

Racemic 2-bromobutane-(1,1,1- d_3) was prepared by the action of PBr_3 on 2-butanol-(1,1,1- d_3).^{142,143}

2-Butanol-(1,1,1- d_3) (2.5 g, 0.032 mol) was placed in a test tube and was cooled in an ice bath for 15 minutes. PBr_3 (2 mL, 0.021 mol) was added slowly over a ten minute period. The test tube was fitted with a CaCl_2 drying tube and allowed to stand in the ice bath for ~30 minutes. It was then taken out and allowed to stand for ~24 hours. Water (~7 mL) was carefully added over a period of about ten minutes. The mixture was allowed to cool and the organic and aqueous layers separated with a separatory funnel. The organic layer was dried with Na_2SO_4 yielding a colourless liquid (~1.5 mL, ~42 % yield). The liquid was examined with high resolution ^1H NMR spectroscopy and the spectrum was compared to that of pure 2-bromobutane. The NMR analysis confirmed that the sample was indeed 2-bromobutane of very high chemical purity. The fraction of ^2H on the C1 position was determined to be 65 % based on the integration of resonances in the ^1H NMR spectrum.

I.5. Preparation of (*R*)(*S*)-2-Butanol-(2- d_1)

Racemic 2-butanol-(2-d₁) was prepared via the reduction of 2-butanone with LiAlD₄.

LiAlD₄ (2 g, 0.048 mol) was added to 50 mL of dry ether in a three necked 250 mL round bottom flask equipped similarly to the one shown in figure 17, with the septum replaced by a stopper. 2-Butanone (16 mL, 0.18 mol) was dissolved in 50 mL of dry ether and added to the reducing agent via the addition funnel at such a rate that the ether refluxed gently. After the addition was complete the reaction mixture was allowed to stand for an additional hour. Water (50 mL) was added carefully through the dropping funnel to the reaction mixture. Sufficient 6 M HCl was then added to dissolve the solid. The ethereal and aqueous layers were separated and the aqueous layer was washed several times with ether. All of the ethereal extracts were combined and dried with Na₂SO₄. The ether was removed by flash distillation leaving a colourless liquid which in turn was fractionally distilled. Some unreacted 2-butanone was recovered (b.p. ~78°C). The fraction boiling between 90 and 100°C was collected (~5 mL, 30 % yield). A high resolution ¹H NMR spectrum was obtained for this liquid and indicated that it was indeed 2-butanol-(2-d₁) (no unlabelled 2-butanol was detected) contaminated with ~15 % 2-butanone. No further attempts were made to purify the sample. It was used as a starting material in the preparation of 2-bromobutane-(2-d₁).

I.6. Preparation of (*R*)(*S*)-2-bromobutane-(2-d₁)

The impure 2-butanol-(2-d₁) obtained from section I.5. above was converted to 2-bromobutane-(2-d₁) by the method described in section I.4..

A ¹H NMR analysis of the isolated product revealed it to be free of 2-butanone. The extent of deuteration on the C2 position was determined to be 92 % based on the integration of resonances in the spectrum.

I.7. Preparation of (*R*)(*S*)-2-Butanol-OD

2-Butanol (15 mL, 0.16 mol) was added to 20 mL D₂O (1.0 mol) in a 100 mL round bottom flask equipped with a reflux condenser. The mixture was refluxed for four hours, to facilitate H/D exchange, and allowed to cool. Ether (25 mL) was added to the cool mixture, with shaking, and the aqueous and ethereal layers were separated. The aqueous layer was washed several more times with ether and all of the ethereal extracts were combined. The ether was removed by flash distillation, leaving the labelled alcohol. The extent of deuteration on the hydroxyl group is expected to be 93 % based on a complete statistical exchange. This, however, was not tested.

I.8. Preparation of 2-Bromopropane-(1,3-d₆)

2-Bromopropane was prepared from 2-propanol-(1,3-d₆) (MSD isotopes) by the method described in I.4.

The reaction product was examined by high resolution ¹H NMR spectroscopy. The sample was very pure and the extent of deuteration on the C1 and C3 positions was determined to be 91 %.

I.9. Preparation of HBr Gas

Hydrogen Bromide gas was prepared by the bromination reaction of tetrahydronaphthalene.¹⁴⁴

Tetrahydronaphthalene (~100 mL) was placed in a standard 250 mL suction flask fitted with an addition funnel charged with Br₂. The side arm of the flask was fitted with rubber tubing which, on the other end, was attached to a glass tube. The glass tube was fitted through a rubber stopper which in turn topped a second suction flask filled with more tetrahydronaphthalene. The glass tube was positioned near the bottom of the second flask well below the surface of the liquid. Rubber tubing attached to the side arm of the second flask acted as a vent for the HBr gas while Br₂ was being added via the addition funnel. The purpose of the second flask was

to ensure that the gas produced was free of gaseous bromine. It was found that a steady flow of HBr could be produced for several hours with the slow dropwise addition of ~100 mL of Br₂.

All other reagents used as guest materials in this work were purchased and used without further purification.

II. Preparation of Clathrates

Many TOT clathrates were prepared throughout the course of this work. Many of these were prepared by the same method under the same conditions. It would, therefore, be redundant to describe, in detail, the preparation of each one. Instead, all of the clathrates are listed in table 3 along with a reference to one or more of the following sections which provide a general description of the preparation. All of the clathrates were prepared from guest free TOT.

II.1. - TOT (200-500 mg) was mixed with the pure liquid guest material. The mixture was heated to a boil and more guest was added until all of the TOT was dissolved. The solution was allowed to cool slowly to room temperature allowing some of the clathrate to crystallize. The mixture was then cooled in an ice bath and the clathrate collected by suction filtration. In some cases the mother liquor was allowed to evaporate leaving more of the clathrate.

II.2. - TOT (200-500 mg) was mixed with a small amount of the pure liquid guest (typically 2-5 mL) in an appropriately sized glass vial. The mixture was heated to the boiling point with a heat gun and briefly allowed to settle. The hot supernatant solution was removed with a Pasteur pipette and placed in another vial where it was

Table 3

CLATHRATE	REFERENCE
TOT / Acetone	II.1.
TOT / Acetone-(d ₆)	II.2.
TOT / Acetone-(2- ¹³ C)	II.3.
TOT / Benzene	II.4., II.5.
TOT / Benzene-(d ₆)	II.2., II.5.
TOT / (R)(S)-2-Butanol	II.4.
TOT / (R)(S)-2-Butanol-(1,1,1-d ₃)	II.2.
TOT / (R)(S)-2-Butanol-(OD)	II.2.
TOT / (S)-2-Butanol	II.2.
TOT / (R)-2-Butanol ^a	II.2, II.6
TOT / (R)(S)-2-Bromobutane	II.1.
TOT / (R)(S)-2-Bromobutane-(1,1,1-d ₃)	II.2., II.5.
TOT / (R)(S)-2-Bromobutane-(2-d)	II.2.
TOT / 2-Bromopropane	II.4.
TOT / 2-Bromopropane-(1,3-d ₆)	II.2.
TOT / Chlorocyclohexane	II.4.
TOT / 2-Chloropropane	II.4.
TOT / Cyclohexene oxide	II.4.
TOT / Dimethylsulfoxide	II.4.
TOT / Dimethylsulfoxide-(d ₆)	II.2.
TOT / <i>cis</i> -2,3-epoxybutane	II.2.
TOT / <i>trans</i> -2,3-epoxybutane	II.2.
TOT / 2-Propanol	II.1.
TOT / 2-Propanol-(1,3-d ₆)	II.7.
TOT / Pyridine	II.4.
TOT / Pyridine-(d ₅)	II.2.

a: One of these samples was prepared from TOT enriched in one of the enantiomers. See chapter four for details.

allowed to cool and crystallize. In some cases the vial was placed in an ice bath. The cooled supernatant solution was removed from the second vial with a Pasteur pipette and placed back in the original one. This process was repeated (typically 5-15 times) until all of the guest free TOT had been dissolved and recrystallized. In some cases the remaining solution was allowed to evaporate leaving more of the clathrate.

II.3. - TOT / acetone-(2-¹³C) was prepared from guest free TOT and ¹³C enriched acetone as in II.2. The guest was prepared by mixing 0.5 g of acetone-(2-¹³C) (M.S.D. isotopes) with 4.5 mL of unlabelled acetone (12 mol % isotopic purity).

II.4. - TOT (200-500 mg) was dissolved in a minimum of hot guest material. The solution was placed in a petri dish where it was allowed to evaporate leaving the powdered clathrate as a residue.

II.5. - Single crystals of clathrates were grown by dissolving the guest free TOT (50-100 mg) in a minimum amount of pure liquid guest at 90-95°C in a test tube. The test tube was immersed in a dewar of water at 90-95°C (see figure 18). The dewar was allowed to stand undisturbed for several days and then placed in a refrigerator for several more days. When removed from the refrigerator, the mixture in the test tube was filtered leaving large single crystals (typically 0.5-3 mm on edge).

II.6. - TOT (200-500 mg) was mixed with the pure liquid guest material. The mixture was heated to a boil and more guest was added until all of the TOT was dissolved. The solution was allowed to cool slowly to room temperature using the

apparatus shown in figure 18. The mixture was then allowed to evaporate slowly over a five week period.

II.7. - TOT (~300 mg) and 2-propanol-(1,3-d₆) (2.5 g) were added to a specially made heavy walled glass tube (~8 mm O.D. and ~100 mm in length). The tube was connected to a vacuum line. The contents were frozen with liquid nitrogen and the tube evacuated. Two more freeze-pump-thaw cycles were carried out and the tube was then sealed with a torch with the contents frozen, and evacuated. The tube was allowed to warm to room temperature and then it was placed in an oven at ~100°C 19 days. After being removed from the oven the contents were allowed to cool to room temperature. They were then frozen with liquid nitrogen and the tube was opened. After thawing, the mixture was placed in a petri dish where the excess guest was allowed to evaporate, leaving the clathrate.

III. NMR Experiments.

III.1. Solid State ¹³C CP/MAS NMR Experiments.

Unless otherwise stated, all of the ¹³C CP/MAS NMR spectra were run at 45.3 MHz on a Bruker CXP 180 pulse NMR spectrometer using a double tuned probe (¹³C and ¹H) from Doty scientific. The magic angle spinning assembly in this probe is of the double bearing type and accepts rotors of 7 mm in diameter. The rotors used were composed of sapphire tubes with press-fit Kel-F® top and bottom caps. The fluted top cap of the rotor was driven with 20-40 p.s.i. of compressed air. This allowed typical spinning rates of 3.5 - 5 kHz. The spinning rate was monitored with a device able to pick up the frequency of the rotor by way of an antenna placed

near the spinner assembly. On occasion the spinning rate was measured directly from the spinning sidebands in the NMR spectrum. The magic angle was coarsely set by using a standard sample of hexamethylbenzene which gives a symmetric aromatic resonance when the angle is properly set and an asymmetric resonance otherwise. The angle was set more accurately using a sample of the TOT / acetone clathrate. The angle was adjusted to give the sharpest aromatic and carbonyl resonances (usually 10-15 Hz). The probe was also equipped with a variable temperature accessory consisting of an internal thermocouple, an internal electric heater and an external temperature control unit. The experiments were conducted by driving the spinner with cold N_2 gas (for temperatures below room temperature) or room temperature air (for temperatures above room temperature). The driving gas was heated in the probe via the electric heater whose current was controlled by the temperature control unit. Samples were allowed to equilibrate for at least 5 minutes between temperature changes. The temperatures could be maintained to within 1 K and were read directly from the variable temperature control unit.

When the observation of spinning sidebands was important, the conventional cross polarization pulse sequence was used with a single contact. The pulse sequence included a phase cycling routine to eliminate determinate errors in the spectrum. The 90° pulses used were typically 3-4 μsec . When sidebands were a problem the conventional cross polarization sequence was modified using the pulse sequence of Hemminga and de Jager.⁸⁰ This sequence contains two additional 180° carbon pulses and two additional delays which depend on the sample spinning rate.

This experiment effectively eliminates the first order spinning sidebands and inverts the second order ones. Both of these pulse sequences were used on occasion with the dipolar dephasing technique described in chapter one. For most of the spectra reported herein 3-4 k data points were collected with a sweep width of 20 kHz. The free induction decays were typically zero filled to 16 k prior to Fourier transformation. Unless otherwise stated, the data was not subject to any broadening or resolution enhancement procedures.

III.2. Solid State ^2H NMR Spectra of powders

Unless otherwise stated all of the ^2H NMR spectra collected on powdered samples was done so on the Bruker CXP 180 NMR spectrometer described above at 27.6 MHz. The probe used was of the horizontal solenoid type with a silver coil able to accommodate short tubes of 10 mm in diameter. This probe contained an internal electric heater surrounded by a dewared glass tube and an internal thermocouple placed just below the sample coil. In carrying out variable temperature experiments, the current of the internal heater was controlled by a Bruker temperature control unit. Cold N_2 gas was passed over the heater and directed at the sample. The pressure required was typically less than 5 p.s.i. For spectra acquired at temperatures >298 K, room temperature air was used instead of cold N_2 gas. The samples were allowed to equilibrate for at least 5 minutes between temperature changes. The temperature of the sample was measured immediately after the collection of data by lowering a thermocouple down the top

of the magnet, into the probe and positioning it directly on the sample tube. These temperature are thought to be good to within 1°.

In all cases the quadrupolar echo pulse sequence, with phase cycling, was used to record the spectra. The 90° pulses were typically 3 μ sec and the echo delays were typically 35 μ sec. The second delay was always made at least 2 μ sec shorter than the first. Doing this allowed precise location of the echo maximum. The number of points collected and the sweep width depended on the nature of the spectrum. All data points before the top of the echo were eliminated. The echo decays were typically zero-filled to 4 - 8 k points and multiplied by an exponential function before Fourier transformation. The exponential multiplication served to broaden the transformed spectrum and artificially enhance the signal / noise ratio. The broadening was never chosen such that any spectral features would be significantly distorted. Another means used to enhance the signal / noise ratio, was to reverse the transformed spectrum and add it to the original spectrum. This was only done when the spectrum was very close to being symmetric about the centre. Measurements of spin lattice relaxation times were carried out by the inversion recovery technique, described in chapter one, using the quadrupolar echo pulse sequence to measure the partially relaxed spectrum.

III.3. ^2H NMR Spectra of Single Crystals

All of the ^2H NMR spectra reported herein were obtained on a Bruker MSL 300 pulse NMR spectrometer operating at 46 MHz. The probe was of the horizontal solenoid type. The coil, wound from copper wire accommodated short

tubes of 5 mm in diameter. The portion of the tube not in the coil was inserted into a hole, bored in the centre of a gear which, in turn, was part of a single axis goniometer. The tube could be rotated about the axis of the coil by way of a second gear affixed to a rod extending to the bottom of the NMR probe. The ratio of the gears was such that 400 revolutions of the adjustment rod was equivalent to a 360 degree rotation of the sample tube. The number of turns could be read by a rotary scale attached to the adjustment rod. The error in angle over the course of a full rotation was deemed to be less than 1 degree. This was tested with a single crystal of the TOT / 2-bromobutane-(1,1,1-d₃) clathrate which gave an identical NMR spectrum before and after the adjustment rod was turned 400 times.

The quadrupolar echo pulse sequence described previously was used to acquire the single crystal NMR spectra. The echo delays were set equal to one another. 1 k data points were collected and the echo delay was multiplied by an exponential function. The signal was zero filled to 8 k points prior to Fourier transformation. The transformed spectra were symmetrized as described above to increase the signal / noise ratio.

Figure 15: 45.3 MHz ^{13}C CP/MAS NMR spectrum of TOT / acetone. A: Alkyl region. B: Aromatic / carbonyl region. C: Full spectrum. The spectrum was obtained using a pulse sequence to suppress first order spinning sidebands.⁸⁰ The repetition time was 2 seconds and the contact time was 3 msec. The resonances due to the acetone are at 206.6 and 30.1 ppm from externally referenced TMS.

2

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Figure 16: 45.3 MHz ^{13}C CP/MAS NMR spectrum of the oven dried TOT / Acetone clathrate. The sample was dried at 150 °C for 48 hours. The spectrum was obtained using a pulse sequence to suppress first order spinning sidebands.⁸⁰ The repetition time was 1 second and the contact time was 3 msec. Note the absence of acetone.

Figure 17: A schematic representation of the apparatus used for the preparation of 2-butanol-(1,1,1-d³). See text for details.

Figure 18: A schematic representation of the apparatus used to grow large single crystals of TOT clathrates.

CHAPTER FOUR

Chiral Selectivity: TOT / 2-Bromobutane and TOT / 2-Butanol

The purpose of this chapter is to present and discuss the data collected for the TOT / 2-bromobutane and TOT / 2-butanol clathrates. Despite the similarity between the guest molecules and the host lattice, it has been reported that the enantiomeric excess of TOT enclathrated 2-bromobutane is ~7 times that of 2-butanol.¹¹⁹ The reasons for this are not clear. The preparations of 2-bromobutane-(1,1,1-d₃), 2-bromobutane-(2-d₁), 2-butanol-(1,1,1-d₃) and 2-butanol-(OD) are described in chapter three along with the preparation of their TOT clathrates. First, ¹³C CP/MAS NMR data will be used to examine the chiral selectivity of the TOT host towards the chiral guest. Solid state ²H NMR data collected for powdered samples of TOT / 2-bromobutane-(1,1,1-d₃), TOT / 2-bromobutane-(2-d₁), TOT / 2-butanol-(1,1,1-d₃) and TOT / 2-butanol-(OD) will be used to examine both, the chiral selectivity of the TOT host and the molecular motion of the guests. In the case of TOT / 2-bromobutane-(1,1,1-d₃) a ²H NMR single crystal study will be presented with an attempt at defining the orientation of the guest molecule inside the clathrate cage.

I. TOT / 2-Bromobutane

I.1. ¹³C CP/MAS Data

The X-ray crystal structure of *M*-TOT / (*R*)(*S*)-2-bromobutane, at 125 K has been published.¹⁰⁸ The 2:1 clathrate was found to be of the $P3_121$ cage type with one TOT molecule in the asymmetric unit and six TOT molecules in the unit cell. In solving this crystal structure, the authors calculated a minimum energy conformation for free (*R*)-2-bromobutane and used it as a rigid substructure in the refinement of the X-ray data. The (*S*) isomer could not be located experimentally and therefore an enantiomeric excess, based on the structural data, could not be reported. The 2-bromobutane was found to exhibit two-fold disorder, with the Br atom on the crystallographic two-fold axis.

Figure 19 shows the 45.3 MHz ^{13}C CP/MAS NMR spectrum of TOT / 2-bromobutane obtained using the conventional CP/MAS pulse sequence (19 A) and the pulse sequence described in reference 80 to suppress first order spinning sidebands (19 B). The most intense resonances are due to the TOT host. Each resonance of the host is split into three, with many of the triplets fully resolved (19 C, 19 D). Since there is only one TOT molecule in the asymmetric unit, the triplets cannot be due to crystallographically inequivalent molecules. Instead, they are due to the loss of three-fold molecular symmetry in the crystalline state. Each carbon atom in the TOT molecule is unique. The weaker resonances in the spectrum are due to the enclathrated 2-bromobutane, these are assigned in the figure. The C1 resonance is masked by the spectrum of the host. The C2 and C4 resonances are split into doublets. The C3 resonance appears slightly broader than the others and may in fact be an unresolved doublet as well. In order to account for the splitting,

one must consider all of the possible combinations of guest and host. These are shown below:

Of the four possible combinations, there are four pairs of diastereomorphs and two pairs of enantiomorphs. The enantiomorphs cannot be distinguished from one another in the NMR experiment, whereas, the diastereomorphs may give rise to separate spectra.¹³⁹

Consider first, a powder made by crushing a single crystal composed of only *P*-TOT molecules. This powder contains both (*R*) and (*S*) guest molecules. The *P*-(*R*) and *P*-(*S*) combinations are diastereomorphs and may give rise to different NMR spectra. Because of the overwhelming size difference between the clathrate cage and the guest molecule, the influence of the host on the environment of the guest is expected to be much greater than that of the guest on the host. One would, therefore, expect the resonance lines of the guest to be split to a much larger extent than those of the host. In the extreme case, where the guest has very little influence on the host, (as is the case with the isostructural *P*_{3,21} TOT clathrates) one would expect to see a large splitting of the guest resonances with no doubling of the host resonances at all. The components of the guest doublets represent the (*R*) and (*S*) isomers of the guest, respectively. These resonances can be integrated to determine the enantiomeric excess of the guest material. Now, consider a similar powder made

by crushing a crystal composed of only *M*-TOT molecules. This crystal is the enantiomer of the *P*-TOT crystal and its powder would therefore give an identical NMR spectrum to that of the *P*-TOT crystal. Since the powders of both crystals give the same NMR spectrum, then a polycrystalline powder, composed of both *P* and *M* crystals, would also give the same spectrum. Furthermore, the components of the guest doublets in the spectrum of the polycrystalline sample could be integrated to give the enantiomeric excess, eliminating the need to produce large single crystals. When interpreting the doubled resonances of the guest in polycrystalline TOT clathrates, one must refer to the *major* and *minor* enantiomers rather than (*R*) and (*S*) isomers since, for example, the resonance of the (*R*) isomer in the *M* crystal has the same chemical shift value as the (*S*) isomer in the *P* crystal.

In order to obtain a quantitatively reliable measurement of the enantiomeric excess from ^{13}C CP/MAS data, one must be sure that the spectrum itself is quantitatively reliable. All of the carbon resonances must be cross polarized to the same extent. This can be confirmed by examining the ^{13}C CP/MAS NMR spectrum as a function of the contact time specified by the pulse sequence. This experiment was carried out for the TOT / 2-bromobutane-(1,1,1- d_3) clathrate, which gives an identical ^{13}C NMR spectrum to that of the unlabelled clathrate. The data are plotted in figure 20. The slopes of the lines, which define the proton $T_{1\rho}$, are identical within experimental error. This indicates that all of the protons are highly coupled to a common lattice by the dipolar interaction. It can be seen from the data that a contact time of ≥ 4 msec is sufficient to obtain a quantitative spectrum.

The enantiomeric excess was calculated from the ratio of the integrals of the doublet peaks at the intercept. It was found to be 16 ± 6 %, based on the C2 doublet and 16 ± 4 % based on the C4 doublet. The relatively large uncertainty in these values can be attributed to noise in the spectra. These values are lower than those reported previously.^{110,121,124} In the previous studies the samples used were produced by slow recrystallization under equilibrium conditions whereas the TOT / 2-bromobutane-(1,1,1-d₃) used in this experiment was produced by rapid recrystallization (see chapter 3 section II.2). This implies that the chiral selectivity may depend on the rate at which the clathrate is crystallized. Further experimentation, however, would be required in order to establish this.

In table 4, the chemical shifts of the carbon atoms of TOT enclathrated 2-bromobutane are compared to those measured in solution.¹⁴⁵ The chemical shifts, reported for the enclathrated 2-bromobutane, were externally referenced to the methyl resonance of solid hexamethyl benzene, which was assigned a chemical shift of 16.9 ppm relative to TMS at 0 ppm. One can see that the chemical shifts of both the major and minor enantiomers of the enclathrated guest not only differ from one another but, differ significantly from those measured in solution. From the data, one can conclude first, that the electronic shielding is different for the major and minor enclathrated enantiomers and second, that the shielding of the enclathrated guests is different from that of the molecule in solution. It is not unusual for the molecules of solids to have different chemical shifts than those in the liquid state or in solution. The differences are usually attributed to the changes in molecular

geometry imposed by the crystal packing forces of the solid. This reason may also account for the chemical shift difference between the favoured and unfavoured enantiomers in the solid clathrate. That is, the favoured and unfavoured enantiomers may experience different crystal packing forces and have different average geometries in the same host lattice. In order to test this idea, some minimum energy calculations were performed to obtain the most favourable molecular geometry for each enantiomer of the 2-bromobutane in a fixed TOT clathrate cage of given handedness. These geometries were compared to those calculated for the free molecule.

Table 4

¹³ C Chemical Shifts for 2-bromobutane (ppm from TMS)			
Carbon	Clathrate	Solution	Δ
C1	-	26.0	-
C2 major	59.0	53.1	5.9
C2 minor	60.7	-	7.6
C3	33.5	34.2	-0.7
C4 major	13.3	12.1	1.2
C4 minor	11.4	-	-0.7

The calculations were conducted with a commercially available molecular graphics program,¹⁴⁶ able to perform molecular mechanics calculations. The molecular mechanics strategy¹⁴⁷⁻¹⁶⁴ is an empirical one, designed to find a molecular geometry, where the difference in energy between the calculated geometry and an "ideal" one is a minimum. In order to do this the program employs a reference

table, containing typical bond lengths, bond angles, torsion angles, force constants, van der Waals radii and other details for a large number of bonding situations. The table, referred to as a force field, is based on a large body of previously collected data. A molecule is first presented to the program with an initial set of coordinates. The difference in energy, E , between the input molecule and one of "ideal" geometry is then calculated from the following equation:

$$E = E_{str} + E_{bend} + E_{oop} + E_{tors} + E_{vdw} + E_{ele} \quad (68)$$

E_{str} is the bond stretching energy; E_{bend} , the bending energy; E_{oop} , the out of plane distortion energy; E_{tors} , the torsional energy; E_{vdw} , the van der Waals energy and E_{ele} , the electronic energy. The individual energy terms are defined in appendix 2. The positional coordinates of all of the atoms are then varied and the energy recalculated. A derivative based minimization procedure is used to find a minimum on the energy surface. When a minimum is reached the new coordinates of the molecule are then given as output and displayed graphically. The fundamental problem with this procedure is that it is impossible to distinguish between a local and a global energy minimum. In order to find the global energy minimum, one must repeat the calculation for many, quite different, starting geometries and then compare the calculated minimum energies upon convergence. Even when this approach is taken, however, there is still a chance that the minimum energy found is local rather than global. The success of the strategy depends on the complexity of the energy surface. One way to gain confidence in finding a global, rather than a local minimum, is to start with crystallographic coordinates as input.

The energy of the free 2-bromobutane molecule was minimized using an input geometry where the C1-C2-C3-C4 torsion angle was 180°. As expected, the same energy minimum was reached for both the (*R*) and (*S*) free molecules. The calculation of the minimum energy for the favoured enclathrated enantiomer was conducted, first, by inputting the crystallographic coordinates for the *M*-TOT / (*R*)-2-bromobutane clathrate. The space group symmetry elements were used to generate several unit cells. From the unit cells, the eight molecules bordering a cage were picked out. This was accomplished by determining the mean distances of the host molecules from the guest and choosing the eight closest host molecules. All molecules, other than the eight cage molecules and a single guest, were ignored. The coordinates of the atoms comprising the cage molecules were held constant throughout the entire calculation. The energy of the system was then minimized, allowing only the coordinates of the flexible (*R*)-2-bromobutane to change. The same calculation was carried out for the *M*-TOT / (*S*)-2-bromobutane clathrate. Several starting geometries of the guest molecule were tried, with the Br atom near the two-fold crystallographic axis. All gave the same minimum energy and optimized geometry. The difference in energy between the *M*-(*S*) and *M*-(*R*) combinations was found to be 0.538 kcal/mol. Based on a Boltzman ratio, this energy difference implies an enantiomeric excess of 42.5 % for a sample prepared under equilibrium conditions at 298 K. This value agrees reasonably well with those measured experimentally by others^{110,121,124} on samples prepared under equilibrium conditions. The good agreement between the calculated and measured enantiomeric excesses,

however, must be interpreted with caution, as only a single guest in a single cage was considered.

