1

MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS
STANDARD REFERENCE MATERIAL 1010a
(ANSI and ISO TEST CHART No 2)

National Library
of Canada

Bibliothèque nationale
du Canada

Canadian Theses Service

Service des thèses canadiennes

Ottawa, Canada
K1A 0N4

NOTICE

The quality of this microform is heavily dependent upon the quality of the original thesis submitted for microfilming. Every effort has been made to ensure the highest quality of reproduction possible.

If pages are missing, contact the university which granted the degree.

Some pages may have indistinct print especially if the original pages were typed with a poor typewriter ribbon or if the university sent us an inferior photocopy.

Reproduction in full or in part of this microform is governed by the Canadian Copyright Act, R.S.C. 1970, c. C-30, and subsequent amendments.

AVIS

La qualité de cette microforme dépend grandement de la qualité de la thèse soumise au microfilmage. Nous avons tout fait pour assurer une qualité supérieure de reproduction.

S'il manque des pages, veuillez communiquer avec l'université qui a conféré le grade.

La qualité d'impression de certaines pages peut laisser à désirer, surtout si les pages originales ont été dactylographiées à l'aide d'un ruban usé ou si l'université nous a fait parvenir une photocopie de qualité inférieure.

La reproduction, même partielle, de cette microforme est soumise à la Loi canadienne sur le droit d'auteur, SRC 1970, c. C-30, et ses amendements subséquents.

**^{13}C NMR Conformational Analysis of
Dicyclohexyl-12,13 and 14Crown4 Ethers
and Their Complexes.**

by
R.A.Kirby

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

Doctor of Philosophy

Carleton University
Ottawa, Ont.
Nov.1990.

National Library
of Canada

Bibliothèque nationale
du Canada

Canadian Theses Service Service des thèses canadiennes

Ottawa, Canada
K1A 0N4

The author has granted an irrevocable non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of his/her thesis by any means and in any form or format, making this thesis available to interested persons.

The author retains ownership of the copyright in his/her thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without his/her permission.

L'auteur a accordé une licence irrévocable et non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de sa thèse de quelque manière et sous quelque forme que ce soit pour mettre des exemplaires de cette thèse à la disposition des personnes intéressées.

L'auteur conserve la propriété du droit d'auteur qui protège sa thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

ISBN 0-315-68914-5

The undersigned hereby recommend to
The Faculty of Graduate Studies and Research
acceptance of the thesis, submitted by

Robert A. Kirby #135866
in partial fulfilment of the requirements
for the degree of Doctor of Philosophy.

.....
Chairman, Department
of Chemistry

.....
Thesis Supervisor

.....
External Examiner

Carleton University

Abstract

The synthesis and X-ray crystallographic characterization of the cis-syn-cis and cis-anti-cis isomers of dicyclohexyl-12,13 and 14-crown-4 ethers and their lithium complexes are reported. The solid phase conformations of these compounds and their LiSCN or LiClO₄ complexes are described employing the X-ray results and conformational changes induced by complexation are discussed.

Solid phase ¹³C CPMAS spectra are analysed in light of X-ray data with individual chemical shift assignments made by reference to torsional angles. Low temperature high resolution ¹³C chemical shifts are compared with solid phase CPMAS ¹³C chemical shifts and similarities between solid and liquid phase conformations are noted.

Barriers to cyclohexyl ring inversion are reported from ¹³C coalescence temperature measurements for 12 and 14 membered macrocycles. Comparisons are made for free energies of cyclohexane chair to chair interconversion for these crown ethers and their complexes. Flexibility and complexational differences between configurational isomers and between crown ethers having different cavity sizes are reported. This analysis is supplemented by ¹³C T₁ measurements of molecular mobilities in solution. Also, correlation between solid phase torsional strain, solid and liquid phase chemical shifts and liquid phase mobilities are reported.

Analysis of these crown ethers and their complexes suggest the larger macrocycles permit greater molecular flexibility and are

superior complexing agents. The cis-anti-cis-dicyclohexyl-12,13 and 14-crown-4 ethers were found resistant to formation of solid complexes with lithium salts while the cis-syn-cis isomers all formed stable complexes. These cis-syn-cis complexes exhibit increasing lithium cation distances above the mean plane of the four oxygen atoms as cavity size is decreased.

Complexation of the cis-syn-cis-dicyclohexyl-12 and 14-crown-4 ligands occurs via a ring inversion of one of the cyclohexyl substituents. Also, effective complexing geometries have ethereal oxygen lone pairs directed toward the cation. Low temperature solution analysis of the 12 and 14 membered systems indicate the cis-anti-cis isomers have two conformations in equilibrium while the corresponding cis-syn-cis isomers exhibit a single conformer. Cis-anti-cis-dicyclohexyl-12-crown-4 is more flexible than its configurational isomer in solution while the reverse is true in the 14-crown-4 series.

Individual chemical shift assignments are made using conventional wisdom concerning cyclohexane substitution patterns. This empirical knowledge of conformationally dependant ^{13}C chemical shift behavior is supplemented by computational data describing the correlation between torsional angle and chemical shift.

Due to the importance of computational results describing the ^{13}C chemical shift dependencies and to determine the mechanism responsible for conformationally dependant chemical shifts, two torsional systems have been studied. Chemical shift variations due to torsional angle changes for n-butane and methoxyethane are

reported using LORG type ab initio MO calculations of ^{13}C shielding tensors. Individual bond anisotropic contributions for the significant shielding components of these two systems are reported. Comparison between LORG results obtained in this study and earlier calculations on the butane system by Seidman and Maciel⁽³¹⁾ and Barfield and Yamamura⁽³⁴⁾ are made.

A mechanism explaining conformationally dependant ^{13}C chemical shifts is proposed. This mechanism is contingent upon ring currents acting as deshielding influences and is based upon anisotropic shielding tensor evidence in the computational results for the two systems studied herein.

ACKNOWLEDGEMENTS

I take this opportunity to thank:

Dr. G.W. Buchanan for suggesting this project and for his many useful comments throughout;

Dr. J. Tse for running ab initio programs and for numerous useful comments on computational chemistry;

Dr. J.P. Charland for X-ray analysis;

Dr. J.A. Ripmeester and Dr. C.I. Ratcliffe for running solid phase samples;

Dr. A. Jay and Kane Denike for advice on Macintosh software;

Karl Diedrich and Robert Kehle for extensive assistance and advice;

Keith Bourque for running NMR samples;

Administrative people in the Chemistry department, Barb, Donna and Marilyn.

TABLE OF CONTENTS

	page
ACCEPTANCE SHEET	i i
ABSTRACT.....	i i i
ACKNOWLEDGEMENTS.....	v i
TABLE OF CONTENTS	v i i
LIST OF ORTEPS.....	v i i i
LIST OF FIGURES.....	i x
LIST OF GRAPHS	x
CHAPTER 1: Introduction.....	1
CHAPTER 2: Theory and Background	
2.1 Basic Theory	6
2.2 NMR Experimental	18
2.3 Chemical Shifts	24
2.4 Molecular Dynamics	37
2.5 Crown Ethers	53
CHAPTER 3: Results and Discussions	
3.1 CAC and CSC Dicyclohexyl14crown4 and Complexes ..	70
3.2 CAC and CSC Dicyclohexyl12crown4 and Complexes ..	102
3.3 CAC and CSC Dicyclohexyl13crown4 and Complexes ..	132
CHAPTER 4: Molecular Dynamics	147
CHAPTER 5: Computational ¹³ C NMR	160
CHAPTER 6: Conclusion	206
CHAPTER 7: Experimental	207
REFERENCES:	221
APPENDIX 1	1-12
APPENDIX 2	1-19

List of ORTEPS

ORTEP	TITLE	Page
1.	CACDC14C4	71
2.	CSCDC14C4	84
3.	CSCDC14C4:LiSCN	92
4.	CSCDC14C4:LiClO ₄	99
5.	CSCDC12C4	102
6.	CSCDC12C4:LiSCN	114
7.	CACDC12C4	124
8.	CACDC13C4	132
9.	CSCDC13C4:LiSCN	138
10.	CSCDC13C4:LiClO ₄	142
11.	DiBenzo12C4	145

List of Figures

Figure	Title
1.	Angular Momentum
2.	Dipolar Interaction
3.	Magic Angle Spinning
4.	Pulse Sequence For Cross Polarization
5.	Magnetization Vectors
6.	FID
7.	Diamagnetic Shielding
8.	Butane Conformational Energy
9.	Energy of Activation
10.	Dipolar Relaxation
11.	Dibenzo18Crown6
12.	Gauche Versus Anti Conformations
13.	12C4
14.	12C4:LiSCN
15.	14C4
16.	1,3,8,10-tetraoxacyclotetradecane
17.	Chair to Chair Conversion
18.	Butane
19.	Ethyl-methyl Ether
20.	Butane 120 Degree
21.	Ethyl-methyl Ether
22.	Butane 120 Degrees Along X Axis
23.	Ethyl-methyl Ether 120 Degrees Along X Axis

CHAPTER 1

INTRODUCTION

Conformational analysis has been a part of organic chemistry since tetrahedral geometry at saturated carbon was first proposed.⁽¹⁾ The first application of such analysis dates back to 1890 when Sachse⁽²⁾ suggested there were two shapes of cyclohexyl rings in which all valence angles were tetrahedral. These are now known as the chair and boat forms. The existence of two types of bonds for cyclohexyl substituents, now called axial and equatorial, was first demonstrated by Kohlrausch et al in 1936.⁽³⁾ An explosion of interest in conformational analysis began in 1950 when it was demonstrated conformational preference had significant influence on chemical reactivity.⁽⁴⁾ In the present research environment it is now understood that molecular conformations dictate the course of a wide range of biological reactions. One example of this is the complex folding of polypeptide chains in enzymes to bring a number of amino acids together creating active sites where reacting molecules or substrates fit in orientations which dictate reaction routes.⁽⁵⁾ This has implications for and therefore dictates research initiatives into the design of biologically active structures such as the essentially planar anthracycline family of anticancer drugs. These are believed to take on conformations in solution which permit them to slide into the spiral DNA structure to form weak bonds and inhibit replication.⁽⁶⁾ It is therefore important that chemists continue to characterize the preferred conformations of molecular systems and that the tools of conformational analysis be developed and improved.

One of the most important physical properties in chemistry today is the NMR chemical shift and ^{13}C is premier among all nuclei presently in use. ^{13}C NMR chemical shifts are routinely used for structural analysis (7) and have been used to probe dynamic features for a variety of molecules in solution.(8-13) The existence of conformationally dependent ^{13}C chemical shifts is documented (14-17) and has given rise to the use of ^{13}C NMR as an indicator of molecular conformational isomerism.(18-20)

Generally done for molecules in solution, conformational analysis often requires low temperature experiments since interconversion of conformational isomers occurs rapidly on the NMR timescale at ambient temperatures. However, the advent of cross-polarization magic-angle spinning spectroscopy (CPMAS)(21-23) has afforded reasonable NMR spectra for the solid phase and this has initiated application of the principles of ^{13}C conformational analysis to solid compounds.(24,25) Doing conformational analysis in the solid phase avoids the problems encountered in recording high-resolution spectra at low temperatures. It also permits correlation between ^{13}C chemical shifts obtained in the solid phase with specific conformations as determined by X-ray crystallography. Such comparisons have the potential of defining conformationally dependant shifts by relating the observed resonance with the torsional angles for the nucleus in question. The results of such analysis can also lead to a sharper understanding of the conformations which exist in solution.

The information generated in these experiments also has implications for theoretical calculations of NMR shielding tensors

since the correct molecular geometry is known for a specific chemical shift. The result is that calculations of chemical shifts can be verified against the known isotropic or anisotropic values and this can lead to intelligent selection of computational approaches and methods.⁽²⁶⁾ Recent studies now seek to compare calculated anisotropic shielding tensors with experimental values obtained in single crystal studies capable of measuring the directional shielding properties of the species of interest.⁽²⁷⁾ Comparisons between calculated and experimental chemical shifts are best done for the gas phase since measurements at a selection of pressures permit extrapolation to zero concentration thereby eliminating lattice influences on experimental values.⁽²⁸⁾ However, for the purposes of comparing conformationally dependant chemical shifts, the solid phase is preferable since absolute conformations are known for this phase alone.

A difficulty in comparisons between calculated and experimental conformationally dependant chemical shifts occurs in their respective error magnitudes. Variations in chemical shifts which accompany rotational isomerism are generally up to 8 ppm although at times can be as large as 12 ppm⁽²⁴⁾. The errors for calculated ^{13}C values for small molecules using fairly large basis sets are in the order of 6 ppm.⁽²⁸⁾ Errors may be minimized for the solid phase by computational approaches which take into account influences due to the crystal lattice⁽²⁹⁾. However these are expensive to run, are not well developed and have not been used extensively.

Yet, computational analysis of conformationally dependant ^{13}C chemical shifts can be useful because although absolute magnitudes are questionable, experimental trends (30) have been correctly predicted by a number of calculations.(31-34) The most extensively cited explanation for the gauche γ effect, the most commonly cited conformational effect in ^{13}C NMR, is due to Grant et al (35,36). They proposed electron repulsions between interacting C-H systems produce increases in the electron density about the carbon nucleus and therefore increases in magnetic shielding. Subsequent computational results have disputed this as the major cause of ^{13}C conformational shift variations.(31) However, the empirical result that ^{13}C chemical shifts are conformation dependant is employed in stereochemical and conformational assignments in deference to the lack of a comprehensive mechanism explaining the result.

An ideal experiment in this area of chemistry would combine X-ray crystallographic data with solid and solution phase NMR as well as ab initio MO calculations of ^{13}C shielding tensors for a suitable molecule or family of molecules. Results would provide a comprehensive description of the conformational characteristics of the species studied and a theoretical explanation for the source of any ^{13}C shielding variations associated with conformational isomerism. A difficulty in designing such an experiment is in finding organic molecules capable of conformational isomerism which form x-ray suitable crystals and yet are small enough to be represented by an acceptably sized basis set. Small organic molecules are gaseous or liquid at ambient temperatures(37) and larger species introduce computational difficulty and error through the

requirement that they be represented by small basis set calculations⁽³⁸⁾ and these limit result accuracies.⁽³⁹⁾

A compromise solution initiated by this research project has been to study small ring dicyclohexyl crown ethers and their complexes by ^{13}C NMR and X-ray crystallography. This is supplemented by ab initio MO ^{13}C shielding tensor calculations on algorithms which represent segments of the ethers in question. This affords conformational analysis of a previously undescribed segment of the important crown ether family and their complexes while generating computational analysis of the contributions making up ^{13}C conformationally dependent ^{13}C chemical shift variations for these systems.

This study has therefore undertaken the synthesis and X-ray crystallographic analysis of the cis-syn-cis and cis-anti-cis dicyclohexyl 12,13, and 14-crown-4-ethers and their lithium complexes. This is supported by solid and liquid phase ^{13}C NMR analysis of the preferred conformations of these ligands and their complexes. The IUPAC nomenclature for these compounds is 2,3,8,9-dicyclohexyl-1,4,7,10-tetraoxacyclododecane, commonly (dicyclohexyl-12-crown-4), 2,3,9,10-dicyclohexyl-1,4,8,11-tetraoxacyclotridecane, commonly (dicyclohexyl-13-crown-4) and 2,3,9,10-dicyclohexyl-1,4,8,11-tetraoxacyclotetradecane commonly (dicyclohexyl-14-crown-4). The source of conformationally dependent chemical shift variation for these compounds is studied using LORG type ab initio MO calculations of shielding tensors for butane and methoxyethane.

Chapter 2.

Background And Theory

2.1 NMR:The Basic Theory

The NMR experiment depends upon the fact that some nuclei behave as if they are spinning. This follows from the individual spins of neutrons and protons which make up the nucleus and the nuclear spin is the composite of the spins of its components. Although the laws governing the addition of nuclear spins are not presently defined, experimental results can indicate the net spin of a given nucleus. In fact some generalizations can be made based upon the spin quantum number I and the total number of neutron and protons of a nucleus. If the total number of protons and neutrons is odd, the nucleus has a half integral spin quantum number. When the total mass number is even the spin quantum number has integral values. Thus, the ^1H nucleus has a spin quantum number of $1/2$ and when a neutron is added to give ^2H , the proton and neutron could combine to produce a net spin of 1 or 0. Experiment tells us the ^2H nucleus has a spin quantum number of 1.

When a nucleus, or any other body, has a spin then it has associated with this spin an angular momentum directed along the axis of rotation. According to classical mechanics the momentum of a rotating body is constant in the absence of external forces and can take on any value depending upon the force used to set the body in motion. However, at the atomic level where quantum mechanics is operational, momentum like energy is quantized and can only take on values which are some multiple of Planck's constant, h . Therefore,

the angular momentum of any nucleus having a net spin is given by the relation

$$p = h[I(I+1)]^{1/2}/2\pi \quad (1)$$

where I is the spin quantum number and angular momentum p , is a vector.

A rotating charge acts in the same manner as a current loop and has associated with it a magnetic field. This field is described by the magnetic moment of a nucleus and this is also directed along the axis of rotation and is related to the angular momentum by Equation (2)

$$\mu = \gamma p \quad (2)$$

The proportionality constant relating magnetic moment and angular momentum vectors is called the magnetogyric ratio and is constant for each nucleus. The parameter γ is defined by Equation (2) and relates the area taken up by a nucleus with the nuclear charge experiencing rotation. Since it involves areas of atomic dimension, γ is non-classical in origin and must be determined experimentally for each nucleus.

Angular momentum and magnetic moment are therefore vectors which take up the same number of orientations as the nuclear spin. The total number of spin, angular momentum and magnetic moment vectors, is given by the relation $2I+1$, where I is the spin quantum number. The reference axis is designated the Z axis and corresponds

to the direction of an externally applied magnetic field and the components of the vector must be integral or half integral multiples of $h/2\pi$. Thus for a spin $1/2$ nucleus such as ^{13}C there are two possible orientations of nuclear spin, angular momentum and magnetic moment. These are typically represented as shown in Figure 1 below.

Figure 1. Representation of angular momentum or magnetic moment for a spin $1/2$ nucleus.

When the magnetic moment interacts with an externally applied field B_0 it experiences a torque T which is given by the cross product of the magnetic moment and applied field vectors.

$$T = \mu \times B_0 \quad (3)$$

This causes the magnetic moment to precess about the applied field with an angular velocity and direction which depends upon the

strength and direction of B_0 . This angular velocity is given by the product of B_0 and the magnetogyric ratio.

$$\omega = -\gamma B_0 \quad (4)$$

The frequency of precession is therefore given by the relation

$$\nu = \omega/2\pi = \gamma B_0/2\pi \quad (5)$$

and is termed the Larmor frequency. Each nucleus therefore has a unique Larmor frequency since magnetogyric ratios for different nuclei are distinct.

In the presence of an applied field the $2I+1$ spin levels of a nucleus are separated into different energy levels. Quantum mechanics tells us the energy of interaction of each orientation of the magnetic moment with an externally applied field is equal to the component of the magnetic moment along the field multiplied by the magnitude of the field.

$$E = -\mu_z B_0 \quad (6)$$

The selection rule $\Delta M = +\text{or}-1$ applies to transitions between spin levels so transitions can only occur between adjacent levels. When a transition occurs it is induced by the absorption of energy from an electromagnetic field B_1 . The energy absorbed is described by the Planck relationship $E = h\nu$ giving a transition energy of

$$\Delta E = h\nu = h\gamma B_0 / 2\pi. \quad (7)$$

The implications of this are that the energy differences between levels get larger as the applied field B_0 increases and that at a given field strength all transitions are essentially equal.

In a macroscopic sample, in the absence of an applied field, nuclei are randomly oriented. The effect of a strong B_0 is to align these nuclei so $(2I+1)$ orientations exist and for the ^{13}C example nuclei are aligned with B_0 or against it. At thermal equilibrium the spins are distributed according to Boltzmann's law and the population ratio of the lower to upper states is

$$N_L/N_U = \exp(2\mu_z B_0 / kT) \quad (8)$$

where k is Boltzmann's constant and T is the temperature. Although this amounts to a small difference with the lower energy level receiving an excess population, the difference is enough to establish a net macroscopic magnetization. This excess permits energy absorption to occur since equal populations of all levels would cause upward transitions to equal downward transitions and no net absorption would be observed. The net magnetization is a product of the vector B_0 , the energy difference between levels and the number of nuclei per unit volume N .

$$M = N\mu_z^2 B_0 / kT \quad (9)$$

This macroscopic magnetization is therefore also a vector quantity possessing the same orientation as the applied field.

The NMR experiment is useful to chemists because all nuclei in a sample do not resonate at precisely the same Larmor frequency. When nuclei in a sample are in different magnetic environments for one reason or another they resonate at a characteristic frequency shifted away from the Larmor frequency. These shifts are generally small and are in the range of 10^{-3} to 10^{-5} MHz for most nuclei. This shift difference, or screening effect, arises from the magnetic effect of electronic currents induced in the atom or molecule by the applied magnetic field. These induced currents create their own magnetic fields which may add or subtract from the applied field causing the nucleus in question to experience a net magnetic field dependant upon its electronic environment. Thus nuclei can be distinguished based upon their electronic-magnetic environment and this is the basis of the extensive application of the NMR experiment.

Since the observed magnetic field at a given nucleus is a function of the applied field it is possible to describe the net field in terms of B_0 . Thus

$$B_{\text{obs}} = (B_0 - B_0 \sigma_i) \quad (10)$$

$$\sigma_T = 1 - B_{\text{obs}}/B_0 \quad (10a)$$

$$\sigma_T = (\sigma_{xx} + \sigma_{yy} + \sigma_{zz})/3 \quad (10b)$$

defines the shielding parameter σ_i which is a field independent constant for a given nuclear environment. Atomic and molecular orbitals describing the shapes of electronic motion are not always

spherically symmetrical and the shielding constant is therefore a tensor value having X,Y and Z components. However most solution and solid phase spectra record an effective shielding given by Equation (10b).

The magnitudes of chemical shifts are much smaller than those of dipolar interactions and would be obscured without isotropic averaging. This is because a spinning nucleus acts like a small magnet generating a local magnetic field experienced by its neighbors. The field at a distance r from a local source is given by the relations

$$B_r = \mu_0(4\pi)^{-1}2\mu r^{-3}\cos\psi \quad (11a)$$

$$B_\psi = \mu_0(4\pi)^{-1}2\mu r^{-3}\sin\psi \quad (11b)$$

where μ is the nuclear magnetic moment, μ_0 is the permeability constant ($4\pi \times 10^{-7} \text{ kg m s}^{-2}\text{A}^{-2}$) and ψ is the angle between the magnetic moment vector and the line between the nucleus and its neighbor (Figure 2 below).

Figure 2. Dipolar interaction.

When the angle ψ is small, the local field is close to $(\mu_0/4\pi) \times (2\mu/r^3)$, which for typical interatomic distances is of the order of 0.2 mT. This is small compared with B_0 but is significant when compared to coupling constants or chemical shifts which are in the range of μT since they are expressed in ppm at applied fields between 2 and 12 Tesla.

Therefore when the nucleus precesses about the large applied field, B_0 directed along the Z axis, the local field will contain a static component in the direction of r and a fluctuating component at right angles to this. Both of these will be modulated by any motion of the two interacting nuclei with respect to B_0 and each nucleus interacts with all its neighbors. In classical physics the energy of interaction through space between two magnets having magnetic moments μ_1 and μ_2 is

$$U = \left\{ (\mu_1 \times \mu_2)/r^3 - 3(\mu_1 \times r)(\mu_2 \times r)/r^5 \right\} \mu_0/4\pi \quad (12)$$

where r is the distance between the two magnets. This is converted to the quantum mechanical Hamiltonian by use of the relation $\mu = \gamma \hbar I / 2\pi$ to give

$$H_{dd} = \gamma_1 \gamma_2 \hbar \left\{ (I_1 \times I_2) / r^3 - 3(I_1 \times r)(I_2 \times r) / r^5 \right\} \mu_o / 4\pi. \quad (13)$$

When the cross products are expanded and the coordinate system is converted to polar from cartesian coordinates the Hamiltonian has terms in $(3\cos^2\theta - 1)$ and $(\exp(i\theta))$.

The average of an exponential over all values is zero and thus all terms having the $\exp(i\theta)$ factor disappear. The average value of a function of θ is given by integration from zero to π of that function multiplied by a distribution equal to $1/2$. The result is as θ is varied between zero and π

$$\langle (3\cos^2\theta - 1) \rangle = 1/2[\cos^3\theta] + 1/2[\cos\theta] = 0 \quad (14)$$

and the average value is equal to zero. When intramolecular dipolar interactions are considered in solution, rapid isotropic tumbling tends to average all contributions. The result is that dipolar interactions do not affect the transition energies or intensities for high resolution NMR spectra of isotropic solutions. However in solid samples or solutions in liquid crystals averaging does not occur and dipolar effects become important.

Therefore to obtain spectra for solid samples it is necessary that isotropic tumbling be approximated. This is achieved by taking

the average of $(3\cos^2\theta-1)$ about the conical path traced out by r (Figure 3 below).

Figure 3. Geometric relationships used to describe Magic Angle Spinning.

Thus it can be shown this average is

$$\langle 3\cos^2\theta-1 \rangle = 1/2(3\cos^2\beta-1)(3\cos^2\chi-1) \quad (15)$$

where the angles θ , β and χ are as defined in figure 3. Therefore the angle β is under the experimentalist's control and when set to 54.7 degrees gives a value of zero for $(3\cos^2\beta-1)$. Thus for all values of χ the dipolar influence is eliminated and resolution of chemical shifts for most solid phase samples is possible. This is called magic-angle spinning and the 54.7 degree angle is termed the magic angle.

A second problem in obtaining high resolution spectra in the solid phase for dilute spin systems such as ^{13}C is that spin-lattice

relaxation times can be very long making multipulse methods impractical. This follows from the lack of neighboring atoms having spin to transfer energy to, and that the essentially rigid lattice is not conducive to magnetic field fluctuations required for energy transfer. This difficulty has been overcome for ^{13}C by a method which transfers magnetization from ^1H to the ^{13}C spins. This is known as cross-polarization and is achieved by making the protons and carbons precess in their respective rotating frames of reference at the same rate. This allows energy transfer from hydrogen to carbon nuclei to occur and is accomplished when the condition in Equation 16 applies.

$$\gamma_{\text{H}}B_{1\text{H}}=\gamma_{\text{C}}B_{1\text{C}} \quad (16)$$

Since the proton spins are abundant and the carbon spins are dilute there is an energy transfer in which the protons lose a small part of their magnetization which the carbons gain. The enhanced magnetization for ^{13}C increases resolution as desired.

The method of cross-polarization is achieved by applying a 90 degree pulse to the ^1H magnetization and locking this on the Y axis. The ^{13}C magnetization is then turned on and the $B_{1\text{C}}$ magnetic field is adjusted so Equation (16) applies. The pulse sequence which achieves this is described in Figure 4 below.

Figure 4. Pulse sequence used to obtain cross-polarization.

Contact between the carbon and hydrogen channels ensures the carbon relaxation times are not a factor since they become dominated by relaxation times of the order of the ^1H nuclei which are shorter than ^{13}C relaxation times. The effect of this is ^{13}C solid phase spectra of acceptable resolution can be obtained when cross-polarization techniques are coupled with magic-angle spinning (CPMAS).

2.2 NMR Experimental

The NMR spectrometer is equipped with the same basic components as any spectrometer. These include a radiation source, a sample compartment, a detector, an amplifier and a recording device. In addition to these the NMR spectrometer requires the presence of a strong magnetic field as described in Equations (3) to (10).

A critical part of NMR spectrometers is the large applied field B_0 which must be as homogeneous as possible at the sample. This field is created by superconducting electromagnets and field homogeneity is achieved by varying current in shim coils at the poles of the magnet. Rapid rotation of the sample also helps to randomize out inhomogeneous portions of the field. Fields can also drift if the temperature of the coils change and this is controlled by a locking circuit which monitors the field and references it to a lock sample bringing it back to the desired position by varying the system voltage.

Since magnetic fields used in NMR applications vary between 2 and 12 Tesla and magnetogyric ratios range between 0 and 27×10^{-7} rad/s/T, the energy of absorption from Equation (7) is in MHz. Therefore the radiation source in the NMR experimental is a radio frequency transmitter. In Fourier transform NMR the transmitter generates a pulse of energy centered at the Larmor frequency with a

range wide enough to include all resonating species. This range is controlled by the pulse width in the relation

$$\text{frequency range} \propto + \text{ or } -(1/t_p) \quad (17)$$

where t_p is the duration of the pulse. Thus a single pulse of energy can excite all nuclei in a sample at the same time. The range of Larmor frequencies for ^{13}C nuclei in different chemical environments is about 5000 Hz at a field strength of 2 T and therefore a pulse width of 0.4 milliseconds is required. In practice shorter pulse widths are used and values between 1 to 100 μs are common.

Therefore all nuclei in a sample can be excited at the same time and the problem of detecting their simultaneous absorption of energy arises. This is accomplished in modern spectrometers by a receiver coil which detects the component of total magnetization along the Y axis. Thus when a nucleus is in the field of B_0 it precesses about B_0 with its Larmor frequency determined by $\omega = \gamma B_0$. When an oscillating current is applied to a coil along the X-axis a magnetic field B_1 is generated which causes nuclei to also precess about B_1 at a rate equal to $\gamma \cdot B_1$. This precessing of the total magnetization M about B_1 causes it to move toward the X-Y plane by an angle proportional to the duration of the pulse t_p . The angular speed, ω , the net magnetization moves with is γB_1 and the angle it will move through is

$$\varphi = \gamma B_1 t_p. \quad (18)$$

Thus a pulse of the correct time duration can tip the net magnetization vector 90 degrees onto the Y axis or 180 degrees onto the -Z axis as described in Figure 5 below.

Figure 5. Three positions of M ; (a) before pulse, (b) 90 degree pulse, (c) 180 degree pulse.

In fact the coordinate axes represented in Figure 5 are termed the laboratory frame since the entire system is rotating about the true Z axis at the Larmor frequency. This convention is used to simplify discussions of rotations of the net magnetization vector since the actual situation has rotations about B_0 superimposed upon rotations about B_1 . When the transmitter is turned off nuclei tend to lose the energy gained during the pulse by transmitting it back to their surrounding environment. At this time the transmitter coil is used as a receiver to monitor the net magnetization along the Y axis.

The Y component of the magnetization vector decreases exponentially after the pulse is switched off. This exponentially decreasing magnetization induces a current into the receiver coil. Since the exponential decrease is superimposed upon rotation about the Z axis at the Larmor frequency, the signal detected is an exponential decrease imposed upon a sinusoidal wave. The difference between this signal and a reference signal is amplified and stored in a computer memory as a function of voltage versus time (Figure 6).

Figure 6. Free Inductive Decay

When the Free Inductive Decay (FID) has the exponential decay of more than one nucleus the different Larmor frequencies are present and superimposed on one another. The resulting FID is a complex composite of the two relaxing magnetizations and when there are more than two sets of nuclei at different Larmor frequencies the FID becomes very complex. If the sample is dilute or the nucleus in question has a low sensitivity the pulse can be repeated several times until the signal to noise is improved to a satisfactory level.

The FID can be converted into a conventional frequency versus intensity spectrum by the use of Fourier transformation. This is a simple mathematical conversion of time into frequency dependent functions given by the relation

$$F(\omega) = \int f(t) e^{-i\omega t} dt. \quad (19)$$

Conversion is done by a computer algorithm which can complete the process quickly after which the frequency dependent spectrum is stored in computer memory.

In practice the 90 degree pulse is not used to tip the magnetization onto the Y axis since this is not an efficient flip angle. Here the flip angle is defined as the angle between the Z axis and the rotated magnetization at the end of the pulse. When a 90 degree pulse is used relaxation back to the Z axis takes too long a time and optimum signal to noise is obtained by using the Ernst Equation to determine the flip angle (Equation 20 below).

$$\cos\phi = e^{-D/T} \quad (20)$$

In this Equation D is the time between pulses, ϕ is the optimum flip angle and T is the relaxation time necessary for the magnetization to return to equilibrium.

Therefore in a typical solution phase ^{13}C experiment a sweep width of 10,000 Hz is used requiring a pulse width of 0.1 ms. The acquisition time, defined as the time the magnetization is monitored, is typically 1.0 s. The tip angle is around 30 degrees and

high power ^1H decoupling is turned on with the total number of acquisitions for 0.1 M solutions being around 500 for satisfactory signal to noise. Chemical shifts are reported relative to internal TMS and field homogeneity is maintained by locking to internal deuterium. Recording of solid phase ^{13}C spectra is done with magic-angle spinning rates of 3 kHz, cross polarization times of 3ms, sweep widths of 10-20 kHz and around 500 acquisitions. Chemical shifts are measured relative to an external solid compound, typically hexamethylbenzene, and then converted to the TMS scale by an appropriate factor.

2.3 ^{13}C NMR: Chemical Shifts

The objective of a conformational analysis using ^{13}C NMR is to correlate systematic changes in ^{13}C chemical shifts with corresponding changes in the stereochemistry of a molecular system. This is possible only if correlations exist and are understood. There are two ways of studying ^{13}C conformational chemical shift dependencies. The first is to investigate systems of known geometry and to correlate dihedral angles with experimental chemical shifts. When enough variety in the molecular geometries of a group of molecules studied in this way is found, a systematic correlation between chemical shift and molecular geometry can be established. A second approach involves doing MO computational NMR shielding tensor studies on a system as molecular geometry is varied.

The experimental approach has the inherent difficulty of finding systems of known geometries in which suitable variation in substitution patterns and dihedral angles exists. In some part, the advent of CPMAS has aided in the study of geometry dependant ^{13}C chemical shifts and this is seen in the recent comparison between the number of ^{13}C resonances and differing torsional angles for 18-crown-6 and its KNCS complex⁽⁴⁰⁾. In the liquid phase Lambert and Vagenas⁽³⁰⁾ have looked at the γ effect for ^{13}C chemical shifts versus dihedral angle for a series of monosubstituted and rigid cyclohexane and nonbornane compounds. They found that, when differences due to the varying electronegativities of substituents

were omitted by graphical analysis, an approximately linear stereochemical dependence existed for compounds having the same geometry.

The computation tact also has inherent difficulties. Large molecules cannot be studied at the *ab initio* level since basis sets large enough to give acceptable results cannot be reasonably handled by modern computers. Also comparison between computational and experimental results are difficult since lattice influences are difficult to incorporate into a calculated chemical shift value and difficult to exclude from an experimental result. One advantage of the computational approach to studying NMR conformational phenomena is, it is possible to correlate between chemical shifts and such molecular properties as electron densities, electron occupancies, hybridization and geometries. The theory behind computational NMR is mature although hardware limitations cause a large number of systems to be inaccessible by this approach.

A number of reviews and texts are available which describe the theoretical construct behind NMR shielding tensor calculations⁽⁴¹⁻⁴⁸⁾. The work is derived from the early Van Vleck⁽⁴⁹⁾ approach to calculating magnetic susceptibilities (induced dipole moment per unit applied magnetic field). Lamb⁽⁵⁰⁾ developed a theory for describing the chemical shielding for individual atoms and Ramsey^(51,52) developed the approach used today for calculating shielding tensors in molecules.

The Lamb method used the Larmor precession theorem which states a uniform external magnetic field B_0 superimposes a precession of angular frequency, ω , onto the electron orbits. Here

$$\omega = eB_0/2mc \quad (21)$$

where e is the electronic charge, m is the electronic mass and c is the speed of light. If an electron circles a loop at angular velocity ω , then the current in this loop is given by the relation

$$I = (-e\omega/2\pi) = -e^2B_0/4\pi mc. \quad (22)$$

The field at a point on the axis of a circular loop of radius r and carrying a current I is given by the relation

$$B' = (2\pi I \sin^2\theta)/cr. \quad (23)$$

Therefore the induced field due to the current in a single ring of a sphere is

$$B' = -e^2B_0 \sin^2\theta / 2mc^2r \quad (24)$$

and the total shielding field is obtained by integration over all values of r and θ . This must then be combined with the appropriate charge density factor since the electron has access to all volume elements. This is achieved by assuming $p(r)d\tau$ is the probability of finding an electron in a volume $d\tau$ at a distance r from the origin. Thus

$$p(r) = (\Psi(r))^2 \text{ and } d\tau = 4\pi r^2 dr \quad (25)$$

and since $\sin^2\theta$ averaged over polar angles is $2/3$ the net field at the nucleus upon integration from zero to infinity is

$$B' = -e^2 B_0 / 3mc^2 \int (1/r) \rho(r) 4\pi r^2 dr. \quad (26)$$

Therefore from Equation (10a) the shielding parameter σ is known and Equation (26) is referred to as Lamb's formula.

The chemical shielding described by Lamb's formula is called diamagnetic shielding because it has a current flow which sets up a magnetic field opposed to the applied field (Figure 7 below).

Figure 7. Diamagnetic shielding induced by B_0 .

This secondary field B' is opposed to the applied field and therefore to achieve the resonance condition a greater B_1 must be applied to this shielded nucleus.

When the electronic distribution is asymmetric, as is the case for molecules, Lamb's theory fails and the situation becomes considerably more complex. Here Ramsey's approach is used and this theory assumes the nucleus in question can be represented as a magnetic moment, μ , directed in the same direction as the applied field B_0 . The electromagnetic relationship giving the energy for a dipole in a magnetic field is

$$E = -\mu B' \quad (27)$$

Thus, by calculating the energy of a molecular system in the presence of μ and B_0 , collecting all terms linear in μ and B_0 and assigning these as the energy of interaction between the magnetic field and the dipole, it is possible to obtain σ from the relationship $\sigma = B'/B_0$.

