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**Structural Investigations of
Oxygenated Organic Compounds Using
Nuclear Magnetic Resonance and X-ray Crystallography**

By

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Abstract

Solution and ^{13}C cross polarization/magic angle spinning NMR spectra indicate large amplitude motion in 15C5 and 21C7 complexes. In order to study solid state rearrangements in the macrocyclic moieties, the X-ray structure of 15-crown-5 $\cdot$ NaI was obtained, 15-crown-5- d_n $\cdot$ NaX ($n = 4, 8$; X = I, ClO_4) and 21C7- d_{12} $\cdot$ KI prepared. The motion in the low temperature phases are probable up-down flips of the CD_2 groups. In the high temperature phases, all the deuterons become equivalent, suggesting reorientation around the ring accompanied by up-down flips.

The X-ray structure of 1,2-dimethoxybenzene (mp = 15°C) revealed the two methoxy groups to be *trans*-coplanar. Utilizing variable-spinning cross polarization/magic angle spinning NMR, a ^{13}C NMR shielding tensor analysis of anisole, 1,2-dimethoxybenzene, 1,4-dimethoxybenzene and 1,3,5-trimethoxybenzene allowed a determination of the principal shielding elements of static benzene ($\sigma_{11} = 222$ ppm, $\sigma_{22} = 147$ ppm, $\sigma_{33} = 14$ ppm, $\sigma_{\text{iso}} = 128$ ppm) and subsequently the *ipso*, *ortho*-cis, *ortho*-trans, *meta* and *para* substituent chemical shifts of a planar methoxy group. The results show additivity at all sites in 1,2-dimethoxybenzene except at the *ipso* positions where σ_{22} and σ_{33} are inverted. The ^{13}C cross polarization/magic angle spinning NMR spectrum of 1,3-dimethoxybenzene (mp = -52°C) reveals this molecule to adopt the asymmetric planar conformation in the solid state, based on isotropic solid state methoxy substituent chemical shifts.

The ^{13}C cross polarization/magic angle spinning NMR spectrum and X-ray structure are obtained for 2,3-dimethoxynaphthalene which show similar features to 1,2-dimethoxybenzene with up to 1.9 ppm splitting of symmetry related aromatic sites. Both of these compounds exhibit specific van der Waals *intermolecular* C-H $\cdots\pi$ contacts in the crystalline state

2,3,5,6,7-5H-1,4,8-Benzotrioxacyclodecin (benzo-10-crown-3) and (benzo-10-crown-3) $_2\cdot$ LiClO_4 were prepared and studied by X-ray crystallography and ^{13}C cross polarization/magic angle spinning NMR. The hexa-covalent Li-complex illustrates for the

first time, a puckering of the benzene ring (torsional distortions up to 14°) in the absence of any non-bonded steric interactions.

Benzo-10-crown-3 is synthesized, in part to study the effect of the $C_{ar}-C_{ar}-O-C$ dihedral angle on aromatic ^{13}C shifts in benzo-crown ethers. The experimental trends are confirmed by gauge invariant atomic orbital ^{13}C shielding calculations on anisole and 1,2-dimethoxybenzene with incremental methoxyl rotations of 10° . It is confirmed that the protonated aromatic sites are directly related to the twist angle about the $C_{ipso}-O$ bonds and that the *meta* isotropic substituent chemical shift of a non-planar methoxy group is independent of the twist angle.

The *cis*-2,5,9-trioxabicyclo-[8.4.0]-tetradecane and *cis*-2,5,8,12-tetraoxabicyclo-[11.4.0]-heptadecane ethers were prepared along with deuterated analogues. For each compound, two isomers were detected at 210 K in solution by 1H and ^{13}C NMR. Equilibrium constants for cyclohexane ring inversion are 4.7 ± 0.8 and 2.2 ± 0.4 for the ten- and thirteen-membered crowns respectively. Results of molecular mechanics calculations indicate a conformational preference for the propoxy unit as equatorial.

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CHAPTER 1

Crown Ethers and Derivatives

*Everything that we can see, everything that
we can understand is related to
structure- perception is in patterns not
fragments.*

CYRIL S. SMITH

A- Introduction

Looking at the configuration of nuclei that make up a crystal is a little like looking at the stars in the sky. Unless you have a clear ordering principle, the patterns appear chaotic or random. Just as constellations are formed from the arbitrary ordering of the stars, there are many possible ordering principles that can describe the positions of atoms in a crystal.

B- The abridged Approach for Structure Determination

X-ray crystallography and solid state NMR are analytical tools that can be used independently or in combination for studying the structure and properties of solids^{(1),(2)}. X-ray diffraction is sensitive to long-range order, describes the unit cell over a nearly infinite volume and provides results which are averages over long time periods relative to molecular motion. Therefore at a given temperature, X-ray crystallography does not differentiate between static and dynamic disorder.

Solid state NMR determines the primary molecular structure and evaluates the effect of local *intermolecular* interactions on individual nuclei.

Ab initio ¹³C shielding calculations (LORG⁽³⁾ and GIAO⁽⁴⁾ methods) were used in

an attempt to understand the stereoelectronic contributions to ^{13}C chemical shifts.

This *abridged* approach for structure determination is a major theme of this thesis (Fig 1) and was used to investigate the parameters (motion, packing forces, torsional dependence, host-guest interactions,...) controlling and describing anisotropy in the solid state.

Fig. 1 The *abridged* approach for structure determination

3*n*-oxacrown-*n* (*n* = 5, 7) and some dialkoxyarylsystems (Fig 2) were used as model compounds for such an investigation.

C- Crown Ethers⁽⁵⁾⁻⁽⁸⁾

Coronands

Large amplitude motions in solid 12-crown-4 and 18-crown-6 complexes^{(9),(10)} have previously been detected, rapid on the NMR timescale about room temperature, and in the case of 18-crown-6· 2 CH₃(CN)₂ described as a "merry-go-round" motion. Further work is required to assess if the already known motional trends are an individual or collective characteristic of this family of crowns.

Fig. 2 Model compounds under investigation in this thesis

Therefore motional analyses of 15-crown-5· NaX and 21-crown-7· KI are undertaken (Chapter 3).

Benzo-crown ethers and model compounds

Model compounds

Increased ^{13}C NMR spectral multiplicity in the solid state over solution originates from locked molecular conformations⁽¹⁾. The conformational dependence of ^{13}C CP/MAS shifts has been well characterized in the literature^{(11),(12)} however relatively little work has been undertaken to properly document spectral multiplicity originating from packing effects in organic solids. With the X-ray packing diagram of 1,2-dimethoxybenzene and 2,3-dimethoxynaphthalene⁽¹³⁾ in hand, along with *ab initio* shielding calculations, a distinction between molecular *intra*- and *inter*-contributions to the ^{13}C multiplicity in the solid state is realized (Chapter 4).

In order to more fully comprehend the solid state electronic structure, shielding tensor analysis of veratrole⁽¹⁴⁾ and other simple crystalline planar methoxybenzenes is undertaken. The results are discussed in terms of the anisotropic contribution of a planar methoxy group on an aromatic system (Chapter 4).

Benzo-crown ethers

In this class of compounds the ¹³C CP/MAS shifts are clearly related to the molecular conformation. The impact of the torsional changes about the *ipso* carbon-oxygen bonds on the aromatic distribution is presented for 1,2-dialkoxybenz-annelated crown ethers and compared to theoretical trends found for methoxybenzene (Chapter 6)

Host-guest interaction

Crown ethers have been extensively studied as hosts which bind cations or neutral molecules by virtue of dipole-dipole interactions and/or hydrogen-bonding. The selectivity of crown ethers toward alkali metal ions has generally been explained in terms of "hole size selectivity" of the crown ethers⁽²⁰⁾. So the synthesis of a new crown is an inducement to analyze the complexing properties *via* the *abridged* approach (Chapter 5).

Cis-cyclohexano-crown ethers

Motional freedom in unsymmetrical *cis*-cyclohexano-crown ethers (*i.e.*, ring inversion), studied in this thesis, is intermediate between the unsubstituted coronands (motion) and the benzo-crown ethers (locked). So conformational analysis of these cyclic polyethers is undertaken *via* low temperature ¹H and ¹³C solution NMR and Molecular Mechanics calculations (Chapter 7).

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CHAPTER 2

Solid State NMR Spectroscopy

A- Introduction

NMR spectra of dilute nuclei in static powdered solids exhibit broad bands due to the superposition of signals from the randomly oriented single crystals. These broadening effects are effectively averaged in solution due to fast molecular tumbling. The development of multiple-pulse⁽¹⁾⁻⁽³⁾, cross-polarization⁽⁴⁾, dipolar decoupling^{(5),(6)} and magic angle spinning⁽⁷⁾⁻⁽¹⁰⁾ techniques for polycrystalline materials has made it possible to obtain well-resolved ^{13}C NMR line shapes, comparable to those in the liquid state⁽¹¹⁾. So "high resolution" NMR in solid state^{(12),(13)} is achieved at the expense of chemical shift anisotropy information, which is of two types; the first is the chemical shift dispersion which reflects the electronic structure of the solid, while the second is modulation of the dispersion due to molecular motion.

Magic angle spinning (MAS) ^{13}C NMR at different spinning rates^{(14),(15)} is a practical experimental technique to retrieve the information contained in the chemical shift anisotropies.

The effect of restricted molecular motions on dipolar, quadrupolar and chemical shielding NMR interactions is to reduce, but not eliminate the anisotropies. The powder line shapes are often sensitive to the rate of these dynamic processes. With the advent of the quadrupolar-echo technique⁽¹⁶⁾, ^2H line shape studies have become an important source of kinetic information regarding solid-state molecular dynamics^{(17),(18)}.

The theory behind these two techniques will be outlined in this chapter.

B- Fundamental Theory of Solid State NMR

The Hamiltonian experienced by a nucleus of spin I in the general case^{(19),(20)}

$$\mathcal{H} = \mathcal{H}_Z + \mathcal{H}_Q + \mathcal{H}_D + \mathcal{H}_{CSA} + \mathcal{H}_J \quad (1)$$

is composed of $\mathcal{H}_Z$ the Zeeman interaction, $\mathcal{H}_Q$ the quadrupolar interaction, $\mathcal{H}_D$ the nuclear dipolar interaction, $\mathcal{H}_{CSA}$ the chemical shielding interaction and $\mathcal{H}_J$ the J coupling. All of these Hamiltonians are considered as tensor interactions.

The Zeeman Interaction

$$\mathcal{H}_Z = \sum (-\gamma \hbar I_z) \cdot B_0 \quad (2)$$

where γ is the gyromagnetic ratio for the nucleus

$\mathcal{H}_Z$ is responsible for the removal of the degeneracy of the energy levels of any non-zero spin nucleus when placed in a magnetic field. It is the fundamental interaction between a spin $I \neq 0$ nucleus and a static magnetic field, which makes the NMR experiment possible.

The Nuclear Quadrupolar Interaction

The Quadrupolar Hamiltonian

The quadrupolar Hamiltonian represents the interaction between the nuclear quadrupole moment eQ and the electric field gradient (e.f.g.) tensor V at the nucleus and can be written as the double matricial product of a spin vector I and 2nd rank tensor Q (3 x 3 matrix)

$$\mathcal{H}_Q = I \cdot Q \cdot I \quad (3)$$

with $Q = eQ [2I(2I-1)]^{-1} \cdot V$

The e.f.g. tensor has three principal components V_{xx} , V_{yy} , V_{zz} and is defined in a coordinate system attached to the molecule, the principal axis system.

$$\begin{aligned} |V_{zz}| &\geq |V_{yy}| \geq |V_{xx}| \\ V_{xx} + V_{yy} + V_{zz} &= 0 \Leftrightarrow \text{traceless} \\ V_{xy} &= V_{yx} \text{ etc...} \Leftrightarrow \text{symmetric} \end{aligned}$$

the quadrupole Hamiltonian⁽²⁰⁾ becomes

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

with $eq = V_{zz}$

$I_{\pm} = I_x \pm i \cdot I_y$, the "raising" and "lowering" operators respectively.

$$\eta = (V_{yy} - V_{xx})/V_{zz}, \text{ the asymmetry parameter } (0 \leq \eta \leq 1) \quad (5)$$

For quadrupolar nuclei, $\mathcal{H}_Q$ in equation (1) is often much larger than $\mathcal{H}_h$ and $\mathcal{H}_s$, hence the spectrum can be approximated by the following expression.

$$\mathcal{H} = \mathcal{H}_Z + \mathcal{H}_Q \quad (6)$$

If the Zeeman and quadrupolar interactions are of the same order of magnitude, the eigenstates and eigenvalues of equation (6) can be obtained by solving a secular equation of order $2I+1$. In most cases, the Zeeman interaction is dominant, corresponding to the so called high magnetic fields ($E_z \gg E_Q$, E representing the energy of the described interaction). In this case, the quadrupolar interaction is considered as a perturbation of the Zeeman interaction, and the energy levels can be determined using the 2nd order perturbation theory (Fig. 3).

Fig. 3 Quadrupole perturbation of spin $I = 1$ Zeeman energy levels⁽¹⁹⁾
with $A = \frac{3}{8} (e^2 q Q / h) \cdot (3 \cos^2 \theta - 1 + \eta \cos 2\phi \sin^2 \theta)$

Quadrupolar energy levels for a single crystal

For simplification, it is assumed the quadrupole gradient has cylindrical symmetry $V_{xx} = V_{yy}$ so that η vanishes in equation (5). If a new frame of reference is considered Oxyz, so the Oz axis is in the OXZ plane and parallel with the external magnetic field, one can write the following.

$$I_z = I_z \cos \theta + I_x \sin \theta \quad (7)$$

so now equation (4) becomes

$$\mathcal{H}_Q = e^2 q Q [4I(2I-1)]^{-1} \cdot \left[\frac{1}{2} (3 \cos^2 \theta - 1)(3I_z^2 - I^2) + (3/2) \sin \theta \cos \theta \{I_z(I_+ + I_-) + (I_+ + I_-)I_z\} + (3/4) \sin^2 \theta (I_-^2 + I_+^2) \right] \quad (8)$$

The energy levels of the quadrupolar Hamiltonian

$$E = E^{(0)} + E^{(1)} + E^{(2)} + \dots \quad (9)$$

following the 2nd order perturbation theory can be written

$$E_m^{(0)} = -\gamma \hbar B_0 m = -\hbar m \nu_L$$

$$E_m^{(1)} = \frac{1}{4} \hbar \nu_Q (3\mu^2 - 1)(m^2 - a/3)$$

$$E_m^{(2)} = -(\hbar/12)(\nu_Q^2/\nu_L) \cdot [3\mu^2/2 (1 - \mu^2)(8m^2 - 4a + 1) + \frac{3}{8} (1 - \mu^2)^2(-2m^2 + 2a - 1)]$$

here

$$\nu_Q = 3e^2qQ [h2I(2I-1)]^{-1}$$

$$a = I(I+1)$$

$$\mu = \cos\theta$$

$$\nu_L = \gamma B_0/2\pi$$

and m is the quantum number for the z component of the angular momentum I .

The pure Zeeman energy is $E^{(0)}$ while $E^{(1)}$, $E^{(2)}$ are dependent on the magnitude of the quadrupolar frequency. The $E^{(1)}$ term is independent of the Zeeman frequency while $E^{(2)}$ is inversely dependent on the Zeeman frequency.

The resonance frequency⁽²¹⁾ (for $\Delta m = 1$ transitions) is written as the following.

$$\begin{aligned} \nu(m_{-1} \rightarrow m) &= (E_{m-1} - E_m)/\hbar \\ &= \gamma B_0/2\pi \pm \frac{1}{2}\nu_Q \cdot (m - \frac{1}{2}) (3\mu^2 - 1) \end{aligned} \quad (10)$$

For deuterium, the spin angular momentum is 1, therefore two equal intensity transitions $\nu_{(0 \rightarrow 1)}$ and $\nu_{(-1 \rightarrow 0)}$ separated by $\Delta\nu$ are observed.

$$\Delta\nu = \frac{1}{2} \nu_Q \cdot (3\cos^2\theta - 1) \quad (11)$$

In the solid state, the quadrupolar splitting exhibits an angular dependence whereas in the liquid state, rapid molecular reorientation averages the $(3\cos^2\theta - 1)$ term to zero. When there is no cylindrical symmetry of the quadrupole gradient ($\eta \neq 0$) then

$$E_m^{(1)} = eQ [2I(2I-1)]^{-1} \cdot [3m^2 - I(I+1)] \cdot V_{zz}$$

The perturbed eigenstates depend on both polar angles θ and ϕ (Fig. 4), which describe the orientation of the magnetic field in the principal axis system of the e.f.g..

Fig. 4 (a) orientation of the C-D bond with respect to the magnetic field,
 (b) C-D bond showing the orientation of the three e.f.g. components,
 (c) definition of the polar angles θ and ϕ made by the magnetic field vector in the principal axis system of the e.f.g.

Now the perturbed energy can be written as

$$E_m^{(1)} = \frac{1}{4} e^2 q Q \cdot (3m^2 - 2) [\cos^2\theta + \frac{1}{2} \sin^2\theta (\eta \cos 2\phi - 1)] \quad (12)$$

yielding transition frequencies

$$\nu = \gamma B_0 / 2\pi \pm (3e^2 q Q / 4h) [\cos^2\theta + \frac{1}{2} \sin^2\theta (\eta \cos 2\phi - 1)] \quad (13)$$

For the ^2H nucleus in rigid organic compounds, V_{zz} is usually close to being axially symmetric about the C-D bonds, therefore the splitting in equation (11) is sensitive to the orientation of the C-D bond in the magnetic field. The variation in the magnitude of the splitting, as a function of the crystal orientation in the magnetic field, can give the q.c.c. and η directly as well as the orientation of V_{zz} with respect to the crystal axes.

Quadrupolar energy levels for powder samples

For powder samples where many small crystals are randomly oriented, a broad ^2H resonance envelope is obtained. In order to predict the lineshape of a polycrystalline sample, calculation of the contributions from all orientations described by equation (13) is necessary. Each orientation in the powder sample gives two resonances, and these must be given equal statistical weight. The variables in the calculation are the q.c.c., η and, in the case where some motion is present, the rates and directions of the axes of motion. The resultant powder spectrum is characterized by three features (Fig. 5).

$$\text{outer shoulders separated by} \quad \Delta\nu_{zz} = \nu_Q \quad (14)$$

$$\text{inner shoulders separated by} \quad \Delta\nu_{yy} = \frac{1}{2} (1 + \eta) \cdot \nu_Q \quad (15)$$

$$\text{and a pair of singularities separated by} \quad \Delta\nu_{xx} = \frac{1}{2} (1 - \eta) \cdot \nu_Q \quad (16)$$

$$\text{where } \Delta\nu_{zz} \propto |V_{zz}|$$

$$\Delta\nu_{yy} \propto |V_{yy}|$$

$$\Delta\nu_{xx} \propto |V_{xx}|$$

Fig. 5 ^2H lineshapes for different values of the asymmetry parameter
 $\eta = 0, \eta = 0.21, \eta = 1$

Molecular Dynamics

The molecular motion gives rise to a time averaged e.f.g. tensor, which may not have the same orientation as the static tensor. Motions start to affect the lineshape when the rate becomes similar to the linewidth of the individual powder lineshape components, $\Delta\nu_{1/2} = (\pi T_2)^{-1}$, with a maximum effect when the rate is similar to the quadrupole splitting.

Therefore molecular motions can be divided in three regimes;

slow regime for rates $< 10^4 \text{ s}^{-1}$	- static lineshape
intermediate regime	- distorted lineshapes encountered
fast regime for rates $> 10^7 \text{ s}^{-1}$	- narrowed lineshape
	independent of motional rate

The quadrupolar echo experiment cannot distinguish slow moving molecules from rigid molecules, however other pulse techniques can. In the fast motion regime, a new averaged e.f.g. tensor must be invoked in order to simulate the powder lineshape. The fast motion limit (f.m.l.) case is independent of the motional rate, therefore different simultaneous fast motions cannot be distinguished. Only the intermediate regime spectra provide information about the rate and mechanism of the motion⁽²²⁾⁻⁽²⁵⁾.

In order to simulate f.m.l. ^2H spectra, one must first determine the time averaged e.f.g. tensor. To proceed, a description of the e.f.g. tensor in a coordinate frame other than the principle axis system (PAS) is needed, such that the motion is symmetric about the z-axis. This is done by making use of the angles α , β and γ between the two axis systems (Fig.6) known as the Euler angles⁽²⁶⁾ and the rotation matrix $R(\alpha, \beta, \gamma)$ ⁽²⁷⁾

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

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

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

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

The tensor is then described in the new frame by

$$V(\alpha, \beta, \gamma) = R \cdot V_{PAS} \cdot R^{-1} \quad (17)$$

The time averaged tensor $V'(\alpha, \beta, \gamma)$ for each deuteron is a simple average of the tensors $V_i(\alpha, \beta, \gamma)$ at each of the n sites visited by the deuteron given by the following expression.

$$V'(\alpha, \beta, \gamma) = 1/n \cdot \sum V_i(\alpha, \beta, \gamma) \quad (18)$$

This procedure must be carried out for each deuteron affected by the motion. For n -fold rotations, where $n \geq 3$, the averaged spectrum is always axial (*i.e.*, $\eta = 0$).