Table 5
Geometry Parameters for 2-Bromobutane

Angle or Torsion	Clathrate	Free	Δ
C1-C2-C3 major	112.5°	111.1°	1.4°
C1-C2-C3 minor	111.5°	"	0.4°
C2-C3-C4 major	111.3°	112.4°	-1.1°
C2-C3-C4 minor	112.3°	"	-0.1°
Br-C2-C1 major	108.3°	108.5°	-0.2°
Br-C2-C1 minor	108.9°	"	0.4°
Br-C2-C3 major	109.8°	110.8°	-1.0°
Br-C2-C3 minor	111.6°	"	0.8°
C1-C2-C3-C4 major	179.1°	175.6°	3.3°
C1-C2-C3-C4 minor	168.4°	"	7.4°
Br-C2-C3-C4 major	58.4°	63.7°	5.3°
Br-C2-C3-C4 minor	46.4°	"	17.3°

The geometry parameters resulting from the calculations are given in table 5. The data show that there are significant differences between the bond angles and torsion angles of the 2-bromobutane in each of the three different environments. These differences in molecular geometry imply that the electronic environment around the each of the three types of molecules is different. This may account for the chemical shift differences observed. The chemical shifts seem to be particularly

sensitive to the C1-C2-C3-C4 and Br-C2-C3-C4 torsion angles. The differences in bond angles appear to be minor in comparison.

I.2. Solid State ^2H NMR Data

I.2.1. Powder Data

Table 6

Parameters for the Simulated ^2H NMR Spectra of TOT / 2-Bromobutane-(1,1,1- d_3)						
Temperature (K)	Broad Component			Narrow Component		
	$\Delta\nu_{xx}$ (kHz)	$\Delta\nu_{yy}$ (kHz)	$\Delta\nu_{zz}$ (kHz)	$\Delta\nu_{xx}$ (kHz)	$\Delta\nu_{yy}$ (kHz)	$\Delta\nu_{zz}$ (kHz)
186	34.0	42.4	76.4	15.5	28.6	44.1
210	31.0	39.4	70.4	16.0	27.0	43.0
230	31.0	38.5	69.5	16.0	27.0	43.0
252	31.0	37.9	68.9	16.0	27.2	43.2
273	29.5	37.9	67.4	16.0	26.4	42.4
295	28.5	36.3	64.8	16.0	25.0	41.0
315	26.5	33.1	59.6	16.0	24.0	40.0
335	25.0	32.0	57.0	16.0	23.0	39.0
355	23.5	29.4	52.9	15.5	20.5	36.0

The broadline ^2H NMR spectrum of TOT / 2-bromobutane-(1,1,1- d_3) was measured as a function of temperature. The spectra are shown in figure 21. Note the difference in scale between the spectrum taken at 77 K and all of the others. Although the signal / noise ratio is poor, the spectrum at 77 K appears to show little if any axial asymmetry. The splitting of the inner singularities is 127 kHz which gives a quadrupolar coupling constant (e^2qQ/h) of 169 kHz. All of the other spectra are motionally narrowed and appear more complicated. They do not resemble the

lineshapes expected for single electric field gradient tensors. The spectra acquired at temperatures higher than 186 K could be well represented with sums of two fast motional lineshapes obtained by using the computer program described in appendix 1. Representative simulations are shown in figure 21. Table 6 gives the parameters of the simulations for each of the two components in each spectrum. These data are plotted in figure 22. The simulated spectra consist of two subspectra in the ratio 59:41. This ratio was found to be constant throughout the entire temperature range of the simulations. The fits were made by overlaying the experimental and simulated spectra. The uncertainty in each of the parameters of the simulation is estimated to be less than 1 kHz. If each of the subspectra is assigned to the favoured and unfavoured enantiomers, respectively, then the intensity ratio gives an enantiomeric excess of 18 %. This agrees well with that determined from the ^{13}C CP/MAS NMR data obtained on the same sample. The spectra acquired between 77 K and 186 K could not be represented by sums of fast motional lineshapes. This is expected if some sort of molecular motion is occurring at a rate comparable to the time scale of the experiment (10^{-5} - 10^{-6} sec).

The spectrum acquired at 77 K is typical of rigid C-D bonds. The C1 methyl groups of the guest are, therefore, unable to overcome the methyl rotational barrier at 77 K. At temperatures between 77 K and 186 K, the methyl groups begin to undergo rotation about their 3-fold axes at a rate comparable to the time scale of the experiment (10^{-5} - 10^{-6} sec). The spectra obtained at temperatures higher than 186 K exhibit large asymmetry parameters and are narrower than that expected for

simple fast methyl group rotation. For simple methyl group rotation, one would expect an axially symmetric spectrum with an inner splitting of 42 kHz. These higher temperature spectra can be accounted for, if the guest molecules undergo fast methyl group rotation as well as an additional anisotropic molecular libration. Librational processes are able to account for the continual change in the spectral parameters as a function of temperature, however, a precise description of the librations cannot be provided on the basis of this data alone. Since the components of each spectrum have significantly different lineshapes, one is able to conclude that the favoured and unfavoured enantiomers undergo significantly different molecular motions and must, therefore, be in very different chemical environments. Since the unfavoured enantiomer has a narrower spectrum than the favoured one at any temperature, one can make the additional conclusion that the C1 methyl group of the unfavoured enantiomer has a greater degree of molecular mobility. The C1 methyl group of the favoured enantiomer is held more rigidly, but still experiences some librational motion. These conclusions support those made previously, based on a dipolar dephased ^{13}C CP/MAS spectrum.¹²¹

A solid state ^2H NMR spectrum of the TOT / 2-bromobutane-(2- d_1) clathrate was obtained at room temperature and is shown in figure 23 A. The spectrum is not the simple powder pattern expected for rigid C-D bonds. It appears to be the sum of at least two component spectra, both of which are narrower than that expected for rigid C-D bonds. Based on the previous data, it is a reasonable assumption that the contributions are due to the favoured and unfavoured enantiomers. An attempt

was made at simulating this spectrum with the computer program described in appendix 1. The best fitting simulation is shown in figure 23 B. It was obtained by adding two subspectra whose parameters are given in the figure caption. The ratio of the broad component to the narrower component was 55:45. It is lower than the 59:41 ratio observed in the ^2H NMR data for the TOT / 2-bromobutane-(1,1,1- d_3) clathrate. Although the simulation mimics the general shape of the experimental spectrum, it is by no means a perfect fit. It contains outer shoulders which apparently are not present in the experimental spectrum and it also lacks some of the central intensity present in the experimental spectrum. There are at least four reasons which may account for the poor fit and the inconsistent ratio of subspectra.

First, the molecular motion responsible for narrowing of each component may not be in the fast motional régime. This could be tested by repeating the experiment as a function of the echo delay periods in the quadrupolar echo pulse sequence.²⁴⁻²⁷ This experiment, however, was not performed and would be rather time consuming, as the abundance of deuterium in the sample is very low.

Second, the spectrum may be distorted due to chemical shielding anisotropy effects, which become significant at higher magnetic field strengths (see chapter one). Chemical shielding anisotropy removes the bilateral symmetry from the powder spectrum and makes the symmetrization procedure, used here (and described in chapter three, section III.2.1), questionable. The spectrum in figure 23 A was obtained on the MSL-300 where these effects may arise.

Third, the spectrum may not be quantitative due to T_1 relaxation effects. In order to obtain a spectrum in a reasonable period of time, the quadrupolar echo sequence was repeated every 2 seconds. This may not have been enough time for the magnetization of the deuterons to fully relax. It is not uncommon for deuterons to have T_1 relaxation times of the order of tens of seconds. If this was the case the spectrum is not expected to be quantitative. A further complication may result if the T_1 relaxation times are not the same for all frequencies in the powder spectrum.³⁵ This effect would lead, not only to a quantitatively unreliable spectrum, but also to lineshape distortions.

Finally, the finite width of the r.f. pulses used in the quadrupolar echo experiment would lead to lineshape distortions. These distortions usually manifest themselves as diminished intensity in the shoulders of very broad spectra.

Despite the problems, one is able to conclude that the favoured enantiomer is less mobile than the unfavoured one. This is consistent with the previously presented data. The precise mechanism of the molecular motion for each enantiomer still cannot be deduced unambiguously.

1.2.2. Single Crystal Data

Although ^2H NMR powder spectra contain a great deal of information regarding the molecular motion of molecules, they contain no information regarding their orientation with respect to the magnetic field vector. As discussed in chapter one, the ^2H NMR spectrum of a single crystal, containing only one crystallographically unique ^2H species, will consist of a doublet, with a splitting

dependent on the orientation of the V_{zz} component of the electric field gradient tensor with respect to the magnetic field. When fast molecular motion occurs, such as the rotation of a $-CD_3$ group, it is the orientation of the V'_{zz} component of the *averaged* electric field gradient tensor which must be considered. If the unit cell of the crystal contains more than one molecule, then the spectrum will be a superposition of the spectra resulting from each of the constituent molecules in the unit cell.

Consider the magnetic field vector, B_0 , along the z' axis of an orthogonal axis system defined by x' , y' , and z' , and a crystal defined in a different orthogonal axis system defined by X , Y , and Z . If the crystal is aligned such that the Y axis is parallel to B_0 and then rotated about the X axis, the splitting in the spectrum, $\Delta\nu$, is given by:⁴

$$\Delta\nu_X = A_X + B_X \cos(2\theta_X) + C_X \sin(2\theta_X) \quad (69)$$

where θ_X is the rotation angle and A_X , B_X , and C_X are constants. Similar relationships exist when the crystal is lined up such that the Z and X axes are made parallel with B_0 and then rotated about the Y and Z axes, respectively. These relationships define the six additional constants, A_Y , B_Y , C_Y , A_Z , B_Z and C_Z . The constants are defined as follows:⁴

$$A_X = \frac{1}{2}K(\phi_{YY} + \phi_{ZZ}) - \frac{1}{2}K\phi_{XX} \quad (70)$$

$$B_x = \frac{1}{2}K(\phi_{yy} - \phi_{zz}) \quad (71)$$

$$C_x = -K\phi_{yz} \quad (72)$$

$$K = \frac{3eQ}{2h} \quad (73)$$

where ϕ_{ij} represent the components of the electric field gradient tensor in the XYZ crystal axis system. The other six constants are defined similarly by cyclic permutation. The six constants, A and B, are not independent. They are related as follows:

$$A_x + A_y + A_z = 0 \quad (74)$$

$$A_x + B_x = A_z - B_z \quad (75)$$

$$A_y + B_y = A_x - B_x \quad (76)$$

$$A_z + B_z = A_y - B_y \quad (77)$$

If the three mutually orthogonal rotations are carried out the nine constants, A, B and C, can be obtained by fitting the experimental spectral splittings to equation (69) and the tensor components, $K\phi_{ij}$, can then be determined from equations (70)-(72) and checked by equations (74)-(77). The diagonal elements are triply determined, then averaged. The off diagonal elements are determined only once. The tensor, $K\phi_{ij}$, can then be diagonalized. The eigenvalues are the $\Delta\nu_{xx}$, $\Delta\nu_{yy}$ and $\Delta\nu_{zz}$ splittings observed in the powder spectrum, the corresponding eigenvectors

describe the orientation of the XYZ crystal axis system in the principal axis system of the electric field gradient tensor, xyz . If the crystal axis system, XYZ , is chosen to coincide with one or more of the crystallographic axes, abc , and the orientation of the principal axis of the electric field gradient is known with respect to the molecule, then the orientation of the molecule with respect to the crystallographic axes can be deduced.

Since the available X-ray data are only able to define the coordinates of the favoured enantiomer of 2-bromobutane in its TOT clathrate, it was felt that a single crystal ^2H NMR study of TOT / 2-bromobutane-(1,1,1- d_3) would be worth while, in that the orientation of the unfavoured enantiomer inside the TOT cage could be determined. Two suitably large crystals (~1-2 mm on edge) were grown. The crystallographic c axis of each crystal was located with the use of X-rays. The crystals were mounted at the end of glass tubes of outside diameter ~4 mm. The first crystal was mounted such that the crystallographic c axis was parallel to the tube, and the second, such that the c axis was perpendicular to the tube. A crystal coordinate system, XYZ , was defined with the X axis parallel to the crystallographic c axis, the Y axis parallel to the axis of the tube containing the second crystal, and the Z axis orthogonal to the other two. The tubes were cut to a convenient length and inserted into standard 5 mm NMR tubes, whose bottoms had been previously cut off. The concentric tubes were glued into place. The tube containing the first crystal was inserted into the single crystal NMR probe described in chapter three and ^2H NMR spectra were recorded as a function of rotation angle, θ_x , at 5°

intervals over a 180° range. The tube containing the second crystal was then inserted into the probe such that the X axis was perpendicular to the magnetic field (this was done by eye) and ^2H NMR spectra were collected as a function of the rotation angle, θ_Y , at 5° intervals over a 180° range. A third specimen was obtained by cutting the tube containing the second crystal, rotating it 90° (by eye) about the X axis then mounting it on the end of another 5 mm NMR tube. This new tube was inserted into the probe such that the X axis was perpendicular to B_0 and the Y axis parallel to B_0 . ^2H NMR spectra were collected as a function of the rotation angle, θ_Z at 5° intervals over a 180° range.

Some typical spectra for arbitrary orientations are shown in figure 24. The ^2H NMR spectrum for any orientation is expected to contain six doublets, one for each of the three (R) guests in a unit cell and one for each of the three (S) guests in a unit cell. In general, the spectra were not sufficiently resolved to observe all six doublets. The line broadening is thought to be due to $^1\text{H} - ^2\text{H}$ dipolar interactions, which were not removed in the experiment. The spectra are, however, sufficiently resolved to observe the three doublets due to the major enantiomer. The resonances due to the minor enantiomer were often observed only as shoulders on the more intense peaks in the spectrum and it was not possible to follow them as a function of rotation angle.

The three plots of the spectral splittings, for the favoured enantiomer, as a function of rotation angle are shown in figure 25. The splittings are plotted with arbitrary sign. In any two of the three rotation patterns there is a pair of spectra,

one from each series, which are very nearly identical. This is expected, as there is always two identical orientations when comparing two series. This information was used to label each of the doublets and assign a common algebraic sign. The absolute values of the algebraic signs, however, are not known, as the two energy transitions cannot be distinguished from one another. The abscissas of the third and first rotation plots were shifted such that the 0° orientation of the first pattern matched the 90° orientation of the third, the 90° orientation of the first matched the 0° orientation of the second, and the 90° orientation of the second matched the 0° orientation of the third. With these initial orientations the equations, given above, can be used to obtain the magnitudes and directions of the components of the averaged electric field gradient tensor. The corrected rotation plots are given in figure 26.

A nonlinear least squares routine was used to fit all of the rotation patterns to equation (69), thus obtaining the 9 constants, A, B and C , for each of the three major enantiomers in a unit cell. Equations (70)-(77). were used to obtain the tensor components, $K\phi_{ij}$, in the XYZ axis system. These tensors were diagonalized to give the components in the principal axis system, xyz . The absolute values of the eigenvalues, for each molecule, S1, S2 and S3 in the unit cell, are given in table 7 and compared to the splittings in the powder spectrum at room temperature. The agreement is good to within ~ 3 kHz.

If one assumes that the largest component of the electric field gradient tensor lies approximately parallel to the C2-C1 bond, as would be the case for simple fast

Table 7

Principal Splittings for TOT / 2-Bromobutane-(1,1,1-d ₃) (kHz)				
	S1	S2	S3	Powder
$\Delta\nu_{xx}$	28.3	27.8	28.8	28.0
$\Delta\nu_{yy}$	36.8	38.2	37.8	35.5
$\Delta\nu_{zz}$	65.2	66.1	66.5	63.5

Table 8

Angle Between C2-C1 Bond and the Crystallographic <i>c</i> Axis			
	S1	S2	S3
² H NMR	-86.4°	-80.2°	101.4° (-79.6°)
X-ray	-82.5°	-82.5°	-82.5°

methyl group rotation, then the eigenvectors obtained from diagonalizing $K\phi_{ij}$ will give the orientation of this bond with respect to the XYZ axis system. Since the *c* axis of the crystal was parallel to the *X* axis the angles between the C2-C1 bond and the crystallographic *c* axis were calculated and compared to those from the published crystal structure (see table 8). The 101.4° angle obtained for S3 is equivalent to -79.6° since the +*c* axis was not distinguished from the -*c* axis. The angles agree with one another to within 4°. This difference can be accounted for by considering the possible sources of error. Experimental error may be as high as 10% since the second and third crystals were aligned by eye. Another source of error is present in the assumption that V'_{zz} lies parallel to the C2-C1 bond. This is only an approximation since the powder spectra indicated an anisotropic libration in addition

to fast methyl group rotation. This additional librational motion is expected to displace V'_{zz} away from the C2-C1 bond by an amount dependent on the amplitude of the anisotropic libration. Overall, however, the NMR data agree quite well with the X-ray data.

II. TOT / 2-Butanol

II.1. ^{13}C CP/MAS Data

The ^{13}C CP/MAS NMR spectra of TOT / 2-butanol and TOT / 2-butanol-(1,1,1- d_3) are shown in figure 27 A and 27 C, respectively. As before, the most intense resonances are due to the TOT host while the weaker ones are due to the guest. All of the resonances of the guest in figure 27 A are visible. The resonance of the C1 carbon in figure 27 B is not visible due to the ^{13}C - ^2H dipolar interaction. The only resolved doublet, in the resonances of the guest, is that of the C2 carbon. The chemical shift data for enclathrated and neat 2-butanol¹⁴⁵ are compared in table 9. The differences in chemical shift between the enclathrated and neat species are very small and may be due to small distortions resulting from crystal packing forces. These observations are contrary to those made for 2-bromobutane which showed large chemical shift differences between the enclathrated and solution state species. Based on the chemical shift data, it is reasonable to conclude that the conformation of each of the two enantiomers of 2-butanol in a cage of given handedness is very similar.

When a contact time of 3 msec is used in the cross polarization pulse sequence, the components of the C2 doublet appear to have approximately the same

Table 9

¹³ C Chemical Shifts for 2-butanol (ppm from TMS)			
Carbon	Clathrate	Solution	Δ
C1	23.4	22.6	0.8
C2	68.8	68.7	0.1
C2	68.2	"	-0.5
C3	32.2	32.0	0.2
C4	9.7	9.9	-0.2

intensities, suggesting that the enantiomeric excess is very low. Although this observation is in agreement with previous studies,^{110,111,121,126} it is not quantitatively reliable since the intensities of the resonances are expected to be a function of the contact time. The spectrum of TOT / 2-butanol-(1,1,1-d₃) was measured as a function of contact time with hopes of obtaining a quantitative evaluation of the enantiomeric excess. The results are shown in figure 28. The ratio of intensities of the C2 peaks did not appear to change very much as a function of cross polarization time and the lack of resolution and signal/noise prohibited the evaluation of a reliable enantiomeric excess.

In order to establish that TOT does indeed exhibit enantiomeric selectivity towards the enantiomers of 2-butanol a number of clathrates were prepared from the optically pure alcohols. A sample of TOT / (*R*)-2-butanol was prepared by slow recrystallization of guest free TOT. For such a sample only the *P*-(*R*) and *M*-(*R*) diastereomers are possible. The spectrum of the C2 resonance is given in figure 29 B. Only the downfield component of the doublet is present. Since it has been

shown that the *M*(-) TOT cages prefer the (*R*)-2-butanol enantiomer,^{111,132} this resonance must be due to the *M*-(*R*) combination. A similar sample of TOT / (*S*)-2-butanol was prepared by rapid recrystallization. For this sample only the *P*-(*S*) and *M*-(*S*) diastereomers are possible. The spectrum is given in figure 29 C. The C2 resonance consists of an asymmetric doublet. As was the case for the (*R*)-2-butanol clathrate, the downfield peak is dominant. Since the *P*(+) TOT cages prefer the (*S*) enantiomer, the downfield peak must be due to the *P*-(*S*) combination. Thus for the spectrum of the TOT / (*R*)(*S*)-2-butanol, shown in figure 29 A, The downfield peak must be due to the favoured combinations (*P*-(*S*) and *M*-(*R*)). These results are consistent with similar experiments performed on TOT / 2-bromobutane.¹²¹ The TOT / (*S*)-2-butanol clathrate was dried in an oven at 150° for 48 hours. The guest free material, containing a predominance of *P*(+) TOT molecules, was used to prepare the TOT / (*R*)-2-butanol clathrate by rapid recrystallization. If such a recrystallization is carried out fast enough, such that the dissolved TOT molecules do not have a chance to racemize, then the unfavoured combination, *P*-(*R*), should dominate. The spectrum is shown in figure 29 D. Indeed, in this spectrum, the unfavoured component of the doublet is dominant. These experiments demonstrate that TOT is chirally selective towards the enantiomers of 2-butanol and that the proportion of the unfavoured component can change depending on the method of sample preparation.

The ¹³C CP/MAS spectrum of TOT / 2-butanol-(1,1,1-d₃), acquired under dipolar dephasing conditions, is given in figure 30. The C2, C3 and C4 resonances

are all present, indicating that the static $^{13}\text{C}\text{-}^1\text{H}$ dipolar interactions must be averaged by a large scale molecular motion. Both enantiomers of the guest in any given cage must therefore be highly mobile. A solid state ^2H NMR study was carried out in order to obtain a more detailed view of the molecular motions.

II.2 Solid State ^2H NMR Data.

The Solid state ^2H NMR spectrum of TOT / 2-butanol-(1,1,1- d_3) was measured as a function of temperature. Representative spectra are shown in figure 31 A. The spectrum acquired at 77 K has a very low signal/noise ratio and could not be simulated using a fast motion or rigid model. This behaviour is expected if the C1 methyl group is rotating about its three-fold axis at a rate comparable to the frequency spread of the static spectrum (10^4 - 10^6 Hz). At 142 K the spectrum resembles a broadened out Pake doublet whose frequency separations are consistent with fast methyl group rotation. At temperatures above 161 K the spectra consist of two different overlapping powder patterns in a 60:40 intensity ratio. These spectra were simulated using the fast motional lineshape simulation program given in appendix 1. Representative simulations are given in figure 31 B. The spectral parameters are given in table 10 and plotted in figure 32. The errors in the parameters of the simulation are estimated to be less than 1 kHz.

The intensity ratio of the overlapping powder spectra indicates an enantiomeric excess of 20 %. The broader component is the most abundant indicating that the C1 methyl groups of the favoured enantiomer are held more rigidly than those of the unfavoured one. A precise description of the molecular

Table 10

Parameters for the Simulated ^2H NMR Spectra of TOT / 2-Butanol-
(1,1,1- d_3)

Temperature (K)	Narrow Component			Broad Component		
	$\Delta\nu_{xx}$ (kHz)	$\Delta\nu_{yy}$ (kHz)	$\Delta\nu_{zz}$ (kHz)	$\Delta\nu_{xx}$ (kHz)	$\Delta\nu_{yy}$ (kHz)	$\Delta\nu_{zz}$ (kHz)
358	6.7	7.7	1.0	2.6	19.1	21.7
348	6.7	7.7	1.0	2.6	20.0	22.6
335	6.7	7.7	1.0	2.6	20.5	23.1
326	5.8	8.3	2.5	2.6	21.6	24.2
315	5.0	10.0	5.0	2.6	21.6	24.2
305	5.3	10.6	5.3	4.6	22.5	27.1
294	5.5	11.0	5.5	7.2	24.8	32.0
283	2.6	11.6	8.8	7.2	24.8	32.0
273	0	13.5	13.5	8.0	27.6	35.6
262	0	15.0	15.0	8.5	29.3	37.8
250	1.3	16.0	17.3	10.0	30.0	40.0
239	3.5	19.8	23.3	11.0	31.0	42.0
227	7.5	27.0	34.5	13.6	32.0	45.6
218	7.8	25.4	33.2	14.2	31.8	46.0
207	12.2	27.8	40.0	16.9	34.3	51.2
196	15.0	31.0	46.0	19.0	37.7	56.7
183	16.0	32.6	48.6	21.0	36.0	57.0
173	18.0	34.5	52.5	22.4	37.3	59.7
161	21.3	35.5	56.8	26.0	40.4	66.4

motions being experienced by each of the enantiomers would require more information. It can however, be concluded that at temperatures below 77 K the C1 methyl groups are held rigidly. At ~142 K they are undergoing fast ($> 10^7$ Hz) rotation about their 3-fold axes. Above 161 K the molecules themselves are undergoing whole body motions as well as fast C1 methyl rotations. Since the spectra change gradually as a function of temperature, the whole body motion is probably a large scale libration. Also, since the temperature dependence for each subspectrum is different, one can conclude that the motion experienced by the favoured enantiomer is much different than that of the unfavoured one.

The TOT / 2-butanol-(OD) clathrate was prepared (see chapter three). The ^2H NMR spectrum was obtained at room temperature and is shown in figure 33 A. The spectrum fits well to the fast motional lineshape simulation in figure 33 B. The simulation consists of two components in a 60:40 intensity ratio. The frequency separation of the features for the narrow component are $\Delta\nu_{xx} = 10$ kHz, $\Delta\nu_{yy} = 31$ kHz and $\Delta\nu_{zz} = 41$ kHz. Those of the broad component are $\Delta\nu_{xx} = 16$ kHz, $\Delta\nu_{yy} = 66$ kHz and $\Delta\nu_{zz} = 82$ kHz. Both component spectra are narrower than that expected for a hydroxyl group freely rotating about its C-O bond and some additional mobility must therefore be present. The intensity ratio is consistent with that determined from the ^2H NMR spectra of the 2-butanol-(1,1,1- d_3) clathrate except that in this case the narrow component is dominant. This can be justified in a rather simplistic way by imagining that the C2 carbon of the guest molecule remains approximately fixed in the cage as a function of time. Then, if the C1

methyl and the C3-C4 ethyl groups are free to move, the -OD group would be less mobile. Since 40 % of the methyl groups were very mobile relative to the 60 % of those that were less mobile, one would expect 40 % of the -OD groups to be less mobile than the remaining 60 % of higher mobility. The extreme case of this notion is that either the C1 methyl group or the -OD group can become attached to a "binding site" inside the cage. When the C1 methyl group is bound (60 %) then the -OD group is free to move and when the -OD group is bound (40 %) then the C1 methyl group is free to move. This, of coarse, is an over simplification which does not take all of the molecular mobility into account. It does, however, serve as a good qualitative picture. It suggests that the favoured enantiomer in any given cage prefers a dynamic state where the C1 methyl group is less mobile than the -OD group.

Both the solid state ^{13}C and ^2H NMR results show that TOT is chirally selective towards the enantiomers of 2-bromobutane and 2-butanol. The guest molecules exhibit a great deal of dynamic disorder inside the cages. Because such disorder is present, one must use caution when interpreting single crystal X-ray diffraction data. The models used in the refinement of such data have employed conformationally rigid guest molecules with fixed coordinates. The data presented here indicate that this assumption is entirely inappropriate. Solid state NMR and X-ray crystallography are complimentary techniques, each giving only a partial description of the nature of the interactions between guest and host systems.

Figure 19: 45.3 MHz ^{13}C CP/MAS NMR spectra for TOT / 2-bromobutane at room temperature. A: Obtained using the conventional CP/MAS pulse sequence. Notice that the spinning sidebands obscure the C2 resonance of the 2-bromobutane. B: Spectrum similar to that of A, using the pulse sequence described in reference 80. Notice that the C2 resonance of the guest is now visible. C: and D: Expansions of the carbonyl - aromatic and alkyl regions of A.

Figure 20: Semi-Log plot of the integrals of the TOT enclathrated 2-bromobutane-(1,1,1-d₃) ¹³C CP/MAS resonances vs. contact time. The data for each resonance was fitted to a linear model. The slopes of each line are identical within experimental error. All of the spectra used for the plot were collected using the pulse sequence described in reference 80. The ratios used to calculate the enantiomeric excess were those at the intercept of the best fitting lines.