The general approach to getting Ramsey's solution is to obtain electronic wave functions of a system for the ground and excited states in the absence of external magnetic fields. These zero-field eigenfunctions are then used to represent the electronic structure in the presence of a magnetic field. The effect of μ on the system is then determined using perturbation theory and Ramsey used a Taylor series expansion around zero field values of B_0 and μ . This approach is possible when the energy due to perturbations is small compared with the overall energy and this is a valid assumption here.

The electronic Hamiltonian is obtained by separating the nuclear kinetic and electrostatic energy terms from the total Hamiltonian and this gives

$$H_{elec} = (-h^2/8\pi^2m) \sum_i (\text{del})_i^2 - \sum_i \sum_k (Z_k e^2 / r_{ik}) + \sum_i \sum_j (e^2 / r_{ij}) \quad (28)$$

In this equation m is the electron mass, e the electron charge, Z_K the atomic number of the nucleus K , r_{ik} the distance between the electron i and the nucleus K , r_{ij} the distance between electrons i and j and (del) is the Laplacian defined as the sum of second derivatives.

When a magnetic field B_0 is applied to this system, electronic motion can be described by adding $e \cdot A$ to the generalized momentum, where A is the vector potential due to the applied magnetic field and is defined as

$$A = 1/2(B \times r), \text{div } A = 0, \text{curl } A = B \quad (29)$$

The Hamiltonian of the electronic system of a molecule in the presence of a magnetic field is then

$$H_{elec} = (1/2m) \sum_j [(h/2\pi i)(\text{del})_j + e \cdot A_j]^2 + V \quad (30)$$

where $[(h/2\pi i)(\text{del})]$ is the generalized momentum and V is the electrostatic potential energy term. With the applied field in the positive Z direction and the coordinates chosen with their origin at the nucleus for which shielding is to be determined, A_j can be chosen to be

$$A_j = 1/2(B_0 \times r_j) + (\mu \times r_j)/r^3, \quad B_0 = (0,0,B_0) \quad (31)$$

Here, r_j is the radius from the origin at the nucleus to the position of electron j given by

$$r_j = ix_j + jy_j + kz_j \quad (32)$$

where i , j and k are unit vectors.

Since the applied field and the dipole moment are chosen to be in the $+Z$ direction of $B_0 = B_0 k$ and $\mu = \mu_k$

$$A = (1/2 B_0 + \mu r^{-3}) \cdot (-y_i + x_j). \quad (33)$$

It follows that this vector potential gives the proper magnetic field

$$[(\text{del}) \times A] = B_k + i3xz/r^5 + j3yz/r^5 + k[2/r^3 - 3(x^2 + y^2)/r^5] \quad (34)$$

where the first term is the applied field and the following terms give the dipole field. Expanding the Hamiltonian in Equation (30) and using the relations

$$\begin{aligned} (\text{del}) \cdot A &= 0 \\ [(\text{del}) \cdot A + A \cdot (\text{del})] \Psi &= 2 \cdot A (\text{del}) \Psi \end{aligned} \quad (35)$$

the electronic Hamiltonian of Equation (28) becomes

$$H_{elec} = -\hbar^2/8m\pi^2 \sum_j (\text{del})_j^2 + V + eh/imc2\pi \sum_j A_j (\text{del})_j + e^2/2mc^2 \sum_j A_j^2 \quad (36)$$

and this may be written as

$$H_{elec} = H_0 + H_1 + H_2 \quad (37)$$

The result is the separated components of the total Hamiltonian are

$$H_0 = -\hbar^2/8m\pi^2 \sum_j (\text{del})_j^2 + V \quad (38)$$

$$H_1 = eh/imc2\pi \sum_j A_j (\text{del})_j \quad (39)$$

$$H_2 = e^2/2mc^2 \sum_j A_j^2 \quad (40)$$

Here H_0 represents the electronic system without an applied field and the second and third terms are perturbations upon this system.

Perturbation theory is used in determining eigenvalues and eigenfunctions of a system experiencing perturbation when the energy and wavefunction of the unperturbed system is known⁽⁵³⁾. This theory applies when the perturbing energy is small in relation to that of the total system and the first and second order perturbation energies are given by the relations in Equations 41 and 42.

$$E_1 = \langle 0 | H_1 + H_2 | 0 \rangle \quad (41)$$

$$E_2 = \sum_{n=0} [0 | H_1 + H_2 | N] \cdot [N | H_1 + H_2 | 0] / (E_n - E_0) \quad (42)$$

Here zero labels the unperturbed ground state of the system, n labels one of the excited states and H_1 and H_2 are perturbations on H_0 .

Therefore since

$$\Delta E = E_1 - E_2 = \sigma \mu B' \quad (43)$$

the shielding constant σ can be obtained by finding all terms in E which are linear in B' . The first order perturbation to the system, H_1 , has no linear terms in $\mu B'$ since

$$A_j(\text{del})_j = (B'/2 + \mu/r^3) \cdot (X_j \partial/\partial y_j - y_j \partial/\partial x_j) \quad (44)$$

However, H_2 , which is the square of A_j , does have linear terms in $\mu B'$ since

$$A_j^2 = A_j \cdot A_j = (B^2/4 + \mu B/r^3 + \mu^2/r^6) \cdot (x_j^2 + y_j^2) \quad (45)$$

Excluding terms from H_2 that are not linear in B' , placing all remaining terms from Equation (45) into (41) and (42) and using (43), gives a value for the shielding constant. Using the closure approximation and choosing an average excitation energy $\Delta E = E_n - E_0$ gives the shielding tensor along the Z axis as

$$\sigma_{zz} = e^2/2mc^2 \langle 0 | (x^2+y^2)/r^3 | 0 \rangle + (e^2\hbar^2/4\pi^2m^2c^2\Delta E) \langle 0 | \sum_{jj'} r_j^{-3} (\partial^2/\partial\phi_j\partial\phi_{j'}) | 0 \rangle. \quad (46)$$

The first term in Equation (46) can be written differently as

$$\begin{aligned} e^2/2mc^2 \langle 0 | (x^2+y^2)/r^3 | 0 \rangle &= e^2/2mc^2 \int_0^\infty \Psi_0^* (x^2+y^2)/r^3 d\tau \\ &= e^2/2mc^2 \int (\sin^2\theta/r) \rho d\tau \end{aligned}$$

with $\rho d\tau = |\Psi|^2 d\tau$ being the probability of finding an electron in all space $d\tau$ in the ground state molecule. When this is averaged over all directions it is the same as Lamb's formula (Equation 26) and represents the diamagnetic contribution to the total shielding. The second term in (46) represents a contribution to the total field in the same direction as the applied field and therefore is labelled the paramagnetic contribution. This part of the total shielding incorporates the electron orbital angular momentum operator as $(\partial^2/\partial\phi_j\partial\phi_{j'})$ and is negative with respect to the diamagnetic contribution. Thus the total screening constant is the sum of two factors having opposite signs and is

$$\sigma_T = \sigma_d + \sigma_p \quad (47)$$

Since the paramagnetic contribution requires the presence of electrons with orbital angular momentum, it does not apply for

electrons of s character and this explains the relatively small chemical shift range for the hydrogen nuclei.

Although Ramsey's description of nuclear shielding is theoretically sound, the simplifications necessary to make it applicable cause problems that in practice make it unsatisfactory for routine chemical shift calculations. A major disadvantage of Equation (46) termed the gauge problem is that even for fairly small molecules the opposing terms can have large absolute values. The net shielding constant is therefore a difference of two large quantities. These values have errors since the unperturbed wave functions are known imprecisely and the net shielding tensor becomes the difference of two large values each having some error. The result is the net shielding value can be significantly different from its true value as measured by experiment. A second source of error in Equation (46) is the ΔE value in the paramagnetic term since this requires knowledge of the energies of excited levels and these are rarely known with suitable precision. Also, for any but the smaller molecules, accurate calculation of eigenfunctions and eigenvalues is difficult and this also gives imprecise results.

Since Ramsey first articulated his method of molecular shielding calculations a number of solutions to the inherent problems have been realized. The most significant development has been the advent of computers capable of calculating wavefunctions and energies for moderately sized molecules⁽⁵⁴⁻⁵⁶⁾. The problem caused by the addition of large opposing terms has been solved in a number of ways. An early solution comes from Pople⁽⁵⁷⁾ who has

proposed a model for nuclear shielding in which σ is the sum of a number of localized shielding contributions (Equation 48).

$$\sigma_T = \sigma_d(\text{loc}) + \sigma_p(\text{loc}) + \sigma_d(\text{nonloc}) + \sigma_p(\text{nonloc}) + \sigma_d(\text{inter}) + \sigma_p(\text{inter}) \quad (48)$$

The local terms relate to the shielding from electron currents induced by B_0 on the atom of interest, the nonlocal terms are the shielding contributions arising from currents on neighboring nuclei and the interatomic terms are from nonlocalized contributions such as ring currents.

A more recent solution of the gauge problem, and one that has significantly improved both accuracies and the size of basis sets required, has been the gauge-independent approach. This method originated in London's work on diamagnetic susceptibilities⁽⁵⁸⁾ and is expressed in the gauge invariant atomic orbital (GIAO) approach⁽⁵⁹⁻⁶⁰⁾. This involves the use of gauge-invariant atomic orbitals as a basis for linear combination of atomic orbitals (LCAO) molecular wavefunctions. The basis of this method is that the vector potential, A , defined in Equation (29) need not be determined by specifying the magnetic field alone. Instead the gradient of a scalar function ζ can be added to A and the resulting vector potential A' will still correspond to the magnetic field B' , since

$$\begin{aligned} B' &= (\text{del}) \times A \\ A' &= A + (\text{del})\zeta \end{aligned} \quad (49)$$

and

$$\begin{aligned}
 (\nabla) \times A' &= (\nabla) \times [A + (\nabla)\zeta] \\
 &= (\nabla) \times A + (\nabla) \times ((\nabla)\zeta) \\
 &= (\nabla) \times A = B', \quad (50)
 \end{aligned}$$

The last step follows since the curl of the gradient of any scalar is zero. The result is the origins are local and set at the centers of any nuclei and the atomic orbital carries its own complex phase factor determined by the value of the magnetic vector potential at the origin for this orbital.

A more recent solution to the gauge-dependence of NMR shielding calculations, and the one employed by this study, is the localized orbital/local origin (LORG) method developed by Bouman and Hansen⁽⁶¹⁻⁶⁴⁾. This theory of NMR shielding tensors is derived from Ramsey's expressions and uses the approach of expanding angular momentum terms relative to a local origin for each orbital. The expressions for the total tensor can therefore be analysed in terms of intrinsic bond and bond-bond contributions.

2.4 Molecular Dynamics

There are no instances where a molecule remains absolutely rigid and this must be included in any consideration of molecular geometry, structure or conformation. Even the solid phase experiences vibrations which occur in the range of 10^{12} to 10^{14} Hz although these are much too fast to be detectable for the NMR experiment. However the liquid, gas and in some rare instances the solid phases permit interconversion of conformers accessible to the system in question at the temperature of interconversion.

A conformational analysis is the search for the one or few actual conformers a molecular system chooses to take up. These conformations are energetic minima and are one or a few of a nearly infinite number of possibilities available to a system. One of the simplest systems exhibiting conformational isomerism is butane and the energy versus dihedral angle plot in Figure 8 shows that three energy minima exist, two of which are degenerate.

Figure 8. Dihedral angle versus energy for butane.

The energy differential between the more stable anti conformer and the less stable gauche conformer is about 3.5 kJ/mol and therefore both are populated at ambient temperatures. This implies the molecule spends some time in the conformations intermediate between the stable conformers and any conformational analysis is therefore incomplete without some knowledge of a system's flexibility.

In addition to the NMR experiment's usefulness as a probe of molecular conformation it can be used to determine molecular dynamics in solution. This is done using low temperature coalescence data to determine conformational rate processes and this yields information on the free energy of activation for interconversion between conformers. Also, ^{13}C T_1 data describing nuclear relaxation characteristics can generate information on molecular mobility and flexibility in solution.

The first description of the way NMR can be used to study dynamic processes comes from the work of Bloch⁽⁶⁵⁾. He used a

classical macroscopic approach to derive expressions describing the lineshape of a simple spectrum. This description looks at a macroscopic sample containing many identical molecules with each having one magnetic nucleus. The total magnetic moment of such a system is the sum of the magnetic moments of its components. Therefore the total magnetization is

$$M = \sum_i \mu_i \quad (51)$$

Since the magnetic moment is related to angular momentum by Equation (2) in terms of the total spin angular momentum the total magnetization is

$$M = \gamma P \quad (52)$$

The applied field acts on this magnetization to give the system a torque as described in Equation (3) and this changes the angular momentum by the relation in Equation (53)

$$dP/dt = -B_0 \times M \quad (53)$$

but since P and M are related by Equation (52)

$$dM/dt = -\gamma B_0 \times M \quad (54)$$

The solution to this differential equation under the steady state is a precession about the field B_0 at the Larmor frequency and the total

magnetization acts like a single nucleus. Thus for a single magnetic moment in Equation (5) the frequency is $\nu = \gamma B_0 / 2\pi$.

For a spin 1/2 system like ^{13}C the magnitude of M_0 , the equilibrium macroscopic magnetization, is the sum of magnetizations directed along the Z axis and is

$$M_0 = n_\alpha \mu_{z\alpha} + n_\beta \mu_{z\beta} = \Delta n_0 \mu_{z\alpha} \quad (55)$$

where n_α and n_β designate the number of molecules having α and β spins. The energy difference between the two states from Equation (7) can be used in the Boltzmann Equation to give the population difference when N the total number of nuclei is known and

$$n_\alpha - n_\beta = \Delta n_0 = N \Delta E / kT. \quad (56)$$

This leads to an expression for the equilibrium magnetization of a spin 1/2 system of

$$M_0 = N(\gamma h / 2\pi)^2 B_0 / 2kT. \quad (57)$$

Thus when a field B_0 is applied to a system the magnetization goes from zero to M_0 and any description of magnetic motion must include the approach to thermal equilibrium or M_0 .

The assumption is that the components of M decay to M_0 exponentially and the components of M parallel and perpendicular to M_0 decay with different time constants T_1 and T_2 . The change in the

magnitudes of the magnetization vectors along the X,Y and Z axes can therefore be described as

$$dM_z/dt = -(M_z - M_0)/T_1 \quad (58)$$

$$dM_x/dt = -M_x/T_2 \quad dM_y/dt = -M_y/T_2. \quad (59)$$

The decay time along the Z axis can differ from that along the two axes perpendicular to Z because the energy of the spin system depends upon M_z and any change in M_z is accompanied by an energy flow between the nuclear spin and the other degrees of freedom of the system. The relaxation time describing this flow is therefore the T_1 and is known as the spin-lattice relaxation time or the longitudinal relaxation time. T_2 is the corresponding relaxation along the X and Y axes and is known as the transverse or spin-spin relaxation time. This latter term describes the type of relaxation due to T_2 since direct interaction between the spins of different nuclei can cause relaxation of M_x and M_y without energy transfer to either the other degrees of freedom in the system or to the lattice.

The small applied magnetic field B_1 in the NMR experiment which precesses about B_0 can be represented as an oscillating field or $2B_1 \cos \omega t$. This can be resolved into two components rotating in opposite directions about the Z axis in the X-Y plane with angular velocities of $+$ and $- \omega$. These rotating fields have associated with them magnetizations in the X-Y plane which is monitored by the receiver coils of the spectrometer. Neglecting the magnetization

which has angular velocity $+\omega$ the other component has a field acting on the sample of

$$\mathbf{B} = i\mathbf{B}_1 \cos \omega t - j\mathbf{B}_1 \sin \omega t + k\mathbf{B}_0 \quad (60)$$

where i, j and k are unit vectors in the X, Y and Z directions respectively. When this expression is combined with the equation for the motion of the total magnetization (Equation 54) and the relations describing the time dependence of the relaxation processes (Equations 58 and 59) the Bloch Equations are (61-63).

$$dM_z/dt = -\gamma[B_1 \cos \omega t M_Y + B_1 \sin \omega t M_X] - (M_z - M_0)/T_1 \quad (61)$$

$$dM_Y/dt = -\gamma[B_0 M_X - B_1 \cos \omega M_Z] - M_Y/T_2 \quad (62)$$

$$dM_X/dt = +\gamma[B_1 \sin \omega t M_Z + B_0 M_Y] - M_X/T_2 \quad (63)$$

These equations can be simplified by using the rotating frame of reference which precesses about the Z axis at $-\omega$ and the X and Y components perpendicular to B_0 are designated u and v as in Equations (64) and (65).

$$u = M_X \cos \omega t - M_Y \sin \omega t \quad (64)$$

$$v = M_X \sin \omega t + M_Y \cos \omega t \quad (65)$$

Receiver coils detect magnetization by a signal induced by a change in magnetization along the Y axis. Therefore

$$\begin{aligned} du/dt &= dM_x/dt \cdot \cos\omega t - dM_y/dt \cdot \sin\omega t - \omega(M_x \sin\omega t + M_y \cos\omega t) \\ &= +\gamma B_0 v - u/T_2 - \omega v \end{aligned} \quad (66)$$

and the Bloch Equations in the rotating frame of reference are

$$dM_z/dt = -\gamma B_1 v - (M_z - M_0)/T_1 \quad (67)$$

$$du/dt = +(\omega_i - \omega)v - u/T_2 \quad (68)$$

$$dv/dt = -(\omega_i - \omega)u + \gamma B_1 M_z - v/T_2 \quad (69)$$

where ω_i is the Larmor angular velocity about B_0 and ω is the angular velocity about B_1 .

Solution of the Bloch Equations with the time derivatives equal to zero and when $\gamma B_1 \ll (1/T_1 T_2)$ gives a signal proportional to

$$g(v) = 2T_2 / (1 + 4\pi^2 T_2^2 (v_i - v)^2) \quad (70)$$

where $v = \omega/2\pi$. The width of the absorption line at half-height is $(\pi T_2)^{-1}$ and frequently the total observed line width $\Delta v_{1/2}$ is used to define an effective relaxation time T_2 by the relation

$$\Delta v_{1/2} = (\pi T_2)^{-1}. \quad (71)$$

However when chemical exchange between two sites occurs then the linewidth may not be determined by T_2 .

When a molecule is interconverting between two states or a nucleus is exchanging between two molecules such that magnetic environments A and B are interchanging (Equation 72) then if the rate of exchange is fast on the NMR timescale the resulting spectrum is a single average resonance.

$$A_n \text{ interconverting } B_n \quad (72)$$

When this exchange rate is slow the NMR spectra will have two distinguishable resonances with relative intensities dependant upon the populations of the two sites. In the intermediate time the spectrum will be one broad line with a line width equal to the difference in the two chemical shifts and this special case is called the coalescence point.

When the rate of magnetic exchange is on the NMR timescale and the spectrum is affected by exchange, as for the coalescence point, then the situation can be described by invoking the uncertainty principle. Although usually thought of in terms of position and velocity of a particle, this principle is in some instances expressed in terms of the lifetime, Δt , and the uncertainty in the energy, ΔE , of a state.

$$(\Delta t)(\Delta E) \sim h/2\pi \quad (73)$$

This means when the lifetime of a state is infinite the uncertainty in its energy is zero and when the lifetime is short the uncertainty in energy is large. This uncertainty in energy is therefore manifested in an uncertainty in the frequency of a spectroscopic emission or absorption.

Combining Equation (73) with the Planck relationship, $\Delta E = h\Delta\nu$, gives an expression for the uncertainty in the time in terms of the uncertainty in the resonance frequency (Equation 74).

$$\Delta t \sim 1/(2\pi\Delta\nu) \quad (74)$$

Thus when a nucleus is interchanging between sites A and B, which have frequencies of ν_A and ν_B , the uncertainty in the frequency, $\Delta\nu$, covers the range of frequencies between the two shifts. Here the time spent at each site is approximately Δt and since the rate of exchange is the reciprocal of the residence time

$$\text{rate} = k \sim 2\pi\Delta\nu. \quad (75)$$

It can be assumed that line widths at temperatures significantly below the coalescence temperature are negligible compared with the separation of peaks at these temperatures. When this assumption for two exchanging resonances of equal intensity applies, the shape of the signal is $g(\nu)$, where

$$g(\nu) = K \{ \tau(\nu_A - \nu_B)^2 / [((\nu_A + \nu_B)/2 - \nu)^2 + 4\pi^2\tau^2(\nu_A - \nu)^2(\nu_B - \nu)^2] \}. \quad (76)$$

Here K is a normalizing constant, and τ is the residence time defined as the amount of time the nucleus resides in a given magnetic environment. The actual shape is then dependant upon the product $\tau(\nu_A - \nu_B)$ and for large τ two resonances are observed, small values of τ give a single line and the intermediate gives a broad signal. At this mid point $2\pi\tau(\nu_A - \nu_B) = 2^{1/2}$ and therefore

$$\tau_c = (2)^{1/2} / (\pi(\nu_A - \nu_B)). \quad (76a)$$

The values for the two chemical shifts can be found from their values at temperatures well below the coalescence point and since simple A to B exchanges are first-order processes, the rate constant is the inverse of the residence time.

$$k_A = 1/\tau_c \quad (77)$$

The rate of interconversion between A and B is determined by the free energy of activation for the process (Figure 9).

Figure 9. Free energy of activation for A to B conversion.

Rates of interconversion for intramolecular processes are given by the relation in Equation (78) which is one form of the Eyring Equation.

$$k = \kappa \cdot RT/h \cdot \exp(-\Delta G^\ddagger/RT) \quad (78)$$

Here $\Delta G^\ddagger$ is the activation energy from Figure (9) and κ is a transmission coefficient which depends on the nature of the process and is usually taken as unity under the assumption that essentially all individuals having the energy of activation will proceed over the energy barrier between A and B. Therefore, provided the lifetimes of the species are of the order of the NMR timescale, the two sites are equally populated and the process is intramolecular, the energy of interconversion at the coalescence temperature can be determined using Equations (76a),(77) and (78).

Lifetimes accessible to the NMR experiment are in the range around 10^{-2} s for most nuclei and free energy values range between 20 and 100 kJ·mol⁻¹. A large number of molecular systems have been studied using coalescence temperature analysis⁽⁶⁶⁾ which is general and can be used for many different nuclei. Some notable applications include the early Gutowsky study of proton exchanges using ¹H NMR⁽⁶⁷⁾ and a later study of the E to Z energy barrier for a number of aromatic imines⁽⁶⁸⁾. This method has also been used for the determination of activation energies for complexation between 1,4-diazabicyclo[2.2.2]-octane and chloroform⁽⁶⁹⁾ using ¹³C and more recently to study the complexation reaction between the sodium cation and a cryptate ligand using ²³Na⁽⁷⁰⁾.

Much of the analysis of large classes of organic molecules is dependant upon coalescence temperature analysis with conformational dynamics as well as complexation kinetics being accessible by this method. Thus studies in cyclodextrin⁽⁷¹⁻⁷³⁾, calixarene⁽⁷⁴⁻⁷⁸⁾ crown ether⁽⁷⁹⁻⁸¹⁾ and cryptand⁽⁸²⁻⁸³⁾ dynamic stereochemistry are heavily dependant upon the methods of coalescence temperature analysis and much of the available knowledge about such compounds has been derived using this method. Possibly the best known application of NMR coalescence temperature analysis has been the study of ring inversion processes since the free energies of activation fall within the appropriate range of 20 to 100 kJ·mol⁻¹. Numerous studies have looked at the chair to chair inversion process for cyclohexane under numerous substitution patterns⁽⁸⁴⁻⁸⁶⁾ and the unsubstituted alkane has been shown to have a free energy of interconversion of 42.3 kJ·mol⁻¹.

A second way ^{13}C NMR can be used to study molecular dynamics is by the use of spin-lattice relaxation times. As defined in Equation (67) the T_1 measures the time necessary for a nucleus to dissipate absorbed energy back to its surroundings. A molecule's ability to relax is a function of overall and local geometry, bonded and nonbonded interactions and other factors controlling molecular motion such as flexibility and solvent viscosity.

The process of spin-lattice relaxation allows the surrounding lattice to act as a heat sink for energy absorbed by the nucleus upon irradiation. Energy transfer is therefore dependant upon the existence of a mechanism coupling nuclear spins and the surrounding lattice. Since the only property of a nucleus having a $1/2$ spin which depends upon orientation is the magnetic moment, transitions between nuclear spin levels can only be induced by magnetic fields. Thus thermal relaxation to give population distributions predicted by Boltzmann can only occur by fluctuation of random magnetic fields within the sample. A nucleus in a liquid experiences a fluctuating magnetic field due to the magnetic moments of nearby nuclei which are experiencing Brownian motion.

In the case of ^{13}C , a dilute spin system occurring in molecules where protons are typically the only other magnetically active nuclei, relaxation is dominated by C-H dipolar interactions. When a ^{13}C nucleus is directly bonded to a ^1H species the three dipoles present are the two from the ^{13}C and ^1H nuclei and one due to the polarized bond. For the later the dipole moment of the bond is directed from the partially positive proton to the partially negative carbon as demonstrated in Figure 10 below. Relaxation can occur as

a result of the fluctuations of any dipoles present in the system as the system moves in solution. When these fluctuating fields have the same frequency as the Larmor frequency, coupling between these and the magnetic field associated with the excited nucleus permits energy transfer and therefore relaxation (Figure 10 below).

Figure 10. Relaxation by C-H dipolar motion.

Equation (79) describes dipole-dipole relaxation for a carbon bearing hydrogen in a molecule which is an isotropic, rigid tumbler. This relaxation is given in terms of the dipole-dipole relaxation time T_1 and the corresponding rate R_1^{DD} .

$$1/T_1^{DD} = R_1^{DD} = (h^2 \gamma_C^2 \gamma_H^2 r^{-6} \tau_c) / 4\pi^2 \quad (79)$$

Here τ_c is the molecular correlation time which approximates the time for rotation of the C-H vector through 1 radian and Equation (79) applies only in the extreme narrowing limit where τ_c is much

smaller than the reciprocal of the resonance frequency in radians·sec⁻¹. This condition holds for most organic compounds in nonviscous solutions.

Therefore from Equation (79) the strength of the C-H interaction is dependant upon the square of the magnetogyric ratios, the inverse sixth power of the distance between interacting dipoles and upon the rate of molecular motion. The inverse dependance on the sixth power of distance ensures that only nearest neighbors influence relaxation. Also a linear relationship exists between the number of hydrogens attached to a carbon and its relaxation rate. The dependance of the relaxation rate upon τ_c is the relationship of interest in determining molecular mobility since rates corresponding to the Larmor frequency are most efficient at relaxing excited nuclei. For organic molecules in solution τ_c is in the range between 10⁻⁹ and 10⁻¹³ seconds depending on molecular size, solution viscosity and temperature.

Measurement of ¹³C T₁'s is possible by simply exciting a nucleus and monitoring the signals intensity as a function of time. After excitation the nuclear spins return to a Boltzmann distribution and the intensity of a signal goes exponentially to zero. Integration of Equation (58), which defines T₁ in terms of M_z, produces the relation in Equation (80).

$$M_z(t) - M_0 = [M_z(0) - M_0] \exp(-t/T_1) \quad (80)$$

Here M_z(t) is the magnetization after a pulse interval t. Therefore a plot of ln(M_z-M₀) versus pulse interval, t, has a slope of 1/T₁. In

practice M_z is tipped onto the $-Z$ axis by a 180° pulse and after a waiting interval, t , the pulse is given a 90° pulse rotating it onto the Y axis to be monitored for intensity. A delay time, T_D , is given to ensure equilibrium is achieved before the sequence is repeated. When the time interval is varied, a plot giving T_1 can be constructed and the pulse sequence used is described in Equation (81).

$$[180^\circ-t-90^\circ(\text{fid})-T_D]_n \quad (81)$$

A number of investigators have found ^{13}C T_1 analysis to be useful for monitoring changes in molecular motion due to intra and intermolecular interactions.⁽⁸⁷⁻⁸⁹⁾ An example of ^{13}C spin-lattice relaxation usage is the study of potassium ion interaction with the cyclic antibiotics valinomycin and nonactin as well as with two crown ethers.⁽⁹⁰⁾ Complexation of these compounds with the potassium cation make the systems more rigid thereby reducing internal segmental mobility and affecting correlation times and therefore T_1 values. The approach is to compare T_1 values for the uncomplexed ligand with those for the complex and draw conclusions based upon any differences.

2.5 Crown Ethers

The synthesis and characterization of cyclic ethers was reported as early as 1937 by Luttringhaus⁽⁹¹⁾. However, their unusual characteristics were missed until C.J.Pedersen⁽⁹²⁻⁹⁵⁾ reported on the formation of stable complexes between macrocyclic polyethers and salts of alkali and alkaline earth metals. While working for E.I.duPont de Nemours and Company in the mid sixties Pedersen, in an attempt to find new ways of incorporating vanadium with different ligands for potential use as a catalyst for alkene polymerization, isolated the crown ether dibenzo-18-crown-6 (Figure 11) and demonstrated its complexing potential.

Figure 11. Dibenzo18Crown6

Since this discovery numerous efforts have been made to utilize, modify and understand the new area of chemistry that can be described as neutral ligand chemistry. This has lead to the development of new families of compounds having the same

complexing properties as crown ethers such as the cryptands⁽⁹⁶⁻⁹⁸⁾ and calixarenes⁽⁹⁹⁻¹⁰²⁾. Also this discovery has generated renewed interest in natural complexing agents such as the cyclodextrins⁽¹⁰³⁾.

The important property of neutral ligands such as crown ethers is their capacity for forming selective, stable complexes with positive and in some cases neutral⁽¹⁰⁴⁾ species. The complexation process is attributed to electrostatic attraction between the positive end of a cation-anion pair or a polarized neutral molecule and the negative dipolar charge on the heteroatoms in the polyether ring⁽¹⁰⁵⁾. The binding of a ligand with a ligand acceptor has been studied for such cases as the ethylenediamine and nickel⁽¹⁰⁶⁾ reaction with the conclusion that complex formation is a stepwise process in which solvent molecules are consecutively replaced by binding sites on the ligand. The presence of more than one binding site on a single ligand inhibits dissociation. This is based upon the assumption that once a given donor atom separates from the metal, the possibility of the process being reversed by rebinding is enhanced by its linkage to the rest of the molecule which is still bound to the ligand acceptor⁽¹⁰⁷⁾.

The binding of a flexible ligand such as a crown ether to a ligand acceptor requires reorganization of the ether conformation as well as desolvation. However, the degree of reorganization required for a macrocycle to form a complex is significantly less than that required for a linear analogue and as Cram⁽¹⁰⁸⁾ has noted, the energy cost of complex formation is in part prepaid

during the synthesis of the preorganized ligand in terms of conformation and dipole-dipole repulsion.

The preferred conformation of the $-\text{OCH}_2\text{CH}_2\text{O}-$ unit in crown ethers has been studied⁽¹⁰⁹⁻¹¹¹⁾ and it is agreed they prefer to adopt a gauche conformation about the C-C bonds and an anti conformation about the C-O bonds (Figure 12).

Figure 12. Gauche and anti conformations.

Infrared studies⁽¹¹²⁾ on 1,2-dimethoxyethane have shown that this simplest example of the $-\text{OCH}_2\text{CH}_2\text{O}-$ system takes on a range of conformations in the liquid phase but adopts only the gauche conformer in the crystal at -195°C . In the crystal form, polyoxyethylene adopts gauche conformations around the C-C bonds and anti conformations about the C-O axis.⁽¹¹³⁾ It has been shown that the $-\text{OCH}_2\text{CH}_2\text{O}-$ network is approximately $1.7\text{kJ}\cdot\text{mol}^{-1}$ more stable when the oxygens are gauche than when they are anti to one another⁽¹¹⁴⁾.

When discussing crown ethers it is possible to make correlations between the ability of a system to adopt the preferred conformations upon complexation and the propensity for forming a complex. Thus the 18-crown-6 system is the most fully characterized family of crown ethers and therefore the one best suited to comparisons. The parent compound adopts the preferred all gauche conformation upon complexation and has D_{3d} symmetry in both solution⁽¹¹⁵⁾ and the crystalline state^(116,117) and forms the most stable complexes of the 18-crown-6 family^(118,119).

The cis-syn-cis and cis-anti-cis dicyclohexyl isomers can also attain the ideal complexing conformation in the solid^(120,121) and in the liquid⁽¹²²⁾ phases and each readily form complexes. The corresponding trans-syn-trans isomer is rigid to cyclohexyl ring inversion but has the desired all gauche conformation upon complexation and readily forms stable complexes. In contrast the trans-anti-trans compound, also rigid to cyclohexyl ring inversion, is incapable of taking on the desirable complexing conformation and forms the least stable complexes⁽¹²³⁾. Here the cis or trans adjectives describe the stereochemistry at the cyclohexyl substituents and the syn or anti adjectives refer to the relative dispositions of the two cyclohexyl substituents to one another about the macrocyclic ring. A correlation between the free energies of association (ΔG_a) for these systems and their capacity for adopting the preferred conformation is seen in (Table 1). Here the ΔG_a value refers to the energy barrier overcome by the free ligand in passing to its complexed form. Table 1 indicates the more flexible 18-crown-6

system has the largest negative energy while the least conformationally suited isomer (trans-anti-trans) has the smallest negative energy of complexation.

Crown ether	ΔG_a for Na^+ $\text{kJ}\cdot\text{Mol}^{-1}$	ΔG_a for K^+ $\text{kJ}\cdot\text{Mol}^{-1}$
18-crown-6	-24.7	-34.7
c-s-c dc18-C-6	-23.0	-34.3
c-a-c dc18-C-6	-20.9	-30.5
t-s-t dc 18-C-6	-16.7	-23.4
t-a-t dc 18-C-6	-14.2	-18.0

Table 1. ΔG values of complex formation for 18-c-6 systems.

The selectivity exhibited by the 18-crown-6 system for potassium is a function of cavity size versus ion size. This correlation is used to explain the selectivity of crown ethers to certain cations⁽⁹⁵⁾ and is valid with the exception of some of the more flexible polyether systems⁽¹²⁴⁾. This situation is described in a comparison between crown ether cavity diameters and cation diameters below (Table 2).

Cation	Diameter	Crown	Diameter
Li ⁺	1.36	12-c-4	1.2-1.5
Na ⁺	1.94	15-c-5	1.7-2.2
K ⁺	2.66	18-c-6	2.6-3.2
Cs ⁺	3.34	21-c-7	3.4-4.3

Table 2. Cation and crown cavity diameters in Å.

Therefore any design of a crown ether system must consider cavity size as well as the preferred conformations of the free ligand and of the desired complex.

Table 2 suggests the crown ethers best suited for lithium complexation are the 12 to 14 membered macrocycles and this has been found to be the case⁽¹²⁵⁻¹³⁴⁾. However, solvent effects and the initial concentrations of reagents affect complexation trends and stability constants increase with decreasing solvent polarities making it necessary to take care in making comparisons. One comparison is the study of lithium picrate extraction by a number of crown ethers and the results indicate benzo-13-c-4 is the most efficient (Table 3)⁽¹³⁵⁾.

Crown Ether	Percent Picrate Extracted
Benzo-12-c-4	11
Benzo-13-c-4	82
Dibenzo-14-c-4	75
Benzo-15-c-5	43
Dibenzo-18-c-6	51

Table 3. Percent picrate extracted by a series of crowns.

However this contrasts the results of an alternate study on lithium complexation in which extraction efficiency is also used to compare complexation energies. This study of benzyloxy-methyl crown ethers having 13,14,15 and 16 membered macrocycles found the 14-crown-4 system was most efficient at lithium ion complexation.(136). Yet, selectivity comparisons for the compounds in Table 3 and reference (136) cannot include conformational influences since the conformational preferences for these systems are not at this time fully characterized.

However, the conformational characteristics of some 12,13 and 14 membered tetraoxa crown ethers and their complexes have been described. A number of results describe the crystal structures of sandwich complexes between 12-crown-4 systems and sodium salts having a selection of anions(136-138). Results indicate the 12-crown-4 ligand adopts a number of different

conformations upon formation of different complexes. Also, the conformation of the parent 12-crown-4 compound has been characterized at low temperature by X-ray crystallography⁽¹³⁹⁾. The three dimensional stereoview of this structure is described in Figure 13 below.

Figure 13. Stereoview of 12C4 at -150 C.

Thus the compound adopts a pseudo square conformation in the crystal and has a twofold symmetry. The notable aspect of this structure is the deviation from normal gauche and anti orientations for the -O-C-C-O- and -C-O-C-C- units. The closest approach to ideal gauche geometry for the two -O-C-C-O- units is in the $\text{-O}_2\text{C}_3\text{C}_4\text{O}_1\text{-}$ segment which has a torsional angle of 74.5° while the $\text{-O}_1\text{C}_1\text{C}_2\text{O}_2\text{-}$ value is -75.4° . The -C-O-C-C- structures, of which there are four different systems, have only one unit which fits the anti geometry and this is the $\text{-C}_4\text{C}_3\text{O}_2\text{C}_2\text{-}$ system with a torsional angle of 173.6° . The other three corresponding

networks have dihedral angles of 140.2° , 102.7° and 85.2° . This deviation from ideal geometry is also the case when 12-crown-4 is complexed^(136,139) and the complexed geometries can deviate to a greater extent than for the free ligand.