Fig. 6 Diagram showing the three rotations through the Euler angles α , β and γ

The Nuclear Dipolar Interaction

$\mathcal{H}_D$ represents the through-space interaction between magnetic dipoles, and in a strong magnetic field, is treated as a perturbation of the Zeeman interaction. In polar coordinates, the secular (stationary) part of the Hamiltonian can be written as

$$\mathcal{H}_0 = \hbar R (3\cos^2\theta - 1) [-I_1 I_2 + \frac{1}{4} (I_{1-}I_{2+} + I_{1+}I_{2-})] \quad (19)$$

$$\mu_0 = 4\pi \times 10^{-7} \text{ kg m s}^{-2} \text{ A}^{-2}$$

$R = (\mu_0 \gamma_1 \gamma_2 \hbar / 4\pi) (r_{12})^{-3}$ is the dipolar coupling constant

r_{12} is the internuclear vector and θ the angle between r_{12} and B_0 .

In the case of homonuclear interactions, the second term in the Hamiltonian often referred to as the flip-flop term, causes efficient transfer of magnetization throughout the sample by a process known as spin diffusion. This is not true for the heteronuclear case.

$$\mathcal{H}_{\text{Dhetero}} = \hbar R (3\cos^2\theta - 1) (-I_1 I_2) \quad (20)$$

For *dilute* nuclei, the homonuclear interactions are neglected since the dependence is on the cube of the distance between spins.

In a rigid solid, if the sample spins with an angular frequency ω_r about an axis which intersects the external magnetic field at an angle β , then we have

$$\cos\theta(t) = \cos\beta \cos\beta_{12} + \sin\beta \sin\beta_{12} \cos(\omega_r t + \phi_{12}) \quad (21)$$

where β_{12} is the angle between r_{12} and the axis of rotation
and ϕ_{12} is the initial azimuth angle of r_{12} .

By squaring and taking the time average of equation (21), the following is true

$$\cos^2\theta = (1/6) (3\cos^2\beta - 1) (3\cos^2\beta_{12} - 1) + \frac{1}{3} \quad (22)$$

By combining equations (20) and (22), the time averaged value of the truncated dipolar Hamiltonian is obtained

$$\mathcal{H}_D^t = \frac{1}{2} \hbar R (3\cos^2\beta - 1)(3\cos^2\beta_{12} - 1) \cdot [-I_1 I_2 + \frac{1}{4} (I_{1-}I_{2-} + I_{1+}I_{2+})] \quad (23)$$

If a solid sample rotates about an axis inclined at the "magic" angle $\beta = 54.7^\circ$ to the external magnetic field B_0 , then $3\cos^2\beta - 1 = 0$, and the dipolar broadening of the NMR line vanishes, resulting in the same resolution as for liquid samples.

The Chemical Shift Anisotropy

Shielding Tensors

Another source of NMR line broadening in solid samples is chemical shift anisotropy (CSA), the Hamiltonian of which is given by

$$\mathcal{H}_{\text{CSA}} = \sum \gamma \hbar I_{zi} \sigma_i B_0 \quad (24)$$

The electronic shielding of a particular nucleus i is described by the shielding tensor σ_i . It has a three dimensional character and depends on the molecular orientation with respect to the external magnetic field, since the electronic cloud in even the simplest molecule is not spherically symmetric. It can be separated into a symmetric tensor σ_s and an antisymmetric tensor σ_a defined by

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

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

where σ^T is the transpose of σ .

The antisymmetric tensor contributes negligibly to the NMR spectrum and will not be considered further. If the symmetric part of the tensor has principal values σ_{ii} oriented along the principal axes, and if θ_{ii} is the angle made between each of the tensor components with respect to B_0 , then

$$\sigma_{zz} = \sum \sigma_{ii} \cos^2 \theta_{ii} \quad (25)$$

If the solid sample is rotated with an angular frequency ω_r about an axis inclined at an angle β to the magnetic field B_0 and χ_{ii} are the angles with respect to the principal axes of the sample (Fig. 7), then the following relationship exists

$$\cos \theta_{ii} = \cos \beta \cos \chi_{ii} + \sin \beta \sin \chi_{ii} \cos(\omega_r t + \Psi_{ii}) \quad (26)$$

where Ψ_{ii} is the initial azimuthal angle.

So, the time average of σ_{zz} is given by

$$\sigma_{zz} = (3 \sin^2 \beta / 2) \cdot \sigma_i + \frac{1}{2} (3 \cos^2 \beta - 1) \sum \sigma_{ii} \cos^2 \chi_{ii} \quad (27)$$

If $\beta = 54.7^\circ$ ($\cos^2 \beta = 1/3$ and $\sin^2 \beta = 2/3$) then $\sigma_{zz} = 1/3 \cdot \text{Tr}(\sigma)$. Upon spinning at this magic angle, all orientations with respect to B_0 are sampled over time leading to a scalar quantity for the chemical shift tensor. This is the origin of the chemical shift value in solution.

Fig. 7 Relationship of the chemical shift tensor components with respect to the magic angle rotation axis and the magnetic field direction

The CSA interaction as a function of time arises because of sample rotation and can be written as

$$\begin{aligned} \mathcal{H}_{\text{CSA}} = \sum \sum I_{iz} B_o \sigma_{ip} [& \cos^2\beta \cos^2\chi_{ip} \\ & + 2 \cos\beta \sin\beta \cos\chi_{ip} \sin\chi_{ip} \cos(\omega_r t + \Psi_{ip}) \\ & + \sin^2\beta \sin^2\chi_{ip} \cos^2(\omega_r t + \Psi_{ip})] \end{aligned} \quad (28)$$

The interaction contains periodic terms with frequency $\nu_r = \omega_r / 2\pi$. This time dependence gives rise, in the free induction decay (FID), to a series of echoes separated by a time interval $2\pi/\omega_r$. When the FID is Fourier transformed to obtain the spectrum, these echoes give rise to spinning sidebands separated from the central isotropic spectral line at intervals equal to the spinning frequency ν_r . The intensities of the spinning sidebands are related to the CSA, and provide an opportunity to recover the shift parameters.

Shielding tensor analysis of single crystals⁽²⁸⁾⁻⁽³³⁾

The principal elements of the chemical shift tensor, and the orientation of the principal axes on the molecular frame, can be obtained from single crystal measurements. Due to sensitivity limitations, these studies require large crystals (50 mm³ or more) where each unique carbon in the unit cell gives one line (Fig. 8). This technique involves a systematic rotation of the single crystal in three mutually perpendicular directions with respect to the external magnetic field (Fig. 9), which produces rotational patterns (Fig. 10). From these values, the shielding tensors in the bulk crystal frame can be calculated. In order to transform into the molecular frame, the relative orientation of the crystal and laboratory frames (Fig. 11) is needed, as well as an X-ray structure. Finally, diagonalization in the molecular frame gives access to the magnitude and orientation of the principal shielding tensors.

Fig. 8 (a) Naphthalene molecules in the unit cell⁽³⁴⁾. Carbon 1 of the molecule at the origin of the unit cell is blackened, (b) representative ^{13}C spectrum of single crystal naphthalene in which all ten theoretically possible lines are resolved⁽³⁵⁾

Fig. 9 Simple goniometer assembly⁽³⁶⁾

Fig. 10 Rotational plot for a single crystal of acetophenone⁽³²⁾

Fig. 11 Orientation of the rotation axis (z axis of cube x, y, z) and the plane of measurement with respect to the crystal axes a, b and c^* for acetophenone⁽³²⁾

Tensor analysis of powder patterns⁽³⁷⁾

Powdered materials are used for chemical shift studies when; *i*) there are a large number of molecules in the crystallographic unit cell, *ii*) single crystals are not available or *iii*) when only the principal elements of the tensor are of interest. A number of NMR spectroscopic techniques are available to extract the shift anisotropy from a powder spectrum; (a) measurement and analysis of the static powder line shape⁽³⁸⁾, (b) simulation of the variable angle sample spinning line shapes^{(39),(40)}, (c) the magic angle hopping experiment^{(41),(42)}, (d) the dynamic angle spinning technique^{(43),(44)}, (e) the stop-and-go technique⁽⁴⁵⁾ and (f) the technique involving magic angle spinning utilizing rf pulses to regain the CSA information⁽⁴⁶⁾.

a- Static powder samples⁽³⁸⁾

Under static conditions, the ^{13}C NMR spectrum is a broad line shape, containing all orientations with respect to the magnetic field yet there are two techniques to obtain the principal values of the chemical shift tensor. The first is a one pulse experiment with high power ^1H decoupling to remove the ^1H - ^1H and ^1H - ^{13}C dipolar interactions, and the second a cross-polarization (CP) experiment⁽⁴⁾ with ^1H decoupling.

b- Slow magic angle spinning

the method of Moments⁽¹⁴⁾

The second and third moments of the NMR spectra are related to the chemical shift parameters and can, in principle, be used to extract the chemical shift anisotropy from the sideband intensities.

$$M_2 = (\omega_0 \delta)^2 (3 + \eta^2)/15 \quad (28)$$

$$M_3 = 2(\omega_0 \delta)^3 (1 - \eta^2)/35 \quad (29)$$

where $\delta = \sigma_{33} - \sigma_{\text{iso}}$ and $\eta = (\sigma_{22} - \sigma_{11})/\delta$

$\sigma_{33} > \sigma_{22} > \sigma_{11}$ are the principal values of the shielding tensor.

This method requires accurate measurements of the intensities of *all* sidebands, which is seldom feasible, even for moderately complex materials, due to overlap. The alternative is to derive the chemical shift parameters directly from the individual sideband intensities, as outlined next.

the method of Herzfeld and Berger⁽¹⁵⁾

Spinning sidebands are separated by an integral number of rotational frequency $N\omega_r$ from a central isotropic line I_0 . In order to identify the sideband of N^{th} order, S_N , one varies the rotor frequency and identifies S_N as the line that moves by a frequency interval $N\omega_r$ from I_0 . The relative intensity I_N of the N^{th} sideband can be expressed as:

$$I_N = \pi/4 \cdot \int_0^\pi \int_0^{2\pi} |F|^2 d\alpha \sin\beta d\beta$$

α, β : Euler angles

$$F \propto f(\mu, \mu\rho) \quad \text{with} \quad \mu = \gamma H_0 (\sigma_{33} - \sigma_{11})/\omega_r \quad (30)$$

$$\rho = (\sigma_{11} + \sigma_{33} - 2\sigma_{22})/(\sigma_{33} - \sigma_{11}) \quad (31)$$

Contour maps constructed *via* bicubic spline interpolation of I_N/I_0 ($N = \pm 1, \pm 2, \pm 3, \pm 4, \pm 5$) have been developed to assist the experimenter in making the analysis of the sideband intensities (Fig. 12). One takes the I_N/I_0 ratio and identifies the correct curve on the appropriate graph. After identifying as many sidebands as possible, the contour maps are superimposed and the intersection points give rise to μ and ρ . These two parameters, combined with the I_0 give the three principal shifts.

Fig. 12 Contour plots of $I_{\pm N} / I_0$ in the half-strip $\mu \geq 0$ and $-1 \leq \rho \leq 1$ ⁽¹⁵⁾

Fig. 12 continued⁽¹⁵⁾

Fig. 13 Graphical analysis of the sideband intensities from a $\text{Ba}[\text{PO}_2(\text{OEt})_2]$ spectrum to obtain estimates of μ and ρ (circle) with uncertainty (rectangle)⁽¹⁵⁾

c- the hopping experiment⁽⁴¹⁾

This 2D technique separates the isotropic chemical shift from the individual chemical shift anisotropy patterns, by projection onto two different frequency axes (F1, F2 domains, respectively). In this process the sample does not rotate smoothly at the magic angle but rather "hops" in 120° increments between evolution segments t_1 . The hopping is technically demanding but is mathematically equivalent to continuous rotation about the magic angle. The basic pulse sequence (Fig. 14) is repeated four times with different ^{13}C rf phases to give the total magnetization, from which the 2D experiment (F1, F2) is performed.

Fig. 14 Pulse sequence of one of four steps in the magic angle hopping experiment and evolution of the magnetization during this sequence. During the "hop" period the sample is rotated by 120° about the magic angle axis and the ^1H decoupling switched off⁽⁴²⁾

Fig. 15 Magic angle hopping ^{13}C spectrum of 1,4-dimethoxybenzene⁽⁴¹⁾

Tensor analysis by theoretical methods

Calculations of ^{13}C shielding tensors using the coupled Hartree-Fock⁽⁴⁶⁾ theory give good results, but large basis sets are necessary and calculations are limited to small and highly symmetrical molecules. Other methods are available to overcome this problem; GIAO (Gauge Invariant Atomic Orbitals)⁽⁴⁷⁾, IGLO (Individual Gauge for Localized Orbitals)⁽⁴⁸⁾ and LORG (Localized Orbital/ local oRiGin)⁽⁴⁹⁾. Both the GIAO and IGLO methods originate from London's work⁽⁵⁰⁾ on diamagnetic susceptibilities. In the GIAO method, the local origins are the atomic centers and each atomic orbital carries its own complex phase factor determined by the value of the magnetic vector potential at the origin for this orbital. With the IGLO method the centroid of localized orbitals are used as local origins, defining complex phase factors for these molecular orbitals. In the LORG method, the local gauge origin derives from Ramsey's expressions⁽⁵¹⁾ for magnetic shielding, by applying the random phase approximation (RPA)⁽⁵²⁾ in a localized orbital scheme and utilizing the properties of the RPA solutions. The resulting expressions for the shielding tensor can be divided into bond contributions and bond-bond coupling contributions.

The J Coupling Interaction

$\mathcal{H}_J$ is the spin-spin coupling interaction. It must be summed over all like and unlike spins. In order to extract J coupling information, multiple-pulse decoupling techniques are utilized rather than the standard dipolar decoupling, which removes the effects of J coupling from the spectrum completely. Although very important in solution, J-coupling in the solid state is usually only observed with the heavier nuclides, when decoupling is not used.

C- Experimental techniques

Basic Pulse Technique

"Quadrupolar echo" technique^{(16),(53)}

The breadth of the ^2H solid state spectrum requires rapid digitization of the signal, so a simple one-pulse experiment would require the data collection to begin as little as 1 μs after the pulse. During the time required for recording the first few points, the probe and related electronics are recovering from the effects of the pulse. Unfortunately, errors in the first few data points distort both the shape of the peak and the baseline. The distortions are a chronic problem in pulsed NMR studies of wide lines, and are very serious when one must rely on lineshape analysis to interpret the data.

These problems are removed by using an echo technique to generate the spectrum. For ^2H NMR, it is possible to produce a "quadrupolar echo" with a very simple pulse sequence (Fig. 16)

$$(\pi/2)_x - \tau_1 - (\pi/2)_y - \tau_2 - \text{Acquire} \quad (32)$$

After the $(\pi/2)_x$ pulse, the signal is allowed to decay for a time τ_1 , where τ_1 is shorter than

the transverse relaxation time T_2 . After the $(\pi/2)_y$ pulse, the signal builds up again until it reaches a maximum after a time τ_2 . At this point, the receiver is switched on and the echo decay is collected. In principle $\tau_1 = \tau_2 = 50 \mu\text{s}$ however in practice, τ_2 is made shorter than τ_1 , in order to locate the echo maximum more precisely.

While this sequence is easy to describe and use, it cannot be interpreted with a vector model, such as the Hahn echo sequence for T_2 measurements on spin $I = 1/2$ systems in solution. The quadrupolar echo sequence can also be used in conjunction with the inversion recovery method for measuring T_1 relaxation times.

Fig. 16 Depiction of the quadrupolar sequence

Cross-polarization (CP) ⁽⁴⁾

This experiment (Fig. 17) is commonly used to enhance the sensitivity of rare nuclear spins (S), such as ^{13}C , through two mechanisms. Firstly, by increasing the population difference between the "spin up" and "spin down" states and secondly, by effectively shortening the relaxation times hence reducing the time between successive FID's. The CP pulse sequence starts with a strong $\pi/2$ pulse at the resonance frequency of the abundant spins (I), such as ^1H , which rotates the I spin magnetization in the x' - y' plane. This is followed by a phase-shifted pulse (x' direction in the rotating frame) on the I spins which locks the magnetization along the field direction. This spin-locking procedure creates a continuous increase in irradiation along the y' axis, so that the

magnetization will precess about B_{1I} in the rotating frame, while at the same time a pulse, B_{1S} , is applied to the I and S spins. The angular frequencies of the I and S spins are adjusted by varying the oscillating field amplitudes establishing the following equality,

$$\gamma_S \cdot B_{1S} = \gamma_I \cdot B_{1I} \quad (33)$$

where γ_S and γ_I represent the gyromagnetic ratios of the S and I spins respectively.

Under such conditions, the z' components of the magnetization for the I system and the S system have the same time-dependence, and a resonant energy exchange between the two can readily take place, through a mutual spin flip mechanism (flip-flop term of the dipolar interaction). The frequency condition is called the *Hartmann-Hahn* condition⁽⁵⁴⁾. Compared to conventional carbon excitation (where $I = {}^1\text{H}$ and $S = {}^{13}\text{C}$), this transfer results in a four-fold increase (since the gyromagnetic ratio for protons is approximately four times that for ${}^{13}\text{C}$) of the amplitude of the carbon FID, provided that the proton spin-lattice relaxation time in the rotating frame is longer than the rate at which the cross-relaxation occurs. After optimum transfer, the B_{1S} field is turned off, resulting in a free precession signal which may then be digitized, meanwhile keeping the B_{1I} for decoupling purposes.

Fig. 17 Depiction of the cross polarization technique⁽³³⁾

Often, the magnetization transfer can be repeated immediately after the FID has been digitized, making the signal to noise ratio even greater. Another advantage of the CP technique is that the delay between successive sequences is now governed by the usually much shorter relaxation time of the I spins.

Techniques

Cross polarization - magic angle spinning (CP/ MAS) experiment

In the solid state, sources of line broadening such as chemical shielding anisotropy and dipole-dipole interactions, are proportional to $(3\cos^2\theta - 1)$ where θ is the angle between the external magnetic field and the axis about which the sample is caused to spin. The magic angle is defined such that $3\cos^2\theta - 1 = 0 \Rightarrow \theta = (\arccos 1/\sqrt{3}) = 54.7^\circ$, hence spinning at this angle averages these interactions to zero^{(9),(55)-(58),(59)}.

By application of CP, there is a considerable enhancement of intensity in the spectrum but no resolution. Dipolar decoupling combined with CP, gives the recognizable features of a number of overlapping chemical shift powder patterns and finally, the CP/ MAS technique yields the high resolution spectrum. Sample spinning can impart an oscillatory time-dependence to the dipolar interaction between the I and S spins that leads to polarization transfer. Care should be taken since, if the dipolar fluctuation energy conserving mutual spin flips of the S spin is close to the spinning rate, the CP process can be affected resulting in appreciable line broadening of the S spin resonance.

Dipolar dephased CP/ MAS experiment

This is a spectrum editing technique used to suppress S spins strongly coupled to the I spin system (for instance $-\text{CH}_2-$ and $-\text{CH}<$ signals), while signals from quaternary carbons or those with considerable motional averaging, (i.e. CH_3-), where the decay is slower during the time decoupling is withheld, survive. This technique makes use of a

modified CP pulse sequence, where the ^1H field is turned off between the traditional CP step and the acquisition. During this time, the protonated ^{13}C spins dephase very quickly under the influence of the proton dipolar field, relative to those with no attached protons. After a relatively short time (usually 40 μs), the ^1H field is reinstated to decouple the dipolar interactions during the ^{13}C FID acquisition. The non-protonated carbons which were not fully dephased during the delay are hence the sole contributors to the ^{13}C FID.

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CHAPTER 3

Motion Studies of 15-Crown-5 and 21-Crown-7 Complexes

A- Introduction

Crown-ethers were discovered by *Pedersen*⁽¹⁾ in 1967 due to their capacity to form complexes with inorganic salts or polar neutral molecules. Solid state motion in these complexes is evident in the dipolar dephased ¹³C CP/ MAS spectra where residual intensity is observed for the protonated carbons. In order to characterize this motion, one must utilize ²H NMR spectroscopy on a powdered sample at different temperatures. The experimental line shapes can then be simulated using crystallographic data and appropriate models of motion. Deuterium powder line shapes show either two or three pairs of features separated by the frequencies;

$$\begin{aligned}\Delta\nu_{zz} &= \nu_Q \\ \Delta\nu_{yy} &= \frac{1}{2} \cdot \nu_Q (1 + \eta) \\ \Delta\nu_{xx} &= \frac{1}{2} \cdot \nu_Q (1 - \eta)\end{aligned}$$

where $(e^2qQ/h) = 2\nu_Q/3 = \chi$ is the quadrupole coupling constant and $\eta = (\Delta\nu_{yy} - \Delta\nu_{xx})/\Delta\nu_{zz}$ is the asymmetry parameter. The $\Delta\nu_{ii}$ are proportional to the principal axis components of the effective quadrupole coupling tensor, but information regarding the signs is lost.