EXPERIMENT SIMULATION

Figure 21: Representative experimental and simulated 27.6 MHz ^2H NMR spectra of TOT / 2-bromobutane-(1,1,1- d_3) as a function of temperature. All spectra were acquired using the quadrupolar echo experiment. The relaxation delay for the spectrum acquired at 77 K was 5 sec. The spectrum at 116 K was obtained using a relaxation delay of 0.1 sec. All others were obtained using a relaxation delay of 1 sec. Note the difference in scale between the spectrum at 77 K and all the others. The parameters for the simulated spectra are given in table 6. 1.8 kHz of Gaussian broadening was applied to each simulated spectrum.

Figure 22: Plots of ^2H NMR spectral splittings for the TOT / 2-bromobutane-(1,1,1- d_3) clathrate vs. absolute temperature. These points are those taken from the best fitting simulations (see text for explanation).

Figure 23: A: 46.1 MHz ^2H NMR spectrum of TOT / 2-bromobutane-(2- d_1) at room temperature. The spectrum was obtained using the quadrupolar echo technique. B: Fast motional lineshape simulation used to represent the spectrum in A. 4 kHz of Gaussian broadening was applied to each contribution before addition. Narrow component: $(e^2qQ/h) = 77$ kHz, $\eta = 0$. Broad component: $(e^2qQ/h) = 132$ kHz, $\eta = 0.09$. The ratio of the broad : narrow components was 55 : 45.

Figure 24: Typical single crystal 46.1 MHz ^2H NMR spectra of TOT / 2-bromobutane-(1,1,1- d_3) at arbitrary orientations to the magnetic field. The spectra were obtained using the quadrupolar echo technique with 90° pulses of 2.5 μsec and echo delays of 35 μsec . The relaxation delays were 0.5 sec.

Figure 25: Rotation patterns obtained from the single crystal ^2H NMR study of TOT / 2-bromobutane-(1,1,1- d_3). Only the major enantiomer could be followed. (see text for discussion).

Figure 26: Corrected rotation patterns obtained from the single crystal ^2H NMR study of TOT / 2-bromobutane-(1,1,1- d_3). Only the major enantiomer could be followed. (see text for discussion and the description of the corrections used).

Figure 27: A: 45.3 MHz ^{13}C CP/MAS NMR spectra for TOT / 2-butanol at room temperature using the conventional CP/MAS technique. The doubled C2 resonance of the guest is visible among the spinning sidebands B: The alkyl region of the ^{13}C CP/MAS NMR spectrum of TOT / 2-butanol. The C1 resonance is indicated by an asterisk. C: The 45.3 MHz ^{13}C CP/MAS NMR spectrum of TOT / 2-butanol-(1,1,1- d_3) at room temperature using the pulse sequence described in reference 80 to suppress first order spinning sidebands. D: The alkyl region of the spectrum given in C. Note the absence of the C1 resonance.

Figure 28: Partial 45.3 MHz ^{13}C CP/MAS NMR spectra of TOT / 2-butanol-(1,1,1- d_3) obtained as a function of cross polarization time. From top to bottom, the cross polarization times are: ms, 4.0 ms, 4.5 ms, 5.0 ms, 5.5 ms, 6.5 ms, 7.5 ms and 8.5 ms.

Figure 29: The ^{13}C CP/MAS resonances of the C2 carbon of TOT enclathrated 2-butanol under different conditions of sample preparation. A: Clathrate prepared from racemic 2-butanol by rapid crystallization. B: Clathrate prepared from optically pure (*R*)-2-butanol by slow crystallization. C: Clathrate prepared from optically pure (*S*)-2-butanol by rapid crystallization. D: The clathrate from C was desolvated then recrystallized quickly from optically pure (*R*)-2-butanol. This spectrum shows a predominance of the unfavoured enantiomer.

Figure 30: The ^{13}C CP/MAS NMR spectrum of TOT / 2-butanol-(1,1,1- d_3) under dipolar dephasing conditions using first order sideband suppression.

EXPERIMENT SIMULATION

Figure 31: Representative experimental and simulated 27.6 MHz ^2H NMR spectra of TOT / 2-butanol-(1,1,1- d_3) as a function of temperature. All spectra were acquired using the quadrupolar echo experiment. The relaxation delay for the spectrum acquired at 77 K was 10 sec. All others were obtained using a relaxation delay of 1 sec. Note the difference in scale between the spectrum at 77 K and all the others. The parameters for the simulated spectra are given in table 10. 1.8 kHz of Gaussian broadening was applied to each simulated spectrum.

Figure 32: Plots of ²H NMR spectral splittings for the TOT / 2-butanol-(1,1,1-d₃) clathrate vs. absolute temperature. These points are those taken from the best fitting simulations (see text for explanation).

Figure 33: A: 46.1 MHz ^2H NMR spectrum of TOT / 2-butanol-(OD) at room temperature. The spectrum was obtained using the quadrupolar echo technique with a relaxation delay of 1 sec. B: Fast motional lineshape simulation used to represent the spectrum in A. 3 kHz of Gaussian broadening was applied to each contribution before addition. Narrow component: $(e^2qQ/h) = 27$ kHz, $\eta = 0.512$. Broad component: $(e^2qQ/h) = 55$ kHz, $\eta = 0.610$. The ratio of the broad : narrow components was 40:60.

CHAPTER FIVE

TOT / Acetone, TOT / Benzene and TOT / Pyridine

It has been shown, in chapter four, that the enantiomers of 2-bromobutane and 2-butanol have large degrees of molecular mobility inside the cages of their TOT clathrates. A complete description of the molecular motion, however, could not be deduced from the data collected. In this chapter simpler systems will be examined. The molecular motions of TOT enclathrated acetone, benzene and pyridine will be studied in detail by solid state ^{13}C and ^2H NMR. The NMR results will be compared to the X-ray crystallographic data. It will be shown that, for these systems, very detailed quantitative information can be obtained through the use of solid state NMR, and when used to supplement the X-ray data, a complete physical description of the system can be obtained.

I. TOT / Acetone

The X-ray crystal structure of TOT / acetone was determined at room temperature. It was found to be a typical 2:1 $P3_121$ clathrate with cell dimensions, $a=b= 13.4612(11) \text{ \AA}$ and $c= 30.2973(20) \text{ \AA}$. There were 6 TOT molecules and 3 acetone molecules in the unit cell. The experimental details are given in appendix 3 along with tables of coordinates, bond distances and angles and an ORTEP

diagram. Each acetone molecule is inside a cage of 8 TOT molecules. Its carbonyl bond is on the two-fold symmetry axis of the cavity. An ORTEP diagram of the acetone molecule, along with its thermal ellipsoid dimensions, is given in figure 34. Although the thermal ellipsoids are large compared to those of the host, the acetone molecule seems to exhibit limited disorder.

Solid state ^2H NMR spectra were obtained for the TOT / Acetone- d_6 clathrate as a function of temperature and are shown in figure 35 A. The spectrum obtained at 77 K can be well represented by a fast motional spectrum (figure 35 B). Those between 77 K and 134 K have distorted lineshapes due to a molecular motion occurring on the same time scale as the echo experiment. The spectra obtained at temperatures above 134 K are again in the fast motional regime and can be simulated (figure 35 C and D) by the computer program described in appendix 1.

For a completely rigid acetone molecule one expects an axially symmetric spectrum with $\Delta\nu_{xx} = \Delta\nu_{yy} \sim 126$ kHz and $\Delta\nu_{zz} \sim 252$ kHz.¹⁶⁴ For fast symmetric methyl group rotations, one expects the same spectrum scaled down by a factor of $\frac{1}{2}(3 \cos^2\beta - 1)$, compared to that of the rigid spectrum, where β is the tetrahedral angle between the C-D bonds and the rotation axis. For such a motion, the parameters would be $\Delta\nu'_{xx} = \Delta\nu'_{yy} = 42$ kHz and $\Delta\nu'_{zz} = 84$ kHz. The spectral parameters observed at 77 K were $\Delta\nu'_{xx} = 35 \pm 1$ kHz, $\Delta\nu'_{yy} = 48 \pm 2$ kHz and $\Delta\nu'_{zz} = 83 \pm 3$ kHz. These agree well with those measured for pure acetone- d_6 at 77 K.^{165,166} The axial asymmetry observed in the spectrum is not uncommon for rotating methyl groups attached to carbonyl carbons.¹⁶⁵ It can be accounted for if the three

sites visited by the deuterons over the course of the rotation are not equivalent. This is indeed the case for the acetone molecule. The motional narrowing in the spectrum obtained at 77 K is therefore due to fast methyl group rotation. The V'_{zz} components of the averaged electric field gradient tensors are approximately parallel to the C-C bonds in the molecule. The other components are in and out of the molecular plane, however, it is not possible to assign their orientations at this stage.

Above 77 K a new molecular motion begins to occur and is in the fast motional regime at 134 K. Since the averaged spectrum at 134 K is a single powder pattern, i.e. it is not a superposition of two, then the motion must treat both methyl groups in exactly the same way. One such motion is a two-fold flip about the carbonyl bond. This motion would be consistent with the X-ray data since the carbonyl bond was found to be coincident with the two-fold axis of the cage. A discrete two-fold flip about this axis does not give rise to disorder and would not be expected to show up in the X-ray data. The effects on the already averaged electric field gradient tensor at 77 K can be calculated using the method described in chapter one. The new averaged tensor components, V''_{xx} , V''_{yy} and V''_{zz} , are given by the following equations:

$$V''_{xx} = V'_{yy} \sin^2 \beta + V'_{zz} \cos^2 \beta \quad (78)$$

$$V''_{yy} = V'_{xx} \quad (79)$$

$$V''_{zz} = V'_{yy} \cos^2 \beta + V'_{xx} \sin^2 \beta \quad (80)$$

where β , in this case, is the angle between the C-C and carbonyl bond axes. According to microwave data,^{167,168} $\beta = 58^\circ$. Since the orientations of the V'_{xx} and V'_{yy} components at 77 K are not known, one must consider two possible situations: either, V'_{xx} is out of the molecular plane and V'_{yy} is in the molecular plane, or vice versa. Each of these situations leads to a different spectrum. If the former is true, then the splittings in the spectrum at 134 K are expected to be $\Delta v''_{xx} = 11$ kHz, $\Delta v''_{yy} = 35$ kHz and $\Delta v''_{zz} = 46$ kHz ($\eta = .52$). If the latter is true, then $\Delta v''_{xx} = 2$ kHz, $\Delta v''_{yy} = 48$ kHz and $\Delta v''_{zz} = 50$ kHz ($\eta = .92$). The parameters for the observed spectrum were $\Delta v''_{xx} = 11 \pm 1$ kHz, $\Delta v''_{yy} = 29 \pm 2$ kHz and $\Delta v''_{zz} = 40 \pm 3$ kHz ($\eta = .45$). These parameters do not match either of the two situations but are certainly closer to those of the former case than the latter. Furthermore, the parameters of the spectrum undergo further averaging at higher temperatures, see table 11 and figure 36. This is not expected for simple two-fold flips plus methyl group rotations and indicates that the spectrum at 134 K must also be averaged by yet another molecular motion giving rise to the spectral parameters $\Delta v'''_{xx}$, $\Delta v'''_{yy}$ and $\Delta v'''_{zz}$.

If two-fold flips are occurring at 134 K, at a rate fast on the NMR time scale ($> 10^7$ Hz), then the V'_{yy} and V'_{xx} components of the electric field gradient tensor at 77 K must be in and out of the molecular plane, respectively (see figure 37 A). The V''_{xx} component of the spectrum is parallel to the carbonyl bond. The V''_{zz} and V''_{yy} components are in and out of the molecular plane, respectively (figure 37 B).

Table 11

¹ H NMR Spectral Parameters for TOT / Acetone-d ₆ as a Function of Temperature			
Temperature (K) ± 1 K	$\Delta\nu'''_{xx}$ (kHz) ± 1 kHz	$\Delta\nu'''_{yy}$ (kHz) ± 2 kHz	$\Delta\nu'''_{zz}$ (kHz) ± 3 kHz
134	11	29	40
140	10	29	41
154	11	30	41
162	11	28	40
183	11	28	39
200	10	29	38
201	11	28	40
221	10	28	39
231	10	28	38
241	10	27	37
251	11	27	37
261	10	27	38
271	10	26	37
281	10	26	37
298	11	25	36
320	10	24	33
335	10	23	33
340	10	22	32
365	10	21	31
387	10	21	30

It can be seen from figure 36 that the $\Delta\nu'''_{xx}$ component of the high temperature spectra is independent of temperature. The additional motion, present at temperatures ≥ 134 K, must therefore, occur about the V'''_{xx} axis. The gradual change in the other two parameters with temperature suggests that the additional

motion must be a librational process where the libration angle increases with temperature. The tensor components, V'''_{xx} , V'''_{yy} and V'''_{zz} , and spectral parameters, $\Delta v'''_{xx}$, $\Delta v'''_{yy}$ and $\Delta v'''_{zz}$, of the librationaly averaged system can be calculated with the use of a two site libration model:

$$V'''_{xx} = V''_{xx} \quad (81)$$

$$V'''_{yy} = V''_{yy} \cos^2 \gamma + V''_{zz} \sin^2 \gamma \quad (82)$$

$$V'''_{zz} = V''_{yy} \sin^2 \gamma + V''_{zz} \cos^2 \gamma \quad (83)$$

where γ is the libration angle defined in figure 38. Equations (82) and (83) were used to calculate γ for each temperature. The temperature dependence is shown in figure 39 and is the result of the increased thermal motion of the acetone molecule. The librational angle, γ , is $\pm 15^\circ \pm 2^\circ$ at 134 K and $\pm 22^\circ \pm 2^\circ$ at room temperature.

In order to confirm the ^2H NMR results, the chemical shielding tensor of the carbonyl carbon of TOT enclathrated acetone-(2- ^{13}C) was examined at room temperature. From previous studies,^{67,66} it has been shown that the chemical shielding parameters for the carbonyl carbon of solid acetone at 87 K are, $\sigma_{xx} = -58 \pm 6$ ppm, $\sigma_{yy} = -72 \pm 6$ ppm and $\sigma_{zz} = 130 \pm 6$ ppm with respect to the isotropic chemical shift, taken to be 0 ppm. The σ_{zz} component has been shown to be perpendicular to the sp^2 plane. The other two components are parallel and perpendicular to the carbonyl bond in the molecular plane (figure 40). The previous studies were unable to assign the orientations to the σ_{xx} and σ_{yy} components. Both

methyl group rotations and two-fold flips about the carbonyl bond leave this tensor completely unchanged. The librational motion about the carbonyl bond, on the other hand will average the σ_{zz} component as well as one of the other two. One of the components must stay constant. Observation of this behaviour is a good confirmation of the ^2H NMR results. By observing which of the two components remains unchanged in the clathrate at room temperature, it is possible to determine the orientation of σ_{xx} and σ_{yy} at 87 K.

Initially, a static ^{13}C CP spectrum of unlabelled TOT / acetone was obtained and subtracted from a similar spectrum of TOT / acetone-(2- ^{13}C). Since the enrichment of ^{13}C was only 12 mol %, the signal / noise ratio in the difference spectrum was too low to make a reliable measurement of the shielding parameters. Instead, ^{13}C /CP/MAS spectra were obtained for the enriched sample at slow spinning rates so that the graphical sideband analysis of Herzfeld and Berger⁷⁶ could be used to obtain the chemical shielding parameters. The spinning rates used had to be chosen carefully such that the sidebands of the carbonyl carbon of the enclathrated acetone did not overlap with the resonances or sidebands of the TOT host. Four spectra were obtained at spinning rates between 2.176 and 2.389 kHz. The carbonyl peak of the acetone was the most intense resonance in the spectrum and the intensities of the sidebands were measured as a ratio to the centerband. The sideband intensities were used in the graphical analysis⁷⁶ to obtain the shielding parameters: $\sigma'_{xx} = -39 \pm 6$ ppm, $\sigma'_{yy} = -53 \pm 6$ ppm and $\sigma'_{zz} = 92 \pm 9$ ppm. The lineshapes were reconstructed for both the pure acetone at 87 K and the

enclathrated acetone at room temperature using the computer program in appendix 1 and are shown in figure 41. It is obvious from the figure that the σ_{xx} component is averaged in the spectrum, therefore, the libration is confirmed to be about the carbonyl bond. The σ_{xx} component remained essentially unchanged, therefore its orientation must be perpendicular to the carbonyl bond in the molecular plane.

The ^{13}C NMR data can be used to calculate the libration angle at room temperature in the same way the ^2H NMR data were used. The parameters of the librationaly averaged shielding tensor are given by:

$$\sigma'_{xx} = \sigma_{yy} \cos^2 \gamma + \sigma_{zz} \sin^2 \gamma \quad (84)$$

$$\sigma'_{zz} = \sigma_{yy} \sin^2 \gamma + \sigma_{xx} \cos^2 \gamma \quad (85)$$

$$\sigma'_{yy} = \sigma_{xx} \quad (86)$$

The librational angle, γ , was determined to be $24^\circ \pm 5^\circ$ by averaging the angles calculated from equations (84) and (85). This agrees well with that calculated from the ^2H NMR data.

^2H T_1 measurements were carried out for the acetone- d_6 clathrate as a function of temperature. Complete measurements were made using the inversion recovery technique in conjunction with the quadrupolar echo pulse sequence at 298 K, 236 K and 184 K. The intensity measurements were all made at the same point in the spectrum. The T_1 s were calculated using the two parameter model:

$$I(\tau) = I_\infty (1 - 2e^{-\tau/T_1}) \quad (87)$$

Table 12

² H T ₁ 's TOT / Acetone-d ₆		
Temperature (K)	T ₁ (msec)	Method
298	603	Inversion Recovery
298	577	Null
236	92	Inversion Recovery
211	36	Null
200	25	Null
184	19.3	Inversion recovery
184	19	Null
175	20	Null
162	29	Null

where $I(\tau)$ is the intensity of the inner features of the spectrum as a function of the relaxation delay, τ , and I_{∞} is the intensity of the inner singularities for the fully relaxed spectrum. The ²H NMR spectra taken as a function of τ , for the room temperature experiment, are shown in figure 42. Other T₁ estimates were made at 298 K, 211 K, 200 K, 184 K, 175 K and 162 K by finding the τ value that gave a minimum signal, τ_{null} . The T₁ value was obtained from equation (87) by substituting $I(\tau)=0$ and $\tau=\tau_{\text{null}}$. The T₁ estimates made at 298 K and 184 K, using the null method, agreed well with those determined by the inversion recovery technique. The data are summarized in table 12. The errors are estimated to be $\pm 5\%$ for the T₁s measured using the inversion recovery technique and $\pm 15\%$ for those estimated using the null signals. An Arrhenius plot of the data is given in figure 43. The T₁ minimum is ~19 msec at 184 K. The first five data points on the Arrhenius plot give

a straight line whose slope can be used to obtain an activation energy of 13.6 ± 0.8 kJ/mol. This barrier is much higher than those reported for the methyl group rotation in gaseous acetone- d_6 , 3.0 kJ/mol¹⁶⁹ and unlabelled gaseous acetone, 3.3 kJ/mol¹⁶⁹ (3.1 kJ/mol¹⁶⁸). Because of the large difference, the activation barrier measured here must be due to the two-fold flipping motion of the acetone molecule about the carbonyl bond. If it is assumed that the correlation time of the methyl group rotation, τ_{c3} , is much shorter than that of the two-fold flips, τ_{c2} , then the spectral density function, $J(\omega_o)$,¹⁷⁰ introduced in chapter one, can be written:

$$J(\omega_o) = \frac{\tau_{c2}}{1 + (\omega_o \tau_{c2})^2} + \frac{4\tau_{c2}}{1 + (2\omega_o \tau_{c2})^2} \quad (88)$$

where ω_o is the Larmor frequency. The spectral density function has a maximum when $\omega_o \tau_{c2} = 0.6158$ at which point the relaxation is most efficient. Since the Larmor frequency is known, one can easily calculate the correlation time for the two-fold flipping motion at the T_1 minimum (~ 184 K). The correlation time is 3.5 nsec.

From the above discussion one can see that a very detailed dynamic picture of the TOT / acetone clathrate can be obtained by using both X-ray and NMR data. It is difficult, if not impossible, to get such a complete description from each technique individually.

II. TOT / Benzene

Unlike the TOT / acetone clathrate, TOT / benzene is known to exist in more than one crystal form. The typical $P3_121$ cage type clathrate was described by Newman and Powell in 1952.^{104a} This material was made by slowly cooling a

saturated solution of TOT in benzene. Although a complete X-ray structural analysis has never been carried out, the unit cell dimensions have been measured and are typical of the isostructural clathrates. Another, less stable crystalline form has been studied in more detail.¹¹⁷ It was also prepared by slow cooling of a TOT - benzene solution. The authors claimed that if the crystallization of TOT began at an early stage in a benzene solution, the less stable polymorph was formed. When taken out of solution the crystals decomposed within a few minutes giving benzene and a polycrystalline or amorphous powder. The 2 : 2.5 (TOT : benzene) inclusion compound, in space group *P*1, has two independent TOT molecules in the unit cell. The unit cell constants are $a=11.312 \text{ \AA}$, $b=13.147 \text{ \AA}$, $c=25.016 \text{ \AA}$, $\alpha=93.13^\circ$, $\beta=103.24^\circ$ and $\gamma=86.28^\circ$. The structure contains three types of channels. Two channels run parallel to the crystallographic *a* axis and have fairly uniform cross sections. The third runs parallel to the crystallographic *b* axis and is characterized by a series of bulges and constrictions.

A TOT / benzene inclusion compound was prepared by slow recrystallization. The crystals obtained were large and colourless. Since no attempt was made at protecting the crystals from air, it was assumed that the complex was of the cavity type in space group *P*3₁21. The large crystals were ground into a powder and a ¹³C CP/MAS spectrum was acquired under both standard and dipolar dephasing conditions. The spectra are shown in figure 44. The observed chemical shift for the benzene was 128.3 ppm from TMS. This agrees well with that observed for neat liquid benzene, 128.5 ppm.¹⁷¹ Since the benzene resonance appears in the dipolar

dephased spectrum, one must conclude that the benzene molecules are undergoing a molecular motion able to average the static ^{13}C - ^1H dipolar interaction.

A TOT / benzene- d_6 clathrate was made by rapid recrystallization. A ^{13}C CP/MAS spectrum was obtained and is shown in figure 45. The spectrum is complicated and appears to result from a mixture of at least two different materials. It may either be a mixture of the two known polymorphs or a mixture of the $P3_121$ clathrate and an unsolvated powder.

Solid state ^2H NMR spectra were obtained for this material at 77 K and 298 K. The spectra are shown in figure 46. The spectrum of pure benzene- d_6 at 77 K has $\Delta\nu_{xx}=130 \pm 1$ kHz, $\Delta\nu_{yy}=141 \pm 1$ kHz and $\Delta\nu_{zz}=271 \pm 1.5$ kHz.¹⁶⁵ The spectrum taken of the TOT / benzene- d_6 clathrate at 77 K is axially symmetric with separation between the inner singularities of 70 ± 1 kHz. This spectrum is expected if the benzene rings undergo fast in plane rotation about their six-fold symmetry axes. The averaging of the electric field gradient tensor components due to such a motion can be described by the following equations:

$$V'_{xx} = V'_{yy} = \frac{1}{2} (V_{xx} + V_{zz}) \quad (89)$$

$$V'_{zz} = V_{yy} \quad (90)$$

The $\Delta\nu_{xx}$ and $\Delta\nu_{zz}$ components are averaged while the $\Delta\nu_{yy}$ component remains unchanged. At 298 K the spectrum is also axially symmetric with an inner splitting of 61 ± 1 kHz. The reduction in spectral width can be attributed to an out-of-plane libration of the ring where the ring normal moves on the surface of a cone of half

angle θ . The expected reduction in all of the spectral components is then $\frac{1}{2}(3 \cos^2\theta - 1)$ where θ is the half angle of libration. For the observed reduction in spectral width, the half angle of libration is $17^\circ \pm 2^\circ$ at 298 K.

This model for the molecular motion may be deceptively simple. The ^2H NMR spectrum in this case is not sensitive to all possible types of molecular motion. For example, the benzene rings may be able to undergo two-fold flips about any of the three two-fold molecular symmetry axes. Two-fold flipping motions make two of the deuterons inequivalent to the other four. There is no way of determining, from the ^2H NMR spectrum, whether or not this type of motion accompanies the in plane rotation since the in plane rotation results in a single tensor. Two-fold flips superimposed on a fast six-fold in-plane rotation have absolutely no effect on the ^2H NMR spectrum.

The above results show conclusively that the benzene ring, in its $P3_121$ clathrate, undergoes fast in plane ring rotation as well as whole molecule libration. A two-fold flipping motion is also possible. If the deuterium labelled sample also contained some of the other polymorph, then one can conclude that benzene undergoes similar molecular motions in each of the two inclusion compounds.

III. TOT / Pyridine

A single crystal X-ray study of the 2:1 TOT / Pyridine clathrate has been reported.¹¹⁶ Like the TOT / acetone clathrate, the pyridine clathrate belongs to the $P3_121$ space group. It has six TOT molecules in the unit cell with eight molecules forming a cage. There is only one guest molecule per cage. The authors were able

to assign positional coordinates for the atoms of the pyridine guest molecule. The highest peak in the Fourier map of the guest was attributed to the nitrogen atom, which was found to reside on the two-fold axis of the cage. The temperature factors for the pyridine atoms were larger than those of the host molecules, however, the authors concluded that the pyridine had only limited disorder.

A solid state ^{13}C CP/MAS NMR spectrum was obtained for the TOT / Pyridine clathrate at room temperature under standard and dipolar dephasing conditions. The aromatic / carbonyl region of the spectra are shown in figure 47. The observed chemical shift values for the pyridine were 149.3, 124.3 and 137.2 ppm from TMS. These values agree, to within 1 ppm, with those reported for neat liquid pyridine.¹⁷¹ The resonance of the nitrogen bearing carbons is significantly broader than the others due to residual ^{14}N - ^{13}C dipolar coupling which is not averaged by the MAS experiment. The dipolar dephased spectrum is completely free of the resonances of the proton bearing carbon atoms of the host. It does, however, still contain all of the resonances of the pyridine guest with a reduced intensity. The reduction in intensity, for the resonance due to the carbon atom opposite the nitrogen, is much greater than those of the other four carbon atoms. This implies that the ^{13}C - ^1H dipolar interactions are not averaged equally for all of the carbon atoms. The carbon atom opposite the nitrogen is unique and undergoes less motional averaging. The only type of molecular motion consistent with this observation is rotation about the two-fold molecular symmetry axis.

Solid state ^2H NMR spectra were recorded for the TOT / pyridine- d_5 clathrate as a function of temperature and are shown in figure 48. The spectrum at 77 K has $\Delta\nu'_x = 68 \pm 2$ kHz, $\Delta\nu'_y = 136 \pm 3$ kHz and $\Delta\nu'_z = 204 \pm 5$ kHz. This spectrum is considerably narrower than that measured for pure pyridine- d_5 at 77 K which has $\Delta\nu_x = 128 \pm 3$ kHz, $\Delta\nu_y = 138 \pm 3$ kHz and $\Delta\nu_z = 266 \pm 6$ kHz. The narrowing can be attributed to a fast molecular motion. Since the spectrum consists of only one powder pattern, one can conclude that the molecular motion responsible for the narrowing treats all of the deuterons identically. An additional, thermally activated, molecular motion begins to occur at temperatures above 77 K. This motion is in the slow motional regime between 77 K and ~ 196 K, leading to distorted lineshapes. Above ~ 196 K it is in the fast motional regime. At first glance, the high temperature spectra also appear to be single motionally narrowed powder patterns with very high asymmetry parameters. Upon closer examination, however, one is able to identify additional features in the spectra. The ^{13}C data suggested that the pyridine rings were able to undergo rotational motion about the two-fold symmetry axis of the molecule. This leaves one unique deuteron whose ^2H NMR spectrum is unchanged from that at 77 K and whose contribution is only 20 % to the total spectrum at higher temperatures. It is this unique deuteron that accounts for the additional features observed in the spectra at higher temperatures. Table 13 lists the parameters of the high temperature spectra as a function of temperature. The three components of the spectrum for the four equivalent

deuterons, $\Delta\nu''^c_{ii}$, are given along with the separation between the innermost features, $\Delta\nu''^u_{xx}$, of the spectrum due to the unique deuteron.