An example of a 12-crown-4 complex is the 12-crown-4 and LiSCN system which has been isolated and characterized by X-ray crystallography⁽¹⁴⁰⁾. The stereoview of this complex is depicted in Figure 14 below with the LiSCN moiety directed into the -Z direction.

Figure 14. Stereoview of 12C4 and LiSCN at 20 K.

The ligand in this complex takes on the square shape evident in the uncomplexed molecule and although the system no longer has true symmetry there is a pseudo mirror plane dissecting the cation and two oxygen atoms. The interoxygen distances across the cavity are 3.9 Å and 3.7 Å and with dihedral angles of 89° , 96° and 46° a considerable degree of distortion from ideal geometry exists.

The dibenzo-14-crown-4:LiSCN⁽¹⁴¹⁾ and the sym-dibenzo-14-crown-4-oxyacetate:Li[C₂₀H₂₁O₇].7.5H₂O⁽¹⁴²⁾ complexes have been characterized by-X-ray crystallography and in both cases the ligand takes on the same symmetric V shaped conformation with the cation placed about 0.8 Å above the plane of the four oxygens. In this conformation the molecule is inflexible and the four oxygens are locked into a perfect arrangement for square pyramidal co-ordination to Li⁺ which is also bound to the anion. Selectivity towards lithium is ascribed to the cavity size and to the V shaped conformation⁽¹⁴¹⁾ which makes the crown ether cavity accessible from one side alone.

The crystal structures of the benzo-13-crown-4 and benzo-13-crown-4 LiSCN have been solved⁽¹⁴³⁾ and these provide an illustration of the conformational changes which can occur upon complexation. The free ligand is bent forming a 137° angle between the plane of the benzene ring and the mean plane of the four oxygens in the macrocycle. Three of the four oxygens have their lone pairs directed toward the interior of the cavity while the fourth oxygen is directed to the cavity exterior. This is attributed to a repulsive interaction of the lone pairs. Upon complexation all four oxygens are directed toward the convex side of the molecule with the lithium cation pentacoordinated to the four crown ether oxygens and the nitrogen of the anion. The angle between the aromatic plane and the mean plane of the oxygens has changed to 131° and the cation is 0.8 Å above the oxygen plane. Thus complexation has caused a reorganization of

the 13 membered ring to direct all oxygen lone pairs toward the lithium cation.

The conformations of two cis-syn-cis and one cis-anti-cis dicyclohexano-14-crown-4 diols have been described by X-ray crystallography.⁽¹⁴⁴⁾ In each of these cases the average planes of the cyclohexyl substituents are colinear with one another and at an angle with the average plane of the oxygens in the macrocycle. The cis-anti-cis isomer has anti conformations in four -C-O-C-C- systems around the macrocycle and only gauche conformations in the -O-C-C-O- and -O-C-C-C- networks. This situation is repeated without exception for the two cis-syn-cis isomers and demonstrates the preferred conformations of the units in larger crown ethers⁽¹⁴⁵⁻¹⁴⁷⁾ applies to these smaller crown systems.

The conformation of 1,4,8,11-tetraoxacyclotetradecane(14-crown-4) at -150 C has been determined by X-ray analysis⁽¹⁴⁸⁾ and the stereoview of this molecule is displayed in (Figure 15) below.

Figure 15. Stereoview of 14C4.

The rectangular conformation adopted by 14-crown-4 at low temperature is similar to that of the parent alkane(149) and to that of the complementary structure 1,3,8,10-tetraoxacyclotetradecane(150) (Figure 16 below).

Figure 16. Stereoview of 1,3,8,10-tetraoxacyclotetradecane.

Therefore the 14-crown-4 molecule demonstrates the preferred alignment of the $-O-C-C-O-$ and $-O-C-C-C-$ units which in every instance have adopted the familiar gauche conformation. Equally all the $-C-O-C-C-$ units are in the anticipated anti orientation.

The 1,3,8,10-tetraoxacyclotetradecane has no -O-C-C-O- segments but the -O-C-C-C- units are gauche and the -C-O-C-C- systems take up an anti conformation. In both examples the atoms occupying corners are carbon which are participating in gauche systems. Also the oxygens atoms are confined to the linear segments of the molecule. Other systems which exhibit a similar rectangular conformation in the macrocycle are 1,5,9,13-tetraoxacyclohexadecane (16-crown-4)⁽¹⁵¹⁾ and 1,4,7,10,13,16-hexaoxacyclooctadecane (18-crown-6)⁽¹⁵²⁾.

The molecular dynamics of crown ethers have also been studied. In fact ring systems have been investigated since the early sixties and the best documented example of conformational flexibility is for the chair-chair interconversion of cyclohexane⁽¹⁵³⁻¹⁵⁵⁾ (Figure 17).

Figure 17. Chair to chair interconversion.

NMR coalescence temperature analysis has been used to show conformational energy barriers exist in cyclooctane⁽¹⁵⁶⁾, cyclononane⁽¹⁵⁷⁾ as well as cyclodecane, cyclododecane and cyclotetradecane⁽¹⁵⁸⁾ systems. The 1,4,7,10-tetraoxacyclododecane (12-crown-4) and its lithium salt

complexes have been studied⁽¹⁵⁹⁾ and were shown to exhibit two site exchange processes. The free ligand was found to coalesce at -126 C and have a free energy of activation of 28.5 kJ·Mol⁻¹. This process is attributed to a stepwise movement of each corner of a rectangular conformation where the corner carbon is converted to a side carbon by passing through a high energy intermediate. The LiSCN complex of 12-crown-4 was found to coalesce at -96 C and have a free energy of activation of 34.3 kJ·Mol⁻¹ for the interconversion process and a similar mechanism is ascribed to this rate process as for the free ligand

Although there have been no studies done on 12,13 or 14 membered dicyclohexyl crown ethers the cis-anti-cis and cis-syn-cis isomers of dicyclohexyl-18-crown-6 have been studied⁽¹⁶⁰⁾. These compounds exhibit conformational isomerism detectable by NMR methods with different conformers having unequal populations. The existence of more than a single degenerate rate process is attributed to the existence of chair-chair interconversion for the cyclohexyl substituents superimposed upon a conformational rate process associated with the macrocycle itself. Therefore combinations of conformation mobilities can lead to a relatively complex situation in which several dynamic processes may be superimposed.

This leads to a discussion of the rationale for proceeding with a conformational analysis on neutral ligand systems. It is clear the conformation of the free ligand and the degree of change necessary for this system to form a complex plays a role in the energy requirement of complex formation. The reasons for

studying the complexation reaction and seeking to understand and modify this phenomena are numerous. Crown ethers have been useful as phase-transfer catalysts in generating highly reactive anions^(161,162) and strong bases generated by crown ether separations of ion pairs have been used to increase ionic polymerization⁽¹⁶³⁾. Dicyclohexyl-18-crown-6 has been shown to increase oxidation rates by solubilizing potassium permanganate in organic solvents⁽¹⁶⁴⁾ and analytical chemistry has used crown ether ionophilicity to generate metal of high purity⁽¹⁶⁵⁾. Further application of the selective complexation properties of macrocyclic systems such as crown ethers seems inevitable.

The search for new and better crown ethers has therefore lead to the variation of a number of parameters and new systems have incorporated differing numbers of ether oxygen atoms, ring sizes, lengths of the $(CH_2)_n$ bridge, substitutions by other heteroatoms and varied substitution patterns around the macrocycle⁽¹⁶⁶⁾. Also chirality has been introduced into the ring to create optically active crown host compounds with the capability of differentiating between enantiomeric guest molecules^(166,167). Therefore knowledge of the impact a preferred conformation will have upon a new system's ability for forming stable complexes has implications for the design of new crown ether systems.

Useful as the documented applications of neutral ligand chemistry may be, clearly the most exciting use of these compounds is in the developing field of synthetic enzymes. This area of chemistry seeks to design molecular systems with some

of the catalytic prowess of naturally occurring enzymes⁽¹⁶⁸⁾. The motivation for developing this branch of chemistry is based upon the clear superiority of in vivo molecular chemistry over conventional in vitro chemistry. Thus it is not unusual for an enzyme catalyzed reaction to be 10^{10} times as fast as the same reaction without the catalyst⁽¹⁶⁹⁾. Also, enzymatic reactions achieve a degree of selectivity impossible for the conventional chemist. Control of molecular selectivity at the level of biological enzymes could make it possible to design and synthesize molecules capable of chelating with and destroying viruses or able to neutralize cancer cells by selectively inhibiting their replication. Possibly genetic disorders could be corrected on the molecular level by appropriately designed systems which could enter all the cells of the individual and affect repairs.

The first step in an enzyme-catalyzed reaction is the formation of an enzyme-substrate complex. This weak bond holds the substrate to the catalyst in an appropriate orientation to permit reaction to occur before release. It is probable part of an enzyme's ability for recognizing a substrate and knowing when reaction has occurred is based upon conformational changes in the enzyme structure. Therefore the design of a synthetic enzyme must begin with the design of an active site in which a weak bond between substrate is formed and this bond formation must be selective. The study of the conformational preferences of crown ether systems is therefore a step toward the design and control

of a chemistry modelled after the impressive abilities of in vivo molecular enzyme chemistry.

Therefore it is within this context that the present study of the conformational characteristics of 12,13 and 14 membered cis-anti-cis and cis-syn-cis dicyclohexyl crown ethers is undertaken. These compounds were not isolated before this research initiative was undertaken. The information that can be gleaned from the following conformational analysis may be useful in the future design of lithium selective ligands. Also, the application of solid and liquid phase ^{13}C NMR spectroscopy in concert with X-ray analysis can present an example of a useful approach to future conformational investigations.

Chapter 3.0 Results And Discussions

The following conformational analysis of dicyclohexyl-12,13 and 14-crown-4-ethers employs the coordinate system described in Coordinate System 1 below.

Coordinate System 1.

Here a positive rotation about the X axis moves the Y coordinate onto the Z axis, a positive rotation about Y brings the Z axis into X and a similar rotation about Z brings X into Y. Stereoviews can be seen in 3-dimensions by the crossed eye technique but are most easily viewed with 3-D glasses and these give optimal results when the viewer's two eyes are of approximately even strength while experiencing equal amounts of light. The molecular numbering schemes are not consistent with correct IUPAC numbering but are consistent with those assigned by X-ray analysis. Supplemental X-ray data is recorded in Appendix 1 at the end of this study.

3.1 CAC and CSC Dicyclohexyl 14-Crown-4 and Complexes

The *cis-anti-cis*-dicyclohexyl-14-crown-4 isomer was found to recrystallize into the space group $Pbc2_1$ with a local symmetry or point group of C_i since there is a true local or molecular center. This local symmetry is described in the numbering system of the structure described below (ORTEP 1.).

ORTEP 1. CACDC14C4.

This view of the *cis-anti-cis* isomer is also represented in Stereoview 1a (below).

Stereoview 1a. CACDC14C4.

The O_1 to O_1' distance is 4.4 Å and since oxygen has a radius of 1.4 Å an effective cavity of 1.6 Å exists. The cyclohexyl rings are in the anticipated chair conformations and in this numbering scheme C_1 and C_1' have axial oxygen while C_2 and C_2' are attached to equatorial oxygen. The planes of the cyclohexyl rings are coplanar and approximately perpendicular with the mean plane of the macrocycle. Also the lone pairs on O_1 and O_2 are directed up while those on O_1' and O_2' are directed in the opposite direction. This is made evident by a negative rotation of the view seen in (ORTEP 1) about the X axis to look along the plane of the four oxygen atoms (Stereoview 1b).

Stereoview 1b. ORTEP 1 after negative X rotation.

The macrocycle is aligned in a manner which permits all -C-C-O-C- segments to have dihedral angles close to an anti conformation while all -O-C-C-O- and -O-C-C-C- units approximate the gauche orientation. Thus beginning with the $-O_1-$

C₁-C₂-O₂- portion of the molecule and proceeding in a clockwise manner around the macrocycle the first seven unique dihedral angles are documented below (Table1). Comparison between this system and its parent, 14-crown-4 (Figure 15 of this report), is possible and the corresponding angles for this system are also documented in Table 1.

Atomic system	Torsion angle	
	14c4	CACDC14C4
O ₁ C ₁ C ₂ O ₂	77.1	56.9
C ₁ C ₂ O ₂ C ₉ '	-89.1	65.1
C ₂ O ₂ C ₉ 'C ₈ '	167.8	170.4
O ₂ C ₉ 'C ₈ 'C ₇ '	-70.6	61.5
C ₉ 'C ₈ 'C ₇ 'O ₁ '	-64.0	64.1
C ₈ 'C ₇ 'O ₁ 'C ₁ '	179.0	-173.6
C ₇ 'O ₁ 'C ₁ 'C ₂ '	-172.0	157.9

Table 1. Dihedral angles for 14C4 and CACDC14C4.

The results in Table 1 show the gauche angles for the cis-anti-cis isomer are closer to the ideal value of 60° than those in the 14-crown-4 molecule. This may be due to the cyclohexyl substituent which imposes its close to ideal geometry on the O₁C₁C₂O₂ and C₁C₂O₂C₉' networks. A second notable difference between the two compounds in Table 1 is the opposite sign of the dihedral angles for five of the seven unique systems. Thus the anti orientation of the two cyclohexyl substituents imposes a

major reorganization upon the macrocyclic ring. This is seen in the dispositions of oxygen lone pairs. These are directed consecutively up and then down in the 14-crown-4 molecule while in the cis-anti-cis isomer oxygen lone pairs on each cyclohexyl are directed in the same direction. This is evident in Stereoview 1b.

Since the cis-anti-cis-dicyclohexyl-14-crown-4 molecule has twofold symmetry as evident in the X-ray, the CPMAS ^{13}C NMR spectrum should reflect this and such is the case in Spectrum 1a (below).

Spectrum 1a. CPMAS ^{13}C of CACDC14C4.

This twofold symmetry is easiest to see in the oxygenated carbon region of the solid phase ^{13}C NMR spectrum between 60 and 80 ppm where four clearly defined resonances are evident. The completely resolved spectrum should have nine lines and with a single case of peak overlap at 28 ppm Spectrum 1a has nine signals.

The assignment of individual carbon resonances can be made using established substituent effects on ^{13}C chemical shifts. One such documented result is that a cyclohexyl carbon bearing an axial oxygen is shifted upfield relative to one having an equatorial oxygen⁽¹⁷¹⁾. The C_2, C_2' pair therefore account for the least shielded resonance at 78.02 ppm in the CP MAS ^{13}C spectrum of the cis-anti-cis isomer since these have equatorial oxygen. The next line at 72.63 ppm can also be assigned to the methine C_1 and C_1' carbons which have axial substituents. Based upon the well known gauche γ effect the most upfield resonance in this spectrum can be attributed to those carbons in the cyclohexane rings which have oxygen atoms in a gauche γ relationship. The structure in ORTEP 1 indicates these carbons are the C_5, C_5' pair and these therefore accept assignment of the resonance at 20.4 ppm. The next resonance downfield to C_5, C_5' at 24.84 ppm is therefore C_4, C_4' since these are anti γ to oxygen.

The C_7, C_7' and C_9, C_9' pairs bear oxygen and therefore account for the resonances at 60.8 and 63.5 ppm. These are in very similar environments with each having two anti and three gauche torsional angles. However the C_7, C_7' pair have one gauche interaction which deviates significantly from ideality with a

value of 81.5° . Based upon the calculations of Maciel and Seidman⁽³¹⁾, and corroborated by computational analysis done in the course of this study, the 80 degree angle is less shielding than the ideal gauche angle of 60 degrees. Therefore the C₇,C_{7'} pair are assigned the downfield resonance at 63.5 ppm leaving the upfield shift at 60.8 ppm for the C₉,C_{9'} pair. The C₈,C_{8'} pair can be assigned the resonance at 32.6 ppm since these atoms are the only aliphatic carbons which are β to two oxygens and these will therefore be downfield relative to all other other nonoxygenated carbons. The C₃ to C₆ distinction can also be made based upon their respective β relationships to oxygen. The C₆, C_{6'} pair are the least shielded since they are anti to oxygen and the C₃, C_{3'} pair are correspondingly gauche. However in Spectrum 1a these have approximately the same chemical shifts and are assigned the overlapping resonances at 28 ppm.

In solution at room temperature the cis-anti-cis isomer has five lines in its ¹³C spectrum indicating rapid conformational averaging on the NMR timescale (Spectrum 1b).

Spectrum 1b. 100.6 MHz ^{13}C of CACDC14C4 at 298 K.

However when the temperature is reduced to 193 K there are eighteen distinguishable resonances (including a closely spaced doublet at 71.69 and 71.75 ppm) in the ^{13}C spectrum (Spectrum 1c).

Spectrum 1c. 100.6 MHz ^{13}C of CACDC14C4 at 193 K.

If the cis-anti-cis compound experiences a complete loss of symmetry under low temperature conditions there should be eighteen approximately equal intensity lines in the spectrum. This is clearly not the case, just as it is evident the symmetric form with nine lines seen in the solid phase does not account for Spectrum 1c.

The relative intensities of the various resonances at low temperature provides a clue to the probable source of the eighteen lines observed. In the oxygenated carbon region of the spectrum, between 60 and 80 ppm, eight lines are observed in a 2:1 ratio. Other pairs existing in the same ratio are four resonances between 26 and 29 ppm as well as two signals near

20 ppm. In that part of the spectrum associated with the non-oxygenated bridging methylene carbons, near 31 ppm, there are three lines in the ratio of 4:1:1 as seen in an enlargement of the non-oxygenated region of Spectrum 1c below.

Spectrum 1c'. Enlargement of aliphatic region of 1c.

The implication of this is that the C_8 , C_8' bridging pair are split in two lines in one conformer which co-exists with a second conformer in which this pair are equivalent as is the case in the solid phase spectrum. These two conformations are therefore in a 2:1 ratio with the major isomer having equivalent C_8 , C_8' carbons while in the minor isomer these atoms are different. The existence of unequally populated conformational isomers is reminiscent of the dicyclohexyl-18-crown-6 isomers⁽¹⁶⁰⁾. It is

possible the major conformer in the liquid phase is the same as that of the solid phase. This is supported by a comparison of the chemical shifts for the major and minor conformers in solution with those found in the solid phase (Table 2).

carbon	Solid (ppm)	Major(soln) (ppm)	Minor(soln) (ppm)
C ₁ ,C ₁ '	72.6	71.75	71.69
C ₂ ,C ₂ '	78.0	79.21	79.68
C ₃ ,C ₃ '	27.9	28.02	27.80
C ₄ ,C ₄ '	24.8	24.74	unresolved
C ₅ ,C ₅ '	20.4	19.68	19.88
C ₆ ,C ₆ '	27.9	26.61	27.38
C ₇ ,C ₇ '	63.5	63.89	64.75
C ₈ ,C ₈ '	32.6	30.42	31.25, 30.62
C ₉ ,C ₉ '	60.8	62.26	62.87

Table 2. Chemical shifts for CACDC14C4.

The strong similarity between the chemical shifts in the solid phase and those in solution suggests these carbons are in very similar environments. Since symmetry properties are the same for the solid compound and the major conformer in solution, it is reasonable to conclude the solution geometry is very close to that seen in ORTEP 1 and that in the liquid phase the molecule also has an inversion center. The minor conformer in this

interpretation has ten distinct carbons with C_8 and C_8' being different and this could be achieved by a plane which passes through these methylene carbons. This would give the minor conformer C_s symmetry. It is possible a ring inversion of one of the cyclohexyl rings in the structure of ORTEP 1, accompanied by a reorganization of the macrocycle, could produce the minor conformer.

The cis-anti-cis isomer did not form solid complexes with any lithium salts although a number of attempts under a variety of conditions were made. This is a reasonable result when the orientations of the oxygen lone pairs, as seen in Stereoview 1b, are considered. Thus, as evident in this view, the lone pairs on C_1 and C_2 are directed in the positive Y direction while those on C_1' and C_2' are pointed along the negative Y axis. Formation of a solid complex requires that all oxygen lone pairs be pointed in the same direction to afford interaction with the cationic center. This is apparently impossible for this compound and thus a solid complex could not be isolated.

However, in solution a number of combinations are possible. One example of this is that two neutral ligands could complex with a single cation. Also, a single ligand and a combination of solvent molecules could coordinate with the Li^+ species. Clearly there exists some interaction between this cis-anti-cis ligand and the lithium cation in solution. This is evident in the low temperature spectra of a 1:1 mixture between LiSCN and cis-anti-cis-dicyclohexyl-14-crown-4 below (Spectra 1d to 1f).

Spectrum 1d. 75.5 MHz ^{13}C of CACDC14C4+LiSCN at 295 K

Spectrum 1e. 75.5 MHz ^{13}C of CACDC14C4+LiSCN at 225 K

Spectrum 1f. 75.5 MHz ^{13}C of CACDC14C4+LiSCN at 165 K.

These spectra demonstrate there exists a significant difference between the presence of a lithium salt and its absence. This is demonstrated in a comparison between Spectrum 1f and Spectrum 1c above. The 225 K spectrum exhibits nine lines of approximately equal intensity and this is probably due to degenerate double cyclohexane ring inversion. This can be concluded since the observed shift differences at individual carbon sites are similar to those found for other cyclohexane ring inversions⁽¹⁷²⁾. At the extreme low temperature all symmetry is lost and this is evident in the oxygenated carbon region of Spectrum 1f. Here between 64 and 80 ppm eight equally intense resonances are observed. The 18 to 30 ppm region associated with non-oxygenated carbons also indicates asymmetry. In this region ten individual resonances are expected and eight lines are seen with two having double intensity indicating overlap.

The configurational isomer of the cis-anti-cis molecule, cis-syn-cis-dicyclohexyl-14-crown-4, was found to crystallize into space group P21/a. Since the molecule has no true local symmetry it belongs to the point group C_1 . However, the molecule does possess pseudosymmetry in the form of a twofold rotation axis which approximately brings one half of the molecule into the other half. This is evident in the numbering scheme in the ORTEP of this molecule below (ORTEP 2).

ORTEP 2. CSCDC 14 Crown4.

The view of the syn isomer seen in ORTEP 2 and Stereoview 2a (below) shows the two cyclohexyl rings are in the same plane and that this plane is at an angle of approximately 90° with the plane of the four oxygen atoms in the macrocycle.

Stereoview 2a. CSCDC14C4

The disposition of the oxygen lone pairs in this structure are the same as for the parent 14-crown-4 molecule since they are directed consecutively above and below the mean plane of the ring. Also it is notable that the disposition of the cyclohexyl substituents is such that they are both directed onto the same face of the macrocycle leaving the other side essentially open.

In contrast to its configurational isomer the *cis-syn-cis* compound adopts almost the same crystalline form in the macrocycle as does the 14-crown-4 system. This can be demonstrated by viewing the mean oxygen plane of the *syn* compound from the same perspective, Stereoview 2b below, as the 14-crown-4 stereoview of Figure 15 in this study.

Stereoview 2b. CSCDC14C4

The viewing angle in Stereoview 2b shows the compound has adopted the same rectangular shape as seen for the parent. This observation is corroborated by a comparison of dihedral angles between a half unit of the pseudo twofold symmetric cis-syn-cis compound and the 14-crown-4 molecule (Table 2a below).

Atomic system	14C4	CSCDC14C4
O ₁ C ₁ C ₂ O ₂	77.1	64.2
C ₁ C ₂ O ₂ C ₉ '	-89.1	-92.4
C ₂ O ₂ C ₉ 'C ₈ '	167.8	175.6
O ₂ C ₉ 'C ₈ 'C ₇ '	-70.6	-62.6
C ₉ 'C ₈ 'C ₇ 'O ₁ '	-64.0	-58.5
C ₈ 'C ₇ 'O ₁ 'C ₁ '	179.0	-174.8
C ₇ 'O ₁ 'C ₁ 'C ₂ '	-172.0	174.0

Table 2a. Dihedral angles for 14C4 and CSCDC14C4.

Therefore the torsion angles around the macrocyclic ring for this cis-syn-cis isomer do not differ from those of 14-crown-4 by values greater than 8 degrees. This compares with a similar deviation for the cis-anti-cis isomer of 29 degrees. The implication is that the addition of two cyclohexyl substituents in a syn manner onto the macrocycle perturbs the preferred conformation to a

2

MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS
STANDARD REFERENCE MATERIAL 1010a
(ANSI and ISO TEST CHART No. 2)

smaller extent than a corresponding anti addition. Also, the signs of the dihedral angles in Table 2a are the same with the exception of the last two anti conformations which have opposite sign.

The lack of any true symmetry in the X-ray result is expected to be reflected in the CPMAS ^{13}C spectrum of this compound. This expectation is realized in the solid phase spectrum of this system in Spectrum 2a (below).

Spectrum 2a. CPMAS ^{13}C of CSCDC14C4.

Therefore the lack of local symmetry is evident in this spectrum. This is seen in the oxygenated carbon region of the spectrum between 61 and 68 ppm where four clearly distinguished resonances are evident. This indicates the C7, C7', C9, and C9' environments are different. The strong similarity in torsional angles is also evident in this spectrum. Therefore the oxygenated methine carbons bearing axial and equatorial oxygen, between 76 and 82 ppm, are unresolved. Also a number of resonances due to the aliphatic carbons on the cyclohexyl rings are overlapping.

The C1,C1' pair can be assigned the more downfield resonance in Spectrum 2a since these bear equatorial oxygen and this leaves the C2,C2' pair due to the resonance at 76.3 ppm. Distinction between the C7, C7' and C9,C9' pairs can be done based upon computational evidence as described for the cis-anti-cis isomer. Therefore the C9,C9' pair are assigned the upfield doublet at 67.3 and 66.6 ppm due to their participation in a 90° torsion angle. An observation which supports this assignment is that computational results suggest the 90° angle is more deshielding than a corresponding 80° value. Thus it is expected a greater differential between the C7,C7' and C9,C9' chemical shifts for the cis-syn-cis isomer over the cis-anti-cis isomer will be observed. This is the case since the deshielding of the cis-anti-cis C9,C9' pair at 67.3 and 66.6 ppm is greater than the corresponding deshielding of the cis-anti-cis C7,C7' pair at 63.5 ppm.

The C4 and C4' pair which are gauche- γ to oxygen appear at the highest field as a closely spaced doublet at 19.8 and 20.9 ppm. The corresponding pair which are trans- γ to oxygen can be assigned the double intensity line at 25.2 ppm. The C8,C8' methylene carbons on the propano bridges are assigned the resonance at near 32 ppm. The C3,C3' pair which are downfield relative to their C6,C6' counterparts due to their β relationship to equatorial oxygen are assigned the other resonance near 32 ppm leaving the C6,C6' pair the 25.7 ppm shift.

The low temperature solution spectrum of cis-syn-cis-dicyclohexyl-14-crown-4 compound shows a marked similarity to the corresponding solid phase spectrum (Spectrum 2b below).

Spectrum 2b. 50.3 MHz ^{13}C of CSCDC14C4 at 170 K.

The low temperature spectrum of the cis-syn-cis isomer is consistent with a single degenerate process becoming slow on the NMR time scale since the five lines in the room temperature spectrum are each split into two lines at reduced temperatures.

The similarity between the solid and liquid phase chemical shifts is also apparent in Table 2b which documents the chemical shifts for this isomer in the liquid and solid phases.

Carbon	Solid Phase ppm	Solution ppm
C ₁ ,C _{1'}	82.0, 82.0	81.79
C ₂ ,C _{2'}	76.3, 76.3	75.43
C ₃ ,C _{3'}	32.0, 32.0	31.15
C ₄ ,C _{4'}	19.8, 20.9	20.38
C ₅ ,C _{5'}	25.2, 25.2	24.84
C ₆ ,C _{6'}	25.7, 25.7	25.10
C ₇ ,C _{7'}	60.9, 61.8	62.30
C ₈ ,C _{8'}	32.9, 32.9	31.37
C ₉ ,C _{9'}	67.3, 66.6	66.04

Table 2b. Chemical shifts CSCDC14C4.

The strong similarity between the X-ray defined conformations of the macrocycle in the cis-syn-cis compound and the parent 14-crown-4 invites the conclusion that the cis-syn-cis isomer is in an energetically favorable conformation. Also, a strong correlation between the solid and liquid phase chemical shifts leads one to conclude the two conformations are also very similar. The small differences in the C7,C7' and C9,C9' environments which have caused them to be distinguishable as four resonances in the solid are averaged in the liquid phase causing them to resolve as two lines.

The capacity of cis-syn-cis-dicyclohexyl-14-crown-4-ether to adopt the same conformation as its non-substituted parent compound is indicative of a high degree of flexibility. This is a prerequisite to efficient complexation when the free ligand's conformation is not the same as the complexed conformation. In such an instance reorganization of the ligand conformation is necessary before the four oxygen atoms can direct their lone pairs toward a cation centered approximately in the middle of the macrocyclic cavity. The cis-syn-cis isomer is capable of such reorganization and forms stable complexes in both the solid and liquid phases.

The solid phase LiSCN complex of the cis-syn-cis-dicyclohexyl-14-crown-4 isomer is described in ORTEP 3 (below).

ORTEP 3. CSC14C4:LiSCN.

The crystallographic space group adopted by this compound is $Pnma$ and the point group describing the molecular, or local, symmetry is C_s since the molecule has a mirror plane passing through C_8 and C_{10} . The reorganization necessary for the free ligand to form a complex with the lithium salt has caused one of the cyclohexyl rings to invert which is accompanied by a change in the macrocycle conformation. This is evident by comparison between the axial and equatorial oxygens in ORTEP 3 and ORTEP 2. Here the sequence around the macrocycle has changed from axial-equatorial-axial-equatorial to axial-axial-equatorial-equatorial.

The four oxygen lone pairs in the complexed ligand are directed toward the same molecular face. Also the two cyclohexyl

substituents are directed toward the opposite side of the ligand and this is evident in Stereoview 3a (below).

Stereoview 3a. CSCDC14C4:LiSCN.

The mean planes of the two cyclohexyl groups are at an angle with one another in the X-Y plane and perpendicular to the mean oxygen plane in the X-Z plane. A mirror plane runs through carbons 10 and 8 and in Stereoview 3a is in the Y-Z plane. The diagonal distance across the ring between opposite oxygens is 3.88 Å and taking into account the van der Waals radius of oxygen of 1.4 Å the resulting cavity diameter is 1.08 Å. This value is slightly too small for the Li cation to fit easily into since lithium has an effective diameter between 1.18 and 1.52 Å⁽¹⁷³⁾. The result of this is that the lithium cation lies 0.53 Å above the mean plane of the oxygen atoms. This out of cavity disposition is apparent in the view along this mean oxygen plane seen in Stereoview 3c (below).

Stereoview 3b. CSCDC14C4:LiSCN oxygen plane.

The lithium atom is therefore pentacoordinated with the four crown ether oxygens and the nitrogen of the SCN anion in a distorted square-pyramidal geometry. The two Li-O₁ bond lengths of 1.958 Å are short and correspond to the Li-O bonds lengths in tetrahedral complexes. The Li-O₂ distances of 2.074 Å are normal for lithium-oxygen bond distances in pentacoordinated complexes with macrocyclic ligands⁽¹³⁹⁻¹⁴¹⁾. Since the Li-O₂ distances are longer than the Li-O₁ bond lengths, the lithium atom is not directly over the center of the four oxygen plane, but is biased toward the O₁,O₁' side of the molecule. This is also seen in the unsymmetrical nature of the O-Li-NCS bond angles where the O₁-Li-N bond angle is 108.6 degrees and the O₂-Li-N angle is 102.4 degrees.

The mirror plane observed in the X-ray of this complex is clearly reflected in the CPMAS ¹³C spectrum (below).

Spectrum 3a. CPMAS ^{13}C CSCDC14C4:LiSCN.

Thus the C_8 and C_{10} carbons are clearly distinguishable at 30.7 and 32.6 ppm as half intensity resonances indicating these carbons are different as shown by the X-ray. The lowest field resonance at 78.4 ppm is due to the methine carbons bearing equatorial oxygen and therefore from ORTEP 3 these are C_1, C_1' . The next line proceeding upfield in Spectrum 3a is due to the carbons bearing axial oxygen and therefore are assigned the C_2, C_2' pair.

The most upfield line in Spectrum 3a is assigned the carbons having oxygen in a gauche- γ orientation which in this case is the C_4, C_4' pair at 19.1 ppm. At approximately 5 ppm

downfield from this is the anti- γ counterpart which is resolved at 24.2 or 24.9 ppm and one of these lines is assigned to the C_5, C_5' pair. Based upon the usual β to axial oxygen consideration one of the resonances at 24.2 or 24.9 ppm can be assigned to the C_3, C_3' pair. The C_6, C_6' pair, which are β to equatorial oxygen are attributed to the line at 27.0 ppm. The two resonances at 65.2 and 67.6 ppm are due to the C_7, C_7' and C_9, C_9' pairs and since these are both involved in nine torsional networks and have a chemical shift difference of 2.4 ppm, they are essentially indistinguishable.

In a manner similar to that of the uncomplexed ligand, the complex exhibits a low temperature ^{13}C spectrum very similar to the solid phase spectrum. This is apparent in a comparison between the solid phase spectrum (Spectrum 3a) and the solution spectrum below (Spectrum 3b).

Spectrum 3b. 50.3 MHz ^{13}C CSCDC14C4:LiSCN at 183 k

This spectrum is indicative of a single degenerate ring inversion process becoming slow on the NMR timescale. The correlation between the solution and solid phase is also apparent and Table 3a (below) documents the chemical shifts for the solid and liquid phase spectra. Here the largest difference is due to either a C₁₀ or C₈ resonance and this differs for the two phases by 2.41 ppm. All other chemical shifts have a closer chemical shift similarity (Table 3a below).

Carbons	Solid (ppm)	Liquid (ppm)
C ₁ ,C _{1'}	78.4	79.71
C ₂ ,C _{2'}	75.8	75.4
C ₃ ,C _{3'}	27.0	25.47
C ₄ ,C _{4'}	19.1	18.94
C ₅ ,C _{5'} *	24.2	25.05
C ₆ ,C _{6'} *	24.9	24.05
C ₇ ,C _{7'} *	65.2	65.83
C ₈	30.7	29.51
C ₉ ,C _{9'} *	67.6	68.32
C ₁₀	32.6	30.19

Table 3a. Chemical shifts for CSCDC14C4:LiSCN, where
* indicates possible interchange with nearest line.

Therefore as in the case for the uncomplexed ligand, a successive progression from the X-ray to the solid phase ^{13}C spectrum permits chemical shift assignments based upon specific knowledge of the carbon environment. These assignments can then be extrapolated to the liquid phase when the solid and liquid phase spectra are similar. The result is an insight into the liquid phase conformation that would otherwise not be possible. However, in the liquid phase, significant variations may be possible for individual torsional angles since each carbon chemical shift is a complex combination of factors. However, in the instance where ten resonances for the two phases are quite similar as in the case of the complex in ORTEP 3, a conclusion that the two overall conformations are much the same is reasonable. Yet, it must be noted, the liquid phase spectra are almost certainly averaging out conformational mobilities too flexible to be frozen out by those temperatures accessible to the NMR experiment.

When the anionic half of the complexing salt is changed from SCN to ClO_4 the influence upon ligand conformation is negligible. This is apparent upon comparison of the ORTEP for the CSCDC14C4:LiSCN with that of the corresponding CSCDC14C4:LiClO_4 complex (ORTEP 4 below).

ORTEP 4. CSCDC14C4:LiClO₄.

The space group is $A21ma$ and the local symmetry which is C_s , is the same as that for the corresponding LiSCN complex. The numbering scheme in ORTEP 4 reflects this and indicates the presence of a mirror plane passing through C₈ and C₁₀. The lithium cation is 0.48 Å above the oxygen plane which is close to the 0.53 value for the LiSCN example. The Li-O bond lengths of 1.958 and 2.041 Å are very close to those for the LiSCN complex with the largest difference being 0.03 Å. Therefore this ligand adopts essentially identical conformations for the LiSCN and LiClO₄ complexes. This is apparent upon inspection of Stereoview 4a below and the corresponding view for the LiSCN complex (Stereoview 3a). This indicates the conformational preference of this ligand persists when the anionic end of the salt is altered.

Stereoview 4a. CSCDC14C4:LiClO₄

One aspect of interest to neutral ligand chemists is the ability of enzymes to react selectively upon certain substrates and this is achieved by molecular recognition. The *cis-syn-cis* isomer has therefore changed its conformation upon complexation with the LiSCN salt and this qualifies as a form of molecular recognition. However, this ligand experiences a different conformational change upon lithium interaction than upon sodium interaction. This is evident in the low temperature spectrum of this isomer with NaSCN (Spectrum 3c below).

Spectrum 3c. 50.3 MHz CSCDC14C4:NaSCN.at 185 K

Therefore when the cis-syn-cis ligand interacts with the larger sodium cation there are no symmetry elements seen. This can be concluded by observation of eight equal intensity lines in the oxygenated carbon region, between 60 and 80 ppm, of Spectrum 3c. It is not useful to discuss the conformation of this complex beyond the observation of asymmetry since a solid complex amenable to X-ray analysis could not be obtained. However, the manner in which this ligand responds differently to variations in the cation size demonstrates that interactions between ligand and cation has an effect upon the ligand conformation. This type of molecular recognition suggests a mechanism for enzyme selectivities.