Recently *Ratcliffe et al.* have characterized the motion of 1,4,7,10,13,16-hexaoxacyclooctadecane(18C6)⁽²⁾ and 1,4,7,10-tetraoxacyclododecane(12C4)⁽³⁾ complexes where both crowns rotate about the centre of the ring. For 18C6· 2CH₂(CN)₂ the motion is X-ray invisible and involves a six site combined rotation and conformational re-adjustment, similar to that of the merry-go-round. With 12C4· LiSCN, the rotation is accompanied by a rapid flipping of the O-CH₂-CH₂-O units which is manifest as disorder

in the crystal.

To assess whether these models of motion are intrinsic to crown-ether complexes, 15C5 (1,4,7,10,13-pentaoxacyclopentadecane) and 21C7 (1,4,7,10,13,16,19-heptaoxacycloeicosane) are presently investigated. In the Na^+ complexes of 15C5, three different conformers are known to exist⁽⁴⁾, which implies that crystal packing forces exert a significant influence on the ring conformation. In the X-ray structure of 15C5· NaClO_4 , the Na^+ ion is seven-coordinate while for 15C5· NaI , a six-coordinate species is expected. In the present work, an X-ray study on the 15C5· NaI was carried out to examine the effect of seven- *versus* six-coordinate Na^+ on the conformational features of 15C5, and as well to examine the coordination geometry and $\text{Na}\cdots\text{O}$ distances. For 21C7, few single crystal structures are available⁽⁵⁾. This ligand has a cavity radius of 1.7 Å corresponding exactly to the radius of $\text{Cs}^{+(6),(7)}$, but is flexible, so it can wrap around a smaller metal ion such as K^+ .

B- Results and discussion

15C5 as Ligand

NMR Data Characteristic of Motional Behavior

In solution 15C5, rapidly interchanges among many conformations, and only a single ^{13}C or ^1H peak is observed down to 210 K. Similarly, the ^{13}C CP/MAS spectrum of 15C5· NaI shows a single peak at 70.05 ppm with no spinning side bands, down to 210 K. Lowering the temperature broadens the peak from $\Delta\nu_{1/2} = 11.5$ Hz at 330K to 230.0 Hz at 210 K (Fig. 18).

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Fig. 18 ^{13}C CP/ MAS spectrum of 15C5· NaI as a function of temperature
($\delta_c = 70.05$ ppm)

X-ray Structure of 15C5· NaI

The conformation of 15C5· NaI⁽⁸⁾ obtained in the present work by X-ray diffraction at 193 K, is essentially identical to that found for the NaClO₄ complex⁽⁹⁾ (Fig. 19, 20 and Tables 1, 2, 3). All the torsion angles for O-C-C-O units are *gauche* (synclinal) and for

C-O-C-C units *trans* (*antiperiplanar*) with the exception of C3-O2-C2-C1 which is equal to -90.2° (*anticlinal*). The conformation with the 13-angle sequence (ap sc⁻ ap ap sc⁻ ap)₂ ap is the most frequently encountered for this macrocyclic ether⁽¹⁰⁾. Due to the asymmetric conformation, a splitting of the single peak in the low temperature CP/ MAS spectrum is anticipated but was not resolved.

In 15C5· NaI, the oxygen atoms are strongly ligated as evidenced by Na...O distances ranging from 2.40 to 2.44 Å with a mean distance of 2.42 Å, identical to that for 15C5· NaClO₄⁽⁹⁾. The oxygen atoms define a least squares plane, with the consecutive distances from this plane for O1 through O5 being; 0.025, -0.290, 0.486, -0.454, 0.217 Å and an average deviation of 0.28 Å, this latter value identical to 15C5· NaClO₄⁽⁹⁾. The Na⁺ ion resides 0.80 Å from the crown plane on the same side as O2 and O4. By contrast, 15C5· NaClO₄ has three oxygens on the same side as the Na⁺, which is situated 0.77 Å from the plane⁽⁹⁾. The nature of the counterion naturally influences the crystal packing, hence the subtle distortions in the pentagonal pyramidal coordination.

Fig. 19 ORTEP diagram of 15C5· NaI with atomic numbering scheme

Table 1 Cartesian coordinates and Biso factors of 15C5· NaI

	x	y	z	Biso
I	0.24171 (4)	0.99635 (3)	0.108129(22)	2.925 (16)
Na	0.25128 (21)	0.98425 (18)	0.30726 (13)	2.24 (8)
O1	0.4338 (4)	0.8289 (3)	0.36342 (24)	2.60 (16)
O2	0.1553 (4)	0.7735 (4)	0.3438 (3)	2.65 (16)
O3	0.0704 (4)	1.0234 (3)	0.3921 (3)	2.70 (16)
O4	0.2125 (4)	1.2223 (4)	0.3270 (3)	2.96 (17)
O5	0.4651 (4)	1.1010 (4)	0.3726 (3)	2.68 (16)
C1	0.3926 (6)	0.7211 (6)	0.4155 (4)	3.1 (3)
C2	0.2564 (6)	0.6686 (5)	0.3623 (4)	3.2 (3)
C3	0.0732 (6)	0.7871 (6)	0.4095 (4)	3.3 (3)
C4	-0.0177 (6)	0.9094 (7)	0.3848 (4)	3.4 (3)
C5	0.0017 (6)	1.1445 (6)	0.3577 (4)	3.3 (3)
C6	0.1047 (6)	1.2571 (6)	0.3728 (4)	3.5 (3)
C7	0.3340 (7)	1.3014 (5)	0.3508 (4)	3.6 (3)
C8	0.4502 (6)	1.2261 (6)	0.3224 (4)	3.3 (3)
C9	0.5742 (6)	1.0185 (6)	0.3554 (5)	3.7 (3)
C10	0.5653 (6)	0.8855 (6)	0.4018 (4)	3.4 (4)

Table 2 Crystallographic data of 15C5· NaI

Formula	C ₁₀ H ₂₀ O ₅ NaI
fw	370.16
Crystal system	monoclinic
Space group	P2 ₁ /c
a, Å	9.8719 (24)
b, Å	9.9071 (20)
c, Å	15.4065 (23)
V, Å ³	1477.6 (5)
Z (molecules/ cell)	4
D _c (g/ cm ³)	1.664
Crystal dimensions, mm ³	0.2 x 0.2 x 0.2
Radiation (λ, Å)	Mo Kα (1, 0.7107)
Octants measured	h(-11 to +11), k (0 to +11), l (0 to +18)
θ _{max} (°)	24.9
Temperature (K)	193
No. of unique reflections	2613
No. of reflections measured	2772
No. of reflections with I _{net} > 2.5 σI _{net}	1988
I _σ / I ratio	0.012
R _f	0.037
R _w	0.052

Table 2 (continued)

GoF	2.29
Maximum and minimum residual ρ in final difference Fourier map, $\text{e}\text{\AA}^3$	1.97 and -0.61

Table 3a Bond distances ($\text{\AA}$) of 15C5·NaI

Na-I	3.053 (2)	O3-C5	1.429 (7)
Na-O1	2.398 (4)	O4-C6	1.430 (7)
Na-O2	2.405 (4)	O4-C7	1.420 (7)
Na-O3	2.442 (4)	O5-C8	1.453 (7)
Na-O4	2.418 (4)	O5-C9	1.418 (9)
Na-O5	2.444 (4)	C1-C2	1.523 (8)
O1-C1	1.441 (7)	C3-C4	1.512 (9)
O1-C10	1.432 (7)	C5-C6	1.496 (9)
O2-C2	1.431 (6)	C7-C8	1.504 (9)
O2-C3	1.422 (7)	C9-C10	1.509 (9)
O3-C4	1.416 (7)		

Table 3b Bond angles ($^\circ$) of 15C5·NaI

I-Na-O1	105.12 (11)	Na-O3-C4	109.5 (3)
I-Na-O2	109.47 (11)	Na-O3-C5	106.2 (3)
I-Na-O3	130.52 (12)	C4-O3-C5	113.6 (4)
I-Na-O4	96.53 (11)	Na-O4-C6	116.7 (3)
I-Na-O5	104.44 (11)	Na-O4-C7	115.1 (3)
O1-Na-O2	70.20 (13)	C6-O4-C7	114.4 (4)
O1-Na-O3	119.03 (15)	Na-O5-C8	101.3 (3)
O1-N1-O4	134.96 (15)	Na-O5-C9	106.1 (3)
O1-Na-O5	68.16 (13)	C8-O5-C9	113.2 (4)
O2-Na-O3	69.47 (13)	O1-C1-C2	105.6 (4)
O2-Na-O4	137.56 (15)	O2-C2-C1	111.5 (4)
O2-Na-O5	131.51 (15)	O2-C3-C4	106.9 (5)
O3-Na-O4	68.12 (13)	O3-C4-C3	107.1 (4)
O3-Na-O5	111.56 (14)	O3-C5-C6	108.0 (5)
O4-Na-O5	68.39 (13)	O4-C6-C5	107.0 (5)
Na-O1-C1	113.7 (3)	O4-C7-C8	107.7 (4)
Na-O1-C10	117.0 (3)	O5-C8-C7	105.8 (4)
C1-O1-C10	113.1 (4)	O5-C9-C10	107.4 (5)
Na-O2-C2	112.7 (3)	O1-C10-C9	106.2 (5)
Na-O2-C3	113.0 (3)	C2-O2-C3	113.6 (4)

Table 3c Torsional angles (°) of 15C5·NaI

I-Na-O1-C1	-126.6 (3)	I-Na-O1-C10	98.6 (3)
O2-Na-O1-C1	-21.0 (2)	O2-Na-O1-C10	-155.8 (3)
O3-Na-O1-C1	30.3 (2)	O3-Na-O1-C10	-104.6 (3)
O4-Na-O1-C1	117.5 (3)	O4-Na-O1-C10	-17.3 (2)
O5-Na-O1-C1	133.6 (3)	O5-Na-O1-C10	-1.2 (2)
I-Na-O2-C2	88.9 (3)	I-Na-O2-C3	-140.7 (3)
O1-Na-O2-C2	-10.7 (2)	O1-Na-O2-C3	119.6 (3)
O3-Na-O2-C2	-144.0 (3)	O3-Na-O2-C3	-13.6 (2)
O4-Na-O2-C2	-146.7 (3)	O4-Na-O2-C3	-16.3 (2)
O5-Na-O2-C2	-42.9 (3)	O5-Na-O2-C3	87.5 (3)
I-Na-O3-C4	76.9 (3)	I-Na-O3-C5	-46.1 (3)
O1-Na-O3-C4	-73.2 (3)	O1-Na-O3-C5	163.8 (3)
O2-Na-O3-C4	-21.6 (3)	O2-Na-O3-C5	-144.6 (3)
O4-Na-O3-C4	156.4 (3)	O4-Na-O3-C5	33.4 (3)
O5-Na-O3-C4	-149.4 (3)	O5-Na-O3-C5	87.6 (3)
I-Na-O4-C6	128.8 (3)	I-Na-O4-C7	-93.1 (3)
O1-Na-O4-C6	-112.2 (3)	O1-Na-O4-C7	26.0 (3)
O2-Na-O4-C6	0.3 (3)	O2-Na-O4-C7	138.5 (3)
O3-Na-O4-C6	-2.5 (3)	O3-Na-O4-C7	135.7 (3)
O5-Na-O4-C6	-128.3 (3)	O5-Na-O4-C7	9.9 (3)
I-Na-O5-C8	51.0 (2)	I-Na-O5-C9	-67.4 (3)
O1-Na-O5-C8	151.8 (3)	O1-Na-O5-C9	33.4 (3)
O2-Na-O5-C8	-175.5 (3)	O2-Na-O5-C9	66.1 (3)
O3-Na-O5-C8	-94.4 (3)	O3-Na-O5-C9	147.2 (3)
O4-Na-O5-C8	-40.3 (3)	O4-Na-O5-C9	-158.7 (4)
Na-O1-C1-C2	46.7 (3)	C10-O1-C1-C2	-176.7 (6)
Na-O1-C10-C9	-29.0 (3)	C1-O1-C10-C9	-164.2 (6)
Na-O2-C2-C1	39.8 (3)	C3-O2-C2-C1	-90.2 (5)
Na-O2-C3-C4	44.7 (3)	C2-O2-C3-C4	174.7 (6)
Na-O3-C4-C3	52.3 (3)	C5-O3-C4-C3	170.8 (6)
Na-O3-C5-C6	-61.9 (3)	C4-O3-C5-C6	177.7 (6)
Na-O4-C6-C5	-27.5 (3)	C7-O4-C6-C5	-166.0 (6)
Na-O4-C7-C8	22.2 (2)	C6-O4-C7-C8	161.3 (6)
Na-O5-C8-C7	68.6 (3)	C9-O5-C8-C7	-178.3 (6)
Na-O-C9-C10	-62.3 (3)	C8-O5-C9-C10	-172.5 (6)
O1-C1-C2-O2	-57.1 (3)	O2-C3-C4-O3	-65.4 (4)
O3-C5-C6-O4	60.0(4)	O4-C7-C8-O5	-62.5(4)
O5-C9-C10-O1	61.2(4)

Fig. 20 Unit cell of 15C5·NaI

Motion Study of the 15C5 Ligand by ^2H Solid State NMR.

In order to undertake a motional analysis in 15C5, 15C5- d_4 and - d_8 were synthesized (Fig. 21). The cyclization was achieved *via* a modified Williamson ether synthesis^{(11),(12)}, in a polar aprotic solvent not requiring anhydrous conditions, between deuterated analogues of bis-(2-chloroethyl)-ether and triethylene glycol in the presence of NaOH (Na^+ acting as a template) in 40 % yield. The purity of each compound was established by GC/ MS and high resolution ^1H NMR (Chapter 8).

Using NMR relaxation techniques, *Dye et al.* have recently studied the sandwich-type sodide $\text{Cs}^+(\text{15C5})_2\text{Na}^-$, and concluded the line width reduction of the ^{23}Na resonances was consistent with a *merry-go-round* motion, possessing an average activation barrier of 35.4 kJ/mol⁽¹³⁾.

(a) $\text{BF}_3 \cdot \text{Et}_2\text{O}$, CH_2Cl_2 , 75 %; (b) LiAlX_4 ($\text{X} = \text{H}$ or D), anhydrous THF, 95 %; (c) NaOH , 1,4-dioxane, Δ , 24 hr, 36.7 %; (d) TsCl , anhydrous pyridine, 80 %; (e) KOH , 1,4-dioxane, Δ , 57.7 %, 24 hr; (f) SOCl_2 , absolute MeOH, 98 %; (g) SOCl_2 (2 eq.), Δ , 77 %; (h) NaI , CH_2Cl_2 : EtOH (7: 3); (i) KI , CH_3CN , Δ , 24 hr.

Fig. 21 Synthetic pathway for 15C5- d_4 , 15C5- d_8 and 21C7- d_{12}

15C5-d₈ NaI

The ^2H powder spectrum of the NaI complex at 238 K (Fig. 22) indicates that the crown ether is static at this temperature. The values of the static tensor components are $\Delta\nu_{zz} = 242.67$ kHz, $\Delta\nu_{yy} = 129.33$ kHz, $\Delta\nu_{xx} = 113.34$ kHz, $\chi = 161.77$ kHz and $\eta = 0.0659$.

Fig. 22 ^2H static lineshape of 15C5-d_8 NaI at 238 K

As the temperature is increased from 238 K, the line undergoes pronounced changes in shape and intensity with many shoulders, indicative of the deuterons visiting different environments. Above 300 K, the fast motion limit (f.m.l.) is reached, but the line shapes continue to undergo gradual narrowing, due to changes in the amplitude of the motion. At 345 K, a sharp axially symmetric line ($\eta = 0$) appears, indicating that all deuterons have become equivalent (Fig. 23); this sudden change is characteristic of a phase transition.

Fig. 23 ^2H lineshapes of $15\text{C5-}d_8 \cdot \text{NaI}$ as a function of temperature

By differential scanning calorimetry (DSC) two phase transitions were recorded for this complex. The first between 315-335 K has a multi-step character and the second at 345 K is sharp, above which the solid decomposes (Fig. 24).

Fig. 24 Phase transitions in $15\text{C}5\text{-}d_3 \cdot \text{NaI}$ detected by (a) DSC; (b) ^2H NMR lineshape components as a function of temperature (Δv_{xx} : $\blacktriangle$, Δv_{yy} : $\diamond$, Δv_{zz} : $\blacklozenge$)

$15\text{C}5\text{-}d_4 \cdot \text{NaClO}_4$

The ^2H lineshapes of deuterated $15\text{C}5 \cdot \text{NaClO}_4$ (Fig. 25) reflect a higher thermal stability than the NaI complex where three phase transitions at 356, 374 and 383 K are detected (Fig. 26). The static tensor components equal those of the NaI complex and at 380 K, an axially symmetric line is observed. Due to the asymmetry present at 193 K and the equivalence of all the deuterons in the f.m.l., there is no doubt that the macrocycle adopts a new conformation at 380 K.

Discussion

The description of a motion *via* ^2H solid state NMR is based on the ability to simulate the f.m.l. lineshape by reference to a known X-ray structure. The problem encountered herein in the study of $15\text{C}5$ complexes, is that the low temperature X-ray

Fig. 25 ^2H lineshapes of $15\text{C5-}d_4 \cdot \text{NaClO}_4$ as a function of temperature

structure does not correspond to the high temperature conformation, due to the occurrence of phase transitions. This renders the simulation of the motion more difficult since no ground geometry can be used as a pedestal. So far all attempts have failed to reproduce the experimental data. Nevertheless the bulk lineshape features allow some general comments on the motion in the 15C5 systems.

In the low temperature phases, the motion of both 15C5 complexes appear to be quite similar. The intermediate rate lineshapes do not correspond to the *merry-go-round* motion, a more probable mode being up-down flipping of the CD₂ groups. The dynamically averaged lineshape of each crystallographically unique CD₂ group has a different width which results in a f.m.l. lineshape with many complex features.

Fig. 26 Phase transitions in 15C5-*d*₈ · NaClO₄ detected by (a) DSC; (b) ²H NMR lineshapes components as a function of temperature (Δν_{xx}: ▲, Δν_{yy}: ◆, Δν_{zz}: ■)

In the high temperature phase, each complex exhibits a single axially symmetric lineshape which indicates;

- (a) All the deuterons have become equivalent. There are always 4 sets of C-D's, because physical exchange cannot occur within any one O-CD₂-CD₂-O unit. These sets may become equivalent through symmetry as disorder.
- (b) The axial symmetry implies motion about an *n*-fold axis (*n* ≥ 3), in this case

presumably 5-fold.

The only mode of motion satisfying both (a) and (b) is up-down flips of the CD_2 groups about a mirror plane perpendicular to the rotation-axis, accompanied by a reorientation around the ring (Fig. 27). These motions could be simultaneous as in the case of $18\text{C}6 \cdot 2\text{CH}_2(\text{CN})_2$ or occur at different, though rapid, rates such as in $12\text{C}4 \cdot \text{LiSCN}$. Unfortunately this model cannot be confirmed by simulation of the intermediate rate lineshapes, since the latter are obscured by a phase transition.

Fig. 27 Simulated ^2H NMR spectra: (a) mode, 4 sets of C-H 's involved in macrocyclic polyethers; (b) mode, 5-fold rotation.

21C7 as a Ligand

NMR Data Characteristic of Motional Behavior

In solution at 298 K, all 21C7 carbons are equivalent and averaged to a single line at 70.51 ppm in CDCl₃ and for the KI complex, are averaged to 69.94 ppm in acetone-*d*₆.

Motion Study of 21C7 by ²H Solid State NMR

From the 184.5 K powder ²H spectrum of 21C7-*d*₁₂·KI the values for the static tensor components are; $\Delta\nu_{zz} = 244.94$ kHz, $\Delta\nu_{yy} = 131.50$ kHz, $\Delta\nu_{xx} = 113.44$ kHz, $\chi = 163.29$ kHz and $\eta = 0.0737$ (Fig. 28). This low temperature phase reflects a motion which, upon warming to near room temperature (rt) becomes rapid, and again there are numerous f.m.l. features arising from inequivalent deuterons.

The f.m.l. lineshape in the high temperature phase is very interesting. It indicates the motion has made all the deuterons equivalent, but the large asymmetry parameter ($\eta = 1$) clearly rules out rotation about an *n*-fold axis. It seems certain however that the O-CD₂-CD₂-O groups must still exchange around the ring, probably accompanied by other motions. Unfortunately the inability to obtain an X-ray structure for 21C7·KI inhibits the formulation of any model which could be of use in lineshape simulation.

Fig. 26 ^2H lineshapes of $21\text{C7-}d_{12} \cdot \text{KI}$ as a function of temperature

C- Conclusion

Solution and CP/MAS ^{13}C spectra reflect large amplitude motion in both 15C5 and 21C7 complexes. The motions in the low temperature phases are probably up-down flips of the CD_2 groups. In the high temperature phases, the motions involved make all the deuterons equivalent, suggesting reorientation around the rings accompanied by up-down flips.