Table 13

High Temperature ^2H NMR Spectral Parameters for TOT / Pyridine- d_5				
Temperature ± 1 K	$\Delta\nu''^c_{ii} \pm 3$ kHz	$\Delta\nu''^c_{jj} \pm 3$ kHz	$\Delta\nu''^c_{xx} \pm 3$ kHz	$\Delta\nu''^u_{xx} \pm 3$ kHz
196	12	118	130	54
219	7	125	130	52
249	14	112	126	47
281	15	110	125	43
298	12	108	120	40
323	13	104	118	a
a: insufficient signal / noise ratio				

The ^2H NMR spectrum at 77 K can be attributed to hindered in plane rotation of the pyridine ring. This motion treats all of the deuterons identically and also accounts for the fact that one of the components of the averaged spectrum at 77 K is very nearly identical to that of the rigid spectrum. Any in plane motion of the pyridine ring, however, must be limited if the conclusions drawn from the X-ray data are accepted. An exact description of the motion is not obvious. Several models can be examined (see figure 49).

First, the ring may reside in a single broad potential well and undergo in-plane librations. If a two site librational model is used as an approximation, then the half angle of libration must be 23° to account for the spectrum at 77 K. This model also accounts for the separation between the singularities in the high temperature

spectra, resulting from the unique deuteron, as a function of temperature. The half angle of in plane libration at room temperature is 28° .

Secondly, the ring may reside in a three-site symmetric potential well, where the central site is lowest in energy and the other two equivalent sites, 60° on either side, are of higher energy. This model has been developed and applied successfully to pyridinium iodide.¹⁷² The averaging of the electric field gradient tensor components can be described by the following equations:

$$V'_{yy} = V_{yy} \quad (91)$$

$$V'_{xx} = P_1 \left(\frac{1}{2} V_{xx} + \frac{3}{2} V_{zz} \right) + P_2 V_{xx} \quad (92)$$

$$V'_{zz} = P_1 \left(\frac{3}{2} V_{xx} + \frac{1}{2} V_{zz} \right) + P_2 V_{zz} \quad (93)$$

where P_1 ($=P_3$) and P_2 are the populations of the unfavoured and favoured sites, respectively. For such a process:

$$P_1 = P_3 = \frac{1}{2 + e^{\Delta E/RT}} \quad (94)$$

and

$$P_2 = \frac{e^{\Delta E/RT}}{2 + e^{\Delta E/RT}} \quad (95)$$

ΔE is the energy difference between the potential sites and R is the gas constant. The energy difference, ΔE , must be 1.3 kJ/mol to account for the spectrum at 77 K. Although this model works well for pyridinium iodide,¹⁷² it cannot be used here as it predicts that the innermost features in the high temperature spectra, due to the unique deuteron, become further apart with increasing temperature.

Third, the pyridine ring may reside in a symmetric multi-site potential well with an energy barrier on the two-fold axis of the cavity. The spectrum at 77 K can be calculated if the innermost constituent potential wells are separated by $\pm 23^\circ$. This model can be justified qualitatively by imagining that the nitrogen atom is attracted more strongly to points symmetric about the two-fold axis of the clathrate cavity rather than a point on the two-fold axis itself. The quantitative derivation involves representing the potential function with a Fourier series for points on either side of the two-fold cavity axis and then taking the average of the two potential functions (see appendix 4). This model also accounts for the high temperature spectra where two-fold flips occur, if it is assumed that additional in-plane potential sites can be populated at higher temperature and that whole body molecular libration also occurs. The distinction between the first and third models cannot be made with the available data.

Using the spectrum at 77 K as a starting point, the spectrum due to 180° flips about the two-fold molecular axis can be calculated using the same principles as those used for the analysis of the TOT / acetone- d_6 spectra. The result is shown in figure 50. Although the calculated spectrum has the same general appearance as

those observed at temperatures above 196 K, it is broader than the observed spectra and is not expected to exhibit any temperature dependence. The deviation between the real and simulated spectra can be attributed to whole molecular libration effects.

Contrary to the conclusions drawn from the X-ray data, the NMR data show that the pyridine molecule is dynamically disordered in its TOT clathrate. The motional models used to account for the NMR spectra support the X-ray data in that the nitrogen atom of the pyridine ring remains localized in a region of the cage.

By studying the TOT clathrates of acetone, benzene and pyridine by solid state NMR techniques and comparing the findings with the available X-ray data, it has been possible to obtain a detailed description of the structure and dynamics of these systems. Often the X-ray structures paint a deceptively simple picture of the enclathrated guests. Solid state NMR can be used to confirm the existence of dynamic disorder and also to establish quantitative details about the dynamic processes.

Principal Components of Thermal Ellipsoids ($\times 10^2$)

	U_{11}	U_{22}	U_{33}
O	9.9	9.9	32.7
CA1	6.9	6.9	14.0
CA2	9.1	18.8	19.4

Figure 34: ORTEP representation of acetone enclathrated by TOT.

Figure 35: A: Solid state 27.6 MHz ^2H NMR spectra of TOT / acetone- d_6 as a function of temperature. The spectra were acquired, using the quadrupolar echo pulse sequence. B: Simulated spectrum used to represent the spectrum at 77 K the following parameters were used; $(e^2qQ/h) = 55.3$, $\eta = 0.156$, Gaussian broadening = 1.8 kHz. C: Simulated spectrum used to represent the spectrum at 154 K the following parameters were used; $(e^2qQ/h) = 27.3$, $\eta = 0.463$, Gaussian broadening = 1.8 kHz. D: Simulated spectrum used to represent the spectrum at 281 K the following parameters were used; $(e^2qQ/h) = 23.3$, $\eta = 0.432$, Gaussian broadening = 1.8 kHz.

Figure 36: Plot of the frequency separation between the three sets of features in the high temperature solid state 2H NMR spectra of TOT / acetone- d_6 as a function of temperature. The splittings were taken from the best fitting simulated spectra. Notice that one of the components is independent of temperature. The data is compiled in Table 11.

Figure 37: A: Diagram showing the orientations of the averaged electric field gradient tensor components, V'_{xx} , V'_{yy} , and V'_{zz} , resulting from fast methyl group rotation. B: Diagram showing the orientations of the averaged electric field gradient tensor components, V''_{xx} , V''_{yy} , and V''_{zz} , resulting from both fast methyl group rotation and fast two-fold flips about the carbonyl bond.

Figure 38: Schematic representation of both the two-fold flipping and librational motions which occur for TOT enclathrated acetone at temperatures above 134 K.

Figure 39: Plot of the temperature dependence of the librational half angle, γ , for the librational motion of acetone in its TOT clathrate. The data points were calculated from equations (82) and (83) using the observed spectral parameters with calculated values of V''_{yy} and V''_{zz} derived from those given in the text.

Figure 40: Diagram showing the orientation of the σ_{zz} component of the chemical shielding tensor for the carbonyl carbon of solid acetone at 87 K. The previous studies^{67,86} were unable to assign the directions of the σ_{xx} and σ_{yy} components.

TOT / Acetone

Figure 41: A: The chemical shielding tensor for the carbonyl carbon of solid acetone. This spectrum was reconstructed, using the computer program in appendix 1, from the parameters given in the literature^{67,86} B: The same tensor for acetone in its TOT clathrate at room temperature. This spectrum was reconstructed from the parameters obtained from the slow spinning experiments described in the text. Note that the σ_{zz} component is averaged in B.

TOT / Acetone-d₆ T₁ Data at 298 K

Figure 42: 27.6 MHz ^2H NMR spectra obtained from the inversion recovery experiment in conjunction with the quadrupolar echo sequence. All of the spectra were recorded at room temperature. The repetition time was 5 sec. The τ values for the inversion recovery experiment (in msec) from top left to bottom right were: 2000, 1500, 1000, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, 50, and 10.

Figure 43: Arrhenius plot of the T_1 data for TOT / acetone- d_6 . $\ln T_1$ vs. $1000 / T$.

TOT / Benzene

Figure 44: 45.3 MHz ^{13}C CP/MAS NMR spectra of $P3_{21}$ TOT / benzene clathrate under normal, (A), and dipolar dephasing, (B), conditions. Only the carbonyl-aromatic region is shown. The pulse sequence described by Hemminga and de Jager⁸⁰ was used to suppress first order spinning sidebands.

Figure 45: 45.3 MHz ¹³C CP/MAS NMR spectrum of a sample of TOT recrystallized from benzene-d₆. The pulse sequence described in reference 80 was used to suppress the first order spinning sidebands. A: Complete spectrum. B: Carbonyl-aromatic region. C: Alkyl region. Note that this spectrum is broader than that in figure 44. It does not contain discrete triplets due to the host and is probably due to a mixture of materials.

TOT / Benzene-d₆

Figure 46: 27.6 MHz solid state ^2H NMR spectra of a sample of TOT recrystallized from benzene- d_6 at (A), room temperature and (B) 77 K. The spectra were acquired with the quadrupolar echo pulse sequence. The slight narrowing in the room temperature spectrum can be attributed to librational motion (see text for details).

TOT / Pyridine

Figure 47: 45.3 MHz ^{13}C CP/MAS NMR spectra of *P*3₁21 TOT / pyridine clathrate under normal, (A), and dipolar dephasing, (B), conditions. Only the carbonyl-aromatic region is shown. The pulse sequence described by Hemminga and de Jager⁸⁰ was used to suppress first order spinning sidebands. The dipolar dephasing time used in (B) was 40 μsec . The pyridine resonances appear at 149.3 ppm (C1 and C5), 124.3 ppm (C2 and C4) and 137.2 ppm (C3). The C3 resonance is attenuated much more than the other pyridine resonances in the dipolar dephased spectrum suggesting a molecular motion about the two-fold axis of the molecule.

TOT / Pyridine-d₅

Figure 48: 27.6 MHz solid state ²H NMR spectra of TOT pyridine-d₅ as a function of temperature. The spectra were acquired with the quadrupolar echo pulse sequence.

Figure 49: Plots of potential energy vs in-plane rotation angle used in the discussion of the in-plane motion of pyridine in its TOT clathrate. A: One broad potential well allowing the pyridine molecule to undergo large scale in plane librations. B: A symmetric function with a minimum at 0° . This function can be obtained from the calculation given in appendix 4 if the angle, ϕ is assumed to be 0° . C: A symmetric function with a local maximum at 0° . This is derived in appendix 4.

Figure 50: Simulation of the solid state ^2H NMR spectrum of TOT / pyridine-d₅, using the computer program given in appendix 1. Four kHz of Gaussian broadening was applied to the simulated spectra. A: The spectrum of the four equivalent deuterons resulting from the pyridine molecule undergoing both an in plane libration and two-fold flips about the two-fold axis. B: The spectrum of the unique deuteron resulting from in plane libration. The spectrum of this deuteron is invariant to two-fold flips. C: Weighted sum of A and B. This spectrum resembles those measured at temperatures above 196 K.

CHAPTER SIX

Tri-*o*-thymotide Clathrates with Prochiral Guests

In chapter four, TOT clathrates of chiral molecules were examined and the TOT host was found to behave as a solid state chiral chemical shift reagent. Another property of chiral chemical shift reagents is that they are able to make the enantiotopic chemical groups of prochiral molecules distinguishable from one another.^{139,177,178} Such groups are indistinguishable in racemic or achiral environments. In this chapter several TOT clathrates of prochiral molecules containing enantiotopic methyl groups are examined by ^{13}C CP/MAS and solid state ^2H NMR.

Before proceeding, it is perhaps a good idea to define a few terms that are used throughout this chapter. *Prochiral centres* are tetrahedral centres containing two identical ligands and two other nonidentical ligands.¹⁷⁹ Thus, the P atom of compounds with the general formula $\text{R}_2\text{-P}\cdot(\text{X})(\text{Y})$ is a prochiral centre. The identical ligands, R, attached to the prochiral centre are referred to as *prochiral groups*. Prochiral groups can be either *enantiotopic* or *diastereotopic*. If a molecular plane of symmetry, σ , bisecting the R-P-R bond angle exists, then the groups are enantiotopic otherwise they are diastereotopic. Enantiotopic groups are chemical

shift equivalent, or *isochronous*, in achiral or racemic media, whereas diastereotopic groups are chemical shift inequivalent, or *anisochronous*, in all media. The chemical shift difference between prochiral groups is often very small and it is not unusual for the resonances to be unresolved.¹³⁹

The above definitions work well for molecules with prochiral centres, however, the concept of enantiotopic and diastereotopic groups can be applied in a more general way to groups not attached to a common atom. Mislow and Raban¹⁷⁸ have generalized the definition of prochirality to include molecules containing non-geminal groups. They have applied a substitution test to determine the relationship between intramolecular groups. One of the two groups in question is replaced by an achiral test group, not already present in the molecule. This gives a new molecule. The substitution is repeated for the other group in question on the original molecule and the *intermolecular* relationship between the two resultant molecules is examined. If the two molecules are identical then the groups in question are *homotopic* (i.e. symmetrically equivalent). If they are enantiomers of one another then the groups are enantiotopic and if they are diastereomers of one another then the groups are diastereotopic. As with geminal groups on prochiral centres, diastereotopic groups, in general, are anisochronous under all circumstances. Enantiotopic groups are anisochronous only in a chiral environment.

I. TOT / *cis*-2,3-Epoxybutane

cis-2,3-Epoxybutane contains two chemically equivalent chiral centres of opposite absolute configuration and therefore, on the whole, does not exhibit any

optical activity. It contains no prochiral centres. When the substitution test of Mislow and Raban¹⁷⁸ is applied to this molecule, one finds that the methyl groups are enantiotopic. They should, therefore, be isochronous in an achiral or racemic environment and anisochronous in a chiral environment. A conventional ^{13}C high resolution spectrum of *cis*-2,3-epoxybutane in CDCl_3 was obtained. The methyl resonance appeared as a singlet at 12.9 ppm. The oxygen bearing carbon resonance appeared at 52.6 ppm. The ^{13}C CP/MAS NMR spectrum of TOT / *cis*-2,3-epoxybutane is shown in figure 51. The resonance of the oxygen bearing carbons appears as a singlet at 52.4 ppm while the methyl resonance appears as a doublet centred at 13.0 ppm. The separation between the components of the doublet is 1.1 ppm. The chemical shift differences between the resonances of the enclathrated and dissolved molecules is very small. A spectrum of the TOT clathrate was also obtained under dipolar dephasing conditions. The resonance of the oxygen bearing carbon atoms was completely absent. This indicates that the molecule does not undergo a molecular motion capable of averaging the static ^{13}C - ^1H dipolar interactions. The methyl resonances of the guest were present with reduced intensity.

In the case of the TOT clathrate of 2-bromobutane the chemical shift difference between the components of the observed doublets was found to be due to the different conformations of the favoured and unfavoured enantiomers (see chapter four). *cis*-2,3-Epoxybutane is neither a chiral molecule, nor does it have any freedom to adopt different conformations. The doublet arises because the

enantiotopic methyl groups are in a chiral environment and are therefore anisochronous for symmetry reasons. The molecule adopts an orientation in the cage which places each of the methyl groups in a different environment. This is not unreasonable since the two-fold symmetry of the cage is not present in the guest molecule. More will be said about this clathrate, and its reactivity towards HBr, in chapter eight.

II. TOT / 2-Chloropropane.

2-Chloropropane has a prochiral centre on which two methyl groups are attached. When the substitution test of Mislow and Raban¹⁷⁸ is performed, it is easy to verify that the methyl groups are enantiotopic. The conventional ¹³C high resolution NMR spectrum has been reported.¹⁴⁵ The resonance of the methyl groups is a singlet at 26.85 ppm. The chlorine bearing carbon resonance appears at 53.75 ppm. The ¹³C CP/MAS NMR spectrum of the TOT clathrate is shown in figure 52 under standard (52 A) and dipolar dephased (52 B) conditions. The resonance of the chlorine bearing carbon appears at 56.7 ppm in figure 52 A and the resonance of the methyl groups appears as a 1:1 doublet centred at 27.4 ppm. The separation between the components of the doublet is 0.4 ppm. The difference between the chemical shifts for the liquid and enclathrated species may be due to small differences in bond properties or crystal packing forces. The chemical shift difference between the enantiotopic methyl groups of the guest in the TOT clathrate arises because of the chiral environment surrounding the molecule. In the dipolar dephased spectrum the C2 resonance of the guest is absent, indicating that the

enantiotopic methyl groups are in a chiral environment and are therefore anisochronous for symmetry reasons. The molecule adopts an orientation in the cage which places each of the methyl groups in a different environment. This is not unreasonable since the two-fold symmetry of the cage is not present in the guest molecule. More will be said about this clathrate, and its reactivity towards HBr, in chapter eight.

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molecule is undergoing little molecular motion capable of averaging the static ^{13}C - ^1H dipolar interaction at the C2 position. It is interesting to note that the ratio of intensities for the methyl group doublet, in the dipolar dephased spectrum, is not 1:1. This indicates that the ^{13}C - ^1H dipolar interactions must be different for each of the two methyl groups. Aside from the expected 3-fold methyl group rotation,¹⁸⁵ there must be another whole body molecular motion which treats each of the methyl groups differently but does not significantly average the ^{13}C - ^1H dipolar interaction at the C2 position.

III. TOT / 2-Bromopropane

2-Bromopropane can be thought of in exactly the same way as 2-chloropropane. The methyl groups are enantiotopic and are expected to give rise to their own separate ^{13}C NMR resonances while within the chiral cages of TOT. The ^{13}C CP/MAS NMR spectrum of TOT / 2-bromopropane is shown in figure 53 under standard (53 A) and dipolar dephasing conditions (53 B). The resonance of the bromine bearing carbon atom appears at 49.4 ppm while the methyl resonance appears as a 1:1 doublet centred at 28.9 ppm. The difference in chemical shift between the components of the doublet is 0.4 ppm. These chemical shifts should be compared to those reported for the liquid;¹⁴⁵ 44.05 ppm for the bromine bearing carbon and 28.05 ppm for the methyl groups. The differences in the chemical shifts between the liquid and enclathrated species may again be attributed to slight differences in bond parameters or crystal packing forces. As was the case for the TOT / 2-chloropropane clathrate, the resonance of the C2 carbon of enclathrated

2-bromopropane is absent in the dipolar dephased spectrum. This indicates that the motion of the C2 carbon must be limited, such that the static ^{13}C - ^1H dipolar interaction is not significantly averaged. The ratio of intensities in the methyl doublet remains approximately 1:1 in the dipolar dephased spectrum.

In order to further characterize the molecular motion a TOT clathrate was prepared from methyl deuterated 2-bromopropane. The details of the labelling and sample preparation are given in chapter three. The ^{13}C CP/MAS NMR spectrum of the clathrate is shown in figure 54 under standard and dipolar dephasing conditions. The chemical shift of the bromine bearing carbon is 49.1 ppm, 0.3 ppm upfield compared to that of the unlabelled guest. Such isotope shifts are not uncommon.^{39,180-184} The resonance of the CD_3 groups appears as a single broad absorption due to the dipolar interaction between ^{13}C and ^2H . As was the case for the unlabelled material, the C2 resonance is absent in the dipolar dephased spectrum.

Solid state ^2H NMR spectra were recorded for this material as a function of temperature. The spectra are shown in figure 55. They consist of two overlapping powder spectra in a 1:1 intensity ratio. Those recorded at temperatures greater than 191 K can be well represented by simulations of fast motional limit spectra. Simulations were carried out using the computer program given in appendix 1. The frequency separations between the features for each component of the fast motional limit spectra are given in table 14 and plotted in figure 56. The spectrum obtained at 77 K indicates that the methyl groups are nearly rigid on the μsec time scale and

Table 14

^2H NMR Frequency Separations for TOT / 2-Bromopropane-(1,3-d_6) as a Function of Temperature						
Temperature (K)	Methyl Group 1 Splittings (kHz) ± 1.0 kHz			Methyl Group 2 Splittings (kHz) ± 1.0 kHz		
77	128	a	a	128	a	a
191	11.7	27.3	39.0	26.1	38.3	64.4
201	8.9	30.7	39.6	24.2	37.1	61.3
213	7.5	30.0	37.5	23.6	35.4	59.0
222	5.6	30.5	36.1	22.5	35.2	57.7
233	3.6	30.7	34.3	21.4	32.8	54.2
244	1.4	32.3	37.7	19.4	33.0	52.4
254	0	33.0	33.0	19.4	31.0	50.4
264	0	33.0	33.0	18.1	29.5	47.6
274	1.4	33.6	35.0	17.2	28.7	45.9
284	3.3	26.7	30.0	16.6	27.7	44.3
298	5.3	27.8	33.1	15.3	26.6	41.9
316	5.8	24.7	30.5	14.7	24.5	39.2
327	6.7	23.1	29.8	14.2	21.7	35.9
336	7.8	24.0	31.8	13.6	22.2	35.8
347	7.8	23.4	31.2	13.6	21.7	35.3
360	7.8	21.6	29.4	12.8	19.2	32.0
370	7.8	20.1	27.9	12.8	18.4	31.2

a: This spectrum had either a zero or a very small asymmetry parameter. The inner splitting was 128 kHz. The signal to noise ratio was not sufficient to determine the separation between the shoulders or the asymmetry parameter. The frequency separation was measured directly from the spectrum.

have similar quadrupolar coupling constants. Between 77 K and 191 K the molecules are undergoing motions in the intermediate regime ($\sim 10^5$ Hz). This motion could be 3-fold methyl rotations, a whole body molecular motion or a combination of the two. In the fast motional regime ($T > 191$ K), the methyl groups have different degrees of molecular motion giving rise to different ^2H NMR spectra. The mechanism of this motion is not obvious. Each of the two component spectra is narrower than that expected for a simple fast methyl group rotation.¹⁶⁵ Both components have large asymmetry parameters and exhibit a large temperature dependence. The methyl groups are undoubtedly undergoing fast 3-fold rotation as well as a whole body molecular motion. If an analogy is drawn to the cases where the guest molecules possess 2-fold symmetry, (see chapter five), then it would be a reasonable guess that the 2-bromopropane molecule may be rotating about the two-fold axis of the TOT cavity. Such a motion would leave the methyl groups inequivalent to one another in all cases except when the two-fold axis of the cage bisects the C-C-C bond of the guest. The variation in the spectra with temperature may result from the guest molecule adopting different average orientations at different temperatures or from large scale librations. Whatever the motion, it does not average the ^{13}C - ^1H dipolar interaction at the C2 position to any appreciable extent at room temperature. A precise description of the molecular orientation and mechanism for the motion cannot be obtained from this data alone. An X-ray crystal structure would provide a good starting point for the analysis, as it may give

some information regarding the orientation of the guest molecule with respect to the clathrate cage.

IV. TOT / 2-Propanol

The 2-halopropanes have spherically symmetric substituents on the C2 position and when the substitution test of Mislow and Raban¹⁷⁸ is performed, the methyl groups are found to be enantiotopic. The same can be said of 2-propanol, if the hydroxyl group is rotating rapidly about the C-O bond or if the H-O-C-H torsion angle is either 0° or 180°. If the hydroxyl group is fixed into only a single orientation where the H-O-C-H torsion angle is neither 0° nor 180°, then the methyl groups are diastereotopic. In either case the ¹³C resonances of the methyl groups are expected to be anisochronous in the TOT cavity. Since the TOT cage is lined primarily with alkyl protons and guest-guest interactions are expected to be small, it is reasonable to assume that no hydrogen bonding would be possible.¹¹⁹ Without hydrogen bonding the -OH group is not expected to be locked into a single conformation. More likely, it would have a great deal of rotational freedom, as was observed for the TOT enclathrated 2-butanol (see chapter 4). In the gas phase, the barrier to rotation about the C-O bond has been reported to be 7.0 kJ/mol.¹⁸⁶ The motional freedom of the hydroxyl group makes the methyl groups enantiotopic.

The TOT / 2-propanol clathrate was prepared as described in chapter three. The ¹³C CP/MAS NMR spectrum is shown in figure 57 under standard (57 A) and dipolar dephasing (57 B) conditions. The resonance of the C2 carbon is a singlet having a chemical shift value of 63.4 ppm while the methyl resonance is a doublet

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centred at 26.3 ppm. The splitting between the two components of the doublet is 0.2 ppm. The ^{13}C chemical shift values reported for liquid 2-propanol are 63.4 ppm for the C2 carbon and 25.1 ppm for the methyl carbons.¹⁴⁵ The chemical shift differences between the liquid and enclathrated molecules are quite small. Unlike the TOT clathrates of the 2-halopropanes, the C2 resonance of enclathrated 2-propanol is present in the dipolar dephased spectrum. This indicates that the guest molecule undergoes a molecular motion capable of averaging the static ^{13}C - ^1H dipolar interaction at the C2 position. The molecular motion is, therefore, different than that occurring in the TOT / 2-halopropane clathrates. It should be noted that this is similar to the behaviour observed for the analogous 2-substituted butanes (see chapter four).

In order to learn more about the molecular motion, the TOT clathrate of 2-propanol-(1,3- d_6) was prepared. The ^{13}C CP/MAS spectrum was obtained under standard and dipolar dephasing conditions (figure 58). The C2 resonance appears in both spectra at 63.2 ppm. The isotope shift is 0.2 ppm upfield from that of the unlabelled guest. The methyl resonances appear as a single broad absorption due to the ^2H - ^{13}C dipolar interaction.

Solid state ^2H NMR spectra were recorded for the 2-propanol-(1,3- d_6) clathrate as a function of temperature. The spectra are shown in figure 59. The spectrum acquired at 77 K is typical of rigid C-D bonds. It consists of a single powder spectrum, indicating that deuterons of both methyl groups have similar quadrupolar coupling constants. Each spectrum, acquired above 171 K, is the sum

Table 15

¹H NMR Frequency Separations for TOT / 2-Propanol-(1,3-d₆) as a Function of Temperature						
Temperature (K)	Methyl Group 1 Splittings (kHz) ± 1.0 kHz			Methyl Group 2 Splittings (kHz) ± 1.0 kHz		
77	122	a	a	122	a	a
171	5.2	17.0	22.2	14.0	16.0	30.0
192	5.1	16.1	21.2	12.7	14.3	27.0
213	5.1	14.9	20.0	10.7	15.1	25.8
224	5.1	14.9	20.0	9.9	15.0	24.9
233	4.8	14.0	18.8	8.4	14.9	23.3
253	4.2	13.9	18.1	7.0	14.5	21.5
274	4.2	14.0	18.2	4.4	16.2	20.6
298	b	b	b	b	b	b

a: This spectrum had either a zero or a very small asymmetry parameter. The inner splitting was 122 kHz. The signal to noise ratio was not sufficient to determine the separation between the shoulders or the asymmetry parameter. The frequency separation was measured directly from the spectrum.

b: The spectrum acquired at room temperature was in the fast motional limit but was not simulated because of a large spike due to excess solvent.

of two component spectra in a 1:1 intensity ratio. These can be well represented by simulations of fast motional limit spectra. Simulations were carried out using the computer program given in appendix 1. The frequency separations between the features in each of the components of the fast motional limit spectra are given in table 15 and plotted in figure 60. The methyl groups on each molecule are treated differently by the molecular motion. All of the spectra are narrower than that

expected for a simple fast methyl group rotation¹⁶⁵ and have a large temperature dependence. The spectra acquired at temperatures above 171 K are undoubtedly determined by a fast methyl group rotation as well as another fast molecular motion superimposed. Typical barriers to methyl group rotation in the gas phase are between 5 and 13 kJ/mol.¹⁸⁷ Below 171 K, one or more motions must occur at a rate comparable to the time scale of the experiment ($\sim 10^5$ Hz).