3.2 CAC and CSC Dicyclohexyl12Crown4 and Complexes

The cis-syn-cis-dicyclohexyl-12-crown-4 isomer was found to crystallize into the space group $Pca2_1$ with local C_2 symmetry. The C_2 axis is colinear with the Z axis as described in ORTEP 5 (below) and the numbering scheme reflects this.

ORTEP 5. CSCDC12C4.

The mean plane of the four oxygen atoms is coplanar with the mean plane of one cyclohexane substituent and approximately perpendicular to the other. This is evident in the stereoview below which is the same viewing angle of the compound as seen in ORTEP 5 although slightly rotated about the Z axis.

Stereoview 5a. CSCDC12C4.

This stereoview provides approximately the same view of this compound as the view of its parent 12-crown-4 seen in Figure 13 of this report. The conformation of the macrocycle takes on the same essentially square shape for the two compounds although some actual torsional angles differ. This is apparent in a tabulation of the torsional angles for this *cis-syn-cis* isomer and its parent 12-crown-4 compound in Table 5a (below).

Atoms	12C4	CSCDC12C4
O ₁ C ₁ C ₂ O ₂	74.7	55.1
C ₁ C ₂ O ₂ C ₇	-173.6	-155.1
C ₂ O ₂ C ₇ C ₈	102.7	77.2
O ₂ C ₇ C ₈ O ₁ '	-75.4	69.2
C ₇ C ₈ O ₁ 'C ₁ '	140.2	-170.3
C ₈ O ₁ C ₁ 'C ₂ '	-85.2	76.1

Table 5a. Torsional angles for 12C4 and CSCDC12C4.

Therefore both compounds in Table 5a have torsional angles often significantly different from the ideal *gauche* or *anti*

geometry anticipated for the -O-C-C-O- and -C-O-C-C- networks. The constraint of cyclohexyl substituents on the macrocycle should cause the torsional geometries common to both to approach the ideal geometry more closely than for the unhindered parent. This is comparable to the 14-crown-4 systems and is the case for those angles which share the macrocyclic moiety with the cyclohexyl substituents. However, perturbation upon these angles causes those angles away from the cyclohexyl substituents to vary from ideality to a greater extent than is the case for the unconstrained parent compound. This is apparent upon inspection of Table 5a where the O₁C₁C₂O₂ unit has a torsional angle of 55.1° which is significantly closer to the ideal 60° geometry than the corresponding value of 74.5° for the parent compound. Similarly the C₂O₂C₇C₈ unit has a value of 77.2° in the cis-syn-cis isomer and a corresponding value of 102.7° for the parent 12-crown-4. Therefore, in both the cis-syn-cis isomer and in the parent compound, the constraint placed upon the system in forming a twelve membered ring alters torsional angles significantly away from the ideal values seen in larger crown ethers.

The O₁-O₁' and O₂-O₂' distances across the macrocycle are 4.0 and 4.2 Å respectively and this leaves a minimum cavity diameter of 1.2 Å which is smaller than the corresponding value for the 14 member counterpart. However this value is larger than that of the cis-syn-cis-dicyclohexyl-14-crown-4 system when complexed with LiSCN and LiClO₄. Also in contrast to its 14-crown-4 counterpart, this cis-syn-cis isomer has all oxygen lone

pairs directed toward the same side of the macrocyclic ring. This is apparent in Stereoview 5b (below) which looks along the average plane of oxygen atoms.

Stereoview 5b CSCDC12C4 oxygen plane.

As this view demonstrates, the uncomplexed ligand takes on a solid phase conformation which is close to that required for complex formation. This conclusion is based upon the observation that all oxygen lone pairs are directed to an open face of the molecule.

A reasonable expectation would therefore be for the solid phase ^{13}C NMR spectrum to reflect the twofold symmetry evident in the crystal structure of this compound. However, the solid phase ^{13}C NMR spectrum for cis-syn-cis-dicyclohexyl-12-crown-4 does not reflect a local twofold symmetry as evident in Spectrum 5a (below).

Spectrum 5a. CPMAS ^{13}C of CSCDC12C4.

This is evident by reference to the oxygenated carbon region of Spectrum 5a. where six distinguishable lines are present. If this were to reflect the crystal symmetry, four equal intensity lines should be present between 60 and 80 ppm. Also, a large amount of overlapping is evident in the aliphatic region of this spectrum where four equal intensity lines would be present if the CPMAS spectrum reflected a twofold crystal symmetry.

The reason the local molecular symmetry, as evident in the X-ray, is not reflected in the ^{13}C NMR is due to asymmetry existing at the molecular packing level in the crystal. This was established by observation that in the crystal structure the $\text{O}_2\text{C}_7\text{C}_8\text{O}_1'$ units of one molecule are oriented differently with respect to the corresponding $\text{O}_2\text{C}_7\text{C}_8\text{O}_1'$ units of a neighboring

molecule. This situation is described in Figure 17 below which shows the relative orientations of molecules in the crystal lattice which causes splitting of ^{13}C resonances.

Figure 17. Crystal Packing asymmetry for CSCDC12C4.

Therefore, as depicted in Figure 17, crystal packing for this molecule is such that atoms like C_3 on one molecule are in a different magnetic environment than the corresponding C_3 on a neighboring molecule. As a result the solid phase ^{13}C spectrum does not reflect local molecular symmetry due to this crystal field splitting of individual resonances.

This is not an isolated instance of molecular packing causing asymmetry in the solid state ^{13}C NMR spectrum. The ^{13}C CPMAS spectrum of benzo-15-crown-5 was found to have more lines than expected from the X-ray result⁽¹⁷⁴⁾. This result was also attributed to crystal field splitting of individual ^{13}C lines.

However, the X-ray experiment is done on a single crystal while the NMR spectrum uses a large number of crystals. It is therefore possible the microscopic sample studied by X-ray could misrepresent the macroscopic sample studied by NMR. This was established to not be the case here by doing X-ray powder diffraction on the solid state NMR sample. This experiment concluded the sample was homogeneous since the X-ray powder cell parameters were within experimental error of the corresponding cell parameters for the single crystal experiment.

The environments of all carbons of the cis-syn-cis-dicyclohexyl-12-crown-4 molecule were subsequently checked and intermolecular interatomic distances were calculated using published values for van der Waals radii for C,H and O⁽¹⁷⁵⁾. The overall environments of individual carbons were investigated using the general formula for an electric field.

$$\text{Interaction} = Z / (\text{interatomic distance})^2 \quad (82)$$

Here Z is the number of electrons of the atom involved in an intermolecular contact. The individual contributions were then summed for each atom to determine if intermolecular interactions in the crystal could cause the two symmetry equivalent atoms in a molecule to exist in different magnetic environments. The results of this procedure are documented in Table 5a (below).

Atom pair	Difference between sums of [Z/Inter atomic distance]
C ₁ ,C ₁ '	0.10
C ₂ ,C ₂ '	0.0
C ₃ ,C ₃ '	0.0
C ₄ ,C ₄ '	0.89
C ₅ ,C ₅ '	0.81
C ₆ ,C ₆ '	0.81
C ₇ ,C ₇ '	0.46
C ₈ ,C ₈ '	0.23

Table 5a. Difference between sums of interactions for carbon pairs in CSCDC12C4 crystal.

This indicates only the C₁C₁', C₂C₂' and C₃C₃' pairs should not exhibit separate resonances and all other atoms in the molecule should be split by the crystal field. The resonance for C₁ and C₁', which have equatorial oxygen, should be the more downfield in the ¹³C spectrum and, as evident in the CPMAS spectrum for this compound, these carbons have a single double intensity line at 78.4 ppm. Also the C₂,C₂' pair should have a double intensity resonance about 5 ppm upfield from the C₁,C₁' line and a resonance is evident in the spectrum for this compound at 65.5 ppm.

This separation represents an unusually large difference between carbons bearing axial and equatorial oxygen. However, analysis of the X-ray data suggests a reason for this difference. Discounting the torsional angles involving hydrogens these carbons are involved in twelve individual networks. The downfield position is assigned to C₁ since this carbon bears equatorial oxygen. This carbon participates in five torsional angles which have approximately the anti orientation which leaves seven to the gauche position. This contrasts the upfield C₂ situation which has only two anti torsional networks with ten gauche interactions. Based upon the known shielding of the gauche orientation relative to the anti orientation the observed large chemical shift differential between these carbons is reasonable.

In the oxygenated region of this spectrum the C₇,C_{7'} and C₈,C_{8'} carbons which are split by the crystal field should exhibit four single intensity lines. Discounting the C₂,C_{2'} resonance there are four lines between 60 and 70 ppm including a closely spaced pair at 66.4 and 66.6 ppm. Table 5a suggests the C₄,C_{4'} pair should be split to a greater extent than all other atoms in the CPMAS ¹³C spectrum. Since these carbons are gauche-γ to oxygen they should resonate at the most upfield position and Spectrum 5a does have a pair of resonances at 19.1 and 22.1 ppm which are of equal intensity. These are therefore assigned the C₄,C_{4'} carbons. Detailed analysis of the remaining lines in spectrum 5a is not possible since a broad resonance with an unresolved shoulder centered at 26.5 ppm accounts for the greater part of these resonances.

Splittings due to molecular packing phenomena are absent in solution and if the liquid phase conformer is similar to that of the solid phase then the solution ^{13}C NMR spectrum should reflect the local symmetry observed in the crystal. This is the case and the four lines observed in the room temperature spectrum of this compound are split into eight equal intensity lines upon temperature reduction (Spectrum 5b and 5b' below).

Spectrum 5b 50.3 MHz ^{13}C of CSCDC12C4 at 298 K .

Spectrum 5b'. 50.3 MHz ^{13}C of CSCDC12C4 at 193 K .

This is indicative of a single degenerate process becoming slow on the NMR timescale.

In the slow exchange limit a chemical shift difference of 11.26 ppm is observed between the two downfield resonances and this compares to a separation of 12.9 ppm between C_1, C_1' and C_2, C_2' pairs in the solid phase. The downfield resonance is therefore again assigned the C_1, C_1' pair leaving the next upfield line to the C_2, C_2' pair. The next two lines proceeding upfield in Spectrum 5b are due to the oxygenated methylene carbons making up the ethano bridge and these have a chemical shift separation of 2.1 ppm. The close proximity between these lines makes their distinction difficult and examination of dihedral angles in the crystal reveals the five torsional networks for these carbons are very similar (Table 5b below).

C ₇ ,C _{7'} network	Angle in degrees	C ₈ ,C _{8'} network	Angle in degrees
C ₂ O ₂ C ₇ C ₈	77.2	C ₂ O ₂ C ₇ C ₈	77.2
O ₂ C ₇ C ₈ O _{1'}	69.2	O ₂ C ₇ C ₈ O _{1'}	69.2
C ₇ O ₂ O _{1'} C _{1'}	-170.3	C ₇ O ₂ O _{1'} C _{1'}	-170.3
C ₇ O ₂ C ₂ C ₁	-155.1	C ₈ O _{1'} C _{1'} C _{6'}	-158.9
C ₇ O ₂ C ₂ C ₃	84.1	C ₈ O _{1'} C _{1'} C _{2'}	76.1

Table 5b. Torsional networks for C₇,C₈ pairs.

Thus the two torsional networks not shared by C₇ and C₈ are very similar. Based upon this observation a small differential is expected for the chemical shifts in the solid phase which in this case was not observable due to crystal field splitting of these lines. However if the liquid phase conformation is similar to that of the solid phase, the shift differential between these carbons should also be small and this situation is apparent in the low temperature spectrum.

The most shielded resonance at 19.9 ppm is again attributed to the carbon which is gauche γ to axial oxygen which in this case is the C₄,C_{4'} pair. This leaves the C₅,C_{5'} pair as the resonance at 25.1 ppm due to its trans γ relation to equatorial oxygen. The remaining two lines in this spectrum are due to the last four nonoxygenated carbons. Therefore based upon the known β deshielding effect of oxygen on cyclohexyl ring carbons⁽⁸⁾ the more upfield line is due to C₃ and C_{3'} which are β to axial oxygen.

The complex between cis-syn-cis-dicyclohexyl-12-crown-4 and LiSCN crystallized into the space group $P2_12_12_1$ with local C_1 symmetry. This lack of symmetry is reflected in the numbering scheme in the ORTEP for this complex (ORTEP 6 below).

ORTEP 6. CSCDC12C4:LiSCN.

Comparison between the free and complexed ligand shows complexation has occurred by an inversion of one of the cyclohexane rings. This parallels the complexation reaction of the cis-syn-cis isomer of the 14-crown-4 system. Also, as seen in other lithium complexes, the lithium cation is pentacoordinated with the four ethereal oxygens and the nitrogen atom of the SCN⁻ anion. The four oxygens make an approximate plane in which the mean deviation from the least-squares plane connecting them is 0.15 Å. The two cyclohexyl rings are approximately related as

reflections of one another in a mirror plane passing between the two. The planes of the cyclohexyl substituents are at an angle with the mean plane of oxygen atoms. The pseudo twofold symmetry is least evident in the macrocyclic portion of the molecule. This situation is apparent in Stereoview 6a which gives the same view as that of ORTEP 6.

Stereoview 6a. CSCDC12C4:LiSCN.

The diagonal distances across the macrocyclic cavity, O₁ to O₃ and O₂ to O₄, are 3.5 and 4.0 Å respectively to give an adjusted cavity diameter of 0.74 to 1.20 Å. This is smaller than the corresponding cavity diameter for the cis-syn-cis isomer in the 14-crown-4 series and the lithium cation is therefore farther out of the oxygen plane at a distance of 0.95 Å. The coordination geometry around lithium is a distorted square pyramid with the cation approximately in the center of the cavity. The Li-O bond lengths are alternately long and short around the macrocycle and they range from 2.050 to 2.149 Å which gives an average value of 2.11 Å. This represents a longer average Li-O bond length than for the 14-crown-4 LiSCN complex which has a corresponding

average value of 2.08 Å⁽¹⁴⁰⁾. The length of these bonds may indicate lithium is less tightly held by this macrocycle with its relatively small complexing diameter.

The torsional angles around the macrocycle in this system do not adopt the ideal gauche and anti conformations as are the cases for the uncomplexed cis-syn-cis-dicyclohexyl-12-crown-4 species, the parent 12-crown-4 compound and its complexes. These values are apparently distorted from ideal orientations by the requirement of forming a twelve membered ring. Comparison between the conformation adopted by this cis-syn-cis isomer upon complexation with LiSCN and that taken up by the parent compound when complexing the same salt suggests a good degree of similarity exists. Thus a stereoview of the cis-syn-cis isomer and its LiSCN complex using the same viewing angle as that describing the 12-crown-4 and LiSCN complex (Figure 14 of this study) is presented in Stereoview 6b (below).

Stereoview 6b. CSCDC12C4:LiSCN.

The ligand therefore adopts the familiar square shape with the two cyclohexyl rings directed to the same side of the ligand as the LiSCN species. This disposition of the cyclohexyl substituents with respect to the macrocycle contrasts the situation observed for the complexes of the larger cis-syn-cis-dicyclohexyl-14-crown-4. This may explain the reluctance exhibited by this compound for complexing with LiClO₄ which has a more bulky anion than the LiSCN salt. A comparison between the torsional networks of the LiSCN complexes of the parent 12-crown-4 compound and the cis-syn-cis-dicyclohexyl isomer is presented in Table 6a (below).

Carbons	12C4 :LiSCN	CSCDC12C4 :LiSCN
O ₁ C ₁ C ₂ O ₂	63	54.3
C ₁ C ₂ O ₂ C ₇	-173	-161.9
C ₂ O ₂ C ₇ C ₈	74	80.7
O ₂ C ₇ C ₈ O ₃	60	46.6
C ₉ O ₃ C ₈ C ₇	-173	-157.7
C ₈ O ₃ C ₉ C ₁₀	96	166.8
O ₃ C ₉ C ₁₀ O ₄	50	-49.2
C ₁₅ O ₄ C ₁₀ C ₉	-155	-84.6
C ₁₀ O ₄ C ₁₅ C ₁₆	89	104.1
O ₄ C ₁₅ C ₁₆ O ₁	46	50.0
C ₁ O ₁ C ₁₆ C ₁₅	-162	-176.3
C ₁₆ O ₁ C ₁ C ₂	84	76.8

Table 6a. Torsional angles for LiSCN complexes of 12C4 and CSCDC12C4. * numbering scheme for 12C4:LiSCN adjusted to parallel title compound.

Table 6a shows the only torsional networks significantly different between the two complexes are the C₈O₃C₉C₁₀ and C₉C₁₀O₄C₁₅ systems. It is notable that both of these networks incorporate the methine carbons of one of the cyclohexyl substituents and as expected, variation between these is due to the geometry imposed upon the macrocycle by the cyclohexyl

substituents. Also, the $\text{O}_3\text{C}_9\text{C}_{10}\text{O}_4$ torsional network is the only one having opposite signs in the two complexes in Table 6a. This indicates the central difference between these systems occurs in the macrocyclic segment common to one of the cyclohexyl substituents.

The ^{13}C CPMAS spectrum of the cis-syn-cis-dicyclohexyl-12-crown-4:LiSCN complex reflects the lack of symmetry recorded by the X-ray experiment. This is evident in Spectrum 6a below.

Spectrum 6a. CPMAS ^{13}C of CSCDC12C4:LiSCN.

Thus six lines are present in the oxygenated region of this spectrum with two of these having double intensity. The least shielded resonance at 79.7 ppm with double intensity can be assigned to the $\text{C}_1, \text{C}_{10}$ pair which are the methine carbons bearing

equatorial oxygen. These are unresolved due to the strong similarity in their respective environments although a specific rationalization for this is elusive. These two carbons participate in twelve torsional networks excluding those involving lithium and hydrogen. For these twelve, six are gauche and six are anti for C₁ while seven are gauche and four anti with one intermediate for C₁₀. Also C₁ is bonded to an oxygen which is 2.086 Å from the lithium cation while C₁₀ has an oxygen substituent with a comparable distance of 2.136 Å. This is therefore an example of coincidental overlap of chemical shifts which has a complex origin due to a combination of factors and is therefore not easily explained.

The next resonance proceeding upfield in Spectrum 6a is at 69.7 ppm and this has double intensity. Therefore this line can be tentatively assigned to the C₂ and C₉ carbons which bear axial oxygen atoms. These carbons have environments which more closely match than do the C₁,C₁₀ pair since of their twelve carbon or oxygen torsional networks they differ in only one instance with C₂ having two anti networks while C₉ has three. This could also explain the 10.0 ppm difference between axial versus equatorial oxygen bearing carbons. Thus the C₂,C₉ pair have four and three, respectively, more gauche interactions than do their C₁,C₁₀ counterparts and as noted above the gauche orientation is shielding relative to the anti geometry.

With the assumption that the C₂ and C₉ carbons are responsible for the double intensity resonance at 69.7 ppm, four single intensity lines remain in the oxygenated portion of

Spectrum 6a. These can be assigned to the oxygenated methylene carbons in the macrocycle. Careful analysis of the macrocyclic segment of the complex supports the assignment of these lines to the ring carbons since this is the part of the molecule which most deviates from twofold symmetry as described in Stereoview 6a above.

The upfield double intensity line at 19.3 ppm is assigned, as in previous examples, to the C₄,C₁₃ carbons which are gauche γ to oxygen. The resonance approximately 5 ppm downfield from this shift is therefore due to the C₅,C₁₂ carbons which are trans γ to oxygen and in this case are found at 24.2 ppm. The next two double intensity resonances are again assigned by their β relationships to oxygen and the more upfield line at 26.2 ppm is therefore assigned to carbons C₃ and C₁₄ which are adjacent to axial oxygen leaving the resonance at 27.5 ppm due to C₆ and C₁₁.

In the slow exchange limit for this complex the small deviation from mirror symmetry evident in the crystalline X-ray around the macrocycle is lost due to molecular flexibility and the ¹³C spectrum exhibits twofold symmetry. This is apparent in Spectrum 6b which has seven lines with six of equal and one of double intensity.

Spectrum 6b. 50.3 MHz ^{13}C CSCDC12C4:LiSCN at 190 K

Similarities between the chemical shifts for this complex in solution at low temperature and in the solid phase are evident in Table 6b below.

Carbons	Solid ppm	Solution ppm
C ₁ ,C ₁₀	79.7	78.52
C ₂ ,C ₉	69.7	69.63
C ₃ ,C ₁₄	26.2	25.96
C ₄ ,C ₁₃	19.3	18.76
C ₅ ,C ₁₂	24.2	24.18
C ₆ ,C ₁₁	27.5	27.13
C ₇ ,C ₈	66.8,68.3*	64.38
C ₁₅ ,C ₁₆	65.2,63.9*	64.38

Table 6b. Chemical shifts for CSCDC12C4 :LiSCN.

* denotes possible interchange.

Therefore from the above table and Spectrum 6b the chemical shifts for this complex are very similar between the two phases in all regions except that due to the bridging methylene carbons. Here the four lines in the solid phase collapse into a single resonance in solution. This averaging may be due to an exchange process occurring in the macrocyclic portion of the molecule which is too flexible to be observed by the ^{13}C NMR experiment.

The *cis*-*anti*-*cis*-dicyclohexyl-12-crown-4 isomer crystallized into the space group $P2_1/a$ with local C_i geometry denoting a molecular inversion center. This symmetry property is described by the numbering scheme in the ORTEP of this molecule (ORTEP 7 below).

ORTEP 7. CACDC12C4.

The interoxygen distances across the cavity for O_2 to O_2' and O_1 to O_1' are 4.56 and 3.65 Å respectively. The disposition of the oxygen lone pairs is the same as observed for *cis*-*anti*-*cis* dicyclohexyl-14-crown-4 and this is evident in a view along the mean oxygen plane (Stereoview 7a below).

Stereoview 7a. CACDC12C4 oxygen plane.

The overall conformation of the macrocycle is the pseudo square shape adopted by the parent 12-crown-4 molecule. This is seen in a stereoview of this compound using the same viewing angle as that describing 12-crown-4 in Figure 13 of this report. This is arrived at by a 20° rotation about the Z axis of the view in ORTEP 7 and is presented in Stereoview 7b below.

Stereoview 7b. CACDC12C4.

The torsional angles around the macrocycle are tabulated below with the corresponding values for the parent compound.

Carbons	12C4	CACDC12C4
O ₁ C ₁ C ₂ O ₂	74.7	62.2
C ₁ C ₂ O ₂ C ₇	-173.6	-149.4
C ₂ O ₂ C ₇ C ₈	102.7	106.1
O ₂ C ₇ C ₈ O ₁ '	-75.4	-78.2
C ₇ C ₈ O ₁ 'C ₁ '	140.2	-165.4
C ₈ O ₁ C ₁ 'C ₂ '	-85.2	-99.1

Table 7a. Torsional angles for 12C4 and CACDC12C4.

Comparison between the contents of Table 7a and the corresponding data for the cis-syn-cis isomer (Table 5a) shows the cis-anti-cis isomer adopts a conformation more closely matching that of the parent 12-crown-4 compound. The cyclohexyl substituent again imposes a near ideal gauche geometry on the O₁C₁C₂O₂ system and as evident in Table 7a this value is 62.2° for the dicyclohexyl crown and 74.2° for the unsubstituted compound. The loss of flexibility in the portion of the molecule shared between the macrocycle and the cyclohexyl units causes strain in the ethano bridges. This translates into greater deviation from ideal geometry for the O₂C₇C₈O₁' systems and as documented in Table 7a the values for these units is farther from the 60° ideal geometry for the cis-anti-cis isomer than for its parent compound.

The CPMAS ^{13}C spectrum reflects the twofold symmetry recorded in the X-ray analysis (spectrum 7a below).

Spectrum 7a. CACDC12C4.

Thus eight approximately equal intensity lines are resolved in this spectrum. The lowest field absorption at 82.0 ppm is assigned to the C_1, C_1' methine carbons bearing equatorial oxygen and the next upfield line at 77.7 ppm is due to the counterpart methine C_2, C_2' carbons with axial oxygen. The gauche γ effect of axial oxygen causes the C_4, C_4' pair to be shielded by about 5 ppm relative to the C_5, C_5' carbons which are trans γ to oxygen and therefore the line at 19.9 ppm is due to the C_4, C_4' pair and the resonance at 25.6 ppm is assigned to C_5 and C_5' .

The resonances due to the C_3, C_3' and C_6, C_6' pairs are at 29.9 and 28.5 ppm and these are again differentiated by their β relationship to axial versus equatorial oxygen. Therefore the upfield line is due to the C_3, C_3' pair which are adjacent to a

carbon bearing axial oxygen leaving the downfield resonance to the C₆,C₆' pair. The final two lines in this spectrum are at 69.1 and 75.1 ppm and these are due to the methylene carbons bearing oxygen. Differentiation between these two resonances based upon X-ray data is tentative since they have similar torsional networks.

Discounting dihedral angles involving hydrogens these carbons participate in five networks and they share three of these. The torsional angles for the two units not shared by these carbons are documented in Table 7b (below).

Atoms	Dihedral Angle in degrees
C ₇ O ₂ C ₂ C ₁	149.4
C ₇ O ₂ C ₂ C ₃	90.7
C ₈ O ₁ 'C ₁ 'C ₂ '	99.1
C ₈ O ₁ 'C ₁ 'C ₆ '	136.4

Table 7b. Torsional Networks for C₈ and C₇.

These torsional networks are therefore similar and the relatively small differences do not appear to account for the 6 ppm difference in chemical shifts for these two carbons.

Calculated angular dependance of ¹³C chemical shifts find terminal carbons in butane are progressively deshielded as the torsional network is moved from 60° to 120° with shielding beyond this value increasing^(31,34). Applying this to the problem

of differentiating these carbons based upon their respective torsional networks implies the more shielded carbon is C₇. This follows from the observation that the two distinctive C₇ networks are 10° and 13° farther away from the 120° minimum shielding angle than the corresponding values for C₈. The magnitude of chemical shift differential for a dihedral angle variation of 25° is between 2 and 3 ppm for butane. However calculations completed during the course of this study (Chapter 5) suggest the extent of shielding variation increases when a heteroatom is placed into the network as is the case for the ethereal segments in Table 7b.

The low temperature spectrum of this compound suggests the presence of two conformations in equilibrium (Spectrum 7b below).

Spectrum 7b. 50.3 MHz ^{13}C CACDC12C4 at 293 K and 193 K.

The presence of a second degenerate process becoming slow on the NMR timescale is observable in the oxygenated region of this spectrum. Thus four equal intensity lines are accompanied by three clearly defined resonances of lower intensity and one shoulder on a larger intensity line probably accounting for the fourth lower intensity line. The presence of a second conformation observable in the low temperature limit is comparable to the cis-anti-cis isomer of the 14-crown-4 system where the second conformation is more easily observed (Spectrum 1b).

The nature of the two conformations evident in the low temperature ^{13}C NMR spectrum of this compound are impossible to establish with certainty. However, as for the 14-crown-4 analogue, it is reasonable to correlate between the known solid phase conformation and the liquid phase conformers. The chemical

shifts for the major and minor solution conformers as well as those from the solid phase spectrum are documented in Table 7c (below).

Carbons	Solution		Solid
	Major	Minor	
C ₁ ,C ₁ '	80.70	81.68	82.0
C ₂ ,C ₂ '	74.16	75.14	77.7
C ₃ ,C ₃ '	28.23	nr*	28.5
C ₄ ,C ₄ '	19.23	nr	19.9
C ₅ ,C ₅ '	24.91	nr	25.6
C ₆ ,C ₆ '	28.23	nr	29.9
C ₇ ,C ₇ '	67.32	nr	69.1
C ₈ ,C ₈	70.92	69.67	75.1

Table 7c. Chemical shifts for CACDC12C4. * nr denotes not resolved.

Therefore Table 7c gives no conclusive evidence the solution conformers are the same as the solid phase conformation since many lines are unresolved and large differences in chemical shifts exists. The largest differential is due to the C₈,C₈' assignments where approximately 5 ppm difference is seen between the solution resonances and the solid phase shift. This suggests the solution and solid phase conformations differ. A reasonable result this reminds one that variations in conformation due to changes in phase are possible and often encountered.

3.3 CAC and CSC Dicyclohexyl-13-Crown-4 and Complexes

The cis-anti-cis dicyclohexyl-13-crown-4 isomer was found to recrystallize into the space group Pbc_2 with C_1 geometry denoting an absence of local symmetry. The two bridging units in this compound are different and a lack of any local symmetry in the crystalline structure is therefore inevitable. This is seen in the numbering scheme of the ORTEP describing the crystalline conformation adopted by this isomer (ORTEP 8).

Ortep 8. CACDC13C4.

However, since the material was prepared and recrystallized as a racemic mixture equal amounts of each enantiomer are present. This may be the cause of disorder in the crystal structure of this compound in the lattice segments associated with the ethano and propano bridging units. The packing mode is such that the molecule in ORTEP 8 has a second conformation stacked with it which has the same torsional networks around the cyclohexyl units but has ethano

segments in the place of propano units. This causes alternation of the bridging segments through the crystal lattice and a resulting disorder in carbons 8,9 and 17 with the conformation described in ORTEP 8 as 60% of the total and a second conformer taking up the remaining 40%. The nature of this disorder is due to crystal stacking since the disordered positions are centrosymmetrically related from a positional but not an occupancy standpoint and represent nonsuperimposable mirror image sites.

The requirements of forming a crystal lattice in this manner causes the two molecules to become conformational isomers. This is demonstrated in Table 8a which compares some torsional networks in the disordered segments of the two.

-----		-----	
Atoms		Atoms	
60% isomer	θ	40% isomer	θ
-----		-----	
C ₂ C ₁ O ₁ C ₁₇ '	-157.0	C ₁₁ C ₁₀ O ₃ C ₁₇ "	139.6
O ₁ C ₁₇ 'C ₁₆ O ₄	-89.8	O ₃ C ₁₇ "C ₇ O ₂	92.3
O ₃ C ₉ 'C ₈ 'C ₇	63.0	O ₁ C ₉ "C ₈ "C ₁₆	-51.3
-----		-----	

Table 8a. Corresponding torsional networks for two conformers of CACDC13C4.

The actual ratio of enantiomers is 1:1 since mirror related sites in the crystal also contain the two chiral molecules in a 40:60 ratio.

The molecule is chiral and this is evident in Stereoview 8a where the view of ORTEP 8 is seen with its non-superimposable mirror image with the two separated by a X-Z mirror plane.

Stereoview 8a.CACDC13C4 enantiomeric pair.

The interoxygen distances, which are the same for both conformers, are 4.2 and 4.3 Å for the O₁,O_{1'} and O₂,O_{2'} diagonals respectively and this gives a cavity which is, as expected, smaller than that of the corresponding 14-crown-4 molecule with distances of 4.4 and 4.7 Å and larger than that of the 12-crown-4 system with corresponding values of 3.7 and 4.6 Å. The molecule adopts the same staggered conformation seen for the two other cis-anti-cis isomers described previously with the oxygen lone pairs on one side of the macrocycle directed above the mean plane of the macrocycle and the others directed below this plane.

The disposition of the propano bridge in this conformation is very close to that found for this unit in the corresponding 14-crown-4 molecule. However comparison between the ethano bridging units in the cis-anti-cis isomers of the 12 and 13 membered systems shows significant difference. This situation is documented in Table 8b which compares torsional networks for the bridging units in the 12,13 and 14 membered macrocycles.

Atoms numbering from 13 system.	Torsional values in degrees		
	12c4*	13c4	14c4*
Ethano unit			
O ₁ C ₁₇ C ₁₆ O ₄	78.2	-89.8	-
C ₁₇ C ₁₆ O ₄ C ₁₁	-106.1	161.6	-
C ₁₆ O ₄ C ₁₁ C ₁₀	149.4	-79.0	-
Propano unit			
C ₃ C ₉ C ₈ C ₇	-	63.0	64.1
C ₉ C ₈ C ₇ O ₂	-	56.0	61.5
C ₈ C ₇ O ₂ C ₂	-	169.7	170.4
C ₇ O ₂ C ₂ C ₁	-	75.8	65.1

Table 8b. Torsional values for propano and ethano bridges in CAC isomers of 12,13, and 14 systems.

* numbering changed to match that of CACDC13C4.

Therefore the largest difference in the two propano systems is 10° for the $C_7O_2C_2C_1$ network while the differentials for the ethano units are as much as 70° with all torsional angles of opposite sign. It is also notable the dihedral angles are closer to the ideal anti and gauche geometries for the larger 14-crown-4 system in the propano bridges and significantly different from these values in the ethano segments. This is consistent with the concept that the smaller 12 membered ring is considerably more strained than its larger analogues.

The CPMAS ^{13}C spectrum of this compound (Spectrum 8a below) reflects the lack of symmetry although it is difficult to be specific about the precise number of individual resonances due to peak overlap and a relatively high noise level.

Spectrum 8a. CPMAS ^{13}C of CACDC13C4.

The unsymmetric molecule should have eight oxygenated carbon resonances in the 60 to 80 ppm region of the spectrum. However since two conformers are present in the crystal this number is doubled to sixteen. The chemical shift differences between many of these resonances should be small and identification of individual lines is impossible.

The low temperature spectrum of this compound should have eight lines if a single unsymmetric conformer exists. However as in the previously described examples of the cis-anti-cis isomers of the 12 and 14 membered systems a minor conformer could be present in equilibrium with a major conformation. The low temperature spectrum of this species is not presented here since the resolution of individual lines is too poor to accommodate analysis.

The *cis-syn-cis*-dicyclohexyl-13-crown-4 isomer separated from its configurational isomer as an oil which retained its liquid nature at reduced temperatures. However the pure isomer formed stable complexes with LiSCN and LiClO₄ salts and these complexes melted at elevated temperatures and recrystallized into crystals suitable for X-ray analysis. Both complexes formed crystallographic space groups $P2_1/a$ and had an absence of local symmetry with point group geometry C_1 . The LiSCN complex is described below in ORTEP 9 and the numbering scheme reflects the lack of a local molecular symmetry.

ORTEP 9. CSCDC13C4 :LiSCN

adjusted cavity diameter of 0.74-1.25 Å. This is, as for the other complexes described in this study, too small to accommodate the lithium cation (1.18-1.52 Å) and it lies 0.75 Å above the mean plane of the four oxygen atoms in a pentacoordinated geometry with the four oxygens and the SCN⁻ anion. This compares closely with the related benzo-13-crown-4:LiSCN system which has an almost identical effective cavity diameter with the lithium cation slightly farther from the oxygen plane at 0.80 Å. This difference in distance from the oxygen plane is consistent with the expected increase in flexibility of the dicyclohexyl substituted molecule over the benzo substituted system. Also, the oxygens adjacent to an aromatic substituent are expected to be less basic than their aliphatic counterparts due to delocalization of electronic charge into the benzene ring and therefore less attractive to a cation.

The overall conformation of this complex is similar to those of the 12 and 14 membered systems with the two cyclohexyl rings approximately mirror related. However this complex is similar to the CSCDC12C4:LiSCN complex in the side of the macrocycle it accepts the cation from and correspondingly contrasts the 14-crown-4 complex. This is most easily seen by comparing the side of the macrocycle the salt complexes with and the side the two cyclohexyl rings are directed toward. Such a comparison is possible by reviewing the same view as seen in ORTEP 9 described in Stereoview 9a below and those in Stereoviews 3a and 6a which are similar views of the 14 and 12 membered counterparts.

Stereoview 9a. CSCDC13C4:LiSCN.

The conclusion is the Li^+ species preferentially complexes from the convex side of the macrocycle since this is the side of attachment in the larger 14-crown-4 system.

In the CPMAS ^{13}C spectrum of the LiSCN complex with the cis-syn-cis isomer of dicyclohexyl-13-crown-4 the lack of molecular symmetry is evident (Spectrum 9a below).

Spectrum 9a. CPMAS ^{13}C of CSCDC13C4:LiSCN.

Thus in the oxygenated region of this spectrum seven clearly resolved lines are evident with one having double intensity indicative of eight distinct oxygenated carbons as is expected from the X-ray result. The closely spaced pair of lines downfield at 79.2 and 78.4 ppm are due to the two methine carbons bearing equatorial oxygen and distinction between these is not possible. The next two resonances proceeding upfield are at 74.1 and 71.5 ppm and these are due to the C₁,C₁₁ methine carbons with axial oxygen. Their chemical shift difference of 2.6 ppm invites differentiation of these resonances based upon their torsional environments in the crystal. However, excluding torsional networks involving hydrogens and lithium, these carbons participate in twelve different networks and the proximity of the lithium cation's influence is poorly understood as a shielding influence. Therefore any conclusion on individual assignments would be tentative at best. This situation applies equally to the oxygenated bridging methylene carbons which are resolved into two close lines and one double intensity resonance between 64 and 70 ppm .

The non-oxygenated region of this spectrum is less resolved with three single intensity lines and one large heavily overlapped resonance. The two upfield resonances which appear at 18.6 and 20.3 ppm are due to the C₅,C₁₃ pair which are gauche γ to oxygen. The single intensity resonance at 30.3 ppm is due to the C₈ methylene carbon in the propano bridge and the remaining carbons are overlapping in the large line at 26.2 ppm.

The crystal structure of the LiClO_4 complex with cis-syn-cis-dicyclohexyl-13-crown-4 is very similar to its LiSCN analogue in a manner comparable to the two complexes of the 14-crown-4 system. Thus it crystallizes into the same $P2_1/a$ space group with local C_1 symmetry as seen in the numbering scheme in ORTEP 10 below.