A number of phase transitions complicate the interpretation of the dynamics of the crowns. In order to refine models which will accurately simulate the f.m.l. lineshapes, higher temperature phase X-ray structures are needed. Attempts using models based on known X-ray structures have so far failed.

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CHAPTER 4

Crystal Packing Effects in 1,2-Dimethoxybenzene and 2,3-Dimethoxynaphthalene

Foreword

There is a good deal of experimental ^{13}C CP/ MAS and X-ray data on 1,2-dialkoxybenzene systems in which the protonated aromatic carbons show a strong chemical shift dependence on the degree of planarity of the macrocycle relative to the benzene plane. As 1,2-dimethoxybenzene (1,2-DMB) is the parent molecule in these systems it is a good model for study in order to more fully correlate conformationally induced chemical shift trends with X-ray derived structural features.

At an early stage in this research, facilities were not conducive to achieve both the mounting of a 1,2-DMB crystal (mp = 15°C) on an axis in a cold room and the transport of this assembly to the X-ray spectrometer without losing the crystal. So it was decided to investigate 2,3-dimethoxynaphthalene (2,3-DMN) instead, which should act as a shunted model in the study of stereoelectronic shielding effects in 1,2-dialkoxybenzene moieties. Subsequently after a nearly two year period of mistrials and exasperation, the X-ray structure of 1,2-DMB was finally obtained.

In this chapter, the X-ray structures and the CP/ MAS derived principal ^{13}C shielding tensors are presented for 1,2-DMB (Part I) and 2,3-DMN (Part II), in order to more fully document *intramolecular* (stereoelectronic effects) *v.s.* *intermolecular* (packing forces) phenomena in the solid state.

Part I

Solid State Structure of 1,2-Dimethoxybenzene (Veratrole) and Related Methoxybenzenes

A- Introduction

The conformational preference of 1,2-dimethoxybenzene (1,2-DMB)* has been a subject of much controversy over the years. This moiety is common in natural products where there exists an established relationship between bioactivity and conformation⁽¹⁾⁻⁽²⁾. In cyclohomologues, the relative orientation of the oxygens can affect the susceptibility of the benzene ring towards electrophilic substitution⁽³⁾. In this thesis, the X-ray structure and the ¹³C NMR tensor measurements of 1,2-DMB are presented, and together give a clearer understanding of the electronic properties in this material.

In the gas phase, photoelectron spectroscopic data for 1,2-DMB have been interpreted in terms of a non-planar ($\theta_1 = 0^\circ$, $\theta_2 = 90^\circ$) conformation (Fig. 29)⁽²⁾.

Fig. 29

In solution the problem still remains controversial; partition coefficients⁽²⁾, temperature

* MB, DMB, TMB refer to monomethoxy-, dimethoxy- and trimethoxybenzene

dependence of the dipole moment⁽⁴⁾, dielectric relaxation times⁽⁵⁾, the non-linear dielectric effect parameter⁽⁶⁾ and ^{17}O NMR⁽⁷⁾ all require a non-planar conformation for 1,2-DMB. In contrast, however, ^{13}C NMR shifts, spin-lattice relaxation times⁽⁸⁾ and long range ^1H - ^1H coupling constants has been interpreted in terms of 1,2-DMB as a planar molecule. From the average $^5J_{\text{H,CH}_3} = -0.14$ Hz, the trans-coplanar conformer ($\theta_1 = \theta_2 = 0^\circ$) was shown to be predominant with some torsional motions as large as 20° . The planarity of 1,2-DMB was attributed to solvation effects which can overcome the energy barrier between planar and non-planar conformers⁽⁹⁾.

In the solid state, the structure of 1,2-DMB has been characterized likely as a mixture of planar and non-planar conformers, based on multiplicities found in the low-frequency methyl torsion transitions in the Raman spectrum at 130 K⁽¹⁰⁾. This is in contrast to an X-ray survey where 1,2-DMB derivatives (non 3-substituted) prefer planar arrangements^{(2),(11)}. The results of the computation of the crystal lattice energies for some of these derivatives suggest non-planar conformations are favoured *in vacuo* but due to crystal packing, the planar conformations prevail⁽¹²⁾. The X-ray structure of 1,2-DMB- $\text{Cr}(\text{CO})_3$ shows the trans-coplanar 1,2-DMB molecule to possess an effective C_2 symmetry, with one methyl group situated slightly above the aromatic plane by $0.06 \text{ \AA}$ ⁽¹³⁾.

Solid state anisole (MB) has also been investigated using low-frequency Raman spectroscopy at 130 K⁽¹⁴⁾. It was postulated that MB likely exists as two different conformers, as evidenced by the splitting into a doublet of the methyl torsional band of the deuterated analogues. In a recent publication, the ^{13}C tensors of MB were evaluated from the simulated 2D MAT spectrum at 205 K and found to be in agreement with *ab initio* calculations based on an optimized planar structure. Also, a shoulder on the methoxy resonance in the CP/ MAS spectrum at 180 K was attributed to crystal packing effects⁽¹⁵⁾.

Theoretical investigations into the conformational preferences of MB and the dimethoxybenzenes are restricted by the lack of X-ray data which serve as reference

geometries. These compounds have low melting points; MB (mp = -37.5 °C), 1,2-DMB (mp = 15 °C), 1,3-DMB (mp = -52 °C) with the exception of 1,4-DMB (mp = 59 °C)⁽¹⁶⁾. Molecular mechanics (MM) studies have indicated that it is difficult to describe the C_{sp^2} - C_{sp^2} -O- C_{sp^3} torsion because reliable force field parameters are unavailable⁽¹⁷⁾ and the hybridization state of the oxygen remains independent of dihedral angle. MM calculations on 1,2-DMB suggests it can exist in any or all of four conformers: (0°, 0°), (0°, 90°), (0°, 180°), (90°, 270°)⁽¹⁸⁾. Recent *ab initio* molecular orbital calculations on 1,2-DMB at the STO-3G level⁽¹⁹⁾ indicate that the (0°, 0°) conformation is stabilized by 0.5 kcal/mol relative to the perpendicular one (0°, 90°).

Relating isotropic ^{13}C NMR chemical shifts to electronic structure⁽²⁰⁾⁻⁽²¹⁾ is more straightforward in the solid state than in solution, since conformational averaging is usually eliminated in solids. However caution must be exercised since multiplicities can also originate from the presence of non equivalent molecules in the crystallographic unit cell⁽²²⁾ or quadrupolar nuclei⁽²³⁾. With the X-ray structures in hand, much work in this area has been performed on 1,2-benz-annelated crown ethers⁽²⁴⁾⁻⁽²⁵⁾.

Previous work in these laboratories revealed 7 lines in the low temperature ^{13}C CP/MAS powder spectrum of 1,2-DMB⁽²⁶⁾ (Fig. 30), the origin of which can be attributed to (i) a single conformer with approximate C_2 symmetry⁽²⁷⁾ or (ii) two conformers each with C_2 symmetry. Accordingly, a single crystal X-ray structure of 1,2-DMB was required to resolve this problem. The electronic shielding of a nucleus is dependent on the molecular orientation relative to the external magnetic field and is described by the shielding tensor, which has three mutually orthogonal principal elements $\sigma_{11} > \sigma_{22} > \sigma_{33}$ ⁽²⁸⁾⁻⁽³¹⁾. σ_{11} and σ_{22} are mainly π shielding, the former in the direction of the C_{ar} -H and C_{ar} -O bonds while σ_{33} is mainly σ shielding in a direction perpendicular to the benzene plane⁽³²⁾. To complement the X-ray analysis in understanding the electronic properties inherent in this class of compounds, a variable spinning CP/ MAS shielding tensor analysis was undertaken. If the spinning frequency is reduced relative to the chemical shift anisotropy, then the isotropic line in the CP/ MAS spectrum is flanked on both sides by

sidebands spaced at the spinning frequency. The intensities of the spinning sidebands are related to the chemical shift anisotropy and provide an opportunity to recover the shift parameters. The *Herzfeld and Berger*⁽³³⁾ method is a graphical mathematical resolution for this technique and is used herein to obtain the shielding tensors for MB, 1,2-DMB, 1,4-DMB and 1,3,5-TMB.

Fig. 30 50.32 MHz ^{13}C CP/MAS NMR spectrum of 1,2-DMB at 260 K⁽²⁶⁾

A potential drawback in relating these tensors to the 3-D electronic structure is that the benzene parent, which has been shown to adopt a T-shaped lattice, undergoes a rapid in-plane motion at experimentally accessible temperatures, thereby averaging σ_{11} and σ_{22} ^{(34),(35)}. However from our data it proved possible to directly calculate the tensors of static benzene⁽³⁶⁾⁻⁽³⁸⁾. From this, the anisotropic substituent chemical shifts (SCS) of a planar methoxy group were assessed in order to study the 3-D electronic properties of these compounds, particularly 1,2-DMB. In addition *ab initio* shielding tensor calculations on 1,2-DMB using the GIAO⁽³⁹⁾ and LORG⁽⁴⁰⁾ methods were performed.

B- Results and Discussion

X-ray Structure of 1,2-DMB

The ORTEP diagram (Fig. 31) shows the methoxy groups are twisted on the same side out of the aromatic plane $C6-C1-O1-CM1 = 8.6^\circ$ and $C3-C2-O2-CM2 = -5.0^\circ$ (Table 5c). The near coplanarity of the methoxy groups permits good overlap of the oxygen p-type lone pairs with the *ipso* p-orbitals⁽⁴¹⁾. Although the methyl groups in *ortho*-dimethoxy compounds (non 3-substituted) are usually displaced on opposite sides of the ring, the present situation is not unique⁽⁴²⁾.

Fig. 31 ORTEP plot of 1,2-DMB at 150 K

Table 4a Atomic parameters and B_{iso} of 1,2-DMB

Atom	x	y	z	Biso
O1	0.5776(5)	0.87329(24)	0.20661(14)	3.48(9)
O2	0.9151(5)	1.03691(22)	0.15001(14)	3.44(9)
C3	0.4103(7)	0.8585(3)	0.03820(22)	3.24(12)
C2	0.5766(7)	0.9063(3)	0.10644(19)	2.85(11)
C6	0.7719(7)	1.0350(3)	-0.02320(22)	3.34(12)
C1	0.7600(6)	0.9952(3)	0.07633(21)	2.87(11)
CM1	1.0799(7)	1.1420(4)	0.12501(27)	3.99(14)
C4	0.4241(7)	0.9016(3)	-0.06223(21)	3.50(13)
C5	0.6050(8)	0.9878(3)	-0.09199(21)	3.50(13)
CM2	0.3807(7)	0.7926(4)	0.24120(24)	3.96(14)
H3	0.274(8)	0.800(4)	0.0600(24)	3.(1)
H4	0.303(8)	0.860(4)	-0.1148(32)	5.(1)
H5	0.604(9)	1.026(5)	-0.1616(33)	6.(1)
H6	0.890(9)	1.097(4)	-0.0423(28)	4.(1)
HM2B	0.393(0)	0.693(0)	0.2086(0)	5.(0)
HM2C	0.216(0)	0.844(0)	0.2216(0)	5.(0)
HM2A	0.408(0)	0.769(0)	0.3193(0)	5.(0)
HM1C	1.224(0)	1.115(0)	0.0741(0)	5.(0)
HM1B	1.177(0)	1.167(0)	0.1924(0)	5.(0)
HM1A	1.007(0)	1.236(0)	0.0979(0)	5.(0)

Table 4b Crystallographic data of 1,2-DMB

Formula	C ₈ H ₁₀ O ₂
fw	138.17
Crystal system	orthorhombic
Space group	P 2 ₁ 2 ₁ 2 ₁
<i>a</i> , Å	5.5329(4)
<i>b</i> , Å	9.9240(9)
<i>c</i> , Å	13.3473(11)
<i>V</i> , Å ³	732.88(10)
<i>Z</i> (molecules / cell)	4
<i>D_c</i> (g / cm ³)	1.261
Crystal dimensions, mm ³	0.10 x 0.25 x 0.35
Radiation (λ, Å)	CuK _α (1, 1.54056)
Octants measured	<i>h</i> (0 to +6), <i>k</i> (0 to +11), <i>l</i> (0 to +16)
Max 2θ	139.3
Temperature	-120°C
No. of unique reflections	832
No. of reflections measured	931
No. of reflections with <i>I</i> _{net} > 2.5 σ <i>I</i> _{net}	732
<i>I_c</i> / <i>I</i> ratio	0.011
<i>R_f</i>	0.055
<i>R_w</i>	0.072
GoF	1.94
Maximum and minimum residual <i>ep</i> in final difference Fourier map, eÅ ⁻³	0.220 and -0.220

Table 5a Atomic bond lengths (Å) of 1,2-DMB

O1-C1	1.369(4)	C3-H3	0.99(4)
O2-C2	1.377(3)	C4-H4	1.05(5)
C1-C2	1.403(5)	C5-H5	1.00(5)
C2-C3	1.379(5)	C6-H6	0.93(5)
C3-C4	1.409(4)	CM1-HM1A	1.080(4)
C4-C5	1.375(5)	CM1-HM1B	1.077(4)
C5-C6	1.384(5)	CM1-HM1C	1.083(4)
C6-C1	1.388(4)	CM2-HM2A	1.080(3)
O1-CM1	1.425(4)	CM2-HM2B	1.081(4)
O2-CM2	1.429(4)	CM2-HM2C	1.081(4)

Table 5b Atomic bond angles (°) of 1,2-DMB

C1-C2-C3	120.6(3)	C1-C6-H6	118.9(2)
C3-C4-C5	120.2(3)	C4-C3-H3	119.7(2)
O1-C1-C2	115.94(24)	C6-C5-H5	119.0(3)
O2-C2-C3	124.2(3)	C2-C3-H3	120.9(2)
C1-C6-C5	120.5(3)	O1-CM1-HM1A	118.2(3)
C6-C5-C4	120.3(3)	O1CM1-HM1B	106.9(3)
O1-C1-C6	124.9(3)	O1-CM1-HM1C	115.7(3)
C1-O1-CM1	117.01(24)	O2-CM2-HM2A	109.0(3)
C2-C3-C4	119.2(3)	O2-CM2-HM2B	109.5(3)
C2-C1-C6	119.2(3)	O2-CM2-HM2C	107.4(3)
O2-C2-C1	115.1(3)	HM1A-CM1-HM1B	105.7(3)
C2-O2-CM2	116.4(3)	HM1A-CM1-HM1C	106.5(3)
C3-C4-H4	118.6(2)	HM1B-CM1-HM1C	102.3(3)
C4-C5-H5	119.0(3)	HM2A-CM2-HM2B	100.5(3)
C5-C6-H6	120.6(2)	HM2A-CM2-HM2C	117.1(3)
C5-C4-H4	121.0(2)	HM2B-CM2-HM2C	113.0(3)

Table 5c Torsional angles (°) of 1,2-DMB

CM1-O1-C1-C6	8.6	HM2C-CM2-O2-C2	- 55.4
CM1-O1-C1-C2	-170.9	HM1B-CM1-O1-C1	175.9
CM2-O2-C2-C1	174.6	HM2A-CM2-O2-C2	176.6
CM2-O2-C2-C3	- 5.0	HM1C-CM1-O1-C1	- 70.9
HM1A-CM1-O1-C1	56.9	HM2B-CM2-O2-C2	67.6

Table 6 Closest intermolecular X...H contacts in the 1,2-DMB unit cell

Contact	Numbering Scheme	Distances (Å)
O2 ... HM1B	1	2.30
O1... HM2C	2	2.70
O1... H5	3	2.59
O2 ... H5	4	2.68
C3 ... H3	5	2.82
C4... H3	6	2.88

The C_{ar}-O vectors are bent towards each other presumably to reduce the steric repulsion between the methyl protons and *ortho*-aromatic protons⁽⁴³⁾ where the C6-C1-O1 and C3-C2-O2 bond angles $\sim 124.5^\circ$ (Table 5b)*. In contrast, methyl vinyl ether exists in the more sterically congested *syn*-planar conformation based on vibrational spectroscopy⁽⁴⁴⁾, electron diffraction studies⁽⁴⁵⁾ and *ab initio* calculations. Theoretical calculations on methyl vinyl ether and related hetero-analogues show the *syn*-planar conformation has the lowest overall molecular dipole moment. The calculated⁽⁴⁶⁾ and experimental⁽⁴⁷⁾ *syn/anti* energy difference was found to be 2.82 and 1.26 kcal/ mol respectively.

In the packing diagram, looking down the c-axis, roughly coplanar (23°) 1,2-DMB units are arranged in a mutually perpendicular fashion (Fig. 32).

The closest X...H *intermolecular* contacts (Fig. 33) are all within the appropriate van der Waals radii (Table 6). The perpendicular molecules undergo mutual contacts C3...H3 involving the same side of the aromatic plane. The other perpendicular contacts involve O1...HM2C and O2...HM1B. There are also O2...H5 and O1...H5 contacts between parallel molecules.

Assignment of the Solid State ¹³C Shifts of 1,2-DMB

Solid-state assignments were facilitated by the synthesis of *ortho-d* 1,2-DMB⁽⁴⁸⁾. The 125.8 MHz ¹³C solution spectrum of this compound (Fig. 34) clearly shows a single deuterium bonded to the most shielded aromatic resonance at 111.4 ppm, well known to be the *ortho* site⁽⁴⁹⁾. The 400 MHz ¹H aromatic region of *ortho-d* 1,2-DMB was well simulated as an ABC spin system⁽⁵⁰⁾ (Fig. 35).

* In non planar conformations the C-C-O bond angles are significantly smaller $119.5 \pm 0.7^\circ$.

Fig. 32 Packing diagram of 1,2-DMB

Fig. 33 Relative orientation of 1,2-DMB molecules within the unit cell

Fig. 34 125 MHz solution ^{13}C spectrum of *ortho*-d 1,2-DMB

Fig. 35 400 MHz ^1H spectrum (aromatic region) of *ortho*-d 1,2-DMB

α : simulation by the LAOCOON program⁽⁵⁰⁾

In the CP/MAS dipolar dephased spectrum of this compound (Fig. 36b), there are two resonances within 1.0 ppm of the *ortho* site solution value (Table 7), at half the intensity of the *ipso* and methyl peaks. Clearly the resonances at 110.4, 112.0 ppm and 121.1, 122.8 ppm are assigned to the *ortho* and *para* carbons respectively.

It has been demonstrated in 1,2-dialkoxybenzene moieties that twisting out of the plane by ca. 40° has little effect on the *para* carbon shifts whereas the *ortho* carbons, being more sensitive to the steric environment, are deshielded by ca. 5-6 ppm^{(51),(52)}. Similarly, the methoxy carbon of anisole becomes deshielded as the twist angle increases, based on *ab initio* LORG calculations⁽²⁴⁾.

In order to assess whether these trends are operative, *ab initio* shifts were calculated for 1,2-DMB with the GIAO⁽³⁹⁾ and LORG⁽⁴⁰⁾ methods using the X-ray data as input (Table 7). The results consistently show the most shielded *ortho* and methoxy carbons associated with the most out of plane O1-CM1, $\theta = 8.6^\circ$. Clearly these calculated shielding trends in solid 1,2-DMB are not consistent with *intramolecular* effects.

Theoretical calculations have shown the conformational preferences of 1,2-DMB impact the geometry of the methoxyl group and aromatic ring⁽¹⁹⁾ and in turn, solvation effects can overcome the energy difference between planar and non-planar conformers. Therefore packing forces are expected to be of sufficient relative magnitude to locally distort the molecule and this is reflected as CP/ MAS multiplicities. The *inter*-aromatic contacts are deemed to be of the C-H... π type as found in other systems^{(27),(53)}.

¹³C Shielding Tensor Analysis

In order to obtain shielding tensor measurements, a static solid is required or some degree of order in the tumbling motions of the solid. Using variable spinning CP/ MAS at 260 K, the principal shielding tensors were measured for 1,2-DMB (Fig. 37)⁽³³⁾.

Fig. 36 (a) Normal and (b) dipolar dephased ^{13}C CP/MAS spectra of *ortho*-d 1,2-DMB at 260 K

Fig. 37 Variable spinning rate ^{13}C CP/MAS spectra of 1,2-DMB at 260 K

Fig. 38 Variable spinning rate ^{13}C CP/MAS spectra of 1,4-DMB at 298 K

Fig. 39 Variable spinning rate ^{13}C CP/MAS spectra of 1,3,5-TMB at 298 K

Tensor measurements on 1,4-DMB (Fig. 38) and 1,3,5-TMB (Fig. 39) (both planar, X-ray structures known) were also measured and found to be ± 3 and ± 2 ppm respectively from the literature single crystal derived tensors⁽³²⁾. The C3 sites of 1,2-DMB and 1,4-DMB are γ -eclipsed by an *ortho* methoxy group to within a 5° torsion, hence are expected to be isoelectronic. Indeed, there is only a 1 ppm difference between the respective principal tensors of these two molecules at this site (Table 8).