The ^2H NMR spectra of TOT / 2-propanol-(1,3- d_6) are much narrower than those of TOT / 2-bromopropane-(1,3- d_6), suggesting that the alcohol has much more motional freedom inside the TOT cages than the bromide. These observations parallel those made in the ^2H NMR data collected for the clathrates of the sec-butyl analogues (see chapter four). Perhaps the presence of the large, massive bromine atom restricts the motion of the molecule. The -OH group is much lighter in comparison. More experiments are required to establish the details of the molecular motions occurring. The important conclusion is that both ^{13}C CP/MAS and ^2H NMR can be used to discriminate between the enantiotopic methyl groups in the molecule.

V. TOT / Dimethylsulfoxide.

Although dimethylsulfoxide does not have four substituents on its central atom, it is still similar in geometry to the isopropyl compounds discussed above. When the substitution test of Mislow and Raban¹⁷⁸ is carried out, one sees that the two methyl groups are indeed enantiotopic. Therefore, TOT enclathrated dimethylsulfoxide is expected to have two anisochronous methyl ^{13}C NMR resonances. Figure 61 shows

the ^{13}C CP/MAS NMR spectrum of TOT / dimethylsulfoxide under standard and dipolar dephasing conditions. Unlike all of the other examples presented, the methyl resonance does not appear as a doublet. It is a very sharp singlet at 41.1 ppm (the chemical shift of neat liquid is 40.80 ppm ¹⁴⁵). The chemical shift difference between the methyl resonances must therefore be too small to observe. The methyl resonance is still present in the dipolar dephased spectrum due to the reduced ^{13}C - ^1H dipolar interaction resulting from methyl group rotation.

The TOT / dimethylsulfoxide- d_6 clathrate was prepared by recrystallization. Solid state ^2H NMR spectra were acquired as a function of temperature. A sample of the spectra are shown in figure 62. The spectrum acquired at 77 K is characteristic of rigid C-D bonds. It consists of only one powder spectrum, therefore, the deuterons of the methyl groups have common quadrupolar coupling constants. Simulations show that the spectra acquired at temperatures above 179 K are in the fast motional limit and consist of superpositions of two component powder spectra in a 1:1 intensity ratio. The molecular motion responsible for the averaging must therefore treat each of the methyl groups differently. The methyl groups of dimethylsulfoxide have also been found to be inequivalent for the molecule trapped inside a clay mineral¹⁸⁸ and in the pure solid,¹⁸⁹⁻¹⁹¹ due to crystal packing effects. The spectra are narrower than those expected for a fast methyl group rotation.¹⁶⁵ They also have large asymmetry parameters. The barrier to methyl group rotation for dimethyl sulfoxide has been measured to be 11.9 and 12.8 kJ/mol in the gas phase.^{192,193} Below 179 K, at least one of the molecular motions

Table 16

^2H NMR Frequency Separations for TOT / Dimethylsulfoxide-d_6 as a Function of Temperature						
Temperature (K)	Methyl Group 1 Splittings (kHz) ± 1.0 kHz			Methyl Group 2 Splittings (kHz) ± 1.0 kHz		
77	122	a	a	122	a	a
179	9.6	40.8	50.4	15.2	42.4	57.6
199	9.6	40.8	50.4	15.2	42.4	57.6
212	11.3	40.6	51.9	14.7	42.9	57.6
220	9.6	40.0	49.6	13.6	42.4	56.0
233	11.3	39.5	50.8	13.5	41.8	55.3
242	9.6	40.0	49.6	14.4	41.6	56.0
253	10.2	39.5	49.7	13.5	40.6	54.2
263	10.4	38.4	48.8	12.8	40.0	52.8
272	10.2	38.4	48.6	13.5	39.5	53.0
283	9.6	36.8	46.4	12.8	39.2	52.0
298	9.6	37.6	47.2	12.8	37.6	50.4
a: This spectrum had either a zero or a very small asymmetry parameter. The signal to noise ratio was not sufficient to determine the separation between the shoulders or the asymmetry parameter. The frequency separation was measured directly from the spectrum.						

responsible for the spectral averaging is occurring at a rate comparable to the timescale of the quadrupolar echo experiment ($\sim 10^5$ Hz). The parameters for each of the components of the fast motional spectra ($T \geq 179$ K) were measured directly from the experimental data and are given in table 16 and plotted in figure 63. Unlike the ^2H NMR spectra of the isopropyl compounds, these spectra do not

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exhibit a large temperature dependence. This is typical for molecules in the fast motional regime with little librational motion. The spectral components are not unlike those observed for TOT / acetone- d_6 which was found to undergo fast methyl group rotation and two-fold flips about both the carbonyl bond of the guest and the coincident 2-fold axis of the TOT cavity (see chapter five). Unlike acetone, the dimethylsulfoxide may adopt an orientation inside the cage such that the two-fold cavity axis does not bisect the C-S-C bond. The molecule may then be free to undergo two-fold flips about the two-fold axis of the cage. This type of motion would treat each of the methyl groups differently. Since the components of the observed spectra do not have large differences, one can imagine that the two-fold cage axis is not far off the C-S-C bisector. An X-ray crystal structure may confirm this model.

From the above discussion it has been shown that solid state NMR is able to differentiate between the enantiotopic methyl groups of TOT enclathrated prochiral molecules. In this respect, tri-*o*-thymotide behaves as either a "solid state chiral solvent" or a "solid state chiral chemical shift reagent". In some cases, where the ^{13}C NMR data are unable to resolve the enantiotopic methyl groups, due to small chemical shift differences, ^2H NMR experiments can reveal the inequivalence.

TOT / *cis*-2,3-Epoxybutane

Figure 51: Partial ^{13}C CP/MAS NMR spectrum of TOT / *cis*-2,3-epoxybutane with first order spinning sidebands suppressed.⁸⁰ The resonances marked with asterisks are those of the guest. The $\pi/2$ pulse length was 3.8 μsec . 3 msec was used as a contact time with a 2 sec repetition time.

TOT / 2-Chloropropane

Figure 52: Partial ^{13}C CP/MAS NMR spectrum of TOT / 2-chloropropane with first order spinning sidebands suppressed.⁸⁰ A: under standard conditions and, B: under dipolar dephasing conditions using a dipolar dephasing time of $40\ \mu\text{sec}$. The resonances marked with asterisks are those of the guest. The $\pi/2$ pulse length was $3.8\ \mu\text{sec}$. 3 msec was used as a contact time with a 1 sec repetition time.

TOT / 2-Bromopropane

Figure 53: Partial ^{13}C CP/MAS NMR spectrum of TOT / 2-bromopropane with first order spinning sidebands suppressed.⁸⁰ A: under standard conditions and, B: under dipolar dephasing conditions using a dipolar dephasing time of 40 μsec . The resonances marked with asterisks are those of the guest. The $\pi/2$ pulse length was 3.8 μsec . 3 msec was used as a contact time with a 1 sec repetition time.

TOT / 2-Bromopropane-(1,3-d₆)

Figure 54: Partial ^{13}C CP/MAS NMR spectrum of TOT / 2-bromopropane-(1,3-d₆) with first order spinning sidebands suppressed.⁸⁰ A: under standard conditions and, B: under dipolar dephasing conditions using a dipolar dephasing time of 40 μsec . The resonances marked with asterisks are those of the guest. The $\pi/2$ pulse length was 3.8 μsec . 3 msec was used as a contact time with a 1 sec repetition time.

TOT / 2-Bromopropane-(1,3-d₆)¹⁷⁹

Figure 55: Solid state ²H NMR spectra of TOT / 2-bromopropane-(1,3-d₆) as a function of temperature. The quadrupolar echo pulse sequence was used with $\pi/2$ pulse lengths of 3.5 μ sec. The delay between pulses was set at 35 μ sec. The repetition time was 2 sec in all cases except for the spectrum collected at 77 K, where a 10 sec delay was used. The parameters of the simulations are given in table 14. Note the difference in scale for the spectrum acquired at 77 K.

TOT / 2-Bromopropane-(1,3-d₆)

Figure 56: Plot of the frequency separations in the fast motional limit ²H NMR spectra of TOT / 2-bromopropane-(1,3-d₆) as a function of temperature. A and B represent the inequivalent methyl groups.

TOT / 2-Propanol

Figure 57: Partial ^{13}C CP/MAS NMR spectrum of TOT / 2-propanol with first order spinning sidebands suppressed.⁸⁰ A: under standard conditions and, B: under dipolar dephasing conditions using a dipolar dephasing time of $40\ \mu\text{sec}$. The resonances marked with asterisks are those of the guest. The insets are expansions of the alkyl regions of the spectra, used to show the methyl group doublet resulting from the guest. The $\pi/2$ pulse length was $3.8\ \mu\text{sec}$. 3 msec was used as a contact time with a 2 sec repetition time.

TOT / 2-propanol-(1,3-d₆)

Figure 58: Partial ^{13}C CP/MAS NMR spectrum of TOT / 2-propanol with first order spinning sidebands suppressed.⁸⁰ A: under standard conditions and, B: under dipolar dephasing conditions using a dipolar dephasing time of 40 μsec . The resonances marked with asterisks are those of the guest. The $\pi/2$ pulse length was 3.8 μsec . 3 msec was used as a contact time with a 3 sec repetition time.

Figure 59: Solid state ^2H NMR spectra of TOT / 2-propanol-(1,3-d₆) as a function of temperature. The quadrupolar echo pulse sequence was used with $\pi/2$ pulse lengths of 3.5 μsec . The delay between pulses was set at 35 μsec . The repetition time was 2 sec in all cases except for the spectrum collected at 77 K, where a 0.5 sec delay was used. The parameters of the simulations are given in table 15. The spectrum at 77 K is not expected to be fully relaxed however, it is of sufficient quality to show that the methyl groups are rigid on the time scale of the experiment. Note the difference in scale for the spectrum acquired at 77 K.

TOT / 2-Propanol-(1,3-d₆)

Figure 60: Plot of the frequency separations in the fast motional limit ²H NMR spectra of TOT / 2-propanol-(1,3-d₆) as a function of temperature. A and B represent the inequivalent methyl groups.

TOT / Dimethylsulfoxide

Figure 61: ^{13}C CP/MAS NMR spectrum of TOT / dimethylsulfoxide with first order spinning sidebands suppressed.⁸⁰ A: under standard conditions and, B: under dipolar dephasing conditions using a dipolar dephasing time of 40 μsec . The resonance marked with an asterisk is due to the methyl groups of the guest. The $\pi/2$ pulse length was 3.8 μsec . 3 msec was used as a contact time with a 3 sec repetition time.

Figure 62: Solid state ^2H NMR spectra of TOT / dimethylsulfoxide- d_6 as a function of temperature. The quadrupolar echo pulse sequence was used with $\pi/2$ pulse lengths of $3.5 \mu\text{sec}$. The delay between pulses was set at $35 \mu\text{sec}$. The repetition time was 2 sec. The parameters of the simulations are given in table 16. Note the difference in scale for the spectrum acquired at 77 K.

Figure 63: Plot of the frequency separations in the fast motional limit ^2H NMR spectra of TOT / dimethylsulfoxide- d_6 as a function of temperature. A and B represent the inequivalent methyl groups.

CHAPTER SEVEN

TOT / Chlorocyclohexane

It has been shown, for the case of TOT / 2-bromobutane (see chapter four), that flexible molecules may adopt unusual conformations while trapped in confined spaces. This is also true of chlorocyclohexane in its thiourea inclusion compound^{194,195} where it prefers an axial rather than the otherwise preferred equatorial conformation. In this chapter the tri-*o*-thymotide clathrate of chlorocyclohexane is examined by ¹³C CP/MAS NMR. The data will be used to learn more about the conformation and dynamic state of the guest.

The X-ray crystal structure and infrared spectrum of the TOT / chlorocyclohexane clathrate have been reported.¹¹² The clathrate is a typical host:guest = 2:1, *P*3₁21 cage clathrate with six host molecules per unit cell. The equatorial chair conformation, which is thermodynamically favoured in solution, was not observed inside the clathrate cage. Its absence has been justified by comparing the Van der Waals volume of the molecule to the accessible volume of the TOT cage. The equatorial chair is simply too large. The axial chair and axial boat, on the other hand, are very close fits. The authors concluded that the guest took on both an axial chair and an axial boat conformation in a 2:1 population ratio. This

conclusion was supported by the refinement of the X-ray data (based on rigid guests), infrared data, and force field calculations. There are a number of problems with interpreting such data. First of all, the refinement of the X-ray data required the initial assumption of both guest conformations in the 2:1 population ratio. There is no way of knowing that the refined conformations of the guest or their population ratio are unique. Secondly, since the axial boat conformation has never been observed by infrared spectroscopy, it is risky to assign specific conformations of the TOT enclathrated guest based on the infrared data. Finally, force field calculations often converge at any one of many local energy minima,¹⁴⁹ especially for such a complex system. Like the X-ray data refinement these calculations also rely on the geometry of the guest as input.

With hopes of alleviating some of the ambiguity associated with this clathrate a variable temperature ^{13}C CP/MAS NMR study was carried out. Since it has been demonstrated that ^{13}C chemical shifts are very sensitive to molecular conformation, (see chapter four) one would expect that the chemical shift values for the carbon atoms of the axial conformers be quite different compared to those of the equatorial chair conformation reported in solution. If both the axial chair and boat conformations of the molecule are indeed present in the clathrate cages, are they in dynamic equilibrium with one another or are they present with static disorder? In the former case one might expect to see dynamic effects in the ^{13}C CP/MAS NMR spectrum provided that the interconversion rate is on the order of tens of microseconds.⁹² In the latter case one would expect to see two distinct sets of

resonances for the guest whose intensity ratio agrees with that reported previously.¹¹² The spectra are shown in figure 64. The guest resonances changed dramatically with temperature while the resonances of the host (not shown in the figure) were unchanged. The observed chemical shifts at room temperature are given in table 17 and compared to those measured by others.^{195,196} Since a variable contact time experiment was not carried out, it is not known whether or not the integrated intensities of the resonances are reliable.

Table 17

¹³ C Chemical Shift Values for Chlorocyclohexane				
	Equatorial Chair ¹⁹⁶	Axial Chair ¹⁹⁶	Thiourea Inclusion Compound ¹⁹⁵	TOT Clathrate ^{a, b}
C1	60.3	61.4	-	62.5
C2, C6	38.1	34.4	35.4	42.5
C3, C5	27.4	20.9	21.8	33.8 ^c
C4	25.7	26.5	27.0	28.7

a: These assignments are tentative.

b: Shifts reported for the spectrum acquired at room temperature.

c: This resonance appeared as a doublet at temperatures below 260 K.

The chlorine bearing carbon (C1) is present in the spectrum, unbroadened by the chlorine-carbon dipole-dipole interaction. This is another example of self decoupling^{93b} as was observed for the TOT clathrates of the other halogenated guests (see chapters four and six). It is not possible to tell whether all of the guest resonances are visible in the spectrum. Some may be masked by the resonances of the TOT host. This possibility hinders a complete assignment of the peaks. One

can see, however, that the observed chemical shift values for the carbon atoms of the guest are quite different than those of chlorocyclohexane in either the equatorial or axial chair conformations. This seems to suggest that neither of these two conformations is present in a rigid state, and since the observed resonances do not lie between those expected for the axial and equatorial chairs, it is doubtful that a fast dynamic equilibrium exists between them. The fact that the observed chemical shift values are unusual may give support for the existence of the axial boat conformation whose chemical shifts have never been reported.

It is obvious from the spectra that some sort of dynamic processes are occurring. The C1 resonance of the chlorocyclohexane is sharp at low temperatures. As the temperature is increased it broadens and "fades out" at ~ 320 K. At higher temperatures it reappears. This behaviour is typical of a dynamic process.⁹² The correlation time of the process at the fade out point is of the order of the reciprocal decoupler field strength ($\sim 10^{-5}$ sec.). The resonance at 33.8 ppm shows similar behaviour, however, in this case the resonance is a doublet at low temperatures. Since both the C1 resonance and the resonance at 33.8 ppm fade out at the same temperature, their behaviour must be the result of the same dynamic process. The origin of the doublet, however, is in question. It may be the result two different conformations of the guest in slow exchange with one another. It may also reflect the inequivalence between the C3 and C5 enantiotopic carbon atoms of a single mobile conformation in the chiral TOT cage. The doubling in this case would be analogous to that observed for the enantiotopic methyl groups of the isopropyl TOT

guests studied in chapter six. At temperatures well above the fade out region, it is not known whether or not the doublet reappears.

There appears to be a second dynamic process causing line broadening in both the resonances at 42.5 and 28.7 ppm. These resonances are quite sharp at high temperatures and broaden out at lower temperatures. Spectra acquired at temperatures low enough to observe a complete fade out were not obtained. This process must have a shorter correlation time than the one discussed above.

In light of all the available information one can only say that a complete description of TOT enclathrated chlorocyclohexane is very complicated. The solid state ^{13}C NMR results show unusual chemical shifts and provide evidence for the existence of at least two different dynamic processes. The X-ray and infrared data point to the existence of more than one conformation. Much more experimentation is needed to provide a detailed description of this very complicated system.

Figure 64: Partial ^{13}C CP/MAS NMR spectra of TOT / chlorocyclohexane as a function of temperature. The pulse sequence described in reference 80 was used to suppress the first order spinning sidebands. The $\pi/2$ pulses were $3.8\ \mu\text{sec.}$ in duration, the delay time between acquisitions was 2 sec. and the contact time was 3 msec.

CHAPTER EIGHT

Chemical Reactions of Guest Molecules in Tri-*o*-thymotide Clathrates

The four previous chapters dealt with the orientation and molecular motion of guest molecules in the cages of tri-*o*-thymotide clathrates. In this chapter, the chemical behaviour of a few enclathrated guests is explored. Only a handful of such studies have been published.^{115,119,120,127,130,138} These were introduced in chapter two. The chemical reactions of TOT enclathrated *cis*-2,3-epoxybutane, (2*R*,3*R*)(2*S*,3*S*)-*trans*-2,3-epoxybutane and cyclohexene oxide with HBr gas are examined here using ¹³C CP/MAS NMR. These experiments not only provide information about the identity of the product but may also indicate whether or not a significant change occurs in the TOT host.

I. TOT / *cis*-2,3-Epoxybutane.

The reaction of TOT / *cis*-2,3-epoxybutane with HBr has been studied by Gerdil and Barchietto.¹³⁰ Crushed crystals of M(-) TOT / *cis*-2,3-epoxybutane were exposed to HBr gas. After reaction, the volatile guest material was pumped off at high temperature and collected in a liquid nitrogen trap, then analyzed. It was identified as 3-buten-2-ol (98 %). The HBr, therefore, behaved as a catalyst for the

rearrangement of the epoxybutane. Traces of 3-bromo-2-butanol were also detected. Polarimetric measurements showed that the 3-buten-2-ol contained more of the (*R*) than the (*S*) enantiomer (*ee*=5%) suggesting that the chirality of the host had an influence on the chirality of the reaction product. A concerted reaction mechanism was proposed where the proton of the HBr molecule adds to the oxygen of the *cis*-2,3-epoxybutane, breaking both the C-O and the H-Br bonds. The bromide abstracts a proton from one of the methyl groups to reform an HBr molecule and a C=C double bond is formed in the product (see figure 65).

This study shows that an unusual reaction occurs. The expected reaction product in solution, under acidic conditions, is 3-bromo-2-butanol.¹⁷³ Only under extremely basic conditions is 3-buten-2-ol the principal reaction product.¹⁷⁴⁻¹⁷⁵ The question as to whether or not the reaction occurs at ambient temperature inside the clathrate cage must be addressed. Perhaps the very extreme conditions used in the desolvation process provide a suitable environment for the observed reaction. This question is conveniently answered by monitoring the progress of the reaction with ¹³C CP/MAS NMR where extremes in temperature can be avoided entirely.

A powdered TOT clathrate of *cis*-2,3-epoxybutane, containing equal numbers of P(+) and M(-) crystallites, was prepared as described in chapter three. This material was placed in the apparatus shown in figure 66 and exposed to a stream of dry HBr gas for 15 minutes then flushed with He gas for ~ 30 seconds. The sample was removed from the apparatus and a ¹³C CP/MAS spectrum was obtained. After

acquisition of the spectrum, the sample was returned to the apparatus and the process repeated. The spectra are shown in figure 67.

The spectrum of the starting material (TOT / *cis*-2,3-epoxybutane) in figure 67A has a guest molecule resonance at 52.4 ppm, due to the ring carbons, and a doublet of resonances, due to the methyl carbons, centred at 13.0 ppm (see chapter six). As the reaction with HBr proceeds (figure 67B and 67C) new guest resonances at 67.6 and 112 ppm appear at the expense of the original ones. These are consistent with the C2 and C4 resonances of 3-buten-2-ol, respectively.¹⁷⁶ The C1 and C3 resonances are buried by the spectrum of the TOT host. On close inspection, it can be observed that the resonance at 112 ppm is actually an asymmetric doublet analogous to those observed for the C2 and C4 resonances of 2-bromobutane in its TOT clathrate. The asymmetry of the doublet indicates that, in any given TOT crystallite, there is a small enantiomeric excess of 3-buten-2-ol. Only minor changes in the spectrum of the TOT host are observed, indicating that the cage structure remains intact and that the spectra of the reactant and product clathrates are very similar.

The ¹³C CP/MAS spectra confirm the principal reaction product identified previously¹³⁰ as well as the small enantiomeric excess observed. Unfortunately, the resolution in the C4 doublet in the spectrum of the product, collected here, is not sufficient to allow a reliable quantitative measurement of the enantiomeric excess.

II. TOT / (2*R*,3*R*)(2*S*,3*S*)-*trans*-2,3-Epoxybutane.

The reaction of TOT / *trans*-2,3-epoxybutane with HBr gas has also been studied by others.¹³⁸ The starting material used was a powder consisting of 90-100 % M(-) TOT crystallites. M(-) TOT preferentially includes the (2*R*,3*R*) enantiomer with an enantiomeric excess of 47-55 %.^{110,120,138} After complete reaction, (the precise time was not reported) the product was isolated from the clathrate, analyzed and its optical rotation measured. The only reaction product reported was (2*R*,3*S*)-3-bromo-2-butanol which is the product expected in solution, under acidic conditions, for the reaction of (2*R*,3*R*)-*trans*-2,3-Epoxybutane with HBr.¹⁷³ The oxygen of the epoxide is protonated by the HBr, giving an intermediate with some cationic character. The intermediate undergoes a nucleophilic attack by the bromide, leaving a halohydrin (see figure 68). The same bromohydrin is expected regardless of which of the C-O epoxy bonds are broken. No mention was made of the (2*S*,3*R*) product expected from the reaction of the (2*S*,3*S*)-*trans*-2,3-epoxybutane present in the original sample. There is no direct evidence to suggest that the reaction occurs inside the clathrate cage. One possibility, not considered, is that the HBr may displace the original guest from the cage, allowing the reaction to occur outside of the clathrate. This hypothesis can be tested by monitoring the progress of the reaction with ¹³C CP/MAS NMR. If a liquid is present on the surface of the clathrate crystals, it is not expected to contribute to the spectrum as the cross polarization technique discriminates against it.

A powdered TOT clathrate of (2*R*,3*R*)(2*S*,3*S*)-*trans*-2,3-epoxybutane, containing equal numbers of P(+) and M(-) crystallites, was prepared as described in chapter three. The sample was exposed to a stream of HBr gas as described above. The ^{13}C CP/MAS NMR spectra used to monitor the progress of the reaction are shown in figure 69. Figure 69A shows the spectrum of the starting clathrate. The only visible resonance due to the *trans*-2,3-epoxybutane is that of the ring carbons appearing at 55.1 ppm. The resonance at 29.9 ppm is due to an acetone impurity which remained constant over the course of the reaction and did not contribute significantly to the spectrum of the host. Unfortunately, the methyl resonance of the *trans*-2,3-epoxybutane is obscured by the host spectrum. Although not visible, it is likely to consist of a doublet, analogous to that observed for the C4 methyl groups of TOT enclathrated 2-bromobutane. If such a doublet was visible, it would be possible to estimate the enantiomeric excess in exactly the same way it was for 2-bromobutane.

As the reaction with HBr gas proceeds new resonances appear at 60.1 ppm and 69.5 ppm. These may be assigned to the C3 and C2 carbons of 3-bromo-2-butanol, respectively. The NMR data alone, cannot confirm whether or not the product is the erythro, (2*R*,3*S*)(2*S*,3*R*) or threo, (2*R*,3*R*)(2*S*,3*S*) form. If the $\text{S}_{\text{N}}2$ mechanism is accepted, then only the erythro isomers are possible. Upon closer examination, one finds that the resonance at 69.5 ppm is actually an asymmetric doublet. If it is assumed that this doublet is analogous to those observed for the TOT / 2-bromobutane clathrate and that only the erythro isomers of the product are

formed, then it can be concluded that the enantiomeric excess of the 3-bromo-2-butanol is $51 \pm 10 \%$ based on the intensity ratio of the doublet. This agrees well with the enantiomeric excess reported for the *trans*-2,3-epoxybutane.^{110,120,138} The reaction of the enclathrated species can conveniently be represented as follows:

The reaction of TOT / *trans*-2,3-epoxybutane occurred much less readily than that of TOT / *cis*-2,3-epoxybutane. Even after 270 minutes of exposure to HBr gas the reaction was not complete, as can be seen from the mixture of guests present. The mixture of reactant and product clathrates not only shows up in the resonances of the guests but also in the spectrum of the TOT host (see figure 70). With a mixture of two clathrates, there is no question that the reaction does indeed occur within the clathrate cages and not on the surface of the crystallites. The HBr is able to penetrate the crystalline network. The slower reaction rate observed for the reaction of TOT / *trans*-2,3-epoxybutane with HBr compared to that of TOT / *cis*-2,3-epoxybutane may be related to the size of the reaction product. The 3-bromo-2-butanol is a much larger guest than 3-buten-2-ol and would not fit as well into the

clathrate cages. The extra energy required to accommodate the larger guest may be reflected in a higher activation barrier and hence a slower reaction rate.

III. TOT / Cyclohexene Oxide.

The reaction of M(-) TOT / cyclohexene oxide with HBr gas has also been studied by Gerdil and Barchietto.¹³⁰ The study was conducted in the same way as that described for M(-) TOT / *cis*-2,3-epoxybutane. They concluded that a reaction occurred in the clathrate cavity yielding 3-bromocyclohexene (% ee not measured) and (1*R*,2*R*)-*trans*-2-bromocyclohexanol (ee = 10 %). The ratio of these products was found to depend greatly on temperature. The ratios of 3-bromocyclohexene to *trans*-2-bromocyclohexanol were 88:12 and 5:95 at 30° C and -12° C, respectively. The mechanisms depicted in figure 71 were proposed. Again, however, the question as to whether or not the reactions occur inside the clathrate cage must be addressed.