ORTEP 10. CSCDC13C4:LiClO₄.

Thus the interoxygen distances across the macrocycle are the same as those in the LiSCN complex and bond lengths, angles and dihedral angles are essentially the same with one exception.

This difference is probably due to steric interaction between the larger ClO_4^- anion and the propano bridge and results in a rotation of approximately 12° around the $\text{O}_2\text{-C}_2$ bond. Since the propano segment is less strained than the corresponding ethano group on the other side of the macrocycle, it is more capable of reorganizing to accommodate the bulky anion. However the

difference in torsional networks is not large and is best seen in the bond angles joining the crown ether oxygen atoms with the anionic segment of the complexing salt. The situation is therefore documented in Table 10a where corresponding bond angles are compared.

Atoms	Angle in degrees
LiSCN	
O ₂ -Li-N	116
O ₄ -Li-N	125
C ₁ C ₂ O ₂ C ₇	146.9
C ₂ O ₂ C ₇ C ₈	167.9
LiClO ₄	
O ₂ -Li-O ₅	123
O ₄ -Li-O ₅	112
C ₁ C ₂ O ₂ C ₇	173.8
C ₂ O ₂ C ₇ C ₈	134.6

Table 10a. Bond and torsional angles for two complexes of CSCDC13C4.

This situation can also be seen in the following comparison of the two complexes using approximately the same viewing angle (Stereoview 10 a).

Stereoview 10a. LiSCN and LiClO₄ complexes of CSCDC13C4.

However, since the ^{13}C CPMAS spectra for these two complexes are not conducive to facile interpretation in the regions associated with the propano chain, it is not possible to find differences in the NMR spectra which could be associated with this relatively small difference in crystalline forms. Therefore the CPMAS ^{13}C spectrum for the LiClO₄ complex of the cis-syn-cis-dicyclohexyl-13-crown-4 isomer is not presented.

Additional evidence on the relative rigidity of the ethano bridging unit in small ring crown ethers has been collected in the course of making the dicyclohexyl crown compounds described above. Thus dibenzo-12-crown, which is a precursor to the dicyclohexyl-12-crown-4 molecules analysed in this study, has been isolated and characterized. The ORTEP of this compound is therefore described in ORTEP 11 (below).

ORTEP 11. Dibenzo12Crown4.

This compound crystallized into space group $Pbca$ with a local inversion center. This C_i geometry is evident in the numbering system in ORTEP 11. The system adopts a conformation in the solid phase similar to those taken up by the cis-ant-cis isomers discussed above and this is seen in the stereoview presented below.

Stereoview 11a.Dibenzo12Crown4

This compound further demonstrates the relative rigidity of the 12 membered macrocycle since at reduced temperature the resonances due to the C₇ and C₈ carbons begin to enter coalescence. This relative strain in the macrocyclic portion of the molecule is also indicated in the inability of this compound to form complexes. This conclusion was reached by Pedersen and confirmed during the course of this study.

Chapter 4. Molecular Dynamics

The coalescence temperature analysis using the Eyring equation, described in the theoretical section of this report, can be utilized to examine the low temperature spectra obtained in the course of this conformational analysis. Since the compounds investigated have cyclohexyl substituents the chair to chair interconversion of these substituents occurs on a timescale accessible to the NMR experiment. Also, the flexibility of a compound will determine its free energy of activation for cyclohexane interconversion and these values can be compared between different crown compounds and for the complexed and uncomplexed species. However, it must be noted that since coalescence occurs for different lines at different temperatures and the $\Delta G^\ddagger$ values obtained by coalescence temperature analysis are a function of temperature due to their $T \cdot \Delta S$ factor, these comparisons are approximate. Yet, the temperature effect is small and similar values for the different lines in a given molecule were obtained. The presence of exchange processes in the macrocycles of the crown ethers described in this report is also a possibility. Therefore the results of coalescence temperature analysis on the two isomers of dicyclohexyl-12-crown-4 and dicyclohexyl-14-crown-4 systems and their LiSCN complexes are presented in Tables 11a and 11b.

Since the cis-syn-cis isomers were shown to form stable complexes with LiSCN and to exhibit a single degenerate process becoming slow on the NMR timescale upon temperature reduction the

coalescence data for these compounds and their complexes is collected together in Table 11a.(below). It is therefore notable that the free energy of activation for the interconversion of cyclohexyl substituents in the uncomplexed cis-syn-cis-dicyclohexyl-12-crown-4 species is 3 to 4 kJ/mol higher than the 42.3kJ/mol⁽⁸⁴⁾ for the free cyclohexane molecule. This contrasts the situation for the corresponding dicyclohexyl-14-crown-4 isomer which has activation energies of interconversion almost the same as that for unsubstituted cyclohexane. The flexibility differences between the cis-syn-cis isomers of the 12 and 14 membered systems supports the observation that cis-syn-cis-dicyclohexyl-14-crown-4 adopts essentially ideal gauche or anti geometries in the solid phase while the corresponding 12 membered species exhibits strain.

Compound	Carbons	$\Delta\nu$ (Hz)	$T_c(^{\circ}\text{K})$	$\Delta G^{\ddagger}$ (kJ/mol)
CSCDC12C4	1,1',2,2'	566.85	249	45.8
	7,7',8,8'	106.35	232	45.7
	3,3',6,6'	75.25	232	46.4
	4,4',5,5'	258.15	240	45.6
CSCDC12C4 +LiSCN	1,1',2,2'	447.17	252	46.8
	7,7',8,8'	unresolved	-	-
	3,3',6,6'	58.85	230	46.5
	4,4',5,5'	272.63	245	46.5
CSCDC14C4	1,1',2,2'	319.0	223	41.9
	7,7',9,9'	189.0	218	43.6
	8,8'	unresolved		
	3,3',6,6'	305.0	223	41.9
	4,4',5,5'	225.0	220	41.8
CSCDC14C4 +LiSCN	1,1',2,2'	201.0	238	45.8
	7,7',9,9'	125.0	243	47.7
	8,10	32.0	223	46.2
	3,3',6,6'	21.0	223	46.9
	4,4',5,5'	256.0	253	48.3

Table 11a ^{13}C coalescence data for CSCDC12C4, CSCDC14C4 and LiSCN complexes at 50.3MHz. Errors in $\Delta G^{\ddagger}$ are estimated to be 0.5 to 1.0 kJ/mol.

Comparison of free energies of activation for interconversion between the complexed and uncomplexed species in Table 11a supports the concept that the 14-crown-4 species is a more effective complexing agent for lithium than for its 12-crown-4 counterpart. Thus the difference between $\Delta G^{\ddagger}$ values for the

complexed and uncomplexed 14-crown-4 isomer has an average of approximately 5kJ/mol while the corresponding difference for the free 12-crown-4 molecule and its complex is about 0.7kJ/mol. The free 14-crown-4 molecule has the lowest activation energy for interconversion in Table 11a while its LiSCN complex has the highest free energy of activation. This suggests the cis-syn-cis-dicyclohexyl-14-crown-4 molecule is highly flexible as a free ligand and therefore able to adopt a desirable complexing geometry. This results in the formation of a strong complex between the ligand and lithium salt and the system becomes rigid with a relatively high free energy of activation for the chair to chair interconversion process.

Coalescence temperature analysis data for the cis-anti-cis-dicyclohexyl12 and 14-crown-4 systems is presented in Table 11b (below). The presence of more than one degenerate process in the low temperature spectra of these compounds complicates analysis. This complication occurs since splitting of one line into more than two resonances makes the actual coalescence temperature for the separate processes difficult to establish and the data obtained applies mainly to the major conformations of the two cis-anti-cis isomers alone. Therefore free energies of activation for the dynamic processes of the cis-anti-cis isomers for free and complexed 12 and 14 membered macrocycles are documented in Table 11b (below).

Compound	Carbons	$\Delta\nu$ (Hz)	$T_c(^{\circ}\text{K})$	$\Delta G^{\ddagger}$ (kJ/mol)
CACDC12C4 major	1,1',2,2'	328.9	225	42.3
	7,7',8,8'	181.0	215	41.3
	3,3',6,6'	unresolved -	-	-
	4,4',5,5'	285.7	220	41.5
CACDC12C4 +LiSCN major	1,1',2,2'	223.8	220	42.0
	7,7',8,8'	unresolved -	-	-
	3,3',6,6'	unresolved -	-	-
	4,4',5,5'	271.6	223	42.6
CACDC14C4 major	1,1',2,2'	378.4	223.15	43.9
	7,7',9,9'	unresolved -	-	-
	3,3',6,6'	unresolved -	-	-
	4,4',5,5'	unresolved -	-	-
	8,8	unresolved -	-	-
CACDC14C4 +LiSCN Process#1	1,1',2,2'	314.0	250	47.2
	7,7',9,9'	180.0	242	46.7
	3,3',6,6'	72.0	239	47.9
	4,4',5,5'	380.0	250	46.8
	8,8'	unresolved -	-	-
CACDC14C4 +LiSCN Process#2	1,1',2,2'	194.0	215	41.1
	7,7',9,9'	202.0	215	40.9
	7,7',9,9'	30.0	183	37.6
	8,8'	62.0	195	39.0

Table 11b ^{13}C coalescence data for CACDC12C4, CACDC14C4 and LiSCN complexes at 50.3MHz except CACDC14C4+LiSCN at 75.4MHz.

Errors in $\Delta G^{\ddagger}$ are estimated to be 0.5 to 1.0 kJ/mol.

The uncomplexed cis-anti-cis-dicyclohexyl-12-crown-4 isomer exhibits two dynamic processes the first of which is described in Table 11b. This process, with an activation energy close

to that of 1,2 substituted cyclohexanes, can be attributed to double cyclohexane ring inversion. The second process however, which was not well enough resolved to measure activation energies, is probably attributable to the type of two site exchange observed for the non-substituted parent 12-crown-4 species⁽¹⁵⁹⁾.

The average value for the free energy of activation for the free cis-anti-cis isomer is within experimental error of that for the ligand in the presence of LiSCN. The conclusion that, interaction between this compound and the lithium salt occurs in solution is therefore tentative, although chemical shift differences indicative of some interaction were noted. The activation energy for the cis-anti-cis-dicyclohexyl-12-crown-4 isomer is about 4kJ/mol lower than for its free configurational isomer. This suggests the cis-anti-cis compound is more flexible than the cis-syn-cis isomer. This supports the X-ray result which found the cis-anti-cis isomer adopted a conformation closer to that of the unsubstituted parent 12-crown-4 than did the cis-syn-cis compound.

The $\Delta G^\ddagger$ value for the free cis-anti-cis-dicyclohexyl-14-crown-4 isomer is within experimental error of that for the corresponding value for non-substituted cyclohexane and close to this value for the corresponding dicyclohexyl-18-crown-6 molecule⁽¹⁷⁶⁾. This supports the X-ray data which found this compound adopted a conformation close to the relatively flexible parent 14-crown-4 molecule (Figure 15 and Stereoview 1a). A significant change is observed for this compound upon addition of an equal equivalent of LiSCN salt. This is evident in Table 11b since the

free energy of activation for interconversion of cyclohexane rings has increased to a value close to 47kJ/mol. This can be attributed to degenerate double cyclohexane ring inversion since the observed shift differences at individual carbons sites are very similar to those found for cyclohexane ring inversion in similar molecules⁽¹⁷⁷⁾. However, the second degenerate process for the complex of the cis-anti-cis isomer has activation energies near 39kJ/mol which is approximately 4kJ/mol less than that for unsubstituted cyclohexane. It is therefore probable this second process is, as in the corresponding 12-crown-4 instance, attributable to a dynamic process associated with the macrocycle. This concept is supported by reference to the low temperature spectrum of this compound and LiSCN (Spectrum 1f) where the lines which are farthest from the macrocycle are overlapping while those in the macrocycle due to the non-oxygenated methylene carbons in the propano bridge close to 30 ppm are well resolved.

Comparison of the results for the 14 membered configurational isomers in Tables 11a and 11b suggests the two free ligands are of approximately equal flexibility with both having interconversion energies close to that for cyclohexane. Also the cyclohexane interconversion activation barriers for the complexes of the 14-crown-4 configurational isomers are close to 5kJ/mol higher than the corresponding values for the free ligands. The 14 membered systems are consistently more flexible than their 12 membered counterparts and complexation by LiSCN has a greater effect on the larger macrocycles. This is consistent with results obtained by

conformational analysis since torsional networks for the larger system were consistently closer to ideal gauche and anti orientations than for the smaller crown ethers. Also, complexation was expected to have a greater influence upon the macrocyclic cavity closest to the effective lithium cation diameter since this allows better insertion in the macrocyclic center.

The solution characteristics of the dicyclohexyl 12 and 14-crown-4 isomers and their complexes can also be studied by measuring spin-lattice relaxation times as described in the background and theory section of this report (Chapter 2). Measurements of nuclear Overhauser enhancements indicate spin-lattice relaxation in similar molecules is dominated by the dipole-dipole mechanism (Equation 79) to an extent exceeding 90% for all carbons. Therefore since these molecules have molecular weights which place them in the region where the motional limit applies the correlation time τ_c for the C-H vector is proportional to $1/T_1$. Thus the more flexible molecular systems have smaller correlation times and longer T_1 values. The T_1 data for the dicyclohexyl 12 and 14-crown-4 isomers and their complexes is collected in Tables 12a and 12b below.

Therefore in Table 12a the T_1 values for the different sites of the cis-syn-cis 12 and 14 membered systems and their LiSCN complexes are compared. The larger change caused by complexation for the 14-crown-4 over the 12-crown-4 molecule supports conformational and lineshape results which indicate the larger macrocycle is the better lithium complexing agent. Also comparison

of T_1 values for individual sites indicates the 14-crown-4 system is the more flexible of the two free ligands.

The T_1 values for the methine carbons of the CSCDC12C4 molecule change from 1.76 to 1.29 s upon complexation with LiSCN. This contrasts the situation for the C8,C8' and C7,C7' methylene bridging carbons which upon complexation exhibit no measurable change in T_1 values. This implies the uncomplexed molecule is relatively inflexible in the bridging units and complexation does not change this enough to alter T_1 values. This result parallels the observation in the crystal structures of this isomer and its complex that torsional angles in this region of the molecule often deviate significantly from the energetically favorable gauche and anti orientations. This contrasts the situation for the 14-crown-4 system where complexation significantly changes T_1 values in the propano bridge as seen by the decrease in relaxation times for the C7,C7',C8,C8' and the non-oxygenated C8,C8' sites.

Site	Compound	T ₁ sec.*
C1,C1',C2,C2'	CSCDC12C4	1.76
C1,C1',C2,C2'	CSCDC12C4:LiSCN	1.29
C1,C1',C2,C2'	CSCDC14C4	2.68
C1,C1',C2,C2'	CSCDC14C4:LiSCN	1.24
C7,C7',C8,C8'	CSCDC12C4	0.79
C7,C7',C8,C8'	CSCDC12C4:LiSCN	0.78
C7,C7',C9,C9'	CSCDC14C4	1.60
C7,C7',C9,C9'	CSCDC14C4:LiSCN	0.75
C3,C3',C6,C6'	CSCDC12C4	0.82
C3,C3',C6,C6'	CSCDC12C4:LiSCN	0.82
C3,C3',C6,C6'	CSCDC14C4	1.45
C3,C3',C6,C6'	CSCDC14C4:LiSCN	0.88
C4,C4',C5,C5'	CSCDC12C4	0.82
C4,C4',C5,C5'	CSCDC12C4:LiSCN	0.76
C4,C4',C5,C5'	CSCDC14C4	1.39
C4,C4',C5,C5'	CSCDC14C4:LiSCN	0.73
C8,C8'	CSCDC14C4	1.27
C8,C8'	CSCDC14C4:LiSCN	0.88

Table 12a. T₁ Data for CSCDC12C4, CSCDC14C4 and LiSCN complexes.* typical errors 0.1 sec.

Comparison of T₁ values for the uncomplexed dicyclohexyl-12-crown-4 isomers from Tables 12a and 12b shows that in every case the cis-anti-cis isomer has longer relaxation times than its cis-syn-cis counterpart. This supports the observation that the cis-anti-cis isomer has a solid phase conformation similar to that of the nonsubstituted 12-crown-4 molecule. Also consistent with this

is the low temperature detection of a second conformational process and the result that cyclohexyl ring inversion has a slightly lower free energy of activation for the cis-anti-cis molecule than for its configurational isomer.

Site	Compound	T ₁ sec.*
C1,C1',C2,C2'	CACDC12C4	2.84
C1,C1',C2,C2'	CACDC12C4+LiSCN	2.06
C1,C1',C2,C2'	CACDC14C4	2.08
C1,C1',C2,C2'	CACDC14C4+LiSCN	1.27
C7,C7',C8,C8'	CACDC12C4	1.72
C7,C7',C8,C8'	CACDC12C4+LiSCN	1.23
C7,C7',C9,C9'	CACDC14C4	1.19
C7,C7',C9,C9'	CACDC14C4+LiSCN	0.75
C3,C3',C6,C6'	CACDC12C4	1.68
C3,C3',C6,C6'	CACDC12C4+LiSCN	1.49
C3,C3',C6,C6'	CACDC14C4	1.33
C3,C3',C6,C6'	CACDC14C4+LiSCN	0.77
C4,C4',C5,C5'	CACDC12C4	1.52
C4,C4',C5,C5'	CACDC12C4+LiSCN	1.42
C4,C4',C5,C5'	CACDC14C4	1.22
C4,C4',C5,C5'	CACDC14C4+LiSCN	0.75
C8,C8'	CACDC14C4	1.33
C8,C8'	CACDC14C4+LiSCN	0.77

Table 12b. T₁ Data for CACDC12C4,CACDC14C4 and LiSCN complexes.* typical errors 0.1 sec.

The T₁ values for the parent 12-crown-4 molecule and some of its complexes have been measured⁽¹⁷⁸⁾ and the free ligand has a

spin-relaxation time near 6 s while its LiCl complex reduces this to 3 s. This 50% reduction in T_1 values is, as expected, larger than the reduction for the cis-anti-cis and cis-syn-cis isomers studied in this analysis. The changes in T_1 values upon complexation for the more mobile cis-anti-cis compound are, within experimental error, zero for all except the carbons bearing oxygen. This confirms the implication of a weak interaction found in the coalescence temperature analysis for this compound where a small increase in interconversion energy was noted upon complexation. The T_1 changes for the cis-syn-cis isomer upon complexation are larger than experimental error for all except the oxygenated methine carbons which experience a proportionately smaller reduction in relaxation times than do their cis-ant-cis counterparts. Therefore the parent compound experiences a significant reduction in T_1 values upon complexation while the two dicyclohexyl substituted compounds examined in this study exhibit only modest T_1 reductions. This suggests the diyclohexly substitution pattern significantly impairs the capacity of this macrocycle for making the reorganization necessary for accommodation of the lithium cation.

Comparison between T_1 values for the configurational isomers of the 14-crown-4 system indicates the two free ligands have approximately the same flexibilities in the non-oxygenated carbons. However in the oxygenated carbons greater mobility is observed for the cis-syn-cis isomer. The largest difference is for the carbons in the propano bridges which are 34% higher for the cis-syn-cis compound over its configurational isomer. This observation supports

the lineshape evidence which found the free energy of interconversion for the cyclohexyl substituents to be slightly lower for the cis-syn-cis isomer. Also, X-ray analysis found the solid phase conformation of the cis-syn-cis isomer is closer than that of the cis-anti-cis compound to that of the free parent 14-crown-4 species.

Comparison of the change in relaxation times caused by complexation for individual sites in the 14-crown-4 molecules indicates the largest changes occur for those carbons bonded to oxygen. This parallels the situation for the dicyclohexyl-12-crown-4 isomers and is consistent with the observed binding of these ligands by X-ray crystallography. This pattern with which complexation influences T_1 values for these compounds makes it possible to discuss how complexation influences molecular motion. Two types of molecular motion are available to these molecules since they have internal segmental motion as well as overall tumbling in solution. Since the molecular weight of the complex is not significantly larger than that of the free ligand the tumbling characteristics of the complexed and uncomplexed ligands should be approximately the same. However complexation of these compounds with a lithium cation restricts segmental motion in the bonds closest to the complexing oxygens. This is the case for the crown ethers studied in this T_1 analysis and segmental motion in the oxygenated methylene carbons is evident in the values recorded in Tables 12a and 12b.

5.0 Computation Analysis

The objective in doing this ^{13}C computational analysis has been to explain the origin of ^{13}C conformational shift dependances and in doing this to predict the trends which occur. Within the context of this study an ideal result would have been to calculate the ^{13}C chemical shifts for the same molecules examined by solid phase NMR and X-ray crystallography. However, the difficulties in computing with basis sets large enough to represent the crown ethers investigated in this study make calculations for such systems impractical. The compromise solution taken by this study has been to investigate small analogues of the macrocycles of interest. Therefore the ab initio approach to calculating shielding tensors, as outlined in the theory section of this report, has been used in a conformational analysis of butane and ethyl-methyl ether using the LORG approach to obtaining ^{13}C NMR shielding tensors.

Therefore using the Gaussian 80 program to generate DZ basis sets and the LORG approach to shielding tensor calculations conformational chemical shift dependancies have been studied. The subjects of this analysis have been butane (Figure 18) and methoxyethane (commonly ethyl-methyl ether Figure 19).

Figure 18. Butane

Figure 19. Ethyl-methyl ether.

Corresponding with the convention used in computational analysis the Z axis is designated the main axis of the molecule and is therefore assigned as colinear with the C3-C1 bond in Figure 18 and the O3-C1 bond in Figure 19. This leaves the X axis in the vertical of the page with the Y axis directed out of the page and this coordinate system is used throughout the following description of ^{13}C shift

dependencies. The approach employed by this study has been to do a rotation of the C1-C2 segments of the two molecules about the Z axis in 20° increments. This rotation direction is such that it brings the Y axis into the X axis in this coordinate system and therefore the C2 segments are moved into the negative Y direction as rotation occurs. The ^{13}C shielding tensors for the carbons in each network were then calculated at each 20° interval between 0 and 180 degrees.

This analysis of butane represents a repeat of one of the calculations performed by Seidman and Maciel and⁽³¹⁾ published in 1977. They performed semiempirical calculations, using the modified-INDO finite perturbation theory of ^{13}C chemical shifts, on three different conformations of butane. Their conclusion was that C-H bond polarization by nonbonded hydrogens was not sufficient to explain the origins of the chemical shift difference between gauche and trans γ substitution. Barfield and Yamamura⁽³⁴⁾ also did calculations on the conformational chemical shift dependencies of butane and published in 1990. Their ab initio IGLO studies found the only significant variation in chemical shift accompanying changes in torsional angle occurred in the individual bond paramagnetic contributions of directly bonded atoms. Therefore this calculation on the butane conformation in Figure 18 is useful as a comparison between the results obtained by the LORG approach used herein and those obtained by other methods. However, this study of the shift dependencies of butane also represents an analysis of one of the torsional units present in the dicyclohexyl crown ethers described in

this study. The analysis of ethyl methyl ether in this study represents the investigation of a system previously not studied in this manner. However, as in the case of butane, the ether in Figure 19 approximates a torsional unit in the crown ethers described in this report.

Therefore the total isotropic shielding tensors, σ_T , for the four carbons in the butane structure of Figure 18, are plotted as a function of dihedral angle between 0 and 180 degrees in Graphs 1 and 2 (below). Here the responses of the similar terminal methyl carbons are grouped together in graph 1 and those of the two central methylene carbons are in Graph 2.

The shapes of the four plots in Graphs 1 and 2 are very similar to those obtained by Seidman and Maciel in their calculation on this structure. The decrease in total shielding evident at 120° is also consistent with the results obtained by Barfield and Yamamura. This result also reflects experimental data since the relative deshielding of the 180° angle relative to the 60° angle is well documented in ^{13}C NMR spectroscopy⁽¹⁷¹⁾.

However the question remains as to what mechanism is responsible for the chemical shift variation observed in Graphs 1 and 2. The attempt at finding an answer to this leads to the investigation of a number of possible sources of chemical shift variation. Therefore to examine the possibility that steric interaction between H7 and H13 or H14 could cause chemical shielding to occur, as suggested by Grant et al⁽³⁵⁾, the H7 to H13 and H14 internuclear distances are plotted in Graph 3 (below).

Comparison between the internuclear distances of Graph 3 and the shielding variation in Graphs 1 and 2 provides little reason to conclude these are related.

However, if Grant's⁽³⁵⁾ suggestion is correct and the close approach between nonbonded hydrogen atoms can cause electron density to be distributed down the H-C, then this should be manifest in the carbon electron densities. The plot of electron densities as a function of torsional angle for the four butane carbons, in Graph 4 below, should in this case have a response similar to that of the total tensors in Graphs 1 and 2.

This plot therefore indicates electron densities at individual carbons do not account for variation in chemical shifts.

It is also of interest to examine the response of the system energy as torsional angle is varied to look for a correlation between this and the variation of σ_T . Therefore the total energy of the butane structure is plotted against the differing torsional angles in Graph 5 below.

Butane figure 18

The shape of this plot resembles the inverse of the plot describing the variation of carbon 4 with dihedral angle but does not resemble the shapes of other plots in Graphs 1 and 2. Similarities are therefore attributable to coincidence and the energy plot is useful only to confirm the energy minimum at 180° is lower in energy than the value at 60° . If a hydrogen to hydrogen interaction were important to the system the total repulsive energy could possibly reflect this which is not the case in the plot of repulsive energy as a function of dihedral angle in Graph 6 below.

Butane figure 18

However examining the curve describing the change in total kinetic energy as a function of variation in dihedral angle (Graph 7 below) explains the source of the total energy shape in Graph 5.

Butane figure 18

Thus the variations in total energies in Graphs 5 through 7 do not suggest a correlation to the chemical shift.

The observation noted by Barfield and Yamamura⁽³⁴⁾ and by

this study is that changes in the total tensor are due to changes in the paramagnetic bond contributions due to bonds connecting the atom of interest with its four bonded neighbors. Computational results show the diamagnetic contributions arise essentially from the carbon 1s and 2s orbitals and remain constant while torsional angles are varied. The paramagnetic contributions from nonbonded atoms are negligible and therefore a study of the paramagnetic contributions from the four attached bonds is necessary in any description of the contributions to σ_T which cause it to vary with torsional angle.

Therefore considering the C4 atom: from the structure of Figure 18 this atom exhibits a change in its total shielding tensor of approximately 5 ppm when the torsional angle is changed from 60 to a 180°. Also, as described in Graph 2, the overall response of σ_T as the dihedral angle is changed from 0 to 180 is to vary from 176 ppm at 0° up to 185 ppm at 60°, down to 170 ppm at an angle of 120° and again up to 176 ppm at 180°. Therefore a maximum variation of 9 ppm is reported for this atom over the 180° range of torsional angles.

The four contributions due to the bonds connecting atom C4 with its neighbors are therefore plotted in Graph 8 (below).

Thus as Graph 8 denotes the increase in total shielding between 0 and 60 degrees is due to an increase of slightly more than 4 ppm in the C4-H12 contribution. Also, the decline in the value of the total tensor between 60 and 120 degrees corresponds to decreases in the C4-H12 and C3-C4 contributions of 3 and 2 ppm respectively. The C4-H13 and C4-H14 contributions are largely flat across the variation of torsional angles with a minor increase of less than 2 ppm in the 0 to 60 degree portion of Graph 8. The shapes of the curves in Graph 8 are almost exactly those obtained in the Barfield and Yamamura study⁽³⁴⁾ for a terminal carbon having the same disposition of hydrogen atoms. This is not surprising since comparisons between the IGLO and LORG approaches to shielding tensor calculations find the two methods give similar results for the same basis sets (63).

However, the Barfield and Yamamura study does not proceed to the next logical step in a search for the mechanism behind shielding tensor conformational variations. This step is to further dissect the

individual paramagnetic bond contributions to search for anisotropic effects that may be present. This is done for the C3-C4 contribution to the C4 shielding tensor in Graph 9 below.

This Graph shows the slow decrease in shielding due to the C3-C4 bond is due to a corresponding decrease in shielding along the Y axis and that the anisotropic shielding tensors along the X and Z axes remain essentially constant.

The other important contribution to the variation of the total tensor in Graph 8 is the C4-H12 contribution. The anisotropic contributions to the C4-H12 bond are plotted in Graph 10 (below).

This graph shows the sharp rise in shielding between 0 and 60 degrees in this bond is due to an increase in the X component and that the decrease in shielding between 60 and 120 degrees is due to a decrease in both X and Y directions. The C4-H13 and C4-H14 components, which make the smallest contribution to the total tensor, exhibit very similar variations as the torsional angle is changed. This is evident in Graph 11 below which describes the C4-H13 response as the torsional angle is varied.

Thus apart from an increase of approximately 5 ppm between 0 and 60 degrees due to the contribution along the X axis little variation occurs for the C4-H13 influence.

A similar analysis on the C3 atom of the butane structure of Figure 18 indicates its variational response to dihedral angle changes also has an anisotropic nature. Thus, as demonstrated in Graph 2 above, the C3 isotropic ^{13}C shielding tensor decreases smoothly from its maximum value close to 185 ppm down to its minimum at 170 ppm while the torsional angle is varied from 0 to 120 degrees. Beyond the 120 degree angle the total shielding tensor increases to 173 ppm at a 180 degree torsional angle.

The division of this total tensor quantity into its four significant contributions is plotted in Graph 12 (below).

Therefore the largest contributions to the total deshielding of this carbon are due to the C3-C1 and C3-C4 bonds. However the variations in the total shielding tensor is a result of changes as a function of dihedral angle of all four contributors. An important feature in Graph 12 is the deshielding due to the C3-C1 bond which varies from its maximum value at 0 degrees to its minimum at 120 degrees with a net change of close to 5 ppm.

The anisotropic contributions which constitute this C3-C1 shielding effect are plotted in Graph 13 (below).

The three components of the C1-C3 tensor seen in Graph 13 make it clear the large decrease in shielding around the 120 degree torsional angle in the total contribution is mainly due to a component in the X direction. The contribution in the Z direction is zero without fluctuation. This is a reasonable result since the C1-C3 bond, which is colinear with the Z axis, therefore appears as a small circular shape when viewed along the Z axis and as a result has essentially no paramagnetic contribution to the shielding tensor.

The anisotropic components of the C3-C4 contribution to the total C3 shielding tensor are documented in Graph 14 (below).

The sloping decrease in net shielding at C3 due to the C3-C4 contribution as the torsional angle approaches 180 degrees seen in Graph 12 above is therefore mainly due to deshielding along the Y axis. The relatively small influence upon the total shielding due to the X component is, as the case for the Z component in Graph 13, due to its approximate colinearity with the X axis.

The two influences to the C3 shielding tensor due to bonded hydrogens described in Graph 12 indicates that shielding decreases to minima at torsional angles of 80 and 120 degrees for the C3-H10 and C3-H11 contributions respectively. The anisotropic components of the C3-H10 contribution to the total C3 shielding tensor are described in Graph 15 (below).

Therefore the dominant feature of the three plots in Graph 15 is the distinct minimum in shielding along the X axis at a dihedral angle of 100 degrees. This is comparable to the situation for the anisotropic contributions to the C3-H11 component of the total C3 shielding tensor described in Graph 16 (below).

The decrease in shielding due to the C3-H11 contribution around the 120 degree torsional angle is therefore due to a distinctive

component along the X axis.

A similar analysis of the smooth decrease in shielding from 186 to 180 ppm for C1 in Graph 2 has anisotropic components and the four important contributions to the C1 shielding tensor are described in Graph 17 (below).

Therefore deshielding of this carbon is again dominated by contributions from the bonds to neighboring carbon atoms and the bonds to nearby hydrogens have a shielding variation similar to that for the corresponding hydrogen bond influences upon the C3 tensor.

The anisotropic components of the C1-C3 bond contribution to the C1 chemical shift are plotted in Graph 18 (below).

The decrease in shielding is therefore related to a minimum in the Y axis contribution centered around the 120 degree dihedral angle. However the reason the C1-C3 contribution levels between the 120 and 180 degree angle in Graph 17 is due to a shielding decrease in the X component.

The approach employed in NMR computations is to calculate the shielding tensor along the X,Y and Z axes and to mathematically mix these to obtain an isotropic shielding tensor. Therefore the anisotropic component of a given tensor is affected by the relative orientation of a bond with the axis being calculated. The result is when a bond changes its exposure to a give axis the shielding tensor is also changed. This is seen in the anisotropic components of the C1-C2 contribution in Graph 19 (below).

Therefore since the C1-C2 bond in Figure 18 is changing its exposure to the X and Y axes as the C1-C2 segment rotates about the Z axis this is reflected in the anisotropic shielding tensor. Since the C1-C2 exposure to the Y axis is maximum at a 0 degree dihedral angle for the structure of Figure 18, this orientation has a maximum deshielding contribution for the C1-C2 bond in the Y direction. This is evident in Graph 18 where maximum deshielding occurs at the 0 degree angle for the Y component of the isotropic tensor. The fluctuations due to the exposure of a bond to a specific axis are therefore described by a sinusoidal function and this is seen in Graph 18 for the X and Y anisotropic contributions. The fluctuations which cause the net C1-C2 influence to vary are therefore superimposed upon this sinusoidal response due to rotation. In this instance the X component is symmetrically sinusoidal and it is a fluctuation at 0 and 180 degrees in the Y component which gives the C1-C2 influence upon the total C1 tensor its variational characteristics. This is described above in Graph 17 above where

deshielding due to the C1-C2 contribution is at the 0 and 180 degree torsional angles.

This is also the case for the C1-H5 influence in Graph 20 (below).

Here a distinctive deshielding near the 120 degree angle is imposed upon the sinusoidal response of the Y component of the C1-H5 shielding contribution to the total C1 tensor. This accounts for the decrease in shielding due to the C1-H5 influence upon C1 around the 120 degree angle documented in Graph 17 above.

The C1-H6 contribution to the C1 shielding tensor seen in Graph 17 also has an anisotropic character and the deshielding seen between 60 and 80 degrees in the total C1-H6 tensor of Graph 17 is due to a Y component superimposed upon the normal sinusoidal variation (Graph 21 below).

The response of C2 in the structure in Figure 18 to the changes in torsional angle, as documented in Graph 1 above, is to peak at 190 ppm at an angle of 20 degrees and then to decrease in shielding to a value of 174 ppm at a torsional angle of 120 degrees. The shielding tensor then increases smoothly to 182 ppm at an angle of 180 degrees. This represents a shielding tensor differential between the gauche and anti conformations of approximately 3 ppm which is 2 ppm smaller than the usual difference. However the overall variation in chemical shift for this carbon is significant and its important contributions are described in Graph 22 below.

Graph 22
Individual contributions to C2 shift

This graph demonstrates the large deshielding at a torsional angle of 120 degrees seen in the total tensor for C2 is due to a corresponding decrease in shielding at this angle for the C1-C2 and C2-H7 contributions.

The anisotropic components of the C1-C2 contribution to the total C2 shielding tensor are therefore described in Graph 23 below.

Graph 23
Anisotropic C1-C2 cont. to C2 shift

3

of/de

3

Thus as the C2 carbon is rotated around the Z axis its exposure from a view looking down this axis is constant and no sinusoidal fluctuation of the shielding tensor is recorded. Also evident in Graph 23 is the lack of shielding tensor variation due to the Z component. The source of the large deshielding around the 120 degree torsional angle is therefore from the X and Y contributions to the C1-C2 influence upon the C2 response. Therefore comparison between the values of σ_{xx} and σ_{yy} at dihedral angles of 60 and 120 degrees shows the 120 degree angles experience a greater degree of shielding than do the 60 degree angles. This deshielding along the X and Y axes therefore accounts for the large deshielding seen in Graph 22 above for the C1-C2 contribution to the total C2 shielding tensor.

The C2-H7 contribution which also exhibits deshielding at the 120 degree angle in Graph 22 has an anisotropic character as apparent in Graph 24 (below).

Therefore as for the anisotropic components of the C1-C2 contribution to the total C2 chemical shift the Z axis contribution is constant and variation occurs in the X and Y components. These can be seen in a comparison between the 60 and 120 degree angles for the X and Y contributions where deshielding occurs at the 120 degree geometry relative to that at the 60 degree orientation.

The anisotropic components of the C2-H8 contribution to the C2 shift are documented in Graph 25 (below).

Dissection of the variational character for the shielding tensors of the three ether carbons in Figure 19 indicates anisotropic shielding also occurs here. The responses of the ^{13}C shielding tensors for these three carbons upon changes in torsional angle are characterized in Graph 27 (below).

Graph 27 shows carbons 1 and 4 exhibit deshielding at a 120 degree torsional angle and that all three carbons are more shielded at the gauche than at the anti geometry. As in the instance of the butane structure discussed above, correlation does not exist between shielding fluctuations due to changes in torsional angle and interatomic distances, individual carbon charge densities or total system energies. However, the total shielding tensors variation for the three carbons of this system are due to four main contributions which can be dissected into anisotropic components.

Therefore, the four significant components of the total C2 shielding tensor are plotted in Graph 28 (below).

The major contribution to the total C2 chemical shift is therefore due to the C2-C1 bond. This contribution, as well as that due to the C2-H7 bond, exhibit deshielding near the 120 degree geometry. The two contributions due to the C2-H8 and C2-H9 bonds are similar and largely unimportant in the variational response of the total C2 chemical shift.