Table 7 Experimental and theoretical ^{13}C chemical shifts of 1,2-DMB

		C1	C2	C3	C4	C5	C6	CM1	CM2
solution^a	σ_{iso}	149.1	149.1	111.4	120.9	120.9	111.4	55.7	55.7
solid^b	σ_{iso}	149.4	149.4	112.0	122.8	121.1	110.4	55.0	56.9
	σ_{11}	209	209	185	215	210	184	82	84
	σ_{22}	168	168	137	139	134	134	68	68
	σ_{33}	71	71	14	14	19	13	15	19
LORG, D95V	σ_{iso}	157.4	158.4	117.9	128.7	122.4	112.7	52.8	56.8
	σ_{11}	236.9	240.0	218.9	246.2	237.2	213.6	79.6	81.1
	σ_{22}	167.8	170.3	130.7	132.4	129.6	125.5	70.1	75.5
	σ_{33}	67.4	64.8	4.2	7.4	0.4	-0.9	8.8	13.9
GIAO, 6-31G⁺	σ_{iso}	142.9	142.9	102.1	113.3	108.0	99.6	48.8	52.3
	σ_{11}	201.8	198.2	185.2	209.0	204.4	181.8	78.6	78.6
	σ_{22}	159.8	162.5	119.6	124.1	120.5	120.0	68.6	73.3
	σ_{33}	67.2	68.1	1.4	6.7	-0.8	-3.1	-0.7	5.1

a: referenced to TMS ± 0.1 ; 0.1 M in CDCl_3

b: errors given in Appendix A (see page 194)

Table 8 Principal ^{13}C shifts^a of several methoxybenzenes

	C1	C2	C3	C4	C5	C6	CM1	CM2	CM3
MB									
σ_{150}	159.5	117.4	129.6 ^b	121.0	131.0 ^b	110.2	52.8		
σ_{11}	236	195	-	214	-	-	-		
σ_{22}	168	133	-	138	-	-	-		
σ_{33}	75	24	-	11	-	-	-		
1,2-DMB									
σ_{150}	149.4	149.4	112.0	122.8	121.1	110.4	55.0	56.9	
σ_{11}	209	209	185	215	210	184	82	84	
σ_{22}	168	168	137	139	134	134	68	68	
σ_{33}	71	71	14	14	19	13	15	19	
1,3-DMB									
σ_{150}	160.4	101.1	160.4	109.4	129.8	101.1	54.0	54.0	
1,4-DMB									
σ_{150}	154.0	117.7	112.0	154.0	117.7	112.0	54.8	54.8	
σ_{11}	230	194	186	230	194	186	82	82	
σ_{22}	159	131	137	159	131	137	67	67	
σ_{33}	73	28	13	73	28	13	15	15	
1,3,5-TMB									
σ_{150}	162.2	98.7	162.2	87.9	162.2	93.1	54.7	54.7	54.7
σ_{11}	242	155	242	151	241	152	87	87	87
σ_{22}	168	107	168	110	168	107	65	65	65
σ_{33}	77	34	77	3	77	20	12	12	12

^a: errors given in Appendix A (see page 194)^b: possible interchange of assignments

Low temperature measurements were also attempted on MB and 1,3-DMB and it was possible to extract tensor values for three MB sites; C1 (*ipso*), C2 (*ortho-trans*) and C4 (*para*). Tensor comparison of these MB sites to C1 of 1,3,5-TMB, C2 of 1,4-DMB and C5 of 1,2-DMB respectively (Fig. 40, Table 8), clearly support MB as a planar molecule.

Fig. 40 Solid state conformations of some planar methoxybenzenes

By parameterizing the observed shieldings of these four methoxybenzenes in terms of *ipso*, *ortho-trans*, *ortho-cis*, *meta*, *para* relative to a planar methoxy and ϕ (the benzene parent), one may set up a series of equations. Considering the aromatic sites for which tensor data were experimentally determined* (Fig. 40), one obtains three systems of equations each of which yield the shielding tensors for static benzene. The averaged values are $\sigma_{11} = 222$ ppm, $\sigma_{22} = 147$ ppm, $\sigma_{33} = 14$ ppm with $\sigma_{iso} = 128$ ppm, which are quite close to the literature values (Table 9). Subtraction of the benzene values from the C1, C2 and C4 sites of MB give the *ipso*, *ortho-trans* and *para* shielding of a planar

* This parameterized incremental shielding analysis takes into account those sites which have similar steric environments as MB therefore the C1, C2 sites of 1,2-DMB and C4, C6 sites of 1,3,5-TMB are excluded (Fig. 40). Note the average C3, C6 and C4, C5 anisotropic values of 1,2-DMB are used hereforth since there is no conformational basis for assignments.

methoxy group. The differences between these and the related sites; C1 of 1,3,5-TMB, C2 of 1,4-DMB, C5 of 1,2-DMB can then be averaged to obtain the *meta* shielding. The *ortho-cis* effect was calculated by subtracting the benzene and *meta* values from the averaged C3 sites of 1,2-DMB and 1,4-DMB (Table 10).

Table 9 Principal ^{13}C shifts of benzene

	σ_{11}	σ_{22}	σ_{33}	σ_{iso}
CP at 223K ⁽³⁶⁾	191	191	11	131
CP at 14K ⁽³⁵⁾	217	140	1	119
CP at 20K ⁽³⁴⁾	234	146	9	130
this study	222	147	14	128

Table 10 Principal substituent ^{13}C shifts of a planar methoxy group.

	σ_{11}	σ_{22}	σ_{33}	σ_{iso}
<i>ipso</i>	13 ± 2	21 ± 1	60 ± 3	32 ± 2
<i>ortho-cis</i>	-36 ± 3	-9 ± 1	-5 ± 3	-17 ± 2
<i>ortho-trans</i>	-27 ± 2	-14 ± 1	9 ± 3	-10 ± 2
<i>meta</i>	-1 ± 1	-1 ± 1	4 ± 2	1 ± 2
<i>para</i>	-8 ± 2	-9 ± 1	-3 ± 2	-7 ± 2

in ppm from static benzene at $\sigma_{11} = 222 \pm 2$ $\sigma_{22} = 147 \pm 1$ $\sigma_{33} = 14 \pm 3$ $\sigma_{\text{iso}} = 128 \pm 1$

For a planar methoxy substituent, the *ipso* position is greatly deshielded in the σ_{33} direction by 60 ppm due to the σ inductive effect of the electronegative oxygen. This carries through to the *ortho*-trans position where the σ_{33} is still deshielding. The *ortho*-trans and *ortho*-cis isotropic values are -10 and -17 ppm respectively. The 7 ppm extra *ortho*-cis shielding originates mainly from the σ_{33} direction, which is consistent with an in-plane steric compression of the σ C_{ar}-H electrons⁽⁵⁴⁾. The shielding at the *para* site is due mainly to the σ_{11} and σ_{22} components which supports the π -donor resonance model of a methoxy group. The *meta* effect is the smallest, consistent with the σ acceptor and the π donor behavior of the methoxy group.

Low Temperature CP/MAS on MB and 1,3-DMB

For planar MB, it is anticipated that 7 lines will be resolved in the 210 K ^{13}C CP/MAS spectrum, and indeed at 4.5 kHz this is observed (Fig. 41). The shoulder on the methoxy peak indicates the presence of two conformers, but without an X-ray one cannot speculate any further.

From the CP/MAS spectrum of 1,3-DMB at ~ 150 K (Fig.42), the isotropic shifts are reported (Table 8). Both methoxy carbons resonate at 54.0 ppm, a value characteristic of planarity. Utilizing the isotropic SCS parameters (Table 10), two of the three possible planar conformers are quickly ruled out. Thus, 1,3-DMB appears to adopt the asymmetric planar conformation in the solid state (Fig. 42).

Fig. 41 ^{13}C CP/ MAS spectrum of MB at 210 K

Fig. 42 ^{13}C CP/ MAS spectrum of 1,3-DMB at 150 K

C- Conclusion

In summary, the solid phase spectral multiplicities of 1,2-DMB reflect crystal packing forces and are consistent with the observation that the asymmetric unit in the crystal is one molecule.

The C1, C2 sites of 1,2-DMB exhibit isotropic but not anisotropic SCS additivity. Here the differences between the experimental and calculated σ_{11} , σ_{22} , σ_{33} are 1, 10, -11 ppm respectively. If anisotropic additivity were upheld, the C1-C2 bond would be relatively σ electron deficient, due to the inductive effect of the oxygens acting on the *ipso* and *ortho* sites. The offsetting nature of σ_{22} and σ_{33} reveals a compensatory distribution of π and σ density in the C1-C2 bond. Therefore both additive and non-additive anisotropic shifts can be rationalized in a manner consistent with the 3-D electronic structure.

Part II

2,3-Dimethoxynaphthalene

A- Introduction

Polycyclic aromatic compounds are of interest experimentally in the study of coals⁽⁵⁵⁾ and theoretically, in the study of aromatic character leading to a better understanding of the structural and chemical nature of these molecules. More specifically, dimethoxynaphthalenes form charge transfer complexes with π acceptors such as tetracyanoethylene or chloranil, and have technologically important applications^{(56),(57)}. The specific position of the methoxy group on the naphthalene skeleton was suggested to play a role in the efficiency of fluorescence quenching by π acceptors^{(58),(59)}. The methoxy group is an electron donor and on the whole increases the electron density on the aromatic ring, and the more such groups are present, the more basic the aromatic ring becomes. Hence these two factors are responsible for the raised quenching. On the contrary, steric hindrance associated with mutually adjacent methoxy groups, decreases charge transfer from the substituents to the ring. The rate of quenching of 2,3-dimethoxynaphthalene (2,3-DMN) is then expected to be lower than for those isomers lacking steric substituent interactions, as is found experimentally.

A lot of work has been previously reported on the unambiguous assignment of the solution ^{13}C shifts for 2,3-DMN^{(60),(61)} but, to our knowledge, nothing has been undertaken in the solid state. It has presently been found that 2,3-DMN is excellent as a model to more properly document the nature of packing effects in the solid state⁽²⁷⁾. Herein is presented the X-ray structure and the anisotropic ^{13}C chemical shifts of 2,3-DMN. The electronic shielding effect of *ortho* dimethoxy substitution is delineated by comparison to the known single crystal derived tensors of naphthalene^{(62),(63)}.

The electronic shielding of a nucleus is dependent on the molecular orientation relative to the external magnetic field and is described by the shielding tensor⁽²⁸⁾⁻⁽³¹⁾. The shielding tensors for fused aromatic hydrocarbons are characterized by σ_{11} , σ_{22} at lowfield and σ_{33} at upfield, oriented in and perpendicular to the molecular plane respectively. The σ character of σ_{33} originates in its relative independence of the π electron structure, responsible for the large down-field shift of the two in-plane σ_{11} , σ_{22} components⁽³²⁾. Based on single crystal studies, enough information has been gathered on the orientation of the principal elements of the shielding tensor in condensed aromatic hydrocarbons, to develop some rules in terms of the bond orders of adjacent bonds⁽⁶⁴⁾. For protonated carbons, the σ_{11} axis is oriented perpendicular to the bond with the largest π -bond character. For quaternary carbons, if the symmetry of the molecule is such that two of the three C-C bonds have an equal π -bond order which is larger (smaller) than the third, then σ_{11} lies perpendicular to (along) the latter. When all three bonds are different, σ_{11} will be perpendicular to (along) the greatest (smallest) π bond order. For bridgehead carbons, if all three attached C-C bonds have the same bond order then $\sigma_{11} = \sigma_{22}$ and an axially symmetric tensor is obtained, barring inequivalence due to long range effects.

In naphthalene, the bridge carbons have σ_{11} oriented perpendicular to the plane, in accordance with the bond order for C₉-C₁₀ being larger than the other two C-C bonds^{(62),(63)}. So orientation of the principal shielding elements in 2,3-DMN is intuitively known and no single crystal study is required.

B- Results and discussion

Conformation in Solution

In the solution ¹³C spectrum, six lines are observed for 2,3-DMN which have been unambiguously assigned by deuterium substitution studies^{(60),(61)}. From a consideration of the canonical forms of 2-MN, shielding is expected at all sites which bear a partial negative charge (other than *ipso*), which is indeed the case (Table 11). The *ortho* sites are the most sensitive probes to the conformation of the methoxy group, due to the γ -*gauche*

effect⁽⁶⁵⁾. For anisole, the methoxy group spends an equal amount of time in both planar conformers, but for 1,2-DMB this rotation is restricted, and the *ortho* sites are shielded by 3.4 ppm over what is expected based on solution SCS additivity correlations⁽⁶⁶⁾. There is much better additivity with 2,3-DMN, where the *ortho* sites C1, C4 are calculated as too deshielded by only 1.0 ppm (Table 11). This supports the observation that the methoxy group in 2-MN prefers a planar *cis* disposition to C1⁽⁶¹⁾ and thus 2,3-DMN prefers the planar arrangement in solution to a higher degree than 1,2-DMB.

Table 11 Solution ¹³C shifts of 2-MN, 2,3-DMN and calculated 2,3-DMN ¹³C shifts

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
N ⁽⁵⁹⁾	127.7	125.6	125.6	127.7	127.7	125.6	125.6	127.7	133.4	133.4
2-MN ^{a,(59)}	105.7	157.5	118.7	129.3	127.6	123.4	126.3	126.7	134.6	129.0
2,3-DMN calc.	106.3 107.3	149.4 150.6	149.4 150.6	106.3 107.3	127.0 126.6	124.6 124.5	124.6 124.5	127.0 126.6	130.2 131.2	130.2 131.2

^a: referenced to TMS $\pm$ 0.1; 0.1M in CDCl₃

X-ray Structure

2,3-DMN crystallizes in the P2₁2₁2₁ space group and 4 crystallographically equivalent molecules reside in the unit cell (Fig. 43 and 44).

Inspection of the torsional networks verify that both methoxy groups are nearly coplanar with the naphthalene unit where C11-O1-C2-C1 = -2.8° and C12-O2-C3-C4 = -3.6° (Table 13c). Steric interactions between the methyl groups and the *ortho* protons and/or favourable dipole interactions⁽⁴³⁾, are responsible for a widening of the C_{ortho}-C_{ipso}-O angles to 125.6° and 125.9° with a concomitant compression of the C_{ipso}-C_{ipso}-O angles to 114.1° and 114.0° (Table 13b).

Fig. 43 ORTEP diagram of 2,3-DMN

Fig. 44 Crystal packing diagram of 2,3-DMN

Fig. 45 DSC plot of 2,3-DMN on warming

Table 12 Crystallographic data of 2,3-DMN

Formula	$C_{12}H_{12}O_2$
fw	188.22
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a , Å	12.2873(7)
b , Å	13.1725(8)
c , Å	6.0278(5)
V , Å ³	975.63(7)
Z (molecules/cell)	4
D_c (grams/cm ³)	1.281
Crystal dimensions, mm	0.20 x 0.20 x 0.20
Radiation (λ , Å)	MoK α , 0.70930
Octants measured	$h(0 \text{ to } 14), k(0 \text{ to } 15), l(0 \text{ to } 7)$
Max 2θ (°)	49.9
Temperature (°C)	-110
No. of unique reflections	1026
No. of reflections measured	1026
No. of reflections with $I_{net} > 2.5 \sigma I_{net}$	886
$I\sigma/I_{ratio}$	0.121
R_f	0.027
R_w	0.030
GoF	1.57
maximum and minimum residual ep in final difference Fourier map, e Å ⁻³	0.120 and -0.150

Table 13a Atomic bond distances (Å) of 2,3-DMN

O1-C2	1.368(2)	C3-C4	1.366(3)
O1-C11	1.432(3)	C4-C10	1.430(3)
O2-C3	1.367(2)	C5-C6	1.367(3)
O2-C12	1.436(3)	C5-C10	1.414(3)
C1-C2	1.364(3)	C6-C7	1.402(3)
C2-C3	1.434(3)	C7-C8	1.367(3)
C1-C9	1.424(3)	C8-C9	1.413(3)
C9-C10	1.421(3)		

Table 13b Atomic bond angles (°) of 2,3-DMN

C2-O1-C11	116.6(2)	C1-C9-C8	121.9(2)
C3-O2-C12	116.8(2)	C4-C10-C5	122.3(2)
O1-C2-C1	125.6(2)	C1-C10-C9	119.5(2)
O2-C3-C4	125.9(2)	C8-C9-C10	118.6(2)
O1-C2-C3	114.1(2)	C4-C10-C9	118.6(2)
O2-C2-C3	114.0(2)	C5-C10-C9	119.1(2)
C1-C2-C3	120.3(2)	C7-C8-C9	120.9(2)
C2-C3-C4	120.0(2)	C2-C1-C9	120.6(2)
C6-C5-C10	120.6(2)	C6-C7-C8	120.4(2)
C3-C4-C10	121.0(2)	C5-C6-C7	120.3(2)

Table 13c Selected torsional angles (°) of 2,3-DMN

C11-O1-O2-C1	-2.8(1)	C10-C4-C3-O2	-179.8(2)
C12-O2-C3-C4	-3.6(1)	C11-O1-C2-C3	177.6(2)
O1-C1-C2-C9	-180.0(1)	C12-O2-C3-C2	176.7(2)
C3-C2-C1-C9	-0.4(1)	O1-C2-C3-C4	179.9(2)
O1-C2-C3-O2	-0.4(1)	C2-C1-C9-C10	0.3(1)
C1-C2-C3-O2	180.0(2)	C1-C9-C10-C4	-0.2(1)
C2-C1-C9-C8	-177.9(2)	C6-C5-C10-C4	-178.7(2)
C9-C10-C4-C3	0.1(1)	C10-C4-C3-C2	-0.1(1)

Table 14 Atomic parameters x, y, z and Biso of 2,3-DMN

	x	y	z	Biso
O1	0.43187(11)	0.89795(10)	0.03811(23)	3.10(6)
O2	0.38386(10)	1.00420(11)	-0.30179(23)	3.21(6)
C1	0.58959(15)	1.00153(14)	0.1269 (3)	2.39(8)
C2	0.50133(15)	0.97720(13)	0.0003 (3)	2.35(7)
C3	0.47412(14)	1.03717(13)	-0.1904 (3)	2.39(8)
C4	0.53693(14)	1.11877(14)	-0.2465 (3)	2.48(8)
C5	0.69586(15)	1.23081(14)	-0.1695 (3)	2.76(8)
C6	0.78558(16)	1.25320(15)	-0.0447 (4)	3.12(9)
C7	0.81367(15)	1.19217(15)	0.1372 (4)	3.17(9)
C8	0.75013(16)	1.11119(14)	0.1952 (3)	2.74(8)
C9	0.65630(14)	1.08615(13)	0.0712 (3)	2.26(7)
C10	0.63011(15)	1.14598(13)	-0.1174 (3)	2.28(7)
C11	0.45752(17)	0.83306(15)	0.2214 (4)	3.37(9)
C12	0.34884(16)	1.06428(16)	-0.4874 (4)	3.29(9)
H1	0.6070 (14)	0.9582 (12)	0.256 (3)	3.4(4)
H4	0.5205 (14)	1.1599 (13)	-0.383 (3)	3.3(4)
H5	0.6746 (12)	1.2775 (12)	-0.307 (3)	2.5(4)
H6	0.8343 (14)	1.3151 (12)	-0.084 (3)	2.6(4)
H7	0.8773 (14)	1.2070 (12)	0.226 (3)	3.6(5)
H8	0.7661 (13)	1.0693 (11)	0.326 (3)	2.8(4)
H11A	0.3988 (15)	0.7810 (13)	0.221 (3)	4.3(5)
H11B	0.5333 (15)	0.8023 (13)	0.201 (4)	4.9(5)
H11C	0.4534 (14)	0.8725 (12)	0.363 (3)	3.5(4)
H12A	0.2833 (15)	1.0312 (13)	-0.544 (3)	4.3(5)
H12B	0.4070 (16)	1.0717 (13)	-0.607 (3)	4.8(5)
H12C	0.3266 (15)	1.1398 (14)	-0.446 (4)	4.6(5)

Biso is the Mean of the Principal Axes of the Thermal Ellipsoid
E.S.D.s refer to the last digit printed

A survey of the literature indicates that no X-ray crystallographic results have been reported for materials containing the 2,3-dimethoxynaphthalene moiety, however many structures containing the related *ortho*-dimethoxybenzene moiety have been resolved^{(2),(12),(67)}. Of 32 structures reported, 30 contain *trans* coplanar methoxy groups.

There are four intermolecular C...H van der Waals contacts⁽⁶⁸⁾ involving distances of 2.48- 2.70 Å (Table 15), where the C...H direction is almost perpendicular ($90 \pm 18^\circ$) to the aromatic plane.

Table 15 Closest interatomic distances in 2,3-DMN (Å)

H1...H8	2.477
H5...H4	2.489
C1...H8	2.700
C5...H4	2.670

Assignment of the Solid State ^{13}C Shifts

In the 298 K CP/ MAS spectrum of 2,3-DMN, there are 10 lines (Fig. 46). If the origin of the CP/ MAS multiplicities was *intramolecular i.e.*, due to the small difference in the methoxy torsions of -2.8° and -3.6° , one would expect the conformationally sensitive *ortho* sites C1, C4 to be the most affected. In fact, the largest splitting of 1.2 ppm occurs for the distant C5, C8 sites. DSC measurements (Fig. 45) record no phase transition between -60°C and the mp = $117\text{--}118^\circ\text{C}$ therefore the origin of the CP/ MAS multiplicities are due to *intermolecular* effects. Splittings of peaks for crystalline solids originating from *intermolecular* contributions can be due to either bond distortion by crystalline packing or variation in local susceptibility⁽⁶⁹⁾. A better understanding of these effects in 2,3-DMN could give us some answers about the magnitude of these *intermolecular* forces, as reflected in the observed ^{13}C splittings for 1,2-DMB⁽²⁶⁾.