A powdered sample of cyclohexene oxide, containing equal numbers of P(+) and M(-) crystallites was prepared as described in chapter three. As with the others, the progress of this reaction was followed by ¹³C CP/MAS NMR. The results are shown in figure 72. The spectrum of the pure reactant clathrate in figure 72A shows a single guest resonance at 52.2 ppm due to the oxygen bearing carbon atoms of the fused ring system. Presumably, the other resonances of the guest are obscured by the spectrum of the host. As the reaction proceeds, the guest resonance diminishes and no other guest resonances appear. In addition, the resonances of the host shift and broaden out significantly (figure 73). There are at least three possible explanations of these observations. First, a reaction may have occurred inside the

clathrate cavity producing a mixture of reaction products. The mixture of clathrates would account for the apparent broadening of the host spectrum. The fact that no new guest resonances appear may be explained if the guests are undergoing conformational changes inside the cages with correlation times of the order of the decoupling frequency.⁹² This type of behaviour was observed for the TOT clathrate of chlorocyclohexane (see chapter seven). Second, the HBr gas may have displaced the cyclohexene oxide from the cages and collapsed the clathrate structure, leaving a poorly ordered powder. Not having the local order of a crystalline clathrate, the spectrum of the powder is expected to be broad. The liquid on the surface of the solid may have reacted with the HBr. This, however would not show up in the ^{13}C CP/MAS NMR spectrum as the cross polarization technique discriminates against the liquid. Finally, a reaction may have occurred inside the cages yielding products too large to be accommodated by the clathrate. This would result in the destruction of the clathrate cages leaving a poorly ordered solid. Again, the liquid products on the surface of the solid would not contribute to the NMR spectrum.

In order to see whether or not a guest was present in the product, it was dissolved in CDCl_3 and a high resolution ^{13}C NMR spectrum was acquired. No resonances of significant intensity, other than those of the TOT were detected. This suggests that the clathrate cages were destroyed. The reaction products characterized by Gerdil and Barchietto¹³⁰ may have been on the surface of the solid.

The results described above for the three reactions show, unambiguously, that HBr gas is able to penetrate the TOT cage network. In some cases, chemical

reactions are able to occur inside the TOT cages. These can be conveniently followed by ^{13}C CP/MAS NMR. Chemical reactions, with HBr gas, were observed to occur in the TOT clathrates of *cis* and *trans* 2,3-epoxybutane with chiral reaction products. In the case of TOT / *cis*-2,3-epoxybutane, the chirality of the reaction product, was influenced by the chirality of the host. It is surprising that the reaction products of the enclathrated *cis* and *trans* 2,3-epoxybutanes, with HBr, are so different. With the symmetry differences in the two reactant guests, it is easy to imagine that each will have a different orientation in the TOT cages. The products of the reaction must depend on the orientation of the original guests in the clathrate cages, as well as the available space to accommodate the in-coming HBr molecule. The rates of these reactions may depend on the size and shape of the product guest molecules. For the case of the cyclohexene oxide clathrate, no chemical reaction was directly observed inside the cage. The reason for this may possibly be that there is not enough room in the TOT cage to accommodate both reactant molecules or the large reaction products. The cage must therefore be destroyed, leaving a poorly ordered powder unable to hold a guest.

Figure 65: The reaction mechanism proposed by Gerdil and Barchietta¹³⁰ for the formation of 3-buten-2-ol from TOT enclathrated *cis*-2,3-epoxybutane. The configuration of the reaction product depends on which of the C-O bonds is cleaved.

Figure 66: The apparatus used to expose the solid clathrates to HBr gas.

Figure 67: (a): Solid state ^{13}C CP/MAS NMR spectrum of TOT / *cis*-2,3-epoxybutane. (b) and (c): Spectra acquired after the clathrate in (a) was exposed to HBr gas for 15 and 120 minutes, respectively. The spectra were acquired using the pulse sequence described in reference 80 to suppress first order spinning sidebands. The 90° pulse length was $3.8\ \mu\text{sec}$. Contact times of 3 msec were used. The repetition time was 2 sec.

Figure 68: The accepted mechanism of reaction for the cleavage of an epoxide ring under acidic conditions in solution. The oxygen is first protonated, giving the intermediate some cationic character, then one of the ring carbons undergoes nucleophilic attack. For this reaction, the chirality of the product depends on the chirality of the reactant.

Figure 69: (a): Solid state ^{13}C CP/MAS NMR spectrum of TOT / *trans*-2,3-epoxybutane. (b) - (e): Spectra acquired after the clathrate in (a) was exposed to HBr gas for 90, 150, 210 and 270 minutes, respectively. The spectra were acquired using the pulse sequence described in reference 80 to suppress first order spinning sidebands. The 90° pulse length was $3.8\ \mu\text{sec}$. Contact times of 3 msec were used. The repetition time was 1 sec.

Figure 70: Expansion plots of the spectra shown in figure 69.

Figure 71: (a): The accepted mechanism of reaction for the cleavage of an epoxide ring under acidic conditions in solution. The oxygen is first protonated, giving the intermediate some cationic character, then one of the ring carbons undergoes nucleophilic attack. For this reaction, the chirality of the product depends on which of the two carbon atoms is attacked by the bromide. (b): The reaction mechanism proposed by Gerdil and Barchietto¹³⁰ for the formation of 2-cyclohexen-1-ol from TOT enclathrated cyclohexene oxide. The configuration of the reaction product depends on which of the C-O bonds is cleaved. The authors also proposed that this product may be able to undergo a further S_N2 attack with HBr.

Figure 72: (a): Solid state ^{13}C CP/MAS NMR spectrum of TOT / cyclohexene oxide. (b) - (e): Spectra acquired after the clathrate in (a) was exposed to HBr gas for 15, 45, 105 and 175 minutes, respectively. The spectra were acquired using the pulse sequence described in reference 80 to suppress first order spinning sidebands. The 90° pulse length was $3.8\ \mu\text{sec}$ and contact times of 3 msec were used. The repetition time was 1 sec.

TOT / Cyclohexene Oxide

Figure 73: Expansion plots of the spectra shown in figure 72.

CHAPTER NINE

Conclusions and Suggestions for Future Work

I. TOT / 2-Bromobutane and TOT / 2-Butanol

TOT can be considered as a solid state chiral chemical shift reagent for small chiral guest molecules. It has been shown that for the TOT / 2-bromobutane clathrate, both solid state ^{13}C CP/MAS and ^2H NMR can be used to evaluate the enantiomeric excess of the enclathrated guest molecule directly. This has been done on polycrystalline samples containing both *P*(+) and *M*(-) crystals. The, often tedious, procedure of growing large single crystals to obtain the same information is no longer necessary. For a sample prepared by fast recrystallization the enantiomeric excess has been evaluated at $16 \pm 6 \%$ by ^{13}C CP/MAS NMR and $18 \pm 2 \%$ by solid state ^2H NMR. These values differ from those reported previously for samples grown by slow recrystallization.^{110,121,124} This demonstrates for the first time that the chiral selectivity depends on the method of sample preparation. Samples not prepared under equilibrium conditions show less chiral selectivity. An evaluation of the enantiomeric excess for a series of samples prepared at different rates and different temperatures would help substantiate this and possibly lead to some insight into the mechanism of the selectivity.

The ^{13}C chemical shift values for both the favoured and unfavoured enantiomers of enclathrated 2-bromobutane were not only different from one another but also very different from those reported in solution.¹⁴⁵ This was interpreted as a conformational effect. The preferred conformation of the favoured enantiomer is different than that of the unfavoured one and each of these conformations is, in turn, different than the preferred conformation in solution. This was substantiated by molecular mechanics calculations. All other attempts at performing such calculations assumed a rigid guest molecule inside the cage. The calculations carried out in this work allowed the conformation of the guest molecule to "find" its own energy minimum in a single rigid cage. This represents the first attempt to take this freedom into account. The calculations allowed the evaluation of the energy difference between the favoured and unfavoured combinations of guest and host. The energy difference was 0.538 kcal/mol. Using this as a Boltzman energy difference the enantiomeric excess can be calculated as 42.5 %. This agrees well with the enantiomeric excesses reported for samples prepared under equilibrium conditions. The calculations carried out by others,^{119,125,126} using rigid guest molecules, found the energy difference to be greater than that calculated here by an order of magnitude.

The major difference in the molecular conformations of the favoured and unfavoured guests was in the C1-C2-C3-C4 and Br-C2-C3-C4 torsion angles. The ^{13}C chemical shifts are therefore very sensitive to these parameters. Future work could embody the determination of the conformations for the entire 2-halobutane

series inside the TOT cage. This would give an empirical relationship between the molecular torsion angles and the chemical shifts. The evaluation of the energy differences between the favoured and unfavoured combinations for this series could perhaps establish molecular mechanics calculations as a semi-quantitative means of evaluating enantiomeric excesses. The molecular mechanics approach can also be applied to many other clathrate systems. The possibility of carrying out a full molecular dynamics simulation to characterize the dynamic behaviour of enantiomers also exists.

The ^2H NMR spectra for the powdered TOT / 2-bromobutane-(1,1,1- d_3) clathrate consisted of two overlapping powder spectra in a 59:41 intensity ratio, one for each of the favoured and unfavoured enantiomers. Each of the components are narrower than that expected for simple fast methyl group rotation indicating that each undergoes a molecular motion. The parameters of each component spectrum change gradually with temperature suggesting that the molecular motions may be thermally activated large scale librations. The results indicate that the favoured enantiomer is held more rigidly than the unfavoured one. This conclusion was confirmed in the ^2H NMR spectrum of TOT / 2-bromobutane-(2- d_1). In light of these new NMR results, it not surprising that the X-ray crystal structure data were unable to locate the minor enantiomer. The obviously high degree of molecular motion exhibited by the guest molecules causes one to look very cautiously at the conclusions drawn from X-ray crystal structure data. The assumption of rigid guest molecules, often made for refining the data, is often completely unfounded. A

future study could include a complete ^2H NMR study of TOT enclathrated 2-bromobutane labelled on the C3 and C4 positions. These results combined with those reported here may lead to a detailed description of the molecular motion of the guest molecule. An obvious extension of this work is simply to investigate many more systems to see if the different degrees of molecular motion in the favoured and unfavoured enantiomeric guests is general.

The ^2H NMR data collected for a single crystal of TOT / 2-bromobutane allowed the determination of the orientation of the C2-C1 vector of the major enantiomer with respect to the crystallographic *c* axis. This determination relied on the assumption that the largest component of the averaged electric field gradient tensor is parallel to the C2-C1 bond. The orientation determined was consistent with the X-ray results. A future ^2H NMR single crystal study could use high power proton decoupling to remove the ^1H - ^2H dipolar interaction responsible for broadening the ^2H NMR resonances. Using this technique may allow the determination of the orientation of the minor enantiomer with respect to the crystallographic axes. Its orientation has not been determined by any other technique.

The resonances of the guest in the ^{13}C CP/MAS NMR spectrum of TOT / 2-butanol consisted of three singlets and only one doublet (the C2 carbon). The intensities of the components of this doublet were too similar and the signal / noise ratio too low to give a reliable estimate of the enantiomeric excess, however the ^2H NMR data collected for the TOT / 2-butanol-(1,1,1- d_3) and TOT / 2-butanol-(OD)

clathrates were consistent with an enantiomeric excess of 20 ± 2 %. These data disagree with the 5 % enantiomeric excess reported by others^{120,126} using wet chemistry techniques. The ^{13}C Chemical shift values of the TOT enclathrated 2-butanol were very similar to those reported for the neat liquid suggesting that the molecule does not adopt unusual conformations. This is not true of the enclathrated 2-bromobutane and seems to suggest that the functional group on the guest molecule has an influence on its favoured conformation inside the clathrate cage. An interesting study for the future would be a survey of the ^{13}C chemical shifts of many TOT enclathrated, conformationally flexible guest molecules with a variety of functional groups. This would show, in a general way, whether or not the functionality of the guest molecule controls its preferred conformation.

As was true for the TOT / 2-bromobutane clathrate, the proportion of favoured and unfavoured combinations of guest and host for the TOT / 2-butanol clathrate was a function of the method of sample preparation. When the 2-butanol clathrate was prepared from the optically pure alcohols it was found that more of the favoured combination was obtained at slower recrystallization rates. It was discovered, for the first time, that a predominance of the unfavoured combination could be achieved when the desolvated clathrate of one of the optically pure alcohols was quickly recrystallized from the other enantiomer such that the TOT molecules did not have time to fully racemize in solution. It would be interesting to see whether or not this situation would arise under equilibrium conditions. Such an experiment cannot be carried out in solution since the TOT molecules would

then have time to fully racemize. It can, however, be carried out by exposing the desolvated TOT to the vapour of the appropriate guest. The TOT clathrate of one of the optically pure guests could be prepared and desolvated. The desolvated material could then be exposed to the vapour of the other guest enantiomer under equilibrium conditions. This would establish whether or not the enclathration of the unfavoured guest is thermodynamically or kinetically controlled.

The ^2H NMR data show that the 2-butanol guest is much more mobile inside the TOT cage than the 2-bromobutane. This supports the previous conclusions drawn from the ^{13}C NMR dipolar dephasing experiments.¹²¹ For both the favoured and unfavoured guest enantiomers, the C1 methyl group undergoes fast ($\geq 10^7$ Hz) three-fold rotation and the hydroxyl group undergoes fast rotation about the C2-O bond. The C1 methyl carbon of the favoured enantiomer is less mobile than that of the unfavoured one whereas, the hydroxyl group of the favoured enantiomer is more mobile than that of the unfavoured enantiomer. This data was qualitatively interpreted in terms of a binding site model. For the favoured enantiomer the rotating C1 methyl group prefer to be held in a semi-rigid manner to the cage wall, allowing the hydroxyl and ethyl groups to be more mobile. For the unfavoured enantiomer, the rotating hydroxyl group is held nearest the cage wall leaving the methyl and ethyl groups in a more mobile state. This model is not consistent with the data collected for the TOT / 2-bromobutane clathrate, suggesting that there are significantly different host-guest interactions responsible for its enclathration. Although the model does not take the full degree of molecular mobility into

account, it does serve as a qualitative explanation of the observed behaviour of the enclathrated alcohol. The model could be substantiated further by incorporating ^2H on the ethyl group of the alcohol and measuring the ratio of intensities in the component ^2H NMR spectra. The narrower spectrum, showing more mobility, should be dominant.

From the above discussion, it can be concluded that the host-guest interactions for the TOT clathrates of 2-bromobutane and 2-butanol are very different despite the obvious similarity in molecular shape. These differences account for the preferred conformations of each of the guests as well as their differences in mobility. Perhaps the mass of the C2 substituent is an important factor in the degree of molecular mobility. The heavier bromine substituent may be the reason for the lower degree of molecular mobility in the TOT / 2-bromobutane clathrate compared to that of the TOT / 2-butanol. This hypothesis can be investigated further by examining the ^2H NMR spectrum of TOT / 2-iodobutane-(1,1,1- d_3).

II. TOT / Acetone.

The X-ray crystal structure of TOT / acetone was determined and it was found to be a typical $P3_121$ clathrate. The carbonyl bond of the acetone guest was found to lie on the two-fold axis of the clathrate cavity. The thermal parameters of the guest were larger than those of the host but there was no evidence of disorder.

The ^2H NMR spectra of TOT / acetone- d_6 acquired as a function of temperature showed that, at 77 K, the methyl groups of the acetone undergo three-

fold rotation at a rate $\geq 10^7$ Hz. At higher temperatures the molecule also undergoes two-fold flips about the coincident molecular and cage two-fold symmetry axes. At 134 K this process is occurring at a rate $\geq 10^7$ Hz. Variable temperature T_1 measurements were used to show that this process has a activation barrier of 13.6 ± 0.8 kJ/mol and a correlation time of 3.55 nsec. at ~ 184 K. The ^2H and ^{13}C NMR results indicate that there is also a libration of the acetone molecule about the carbonyl bond. This libration was found to have an amplitude of $15^\circ \pm 2^\circ$ at 134 K and $22^\circ \pm 2^\circ$ at room temperature. From the ^{13}C NMR data, the orientations of the σ_{xx} and σ_{yy} components of the chemical shielding tensor for the carbonyl carbon of acetone were determined for the first time. The σ_{xx} component was found to be perpendicular to the carbonyl bond in the sp^2 plane while the σ_{yy} component was found to be parallel to the carbonyl bond.

The X-ray and NMR data are fully consistent with one another and together, were used to obtain a relatively complete description of the enclathrated acetone molecule. Neither technique on its own can provide such a total picture. The techniques are very much complimentary. Future studies may include both X-ray and solid state NMR studies of other two-fold symmetric molecules to see whether or not the alignment of the two-fold axis of the guest with that of the cage is a general phenomenon. The NMR studies would establish whether or not the two-fold flipping of such enclathrated molecules is general.

III. TOT / Benzene

The NMR results indicate that the benzene guest in the $P3_121$ TOT clathrate is undergoing fast ($\geq 10^7$ Hz) rotation about the symmetry axis perpendicular to the ring plane. It is not known whether or not this motion is a six-fold jump or a continuous rotation. The ring was also found to undergo a large amplitude libration such that the axis perpendicular to the ring moves on the surface of a cone of half angle 17° at 298 K. It is not known whether or not the ring undergoes any two-fold flipping motion as the in-plane averaged electric field gradient tensor is invariant to such a motion.

The X-ray crystal structure of the $P3_121$ clathrate has never been determined. The data from this structure would be interesting as they may establish an orientation for the guest inside the cage. It may also establish whether or not the in-plane rotation is six-fold or continuous. An interesting NMR study for the future would be a ^2H NMR investigation of the TOT / benzene- d_6 inclusion compound in space group PT , for which the crystal structure has been determined.¹¹⁷ This would establish whether or not the benzene is able to undergo in-plane rotation in all of the possible environments within this inclusion compound.

IV. TOT / Pyridine

The ^2H NMR data collected for TOT / pyridine- d_5 as a function of temperature indicate that at least two independent molecular motions are occurring, one fast motion ($\geq 10^7$ Hz) at 77 K and another motion superimposed at higher temperatures. The second molecular motion was found to be in the fast motional regime at 196 K and it left one of the deuterons unique. The spectrum acquired at

77 K, can be attributed to an in-plane motion. Two models were used to explain the spectrum. First, the ring may reside in a single broad potential well and undergo an in-plane libration with an amplitude of 23° at 77 K and 28° at room temperature. Secondly, the ring may reside in a multi-site potential well with a local maximum at a position where the nitrogen atom lies on the two-fold axis of the cavity. The two innermost sites would be separated by 23° at 77 K. Both models explain the results. The higher temperature spectra, consisting of two overlapping powder patterns, can be attributed to the in-plane motion plus a two-fold flipping about the two-fold molecular symmetry axis. The two-fold flipping motion is consistent with the ^{13}C CP/MAS dipolar dephasing data collected at room temperature which indicated that the carbon atom opposite the nitrogen was dynamically unique.

The X-ray crystal structure places the pyridine nitrogen on the two-fold axis of the cavity and suggests that it has only limited disorder. At a glance one might assume that the guest is completely rigid inside the cage. The NMR data are consistent with the fact that the nitrogen atom is localized within a specific region of the cage but they give evidence for dynamic disorder. The X-ray and solid state NMR techniques are again shown to be complimentary.

It would be useful to label the pyridine ring with ^2H on the position opposite the nitrogen and examine the ^2H NMR spectrum of the clathrate. This would provide more direct evidence of the two-fold flipping. The same information may be obtained by examining the ^{15}N chemical shielding tensor of the enclathrated

pyridine. ^2H T_1 measurements could also be made to determine the activation energy and correlation time of the two-fold flipping motion.

V. TOT with Prochiral Guests

^{13}C CP/MAS NMR has been used to discriminate between the enantiotopic methyl groups of TOT enclathrated prochiral guest molecules. In this respect, TOT behaves as a "solid chiral solvent" or a solid state chiral chemical shift reagent. For the TOT clathrates of *cis*-2,3-epoxybutane, 2-chloropropane, 2-bromopropane and 2-propanol, the ^{13}C chemical shift difference between the resonances of the enantiotopic methyl groups was between 0.2 and 1.1 ppm. The enantiotopic methyl carbons of TOT enclathrated dimethylsulfoxide were unresolved.

Solid state ^2H NMR spectra for all of the TOT enclathrated methyl labelled guests, including dimethylsulfoxide- d_6 , were superpositions of two powder spectra in a 1:1 intensity ratio. Where ^{13}C NMR failed to resolve the resonances of the methyl groups, ^2H NMR succeeded.

The ^{13}C CP/MAS dipolar dephased spectra of TOT enclathrated *cis*-2,3-epoxybutane, 2-chloropropane and 2-bromopropane indicated that these molecules did not undergo extensive whole body molecular motions. This was not true of the 2-propanol clathrate. For all of the clathrates examined, the ^2H NMR data indicate that the methyl groups of the guest molecules undergo fast three-fold rotation as well as another type of molecular motion at higher temperatures. The spectrum of the methyl labelled 2-propanol is much narrower than that of the other molecules. This confirms the ^{13}C NMR result suggesting that the alcohol is much more mobile

than the other guests. This behaviour parallels that of the TOT enclathrated 2-butanol compared to 2-bromobutane. The relative mass of the -OH substituent compared to that of -Br may be responsible for this effect. The splittings in the ^2H NMR spectra of the 2-bromopropane and 2-propanol guests were very temperature dependent. This is indicative of large amplitude librational motion. A strong temperature dependence was not observed for similar spectra acquired for the dimethylsulfoxide- d_6 clathrate.

Although the data do not lead to a complete description of the molecular motions in these cases, one reasonable model of the motions is a two-fold flip of the molecule about the two-fold symmetry axis of the cavity. If this axis does not bisect the central bond angle of the molecules then the methyl groups are expected to give different ^2H NMR spectra. This appears more obvious for the dimethylsulfoxide- d_6 clathrate than for the others. In that case the spectrum bears a close resemblance to that of TOT / acetone- d_6 which was found to undergo two-fold flips about the coincident molecular and cavity two-fold axes.

Single crystal X-ray data has not been obtained for these clathrates. This data would be particularly valuable as it may establish that the guests exhibit two-fold disorder inside the cavity and coupled with the NMR data may give a complete description of the dynamic state of the guests.

VI. TOT / Chlorocyclohexane

The ^{13}C CP/MAS NMR data collected for the TOT / chlorocyclohexane clathrate suggest that the guest is very mobile with at least two dynamic processes

occurring. The rate of these processes is on the order of tens of microseconds. The chemical shift values of the carbon atoms of the guest do not agree with any previously measured values in solution or in other inclusion compounds. This suggests that there may be unusual conformations present.

A ^2H NMR study of the TOT clathrate of a ^2H labelled guest may provide a more detailed description of the dynamic processes occurring. A molecular mechanics study, similar to the one carried out for the TOT / 2-bromobutane clathrate, using the X-ray data as input may provide some information regarding the possible conformations.

VII. Reactions of Guest Molecules in TOT Clathrates

Solid - gas chemical reactions were carried out for TOT / *cis*-2,3-epoxybutane, TOT / *trans*-2,3-epoxybutane and TOT / cyclohexene oxide with HBr gas. For the TOT / *cis*-2,3-epoxybutane and TOT / *trans*-2,3-epoxybutane clathrates the ^{13}C CP/MAS data indicated that chemical reactions occurred inside the clathrate cages. The products for each of the reactions of the clathrates were 3-buten-2-ol and 3-bromo-2-butanol, respectively. The 3-buten-2-ol produced was present with a slight enantiomeric excess indicating that the chirality of the clathrate cage has an effect on the chirality of the reaction product. The 3-bromo-2-butanol produced was present with an enantiomeric excess of $51\% \pm 10\%$. This agrees with the reported enantiomeric excess of TOT enclathrated *trans*-2,3-epoxybutane. The rates of these reactions seemed to depend on the size of the reaction products. The reaction producing the larger product occurred at a slower rate.

The reaction of TOT / cyclohexene oxide with HBr gas produced a poorly ordered TOT powder which appeared to contain no guest. These observations can be explained in at least three ways. First, a reaction may have occurred inside the cage giving a product whose resonances are broadened out due to molecular motion.⁹² Second, the HBr may have displaced the guest and collapsed the cages. Finally, the cages may not be large enough to accommodate either both of the reactant molecules or the large products. This would force the cages to break apart, leaving a poorly ordered powder.

It would be possible to confirm or discount the first possibility by conducting a variable temperature ^{13}C CP/MAS study. If the guest resonances are broadened out by molecular motion they will become sharper at either higher or lower temperatures. It would also be productive to examine the powder X-ray diagrams of the materials before and after exposure to HBr gas. This may confirm whether or not the crystalline host network stays intact.

VIII. Conclusion

From the work carried out in the production of this thesis, one can see that solid state NMR has a definite role in characterizing clathrate systems. It is particularly useful when used in conjunction with X-ray crystallography. There is still much room for further study of TOT clathrates by solid state NMR as well as other methods. It is hoped that this study has improved the understanding of this very interesting chemical system.