The anisotropic components of the C2-C1 paramagnetic contribution to the C2 chemical shift are plotted in Graph 29 (below).

Deshielding, seen in Graph 28 near the 120 degree geometry, for the C2-C1 contribution to the total C2 shielding tensor is due to a Y component. This is seen in a comparison between the 60 and 120 degree values for the shielding tensor along the Y axis where the anisotropic shielding tensor has a larger negative value at the 120 degree geometry.

The C2-H7 contribution to the C2 chemical shift exhibits deshielding near the 0 degree torsional angle and this is due to a component along the X axis. This is seen in the plot of anisotropic contributions to this tensor in Graph 30 (below).

Contributions from the C2-H8 and C2-H9 bonds to the C2 shielding tensor are relatively unimportant, as evident in Graph 28, and this is seen in the nearly symmetrical variations of the anisotropic contributions to these described in Graphs 31 and 32 (below).

The C2-H9 component of the C2 shielding tensor exhibits greater deshielding than the C2-H8 bond in Graph 28. This is due to a Y component in the C2-H9 contribution to the C2 shift. Also, comparison between Graphs 31 above and 32 (below) shows the X and Y fluctuations are offset by the difference in the respective angles of exposure these bonds present to the X and Y axes.

Variation of the torsional angle between 0 and 180 degrees causes the C1 shielding tensor (Graph 27 above) to exhibit deshielding around the 120 degree angle. Individual contributions to the total C1 tensor plotted in Graph 33 (below) indicate deshielding at 120 degrees is due to a combination of contributions from the O3-C1 and C1-H5 bonds.

Also, the C1-H6 component of the total C1 tensor has a minimum value near the 80 degree torsional angle and the C1-C2 influence is to deshield C1 for geometries between 100 and 180 degrees.

Anisotropic contributions to the C1-C2 component of the C1 chemical shift are plotted below in Graph 34 (below).

Deshielding in the C1-C2 component is therefore due to an anisotropic contribution along the Y axis as seen in Graph 34. Here σ_{yy} has a value approximately 6 ppm more negative at the 180 than at the 0 degree geometry.

The shielding minimum at 120 degrees for the C1-O3 contribution to the C1 chemical shift is also due to a Y axis component as evident in the plot of anisotropic contributions to shielding due to this bond in Graph 35 (below).

Also, the C1-H5 contribution to the C1 shielding tensor has a Y component which deshields at the 120 degree geometry and this is seen in the decomposition of this component in Graph 36 (below).

Deshielding around the 80 degree geometry due to the C1-H6 contribution to the C1 shift in Graph 33 also has a Y axis component and this is evident in the plot of anisotropic components in Graph 37 (below).

The four significant contributions to the C4 chemical shift are presented in Graph 38 (below).

Notable fluctuations in these four influences upon the C4 shielding tensor are the consistent deshielding evident around the 120 degree geometry in Graph 38. The anisotropic nature of the contribution from the C4-O3 bond is described in the plot of Graph 39 (below).

Therefore, again the 120 degree geometry experiences deshielding along the Y axis.

This is also true for the contribution from the C4-H10 bond which deshields carbon 4 via a component directed along the Y axis. This is demonstrated in the plot of Graph 40 (below).

The two contributions from the C4-H11 and C4-H12 bonds are almost identical in Graph 38 above and their anisotropic components are also very similar. Therefore the C4-H11 bond anisotropic contributions are presented and these are plotted in Graph 41 (below).

This graph shows some deshielding occurs along the Y and Z axes near the 120 degree geometry.

In each of the seven carbons of the two systems studied throughout the course of this research initiative, anisotropic contributions account for variations of ^{13}C NMR shielding tensors when the torsional angle is altered. This anisotropy occurs in the paramagnetic components of carbon-carbon and carbon-hydrogen bonds. The position of this study is that essentially the same mechanism which accounts for anisotropy in the shielding tensors of unsaturated systems also operates in these saturated molecules.

Unsaturated systems such as benzene experience ring currents typically attributed to the flow of delocalized π electrons. This occurs when the applied field is perpendicular to the plane of an aromatic molecular ring having geometry suitable for electron flow to occur. The current flow in a suitable circuit induces a magnetic field which opposes the applied field B_0 inside the current loop and adds with the applied field outside the loop. Outside this current loop nuclei are deshielded while inside they experience a net shielding. Measurement of the three anisotropic shielding tensors on aromatic molecules⁽²⁷⁾ using single crystal NMR methods have shown the tensor values perpendicular to the molecular plane have a shielding contribution at times over 100 ppm different from the tensors along other axes. Since electrons are less available for circulation in saturated molecules the difference between individual shielding components is expected to be significantly below that for unsaturated molecules. Reference to the graphical analysis of the two saturated compounds described above indicates this expectation is consistent with calculated results.

The sources of electrons for the proposed current flow in this mechanism explaining conformational chemical shift variation are C-C and C-H bonds. The thesis is that the force exerted upon the bonding electrons by the applied field causes these electrons to leak out of the bonding orbitals into nearby available bonding or antibonding orbitals. This occurs only when the molecular geometry is such that a current circuit can be completed and therefore the source of conformationally dependant chemical shifts.

Therefore this mechanism can be applied to explain the calculated deshielding at the 120 degree angle for the ether system investigated herein. Graphical analysis of the shielding tensors for this compound indicates deshielding often occurs along a Y axis component of the individual contributions. This result would be consistent with a large applied magnetic field inducing electron flow in a manner described in Figure 20 (below).

Figure 20. Ethyl-methyl ether at a 120 degree angle.

Thus an applied field directed along the Y axis, and therefore out of the page, induces electron flow as described by the arrow in Figure 20. This electron flow then sets up a small field opposed to the applied field, B_0 , which is directed into the page inside the current

loop and out of the page outside this circuit. The result is any carbon nucleus inside such a current loop will experience a net shielding while those outside the loop will be deshielded. Such deshielding will be due to the bonds in which electron flow occurs and will be observed only when the applied field is directed along an appropriate axis for electron flow to occur. Evidence for the existence of the current loop described in Figure 20 is in the anisotropic shielding contributions for the four bonds making up this circuit. Therefore the C1-O3 contribution to the C1 chemical shift has a deshielding influence along the Y axis in Graph 35. The C1-H5 bond is deshielding to C1 at the 120 degree geometry in Graph 36 and the C4-O3 influence upon the C4 chemical shift is deshielding along the Y axis in Graph 39. Also the C4-H10 bond in Graph 40 is deshielding to C4 along the same Y axis at the designated 120 degree torsional angle.

A similar current loop is apparent in the butane structure and this is depicted in Figure 21 (below).

Figure 21. Butane at 120 degree geometry.

Evidence for the existence of the current flowing as described by Figure 21 is in Graph 18 above where the anisotropic C1-C3 contribution to the C1 shift shows Y axis deshielding at the 120 degree angle. Also, the C1-H5 bond in butane is Y axis deshielding to C1 at the 120 degree geometry in Graph 20 and the C3-C4 contribution to the C4 shift is deshielding along the Y axis in Graph 9.

The existence of a single current loop at the 120 degree geometry does not permit conclusion that all conformational shift variations are due to induced electron flow. However, evidence for the existence of other current flow is present in the analysis of these compounds. A deshielding influence consistent with a current flow perpendicular to the X axis in the two compounds studied is also evident. This situation occurs near the 100 degree geometry. In the butane structure bonds exhibiting X axis anisotropy are the C1-C2, C1-C3, C2-H7, C3-H10 and C3-H11. The evidence of X axis deshielding in these bonds in the same order as the bonds are listed is found in Graphs 23,13,24,15 and 16. The electron flow that could create shielding in these bonds is described in Figure 22 below which provides a view of the butane molecule in the 120 degree geometry looking along the positive X axis from below the structure in Figure 21.

Figure 22. Butane at 120 degree angle along X axis.

A similar X axis deshielding is also present in the calculations on the ether studied in this analysis. This situation is described in Figure 23 (below).

Figure 23. Ethyl-methyl ether at 120 degree angle X axis.

The evidence for the existence of this current is seen in Graph 30 where the C2-H7 contribution to the C2 shielding tensor has an X axis deshielding influence. Also Graph 33 documents the x axis shielding of the O3-C1 bond upon the C1 chemical shift. This current loop is completed by a C2-C1 X axis deshielding component in Graph 29 although the symmetric nature of the normal shielding tensor variation due to bond exposure to the X axis makes this shielding tensor difficult to establish as X axis dependant.

Commonality exists between the orientations of the atoms in the current loops described in Figures 20 through 23. This is the

approximately planar orientation of two carbon-carbon or carbon-oxygen bonds and one or two carbon-hydrogen bonds. Therefore the question arises as to why this orientation can support the presence of electron flow while other geometries do not. An example of a geometry which appears suitable for an efficient electron flow is the 0 degree orientation in Figures 18 and 19 above. In the aromatic examples of ring current the diffuse π bonds are overlapped to permit access for circulating electrons. Something similar to this may be the case for the saturated systems under discussion here since the C-H antibonding orbital is known to be diffuse⁽¹⁷⁹⁾. Therefore if leakage from bonding C-C and C-O orbitals into antibonding C-H orbitals were to occur the presence of an appropriately placed C-H bond would be necessary for electron flow to occur. The antibonding orbitals for sp^3 hybridized systems are small⁽¹⁷⁹⁾ and therefore less accessible to electron flow and this may explain the inability of the 0 degree geometry to support electron flow. However this is speculative and concrete evidence concerning the movements of electrons in saturated systems is needed to complete this theoretical description of conformationally dependant ^{13}C chemical shifts.

Evidence also exists in this graphical analysis for the presence of less intense electron circuits. This is seen around the 0 degree geometry for butane which exhibits shielding in the C4-H12, C4-H13 and C4-H14 bonds due to an X axis contribution evident in Graphs 10 and 11. The presence of these secondary electron loops, if in fact it is electron flow which accounts for these deshielding influences,

complicates the problem of presenting a comprehensive description of the source of shielding tensor conformation dependencies.

Therefore further computational analysis of saturated systems is required before a conclusive description of their conformational ^{13}C NMR characteristics can be considered to be complete. Further analysis could do electron density mapping to verify the presence of charge density in a circular path. Also calculations of molecular orbital geometries in the presence of strong magnetic fields can be used to determine where overlap occurs and therefore when current flow is possible.

Chapter 6 Conclusions

This study has demonstrated the utility of ^{13}C conformationally dependant chemical shifts and presented a mechanism to account for this phenomena.

The saturated crown ethers investigated during the course of this study have exhibited lithium complexing properties and the conformational changes which accompany complexation have been described. Evidence has been presented that the propano bridge in the dicyclohexyl-14-crown-4 and dicyclohexyl-13-crown-4 systems is more flexible than the ethano bridge in the dicyclohexyl-13-crown-4 and dicyclohexyl-12-crown-4 systems. The flexibility associated with the propano bridge coupled with the larger ring cavity of the 13 and 14 membered systems increase the complexing efficiencies of these molecules.

X-ray analysis of the crown ethers investigated during the course of this study has been employed to assist in making ^{13}C chemical shift assignments. When assignments have been tentative, the computational analysis of analogues of the crown ether systems under study have been used. The conclusion is therefore that X-ray analysis in concert with experimental and computational ^{13}C NMR spectroscopy provides an effective window upon the conformational preferences molecular systems choose to adopt.

Chapter 7 Experimental

Synthesis of Crown Ethers

Starting materials for this study were obtained as follows; Guaiacol (99%, Sigma), 1,2-dibromoethane (99%, Sigma) and 1,3-dibromopropane (Sigma) 5% ruthenium on alumina (Aldrich). All 12,13 and 14-crown-4 ethers in this study were synthesized from these starting materials using the synthetic route exemplified below for the synthesis of the cis-syn-cis and cis-anti-cis isomers of dicyclohexyl-12-crown-4 (Scheme 1) with the substitution of 1,3,dibromopropane in appropriate instances..

Scheme 1. Synthetic route to dicyclohexyl crown ethers.

A typical experimental procedure for the synthesis of 12,13 and 14-crown-4 ethers is as described below for the generation of the mixture of dicyclohexyl-12-crown-4 isomers.

Preparation of 1,2 Bis(o-methoxyphenoxy)ethane. (Structure II Scheme I).

Into 250 ml of water 12 g (.097 mol) of o-methoxyphenol was mixed with 3.9 g (.098 mol) of sodium hydroxide and the mixture was stirred until the base was dissolved and a dark color was observed. To this solution 4.18 ml (.049 mol) of 1,2 dibromoethane was added and the mixture was refluxed with stirring for 24 hours. The solid dark white material formed was extracted into CH₂Cl₂ and extracted twice with 50 ml aliquots of 5% NaOH solution to remove any remaining phenolic material. White needle crystals 9.97g (.037) mol were collected from CH₂CL₂ and hexanes, which represents a 75% yield of the desired product (structure II scheme I, mp 136-138°C).

Preparation of 1,2 Bis(o-hydroxylphenoxy)ethane. (Structure III Scheme I)

A mixture of 8 g (.029 mol) of 1,2 Bis(o-methoxyphenoxy)ethane and 0.47 ml (.070 mol) of trimethysilyl

iodide (180) was dissolved in 200 ml of dry CH_2Cl_2 . The solution was refluxed with agitation for 20 hours, then 100 ml of water was added and heating was stopped with continued stirring for 1 hour. The aqueous and organic phases were separated and the organic phase was washed twice with 50 ml aliquots of water. The dried organic phase was roto-evaporated to yield 7.01 g (.028 mol) of crude material. This was purified by recrystallization from CH_2Cl_2 and hexanes to produce 5.01g (.020 mol) which represents a 69% yield of the desired product (structure III scheme I mp. $108 - 110^\circ\text{C}$).

Preparation of 2,3,8,9-dibenzo-1,4,7,10-tetraoxacyclododecin-2,8-diene. (dibenzo-12-crown-4) Structure IV Scheme I.

Into 200 ml of 1:1 butanol/water mixture 5 g (0.020 mol) of 1,2 bis(o-hydroxyphenoxy) ethane was placed with 1.8 g (.043 mol) of $\text{LiOH}\cdot\text{H}_2\text{O}$ and agitated for 1 hour until the solid base had dissolved. To this solution 1.72 ml (0.020 mol) of 1,2 dibromoethane was added with stirring and this was refluxed for 30 hours. The butanol/water solvent was roto-evaporated and the residue was dissolved in 100 ml of CH_2Cl_2 to be extracted twice with 50 ml aliquots of 5% sodium hydroxide solution and dried. Upon evaporation to dryness the residue was purified by recrystallization from a solvent mixture CH_2Cl_2 and hexanes to produce 0.69g (.0025 mol) of the desired product, yield 12% MP $208-210^\circ\text{C}$.

Preparation of the cis-syn-cis and cis-anti-cis isomeric mixture of 2,3,8,9-dicyclohexyl-1,4,7,10-tetraoxacyclododecane (dicyclohexyl-12-crown-4)

Into 60 ml of dry 1-butanol 2.0g (0.0074 mol) of dry dibenzo-12-crown-4 was dissolved and to this 0.40g of 5% ruthenium on alumina catalyst was added. A pressure of H₂ gas equal to 1200 psi was applied using an American Instrument Co. 50 000 psi maximum pressure high pressure apparatus and the reaction was maintained at 120°C for 12 hours.

The catalyst was then removed by gravity filtration and when the butanol was removed by rotary evaporation 1.9g of clear oil was collected representing a 90% yield of the isomeric mixture.

The only significant difference in the synthesis of the 13 and 14 membered analogues of the 12 membered macrocycles described in the above outlined synthesis was in the yields of the cyclization reactions. In the case of cyclization to dibenzo-13-crown-4 a typical yield from the diol precursor was 33%. A corresponding yield for dibenzo-14-crown-4 was around 35%.

Separation of Isomers

The hydrogenated material from reaction of dibenzo-12-crown-4 was estimated by ¹³C NMR to contain two isomers in a ca. 20:1 ratio. These were separated as follows. Using (70-230, mesh silica gel in a column washed with a 30:1 hexanes to diethyl ether, the oily mixture obtained by hydrogenation was evolved by column chromatography. Initial fractions contained a 50:50

mixture of isomers and the later aliquots were essentially pure dominant isomer cis-syn-cis (mp 69-71°C). The mixture obtained in the early fractions was again columnated until the cis-anti-cis isomer was isolated (mp 101-103°C). The stereochemistry of both isomers was established by X-ray crystallography.

The dicyclohexyl-13-crown-4 mixture from hydrogenation appeared to be in a 2:1 ratio of isomers from ^{13}C NMR. The clear, viscous oil was separated into its component isomers by an activated silica gel column (mesh size 100-200). The column was run by progressively increasing the content of diethyl ether in hexanes and the cis-anti-cis isomer (mp 78-80°C) was obtained in the early aliquots and the pure major isomer, cis-syn-cis was obtained in the later fragments and was a clear oil at room temperature and below -25°C. The stereochemistry of the two isomers was determined by X-ray analysis of the cis-anti-cis isomer and of two complexes of the cis-syn-cis isomer.

The solid white mixture which contained a 2:1 ratio of dicyclohexyl-14-crown-4 isomers was separated as follows. Recrystallization from a CH_2Cl_2 :hexanes solvent pair in two consecutive recrystallizations gave the pure minor cis-anti-cis isomer (mp 149-151°C). The mother liquors from this recrystallization were evolved on a silica gel column (mesh 100-200) using a CH_2Cl_2 :diethyl ether solvent pair. The mixture of isomers was established onto the column by passing 100ml of CH_2Cl_2 after which a mixture of 10:1 of CH_2Cl_2 :diethyl ether eluent was used. Initial aliquots contained a mixture of isomers and later fractions were almost the pure cis-syn-cis major

isomer. This was purified by recrystallization from hexanes and CH_2Cl_2 (mp 96-98°C).

Complexation of Crown Ethers

All complexation reactions were carried out in essentially the following manner. Equimolar amounts of the neutral ligand and the lithium salt were dissolved in a minimum quantity of dry methanol and this was permitted to stand for a few minutes before evaporation of the solvent. The resulting solid was recrystallized from a solvent mixture of CH_2Cl_2 :hexanes as well as small amounts of methanol when the complex was poorly soluble in the non-polar solvent pair and essentially quantitative amounts of complex was recovered. Crystals were analysis by X-ray crystallography, solid and solution phase ^{13}C NMR and melting points were recorded (table I).

compound	mp degrees C Range
db12c4	208-210
cscdc12c4	69-71
cscdc12c4+LiSCN	202-204
cacdc12c4	101-103
db13c4	134-136
cscdc13c4	oil
cscdc13c4+LiSCN	210-212
cscdc13c4+LiClO ₄	225-228
cacdc13c4	78-80
db14c4	149-151
cscdc14c4	96-98
cscdc14c4+LiSCN	206-208
cscdc14c4+LiClO ₄	214-117
cacdc14c4	147-149

Table I. Table of melting point ranges for crown ethers and complexes.

NMR Analysis of Crown Ethers

Columns were run using Davison Chemical commercial grade H silica gel. Solvents used for recrystallizations and columns were distilled and stored over molecular sieves. DMF used in T1 analysis was dried by distillation under reduced pressure from CaO and stored sealed over molecular sieves.

The ^{13}C spectra were obtained using a Varian XL-200 spectrometer operating at 50.3 MHz, a MSL 300 at 75.2 MHz or a MSL 400 at 100.6 MHz. Sample concentrations were approximately 0.2 M in CD_2CL_2 solutions contained in 5 mm o.d. tubes. Routinely spectra were recorded with complete ^1H noise decoupling. Normal operating conditions were as follows: sweep width = 5kHz with 16K data points; pulse width = $6\mu\text{s}$ (45°) and a repetition rate of 1.0 s. The number of accumulations for the low temperature spectra was typically 1000-2000. Temperatures were calibrated using a copper-constantine thermocouple in a dummy NMR tube.

The ^{13}C spectra at 75.5 MHz were recorded on a Bruker MSL-300 instrument. For the low temperature experiments a sweep width of 7 kHz was employed using 8K data points. Resonances due to solvent were eliminated via the DEPT⁽¹⁸¹⁾ sequence using a 60° sorting pulse. The sequence was carried out assuming a J value of 140 Hz. An acquisition time of 0.6 s and a pulse delay of 2.0 s were employed. Typically under these conditions 400

accumulations provided adequate signal to noise ratios. The $\pi/2$ ^1H and ^{13}C pulses were 19 and 9.2 μs respectively.

^{13}C spin-lattice relaxation times were determined at 50.3 MHz via the inversion recovery method sequence^(182,183) was employed and data were processed using the standard XL-200 software. T1 experiments were done as 0.2 M solutions, in DMF in 10 mm NMR tubes with D_2O internal lock as an insert into the large tube in a 5 mm NMR tube. Samples analysed were dried for 24 hours under reduced pressure and solutions were degassed by bubbling with nitrogen gas.

The solid phase ^{13}C spectra were obtained as follows. The ^{13}C CP MAS spectra were recorded at 45.3 MHz on a Bruker CXP-180 spectrometer. Cross polarization times were typically 3 ms, with the radio frequency field amplitude being 60 kHz. Satisfactory signal-to-noise ratios were obtained after a maximum of 400 spectral accumulations. The sweep width was 20kHz with a recycle time of 4-8 s. Normally 2K points were collected with zero filling to 8K before Fourier transformation. Magic-angle spinning rates of ca. 3kHz were obtained with use of Kel-F spinners of the Andrew-Beams type. Chemical shifts were measured relative to external solid hexamethylbenzene (HMB) and converted to the TMS scale via the factor of 16.9 ppm, which is the chemical shift of the CH_3 group of HMB.

Crystallographic Measurements and Structure Solutions.

Single crystals were mounted on a Nonius CAD4 diffractometer controlled by the CRCCAD software⁽¹⁸⁴⁾ while an automated Picker 4-circle diffractometer was used in on some crystals. Accurate cell parameters and intensity data were obtained at room temperature with use of graphite-monochromatised Cu K radiation or graphite-monochromatised Mo K radiation.

After isotropic refinement of all non-hydrogen atoms of C-A-C-dicyclohexyl-13-crown-4 and close inspection of the refined positions, some carbons of the ethano and propano bridges had large isotropic parameters and distorted geometries, suggesting possible disorder and (or) the presence of highly mobile bridging units. Refinement was resumed with the ethano and propano carbon atoms having U_{iso} values fixed at $0.07 \text{ \AA}^2$ (based on the average U_{iso} value from a Wilson plot) and varying occupancies. A subsequent D-map gave split peaks for three of the ethano and propano carbon atoms. These were included and refined also on occupancy with fixed thermal parameters. At convergence the disordered positions showed occupancy factors in a 60:40 ratio. Despite the 60:40 conformer ratio, the unit cell of c-a-c-dicyclohexyl-13-crown-4 contains equal amounts of each enantiomer. Refinement was pursued and H atoms of the two cyclohexyl rings were located on the next D-map. Non-hydrogen atoms were refined anisotropically and ethano and propano

hydrogen atoms were introduced at calculated positions(sp^3 hybridized C-H distances of 1.08 Angstrom) and taking into account the two disordered orientations. All computations were performed with the NRCVAX crystal structure package.

Computational Analysis

Calculations of the ^{13}C shielding tensors were done using the NRC IBM-3090 computer system at a cost of 100.00 dollars per hour CPU time. The gaussian 80 program was used to generate wavefunctions using a double zeta basis set and the LORG program for calculating NMR shielding tensors was obtained from DR T.D.Bouman of the University of Southern Illinois.

The bond lengths and bond angles for the butane and ethyl-methyl ether were taken from experimental values listed in the HCP(185) and some values used are listed below.

Butane	Parameter	Value	

C1-C2	bond length	1.540	Å
C1-C3	"	1.539	"
C3-C4	"	1.540	"
C4-H12	"	1.084	"
C4-C3-C1	bond angle	109.49°	
C3-C1-C3	"	109.49°	
H9-C2-C1	"	109.50°	

E-M-ether	Parameter	Value	

C1-C2	bond length	1.540	Å
C1-O3	"	1.431	"
O3-C4	"	1.427	"
C2-H7	"	1.084	"
C1-O3-C4	bond angle	114.10°	
O3-C1-C2	"	109.49°	
C1-C2-H7	"	109.49°	

Table II. Bond angle and lengths for computations.

Thesis Preparation

This report was prepared on a Macintosh SE computer in the MS Word wordprocessing package. Figures were prepared using Chemdraw and Macdraw software packages. ORTEP and stereoview constructions were done using the Chem.3D. 2.01 package. Spectra were scanned by a Macintosh graphics scanner and stored in a Deskpaint software package. Original spectra are available upon request.

References

1. J.H. van't Hoff, Bull, Soc.Chim. France, 23, 295 (1875)
2. H. Sachse, Ber., 23, 1360 (1890)
3. K.W.F. Kohlrausch, A.W. Reitz, and W. Stockmair, Z. Physik. Chem., B32, 229, (1936)
4. D.H.R. Barton, Experientia, 6, 316 (1950)
5. H. Curtis, Biology 4th Ed. by Worth Publishers, New York, 1983, p. 169
6. R.C.E. Arcamone, Doxorubicin Anticancer Antibiotic, Academic Press, New York, 1981
7. M.C. Fedarko, J. Magn. Reson. 12, 30 (1973)
8. H.J. Schneider and V. Hoppen, Tet. Lett. 7, 579 (1974)
9. G.C. Levy and G.L. Nelson, Carbon-13 Nuclear Magnetic Resonance for Organic Chemists, Wiley-Interscience, New York (1972)
10. J.B. Stothers, Carbon-13 NMR Spectroscopy, Academic Press, New York (1972)
11. R.J. Abraham and P. Loftus, Proton and Carbon-13 NMR Spectroscopy, John Wiley & Sons, New York (1983)
12. R.K. Harris, Nuclear Magnetic Resonance Spectroscopy, Pitman Books Limited, (1983)
13. I. Bertini and C. Luchinat, NMR of Paramagnetic Molecules in Biological Systems, Benjamin Cummings Pub. Co., (1986)
14. P.C. Luuterbur, J.Chem.Phys. 38, 1406, (1963)
15. G.W. Buchanan, D.A. Ross and J.B. Stothers, J.Am.Chem.Soc. 88, 4301 (1966)

16. G. Govil and R.V. Hosar, Conformation of Biological Molecules New Results, Springer Verlag, Berlin (1982)
17. E.L. Eliel, N.L. Allinger, S.J. Angyal, G.A. Morrison, Conformational Analysis, Interscience Publishers, New York, (1965)
18. H. Saito, ACS Symp.Ser. No. 150, 125 (1981)
19. G.W. Buchanan, M.Z.Khan,J.A.Ripmeester,J.W.Bovenkamp and A.Rodrigue, Can.J.Chem. 65,2564 (1987)
20. G.W. Buchanan. J.W. Boenkamp, A. Rodrigue, R.A.B. Bannard and R.Y. Moir, Can.J.Chem. 63, 600 (1985)
21. A. Pines, M.G. Gibby, and J.S. Waugh, J.Chem.Phys. 59, 569, (1973)
22. C.A. Fyfe, Solid State NMR for Chemists, CFC Press, Guelph, (1983)
23. J. Schaefer and E.O. Stejskal, J.Am.Chem.Soc. 98, 1031 (1976)
24. H. Saito, Mag. Res. in Chem, 24, 835, (1986)
25. K.W. Zilm, R.T. Conlin, D.M. Grant, and J. Michl, J.Am.Chem.Soc. 102, 6672, (1980)
26. N.J. Clayden, Mag. Res. in Chem. 27, 692 (1989)
27. C.M. Carter, J.C. Facelli, D.W. Alderman, D.M. Grant, N.K. Dalley and B.E. Wilson, J.Chem.Soc. Faraday Trans 1, 84, 3673, (1988)
28. C.M. Rohlfing, L.C. Allen, and R. Ditchfield, Chem.Phys, 87, 9 (1984)
29. K. Kobayashi and M. Tsakada, Phys.Rev.B. 38, 8566, (1988)
30. J.B. Lambert and A.R. Vagenas, Org. Mag. Res. 17, 265 (1981)
31. K. Seidman and G.E. Maciel, J.Am.Chem.Soc. 99, 659, (1977)

32. S. Li and D.B. Chesnut, *Mag. Res. in Chem.* 23, 625, (1985)
33. S. Li and D.B. Chesnut, *Mag. Res. in Chem.* 24, 93 (1986)
34. M. Barfield and S.H. Yamamara, *J.Am.Chem.Soc.* 112, 4747, (1990)
35. W.R. Woolfenden and D.M. Grant, *J.Am.Chem.Soc.* 88, 1496, (1966)
36. D.M. Grant and B.V. Cheney, *J.Am.Chem.Soc.* 89, 5315 (1967)
37. T.W.G. Solomons, Organic Chemistry 2nd Ed. John Wiley & Sons, (1980) p. 96
38. E.R. Davidson and D. Feller, *Chem.Rev.* 86, 681, (1986)
39. D.B. Chesnut and C.K. Foley, *Chem.Phys.Lett.* 118, 316, (1985)
40. G.W. Buchanan, R.A. Kirby, J.A. Ripmeester and C.I. Ratcliffe, *Tetrahedron Letters*, 28, 4783, (1987)
41. C.P. Slichter, Principles of Magnetic Resonance, by Harper and Row, (1963)
42. I. Ando, and G.A. Webb, Theory of NMR Parameters, by Academic Press, (1983)
43. J.D. Memory, Quantum Theory of Magnetic Resonance Parameters, by McGraw-Hill, (1968)
44. A. Hinchliffe, Ab Initio Determination of Molecular Properties, by Adam Hilger, Bristol, (1987)
45. R. Ditchfield, in Critical Evaluation of Chemical and Physical Structural Information, ed. by D.R. Linde, and P.A. Martin, pub. by National Academy of Sciences, (1974), pp. 565-590
46. W.N. Lipscomb, *Adv. Magn. Reson.* 2, (1966) pp. 137-176
47. J.I. Musher, *Adv. Magn. Reson.* 2, (1966) pp. 177-224

48. M. Schindler, and W. Kutzeinigg, , J. Chem. Phys. 76(4), (1982), pp. 1919-1933
49. J.H. Van Vleck, The Theory of Electric and Magnetic Susceptibilities, by Oxford University Press, (1932)
50. W.E. Lamb, Phys. Rev. , 60, (1941) p. 817
51. N.F. Ramsey, Phys. Rev. , 77, (1950) p. 567
52. N.F. Ramsey, Phys. Rev. , 78, (1950) p. 699
53. W. Pauliz, General Principles of Quantum Mechanics, Springer-Verlag, (1980), pp. 79-91
54. D.B. Chesnut and Foley, C.B., J. Chem, Phys. 85(5), 2814 (1986)
- 55.. D.B. Chesnut and C.K. Foley, Chem. Phys. Lett. 118, 316 (1985)
56. S.K. Garg and Tse, J.S., Chem. Phys. Lett. 92, 150 (1982)
57. J.A. Pople Disc. Faraday Soc. 34, 7 (1962)
58. F. London, J. Phys. Rad, 8, 397 (1937)
59. C. McMichael Rohlfing, L.C. Allen and R. Ditchfield, Chem Phys. 87, 9 (1984)
60. C. Giessner-Prettre and B. Pullman, J.Am.Chem.Soc. 104, 70 (1982)
61. A.E. Hansen and T.D. Bouman, J.Chem. Phys. 82, 11 (1982)
62. T.D. Bouman and A.E. Hansen, Chem.Phys.Lett. 149, 510 (1988)
63. J.C.Facelli, D.M.Grant, T.D.Bouman and A.E.Hansen, J. Comp. Chem. 11,32 (1990)
64. A.E.Hansen and T.D.Bouman, Adv.Chem.Phys. 44, 545 (1980)

65. F.Bloch, Phys.Rev. ,102,104 (1956)
66. M. Oki, Applications of Dynamic NMR Spectroscopy to Organic Chemistry, Deerfield Beach,Fl; VCH Publishers, 1985
67. H.S.Gutowsky and A.Saika, J.Chem.Phys. 21,1688 (1953)
68. G.W.Buchanan and B.A.Dawson, Org.Mag.Res. 13,293 (1980)
69. H.Negita,T.Suzuki,T.Kubo,M.Maekawa,S.Gima and T.Okuda, Bull.Chem.Soc.Jpn. 57,3378 (1984)
70. S.F.Lincoln, I.M.Brereton and T.M.Spotswood, J.Chem.Soc.,Faraday Trans. 81,1623 (1985)
71. J.F.Wojcik, 'Bioorganic Chemistry , 12,130 (1984)
72. R.Breslow, Science ,218,532 (1982)
73. J.Szejtli,Cyclodextrins and their Inclusion Complexes,Adademiai Kiado, Budapest, (1982)
74. R.Breslow and L.E.Overman, J.Am.Chem.Soc. 92,1075 (1970)
75. C.D.Gutsche, Acc.Chem.Res. ,16,161 (1983)
76. C.D.Gutsche,B.Dhawan,J.A.Levine,K.H.No and L.J.Bauer, Tetrahedron ,39,409 (1983)
77. C.D.Gutsche and L.J.Bauer, Tet.Lett. ,22,4763 (1981)
78. C.D.Gutsche and K.H.No, J.Org.Chem. 47,2708 (1982)
79. G.W.Buchanan,R.A.Kirby and K.Bourque, Can.J.Chem. ,67,449 (1989)
80. G.W.Buchanan and R.A.Kirby, Tet.Lett. ,28,1507 (1987)
81. C.W.Buchanan,R.a.Kirby,K.Bourque and C.Morat, Can.J.Chem. ,66,2204 (1988)

82. A.I.Popov and J.M.Lehn, in Coordination Chemistry of Macrocyclic Compounds, G.A.Melson, ed. Chap.9, Plenum Press, New York (1979)
83. J.M.Lehn, Pure And Appl. Chem. ,52,2303 (1980)
84. H.J.Schneider and V.Hoppen, Tet.Lett. ,7,579 (1974)
85. F.R.Jensen, D.S.Noyce, C.H.Sederholm and A.J.Berlin, J.Am.Chem.Soc. ,82,1256 (1960)
86. H.J.Schneider, J.Am.Chem.Soc. 94,3636 (1972)
87. G.C.Levy, J.Magn.Resonance ,8,122 (1972)
88. A.Allfrhand, D.Doddrell and R.Komoroski, J.Chem.Phys. ,55,189 (1971)
89. S.Sorriso, J.Chem.Soc., Faraday Trans. 80,933 (1984)
90. M.C.Fedarko, J.Mag.Res. 12,30 (1973)
91. A.Luttringhaus, Ann.Chem. 528,181 (1937)
92. C.J.Pedersen, J.Am.Chem.Soc. 89,7017 (1967)
93. C.J.Pedersen, J.Am.Chem.Soc. 89,2495 (1967)
94. C.J.Pedersen, J.Am.Chem.Soc. 92,386 (1970)
95. C.J.Pedersen and H.K.Frensdorff, Angew.Chem.int.Ed. 11,16 (1972)
96. J.M.Lehn, Structure and Bonding ,16,1 (1973)
97. J.M.Lehn, Acc.Chem.Res. 11,49 (1978)
98. J.M.Lehn, Pure Applied Chem. 49,857 (1977)
99. C.D.Gutsche, B.Dhawan, K.H.No and R.Muthukrishnan, J.Am.Chem.Soc. 103,3782 (1981)

100. C.D.Gutsche and R.Muthukrishnan, J.Org.Chem. 43,4905 (1978)
101. J.R. Munch, Makromol. Chem. 178,69 (1977)
102. A.I. ^{أبو}Al-Jarva and H. Matsuda, Makromol. Chem.,Rapid Commun. 3,6 (1982)
103. M.L.Bender and M.Komiyama, Cyclodextrin Chemistry, Springer-Verlag, New York, (1977)
104. C.J.van Stsveren,V.M.L.J.Aarts,P.D.J.Grootenhuis,J.van Eerden,S.Harkema and D.N.Reinhoudt. J.Am.Chem.Soc. 108,5271 (1986)
105. J.J.Christensen,D.J.Eatough and R.M.Izatt, Chem.Rev. 74,351, (1974)
106. A.E.Martell and R.D.Hancock, Comments Inorg.Chem. 6,237 (1988)
107. D.W.Margerum,G.R.Cayley,D.C.Weatherburn and G.K.Pagenkopf, Coordination Chemistry,p.1-194,Vol.2, Ed. by A E.Martell, American Chemical Society, ACS Monograph 174, Washington D.C.,1978
108. D.J.Cram, J.Inclusion.Phenom. 6,397 (1988)
109. J.Dale, Tetrahedron 30,1683 (1974)
110. N.S.Zefirov,V.V.Samoshin,O.A.Subbotin,V.I.Baranenkov and S.Wolfe, Tetrahedron 34,2953 (1978)
111. J.P.Desvergne and H.Bouas Laurent, J.Chem.Soc.,Chem.Comm. ,403 (1978)
112. R.G.Snyder and G.Zerbi, Spectrochim. Acta. 23A,391 (1967)
113. H.Tadokoro,Y.Chantani,T.Yoshihara,S.Tahara and S.Murahashi, Makromol.Chem. 73,109 (1964)
114. A.Abe and J.E.Mark, J.Am.Chem.Soc. 98,6468 (1976)