Tabulation of the four closest *intermolecular* contacts reveals participation of the C1, C4, C5 and C8 sites only (Table 15). The largest symmetry breaking in the CP/ MAS spectrum also occurs at these sites (Table 16). Previous work by Etter *et al.* encountered the existence of close intermolecular H ... π contacts in the crystal structure of a β -triketomethane⁽⁷⁰⁾. The observed splittings in 2,3-DMN are likely due to a perturbation of the π orbital on the atom in question caused by a nearby proton. If so, the largest anisotropic shift differences between symmetry related carbons should be associated with the σ_{11} and σ_{22} components. Note that the π orbitals on C4 and C8 are not directly

Fig. 46 Solution and solid state ^{13}C spectra of 2,3-DMN

involved in the close contacts. In confirmation, shielding tensor measurements were undertaken on powder 2,3-DMN using the method of *Herzfeld and Berger*⁽³³⁾.

Table 16 ^{13}C shifts of 2,3-DMN

	solid phase ^a	solution ^b
C1	(105.8) ^c	106.3
C2	150.4	149.4
C3	150.4	149.4
C4	(106.7) ^c	106.3
C5	(126.8) ^d	127.0
C6	123.8	124.6
C7	123.8	124.6
C8	(128.0) ^d	127.0
C9	(129.7) ^e	130.2
C10	(130.0) ^e	130.2
C11	(54.8) ^f	55.8
C12	(55.0) ^f	55.8

^a referenced to hexamethylbenzene; brackets denote possible assignment interchange

^b referenced to TMS ± 0.1 ; 0.1M in CDCl_3

^{13}C Shielding Tensor Analysis

The principal components of the aromatic ^{13}C shifts in 2,3-DMN were measured using variable spinning CP/MAS techniques (Fig. 48). If the spinning frequency is reduced relative to the chemical shift anisotropy, then the isotropic line in the CP/ MAS spectrum is flanked on both sides by sidebands spaced at the spinning frequency. The intensities of the spinning sidebands are related to the chemical shift anisotropy and provide an opportunity to recover the shift parameters. The *Herzfeld and Berger* method⁽³³⁾ is a graphical mathematical resolution for this technique and will be used herein to extract the desired principal shifts of 2,3-DMN. Before embarking on this exercise, the solid state structure of the parent naphthalene will be reviewed.

It has proved impossible to use the *Herzfeld and Berger* method to extract the tensors of naphthalene, due to very long ^1H spin-lattice relaxation times (Fig. 47). Fortunately, the principal elements of the shielding tensors are known from a single crystal study^{(62),(63)}.

Naphthalene crystallizes in the $P2_1/a$ space group with two molecules in the unit cell, related by a two-fold rotation about the b crystal axis. X-ray diffraction studies⁽⁷¹⁾⁻⁽⁷⁶⁾ are unable to detect any distortion of the molecule in the crystal, where a crystallographic inversion center renders the asymmetric unit as one-half of the molecule. However greater multiplicity is observed in the principal elements of the ^{13}C shift tensors over what is expected based on X-ray data⁽⁶³⁾ (Table 17). Note this reduction in symmetry is invisible isotropically.

In naphthalene, the deviations from the mmm symmetry^{(62),(63)} are centered on the C1 and C4 sites. The effects involve both the π and σ populations, reflected in a difference of 5.3 ppm in the σ_{22} values and 2.4 ppm in the σ_{33} values. It was suggested that this symmetry breaking in the shielding tensor data was due to *intermolecular* close contacts within the lattice. In particular, a close $\text{H} \cdots \text{H}$ contact of 2.40 Å was detected between H1 of the reference molecule and H2 at (1/2, 1/2, 1).

For 2,3-DMN, the largest symmetry breaking occurs at the C1/ C4 and C5/ C8 sites (Table 18). The closest *intermolecular* contacts in the 2,3-DMN crystal involve $\text{H} \cdots \text{H}$ and $\text{H} \cdots \text{C}$ between mutually perpendicular molecules (Table 15). If the CP/ MAS splittings reflect $\text{H} \cdots \text{H}$ packing forces, then the largest anisotropic shift differences between symmetry related sites should reside in σ_{33} , the component most sensitive to changes in σ electron density. By contrast $\text{H} \cdots \pi$ packing should perturb the σ_{11} , σ_{22} components of the carbon bearing the π orbital.

Fig. 47 50.32 MHz ^{13}C CP/ MAS spectrum of naphthalene
($\nu_r = 4.0$ kHz; $D_1 = 10$ min)

Table 17 ^{13}C shielding tensors of naphthalene^a

	σ_{11}	σ_{22}	σ_{33}	σ_{iso}
C1, C5	224.7	140.3	22.8	129.3
C2, C6	227.6	139.3	11.1	126.0
C3, C7	227.6	138.2	10.4	125.4
C4, C8	223.9	145.6	20.4	129.9
C9, C10	208.5	202.2	-5.9	134.9

^a: referenced to TMS $\delta = 191.7$ ppm⁽⁶³⁾

Fig. 48 Variable spinning rate ¹³C CP/MAS spectra of 2,3-DMN

Table 18 ^{13}C shielding tensors of 2,3-DMN

	σ_{11}	σ_{22}	σ_{33}	σ_{iso}	$\Delta\sigma_{11}$	$\Delta\sigma_{22}$
C1, C4	169.9 ± 2.0	121.5 ± 2.0	25.9 ± 2.0	105.8 ± 2.0	4.0	2.7
	173.9 ± 2.0	118.8 ± 2.0	27.4 ± 2.0	106.7 ± 2.0		
C5, C8	208.4 ± 7.0	144.5 ± 3.0	27.5 ± 7.0	126.8 ± 6.0	9.8	4.4
	218.1 ± 2.0	140.1 ± 2.0	25.7 ± 2.0	128.0 ± 2.0		

The average differences for σ_{11} , σ_{22} and σ_{33} between the sites in question are 6.9, 3.6 and 1.6 ppm respectively (Table 18). Therefore the isotropic CP/ MAS splittings of 0.9 and 1.2 ppm support packing forces involving a π perturbation of the aromatic ring.

C- Conclusion

Deviations from C_2 symmetry in the ^{13}C CP/ MAS spectrum of 2,3-DMN are in agreement with the existence of specific van der Waals close contacts between two equivalent molecules within the unit cell (Table 15). Specific assignment of the CP/ MAS anisotropic shifts could be accomplished if tensors for the parent naphthalene of true C_1 symmetry were known. In the X-ray structure for the symmetric 2,7-DMN, the asymmetric unit is also the whole molecule⁽⁷⁷⁾, which implies that packing is at the origin of the reduction in symmetry. For 1,2-DMB, *interatomic* contacts resulting in CP/ MAS symmetry breaking involve the *ortho* ($\Delta = 1.6$ ppm) and the *para* ($\Delta = 1.7$ ppm) sites. Unlike 2,3-DMN though, oxygen...aromatic close contacts are also encountered, which split the methoxy groups by 1.9 ppm isotropically. The packing forces in crystalline 1,2-DMB are therefore somewhat different, and the tensors give no conclusive information as to the three-dimensional nature.

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CHAPTER 5

Solid State Structure of Benzo-10-Crown-3 and its LiClO_4 Complex

Part I

Benzo-10-Crown-3

A- Introduction

Recent work in the laboratories of Pr G. W. Buchanan on benzo-9-crown-3⁽¹⁾ has shown that differences in torsion angles about the $\text{C}_{\text{ar}}\text{-O}$ bonds determined crystallographically are reflected in the aromatic ^{13}C CP/ MAS shifts. There is a stereoelectronic shielding effect operative in such systems which is dependent on the orientation of the aryl oxygen lone pairs relative to the aromatic π system. To further explore the scope of such effects, benzo-10-crown-3 (1) and its deuterated analogues (2, 3) were examined.

The parent compounds of 1 are the n -oxacyclodecenes ($n = 0 \rightarrow 3$). A literature search has shown these materials are relatively unknown except for $n = 0$. For *cis*-cyclodecene, calculations based on Hendrickson's treatment⁽²⁾ of conformational energy⁽³⁾⁻⁽⁵⁾ conclude that asymmetric conformations have the lowest energies.

B- Results and Discussion

X-ray Structure

The X-ray structure at -100°C reveals that **1** (mp $30\text{--}31^{\circ}\text{C}$) crystallizes in the $P2_1/c$ space group and DSC measurements show there is no phase transition between -100°C and the mp (Fig. 51).

In **1**, the two ether carbons closest to the aromatic ring lie in an *antiperiplanar* fashion, twisted $73.6(1)^{\circ}$ (C3-C2-O2-C7) and $61.8(1)^{\circ}$ (C6-C1-O1-C11) respectively from the plane (Fig. 49).

For an alkoxy substituent planar with the benzene ring, there exists a distortion of the trigonal *ipso* carbon geometry, reflected in the two C-C-O bond angles. The *cis*-alkoxy bond angle expands to *ca.* 125° while the *trans* is compressed to *ca.* 115° . When the alkoxy moiety is twisted out of the plane, this angular strain is reduced. For each *ipso* carbon in **1**, the difference between the *cis* and *trans* C-C-O angles is $2.2^{\circ} \pm 0.5$.

In **1**, the crown cavity can be viewed to be composed of an ethylenoxy and a propylenoxy unit. Theoretical calculations in the gas phase on 1,2-dimethoxyethane^{(8),(9)} indicate a preference for the *gauche* form around the C-C bond by 0.5 kcal/ mol, the origin of which remains controversial. This is supported in the X-ray structures of crown ethers, where there is a strong preference of the O-C-C-O unit to adopt a *gauche* geometry regardless of ring size^{(1),(6),(7)} (Table 21). Conformational energy calculations and gas phase NMR on 1,3-dimethoxypropane⁽¹⁰⁾ also show a preferred *gauche* geometry around the C-C bonds, where the g^+g^- rotational state is destabilized 1.97 kcal/ mol over the g^+g^+ arrangement due to repulsive 1,5-diaxial type O... O interactions⁽¹¹⁾⁻⁽¹³⁾. The ten-membered ring of **1** exhibits a *gauche* O1-C11-C10-O3 torsion angle of 58.6° , and g^-g^- torsion angles in the O2-C7-C8-C9-O3 segment of 55.5° and 55.4° , all in agreement with literature precedent.

Fig. 49 ORTEP diagram of 1 at -100°C

Fig. 50 Unit cell of 1

Table 19 Crystallographic data of 1

Formula	$C_{11}H_{14}O_3$
fw	194.23
Crystal system	monoclinic
Space group	$P 2_1/c$
a , Å	7.2705 (20)
b , Å	10.825 (3)
c , Å	12.790 (5)
V , Å ³	1004.7 (6)
Z (molecules/ unit cell)	4
D_c (g/ cm ³)	1.284
Crystal dimensions, mm	0.20 x 0.20 x 0.20
Radiation (λ , Å)	MoK α , 0.70930
Octants measured	$h(-8 \text{ to } 8)$, $k(0 \text{ to } 12)$, $l(0 \text{ to } 15)$
Max $2\theta^\circ$	49.9
Temperature	-100°C
No. of unique reflections	1768
No. of reflections measured	1912
No. of reflections with $I_{net} > 2.5 \sigma I_{net}$	1456
Largest shift/ error in final least squares cycle	0.068
R_f	0.035
R_w	0.041
GoF	2.11
Maximum and minimum residual ep in final difference Fourier map, eÅ ⁻³	0.160 and -0.160

Fig. 51 DSC plot of 1 upon warming

Table 20 Atomic parameters and Biso factors of 1

	x	y	z	Biso
O1	0.62606 (15)	0.22780 (9)	0.15770 (8)	2.75 (4)
O2	0.49713 (13)	0.47425 (9)	0.16146 (8)	2.43 (4)
O3	0.28505 (15)	0.24504 (10)	0.03376 (9)	3.11 (5)
C1	0.71406 (20)	0.31613 (13)	0.22056 (11)	2.30 (5)
C2	0.64737 (19)	0.43691 (13)	0.22531 (11)	2.21 (6)
C3	0.73558 (22)	0.52202 (14)	0.29186 (12)	2.68 (6)
C4	0.88958 (23)	0.48726 (15)	0.35486 (12)	2.97 (6)
C5	0.95389 (21)	0.36711 (15)	0.35159 (12)	2.92 (6)
C6	0.86739 (21)	0.28209 (14)	0.28407 (12)	2.67 (6)
C7	0.32163 (20)	0.43087 (14)	0.19317 (12)	2.51 (6)
C8	0.18485 (21)	0.43939 (14)	0.09960 (12)	2.87 (6)
C9	0.24703 (22)	0.37069 (15)	0.00553 (13)	3.05 (6)
C10	0.45050 (3)	0.19653 (16)	-0.00485 (13)	3.46 (7)
C11	0.62387 (23)	0.25064 (15)	0.04647 (13)	3.06 (7)
H3	0.68700 (21)	0.60810 (14)	0.2917 (11)	2.9 (3)
H4	0.94510 (22)	0.54870 (14)	0.3999 (12)	3.4 (4)
H5	1.05850 (22)	0.34360 (15)	0.3953 (12)	3.6 (4)
H6	0.91180 (22)	0.19900 (14)	0.2792 (12)	3.3 (4)
H7A	0.33500 (18)	0.34300 (12)	0.2169 (10)	1.8 (3)
H7B	0.28620 (21)	0.48080 (13)	0.2524 (11)	2.7 (3)
H8A	0.16560 (20)	0.52970 (13)	0.0818 (11)	2.6 (3)
H8B	0.06920 (22)	0.41070 (15)	0.1218 (12)	3.4 (3)
H9A	0.36030 (21)	0.40570 (13)	-0.0198 (11)	3.0 (3)
H9B	0.14870 (22)	0.37240 (15)	-0.0536 (12)	3.4 (4)
H10A	0.45160 (23)	0.20940 (16)	-0.0821 (13)	4.2 (4)
H10B	0.44570 (22)	0.10400 (15)	0.0110 (12)	3.5 (4)
H11A	0.73290 (23)	0.21090 (15)	0.0184 (13)	4.0 (4)
H11B	0.63240 (21)	0.34270 (13)	0.0323 (11)	2.7 (3)

Table 21a Atomic bond distances (Å) of 1

O2-C2	1.38 (2)	O2-C7	1.44 (2)
O1-C1	1.38 (2)	O1-C11	1.44 (2)
O3-C10	1.42 (2)	O3-C9	1.42 (2)
C2-C3	1.38 (2)	C1-C2	1.39 (2)
C3-C4	1.39 (2)	C4-C5	1.38 (2)
C5-C6	1.38 (2)	C6-C1	1.38 (2)
C11-C10	1.50 (2)	C8-C9	1.50 (2)
C7-C8	1.51 (2)		

Table 21b Atomic bond angles (°) of 1

C2-O2-C7	114.79 (11)	C1-O1-C11	115.60 (11)
C10-O3-C9	114.60 (12)	O2-C2-C3	119.19 (13)
O2-C2-C1	120.75 (12)	C3-C2-C1	120.03 (13)
C2-C3-C4	120.15 (14)	C3-C4-C5	119.89 (14)
C4-C5-C6	120.11 (14)	C5-C6-C1	120.38 (14)
O1-C1-C2	121.58 (13)	O1-C1-C6	118.93 (13)
C2-C1-C6	119.42 (13)	O1-C11-C10	108.78 (13)
O3-C10-C11	114.02 (13)	O3-C9-C8	109.31 (12)
C9-C8-C7	112.77 (13)	O2-C7-C8	107.96 (12)

Table 21c Torsional angles (°) of 1

C7-O2-C2-C3	-106.4 (1)	C5-C6-C1-O1	-177.1 (2)
C2-O2-C7-C8	-160.4 (2)	O1-C11-C10-O3	58.6 (1)
C11-O1-C1-C6	-118.2 (1)	C9-C8-C7-O2	55.5 (1)
C9-O3-C10-C11	69.9 (1)	C7-O2-C2-C1	75.8 (1)
O2-C2-C3-C4	-178.4 (2)	C11-O1-C1-C2	64.9 (1)
C1-C2-C3-C4	-0.6 (1)	C1-O1-C11-C10	-148.9 (2)
O2-C2-C1-O1	-4.4 (1)	C10-O3-C9-C8	-136.3 (2)
C3-C2-C1-O1	177.8 (2)	O2-C2-C1-C6	178.7 (2)
C2-C3-C4-C5	-0.5 (1)	C3-C2-C1-C6	0.9 (1)
C3-C4-C5-C6	1.3 (1)	C5-C6-C1-C2	-0.1 (1)
C4-C5-C6-C1	-1.1 (1)	O3-C9-C8-C7	55.4 (1)

Considering only the bulk macrocyclic conformation (i.e., O3 as a CH₂), there exists a C₂ axis connecting the mid-points of the C1-C2 and C9-O3 bonds. Based on Hendrickson's treatment, previous calculations on *cis*-cyclodecene locate this conformation "Form G" as the fourth lowest in energy at 6.6 kcal/ mol⁽⁵⁾, with the largest torsional angle difference to **1** being 16.4°. In our MM3 minimization on **1**, keeping the ethyleneoxy unit *gauche*, the three lowest energy structures (all within 3 kcal/ mol), each have a *ca.* 35° torsion angle about one C_{*ipso*}-O bond and a perpendicular disposition about the other. Therefore an additional constraint of an "up-down" geometry about the benzene ring was added, resulting in the location of the experimental conformation as the fourth overall lowest at 3.4 kcal/ mol. Lacking in this structure is a stabilizing dihedral angle energy term, varying from 2.0 to 4.8 kcal/ mol, arising from the near coplanarity of one of the oxygen lone pairs with the *ipso p* orbital, present in the first three structures.

Solution NMR Studies

The ¹H and ¹³C solution NMR spectra of **1** have been recorded as a function of temperature between 200 and 300 K. No coalescence phenomena were observed, indicating that conformational interconversions remain fast on the NMR timescale. Iterative computer analysis of the aliphatic region of the 400 MHz ¹H spectrum at 300 K was carried out, treating the C10, C11 protons as an AA'BB' spin system and the C7, C8, C9 protons as an AA'MM'XX' case. The C10 and C11 methylene protons have vicinal coupling constants of 6.39 and 2.29 Hz, in agreement to those found in related molecules⁽¹⁴⁾, and are consistent with a situation in which there is rapid interconversion between rotamers in which the oxygen atoms are in a *gauche* relationship. The vicinal couplings in the C9-C8-C7 unit are conformationally averaged to values of 5.41, 5.20, 5.07 and 4.49 Hz (Table 22). Signal assignments in the ¹H spectrum were facilitated by the results of a NOESY experiment in which correlations were noted between the H7, H11 multiplet at *ca.* 4.2 ppm and the *ortho* aromatic protons (Fig. 52). A COSY experiment reveals that H8 has a crosspeak to the downfield component of the 4.2 ppm multiplet, thereby assigning it as H7 (Fig. 53). Remaining proton assignments are

Table 22 ^1H NMR data for the methylene protons of 1
 $(\delta_{\text{H}}$ from TMS ± 0.001 ; $^n\text{J} \pm 0.01$, $n = 2, 3$)

Proton	δ_{H} (ppm)	^2J (Hz)	^3J (Hz)
7	4.199	-14.35	5.07, 4.49
8	1.885	14.25	5.41, 5.20 5.07, 4.49
9	3.897	-12.52	5.41, 5.20
10	3.799	-12.23	6.39, 2.29
11	4.181	-12.87	6.39, 2.29

Fig. 52 NOESY spectrum of 1

Fig. 53 COSY spectrum of 1

Fig. 54 HETCOR spectrum of 1

straightforward by COSY and by comparison to **2** and **3**. With the ^1H assignments in hand, the ^1J HETCOR (HMQC) experiment gives shifts for the directly bonded carbons (Fig. 54). Also, a long range HETCOR (HMBC) experiment permitted distinction between the quaternary aromatic carbons.

Assignment of the Solid State ^{13}C Shifts

The respective range of solid state shifts for the aromatic and aliphatic carbons are 4.6 and 10.1 ppm, while in solution are 2.5 and 7.1 ppm, due to the lack of conformational averaging in the solid. In the dipolar dephased CP/ MAS spectrum of **1**, the protonated carbon resonances disappear completely, indicative of a static solid devoid of any large amplitude conformational motion in the macrocycle.

Assignment of the aliphatic oxy resonances is accomplished with the aid of well established stereochemically dependent shielding trends. The relevant torsional networks here involve C-O-C-C and C-C-C-O units where the *gauche* geometry is shielding over the *anti* for all carbons^{(15),(16)}. For non-ideal geometries, intermediate between *gauche* and *anti*, a deshielding results with a maximum at 120° . Also for $\text{C}_{\text{ar}}-\text{C}_{\text{ar}}-\text{O}-\text{C}^*$ networks, a steady deshielding of up to *ca.* 5 ppm occurs as $\theta = 0^\circ \rightarrow 90^\circ$ ⁽¹⁾ (Chapter 6).