The routines used in this program were originally written in FORTRAN by Dr. C.I. Ratcliffe.

```
'INITIAL SCREEN
CLS
SCREEN 12
CLS
COLOR (14)
FOR Q% = 1 TO 9
PRINT ""
NEXT Q%
PRINT "
SPECTRAL SIMULATIONS"
PRINT ""
BEEP
PRINT
PRINT
PRINT
PRINT "
PRESS < B > TO BEGIN";
INPUT BEGIN$
IF BEGIN$ = "B" THEN GOTO 2
SOUND (1500), 500

'MAIN MENU
2 CLS
SCREEN 2
CLS
SCREEN 12
COLOR (12)
3 CLEAR
4 PRINT "
MAIN MENU"
6 PRINT ""
PRINT ""
```

```
10 PRINT ""
14 PRINT ""
COLOR (9)
16 PRINT "                WOULD YOU LIKE TO..."
18 PRINT ""
COLOR (14)
PRINT "                0.";
COLOR (11)
PRINT " GO TO THE DATA DIRECTORY MENU"
COLOR (14)
PRINT "                1.";
COLOR (11)
19 PRINT " GENERATE NEW DEUTERIUM SPECTRUM"
COLOR (14)
PRINT "                2.";
COLOR (11)
20 PRINT " ADD TWO EXISTING SPECTRA TOGETHER"
COLOR (14)
PRINT "                3.";
COLOR (11)
21 PRINT " GENERATE NEW SPIN 1/2 SPECTRUM"
COLOR (14)
PRINT "                4.";
COLOR (11)
22 PRINT " PLOT AN EXISTING SPECTRUM"
COLOR (14)
PRINT "                5.";
COLOR (11)
23 PRINT " REVERSE AN EXISTING SPECTRUM"
COLOR (14)
PRINT "                6.";
COLOR (11)
24 PRINT " CONVOLUTE AN EXISTING SPECTRUM"
COLOR (14)
PRINT "                7.";
COLOR (11)
25 PRINT " GENERATE NOISE IN AN EXISTING SPECTRUM"
COLOR (14)
PRINT "                8.";
COLOR (11)
26 PRINT " ADD ISOTROPIC LINE TO EXISTING SPECTRUM"
COLOR (14)
PRINT "                9.";
COLOR (11)
```

```

27 PRINT " QUIT"
28 PRINT ""
COLOR (2)
29 PRINT "                                ENTER NUMBER OF CHOICE";
COLOR (5)
LINE (150, 102)-(504, 280), , B
COLOR (10)
LINE (273, 0)-(355, 15), , B
COLOR (14)
30 INPUT MENU
31 IF MENU = 0 GOTO 50000
32 IF MENU = 1 GOTO 41
33 IF MENU = 2 GOTO 25000
34 IF MENU = 3 GOTO 41
35 IF MENU = 4 GOTO 30000
36 IF MENU = 5 GOTO 32000
37 IF MENU = 6 GOTO 5000
38 IF MENU = 7 GOTO 35000
39 IF MENU = 8 GOTO 40000
    IF MENU = 9 GOTO 1440
    IF MENU > 9 GOTO 40
    IF MENU < 0 GOTO 40

'INPUT PARAMETERS FOR GENERATION OF NEW SPECTRA
40 PRINT ""
PRINT "  ERROR: INAPPROPRIATE ENTRY TRY AGAIN."
PRINT ""
SOUND (250), 10
GOTO 29
41 CLS
SCREEN 12
COLOR (12)
PRINT "                                GENERATING NEW SPECTRA"
42 PRINT ""
44 PRINT ""
46 PRINT ""
COLOR (11)
50 PRINT "  HOW MANY POINTS WOULD YOU LIKE THE SPECTRUM TO
BE  REPRESENTED BY"
PRINT ""
55 PRINT "  (MAXIMUM=1000)";
COLOR 14
60 INPUT M%
COLOR 11

```



```
IF M% > 1000 GOTO 64
IF M% < 1 GOTO 64
GOTO 65
64 PRINT ""
COLOR 12
PRINT " ERROR: YOU MUST ENTER A NUMBER BETWEEN 1 AND 1000"
SOUND (250), 10
GOTO 46
65 PRINT ""
COLOR 11
67 PRINT " WHAT IS THE SWEEP WIDTH IN FREQUENCY UNITS";
COLOR 14
68 INPUT SW
70 PRINT ""
COLOR 11
80 PRINT " WHAT IS THE ASYMMETRY PARAMETER";
COLOR 14
90 INPUT ET
COLOR 11
IF MENU = 1 THEN LET REVADD = 1
IF MENU = 3 THEN LET REVADD = 0
IF ET > 1 GOTO 92
IF ET < 0 GOTO 92
IF ET = 1 THEN LET MENU = 3
GOTO 101
92 PRINT ""
COLOR 12
PRINT " ERROR: THE ASYMMETRY PARAMETER MUST BE A NUMBER
      BETWEEN 0 AND 1";
SOUND (250), 10
GOTO 70
101 IF ET = 1 GOTO 111
IF MENU = 3 GOTO 111
102 PRINT ""
COLOR 11
105 PRINT " WHAT IS THE INNERMOST SPLITTING IN FREQUENCY
UNITS";
COLOR 14
107 INPUT SPL
COLOR 11
IF ((2 * SPL) / (1 - ET)) > SW GOTO 108
GOTO 109
108 PRINT ""
SOUND (250), 10
```

```

COLOR (12)
PRINT "  ERROR: PLOT IS TOO WIDE FOR SCREEN (START AGAIN =S,
      CONTINUE =C)";
COLOR 14
INPUT ER1$
IF ER1$ = "S" GOTO 65
IF ER1$ = "C" GOTO 109
109 IF MENU = 3 GOTO 111
LH = ((3 + ET) / (1 - ET)) * SPL * .5
DR = SW / M%
L = LH / DR
GOTO 120
111 PRINT ""
COLOR (11)
112 PRINT "  WHAT IS THE FULL WIDTH OF THE SPECTRUM IN
FREQUENCY  UNITS";
COLOR 14
113 INPUT FULL
IF FULL > SW GOTO 115
COLOR 11
GOTO 119
115 PRINT ""
SOUND (250), 10
COLOR (12)
PRINT "  ERROR: PLOT IS TOO WIDE FOR SCREEN ( START AGAIN =S,
      CONTINUE =C )";
INPUT ER2$
IF ER2$ = "S" GOTO 65
IF ER2$ = "C" GOTO 119
119 L = FULL / (SW / M%)
120 DIM W(M% + 1)
PRINT ""
140 CLS
150 FOR I% = 0 TO M%
160 W(I%) = 0
180 NEXT I%
190 IF ET = 0 GOTO 15000

'CALCULATE NONAXIAL SPECTRUM
COLOR (1)
192 PRINT ""
COLOR (1)
194 PRINT "  CALCULATING ...."
200 OT = (2 * ET * L) / (3 + ET)

```

```

220 IT = INT(OT + .5)
240 DE = L / (3 + ET)
260 IZ = INT(L - (2 * DE) + .5)
280 SUM = 0
300 LZ = (M% / 2) - IZ

```

'CALCULATES FIRST CURVE OF NONAXIAL SPECTRUM

```

320 FOR I% = 0 TO (IT - 1)
340 J = LZ + I%
360 PF = 1 / (((L - I%) * OT) ^ (.5))
380 E2 = ((L - OT) * I%) / (OT * (L - I%))
400 X = 1
420 GOTO 10000
460 W(J) = PF * PK
480 SUM = SUM + W(J)
500 NEXT I%
502 PRINT ""
510 PRINT "  FIRST ELIPTICAL INTEGRAL DONE"
PRINT ""
PRINT "  CALCULATING ..."

```

'CALCULATES SECOND CURVE OF NONAXIAL SPECTRUM

```

520 FOR I% = (IT + 1) TO L
540 J = LZ + I%
560 PF = 1 / ((I% * (L - OT)) ^ (.5))
580 E2 = (OT * (L - I%)) / ((L - OT) * I%)
600 X = 2
620 GOTO 10000
660 W(J) = PF * PK
680 SUM = SUM + W(J)
700 NEXT I%
702 PRINT ""
710 PRINT "  SECOND ELIPTICAL INTEGRAL DONE"
REM DEFINES THE THREE SINGULARITIES IN THE NONAXIAL
SPECTRUM
720 W(LZ) = W(LZ) / 2
740 W(LZ + L) = W(LZ + L) / 2
760 SUM = SUM - W(LZ) - W(LZ + L)
770 DIF = 1 - SUM
780 W(LZ + IT) = DIF
IF REVADD = 1 GOTO 782
781 IF MENU = 3 GOTO 900

```

'REVERSES AND ADDS THE SPECTRA

```

782 PRINT ""
COLOR (1)
783 PRINT "  REVERSING AND ADDING SPECTRA..."
784 FOR I% = 0 TO (M% / 2)
785 W(I%) = W(I%) + W(M% - I%)
786 W(M% - I%) = W(I%)
788 NEXT I%
900 PRINT ""
905 PRINT "  FINISHED THE UNBROADENED SPECTRUM"

```

'SCALING ROUTINE

'FIND THE LARGEST POINT IN THE SPECTRUM TO SCALE THE PLOT

```

1000 PRINT ""
1002 PRINT "  ABOUT TO PLOT SPECTRUM..."
1004 DIM P(M% + 1)
1010 Z = W(0)
1020 FOR J% = 1 TO M%
1030 IF (Z < W(J%)) THEN Z = W(J%) ELSE 1040
1040 NEXT J%
1050 IF IND = 10 GOTO 35100
1055 IF MENU = 8 GOTO 40100

```

'PLOT SPECTRUM

```

1060 CLS
1070 SOUND (1500), 5
1080 SCREEN 12
COLOR (12)
LINE (0, 100)-(640, 500), , BF
1100 WINDOW (0, 0)-(100, 100)
1110 VIEW (30, 30)-(610, 430)
COLOR (1)
LINE (0, 0)-(100, 70), , BF
COLOR (6)
LINE (0, 0)-(100, 70), , B
1120 FOR I% = 0 TO M%
  1140 P(I%) = ((50 / Z) * W(I%)) + 10
1160 NEXT I%
1200 FOR I% = 0 TO M%
  1220 PSET (((100 / M%) * I%), P(I%))
1240 NEXT I%
1260 FOR I% = 0 TO (M% - 1)
  COLOR (14)
  1280 LINE (((100 / M% * I%), P(I%))-(((100 / M%) * (I% + 1)), P((I%

```

```

+ 1)))
1290 NEXT I%

'PUTS PARAMETERS ON PLOT
COLOR (14)
1294 IF MENU = 2 GOTO 62000
1296 IF MENU = 4 GOTO 1315
1298 IF MENU = 5 GOTO 1315
1299 IF MENU = 6 GOTO 1315
1300 IF MENU = 7 GOTO 1315
1301 IF MENU = 100 GOTO 1315
1302 IF MENU = 3 GOTO 1304
1303 IF MENU = 1 GOTO 1304
1304 PRINT " SWEEP WIDTH = "; SW
IF MENU = 1 GOTO 1307
IF MENU = 3 GOTO 1305
1305 PRINT " LINE WIDTH = "; FULL
1306 GOTO 1308
1307 PRINT " V(XX)="; SPL; " V(YY)="; (1 / 100) * INT(100 * (SPL
* (-1      + ET) / (ET - 1))); " V(ZZ)="; (1 / 100) *      INT(100 * (2
* SPL / (1 - ET)))
1308 PRINT " ASYMMETRY PARAMETER "; (INT(ET * 1000)) / 1000
1310 GOTO 1319
1315 OPEN ((LEFT$(CON$, (LEN(CON$) - 4))) + ".PAR") FOR INPUT AS #1
INPUT #1, MENUP
IF MENUP = 1 GOTO 1316
IF MENUP = 3 GOTO 1317
IF MENUP <> 3 OR MENUP <> 1 THEN GOTO 1318
1316 INPUT #1, SW, ABVXX, ABVYY, ABVZZ, ABET
PRINT " SWEEP WIDTH = "; SW
PRINT " V(XX)="; ABVXX; " V(YY)="; ABVYY; " V(ZZ)="; ABVZZ
PRINT " ASYMMETRY PARAMETER = "; ABET
GOTO 1318
1317 INPUT #1, SW, FULL, ABET
PRINT " SWEEP WIDTH = "; SW
PRINT " LINE WIDTH = "; FULL
PRINT " ASYMMETRY PARAMETER = "; ABET
1318 CLOSE #1
1319 COLOR (11)

'RECORD SPECTRUM UPON REQUEST
PRINT " WOULD YOU LIKE TO SAVE THE SPECTRUM? (Y=YES,
N=NO)";
COLOR 14

```

```

1320 INPUT CD$
IF CD$ = "Y" GOTO 1322 ELSE 1321
1321 IF CD$ = "N" GOTO 1360 ELSE 1340
1322 COLOR 11
PRINT "  ENTER FILE NAME";
COLOR 14
1323 INPUT STO$
1324 OPEN STO$ FOR APPEND AS #1
1326 FOR I% = 0 TO M%
    1328 WRITE #1, W(I%)
1330 NEXT I%
1332 CLOSE #1
STOPA$ = (LEFT$(STO$, (LEN(STO$) - 4))) + ".PAR"
MENUP = MENU
IF MENU = 3 GOTO 1333
ABVXX = SPL
ABVYY = ((1 / 100) * (INT(100 * (SPL * (-(1 + ET) / (ET - 1))))))
ABVZZ = ((1 / 100) * (INT(100 * (2 * SPL / (1 - ET))))))
1333 ABET = (((INT(ET * 1000)) / 1000))
OPEN STOPA$ FOR OUTPUT AS #1
IF MENU = 1 GOTO 1334
IF MENU = 3 GOTO 1335
1334 WRITE #1, MENUP, SW, ABVXX, ABVYY, ABVZZ, ABET
GOTO 1336
1335 WRITE #1, MENUP, SW, FULL, ABET
1336 CLOSE #1
GOTO 1360
1340 SOUND (250), 10
PRINT "  ERROR: YOU MUST ENTER EITHER Y OR N"
GOTO 1319
1360 COLOR (11)
PRINT "  MAIN MENU = M    QUIT = Q ";
COLOR 14
1380 INPUT AB$
1390 SCREEN 12
1400 IF AB$ = "M" GOTO 2 ELSE 1420
1420 IF AB$ = "Q" GOTO 1440 ELSE 1430
1430 SOUND (250), 10
COLOR (12)
PRINT "  ERROR; YOU MUST ENTER EITHER M FOR MAIN MENU OR
Q FOR    QUIT"
GOTO 1360
1440 CLEAR
1460 END

```

'CALCULATES ELIPTICAL INTEGRALS BY ITERATION

```

10000 SM = 1
10020 A = 1
10040 B = 1
10060 C = 1
10080 B = B * A / (A + 1)
10100 C = C * E2
10120 D = B * B * C
10140 CON = .000001
10160 IF (D < CON) GOTO 10240
10180 SM = SM + D
10200 A = A + 2
10220 GOTO 10080
10240 PK = (SM + D) / 2
10260 IF (X = 1) GOTO 460
10280 IF (X = 2) GOTO 660
10300 END

```

'CONVOLUTION ROUTINE

```

5000 CLS
COLOR (12)
PRINT "                CONVOLUTION OF EXISTING SPECTRA"
5030 PRINT ""
COLOR (11)
PRINT "  WHAT IS THE FILE NAME OF THE SPECTRUM YOU WISH TO
        CONVOLUTE";
COLOR 14
INPUT CON$
COLOR 11
PRINT ""
PRINT "  WHAT IS THE SWEEP WIDTH IN FREQUENCY UNITS";
COLOR 14
INPUT SW
COLOR 11
PRINT ""
5035 PRINT "  HAVE YOU PREVIOUSLY ADDED NOISE TO THIS
SPECTRUM?"
PRINT ""
PRINT "  ( Y=YES, N=NO )";
COLOR 14
INPUT NCON$
COLOR 11
IF NCON$ = "Y" GOTO 5040 ELSE 5037
5037 IF NCON$ = "N" GOTO 5040 ELSE 6200

```

```

5040 PRINT ""
PRINT "      WOULD YOU LIKE GAUSSIAN OR LORENTZIAN
BROADENING?"
5052 PRINT ""
PRINT "  G=GAUSSIAN, L=LORENTZIAN ";
COLOR 14
INPUT LB$
COLOR 11
IF LB$ = "G" GOTO 5054
IF LB$ = "L" GOTO 5054
IF LB$ <> "G" GOTO 6300
IF LB$ <> "L" GOTO 6300
5054 PRINT ""
PRINT "  WHAT IS THE HALF WIDTH OF THE BROADENING FUNCTION
IN      FREQUENCY UNITS";
COLOR 14
INPUT HWH
M% = 0
DIM W(1001)
OPEN CON$ FOR INPUT AS #1
DO UNTIL EOF(1)
    INPUT #1, W(M%)
    M% = M% + 1
LOOP
CLOSE #1
M% = M% - 1
HW = HWH / (SW / M%)
CLS
5055 PRINT ""
COLOR (1)
5060 PRINT "  CONVOLUTING ....."
5061 PRINT ""
5063 PRINT "  BE PATIENT! SIT DOWN AND RELAX, I'M DOING ALL OF
THE  WORK."
5065 DIM U(M% + 1)
5067 IF NCON$ = "Y" THEN OP% = 0
5068 IF NCON$ = "Y" THEN OL% = M%
5070 FOR I% = 0 TO M%
5071 U(I%) = W(I%)
5073 NEXT I%
5080 DIM GL(M% + 1)
5100 LF% = 0
5110 FOR J% = 1 TO (M% / 2)
5120 IF U(J%) = 0 GOTO 5200

```



```

5140 IF LF% = 1 GOTO 5200
5160 OP% = J%
5180 LF% = 1
5200 NEXT J%
5220 FOR J% = (M% / 2) TO M%
5240 IF U(J%) <> 0 GOTO 5320
5260 IF LF% = 0 GOTO 5320
5280 OL% = J% - 1
5300 LF% = 0
5320 NEXT J%
5340 HW2 = HW * HW
5360 IF LB$ = "L" GOTO 5480

```

'GAUSSIAN BROADENING

```

5380 BG = (4 * LOG(2)) / HW2
5400 FOR I% = 0 TO OL%
5402 R = BG * I% * I%
5404 IF R > 1000 THEN R = 1000
5420 GL(I%) = EXP(-R)
5440 NEXT I%
5460 GOTO 5600

```

'LORENTZIAN BROADENING

```

5480 BL = 4 / HW2
5500 FOR I% = 0 TO OL%
5520 GL(I%) = 1 / (1 + BL * I% * I%)
5540 NEXT I%
5600 FOR J% = 0 TO M%
5640 U(J%) = 0
5660 NEXT J%
5670 IF NCON = 1 GOTO 5960
5680 FOR I% = OP% TO OL%
5700 FOR J% = 0 TO M%
5720 IJ% = ABS(J% - I%)
5740 U(J%) = U(J%) + GL(IJ%) * W(I%)
5760 NEXT J%
5780 NEXT I%
5882 PRINT ""
5900 PRINT "  FINISHED BROADENING THE SPECTRUM"
5910 FOR I% = 0 TO M%
5920 W(I%) = U(I%)
5930 NEXT I%
5950 GOTO 1000
5960 FOR I% = 0 TO M%

```

```

5980 FOR J% = 0 TO M%
6000 IJ% = ABS(J% - I%)
6020 U(J%) = U(J%) + GL(IJ%) * W(I%)
6040 NEXT J%
6060 NEXT I%
6080 GOTO 5882
6100 END
6200 PRINT ""
SOUND (250), 10
COLOR (12)
PRINT "  ERROR: YOU MUST ENTER EITHER Y OR N."
GOTO 5035
6300 PRINT ""
SOUND (250), 10
COLOR 12
PRINT "  ERROR: YOU MUST ENTER G FOR GAUSSIAN OR L FOR
        LORENTZIAN."
GOTO 5052

```

'CALCULATES AXIAL SPECTRUM

```

15000 PRINT ""
COLOR (1)
15005 PRINT "  CALCULATING SPECTRUM..."
15008 L% = L
15010 IZ% = INT((L% / 3) + .5)
15020 LZ% = (M% / 2) - IZ%
15040 CM = 1 / ((2 * L%) ^ .5)
15060 FOR I% = 1 TO (L% - 1)
15080 J% = LZ% + I%
15100 KJ% = 2 * I%
15120 W(J%) = CM * ((KJ% + 1) ^ .5 - (KJ% - 1) ^ .5)
15140 NEXT I%
15160 W(LZ%) = CM
15180 W(LZ% + L%) = CM * ((2 * L%) ^ .5 - ((2 * L%) - 1) ^ .5)
15190 IF MENU = 3 GOTO 900
15200 GOTO 782
15220 END

```

'ADDITION OF TWO LINESHAPES

```

25000 CLS
COLOR 12
25001 PRINT "                                ADDITION OF TWO SPECTRA"
PRINT ""
PRINT ""

```

```
PRINT ""
COLOR (12)
25005 PRINT " CAUTION, BOTH FILES MUST HAVE THE SAME NUMBER
OF POINTS"
25008 PRINT ""
COLOR (11)
25010 PRINT " ENTER FIRST FILE NAME";
COLOR 14
25020 INPUT F1$
COLOR 11
25030 PRINT ""
25040 PRINT " ENTER MULTIPLIER OF FIRST FILE";
COLOR 14
25060 INPUT M1
XX = 10
IF M1 < 0 GOTO 26010 ELSE 25070
25070 PRINT ""
COLOR (14)
25080 PRINT " ENTER SECOND FILE NAME";
COLOR 11
25100 INPUT F2$
COLOR 14
25110 PRINT ""
25120 PRINT " ENTER MULTIPLIER OF SECOND FILE";
COLOR 11
25140 INPUT M2
XX = 20
IF M2 < 0 GOTO 26010 ELSE 25155
25155 CLS
25156 PRINT ""
COLOR (1)
25158 PRINT " ADDING SPECTRA..."
25160 DIM A(1001)
25180 DIM B(1001)
25190 M% = 0
25200 OPEN F1$ FOR INPUT AS #1
25220 DO UNTIL EOF(1)
25240 INPUT #1, A(M%)
25260 M% = M% + 1
25280 LOOP
25300 CLOSE #1
25320 M% = 0
25340 OPEN F2$ FOR INPUT AS #1
25360 DO UNTIL EOF(1)
```

```

25380 INPUT #1, B(M%)
25400 M% = M% + 1
25420 LOOP
25440 CLOSE #1
25460 M% = M% - 1
25470 DIM C(M% + 1)
25475 DIM W(M% + 1)
25480 FOR I% = 0 TO M%
25500 C(I%) = (M1 * A(I%)) + (M2 * B(I%))
25510 W(I%) = C(I%)
25520 NEXT I%
25660 GOTO 1000
25680 CLEAR
26000 END
26010 PRINT ""
SOUND (250), 10
COLOR (12)
PRINT "  ERROR: YOU MUST ENTER A POSITIVE MULTIPLIER TO
ENSURE  A FULL SPECTRUM"
IF XX = 10 GOTO 25030
IF XX = 20 GOTO 25110

```

'PLOTING AN EXISTING FILE

```

30000 CLS
COLOR (12)
30002 PRINT "          PLOTING AN EXISTING SPECTRUM"
PRINT ""
PRINT ""
PRINT ""
COLOR (11)
30005 PRINT "  WHAT IS THE NAME OF THE FILE YOU WOULD LIKE TO
          PLOT";
COLOR 14
30020 INPUT CON$
30030 M% = 0
30032 DIM ABC(1001)
30040 OPEN CON$ FOR INPUT AS #1
30080 DO UNTIL EOF(1)
30100 INPUT #1, ABC(M%)
30120 M% = M% + 1
30140 LOOP
30150 CLOSE #1
30152 M% = M% - 1
30160 DIM W(M% + 1)

```

```

30180 FOR I% = 0 TO M%
30200 W(I%) = ABC(I%)
30220 NEXT I%
30230 CLS
30240 GOTO 1000
30260 END

```

'REVERSING A SPECTRUM

```
32000 CLS
```

```
COLOR (12)
```

```
32002 PRINT "
```

REVERSING AN EXISTING SPECTRUM"

```
PRINT ""
```

```
PRINT ""
```

```
PRINT ""
```

```
COLOR (11)
```

```
32010 PRINT "  WHAT IS THE FILE NAME OF SPECTRUM TO BE
REVERSED";
```

```
COLOR 14
```

```
32020 INPUT CON$
```

```
32022 M% = 0
```

```
32024 DIM GHI(1001)
```

```
32040 OPEN CON$ FOR INPUT AS #1
```

```
32060 DO UNTIL EOF(1)
```

```
32080 INPUT #1, GHI(M%)
```

```
32100 M% = M% + 1
```

```
32120 LOOP
```

```
32140 CLOSE #1
```

```
32160 M% = M% - 1
```

```
32170 DIM W(M% + 1)
```

```
32180 FOR I% = 0 TO M%
```

```
32200 W(I%) = GHI(M% - I%)
```

```
32220 NEXT I%
```

```
32240 GOTO 1000
```

```
32260 END
```

'ADD NOISE

```
35000 CLS
```

```
COLOR (12)
```

```
35020 PRINT "
```

ADDING NOISE TO AN EXISTING

```
SPECTRUM"
```

```
PRINT ""
```

```
COLOR (11)
```

```
PRINT ""
```

```
PRINT ""
```

```

PRINT " WHAT IS THE FILE NAME OF THE SPECTRUM TO WHICH YOU
WOULD LIKE TO ADD NOISE"
COLOR 14
PRINT " ";
INPUT CON$
COLOR 11
PRINT ""
35030 PRINT " WHAT SIGNAL TO NOISE RATIO WOULD YOU LIKE";
COLOR 14
INPUT SN
IF SN < 0 GOTO 39000
CLS
PRINT ""
COLOR (1)
PRINT " MAKING NOISE..."
DIM W(1001)
IF SN = 0 GOTO 36000
35040 M% = 0
OPEN CON$ FOR INPUT AS #1
DO UNTIL EOF(1)
    INPUT #1, W(M%)
    M% = M% + 1
LOOP
CLOSE #1
35060 M% = M% - 1
DIM N(M% + 1)
IND = 10
GOTO 1004
35100 IF SN = 0 THEN LET NOI = 1
IF SN = 0 THEN LET Z = 1.5
IND = 0
IF SN = 0 GOTO 35102
NOI = Z / SN
35102 RANDOMIZE TIMER
FOR I% = 0 TO M%
    N(I%) = (NOI) * (RND + .5)
    W(I%) = W(I%) + N(I%)
NEXT I%
GOTO 1010
END
36000 OPEN NO$ FOR INPUT AS #1
DO UNTIL EOF(1)
    INPUT #1, W(M%)
    W(M%) = .000001

```

```

    M% = M% + 1
LOOP
CLOSE #1
GOTO 35060
39000 PRINT ""
SOUND (250), 10
COLOR (12)
PRINT "  ERROR: THE SIGNAL TO NOISE RATIO MUST BE POSITIVE."
GOTO 35030

```

```

'ADDITION OF ISOTROPIC LINE
40000 CLS
COLOR (12)
PRINT "          ADDITION OF AN ISOTROPIC LINE TO AN EXISTING
SPECTRUM"
PRINT ""
PRINT ""
PRINT ""
PRINT ""
PRINT ""
PRINT ""
COLOR (11)
PRINT "  WHAT IS THE FILE NAME OF THE SPECTRUM TO WHICH YOU
        WOULD LIKE TO ADD THE"
PRINT "  ISOTROPIC LINE";
COLOR 14
INPUT CON$
COLOR 11
PRINT ""
PRINT "  WHAT IS THE RELATIVE INTENSITY OF THE LINE COMPARED
TO          THE SPECTRUM";
COLOR 14
INPUT RINT
DIM W(1001)
M% = 0
OPEN CCN$ FOR INPUT AS #1
DO UNTIL EOF(1)
    INPUT #1, W(M%)
    M% = M% + 1
LOOP
CLOSE #1
M% = M% - 1
GOTO 1004
40100 LINEE = Z * RINT
40110 PRINT ""

```

```

COLOR 11
PRINT " WOULD YOU LIKE TO PUT THE LINE IN THE CENTRE OF THE
      SPECTRUM?"
PRINT ""
PRINT " ( Y=YES, N=NO );
COLOR 14
INPUT CEN$
IF CEN$ = "Y" GOTO 40120 ELSE 40112
40112 IF CEN$ = "N" GOTO 40120 ELSE 40114
40114 PRINT ""
SOUND (250), 10
COLOR (12)
PRINT " ERROR; YOU MUST ENTER EITHER Y OR N."
GOTO 40110
40120 DIM LI(M% + 1)
IF CEN$ = "N" GOTO 40300
CLS
COLOR (1)
PRINT " GENERATING SPECTRUM..."
FOR I% = 0 TO (M% / 2 - 1)
LI(I%) = 0
NEXT I%
FOR I% = (M% / 2 + 1) TO M%
LI(I%) = 0
NEXT I%
LI(M% / 2) = LINEE
GOTO 40400
40300 PRINT ""
COLOR (11)
PRINT " WHERE WOULD YOU LIKE THE LINE POSITIONED?"
PRINT ""
PRINT " ENTER A NUMBER BETWEEN 0 AND 1"
PRINT ""
PRINT " ( 0=EXTREME LEFT, 1=EXTREME RIGHT );
COLOR 14
INPUT PO
IF PO < 0 GOTO 40310
IF PO > 1 GOTO 40310
GOTO 40340
40310 PRINT ""
SOUND (250), 10
COLOR (12)
PRINT " ERROR; YOU MUST ENTER A NUMBER BETWEEN ZERO AND
1"

```



```

GOTO 40300
40340 CLS
COLOR (1)
PRINT " GENERATING SPECTRUM..."
POSI% = INT(PO * M%)
FOR I% = 0 TO POSI% - 1
LI(I%) = 0
NEXT I%
FOR I% = POSI% + 1 TO M%
LI(I%) = 0
NEXT I%
LI(POSI%) = LINEE
40400 FOR I% = 0 TO M%
W(I%) = W(I%) + LI(I%)
NEXT I%
MENU = 100
GOTO 1010
END

```

'FILE MANAGEMENT

```

50000 CLS
COLOR (12)
PRINT "
FOR Q% = 1 TO 6
PRINT
NEXT Q%
COLOR (14)
PRINT "
PRINT "
PRINT "
PRINT "
PRINT "
PRINT "

```

DIRECTORY MENU"

1. VIEW DATA DIRECTORY"
2. ERASE FILES"
3. RENAME FILES"
4. MAIN MENU"
5. QUIT"

```

COLOR (11)
50010 PRINT "
INPUT DIRMEN
PRINT

```

ENTER NUMBER OF CHOICE ";

```

IF DIRMEN = 1 GOTO 51000
IF DIRMEN = 2 GOTO 52000
IF DIRMEN = 3 GOTO 53000
IF DIRMEN = 4 GOTO 2
IF DIRMEN = 5 GOTO 26000
IF DIRMEN < 1 OR DIRMEN > 5 GOTO 58000
51000