115. D.Live and S.I.Chan, J.Am.Chem.Soc. 98,3769 (1976)
116. J.D.Dunitz and P.Seiler, Acta.Cryst. B29,589 (1973)
117. J.D.Dunitz,M.Dobler,P.Seiler and R.P.Phizackerly, Acta.Cryst. B30,2733 (1974)
118. R.M.Izatt,J.D.Lamb,G.E.Maas,R.E.Asay,J.S.Bradshaw and J.J.Christensen, J.Am.Chem.Soc. 99,2365 (1977)
- 119.R.M.Izatt,J.D.Lamb,R.E.Asay,G.E.Maas,J.S.Bradshaw,J.J.Christensen and S.S.Moore, J.Am.Chem.Soc. 99,6134 (1977)
- 120 .M.F.Truter, Struct. Bonding (Berlin) 16,71 (1973)
121. J.D.Dunitz,M.Dobler,P.Seiber and R.P.Phizackerley, Acta. Cryst Sect.B 30,2733 (1974)
122. R.M.Izatt,N.E.Izatt,B.E.Rossiter,J.J.Christensen and B.L.Haymore, Science 199,994 (1978)
123. R.B.Pettman and J.F.Stoddart, Tet.Lett. 457 (1979)
124. G.W.Gokel,D.M.Goli,C.Minganti and L.Echegoyen, J.Am.Chem.Soc. 105,6786 (1983)
125. U.Osher and J.J.Grudzinski, J.Chem.Soc.Dalton 501 (1981)
126. H.K.Frensdorft, J.Am.Chem.Soc. 93,600 (1971)
127. K.Kimura,M.Tanaka,S.Iketani and T.Shono, J.Org.Chem. 52,836 (1987)
128. C.S.Chen,S.J.Wang and S.C.Wu, J.Heterocyclic Chem. 20,795 (1983)
129. C.S.Chen,S.J.Wang and S.C.Wu, Inorg.Chem. 23,3901 (1984)
- 130.R.A.Bartsch,B.P.Czech,S.I.Kang,L.E.Stewart,W.Walkowiak,W.A.Charewicz,G.S.Heo and B.Son, J.Am.Chem.Soc. 107,4997 (1985)
131. B.Dietrich, J.Chem.Ed. 62,954 (1985)

132. Y.P.Wu and G.E.Pacey, *Anal.Chim.Acta.* 162,285 (1984)
133. E.M.Holt,G.D.Malpass,R.G.Ghirardelli,R.A.Palmer and B.Rubin, *Acta Crystallogr. Sect. C: Cryst. Struct. Commun.* C40,396 (1984)
134. U.Osher, *J.Am.Chem.Soc.* 104,4006 (1982)
135. R.O.Bach, Ed. Lithium Current Applications in Science, Medicine, and Technology, John Wiley and Sons, p.35 (1978)
136. B.P.Czech,D.A.Babb,B.Son and R.A.Bartsch, *J.Org.Chem.* 49,4805 (1984)
137. F.P.Boer,M.A.Neuman,F.P.van Remcortere and E.C.Steiner, *Inorg.Chem.* 13,2826 (1974)
138. B.D.White,K.A.Arnold,R.L.Garrell,F.R.Fronczek,R.D.Gandour and G.W.Gokel, *J.Org.Chem.* 52,1128 (1987)
139. P.Groth, *Acta.Chem.Scand.* A32,279 (1979)
140. P.Groth, *Acta Chem.Scand.* 35,463 (1981)
141. G.Shoham,W.N.Lipscomb and U.Olsher, *J.Chem.Soc.,Chem.Comm.* 208 (1983)
142. G.Shoham,D.W.Christianson,R.A.Bartsch,G.S.Heo,U.Olsher and W.N.Lipscomb, *J.Am.Chem.Soc.* 106,1280 (1984)
143. G.Shoham,W.N.Lipscomb and U.Olsher, *J.Am.Chem.Soc.* 105,1247 (1983)
144. J.D.Owen,J.A.Bandy,D.G.Parsons, M.R.Truter and C.H.L.Kennard, *J.Chem.Soc. Perkin Trans. 2*, 129 (1984)
145. M.E.Fraser,S.Fortier,A.Rodrigue and J.W.Bovenkamp, *Can.J.Chem.* 64,816 (1986)
146. J.D.Dunitz,M.Dobler,P.Seiler and R.P.Phizackerley, *Acta.Cryst.Sect.B* 30,2733 (1974)

- 147 .M.Dobler,J.D.Dunitz and P.Seiler, *Acta.Cryst.Sect.B* 30,2741 (1974)
- 148 .P.Groth, *Acta Chem.Scand.* A32,91 (1978)
149. P.Groth, *Acta Chem.Scand.* A 30,155 (1976)
- 150 .I.W.Bassi,R.Scordamaglia and L.Fiore, *J.C.S.Perkin Trans* 2, 1726 (1972)
- 151 .P.Groth, *Acta Chem.Scand.* 25,725 (1971)
152. J.D.Dunitz and P.Seiler, *Acta.Cryst.Sect.B* 30,2739 (1974)
153. F.R.Jensen,D.S.Noyce,C.H.Sederholm and A.J.Berlin, *J.Am.Chem.Soc.* 82,1256 (1960)
154. F.A.Bovey,F.P.Hood,E.W.Anderson and R.L.Kornegay, *J.Chem.Phys.* 41,2041 (1964)
- 155 .H.J.Schneider and V.Hoppen, *Tet.Lett.* 7,579 (1974)
156. F.A.L.Anet and J.S.Hartman, *J.Am.Chem.Soc.* 85,1204 (1963)
157. F.A.L.Anet and J.J.Wagner, *J.Am.Chem.Soc.* 93,5266 (1971)
158. F.A.L.Anet,A.K.Cheng and J.J.Wagner, *J.Am.Chem.Soc.* 94,9250 (1972)
- 159 .F.A.L.Anet,J.Krane,J.Dale,K.Daavatr and P.O.Kristiansen, *Acta Chem.Scand.* 27,3395 (1973)
- 160 .G.W.Buchanan,K.Bourque,J.W.Bovenkamp and A.Rodrigue, *Can.J.Chem.* 63,2747 (1985)
161. D.J.Sam and H.E.Simmons, *J.Am.Chem.Soc.* 94,4024 (1972)
- 162 .C.L.Liotta and H.P.Harris, *J.Am.Chem.Soc.* 96,2250 (1974)
163. K.Kimura,H.Tamura and T.Shono, *J.Electroanalytical Chem.* 105,335 (1979)
164. D.J.Sam and H.E.Simmons, *J.Am.Chem.Soc.* 94,4024 (1972)

165. .H.Nakamura,M.Takagi and K.Ueno, Anal.Chem. 52,1668 (1980)
166. .S.Patai, The Chemistry of Ethers. Crown Ethers. Hydroxyl Groups and Their Sulphur Analogues, by John Wiley and Sons, (1980)
167. D.G.Parsons, J.Chem.Soc.,Perkin 1,245 (1975)
168. .A.J.Layton,P.R.Mallinson,D.G.Parsons and M.R.Truter, J.Chem.Soc.,Chem.Comm. 694 (1973)
169. .R.Breslow, Acc.Chem.Res. 13,170 (1980)
170. R.S.Boikess and E.Edelson, Chemical Principles 2nd Ed. , Harper and Row, New York, p.618 (1981)
171. .N.K.Wilson and J.B.Struthers, Topics in Stereochem. 8,1 (1973)
172. S.Wolf and J.R.Campbell, Chem.Comm. 874 (1967)
173. .R.D.Shannon, Acta.Crystallogr. A32,751 (1976)
174. P.S.Belton,S.F.Tanner,K.M.Wright,M.P.Payne,M.R.Truter and J.N.Wingfield, J.Chem.Soc.Perkin Trans.II 1307 (1985)
175. J.E.Huheey, Inorganic Chemistry: Principles of Structure and Reactivity, 2nd Ed. Harper and Row, New York (1978)
176. C.J. van Staveren,V.M.L.J.Aarts,P.D.J.Grootenhuis,J van Eerden,S.Harkema and D.N.Reinhoudt, J.Am.Chem.Soc 108,5271
177. S.Wolfe and J.R.Campbell, Chem.Comm. 874 (1967)
178. C.Erk, Spectrosc. Lett. 19,1175 (1986)
179. .M.Karplus and R.N.Porter, Atoms and Molecules, Benjamin Cummings Pub. Co. 1970.p.367.
180. .M.E.Jung and M.A.Lyster, J.Org.Chem. 42,3761 (1977))

- 181 .D.T.Pegg,D.M.Doddrell,W.M.Brooks and M.R.Bendall, J.Mag.Res. 44,32 (1981)
182. R.L.Vold,J.S.Waugh,M.P.Klein and D.E.Phelps, J.Chem.Phys. 48,3831 (1968)
183. R.D.Shannon, Acta Cryst. A32,751 (1976)
- 184 .P.S.White,E.J.Gabe, ACA Meeting Abstr. 14,24 (1986)
185. Ed by R.C.Weast, M.J.Astle and W.H.Beyer, CRC Handbook of Chemistry and Physics, 64th Ed. CRC Press,Inc 1983-1984, pp.F175.

Appendix 1.

All bond lengths in Å and all torsional and bond angles in degrees
 Labelling is excluded if two atoms it is a bond length, three atoms
 bond angle and four atoms torsional angle.

1

CACDC14C4

O(1)-C(1)	1.405(5)	O(2')-C(9)	1.404(7)
O(1)-C(7)	1.436(7)	O(2')-C(2')	1.436(10)
O(2)-C(2)	1.412(10)	C(1)-C(2)	1.504(8)
O(2)-C(9')	11.445(7)	C(1)-C(6)	1.556(9)
O(1')-C(1')	1.433(6)	C(2)-C(3)	1.506(8)
O(1')-C(7')	1.424(6)	C(3)-C(4)	1.552(11)
C(4)-C(5)	1.496(12)	C(2')-C(3')	1.538(8)
C(5)-C(6)	1.535(10)	C(32')-C(4')	1.494(10)
C(7)-C(8)	1.530(7)	C(4')-C(5')	1.536(11)
C(8)-C(9)	1.518(10)	C(5')-C(6')	1.494(10)
C(1')-C(6')	1.529(10)	C(8')-C(9')	1.517(10)
C(1)-O(1)-C(7)	111.9(4)	O(2)-C(2)-C(3)	106.7(5)
C(2)-O(2)-C(9')	114.6(5)	C(1)-C(2)-C(3)	112.6(5)
C(1')-O(1')-C(7')	113.5(4)	C(2)-C(3)-C(4)	111.7(6)
C(9)-O(2')-C(2')	114.5(4)	C(3)-C(4)-C(5)	111.1(6)
O(1)-C(1)-C(2)	107.3(4)	C(4)-C(5)-C(6)	110.9(6)
O(1)-C(1)-C(6)	111.1(40)	C(1)-C(6)-C(5)	110.8(5)
C(2)-C(1)-C(6)	109.7(5)	O(1)-C(7)-C(8)	108.3(4)
O(2)-C(2)-C(1)	114.3(4)	C(7)-C(8)-C(9)	113.6(5)
O(2')-C(9)-C(8)	106.7(5)	C(2')-C(3')-C(4')	111.2(6)
O(1')-C(1')-C(2')	108.4(4)	C(3')-C(4')-C(5')	112.3(6)
O(1')-C(1')-C(6')	110.1(5)	C(4')-C(5')-C(6')	111.7(7)
C(2')-C(1')-C(6')	110.2(5)	C(1')-C(6')-C(5')	112.2(6)
O(2')-C(2')-C(1')	113.7(5)	O(1')-C(7')-C(8')	108.3(4)
O(2')-C(2')-C(3')	107.9(5)	C(7')-C(8')-C(9')	113.8(5)
C(1')-C(2')-C(3')	112.2(5)	O(2)-C(9')-C(8')	106.89(50)

2

CSCDC14C4

O(1)-C(1)	1.42759(22)	O(2')-C(9)	1.4239(23)
O(1)-C(7)	1.4133(23)	O(2')-C(2')	1.4285(22)
O(2)-C(2)	1.4272(23)	C(1)-C(20)	1.523(3)
O(2)-C(9')	1.4239(23)	C(1)-C(6)	1.512(3)
O(1')-C(1')	1.4229(22)	C(2)-C(3)	1.519(3)
O(1')-C(7')	1.4241(23)	C(3)-C(4)	1.507(4)

C(4)-C(5)	1.516(4)	C(2')-C(3')	1.517(3)
C(5)-C(6)	1.527(3)	C(3')-C(4')	1.520(3)
C(7)-C(8)	1.508(3)	C(4')-C(5')	1.513(4)
C(8)-C(9)	1.503(3)	C(5')-C(6')	1.525(3)
C(1')-C(2')	1.522(3)	C(7')-C(8')	1.505(3)
C(1')-C(6')	1.517(3)	C(8')-C(9')	1.499(3)

C(1)-O(1)-C(7)	116.10(14)	O(2)-C(2)-C(3)	106.67(17)
C(2)-O(2)-C(9')	114.29(15)	C(1)-C(2)-C(3)	110.26(18)
C(1')(-O(1')-C(7'))	116.51(15)	C(2)-C(3)-C(4)	111.79(20)
C(9)-((2')-C(2'))	114.56(14)	C(3)-C(4)-C(5)	111.42(22)
O(1)-C(1)-C(2)	106.83(15)	C(4)-C(5)-C(6)	111.28(21)
O(1)-C(1)-C((6)	114.64(16)	C(1)-C(6)-C(5)	110.99(20)
C(2)-C(1)-C(6)	111.05(18)	O(1)-C(7)-C(8)	108.55(17)
O(2)-C(2)-C(1)	111.23(15)	C(7)-C(8)-C(9)	114.39(18)

O(2')-C(9)-C(8)	108.65(17)	C(2')-C(3')-C(4')	111.24(16)
O(1')-C(1')-C(2')	107.29(15)	C(3')-C(4')-C(5')	111.56(20)
O(1')-C(1')-C(6')	114.35(15)	C(4')-C(5')-C(6')	112.26(19)
C(2')-C(1')-C(6')	110.46(17)	C(1')-C(6')-C(5')	110.79(17)
O(2')-C(2')-C(1')	111.31(14)	O(1')-C(7')-C(8')	107.75(18)
O(2')-C(2')-C(3')	107.32(16)	C(7')-C(8')-C(9')	112.94(18)
C(1')-C(2')-C(3')	110.01(17)	O(2)-C(')-C(8')	108.64(17)

CSCDC14C4: LINC

S-C(11)	1.625(6)	O(2)-Li	2.074(6)
O(1)-C(1)	1.449(4)	N-C(11)	1.145(8)
O(1)-C(7)	1.417(4)	N-Li	2.029(10)
O(1)-Li	1.958(6)	C(1)-C(2)	1.508(5)
O(2)-C(2)	1.448(4)	C(1)-C(6)	1.521(6)
O(2)-C(9)	11.428(5)		

C(2)-C(3)	1.533(5)	C(8)-C(7)a	1.513(5)
C(3)-C(4)	1.527(8)	C(9)-C(10)	1.526(5)
C(4)-C(5)	1.513(8)	C(10)-C(9)	1.526(5)
C(5)-C(6)	1.535(6)	Li-O(1)a	1.958(6)
C(7)-C(8)	1.513(5)	Li-O(2)a	2.074(6)

C(1)-O(1)-C(7)	115.6(3)	O(1)-C(1)_C(6)	111.3(3)
C(1)-O(1)-Li	113.98(25)	C(2)-C(1)-C(6)	112.2(3)
C(7)-O(1)-Li	128.5(3)	O(2)-C(2)-C(1)	105.7(3)
C(2)-O(2)-XC(9)	114.7(3)	O(2)-C(2)-C(3)	113.5(3)
C(2)-O(2)-Li	103.21(22)	C(1)-C(2)-C(3)	110.1(3)
C(9)-O(2)-Li	113.4(3)	C(2)-C(3)-C(4)	110.8(4)
C(11)-N-Li	147.7(5)	C(3)-C(4)-C(5)	110.6(3)
O(1)-C(1)-C(2)	105.8(3)	C(4)-C(5)-C(6)	110.9(4)

C(1)-C(6)-C(5)	109.7(4)	O(1)-Li-O(2)a	148.8(5)
O(1)-C(7)-C(8)	108.7(3)	O(1)-Li-N	108.6(3)
C(7)-C(8)-C(7)a	115.2(4)	O(1)a-Li-O(2)	148.8(5)
O(2)-C(9)-C(10)	108.6(4)	O(1)a-Li-O(2)a	81.51(14)
C(9)-C(10)-C(9)a	116.1(4)	O(1)a-Li-N	108.6(3)
S-C(11)-N	179.0(5)	O(2)-Li-O(2)a	88.9(3)
O(1)-Li-O(1)a	91.5(4)	O(2)-Li-N	102.4(3)
O(1)-Li-O(2)	81.51(14)	O(2)a-Li-N	102.4(3)

CACDC13C4 60%

O1-C1	1.416(9)	C4-C5	1.523(17)	C2-O2-C7	115.7(6)	O3-C10-C11	109.3(7)
O2-C2	1.416(9)	C5-C6	1.512(18)	C11-O4-C16	114.8(6)	O3-C10-C15	108.8(8)
O2-C7	1.380(9)	C10-C11	1.482(11)	O1-C1-C2	107.8(6)	C11-C10-C15	109.8(8)
O3-C10	1.390(9)	C10-C15	1.573(15)	O1-C1-C7	109.3(8)	O4-C11-C10	112.7(6)
O4-C11	1.413(10)	C11-C12	1.501(10)	C2-C1-C6	110.8(9)	O4-C11-C12	109.2(6)
O4-C16	1.426(9)	C12-C13	1.520(13)	O2-C2-C1	112.2(6)	C10-C11-C12	112.6(7)
C1-C2	1.479(10)	C13-C14	1.491(15)	O2-C2-C3	107.0(6)	C11-C12-C13	112.5(7)
C1-C6	1.505(15)	C14-C15	1.483(15)	C1-C2-C3	110.8(7)	C12-C13-C14	110.9(8)
C2-C3	1.521(11)	C3-C4	1.516(14)	C2-C3-C4	110.5(9)	C13-C14-C15	112.4(9)
O1-C17'	1.435(16)	C6-C7'	1.542(10)	C3-C4-C5	110.6(8)	C10-C15-C14	109.5(8)
O3-C9'	1.489(14)	C8'-C9'	1.513(18)	C4-C5-C6	110.9(9)	C1-C6-C5	113.5(8)
C7-C8'	1.470(16)			C1-O1-C17	126.0(9)	C7-C8'-O-C9'	109.8(10)
O1-C9'	1.649(22)	C8"-C9"	1.51(3)	O2-C7-C8'	114.3(7)	O3-C9'-C8'	102.1(9)
C7-C17"	1.72(4)	O3-C17"	1.34(4)	C9'-O3-C	106.5(7)		
C8"-C16	1.454(22)			C1-O1-C9"	96.0(8)	C9"-C8"-C16	102.8(14)
				O1-C9"-C8"	101.6(15)	O4-C16-C8"	114.5(10)
				C10-O3-C17"	136.4(15)	O3-C7"-C7	128.0(20)
				O2-C7-C17"	102.5(11)		

CSCDC13C4: LiSCN

S-C18	1.627(3)	C2-C3	1.522(5)	C1-O1-C17	114.00(23)	C1-O1-Li	110.54(19)
O1-C1	1.443(3)	C1-C2	1.501(4)	C17-O1-Li	107.18(19)	O1-C17-C16	111.22(23)
O1-C17	1.430(3)	C3-C4	1.513(6)	C2-O2-C7	115.10(23)	C2-O2-Li	114.41(2)
O1-Li	2.149(5)	C4-C5	1.506(7)	C7-O2-Li	129.27(23)	S-C18-N	178.7(3)
O2-C2	1.441(4)	C5-C6	1.514(5)	C9-O3-C10	115.51(24)	O1-Li-O2	78.40(18)
O2-C7	1.428(4)	C7-C8	1.500(5)	C9-O3-Li	120.30(23)	O1-Li-O3	148.5(3)
O2-Li	1.982(5)	C8-C9	1.504(6)	C10-O3-Li	110.38(19)	O1-Li-O4	79.34(17)
O3-C9	1.430(4)	C10-C11	1.516(4)	C11-O4-C16	114.53(23)	O1-Li-N	108.37(21)
O3-C10	1.433(3)	C10-C15	1.512(5)	C11-O4-Li	112.35(19)	C16-O4-Li	116.69(19)
O3-Li	2.040(5)	O4-Li	2.109(5)	C18-N-Li	173.8(3)	O1-C1-C2	105.59(23)
O4-C11	1.447(3)	C11-C12	1.513(4)	O1-C1-C6	111.08(24)	O2-Li-O3	91.93(20)
O4-C16	1.422(3)	C12-C13	1.511(6)	C2-C1-C6	112.3(3)	O2-Li-O4	118.69(24)
C13-C14	1.514(5)	C14-C15	1.527(4)	O2-C2-C1	106.79(22)	O2-Li-N	115.81(24)
N-C18	1.157(4)	N-Li	1.983(6)	O2-C2-C3	111.4(3)	C1-C2-C3	112.3(3)
C16-C17	1.488(4)			O3-Li-O4	79.37(16)	C2-C3-C4	110.8(3)
C1-C6	1.524(4)			O3-Li-N	102.80(23)	C3-C4-C5	111.9(3)
				C4-C5-C6	110.1(4)	C1-C6-C5	111.7(3)
				O2-C7-C8	108.7(3)	C7-C8-C9	116.3(3)

O4-Li-N	125.36(25)	O3-C9-C8	108.5(3)
O3-C10-C11	109.22(23)	O3-C10-C15	108.3(3)
C11-C10-C15	112.6(3)	O4-C11-C10	103.87(23)
O4-C11-C12	111.35(24)	C10-C11-C12	111.4(3)
C11-C12-C13	111.3(3)	C12-C13-C14	111.4(3)
C13-C14-C15	111.2(3)	C10-C15-C14	110.9(3)
O4-C16-C17	106.8(3)		

CSCDC13C4: LiClO4

C1-O5	1.4316(22)	C1-O6	1.406(3)	O5-C1-O6	108.90(17)	O5-C1-O7	109.63(19)
C1-O7	1.392(3)	C1-O8	1.386(3)	O5-C1-O8	108.03(21)	O6-C1-O7	110.89(21)
C2-C3	1.506(5)	C3-C4	1.514(6)	O6-C1-O8	109.2(3)	O7-C1-O8	110.1(3)
C4-C5	1.495(7)	O1-C1	1.435(3)	C1-O1-C1	114.39(23)	O1-Li-O2	79.38(18)
C5-C6	1.492(7)	O1-C17	1.443(4)	C1-O1-Li	107.53(21)	O1-Li-O3	149.68(25)
C7-C8	1.495(6)	O2-Li	1.955(5)	C17-O1-Li	106.62(20)	O1-Li-O4	79.56(17)
O1-Li	2.170(5)	C8-C9	1.500(5)	C2-O2-C7	114.87(25)	O1-Li-O5	100.85(22)
O2-C2	1.439(4)	C10-C11	1.515(4)	C2-O2-Li	114.99(22)	C7-O2-Li	129.8(3)
O2-C7	1.431(4)	C10-C15	1.499(5)	C9-O3-C10	114.74(23)	C9-O3-Li	119.91(24)
O3-C9	1.429(4)	C11-C12	1.528(4)	C10-O3-Li	109.45(20)	C11-O4-C16	114.68(22)
O3-C10	1.441(3)	C1-C6	1.525(5)	C11-O4-Li	111.86(20)	O2-Li-O3	93.39(21)
O3-Li	2.043(5)	C12-C13	1.507(5)	C16-O4-Li	112.45(21)	O2-Li-O4	123.77(24)
O4-C11	1.434(3)	C13-C15	1.524(5)	C1-O5-Li	136.34(21)	O2-Li-O5	122.9(3)
O4-C16	1.430(3)	C14-C15	1.524(5)	O1-C1-C2	105.61(23)	O1-C1-C6	111.8(3)
O4-Li	2.082(5)	C16-C17	1.476(5)	C2-C1-C6	111.1(3)	O2-C2-C1	107.23(24)
O5-Li	1.957(5)	C1-C2	1.505(4)	O3-Li-O4	80.33(18)	O2-C2-C3	111.7(3)
				O3-Li-O5	107.64(24)	C1-C2-C3	111.8(3)
				C2-C3-C4	110.6(3)	C3-C4-C5	111.7(3)
				C4-C5-C6	111.3(4)	O4-Li-O5	112.03(23)
				C1-C6-C5	113.1(3)	O2-C7-C8	109.2(3)
				C7-C8-C9	115.6(3)	O3-C9-C8	109.1(3)
				O3-C10-C11	108.60(23)	O3-C10-C15	108.71(24)
				C11-C10-C15	112.3(3)	O4-C11-C10	105.00(22)
				O4-C11-C12	111.7(3)	C10-C11-C12	110.6(3)
				C11-C12-C13	111.4(3)	C12-C13-C14	110.7(3)
				C13-C14-C15	111.7(3)	C10-C15-C14	111.3(3)
				O4-C16-C17	107.4(3)	O1-C17-C16	111.4(3)

CACDC14C4				CSCDC14C4		CSCDC14C4:LINCS				
O1	C1	C2	O2	56.9	64.2	O1	C1	C2	O2	55.4
C9'	O2	C2	C1	65.1	-92.4	C1	C2	O2	C9	-178.7
C2	O2	C9'	C8'	170.4	175.6	C2	O2	C9	C1	-176.2
C7'	C8'	C9'	O2	61.5	-62.6	O2	C9	C10	C9'	-71.4
O1'	C7'	C8'	C9'	64.1	-58.5	C9	C10	C9'	O2'	71.4
C1'	O1'	C7'	C8'	-173.6	-174.8	C10	C9'	O2'	C2'	176.2
C7'	O1'	C1'	C2'	157.9	174.0	C9'	O2'	C2'	C1'	178.7
O1'	C1'	C2'	O2'	-57.2	65.5	O2'	C2'	C1'	O1'	-55.3
C9	O2'	C2'	C1'	-63.0	-91.6	C2'	C1'	O1'	C7'	-166.4
C2'	O2'	C9	C8	-169.9	172.1	C1'	O1'	C7'	C8	175.4
C7	C8	C9	O2'	-65.5	-64.3	O1'	C7'	C8	C7	68.9
O1	C7	C8	C9	-61.9	-58.8	C7'	C8	C7	O1	-68.9
C1	O1	C7	C8	172.9	-175.8	C8	C7	O1	C1	-175.4
C7	O1	C1	C2	-158.2	177.3	C7	O1	C1	C2	166.4
C1	C2	C3	C4	-54.7	-56.2	C1	C2	C3	C4	-56.1
C2	C3	C4	C5	54.2	55.4	C2	C3	C4	C5	57.0
C3	C4	C5	C6	-55.7	-54.4	C3	C4	C5	C6	-57.4
C4	C5	C6	C1	57.6	55.1	C4	C5	C6	C1	56.6
C2	C1	C6	C5	-56.5	-56.4	C2	C1	C6	C5	-56.8
C6	C1	C2	C3	55.6	56.7	C6	C1	C2	C3	56.7
C7	O1	C1	C6	82.0	-59.2	C7	O1	C1	C6	-71.4
O1	C1	C6	C5	6.8	-177.6	O1	C1	C6	C5	-175.1
O1	C1	C2	C3	-65.1	-177.7	O1	C1	C2	C3	178.3
C9'	O2	C2	C3	-169.8	147.3	C9	O2	C2	C3	60.4
O2	C2	C3	C4	179.1	64.7	O2	C2	C3	C4	62.2
C6	C1	C2	O2	177.6	-61.5	C6	C1	C2	O2	-66.3
C1'	C2'	C3'	C4'	54.6	-57.6	C1'	C2'	C3'	C4'	56.1
C2'	C3'	C4'	C5'	-52.7	54.5	C2'	C3'	C4'	C5'	-57.0
C3'	C4'	C5'	C6'	53.4	-52.6	C3'	C4'	C5'	C6'	57.4
C4'	C5'	C6'	C1'	-54.3	54.0	C4'	C5'	C6'	C1'	-56.6
C2'	C1'	C6'	C5'	55.4	-57.0	C2'	C1'	C6'	C5'	56.8
C6'	C1'	C2'	C3'	-55.0	59.1	C6'	C1'	C2'	C3'	-56.7
C7'	O1'	C1'	C6'	-81.5	-63.4	C9'	O2'	C2'	C3'	-60.4
O1'	C1'	C6'	C5'	-64.1	-178.2	O2'	C2'	C3'	C4'	-62.2
O1'	C1'	C2'	C3'	65.6	-175.7	C6'	C1'	C2'	O2'	66.3
C9	O2'	C2'	C3'	172.0	148.0	C7'	O1'	C1'	C6'	71.4
O2'	C2'	C3'	C4'	-179.4	63.6	O1'	C1'	C6'	C5'	175.1
C6'	C1'	C2'	O2'	-177.7	-59.7	O1'	C1'	C2'	C3'	-178.3

CACDC13C4 (occupancy factor 60%)

C17'	O1	C1	C2	-157.0(10)	C17'	O1	C1	C6	82.5(9)
C1	O1	X7'	C16	128.5(13)	C7	O2	C2	C1	75.8(6)
C7	O2	C2	C3	-162.4(9)	C2	O2	C7	C8'	169.7(9)
C10	O3	C9'	C8'	-167.8(13)	C9'	O3	C10	C11	161.4(10)
C9'	O3	C10	C15	-78.7(8)	C16	O4	C11	C10	-79.0(6)
C16	O4	C11	C12	155.1(8)	C11	O4	C16	C17'	161.6(10)
O1	C1	C2	O2	56.9(5)	O1	C1	C2	C3	-62.7(6)
C6	C1	C2	O2	176.5(10)	C6	C1	C2	C3	56.9(7)
O1	C1	C6	C5	64.4(8)	C2	C1	C6	C5	-54.3(8)
O2	C2	C3	C4	178.1(11)	C1	C2	C3	C4	-59.3(7)
C2	C3	C4	C5	56.9(7)	C3	C4	C5	C6	-53.1(8)
C4	C5	C6	C1	52.1(8)	O2	C7	C8'	C9'	56.0(8)
C7	C8'	C9'	O3	63.0(8)	O3	C10	C11	O4	-59.6(6)
O3	C10	C11	C12	64.5(6)	C15	C10	C11	O4	-178.9(10)
C15	C10	C11	C12	-54.9(7)	O3	C10	C15	C14	-62.6(8)
C11	C10	C15	C14	57.0(7)	O4	C11	C12	C13	179.4(10)
C10	C11	C12	C13	53.4(6)	C11	C12	C13	C14	-52.2(7)
C12	C13	C14	C15	56.0(8)	C13	C14	C15	C10	-58.2(8)
O4	C16	C17'	O1	-89.8(10)					

CACDC13C4 (occupancy factor =40%)

C9'	O1	C1	C2	-169.5(10)	C9"	O1	C1	C6	70.0(9)
C1	O1	C9"	C8"	173.7(18)	C7	O2	C2	C1	75.8(6)
C7	O2	C2	C3	-162.4(9)	C2	O2	C7	C17"	-153.3(13)
C17"	O3	C10	C11	139.6(16)	C17"	O3	C10	C15	-100.5(16)
C10	O3	C17"	C7	-111.9(21)	C16	O4	C11	C10	-79.0(6)
C16	O4	C11	C12	155.1(8)	C11	O4	C16	C8"	-157.0(11)
O1	C1	C2	O2	56.9(5)	O1	CX1	C2	C3	-62.7(6)
C6	C1	C2	O2	176.5(10)	C6	C1	C2	C3	56.9(7)
O'	C1	C6	C5	64.4(8)	C2	C1	C6	C5	-54.3(8)
O2	C2	C3	C4	178.1(11)	C1	C2	C3	C4	-59.3(7)
C2	C3	C4	C5	56.9(7)	C3	C4	C5	C6	-53.1(8)
C4	C5	C6	C1	52.1(8)	O2	C7	C17"	O3	92.3(21)
C16	C8"	C9"	O1	-51.3(10)	C9"	C8"	C16	O4	-60.6(11)
O3	C10	C11	O4	-59.6(6)	O3	C10	C11	C12	64.5(6)
C15	C10	C11	O4	-178.9(10)	C15	C10	C11	C12	-54.9(7)
O3	C10	C15	C14	-62.6(8)	C11	C10	C15	C14	57.0(7)
O4	C11	C12	C13	179.4(10)	C10	C11	C12	C13	53.4(6)
C11	C12	C13	C14	-52.2(7)	C12	C13	C14	C15	56.0(8)
C13	C14	C15	C10	-58.2(8)					

CSCDC13C4: LINC5

C17	O1	C1	C2	-159.5(3)	C17	O1	C1	C6	78.5(2)
C1	O1	C17	C16	80.6(2)	C7	O2	C2	C1	146.9(3)
C7	O2	C2	C3	-90.3(3)	C2	O2	C7	C8	167.9(4)
C10	O3	C9	C8	178.4(4)	C9	O3	C10	C11	-95.0(3)
C9	O3	C10	C15	142.0(3)	C16	O4	C11	C10	166.6(3)

C16	O4	C11	C12	-73.4(2)	C11	O4	C16	C17	-168.5(3)
O1	C1	C2	O2	52.9(2)	O1	C1	C2	C3	-69.4(2)
C6	C1	C2	O2	174.1(4)	C6	C1	C2	C3	51.8(2)
O1	C1	C6	C5	64.8(3)	C2	C1	C6	C5	-53.2(2)
O2	C2	C3	C4	-172.6(4)	C1	C2	C3	C4	-53.0(3)
C2	C3	C4	C5	56.2(3)	C3	C4	C5	C6	-57.5(3)
C4	C5	C6	C1	55.4(3)	O2	C7	C8	C9	57.2(3)
C7	C8	C9	O3	-82.4(3)	O3	C10	C11	O4	-54.1(2)
O3	C10	C11	C12	-174.1(4)	C15	C10	C11	O4	66.2(2)
C15	C10	C11	C12	-53.8(2)	O3	C10	C15	C14	174.4(4)
C11	C10	C15	C14	53.6(2)	O4	C11	C12	C13	-61.1(2)
C10	C11	C12	C13	54.4(2)	C11	C12	C13	C14	-56.0(3)
C12	C13	C14	C15	56.0(3)	C13	C14	C15	C10	-54.4(2)
O4	C16	C17	O1	55.1(2)					

CSCDC13C4: LiClO4

C17	O1	C1	C2	-162.0(3)	C17	O1	C1	C6	77.0(3)
C1	O1	C17	C16	77.9(3)	C7	O2	C2	C1	134.6(3)
C7	O2	C2	C3	-102.6(3)	C2	O2	C7	C8	173.8(4)
C10	O3	C9	C8	178.0(4)	C9	O3	C10	C11	-93.6(3)
C9	O3	C10	C15	144.0(3)	C16	O4	C11	C10	168.0(3)
C16	O4	C11	C12	-72.1(2)	C11	O4	C16	C17	-168.2(3)
O1	C1	C2	O2	54.5(2)	O1	C1	C2	C3	-68.2(3)
C6	C1	C2	O2	176.0(4)	C6	C1	C2	C3	53.3(3)
O1	C1	C6	C5	65.6(3)	C2	C1	C6	C5	-52.1(3)
O2	C2	C3	C4	-176.0(4)	C1	C2	C3	C4	-55.9(3)
C2	C3	C4	C5	56.7(3)	C3	C4	C5	C6	-55.2(3)
C4	C5	C6	C1	53.0(3)	O2	C7	C8	C9	62.1(3)
C7	C8	C9	O3	-81.4(3)	O3	C10	C11	O4	-54.3(2)
O3	C10	C11	C12	-175.0(3)	C15	C10	C11	O4	65.9(2)
C15	C10	C11	C12	-54.7(2)	O3	C10	C15	C14	174.3(4)
C11	C10	C15	C14	54.2(2)	O4	C11	C12	C13	-60.9(2)
C10	C11	C12	C13	55.6(2)	C11	C12	C13	C14	-56.2(3)
C12	C13	C14	C15	55.4(3)	C13	C14	C15	C10	-54.4(2)
O4	C16	C17	O1	53.8(2)					

CACDC12C4

O1	C1	1.4269(2)	C2	C3	1.520(3)		
O1	C8'	1.416(3)	C3	C4	1.508(4)		
O2	C2	1.426(3)	C4	C5	1.513(3)		
O2	C7	1.415(3)	C5	C6	1.522(3)		
C1	C2	1.507(4)	C7	C8	1.485(3)		
C1	C6	1.504(3)	C8	O1'	1.416(3)		
O1	O1'	3.653(3)	O2	O2'	4.557(3)		
C1	O1	C8'	113.00(13)	C1	C2	C3	110.03(22)
C2	O2	C7	116.69(19)	C2	C3	C4	111.34(22)
O1	C1	C2	111.43(17)	C3	C4	C5	111.74(22)
O1	C1	C6	110.33(15)	C4	C5	C6	111.40(19)
C2	C1	C6	2111.52(18)	C1	C6	C5	110.13(17)
O2	C2	C1	107.98(19)	O2	C7	C8	111.83(17)
O2	C2	C3	109.79(21)	O1	C8	C7	110.30(18)