Inspection of the torsion angles reveal both C7 and C11 are twisted considerably out of the plane by $75.8(1)$ and $64.9(1)^\circ$ respectively, hence gain a large downfield component. Based on this criterion alone, C7 should be more deshielded than C11 due to the 11° greater associated non-planarity. However, the remaining *gauche* and *anti* networks for C7 ($55.4(1)^\circ$, $55.5(1)^\circ$, $-160.4(2)^\circ$) are stronger than for C11 ($58.6(1)^\circ$, $69.9(1)^\circ$, $-148.9(1)^\circ$), resulting in greater shielding for the former. The dipolar dephased CP/ MAS spectrum of **2** unambiguously assigns C11 as the most deshielded resonance at 71.9 ppm (Fig. 55b). Therefore C7 is assigned at 70.7 ppm, shielded by 1.2 ppm over C11. The only notable torsional differences between the remaining two oxy-carbons reside in the $\text{C9}-\text{C8}-\text{C7}-\text{O2} = 55.5(1)^\circ$ and $\text{C1}-\text{O1}-\text{C11}-\text{C10} = -148.9(1)^\circ$ networks, where C9 should be substantially shielded over C10.

Fig. 55 (a) CP/MAS spectrum of 1, and (b) normal and dipolar dephased
CP/ MAS spectra of 2

Table 23 ^{13}C shifts of **1** (δ_{C} from TMS ± 0.1)

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
solution	151.7	151.3	122.4	123.9	124.2	121.7	71.1	29.9	66.6	69.5	73.7
solid	153.7	152.2	128.0	123.4	125.8	125.8	70.7	29.4	61.2	67.5	71.9

Fig. 55 (c) normal and dipolar dephased CP/ MAS spectra of **3**

The dipolar dephased spectrum of **3** unambiguously assigns C9 to the most shielded resonance at 61.2 ppm, upfield 6.3 ppm from C10.

In the aromatic region, there are also well established conformational shielding trends based on stereoelectronic effects *i.e.*, the degree of aryl oxygen lone-pair overlap with the aromatic π system. Steric effects *i.e.*, γ -*gauche* interactions involving the *ortho* sites, are absent in **1** (Chapter 6, Table 30). The greatly deshielded *ipso* carbons are unambiguously assigned due to the inductive effect. In general, carbons *ortho*-trans to a planar alkoxy group are shielded 2- 3 ppm over the *para*. As the twist angle increases, these two sites experience mesomeric deshielding⁽¹⁾ and eventually resonate together at *ca.* 123 ppm for $\theta \approx 50^\circ$ (Chapter 6, Fig. 61), after which the *ortho*-trans becomes more deshielded. In the present case, the twist angles are $64.9(1)^\circ$ and $75.8(1)^\circ$ therefore C3 and C6 are assigned as deshielded relative to C5 and C4 respectively (Table 23). Unambiguous assignment of the aromatic region is in progress by deuterium incorporation *via ortho*-metallation.

Part II

(Benzo-10-Crown-3)₂· LiClO₄

A- Introduction

Cyclic homologues of ethylene oxide $-(\text{CH}_2\text{-CH}_2\text{-O})_n-$, possess remarkable complexing power for alkali and other cations and have attracted much attention^{(17),(18)}.

Crowns are built largely upon the ethylenoxy unit because it is (i) flexible and relatively strain free, (ii) prefers the *gauche* conformation allowing alignment of the C-O dipoles and electron pairs for complexation with cations and (iii) involves precursors which are common industrial chemicals. Other possibilities involve methyleneoxy or propyleneoxy units. The methyleneoxy system $\text{O-CH}_2\text{-O}$ has the disadvantage that, being an acetal, is susceptible to acid catalyzed hydrolysis⁽¹⁹⁾. Crowns with longer carbon chains between successive oxygens experience carbon-carbon backbone interactions that could affect the macro ring conformation.

For *n*-crown-4 ethers ($n = 12 \rightarrow 16$), the cavity sizes are most suited for Li^+ complexation but none exhibit satisfactory Li^+/Na^+ selectivity⁽²⁰⁾⁻⁽²²⁾. Decalino-14-crown-4 was recently synthesized⁽²³⁾. This ionophore exhibits a Li^+/Na^+ selectivity of 20 with 1:1 complexation stoichiometry, has effective extractability of 81 % and is used as the best Li^+ selective electrode system known to date.

Herein a complexation study of **1** with Li^+ is undertaken. Etheral oxygens are hard bases that interact strongly with hard acids such as Li^+ . Two of the oxygen atoms in **1** are less basic due to the presence of the aromatic ring, hence a decrease in the kinetic binding is expected relative to saturated analogues. The macrocycle must adopt a conformation in which all three oxygens are exposed on the same side in order to complex the Li^+ cation. The crown cavity will then provide a good basis for a tetrahedral structure as is encountered with $12\text{C}3 \cdot \text{Li}^+$ (1:1) complexes⁽²⁴⁾.

B- Results and Discussion

X-ray Structure

An attempt was made to form and crystallize a 1:1 complex between **1** and LiClO_4 by the use of a stoichiometric amount of each chemical in ethyl acetate. The recovery of a crystalline compound proved to be a 2:1 sandwich complex (benzo-10-crown-3)₂ · LiClO_4 (**4**) based on X-ray crystallography (Fig. 56, Table 24).

Hexadentate Li^+ selective ligands have previously been encountered in the case of rigid-cage molecules with very small cavity radii, such as cryptands and spherands^{(25),(26)}. In general however, hexadentate ligands seem an unlikely choice for Li^+ selective complexation since they are also expected to effectively bind Na^+ .

In **4** there are two non-equivalent sandwich complexes in the crystal, **4A** and **4B**, each possessing a crystallographic plane of symmetry through the Li (Fig. 54). Also, **4A** is a pseudo-mirror image of **4B** where the largest differences in corresponding torsion angles are $10.2(11)^\circ$ and $-14.0(11)^\circ$ involving the macrocycle and aromatic ring respectively.

Each complex adopts a distorted octahedral geometry with Li^+ coordination number six and an average O-Li-O angle of 82.4° , *ca.* 8° smaller than ideal (Table 27b). The cavity size of 1.34- 1.47 Å is considerably smaller than both the free ligand at 1.41- 1.65 Å and that hypothesized dimension for 10-crown-3· Li^+ at 1.64 Å⁽²⁷⁾. The maximum deviation from the oxygen least squares plane is 0.06 Å for **4A** and is negligible for **4B**. The Li^+ is situated above this plane by 1.31 Å for **4A** and 1.37 Å for **4B**. The average Li...O distance of 2.11 Å is shorter by 0.13 Å than commonly found for lithium-ether complexes⁽²⁸⁾, but is relatively close to that calculated for 10-crown-3· Li^+ (1: 1) at 2.19 Å⁽²⁷⁾.

The aromatic ring is inclined to the oxygen least squares plane by 50.6° and 53.0° for **4A** and **4B** respectively. The two molecules in each complex adopt the head-to-head geometry as in (benzo-14-crown-4)₂· NaClO_4 ⁽²³⁾, in contrast to the head-to-tail geometry found in (benzo-15-crown-5)₂· KI ⁽²⁹⁾.

Fig. 56 ORTEP diagram of **4** at -100°C

Fig. 57 Unit cell of 4

Table 24 Crystallographic data of **4**

Formula	C ₂₂ H ₂₈ O ₁₀ ClLi
fw	494.85
Crystal system	orthorhombic
Space group	P <i>cc</i> 2
<i>a</i> , Å	11.9137 (1)
<i>b</i> , Å	14.2130 (2)
<i>c</i> , Å	14.4007 (2)
<i>V</i> , Å ³	2438.46 (1)
<i>Z</i> (molecules/ unit cell)	4
<i>D_c</i> (g/ cm ³)	1.348
Crystal dimensions, mm	0.20 x 0.20 x 0.20
Radiation (λ, Å)	MoKα, 0.70930
Octants measured	<i>h</i> (-7 to 7), <i>k</i> (-15 to 15), <i>l</i> (-15 to 15)
Max 2θ°	46.4
Temperature	-100°C
No. of unique reflections	3481
No. of reflections measured	9001
No. of reflections with <i>I</i> _{net} > 2.5 σ <i>I</i> _{net}	2974
Largest shift/ error in final least squares cycle	0.084
<i>R_f</i>	0.085
<i>R_w</i>	0.116
GoF	5.80
Maximum and minimum residual ep in final difference Fourier map, eÅ ⁻³	0.820 and -0.370

Table 25 Atomic parameters and Biso factors of **4**

	<i>x</i>	<i>y</i>	<i>z</i>	Biso
O1	0.1195 (4)	0.4603 (4)	0.6046 (4)	4.3 (3)
O2	-0.0322 (5)	0.3580 (4)	0.5105 (5)	6.0 (4)
O3	0.1453 (6)	0.4686 (5)	0.4188 (5)	7.6 (4)
O4	0.3799 (4)	0.0357 (4)	0.0763 (4)	4.5 (3)
O5	0.5265 (5)	0.1392 (4)	0.1700 (4)	4.8 (3)
O6	0.3512 (8)	0.0312 (5)	0.2673 (4)	10.1 (5)
C1	0.1080 (6)	0.3626 (6)	0.6280 (6)	3.9 (4)
C2	0.0277 (8)	0.3120 (6)	0.5756 (7)	4.9 (5)
C3	0.0176 (10)	0.2175 (7)	0.5980 (9)	7.3 (7)
C4	0.0743 (10)	0.1835 (7)	0.6790 (8)	7.9 (7)
C5	0.1498 (9)	0.2302 (7)	0.7207 (7)	6.1 (6)

C6	0.1692 (7)	0.3237 (7)	0.6983 (6)	5.2 (5)
C7	-0.0367 (9)	0.3159 (7)	0.4138 (8)	6.6 (6)
C8	0.0881 (9)	0.3219 (9)	0.3718 (8)	7.6 (7)
C9	0.1219 (15)	0.4149 (9)	0.3534 (13)	12.9 (11)
C10	0.2436 (7)	0.4483 (6)	0.4693 (11)	6.7 (7)
C11	0.2277 (7)	0.4904 (7)	0.5689 (7)	4.7 (5)
C12	0.3871 (7)	0.1309 (6)	0.0547 (6)	4.2 (4)
C13	0.4661 (7)	0.1828 (5)	0.0993 (6)	4.0 (4)
C14	0.4913 (8)	0.2791 (6)	0.0751(7)	4.4 (4)
C15	0.4294 (10)	0.3228 (7)	0.0096 (7)	6.8 (6)
C16	0.3422 (8)	0.2682 (8)	-0.0375 (7)	6.5 (6)
C17	0.3239 (8)	0.1735 (8)	-0.0161 (6)	5.5 (5)
C18	0.5271 (7)	0.1864 (6)	0.2590 (7)	5.0 (5)
C19	0.4190 (10)	0.1874 (7)	0.3050 (7)	7.0 (6)
C20	0.3704 (9)	0.0962 (10)	0.3420 (7)	8.8 (8)
C21	0.2414 (9)	0.0562 (9)	0.2025 (8)	7.4 (7)
C22	0.2692 (7)	0.0078 (10)	0.1125 (9)	7.3 (7)
Li1	0.0000	0.5000	0.5037 (13)	4.4 (11)
Li2	0.5000	0.0000	0.1785 (22)	7.2 (16)

Table 26a Bond lengths (Å) of 4

O1-C1	1.43 (1)	C8-C9	1.40 (2)
O1-C11	1.45 (1)	C10-C11	1.56 (2)
O1-Li1	2.11 (1)	C12-C13	1.35 (1)
O2-C2	1.34 (1)	C12-C17	1.40 (1)
O2-C7	1.51 (1)	C13-C14	1.44 (1)
O2-Li1	2.05 (6)	C14-C15	1.34 (1)
O3-C9	1.24 (2)	C15-C16	1.46 (1)
O3-C10	1.40 (1)	C16-C17	1.39 (1)
O3-Li1	2.16 (1)	C18-C19	1.44 (1)
O4-C12	1.39 (1)	C19-C20	1.51 (2)
O4-C22	1.47 (1)	C21-C22	1.50 (2)
O4-Li2	2.11 (2)	C2-C3	1.38 (1)
C3-C4	1.43 (2)	C4-C5	1.26 (2)
C5-C6	1.38 (1)	C7-C8	1.60 (1)
O5-C13	1.39 (1)	O5-C18	1.44 (1)
O5-Li2	2.00 (6)	O6-C20	1.43 (1)
O6-C21	1.64 (1)	O6-Li2	2.23 (2)
C1-C2	1.41 (1)	C1-C6	1.36 (1)

Table 26b Bond angles (°) of 4

C1-O1-C11	116.9(6)	O4-C12-C17	123.3(8)
C1-O1-Li1	110.9(4)	C13-C12-C17	118.8(9)
C11-O1-Li1	106.1(6)	O5-C13-C12	117.6(7)
C2-O2-C7	117.9(7)	O5-C13-C14	119.4(7)
C2-O2-Li1	106.1(6)	C12-C13-C14	123.0(8)
C7-O2-Li1	110.5(8)	C13-C14-C15	119.5(8)
C9-O3-C10	116.8(10)	C14-C15-C16	117.9(9)
C9-O3-Li1	112.0(10)	C15-C16-C17	121.3(8)
C10-O3-Li1	114.6(8)	C12-C17-C16	119.4(9)
C12-O4-C22	113.3(7)	O5-C18-C19	113.9(7)
C12-O4-Li2	110.4(5)	C18-C19-C20	119.4(9)
C22-O4-Li2	107.2(8)	O6-C20-C19	110.3(9)
C13-O5-C18	116.4(6)	O6-C21-C22	102.4(8)
C13-O5-Li2	113.7(8)	O4-C22-C21	112.3(8)
C18-O5-Li2	113.8(10)	C4-C5-C6	120.6(10)
C20-O6-C21	114.4(8)	C1-C6-C5	118.1(9)
C20-O6-Li2	115.5(8)	O2-C7-C8	107.0(8)
C21-O6-Li2	110.5(9)	O5-Li2-O6	88.0(5)
O1-C1-C2	115.5(7)	C7-C8-C9	112.7(12)
O1-C1-C6	121.0(8)	O3-C9-C8	119.8(14)
C2-C1-C6	123.4(9)	O1-C11-C10	108.6(7)
O2-C2-C3	125.8(9)	O1-Li1-O2	80.3(4)
C1-C2-C3	115.3(9)	O1-Li1-O3	78.1(3)
C2-C3-C4	118.3(10)	O2-Li1-O3	88.5(4)
C3-C4-C5	123.0(10)	O4-Li2-O5	80.1(6)
O4-C12-C13	117.6(8)	O4-Li2-O6	79.3(3)
C11-C10-O3	107.1(7)	O2-C2-C1	118.9(8)

Table 26c Torsional angles (°) of 4

C11-O1-C1-C2	-117.1(15)	C11-O1-C1-C6	64.7(12)
Li1-O1-C1-C2	4.7(9)	Li1-O1-C1-C6	-173.6(15)
C1-O1-C11-C10	70.2(13)	Li1-O1-C11-C10	-54.0(10)
C1-O1-Li1-O2	-4.7(7)	C1-O1-Li1-O3	-95.2(12)
C11-O1-Li1-O2	123.2(14)	C11-O1-Li1-O3	32.7(9)
C7-O2-C2-C1	129.1(17)	C7-O2-C2-C3	-51.6(13)
Li1-O2-C2-C1	-3.0(8)	Li1-O2-C2-C3	176.2(17)
C2-O2-C7-C8	-66.4(13)	Li1-O2-C7-C8	67.4(12)
C2-O2-Li1-O1	4.3(8)	C2-O2-Li1-O3	82.5(13)
C7-O2-Li1-O1	-131.3(15)	C7-O2-Li1-O3	-53.1(10)
C10-O3-C9-C8	69.1(18)	Li1-O3-C9-C8	-65.9(15)
C9-O3-C10-C11	-154.3(24)	Li1-O3-C10-C11	-20.4(9)
C9-O3-Li1-O1	130.2(20)	C9-O3-Li1-O2	49.8(16)
C10-O3-Li1-O1	-5.8(9)	C10-O3-Li1-O2	-86.2(14)
C22-O4-C12-C13	120.7(16)	C22-O4-C12-C17	-65.0(13)
Li2-O4-C12-C13	0.6(11)	Li2-O4-C12-C17	174.8(17)
C12-O4-C22-C21	-62.8(14)	Li2-O4-C22-C21	59.2(14)
C12-O4-Li2-O5	3.2(8)	C12-O4-Li2-O6	93.0(18)
C22-O4-Li2-O5	-120.5(22)	C22-O4-Li2-O6	-30.7(11)
C18-O5-C13-C12	-126.2(15)	C18-O5-C13-C14	55.3(11)
Li2-O5-C13-C12	8.9(11)	Li2-O5-C13-C14	-169.5(16)
C13-O5-C18-C19	67.7(13)	Li2-O5-C18-C19	-67.4(14)
C13-O5-Li2-O4	129.9(21)	C13-O5-Li2-O6	-85.8(17)
C21-O6-C20-C19	-74.7(15)	C18-O5-Li2-O6	50.5(13)
C20-O6-C21-C22	156.5(22)	Li2-O6-C20-C19	55.1(14)
C20-O6-Li2-O4	-128.8(23)	Li2-O6-C21-C22	24.2(12)
C21-O6-Li2-O4	2.9(8)	C20-O6-Li2-O5	-48.5(14)
O1-C1-C2-O2	-1.2(6)	C21-O6-Li2-O5	83.2(17)
C6-C1-C2-O2	177.0(20)	O1-C1-C2-C3	179.5(20)
O1-C1-C6-C5	176.6(20)	C6-C1-C2-C3	-2.4(11)
C2-C1-C6-C5	-1.5(10)	C1-C2-C3-C4	9.3(10)
O2-C2-C3-C4	-169.9(23)	C2-C3-C4-C5	-14.0(11)
C3-C4-C5-C6	10.2(11)	C4-C5-C6-C1	-2.5(11)
O2-C7-C8-C9	-68.7(17)	O3-C10-C11-O1	49.4(11)
O4-C12-C13-C14	172.1(18)	C17-C12-C13-C14	-2.4(9)
C18-C19-C20-O6	-62.5(15)	C7-C8-C9-O3	72.7(19)
O4-C12-C13-O5	-6.2(6)	C17-C12-C13-O5	179.2(19)
O4-C12-C17-C16	-175.5(20)	C13-C12-C17-C16	-1.3(9)
O5-C13-C14-C15	-177.0(20)	C12-C13-C14-C15	4.7(10)
C13-C14-C15-C16	-3.1(9)	C14-C15-C16-C17	-0.5(10)
C15-C16-C17-C12	2.7(9)	O5-C18-C19-C20	69.0(14)
O6-C21-C22-O4	-53.7(12)		

The perchlorate is not ligated to the Li^+ and resides $6.10 \text{ \AA}$ away from the nearest molecule.

In **4**, the macrocycle is bent out of the aromatic plane on the same side, and apart from this, differs from **1** by virtue of *gauche* $\leftrightarrow$ *anti* flips about each of the four O-CH_2 bonds. This conformation possesses no inherent symmetry due to all-*gauche* torsional networks except one *anti* about C10-O3 . In **4A**, there is substantial puckering of the aromatic ring where $\text{C1-C2-C3-C4} = 9.3(10)^\circ$, $\text{C2-C3-C4-C5} = -14.0(11)^\circ$ and $\text{C3-C4-C5-C6} = 10.2(11)^\circ$. Although theoretical studies have shown benzene and cyclohexane to be equally flexible for a range of small torsional deformations ($<15^\circ$)⁽³⁰⁾, only variations of $< 2^\circ$ are encountered in compounds related to **4**. In cyclophanes, *intramolecular* steric interactions are present and initiate torsional distortions of *ca.* 13° ⁽³¹⁾, but in **4A** are absent. There is also an extremely short C4-C5 bond of $1.268(17) \text{ \AA}$ and a severely compressed C1-C2-C3 bond angle of $115.3(9)^\circ$. The known range for aromatic bond lengths and *endocyclic* angles is $1.33\text{--}1.41 \text{ \AA}$ and $118\text{--}122^\circ$ respectively for 1,2-dialkoxy-benz-annelated compounds^{(1),(32)–(34)}. In contrast, the aromatic ring in **4B** remains essentially planar ($\leq 4.7^\circ$) with a particularly long C15-C16 bond of $1.464(16) \text{ \AA}$. Torsional distortions up to 4.4° about the *ipso-ipso* bond into the macrocycle in benzo-crown ethers have been encountered previously⁽¹⁾, but the C14-C13-C12-O4 torsion angle of $172.1(18)^\circ$ in **4B** is unusually large.

Our MM3 calculations on **1** locate the conformation corresponding to **4** as the global minimum, *ca.* 3 kcal/mol lower than the conformation corresponding to the X-ray

structure of **1** (Table 27). In **4A**, there are four torsion angles which deviate 15- 20° from the calculated values, whereas in **4B** there are only two.