```

```

CLS
FILES "*.DAT"
PRINT
COLOR (14)
PRINT " <D> TO RETURN TO DIRECTORY MENU"
PRINT " <M> TO RETURN TO MAIN MENU"
PRINT
51010 PRINT " ENTER CHOICE";
INPUT DIME$
IF DIME$ = "D" GOTO 50000
IF DIME$ = "M" GOTO 2
IF DIME$ <> "D" AND DIME$ <> "M" GOTO 60100
END
52000 CLS
FILES "*.DAT"
PRINT
COLOR (14)
52100 PRINT " WHAT IS THE NAME OF THE FILE YOU WOULD LIKE TO
        ERASE";
INPUT ERAS$
KILL ERAS$
KILL ((LEFT$(ERAS$, (LEN(ERAS$)) - 3)) + "PAR")
CLS
FILES "*.DAT"
PRINT
COLOR (14)
PRINT " <E> TO ERASE ANOTHER FILE"
PRINT " <D> TO RETURN TO DIRECTORY MENU"
PRINT " <M> TO RETURN TO MAIN MENU"
52110 PRINT
PRINT " ENTER CHOICE ";
INPUT DIME2$
IF DIME2$ = "E" GOTO 52000
IF DIME2$ = "D" GOTO 50000
IF DIME2$ = "M" GOTO 2
IF DIME2$ <> "E" AND DIME2$ <> "D" AND DIME2$ <> "M" GOTO 59000
53000 CLS
FILES "*.DAT"
PRINT
COLOR (14)
53100 PRINT " WHAT IS THE NAME OF THE FILE YOU WOULD LIKE TO
        CHANGE";
INPUT FFF1$
PRINT

```

```

PRINT "  WHAT NAME WOULD YOU LIKE THE FILE TO HAVE";
INPUT FFF2$
NAME FFF1$ AS FFF2$
NAME ((LEFT$(FFF1$, (LEN(FFF1$) - 3))) + "PAR") AS ((LEFT$(FFF2$,
      (LEN(FFF2$) - 3))) + "PAR")
CLS
FILES "*.DAT"
PRINT
COLOR (14)
PRINT "  <R>  TO RENAME ANOTHER FILE"
PRINT "  <D>  TO RETURN TO DIRECTORY MENU"
PRINT "  <M>  TO RETURN TO MAIN MENU"
PRINT
53210 PRINT "  ENTER CHOICE  ";
INPUT DIME3$
IF DIME3$ = "R" GOTO 53000
IF DIME3$ = "D" GOTO 50000
IF DIME3$ = "M" GOTO 2
IF DIME3$ <> "R" AND DIME3$ <> "D" AND DIME3$ <> "M" GOTO 60000
54000 END
COLOR (12)
58000 PRINT "  ERROR: TRY AGAIN!"
SOUND (250), 10
GOTO 50010
COLOR (12)
59000 PRINT "  ERROR: YOU MUST ENTER  E, D OR M"
SOUND (250), 10
GOTO 52110
COLOR (12)
60000 PRINT "  ERROR: YOU MUST ENTER  R, D OR M"
SOUND (250), 10
GOTO 53210
60100 SOUND (250), 10
COLOR (12)
PRINT "  ERROR; YOU MUST ENTER EITHER D OR M"
GOTO 51010
END
COLOR (14)
62000 PRINT "  "; M1; "*" "; F1$
      PRINT "  "; M2; "*" "; F2$
      GOTO 1319

END

```

APPENDIX 2

Description of the Energy Terms used in Molecular Mechanics Calculations

The energy terms used to calculate the minimum energy of a system with molecular mechanics calculations have the following descriptions:

$$E_{str} = \sum_{i=1}^{N \text{ bonds}} \frac{1}{2} k_{di} (d_i - d_{oi})^2$$

$$E_{bend} = \sum_{i=1}^{N \text{ bonds}} \frac{1}{2} k_{\theta i} (\theta_i - \theta_{oi})^2$$

$$E_{oop} = \sum_{i=1}^{N \text{ planes}} \frac{1}{2} k_{pi} d_{pi}^2$$

$$E_{tors} = \sum_{i=1}^{N \text{ torsionangles}} \frac{1}{2} V_{\omega i} [1 + S_i \cos (l_{ni} \cdot \omega_i)]$$

$$E_{vdw} = \sum_{i=1}^{N \text{ atoms}} \sum_{j>i}^{N-1} C_{ij} \left(\frac{1.0}{a_{ij}^{12}} - \frac{2.0}{a_{ij}^6} \right)$$

$$E_{ele} = 332.17 \cdot \sum_{i=1}^{N \text{ atoms}} \sum_{j>i}^{N-1} \frac{Q_i \cdot Q_j}{D_{ij} \cdot r_{ij}}$$

k_d , k_θ and k_p are the bond stretching, angle bending and out of plane force constants respectively. The subscript _o indicates the "ideal" value.

d is the bond length.

θ is the bond angle.

d_p is the distance the atom is from the plane.

ω is the torsion angle.

V_ω is the energy barrier to torsional rotation.

n is the periodicity of a torsional rotation.

S takes on a value of +1 for staggered torsion angles and -1 for eclipsed torsion angles.

C is a van der Waals constant.

$$a_{ij} = r_{ij}/(R_i + R_j).$$

r is the distance between nonbonded atoms.

R is the van der Waals radius.

Q is the partial coulombic charge of an atom.

D_{ij} is the value of the dielectric function for atoms i and j .

APPENDIX 3

X-Ray Crystal Structure of TOT / Acetone

These data were obtained by Dr. R. Hynes.

TOTO - NMR/NRC - FEB 91

Space Group and Cell Dimensions Trigonal, P 3121
a 13.4612(11) c 30.2793(20)
Volume 4751.6(5)Å³

Empirical formula : C₆₉ H₇₈ O₁₃

Cell dimensions were obtained from 25 reflections with 2Theta angle in the range 80.00 - 100.00 degrees.

Crystal dimensions : 0.20 X 0.25 X 0.25 mm

FW = 1115.36 Z = 3 F(000) = 1788.00

Dcalc 1.169Mg.m⁻³, mu 0.61mm⁻¹, lambda 1.54056Å, 2Theta(max) 99.7

The intensity data were collected on a Nonius diffractometer, using the theta/2theta scan mode.

The h,k,l ranges are :-- 0 11, 0 11, 0 29

No. of reflections measured 2691

No. of unique reflections 1889

No. of reflections with Inet > 2.5sigma(Inet) 1624

No correction was made for absorption

The last least squares cycle was calculated with 81 atoms, 372 parameters and 1624 out of 1889 reflections. Weights based on counting-statistics were used.

The residuals are as follows :--

For significant reflections, RF 0.043, Rw 0.023 GoF 3.15

For all reflections, RF 0.053, Rw 0.023.

where RF = Sum(Fo-Fc)/Sum(Fo),

Rw = Sqrt[Sum(w(Fo-Fc)**2)/Sum(wFo**2)] and

GoF = Sqrt[Sum(w(Fo-Fc)**2)/(No. of reflns - No. of params.)]

The maximum shift/sigma ratio was 0.007.

In the last D-map, the deepest hole was -0.160e/Å³, and the highest peak 0.150e/Å³.

Secondary ext. coeff. = 0.568309 sigma = 0.043948

Table of Atomic Parameters x,y,z and Biso.
F.S.Ds. refer to the last digit printed.

	x	y	z	Biso
O 1	0.4693(3)	0.8887(3)	0.09431(11)	3.8(3)
O 2	0.3736(4)	0.7233(3)	0.05693(12)	6.7(4)
O 3	0.3389(3)	0.8256(3)	0.17174(11)	3.5(3)
O 4	0.1696(4)	0.7000(4)	0.14217(18)	9.5(4)
O 5	0.3311(3)	0.9896(3)	0.10553(12)	3.8(3)
O 6	0.2087(4)	0.8970(4)	0.05056(14)	6.2(3)
C 1	0.4121(5)	0.7725(5)	0.09096(19)	4.0(5)
C 2	0.4116(5)	0.7170(5)	0.13379(18)	3.4(4)
C 3	0.4511(5)	0.6376(5)	0.13467(19)	4.1(4)
C 4	0.4998(5)	0.6121(5)	0.09453(18)	6.1(5)
C 5	0.4471(5)	0.5865(5)	0.17507(22)	4.7(5)
C 6	0.4047(5)	0.6115(6)	0.21249(18)	4.6(5)
C 7	0.3682(5)	0.6894(5)	0.21237(18)	4.0(4)
C 8	0.3231(6)	0.7162(6)	0.25431(18)	5.5(5)
C 9	0.2258(6)	0.6090(6)	0.27454(19)	7.5(5)
C10	0.4193(6)	0.7785(6)	0.28826(18)	6.8(6)
C11	0.3719(5)	0.7404(5)	0.17247(19)	3.4(4)
C12	0.2314(6)	0.7927(6)	0.15748(21)	4.7(5)
C13	0.2017(5)	0.8846(5)	0.16347(19)	3.6(4)
C14	0.1274(5)	0.8745(6)	0.19763(20)	4.3(5)
C15	0.0710(5)	0.7726(6)	0.22703(19)	5.6(5)
C16	0.1053(6)	0.9650(7)	0.20166(19)	5.0(5)
C17	0.1522(6)	1.0580(6)	0.17361(23)	4.9(5)
C18	0.2245(6)	1.0674(5)	0.13905(21)	4.2(5)
C19	0.2729(6)	1.1673(6)	0.10787(21)	5.3(5)
C20	0.1812(6)	1.1538(6)	0.07495(20)	8.1(6)
C21	0.3229(6)	1.2833(6)	0.13099(24)	8.0(6)
C22	0.2492(5)	0.9794(6)	0.13531(18)	3.7(4)
C23	0.3021(6)	0.9463(5)	0.06375(21)	4.1(5)
C24	0.4118(5)	0.9784(5)	0.03839(18)	3.7(4)
C25	0.4348(6)	1.0432(5)	-0.00042(18)	4.2(5)
C26	0.3510(5)	1.0780(5)	-0.01886(17)	5.7(5)
C27	0.5394(6)	1.0795(5)	-0.02086(18)	4.7(5)
C28	0.6191(5)	1.0537(5)	-0.00417(19)	4.4(4)
C29	0.5985(6)	0.9882(5)	0.03409(19)	3.8(4)
C30	0.6853(6)	0.9611(6)	0.05291(19)	4.8(5)
C31	0.7190(6)	0.8968(7)	0.02087(19)	9.1(7)
C32	0.7948(6)	1.0727(6)	0.06643(22)	8.6(6)
C33	0.4941(6)	0.9527(5)	0.05409(17)	3.6(5)
O	0.7736(6)	0.7736	1/2	14.9(7)
CA1	0.6873(9)	0.6873	1/2	8.2(7)
CA2	0.5839(7)	0.6797(8)	0.4838 (3)	13.4(9)

Biso is the Mean of the Principal Axes of the Thermal Ellipsoid

Table of Calculated Hydrogen Atom Parameters

	x	y	z	Biso
H 4A	0.440	0.579	0.067	7.4
H 4B	0.577	0.688	0.084	7.4
H 4C	0.524	0.549	0.103	7.4
H 5	0.475	0.524	0.175	5.7
H 6	0.407	0.569	0.243	5.7
H 8	0.290	0.772	0.246	6.6
H 9A	0.154	0.567	0.252	7.4
H 9B	0.252	0.548	0.284	7.4
H 9C	0.194	0.627	0.304	7.4
H10A	0.388	0.804	0.316	7.8
H10B	0.453	0.724	0.298	7.8
H10C	0.487	0.855	0.273	7.8
H15A	0.018	0.692	0.210	6.3
H15B	0.133	0.762	0.246	6.3
H15C	0.018	0.782	0.252	6.3
H16	0.054	0.965	0.229	5.8
H17	0.133	1.126	0.179	6.0
H19	0.338	1.168	0.087	6.4
H20A	0.148	1.074	0.057	9.1
H20B	0.111	1.150	0.093	9.1
H20C	0.211	1.224	0.052	9.1
H21A	0.358	1.352	0.107	8.4
H21B	0.257	1.289	0.150	8.4
H21C	0.393	1.294	0.152	8.4
H26A	0.270	1.003	-0.027	6.4
H26B	0.338	1.131	0.004	6.4
H26C	0.384	1.126	-0.049	6.4
H27	0.560	1.129	-0.051	5.4
H28	0.701	1.085	-0.021	4.8
H30	0.654	0.910	0.083	5.5
H31A	0.645	0.816	0.012	11.8
H31B	0.755	0.947	-0.009	11.8
H31C	0.782	0.879	0.035	11.8
H32A	0.861	1.060	0.080	8.8
H32B	0.830	1.125	0.037	8.8
H32C	0.774	1.122	0.089	8.8
HCA2A	0.506	0.598	0.485	13.3
HCA2B	0.560	0.733	0.503	13.3
HCA2C	0.587	0.706	0.450	13.3

Biso is the Mean of the Principal Axes of the Thermal Ellipsoid

(Calculated using C-H distance of 1.08 Å, Biso = 1.1 x Biso of the bonded atom.)

Table of $u(i,j) \cdot 100$ for atoms refined anisotropically.
E.S.Ds. refer to the last digit printed

	u11(U)	u22	u33	u12	u13	u23
O 1	5.9(3)	4.5(3)	3.65(24)	2.4(3)	0.28(22)	0.27(22)
O 2	13.5(5)	4.5(3)	4.9 (3)	2.6(3)	-2.4 (3)	-0.6 (3)
O 3	3.8(3)	4.8(3)	4.64(24)	2.1(3)	-0.30(22)	0.06(22)
O 4	7.9(4)	6.5(4)	23.0 (6)	4.7(4)	-6.9 (4)	-4.9 (4)
O 5	4.6(3)	5.1(3)	4.44(23)	2.2(3)	0.21(24)	-0.51(23)
O 6	4.9(3)	9.0(4)	7.1 (3)	1.5(3)	-1.0 (3)	-2.2 (3)
C 1	5.7(5)	3.7(5)	5.0 (4)	1.7(4)	0.3 (4)	0.7 (4)
C 2	4.2(4)	3.6(4)	4.3 (4)	1.2(4)	-0.1 (3)	0.2 (4)
C 3	5.7(5)	4.7(5)	6.0 (5)	3.2(4)	-0.3 (4)	0.1 (4)
C 4	10.1(6)	7.3(6)	7.9 (4)	6.0(5)	1.9 (5)	-0.1 (4)
C 5	6.5(5)	4.7(5)	7.7 (5)	3.5(4)	-0.1 (4)	1.1 (4)
C 6	6.4(5)	6.7(6)	5.4 (4)	4.1(4)	0.1 (4)	1.8 (4)
C 7	5.0(5)	6.3(5)	4.5 (4)	3.1(4)	0.8 (4)	1.3 (4)
C 8	7.0(6)	10.3(6)	4.9 (4)	5.2(5)	1.4 (4)	2.6 (4)
C 9	7.1(6)	11.5(7)	6.7 (5)	2.2(5)	2.8 (4)	0.6 (5)
C10	9.9(6)	11.0(6)	5.7 (4)	5.9(6)	-0.3 (4)	-0.5 (4)
C11	4.2(4)	4.0(4)	5.0 (4)	2.1(4)	-0.5 (4)	0.5 (4)
C12	6.2(6)	5.7(6)	6.5 (5)	3.3(5)	-1.1 (4)	-0.4 (4)
C13	4.4(5)	4.7(5)	5.2 (4)	2.9(4)	-1.2 (4)	-0.7 (4)
C14	4.7(5)	7.1(6)	5.1 (4)	3.3(5)	-0.8 (4)	-0.4 (4)
C15	5.7(5)	9.0(6)	6.1 (4)	3.3(5)	0.6 (4)	2.2 (4)
C16	5.3(5)	8.5(6)	5.4 (4)	3.5(5)	0.3 (4)	-0.6 (5)
C17	5.1(5)	6.6(6)	7.9 (5)	3.7(5)	-0.5 (4)	-1.6 (4)
C18	5.0(5)	4.2(5)	6.7 (5)	2.2(4)	-0.4 (4)	0.0 (4)
C19	6.4(5)	5.5(5)	9.4 (6)	3.8(5)	0.3 (5)	1.1 (5)
C20	12.6(7)	10.2(7)	8.8 (5)	6.5(6)	-0.5 (5)	3.1 (5)
C21	9.6(7)	5.2(6)	14.2 (7)	2.8(6)	-0.1 (6)	0.6 (5)
C22	4.4(5)	5.0(5)	4.8 (4)	2.3(4)	-0.3 (4)	-0.3 (4)
C23	6.4(6)	3.9(5)	5.1 (5)	2.6(5)	-0.2 (5)	-0.1 (4)
C24	5.1(5)	4.1(5)	3.7 (4)	1.6(4)	0.0 (4)	-0.8 (3)
C25	6.7(6)	4.7(5)	4.4 (4)	2.6(4)	0.0 (4)	0.4 (4)
C26	7.7(6)	6.7(5)	7.0 (4)	3.4(5)	-0.9 (4)	1.8 (4)
C27	7.9(6)	5.0(5)	4.5 (4)	2.8(5)	0.9 (4)	1.3 (4)
C28	5.5(5)	5.2(5)	4.4 (5)	1.6(4)	1.9 (4)	1.1 (4)
C29	4.9(5)	4.7(5)	4.6 (4)	2.3(4)	0.9 (4)	-0.1 (4)
C30	5.3(5)	7.2(6)	5.4 (5)	2.8(5)	0.5 (4)	1.1 (4)
C31	15.3(8)	18.7(9)	7.9 (5)	14.1(8)	0.0 (6)	-1.3 (6)
C32	7.8(6)	10.1(7)	12.4 (7)	2.6(6)	-3.1 (5)	2.1 (6)
C33	6.5(6)	3.8(4)	3.0 (4)	2.3(4)	-0.3 (4)	0.0 (3)
O	9.9(5)	9.9	32.7 (13)	2.0(7)	-1.4 (4)	1.4
CA1	6.9(7)	6.9	14.0 (11)	0.9(9)	0.7 (5)	-0.7
CA2	9.1(8)	18.8(12)	19.4 (10)	4.3(9)	-1.6 (8)	-0.9 (8)

Anisotropic Temperature Factors are of the form

$$\text{Temp} = -2\pi^2 [h^2 u_{11}^* \sin^2 \theta + k^2 u_{22}^* \sin^2 \theta + l^2 u_{33}^* \sin^2 \theta + 2hk u_{12}^* \sin^2 \theta + 2hl u_{13}^* \sin^2 \theta + 2kl u_{23}^* \sin^2 \theta]$$

Table of Bond Angles in Degrees

C(1)-O(1)-C(33)	117.2(4)	C(16)-C(17)-C(18)	121.9(6)
C(11)-O(3)-C(12)	117.0(4)	C(17)-C(18)-C(19)	121.8(6)
C(22)-O(5)-C(23)	118.9(4)	C(17)-C(18)-C(22)	116.1(6)
O(1)-C(1)-O(2)	122.8(5)	C(19)-C(18)-C(22)	122.1(6)
O(1)-C(1)-C(2)	111.7(5)	C(18)-C(19)-C(20)	110.0(5)
O(2)-C(1)-C(2)	125.4(5)	C(18)-C(19)-C(21)	113.6(5)
C(1)-C(2)-C(3)	119.0(5)	C(20)-C(19)-C(21)	109.7(5)
C(1)-C(2)-C(11)	121.7(6)	O(5)-C(22)-C(13)	117.3(6)
C(3)-C(2)-C(11)	119.3(5)	O(5)-C(22)-C(18)	120.0(5)
C(2)-C(3)-C(4)	122.1(5)	C(13)-C(22)-C(18)	122.4(6)
C(2)-C(3)-C(5)	117.1(5)	O(5)-C(23)-O(6)	125.6(6)
C(4)-C(3)-C(5)	120.8(6)	O(5)-C(23)-C(24)	106.9(5)
C(3)-C(5)-C(6)	121.2(5)	O(6)-C(23)-C(24)	127.5(6)
C(5)-C(6)-C(7)	122.4(5)	C(23)-C(24)-C(25)	118.7(6)
C(6)-C(7)-C(8)	121.2(5)	C(23)-C(24)-C(33)	122.3(5)
C(6)-C(7)-C(11)	116.6(5)	C(25)-C(24)-C(33)	118.9(6)
C(8)-C(7)-C(11)	122.2(6)	C(24)-C(25)-C(26)	122.0(6)
C(7)-C(8)-C(9)	111.6(5)	C(24)-C(25)-C(27)	117.6(6)
C(7)-C(8)-C(10)	111.1(5)	C(26)-C(25)-C(27)	120.3(5)
C(9)-C(8)-C(10)	110.0(5)	C(25)-C(27)-C(28)	122.0(5)
O(3)-C(11)-C(2)	118.7(5)	C(27)-C(28)-C(29)	122.0(5)
O(3)-C(11)-C(7)	117.8(5)	C(28)-C(29)-C(30)	122.4(6)
C(2)-C(11)-C(7)	123.3(6)	C(2.)-C(29)-C(33)	115.4(6)
O(3)-C(12)-O(4)	122.5(6)	C(30)-C(29)-C(33)	122.2(5)
O(3)-C(12)-C(13)	112.1(5)	C(29)-C(30)-C(31)	112.8(5)
O(4)-C(12)-C(13)	125.4(6)	C(29)-C(30)-C(32)	110.2(5)
C(12)-C(13)-C(14)	119.1(6)	C(31)-C(30)-C(32)	108.3(6)
C(12)-C(13)-C(22)	119.7(6)	O(1)-C(33)-C(24)	117.6(5)
C(14)-C(13)-C(22)	121.2(6)	O(1)-C(33)-C(29)	118.2(6)
C(13)-C(14)-C(15)	122.9(6)	C(24)-C(33)-C(29)	124.2(5)
C(13)-C(14)-C(16)	115.8(6)	O-C(1a)-C(2a)	121.5(6)
C(15)-C(14)-C(16)	121.3(6)	O-C(1a)-C(2a)a	121.5(6)
C(14)-C(16)-C(17)	122.6(6)	C(2a)-C(1a)-C(2a)a	117.0(10)

Table of Bond Distances in Angstroms

O(1)-C(1)	1.358(7)	C(14)-C(15)	1.486(9)
O(1)-C(33)	1.432(6)	C(14)-C(16)	1.396(10)
O(2)-C(1)	1.194(7)	C(16)-C(17)	1.377(11)
O(3)-C(11)	1.422(7)	C(17)-C(18)	1.391(10)
O(3)-C(12)	1.355(8)	C(18)-C(19)	1.499(9)
O(4)-C(12)	1.194(8)	C(18)-C(22)	1.386(10)
O(5)-C(22)	1.408(7)	C(19)-C(20)	1.525(9)
O(5)-C(23)	1.369(7)	C(19)-C(21)	1.527(10)
O(6)-C(23)	1.160(8)	C(23)-C(24)	1.523(9)
C(1)-C(2)	1.495(8)	C(24)-C(25)	1.402(9)
C(2)-C(3)	1.412(9)	C(24)-C(33)	1.397(10)
C(2)-C(11)	1.388(8)	C(25)-C(26)	1.528(9)
C(3)-C(4)	1.500(8)	C(25)-C(27)	1.384(10)
C(3)-C(5)	1.392(9)	C(27)-C(28)	1.378(10)
C(5)-C(6)	1.383(9)	C(28)-C(29)	1.397(9)
C(6)-C(7)	1.364(9)	C(29)-C(30)	1.499(9)
C(7)-C(8)	1.526(8)	C(29)-C(33)	1.379(9)
C(7)-C(11)	1.378(8)	C(30)-C(31)	1.513(9)
C(8)-C(9)	1.511(9)	C(30)-C(32)	1.544(10)
C(8)-C(10)	1.533(9)	O-C(1a)	1.162(15)
C(12)-C(13)	1.488(9)	C(1a)-C(2a)	1.430(10)
C(13)-C(14)	1.398(9)	C(1a)-C(2a)a	1.430(10)
C(13)-C(22)	1.397(9)		

APPENDIX 4

Derivation of the Potential Energy of Pyridine in a Two-fold Symmetry Site

The general expression for a Fourier series used to represent a periodic function, $f(\theta)$, is given by:

$$f(\theta) = a_0 + \sum_{n=1}^{\infty} \left(a_n \cos\left(\frac{n\pi\theta}{L}\right) + b_n \sin\left(\frac{n\pi\theta}{L}\right) \right) \quad (1)$$

where a_0 , a_n , and b_n are constants. L is half the period of the function and n is an integer. For symmetric functions, i.e. $f(\theta) = f(-\theta)$, this expression can be simplified to:

$$f(\theta) = a_0 + \sum_{n=1}^{\infty} a_n \cos\left(\frac{n\pi\theta}{L}\right) \quad (2)$$

Consider a pyridine molecule interacting with points of attraction on either side of a two-fold symmetry axis:

If the ring rotates about an axis perpendicular to the molecular plane, with rotation angle, θ , then the interaction energy of each of the atoms in the ring with each of the points of attraction can be represented by equation (2) with $L=\pi$. If the potential energy, rather than the energy of attraction is considered then a $(1-\cos\theta)$ rather than a $\cos\theta$ term should be used. Now the potential energy, $E_i(\theta)$, of each atom in the ring, with respect to one of the points of attraction can be expressed as follows:

$$E_N(\theta) = N_o + \sum_{n=1}^{\infty} N_n(1-\cos(n(\theta+\phi)))$$

$$E_{CA}(\theta) = CA_o + \sum_{n=1}^{\infty} CA_n(1-\cos(n(\theta+\frac{\pi}{3}+\phi)))$$

$$E_{CB}(\theta) = CB_o + \sum_{n=1}^{\infty} CB_n(1-\cos(n(\theta+\frac{2\pi}{3}+\phi)))$$

$$E_{CC}(\theta) = CC_o + \sum_{n=1}^{\infty} CC_n(1-\cos(n(\theta+\pi+\phi)))$$

$$E_{CD}(\theta) = CD_o + \sum_{n=1}^{\infty} CD_n(1-\cos(n(\theta+\frac{4\pi}{3}+\phi)))$$

$$E_{CE}(\theta) = CE_o + \sum_{n=1}^{\infty} CE_n(1-\cos(n(\theta+\frac{5\pi}{3}+\phi)))$$

A similar set of six equations can be written to express the potential energy of each of the atoms with respect to the other point of attraction. These equations are exactly as above with the sign of ϕ changed. The constants CA_i , CB_i , CC_i , CD_i and CE_i are approximately equal to one another and will be labelled C_i . C_n becomes smaller with increasing n and can be neglected for terms of order greater than six. The cosine terms can be expanded using standard trigonometric identities and the six equations above as well as their counterparts with $(-\phi)$ can be averaged. The

result is:

$$E(\theta) = K_0 + \sum_{n=1}^5 (K_n (\cos(n\theta) \cos(n\phi))) + K_6 (1 - (\cos(6\theta) \cos(6\phi)))$$

where:

$$K_0 = \sum_{n=0}^5 (N_n + 5 C_n)$$

$$K_i = C_i - N_i \quad i=1 \text{ to } 5$$

$$K_6 = (N_6 + 5 C_6)$$

If the nitrogen has a higher affinity for the points of attraction then the constants K_i are negative. Unlike K_i ($i=1 \rightarrow 5$) which are differences, K_6 is a sum and adds constructively to the potential function. For appropriate constants and angles $E(\theta)$ can take on the following shape:

This figure illustrates that it is possible to have an energy barrier on the two-fold axis. For the above plot the following parameters were used: $N_0=300$ J/mol and $C_0=200$ J/mol. The successive constants were taken as half of the previous constant:

$$C_i = \frac{1}{2} (C_{i-1})$$

$$N_i = \frac{1}{2} (N_{i-1})$$

ϕ was taken as 23° .

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