CSCDC12C4

O1	C1	1.422(7)	C3	C4	1.510(11)
O1	C8'	1.421(6)	C4	C5	1.516(11)
O2	C2	1.440(7)	C5	C6	1.515(10)
O2	C7	1.428(7)	C7	C8	1.515(10)
O1'	C8	1.417(7)	C1'	C2'	1.534(9)
O1'	C1'	1.415(9)	C1'	C6'	1.500(8)
O2'	C2'	1.446(7)	C2'	C3'	1.529(10)
O2'	C7'	1.431(7)	C3'	C4'	1.508(11)
C1	C2	1.529(8)	C4'	C5'	1.515(11)
C1	C6	1.515(9)	C5'	C6'	1.516(11)
C2	C3	1.523(9)	C7'	C8'	1.498(9)
O1	O1'	3.990(7)	O2	O2'	4.180(7)

C1	O1	C8'	114.1(4)	O2	C7	C8	113.4(6)
C2	O2	C7	114.7(5)	O1'	C8	C7	110.1(6)
C8	O1'	C1'	114.7(5)	O1'	C1'	C2'	113.39(5)
C2'	O2'	C7'	114.3(5)	O1'	C1'	C6'	108.1(5)
O1	C1	C2	112.8(5)	C2'	C1'	C6'	112.2(5)
O1	C1	C6	108.2(5)	O2'	C2'	C1'	106.9(5)
C2	C1	C6	112.1(6)	O2'	C2'	C3'	110.4(6)
O2	C2	C1	106.8(5)	C1'	C2'	C3'	110.2(5)
O2	C2	C3	111.3(6)	C2'	C3'	C4'	111.9(6)
C1	C2	C3	110.6(5)	C3'	C4'	C5'	110.1(7)
C2	C3	C4	112.0(6)	C4'	C5'	C6'	111.5(6)
C3	C4	C5	112.1(7)	C1'	C6'	C5'	112.0(6)
C4	C5	C6	111.1(6)	O2'	C7'	C8'	113.7(5)
C1	C6	C5	111.5(6)	O1	C8'	C7'	109.8(5)

CSCDC12C4: LiSCN

S	C17	1.626(5)	C1	C2	1.530(6)
O1	C1	1.447(5)	C1	C6	1.495(7)
O1	C16	1.436(6)	C2	C3	1.530(6)
O1	Li	2.086(8)	C3	C4	1.511(8)
O2	C2	1.433(6)	C4	C5	1.524(8)
O2	C7	1.429(6)	C5	C6	1.536(7)
O2	Li	2.149(8)	C7	C8	1.431(8)
O3	C8	1.444(6)	C9	C10	1.496(6)
O3	C9	1.419(6)	C9	C14	1.508(6)
O3	Li	2.050(7)	C10	C11	1.510(8)
O4	C10	1.454(5)	C11	C12	1.526(9)
O4	C15	1.417(6)	C12	C13	1.497(10)
O4	Li	2.136(8)	C13	C14	1.524(9)
N	C17	1.148(6)	C15	C16	1.497(7)
N	Li	1.969(8)	O1	O3	3.540(6)
O2	O4	4.002(5)			

C1	O1	C16	114.0(3)	O3	C8	C7	110.0(4)
C1	O1	Li	110.2(3)	O3	C9	C10	106.6(4)
C16	O1	Li	105.7(3)	O3	C9	C14	113.3(4)
C2	O2	C7	116.7(3)	C10	C9	C14	112.2(4)
C2	O2	Li	111.6(3)	O4	C10	C9	111.3(4)
C7	O2	Li	105.6(3)	O4	C10	C11	106.9(4)
C8	O3	C9	112.2(4)	C9	C10	C11	112.1(5)
C8	O3	Li	113.6(3)	C10	C11	C12	111.1(6)
C9	O3	Li	115.5(3)	C11	C12	C13	111.1(5)
C10	O4	C15	117.2(4)	C12	C13	C14	111.4(6)
C10	O4	Li	107.5(3)	C9	C14	C13	111.1(4)
C15	O4	Li	110.2(3)	O4	C15	C16	111.7(4)
C17	N	Li	175.3(5)	O1	C16	C15	106.4(4)
O1	C1	C2	109.9(3)	S	C17	N	178.1(4)
O1	C1	C6	107.8(4)	O1	Li	O2	79.2(3)
O2	C1	C6	112.2(4)	O2	Li	O3	117.8(3)
O2	C2	C1	105.0(3)	O1	Li	O4	78.9(3)
O2	C2	C3	111.8(4)	O1	Li	N	125.9(4)
C1	C2	C3	110.4(4)	O2	Li	O3	79.8(3)
C2	C3	C4	112.0(4)	O2	Li	O4	138.1(4)
C3	C4	C5	111.0(5)	O2	Li	N	103.8(4)
C4	C5	C6	110.7(4)	O3	Li	O4	79.5(3)
C1	C6	C5	110.4(4)	O3	Li	N	115.9(4)
O2	C7	C8	112.8(5)	O4	Li	N	118.0(4)

CACDC12C4						CSCDC.12C4		CSCDC12C4LiSCN			
O1	C1	C2	O2	62.2	55.1	O1	C1	C2	O2	54.3	
C7	O2	C2	C1	-149.4	-155.1	C7	O2	C2	C1	-161.9	
C2	O2	C7	C8	106.1	77.2	C2	O2	C7	C8	80.7	
O2	C7	C8	O1'	-78.2	69.2	O2	C7	C8	O3	46.6	
C7	C8	O1'	C1'	165.4	-170.3	C90	O3	C8	C7	-157.7	
C89	O1'	C1'	C2'	-99.1	76.1	C8	O3	C9	C10	166.8	
O1'	C1'	C2'	O2'	-62.2	55.6	O3	C9	C10	O4	-49.2	
C7'	O2'	C2'	C1'	149.4	-152.9	C15	O4	C10	C9	-84.6	
C2'	O2'	C7'	C8'	-106.1	75.4	C10	O4	C15	C16	104.1	
O2'	C7'	C8'	O1	78.2	71.4	O4	C15	C16	o1	50.0	
C1	O1	C8'	C7'	-165.4	-171.8	C1	O1	C16	C15	-176.3	
C8'	O1	C1	C2	99.1	74.6	C16	O1	C1	C2	76.8	
C1	C2	C3	C4	-55.9	-53.7	C1	C2	C3	C4	-53.8	
C2	C3	C4	C5	54.4	54.8	C2	C3	C4	C5	55.2	
C3	C4	C5	C6	-54.0	-54.8	C3	C4	C5	C6	-56.3	
C4	C5	C6	C1	55.3	54.7	C4	C5	C6	C1	57.0	
C2	C1	C6	C5	-57.9	-55.0	C2	C1	C6	C5	-56.7	
C6	C1	C2	C3	58.2	54.0	C6	C1	C2	C3	55.0	
C8'	O1	C1	C6	-136.4	-160.9	C16	O1	C1	C6	-160.6	
O1	C1	C2	C3	-178.0	176.4	O1	C1	C2	C3	174.9	
O1	C1	C6	C5	177.71	80.0	O1	C1	C6	C5	-177.9	
C7	oO2	C2	C3	90.7	84.1	C7	O2	C2	C3	78.3	
O2	C2	C3	C4	62.8	64.9	O2	C2	C3	C4	62.7	
C6	C1	C2	O2	-61.6	-67.3	C6	C1	C2	O2	-65.7	
C1'	C2'	C3'	C4'	55.9	-55.3	C9	C10	C11	C12	54.2	
C2'	C3'	C4'	C5'	-54.4	57.4	C10	C11	C12	C13	-55.3	
C3'	C4'	C5'	C6'	54.0	-56.7	C11	C12	C13	C14	55.8	
C4'	C5'	C6'	C1'	-55.3	55.2	C12	C13	C14	C9	-55.1	
C2'	C1'	C6'	C5'	57.9	-53.4	C10	C9	C14	C13	53.8	
C6'	C1'	C2'	C3'	-58.2	52.9	C14	C9	C10	C11	-54.0	
C8	O1'	C1'	C6'	136.4	-158.9	C8	O3	C9	C14	-69.4	
O1'	C1'	C2'	C3'	178.0	175.7	O3	C9	C10	C11	70.5	
O1'	C1'	C6'	C5'	-177.7	-179.1	O3	C9	C14	C13	-66.9	
C7'	O2'	C2'	C3'	-90.7	87.2	C15	O4	C10	C11	152.7	
O2'	C2'	C3'	C4'	-62.8	62.6	O4	C10	C11	C12	176.5	
C6'	C1'	C2'	O2'	61.6	-67.1	C14	C9	C10	O4	-173.7	

DB12C4

O1	C1'			1.3676(14)	C4	C5			1.370(3)
O1	C8			1.4301(16)	C4	H4			0.952(12)
O2	C2			1.3806(15)	C5	C6			1.3855(21)
O2	C7			1.4376(19)	C5	H5			9.941(14)
C1	O1'			1.3676(14)	C6	H6			0.938(14)
C1	C2			1.3956(19)	C7	C8			1.4971(21)
C1	C6			1.3853(20)	C7	H71			1.026(13)
C2	C3			1.3815(18)	C7	H72			1.042(14)
C3	C4			1.3867(23)	C8	H81			0.985(15)
C3	H3			0.961(13)	C8	H82			1.022(12)
C1'	O1	C8		117.65(9)	C6	C5	H5		120.2(8)
C2	O2	C7		115.70(10)	C1	C6	C5		120.25(140)
O1'	C1	C2		116.05(11)	C1	C6	H6		119.3(7)
O1'	C1	C6		124.47(12)	C5	C6	H6		120.4(7)
C2	C1	C6		119.48(12)	O2	C7	C8		108.56(12)
O2	C2	C1		118.24(10)	O2	C7	H71)		107.6(7)
O2	C2	C3		122.08(13)	O2	C7	H72		107.9(8)
C1	C2	C3		119.67(13)	C8	C7	H71		109.5(7)
C2	C3	C4		120.36(15)	C8	C7	H72		112.9(7)
C2	C3	H3		116.5(7)	H71	C7	H72		110.1(10)
C4	C3	H3		123.1(7)	O1	C8	C7		107.16(11)
C3	C4	C5		120.01(13)	O1	C8	H81		110.1(7)
C3	C4	H4		119.7(8)	O1	C8	H82		108.0(6)
C5	C4	H4		120.2(8)	C7	C8	H81		110.0(7)
C4	C5	C6		120.22(14)	C7	C8	H82		112.5(6)
C4	C5	H5		119.6(8)	H81	C8	H82		109.1(10)
C1'	O1	C8	C7	-157.1(2)	C8	O1	C1'	C2'	155.1(1)
C8	O1	C1'	C6'	-24.6(1)	C7	O2	C2	C1	119.4(1)
C7	O2	C2	C3	-61.6(1)	C2	O2	C7	C8	-136.9(2)
C6	C1	C2	O2	178.4(2)	C6	C1	C2	C3	0.6(1)
O1'	C1	C2	O2	-1.8(1)	O1'	C1	C2	C3	179.2(2)
C2	C1	C6	C56	1.2(1)	O1'	C1	C6	C5	-178.6(2)
C2	C1	O1'	C8'	-155.1(1)	C6	C1	O1'	C8'	24.6(1)
O2	C2	C3	C4	-179.3(20)	C1	C2	C3	C4	-0.4(1)
C2	C3	C4	C5	0.8(1)	C3	C4	C5	C6	-0.2(1)
C4	C5	C6	C1	-0.8(1)	O2	C7	C8	O1	67.8(1)
C1	O1'	C8'	C7'	157.1(2)	C7'	O2'	C2'	C1'	-119.4(1)
C7'	O2'	C2'	C3'	61.6(1)	C2'	O2'	C7'	C8'	136.9(2)
O1	C1'	C2'	O2'	1.8(1)	O1	C1'	C2'	C3'	-179.2(2)
C6'	C1'	C2'	O2'	-178.4(2)	C6'	C1'	C2'	C3'	0.6(1)
O1	C1'	C61	C5'	178.6(2)	C2'	C1'	C61	C5'	-1.2(1)
O2'	C2'	C3'	C4'	179.3(2)	C1'	C2'	C3'	C4'	0.4(1)
C2'	C3'	C4'	C5'	-0.8(1)	C3'	C4'	C5'	C6'	0.2(1)
C4'	C5'	C6'	C1'	0.8(1)	O2'	C7'	C8'	O1'	-67.8(1)

CSCDC14C4: LiClO4

C1	O3		1.426(5)	C1	C6		1.528(7)		
C1	O4		1.420(5)	C2	C3		1.515(8)		
C1	O5		1.417(3)	C3	C4		1.536(8)		
C1	O5a		1.417(3)	C4	C5		1.488(10)		
O1	C1		1.452(5)	C5	C6		1.509(10)		
O1	C7		1.422(6)	C7	C8		1.511(6)		
O1	Li		2.041(7)	C8	C7a		1.511(6)		
O2	C2		1.446(5)	C9	C10		1.516(7)		
O2	C9		1.422(6)	C10	C9a		1.516(7)		
O2	Li		1.958(8)	Li	O1a		2.041(7)		
O3	Li		2.055(14)	Li	O2a		1.958(8)		
C1	C2		1.499(7)						
O3	C1	O4	110.2(3)	C2	C3	C4	110.2(5)		
O3	C1	O5	108.63(23)	C3	C4	C5	111.4(5)		
O3	C1	O5a	108.63(23)	C4	C5	C6	111.6(5)		
O4	C1	O5	110.20(20)	C1	C6	C5	111.8(5)		
O4	C1	O5a	110.20(20)	O1	C7	C8	110.2(5)		
O5	C1	O5a	108.96(22)	C7	C8	C7a	116.7(6)		
C1	O1	C7	116.3(4)	O2	C9	C10	109.1(5)		
C1	O1	Li	103.0(3)	C9	C10	C9a	114.5(7)		
C7	O1	Li	115.4(4)	O1	Li	O1a	91.0(4)		
C2	O2	C9	115.4(3)	O1	Li	O2	82.08(19)		
C2	O2	Li	113.6(3)	O1	Li	O2a	152.2(7)		
C9	O2	Li	128.7(3)	O1	Li	O3	106.6(5)		
C1	O3	Li	146.4(4)	O1a	Li	O2	152.2(7)		
O1	C1	C2	106.2(4)	O1a	Li	O2a	82.08(19)		
O1	C1	C6	113.2(4)	O1a	Li	O3	106.6(5)		
C2	C1	C6	109.8(4)	O2	Li	O2a	91.6(5)		
O2	C2	C1	105.1(4)	O2	Li	O3	101.2(4)		
O2	C2	C3	111.8(4)	O2a	Li	O3	101.2(4)		
C1	C2	C3	112.6(4)						
O4	Cl	O3	Li	180.00	O5	Cl	O3	Li	-59.20
C7	O1	C1	C2	-177.56	C7	O1	C1	C6	-57.03
Li	O1	C1	C2	55.25	Li	O1	C1	C6	175.78
C1	O1	C7	C8	178.00	Li	O1	C7	C8	-61.22
C1	O1	Li	O2	-31.22	C1	O1	Li	O3	68.14
C7	O1	Li	O2	-159.01	C7	O1	Li	O3	-59.65
C9	O2	C2	C1	-167.27	C9	O2	C2	C3	70.32
Li	O2	C2	C1	28.30	Li	O2	C2	C3	-94.11
C2	O2	C9	C10	173.41	Li	O2	C9	C10	-24.97
C2	O2	Li	O1	1.24	C2	O2	Li	O3	-104.23
C9	O2	Li	O1	-160.66	C9	O2	Li	O3	93.87
Cl	O3	Li	O1	48.07	Cl	O3	Li	O2	133.05
O1	C1	C2	O2	-55.57	O1	C1	C2	C3	66.33
C6	C1	C2	O2	-178.29	C6	C1	C2	C3	-56.39
O1	C1	C6	C5	-61.99	C2	C1	C6	C5	56.48
O2	C2	C3	C4	173.09	C1	C2	C3	C4	55.06
C2	C3	C4	C5	-54.06	C3	C4	C5	C6	55.94
C4	C5	C6	C1	-57.25					

Appendix 2 Data for graphical analysis Chapter 5.

Data for graphs 1 and 2 Butane sigma total C1 to C4

Dihedral angle in degrees	C1	C2	C3	C4
0	186.41	188.8	184.29	176.33
20	185.24	189.55	182.99	178.86
40	182.74	187.42	180.07	183.52
60	180.93	184.06	177.01	184.21
80	179.94	180.94	173.83	182.19
100	179.33	177.81	170.66	179.99
120	178.85	176.46	169.07	178.88
140	178.36	178.20	169.92	179.03
160	178.24	181.17	171.97	179.97
180	178.35	182.52	173.03	180.55

Data for graph 3 Butane internuclear distances in Angstrom

Dihedral angle in degrees	H7-H13 in Angstrom	H7-H13 in Angstrom
0	1.634	1.634
20	2.114	1.3724
40	2.6576	1.484
60	3.184	1.895
80	3.65	2.424
100	4.029	2.96
120	4.3038	3.46
140	4.462	3.879
160	4.4976	4.2
180	4.409	4.409

Data for graph 4 Electronic population of individual carbons in butane.

Dihedral angle in degrees	Electronic population in electrons.			
	C1	C2	C3	C4
0	6.281822	6.51484	6.278511	6.54094
20	6.277485	6.499117	6.281742	6.519164
40	6.270016	6.494677	6.283815	6.49237
60	6.260868	6.512365	6.286304	6.492524
80	6.258444	6.518246	6.283491	6.499336
100	6.268482	6.515706	6.27023	6.506942
120	6.274969	6.513929	6.258356	6.510788
140	6.264039	6.516799	6.257512	6.508047
160	6.244258	6.522041	6.263225	6.503191
180	6.234523	6.524749	6.26654	6.50102

Data for graphs 5,6 and 7. Energies of butane versus torsional angle.

Dihedral angle in degrees	Energies of butane in kJ/mol		
	E(total)	E(kinetic)	E(repulsive)
0	-412750.504	414339.926	357534.729
20	-412758.353	414285.538	356754.295
40	-412800.662	414110.475	354671.684
60	-412837.690	413964.847	352117.85
80	-412841.882	413943.894	349794.124
100	-412831.482	413989.098	347923.44
120	-412825.301	414017.519	346481.873
140	-412831.176	413992.432	345409.865
160	-412842.761	413940.839	344722.12
180	-412848.052	413915.359	344481.858

Data for graph 8 Individual contributions to C4 chemical shielding tensor

Dihedral angle in degrees	C3-C4	C4-H12 C4-H13 C4-H14		
		Total values in ppm		
0	-8.29	-7.32	-3.89	-3.89
20	-8.23	-5.85	-2.80	-4.09
40	-8.02	-3.16	-1.88	-3.35
60	-8.42	-2.57	-2.05	-2.53
80	-9.12	-3.66	-2.45	-2.16
100	-9.62	-4.92	-2.62	-2.34
120	-9.89	-5.44	-2.56	-2.65
140	-10.07	-5.02	-2.45	-2.80
160	-10.12	-4.17	-2.40	-2.67
180	-10.1	-3.74	-2.47	-2.47

Data for graph 9 C3-C4 anisotropic paramagnetic shielding tensor contributions to C4 for butane.

Dihedral angle in degrees	σ_{xx}	σ_{yy} σ_{zz}	
		Total values in ppm	
0	-6.14	-45.66	-42.43
20	-5.97	-45.92	-42.00
40	-5.53	-46.86	-40.65
60	-5.45	-48.39	-40.29
80	-5.74	-50.28	-40.22
100	-6.14	-51.71	-39.98
120	-6.44	-52.13	-40.17
140	-6.48	-51.64	-41.16
160	-6.32	-50.79	-42.27
180	-6.21	-50.37	-42.72

Data for graph 10 C4-H12 anisotropic paramagnetic shielding tensor contributions
to C4 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-53.07	-41.7	-0.01
20	-49.63	-40.85	-0.02
40	-42.22	-39.94	-0.02
60	-39.31	-40.7	-0.02
80	-40.23	-42.88	-0.03
100	-41.85	-44.98	-0.04
120	-42.76	-45.60	-0.04
140	-42.5	-44.53	-0.05
160	-41.59	-42.84	-0.04
180	-41.1	-42.04	-0.04

Data for graph 11 C4-H13 anisotropic paramagnetic shielding tensor contributions
to C4 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-34.45	-14.42	-35.17
20	-32.07	-14.00	-34.22
40	-28.89	-13.96	-34.46
60	-28.55	-14.59	-34.77
80	-29.34	-15.34	-34.52
100	-30.11	-15.61	-34.06
120	-30.36	-15.25	-34
140	-30.02	-14.66	-34.57
160	-29.46	-14.37	-35.22
180	-29.31	-14.56	-35.37

Data for graph 12 Individual contributions to C3 chemical shielding tensor

H11	Dihedral angle in degrees	C3-C4	C3-C2	C3-H10	C3-
		Total values in ppm			
	0	-7.34	-6.78	-0.81	-0.81
	20	-7.86	-7.08	-0.83	-1.21
	40	-8.70	-7.44	-2.03	-1.65
	60	-9.64	-7.06	-3.62	-2.49
	80	-10.80	-6.48	-4.42	-3.88
	100	-11.98	-6.65	-4.09	-5.38
	120	-12.51	-7.75	-2.85	-6.18
	140	-12.06	-9.20	-1.74	-5.66
	160	-11.14	-10.18	-1.62	-4.15
	180	-10.68	-10.47	-2.56	-2.56

Data for graph 13 C3-C1 anisotropic paramagnetic shielding tensor contributions

to C3 for butane.

Dihedral angle in	σ_{xx}	σ_{yy}	σ_{zz}
	Total values in ppm		
0	-44.94	-46.46	-0.06
20	-45.69	-47.16	-0.06
40	-48.21	-46.90	-0.04
60	-52.26	-45.64	-0.02
80	-56.63	-44.65	-0.03
100	-59.52	-45.19	-0.05
120	-58.99	-47.23	-0.07
140	-55.40	-49.53	-0.06
160	-51.49	-50.81	-0.03
180	-49.87	-51.11	-0.02

Data for graph 14 C3-C4 anisotropic paramagnetic shielding tensor contributions
to C3 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-6.04	-45.01	-37.43
20	-6.03	-45.24	-38.22
40	-5.95	-45.25	-39.59
60	-5.97	-44.09	-39.67
80	-6.30	-43.29	-38.44
100	-6.91	-44.50	-37.12
120	-7.39	-47.31	-37.16
140	-7.31	-49.97	-38.97
160	-6.89	-51.13	-41.18
180	-6.67	-51.27	-42.13

Data for graph 15 C3-H10 anisotropic paramagnetic shielding tensor contributions
to C3 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-27.68	-13.60	-33.82
20	-27.60	-13.05	-34.67
40	-29.72	-13.42	-35.7
60	-33.56	-13.62	-36.26
80	-36.90	-12.97	-35.88
100	-38.09	-12.09	-34.51
120	-36.16	-11.55	-33.23
140	-32.43	-11.92	-33.2
160	-29.81	-13.10	-34.25
180	-29.93	-14.70	-35.28

Data for graph 16 C3-H11 anisotropic paramagnetic shielding tensor contributions
to C3 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-27.68	-13.60	-33.82
20	-28.14	-13.98	-33.93
40	-29.39	-13.09	-34.74
60	-32.51	-11.99	-35.16
80	-36.61	-12.27	-34.93
100	-39.95	-14.04	-34.27
120	-40.38	-16.21	-34.04
140	-37.23	-17.13	-34.71
160	-32.82	-16.34	-35.44
180	-29.93	-14.70	-35.28

Data for graph 17 Individual contributions to C1 chemical shielding tensor

Dihedral C3-H6 angle in degrees	C1-C2	C1-C3 Total values in ppm		C1-H5
0	-6.61	-6.94	-0.04	-0.04
20	-6.48	-7.54	-0.12	-0.62
40	-6.15	-8.67	-0.71	-1.57
60	-5.54	-9.39	-1.59	-2.24
80	-4.95	-9.84	-2.50	-2.27
100	-5.00	-10.15	-3.19	-1.64
120	-5.79	-10.35	-3.45	-0.78
140	-6.76	-10.44	-3.29	-0.33
160	-7.34	-10.37	-2.61	-0.63
180	-7.49	-10.29	-1.55	-1.55

Data for graph 18 C1-C3 anisotropic paramagnetic shielding tensor contributions
to C1 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-44.08	-46.10	-0.08
20	-45.01	-46.83	-0.07
40	-47.19	-47.82	-0.06
60	-48.34	-48.69	-0.05
80	-47.63	-50.83	-0.05
100	-46.37	-53.23	-0.06
120	-46.06	-54.23	-0.07
140	-47.12	-53.33	-0.06
160	-48.81	-51.19	-0.05
180	-49.65	-50.00	-0.04

Data for graph 19 C1-C2 anisotropic paramagnetic shielding tensor contributions
to C1 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-6.01	-46.84	-35.88
20	-10.51	-41.29	-36.56
40	-21.44	-28.43	-37.5
60	-33.44	-14.85	-37.24
80	-41.31	-6.65	-35.88
100	-41.48	-7.80	-34.82
120	-33.55	-17.86	-35.1
140	-21.10	-31.74	-36.58
160	-10.30	-42.65	-38.18
180	-6.16	-46.55	-38.85

Data for graph 20 C1-H5 anisotropic paramagnetic shielding tensor contributions
to C1 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-27.28	-13.20	-32.23
20	-34.55	-5.75	-32.55
40	-35.72	-5.62	-33.18
60	-30.13	-13.34	-33.57
80	-19.75	-26.62	-33.38
100	-9.20	-39.69	-32.92
120	-4.30	-45.49	-32.8
140	-8.09	-40.70	-33.27
160	-18.27	-28.07	-33.69
180	-29.26	-14.25	-33.36

Data for graph 21 C1-H6 anisotropic paramagnetic shielding tensor contributions
to C1 for butane.

Dihedral angle in	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-27.28	-13.19	-32.23
20	-17.11	-24.55	-32.85
40	-8.34	-34.59	-34.36
60	-4.88	-39.07	-35.27
80	-8.32	-36.20	-34.73
100	-17.58	-26.62	-33.17
120	-28.60	-14.31	-31.85
140	-35.90	-5.80	-31.69
160	-36.07	-5.68	-32.47
180	-29.26	-14.25	-33.37

Data for graph22 Individual contributions to C2 chemical shielding tensor

Dihedral C4-H9 angle in degrees	C2-C1	C2-H7	C4-H8	
	Total values in ppm			
0	-5.61	-6.02	0.03	0.03
20	-5.65	-5.25	0.44	-0.5
40	-6.84	-4.36	0.01	-1.65
60	-8.47	-4.26	-0.99	-1.9
80	-9.77	-4.84	-1.99	-1.72
100	-10.87	-5.79	-2.65	-1.89
120	-11.37	-6.18	-2.62	-2.29
140	-10.88	-5.63	-2.03	-2.32
160	-10.00	-4.71	-1.50	-1.89
180	-9.61	-4.28	-1.48	-1.48

Data for graph 23 C2-C1 anisotropic paramagnetic shielding tensor
contributions to C2 for butane.

Dihedral angle in degrees	σ_{xx}	σ_{yy}	σ_{zz}
	Total values in ppm		
0	-4.59	-44.15	-37.26
20	-9.32	-39.33	-37.46
40	-23.35	-28.37	-38.02
60	-41.09	-15.17	-38.4
80	-54.20	-6.07	-38.19
100	-57.16	-6.65	-37.77
120	-46.60	-18.6	-37.8
140	-27.39	-35.88	-38.39
160	-11.18	-48.89	-39.18
180	-5.27	-53.33	-39.56

Data for graph 24 C2-H7 anisotropic paramagnetic shielding tensor contributions
to C2 for butane.

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-26.40	-47.98	-17.58
20	-27.71	-44.27	-17.47
40	-33.28	-35.56	-17.14
60	-40.72	-27.53	-16.67
80	-47.38	-22.60	-16.37
100	-49.94	-22.89	-16.3
120	-44.80	-29.32	-16.22
140	-34.16	-38.39	-16.21
160	-25.14	-44.61	-16.26
180	-21.91	-46.52	-16.27

Data for graph 25 C2-H8 anisotropic paramagnetic shielding tensor contributions
to C2 for butane.

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-34.29	-13.80	-23.89
20	-28.00	-18.75	-24.02
40	-20.15	-26.80	-25.04
60	-14.52	-34.39	-26.08
80	-14.78	-36.60	-26.67
100	-21.08	-32.26	-26.67
120	-29.15	-24.69	-26.03
140	-35.08	-17.67	-25.27
160	-37.64	-13.78	-25.02
180	-35.64	-15.46	-25.33

Data for graph 26 C2-H9 anisotropic paramagnetic shielding tensor contributions
to C2 for butane.

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-34.29	-13.80	-23.89
20	-35.96	-13.54	-24.22
40	-34.54	-17.68	-25.13
60	-27.21	-25.28	-25.47
80	-19.12	-32.93	-25.24
100	-15.20	-37.37	-25.18
120	-16.09	-37.28	-25.57
140	-21.25	-31.85	-25.94
160	-29.07	-22.85	-25.81
180	-35.63	-15.46	-25.33

Data for graph 27 C1,C2 and C3 total shielding tensors for ethyl-methyl ether
fig.19.

Dihedral angle in degrees	C1	C2 Total values in ppm	C4
0	141.27	175.03	151.33
20	141.24	177.45	152.32
40	140.15	181.09	150.43
60	137.96	180.86	146.40
80	134.71	179.08	142.32
100	131.24	177.56	138.43
120	129.78	176.94	136.75
140	131.39	177.24	138.45
160	134.28	177.87	141.34
180	135.64	178.18	142.63

Data for graph28 Individual contributions to C2 chemical shielding tensor
for ethyl-methyl ether figure 19.

Dihedral C4-H9 angle in degrees	C2-C1	C2-H7	C4-H8	
	Total values in ppm			
0	-8.97	-7.58	-3.79	-3.79
20	-8.70	-6.53	-3.33	-3.45
40	-8.39	-4.56	-2.89	-2.76
60	-8.79	-4.11	-2.78	-2.99
80	-9.35	-4.61	-2.80	-3.44
100	-9.68	-4.98	-3.11	-3.7
120	-9.69	-4.97	-3.48	-3.8
140	-9.43	-4.66	-3.75	-3.81
160	-9.10	-4.32	-3.86	-3.81
180	-8.96	-4.17	-3.85	-3.85

Data for graph 29 C1-C2 anisotropic paramagnetic shielding tensor
contributions
to C2 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy}	σ_{zz}
	Total values in ppm		
0	-6.28	-47.55	-43.11
20	-11.38	-42.56	-42.15
40	-25.12	-29.93	-40.03
60	-41.05	-15.78	-39.38
80	-51.69	-6.77	-39.38
100	-52.15	-7.24	-39.33
120	-42.05	-17.36	-39.16
140	-25.85	-32.77	-38.96
160	-11.27	-46.38	-38.8
180	-5.45	-51.77	-38.73

Data for graph 30 C2-H7 anisotropic paramagnetic shielding tensor contributions
to C2 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-50.91	-41.84	0
20	-47.92	-44.72	0
40	-44.46	-41.98	-0.01
60	-45.24	-39.4	-0.01
80	-47.07	-38.79	-0.01
100	-47.81	-39.03	-0.01
120	-46.40	-40.36	0
140	-42.92	-42.92	0
160	-39.21	-45.62	0
180	-37.61	-46.79	0

Data for graph 31 C2-H8 anisotropic paramagnetic shielding tensor contributions
to C2 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-33.64	-14.37	-35.97
20	-20.59	-26.35	-35.92
40	-8.50	-37.59	-35.3
60	-4.98	-40.86	-34.77
80	-10.49	-35.66	-34.3
100	-22.53	-24.33	-34.52
120	-35.26	-12.23	-35.09
140	-42.36	-5.34	-35.79
160	-40.55	-6.90	-36.4
180	-30.97	-16.26	-36.71

Data for graph 32 C2-H9 anisotropic paramagnetic shielding tensor contributions
to C2 for ethyl-methyl ether

Dihedral angle in degree	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-6.28	-47.55	-43.11
20	-11.38	-42.56	-42.15
40	-25.12	-29.93	-40.03
60	-41.05	-15.78	-39.38
80	-51.69	-6.77	-39.38
100	-52.15	-7.24	-39.33
120	-42.05	-17.36	-39.16
140	-25.85	-32.77	-38.96
160	-11.27	-46.38	-38.8
180	-5.45	-51.77	-38.73

Data for graph33 Individual contributions to C1 chemical shielding tensor
for ethyl-methyl ether figure 19.

Dihedral C1-C2 angle in degrees	O3-C1	C1-H5 Total values in ppm		C1-H6
0	-8.38	-14.45	-14.45	-19.89
20	-8.37	-14.40	-14.48	-19.91
40	-8.50	-14.34	-15.40	-20.08
60	-9.08	-14.74	-16.69	-19.96
80	-10.13	-15.94	-17.31	-19.81
100	-11.24	-17.37	-16.97	-20.25
120	-11.65	-18.01	-15.87	-21.29
140	-11.03	-17.31	-14.62	-22.49
160	-10.03	-15.76	-13.98	-23.38
180	-9.57	-14.40	-14.40	-23.70

Data for graph 34 C1-C2 anisotropic paramagnetic shielding tensor contributions
to C1 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-6.50	-78.07	-42.99
20	-14.57	-70.23	-42.95
40	-35.79	-49.59	-43.12
60	-60.64	-24.63	-43.00
80	-77.11	-8.19	-42.63
100	-77.27	-9.67	-42.47
120	-60.70	-29.00	-43.06
140	-35.49	-56.59	-44.47
160	-14.01	-79.36	-45.93

Data for graph 35 C1-O3 anisotropic paramagnetic shielding tensor contributions
to C1 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-43.59	-41.26	0.05
20	-43.30	-41.45	0.01
40	-42.59	-42.38	-0.04
60	-41.96	-44.63	-0.07
80	-41.50	-48.07	-0.07
100	-41.07	-51.68	-0.06
120	-41.09	-52.80	-0.06
140	-41.97	-50.15	-0.09
160	-43.26	-45.95	-0.13
180	-43.89	-43.98	-0.15

Data for graph 36 C1-H5 anisotropic paramagnetic shielding tensor contributions
to C1 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-54.96	-23.03	-39.76
20	-70.82	-7.32	-39.01
40	-71.63	-6.45	-38.51
60	-56.45	-23.17	-37.94
80	-33.19	-50.42	-37.43
100	-12.79	-75.88	-36.88
120	-4.670	-85.97	-36.49
140	-12.78	-75.66	-36.59
160	-33.04	-50.48	-36.96
180	-55.99	-23.33	-37.22

-

Data for graph 37 C1-H6 anisotropic paramagnetic shielding tensor contributions
to C1 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-54.96	-23.03	-39.76
20	-32.10	-45.50	-40.54
40	-12.10	-67.83	-40.98
60	-3.96	-79.73	-41.01
80	-12.10	-73.76	-40.59
100	-32.92	-52.80	-39.54
120	-56.87	-26.52	-38.34
140	-72.19	-7.88	-37.6
160	-71.52	-6.60	-37.37
180	-55.99	-23.33	-37.23

Data for graph38 Individual contributions to C4 chemical shielding tensor
for ethyl-methyl ether figure 19.

Dihedral angle in degrees	O3-C4	C4-H10	C4 -H11	C1-H12
Total values in ppm				
0	-6.12	-17.66	-12.30	-12.3
20	-6.18	-16.82	-12.60	-12.00
40	-7.18	-15.89	-13.51	-12.6
60	-8.55	-16.18	-14.01	-13.6
80	-9.71	-17.13	-14.45	-14.47
100	-10.67	-18.21	-15.14	-15.23
120	-11.04	-18.62	-15.57	-15.56
140	-10.56	-18.13	-15.32	-15.23
160	-9.79	-17.37	-14.73	-14.66
180	-9.46	-17.05	-14.42	-14.42

Data for graph 39 C4-O3 anisotropic paramagnetic shielding tensor
contributions
to C4 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy}	σ_{zz}
Total values in ppm			
0	-6.72	-37.77	-33.88
20	-6.87	-37.52	-34.13
40	-7.12	-39.74	-34.66
60	-7.25	-43.53	-34.86
80	-7.25	-47.17	-34.53
100	-7.18	-50.43	-34.02
120	-7.18	-51.60	-33.86
140	-7.30	-49.78	-34.24
160	-7.49	-46.91	-34.83
180	-7.59	-45.63	-35.12

Data for graph 40 C4-H10 anisotropic paramagnetic shielding tensor contributions

to C4 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-24.87	-79.76	-23.43
20	-23.66	-78.43	-23.32
40	-22.27	-76.69	-22.89
60	-21.68	-78.00	-22.16
80	-21.27	-81.38	-21.64
100	-21.11	-84.82	-21.5
120	-21.15	-86.06	-21.5
140	-21.29	-84.41	-21.57
160	-21.45	-81.86	-21.69
180	-21.52	-80.76	-21.75

Data for graph 41 C4-H11 anisotropic paramagnetic shielding tensor contributions

to C4 for ethyl-methyl ether

Dihedral angle in degrees	σ_{xx}	σ_{yy} Total values in ppm	σ_{zz}
0	-42.66	-21.92	-46.17
20	-43.77	-21.74	-46.23
40	-45.45	-22.52	-46.65
60	-45.38	-23.47	-47.18
80	-44.48	-24.71	-48.03
100	-43.94	-25.94	-49.36
120	-43.88	-26.33	-50.33
140	-43.99	-25.61	-50.12
160	-44.11	-24.62	-49.12
180	-44.18	-24.30	-48.36

--

END

04.03.92

FIN