Table 27 Torsional conformations of **4A** and **4B**

	4A		4B	MM3 ^a
C3-C2-O2-C7	-51.6	C14-C13-O5-C18	55.3	37.4
C2-O2-C7-C8	-66.4	C13-O5-C18-C19	67.7	69.1
O2-C7-C8-C9	-68.7	O5-C18-C19-C20	69.0	68.1
C7-C8-C9-O3	72.7	C18-C19-C20-O6	-62.5	-52.9
C8-C9-O3-C10	69.1	C19-C20-O6-C21	-74.7	-84.4
C9-O3-C10-C11	-154.3	C20-O6-C21-C22	156.5	166.1
O3-C10-C11-O1	49.4	O6-C21-C22-O4	-53.7	-59.9
C10-C11-O1-C1	70.2	C21-C22-O4-C12	-62.8	-55.2
C11-O1-C1-C6	64.7	C22-O4-C12-C17	-65.0	-81.3

^a calculated global minimum for **1**

For ten membered rings, these changes are apparently sufficient to impart a considerable strain, which is transferred into the aromatic σ system. This is a direct result of the ring cavity being too small and inflexible to provide a perfect octahedral coordination geometry for the Li^+ . How does the structure accommodate this σ -strain from the cycle while keeping the aromatic character of the ring ?

Benzene has been shown to be the site of π and σ driving forces⁽³⁵⁾, the π bonds tend to distort the initial D_{6h} hexagon to a D_{3h} structure while the stronger σ driving force acts in the opposite direction and imposes the regular D_{6h} geometry. When strain is applied to the σ frame, the π bonding reinforces the distortion⁽³⁶⁾, which is particularly well illustrated in **4A**.

From the gathered structural information, the benzo-10-crown-3 system would be a poor Li^+ selective ionophore. It would be worthwhile to obtain a Na^+ complex of **1** to observe if the distortions remain. A more stable complexing agent for Li^+ is anticipated to be *cis*-cyclohexano-10-crown-3, the hydrogenated analogue of **1**, where the constraint from the aromatic system is eliminated.

Assignment of the Solid State ^{13}C Shifts

In **4** there are two non-equivalent benzo-10-crown-3 molecules, hence 22 lines are expected in the ^{13}C CP/ MAS spectrum and indeed 15 lines are resolved, with relative intensities consistent with the presence of accidental overlap (Fig. 58).

Alkoxy carbons

In this region, eight peaks are expected but only 4 are resolved (3: 3: 1: 1), due to conformational similarities in the macrocycles. The C11/ C22 carbons are twisted *ca.* 12° further from the aromatic plane and are involved in one less *gauche* network than C7/ C18. In light of this, the C11/ C22 carbons are assigned as the most deshielded alkoxy resonances at 74.0 ppm. At the shielded end of the arena, C9/ C20 are involved solely in *gauche* networks hence are assigned as the most upfield resonances.

At this point it is clear that symmetry related pairs are separated by 1.8 and 2.5 ppm, which cannot be rationalized on the basis of torsion angle differences. However, by comparing the average of the O-C* and C-C* bond lengths, and also the O-C*-C bond angles between symmetry related carbons in **4A** and **4B**, clearly the largest discrepancies occur at the C9/ C20, C10/ C21 and C7/ C18 sites.

Here C9 is assigned as deshielded over C20 due to a small average associated bond length of 1.32(17) Å and sp^2 bond angle of $119.8(14)^\circ$. The corresponding values for C20 are 1.48(16) Å and $110.3(9)^\circ$ which are close to those in **1**. Therefore C9 and C20 are assigned to 63.9 and 62.1 ppm respectively. Similarly, C21 is assigned as shielded over C10, due to a very long average bond length of 1.567(18) Å and sp^3 bond angle of $102.4(8)^\circ$; for C10 the values are 1.49(16) Å and $107.1(7)^\circ$.

Fig. 58 Normal and dipolar dephased ^{13}C CP/ MAS spectra of 4

Table 28 Solid state and solution ^{13}C shifts for **4**

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
solution ^a	153.7	153.4	122.9	124.6	124.7	122.8	71.4	30.8	66.7	70.0	74.3
solid A	149.4	146.9	117.1	128.7	124.8	127.5	71.5	23.1	63.9	(74.0)	74.0
	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22
solid B	149.4	148.1	119.3	126.3	122.9	127.5	(71.5)	23.1	62.1	71.5	74.0

^a: in acetone- d_6 from TMS ± 0.1 ; brackets denote possible interchange

Finally, C7 should be shielded over C18 due to a long average bond length of 1.56(13) Å and somewhat small bond angle of 107(8)°; the corresponding values for C18 are 1.448(13) Å and 113.9(7)°. The preparation of LiClO_4 complexes with **2** and **3** is in progress to verify the assignments in the aliphatic region.

Aromatic carbons

There are no *intermolecular* close contacts involving either **4A** or **4B**, therefore the aromatic multiplicities have their origin at the *intramolecular* level.

The Li metal ion is symmetrically disposed with respect to the aromatic ring, where all C ... Li distances of symmetry related pairs of aromatic carbons differ by less than 0.1 Å. Therefore the electric fields originating at the lithium ion do not contribute to asymmetric π polarization of the ring, however may affect the absolute values of these chemical shifts.

In **4**, the dihedral angles about the $\text{C}_{ipso}\text{-O}$ bond for a given molecule are *ca.* 53° and 65° respectively where the macrocycle is *cis* to the *ortho* sites. From the experimental dependence of protonated aromatic shifts on twist angle (Chapter 6, Fig. 61), it is expected the observed range to be *ca.* 5 ppm, between 119 and 125 ppm. Inspection of the CP/MAS spectrum shows the actual range to be 10.4 ppm; clearly the 117.1 and 128.7 ppm resonances are highly unusual and are probably associated with the puckered **4A**

structure. Strained benzene systems have been known to shield or deshield. For example, 1,3-benzodioxole⁽³⁷⁾ imparts an in-plane σ strain, reflected in a *ca.* 8 ppm shielding at the *ortho* sites relative to 1,4-benzodioxane. In contrast, the C2 site of [2,2]-*meta*-cyclophane⁽³⁸⁾ is part of a boat-like distortion in the benzene ring and is deshielded by 7.3 ppm relative to the acyclic model 1,2-*bis*-(3-methylphenyl)-ethane⁽³⁹⁾.

The smallest twist angle is $-51.6(13)^\circ$ about C2-O2 in **4A**, hence the *ortho*-cis C3 is expected to be well shielded relative to the *para* (Chapter 6, Fig. 61). The non-planar distortion in **4A** is reflected in long C2-C3 and C3-C4 bonds of 1.387(13) and 1.431(17) Å respectively, followed by an extremely short C4-C5 bond of 1.268(17) Å, and also the large *endocyclic* C4 bond angle of $123.0(10)^\circ$. Based on these trends, the 117.1 and 128.7 ppm resonances are assigned to C3 and C4 respectively.

The two next most shielded resonances are best suited to be associated with the twist angle of $55.3(11)^\circ$ about C13-O5 in the relatively undistorted **4B**. For this twist angle, *ortho*-cis sites are expected to be well shielded relative to the *para* (Chapter 6, Fig. 61), hence C14 and C16 are assigned to 119.3 and 122.9 ppm respectively. In both rings the C6, C17 sites occupy relatively undistorted positions *ortho*-cis to associated twist angles of *ca.* 65° . From the best-fit experimental curve, it is speculated they should resonate at 124- 125 ppm hence are assigned to the 124.8 and 126.3 ppm peaks respectively (Chapter 6, Fig. 61).

By default, the deshielded 127.5 ppm resonance of integral two, is assigned to; (i) C5, although it is *para* to the small $-51.6(13)^\circ$ twist angle in **4A**, it has a very short associated bond length of 1.27 Å and (ii) C15 which is *para* to the large $-65.0(13)^\circ$ angle in **4B**.

Partial verification of these assignments is in progress *via* synthesis and complexation of *ortho* deuterated **1**.

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CHAPTER 6

Aromatic Stereoelectronic Properties of Benzo-Crown Ethers

A- Introduction

The original work by Pedersen^{(1),(2)} and subsequent studies by Frensdorff⁽³⁾ established that macrocyclic polyethers of appropriate ring size complex strongly with cations of the alkali and alkaline earth metals.

Nowadays, the X-ray crystal structures for several mono-benz-annelated crown ethers are available. Specifically, the 15-crown-5⁽⁴⁾, 13-crown-4⁽⁵⁾, 12-crown-4⁽⁶⁾ and 9-crown-3⁽⁷⁾ structures have been reported. In two instances, detailed ¹³C CP/ MAS spectra have been included^{(7),(8)} to illustrate the complementarity of these techniques in examining solid crystal packing phenomena. Protonated aromatic carbons show a strong chemical shift dependence on the degree of planarity of the macrocycle relative to the benzene plane due to stereoelectronic and steric effects. In the present chapter this phenomenon is explored with the aid of *ab initio* ¹³C shift calculations on anisole.

B- Solid State ¹³C Shift Assignment of Benzo-Crown Ethers

Benzo-9-crown-3-d (B9C3-d)

Ortho-metallation⁽⁹⁾ of B9C3 was achieved by the use of the Lochmann- Schlosser base⁽¹⁰⁾ (2 eq. *t*BuOK· BuLi in THF at -78°C followed by D₂O quenching) to give B9C3-*d* with 83 % deuterium incorporation. No hydrogen bonding exists in the X-ray structure, so deuterium substitution leaves the crystal packing unchanged. The dipolar dephased CP/ MAS spectrum of B9C3-*d* confirms the site *ortho* to the alkoxy group bent by 79.9° from the aromatic plane is indeed the most deshielded protonated aromatic resonance at 127.2 ppm, in keeping with the theoretical assignment by LORG⁽⁷⁾. This observation

corroborates that *ortho* carbons exhibit a *ca.* 18 ppm isotropic deshielding as the alkoxy substituent is twisted *ca.* 80-90° out of the plane (Table 30).

Fig.59 Normal and dipolar dephased ^{13}C CP/ MAS spectra of B9C3-*d*

Benzo-12-crown-4 (B12C4)

There are two independent molecules of B12C4 in the asymmetric unit⁽⁶⁾, therefore 24 lines are expected in the CP/ MAS spectrum, however only 9 lines are resolved (Fig. 60). The α alkoxy carbons are symmetrically twisted from the aromatic plane on the same side by 38.8° or 40.4° in each non-equivalent molecule. Due to the small torsional differences about the aromatic plane, the *ortho*-cis shifts accidentally overlap at 117.0 as do the *para* at 121.9 ppm (Table 29). Also the *ipso* resonance is split by 0.5 ppm, probably due to crystal packing, so the aromatic CP/ MAS multiplicity (2 : 2 : 4 : 4) is accounted for. Why are the *para* carbons here not substantially deshielded relative to those of 1,2-DMB ?

Fig. 60 ^{13}C CP/ MAS spectrum of B12C4

This can be understood empirically by considering that mesomeric shielding is dependent on the sum of the overlap for each oxygen lone pair with the lobes of the *ipso* p orbital by the expression $(\cos^2\phi_1 + \cos^2\phi_2)$. Because one lone pair completely overlaps $\phi = 0^\circ$ for a twist angle of $\sim 30^\circ$, this expression only starts to significantly diminish for twist angles $> 30^\circ$.

The conformation of the macrocycle may be described as half-chair, a portion of which is directed towards the center of the ring cavity, resulting in a *trans*-annular H...O contact. The range of aliphatic shifts is 6.2 ppm with a complicated multiplicity and spacing not exceeding 1.8 ppm. Assignment of such a system is not justified without labelling studies, especially since packing effects are likely playing a role.

Table 29 Solution^a and solid state^b ¹³C aromatic shifts for B9C3-*d*, B12C4 and B13C4

	C1	C2	C3	C4	C5	C6
B9C3- <i>d</i>						
solution	151.4	151.3	122.6	123.9	123.8	122.8
solid ^c	149.3	151.7	119.9	125.3	122.6	128.0
	149.2	151.7	119.9	-	-	127.9
B12C4						
solution	150.5	150.5	118.0	122.5	122.5	118.0
solid	152.0	152.0	117.0	121.9	121.9	117.0
B13C4						
solution	150.2	150.2	117.4	122.6	122.6	117.4
solid	148.0	154.8	111.8	126.2	120.3	126.2

^a: referenced to TMS $\pm$ 0.1; 0.1M in CDCl₃

^b referenced to hexamethylbenzene

^c: second line denotes dipolar dephased spectrum

Benzo-13-crown-4 (B13C4) - symmetric isomer

The X-ray structure of B13C4⁽⁵⁾ reveals an interesting conformation of the macrocycle about the aromatic ring, with torsional angles C6-C1-O1-C13 = 69° and C7-O2-C2-C3 = 3°. Both O2 lone pairs exhibit good overlap with the lobes of the *ipso p* orbital, a geometry optimal for conjugative electron release. Therefore more mesomeric shielding is observed at C3 over C6 and C5 over C4. There is also γ -steric shielding operative at C3 due to the eclipsing interaction with the macrocycle. This scenario is similar to B9C3⁽⁷⁾, in which one α alkoxy carbon is *trans*-coplanar to the *ortho* site (170.3°), while the other is approaching a perpendicular (79.9°) disposition.

Fig. 61 (a) ^{13}C CP/ MAS spectrum of B13C4, (b) normal and dipolar dephased ^{13}C CP/ MAS spectrum of B13C4- d_4

Table 30 Dihedral features (θ_1 , θ_2) and ^{13}C CP/ MAS shifts^a of protonated aromatic carbons in benzo-crown ethers^b

	θ_1	θ_2	C3	C4	C5	C6	Ref.
1,2-DMB	5.8	9.1	111.2	120.3	121.9	109.6	(17)
B7C2 ^c	130	130	122.9	122.9	122.9	122.9	(19)
B9C3	170.3	79.9	127.2	121.8	124.6	119.0	(7)
B10C3	118.2	106.4	128.0	125.8	125.8	123.4	(18)
B12C4	38.8	40.4	117.0	121.9	121.9	117.0	(6)
B13C4	3.0	69.0	125.2	120.3	125.2	111.8	(5)
B15C5	13.0	14.0	111.2	119.0	120.0	111.2	(4), (8)
DB24C8	5.4	7.7	111.8	119.7	119.7	111.8	(8), (20)
DB30C10	6.0	26.0	114.8	119.2	120.6	113.8	(8), (21)

a: referenced to hexamethylbenzene

b: absolute value of the $\text{C}_{3,6}\text{-C}_{2,1}\text{-O-C}$ dihedral angle. In Fig. 61 the values of 1,4-DMB and SCS corrected anisole are included

c: in the CP/ MAS spectrum a slight splitting of the ipso and one aromatic site due to crystal packing is neglected here; dihedral angles determined by MM2 and ref.(12)

In light of the experimental shielding trends for B9C3-*d*, the following assignments for B13C4 can be made with certainty; C3 at 111.8 ppm, C4 at 125.2 ppm, C5 at 120.3 ppm and C6 at 125.2 ppm. In the dipolar dephased CP/ MAS spectrum of B13C4-*d*, the assignments of C13 to 75.4 ppm and C7 to 71.8 ppm are made on the basis of an established trend in which α ether carbons become deshielded by *ca.* 5 ppm upon rotation out of the plane by 90° ⁽¹¹⁾.

From a literature survey, additional CP/ MAS ^{13}C aromatic shifts of structurally known benzo-crown ethers are collected (Table 30). Variations in shielding at the *ortho* and *para* sites can be graphically represented as a function of the dihedral angle about the $\text{C}_{\text{ipso}}\text{-O}$ bond (Fig. 63).

Theoretical shielding calculations on anisole as a function of the dihedral angle give a more thorough characterization of this phenomenon, *via* analysis of the calculated aromatic principal shifts.

C- ^{13}C Shielding Calculations as a Function of the $\text{C}_{\text{ar}}\text{-C}_{\text{ar}}\text{-O-CH}_3$ Torsion

Non-planar conformations of sterically unhindered simple methoxybenzenes are unknown in the solid state, however there exists a lot of X-ray and ^{13}C CP/ MAS spectral data on 1,2-benz-annelated crown ethers. Before embarking on a comparative study with these compounds, one must verify that the protonated aromatic sites are directly related to the twist angle about the $\text{C}_{\text{ipso}}\text{-O}$ bonds. It is well known that the *meta* isotropic SCS for a planar methoxy group is small, but what about for non-planar conformations? From shielding calculations on benzene, anisole and 1,2-DMB it will be demonstrated that the *meta* isotropic SCS remains effectively independent of the twist angle.

The shielding tensors of benzene were calculated employing the GIAO method at the 6-31G* basis set level⁽¹³⁾ and found to be $\sigma_{11} = 230.7$ ppm, $\sigma_{22} = 131.3$ ppm, $\sigma_{33} = -11.7$ ppm and $\sigma_{\text{iso}} = 116.8$ ppm relative to TMS.

The optimized planar geometry of anisole at the 6-31G* level is in agreement with theoretical results^{(14),(15)} and structural⁽¹⁶⁾ data; within ± 0.05 Å for bond lengths and $\pm 1^\circ$ for bond angles (Fig. 62). Partial optimizations on anisole were performed at C2-C1-O-CM1 dihedral angle increments of 10° up to 90° in the GIAO shielding calculations (Appendix B). The graphical representation of the calculated SCS for various dihedral angles reveals that the *meta* value remains unchanged (Fig. 64). In support of this, calculations on 1,2-DMB at the 6-31G* level using the X-ray geometry and varying the torsion about C2-O2 up to 90° show only a 0.7 ppm isotropic variation in C4, C6 while C3 and C5 become deshielded by 10.2 and 3.9 ppm respectively (Appendix C).

From the experimental best fit curves (Fig. 63), the variance in the *ortho*-cis, *ortho*-trans and *para* shifts are 16.2, 10.3 and 5.8 ppm respectively. A comparison of the experimental and calculated isotropic SCS shifts show very similar trends as the dihedral angle increases (Fig. 63, 64). If one adds 7.0, 11.0 and 4.6 ppm to the calculated *ortho*-cis, *ortho*-trans and *para* site values respectively, clearly there is very good agreement with experiment (Table 31). The isotropic experimental curve (Fig. 63) reveals that the *ortho*-cis and *ortho*-trans resonances overtake the *para* in a downfield sense at $\theta = 65.8$ and 135.0° respectively. The theoretical curve fails to mimic this intersection behaviour mainly because the *ortho* values are consistently too shielded as evident in the large 7.0 and 11.0 ppm constants needed in Table 31. The experimental trends now can be considered as reflecting the behaviour of anisole itself.

A study of the dependence of theoretical anisotropic shifts of anisole on dihedral angle, allows some insight into the mesomeric and steric origins of the experimental data. It is known from M.O. calculations on anisole and veratrole that *ortho* carbons exhibit a larger π density dependence on dihedral angle than do the *para*^{(22),(23)}. In order to more easily conceptualize the mesomeric shielding contribution, an average of σ_{11} and σ_{22} will be used to reflect π density in the ring. Here the difference between 0° and 90° is 11.4, 10.2 and 7.7 ppm for the *ortho*-cis, *ortho*-trans and *para* carbons respectively, in agreement with M.O. calculations. This trend however, does not account for the large

(a) **(b)** **(c)**

Fig. 62 Optimized geometry of anisole; (a) numbering scheme, (b) bond lengths (Å) where $C_{ar}-H = 1.084$ and $CM1-H = 1.090$ and (c) bond angles ($^{\circ}$)

Fig. 63 Best fit curves for ^{13}C shifts of *ortho* and *para* sites vs. the corresponding dihedral angle in benzo-crown ethers ($R^2 = 0.970$ for the *ortho* curve and 0.870 for the *para* one)

Fig. 64 Theoretical ^{13}C isotropic SCS of a methoxy group as a function of dihedral angle (in ppm from benzene at 116.8 ppm)

variation in the *ortho*-cis shielding. From experimental tensor measurements on 1,4-DMB, the *ortho*-cis shielding originates in σ_{33} , and hence reflects a perturbation of the σ electrons by van der Waals interactions^{(24),(25a)} and/ or electric field effects^(25b).

Table 31 Experimental^a and calculated^b *ortho* and *para* isotropic shifts of some benz-annelated crown ethers

θ	<i>ortho</i> -cis			<i>para</i>		
	calc.	exp.	Δ	calc.	exp.	Δ
0	105.6 + x	111.8	0.8	116.3 + z	120.5	0.4
30	108.4 + x	115.0	0.4	117.0 + z	120.9	0.7
40	110.6 + x	117.6	0.0	117.6 + z	121.8	0.4
50	113.1 + x	120.4	0.3	118.3 + z	122.9	0.0
60	115.7 + x	123.0	0.3	119.2 + z	123.9	0.1
70	117.9 + x	125.2	0.5	120.0 + z	124.7	0.1
80	119.4 + x	126.7	0.3	120.6 + z	125.2	0.0
	<i>ortho</i> -trans			<i>para</i>		
110	117.9 + y	127.1	1.8	120.0 + z	124.8	0.2
120	115.7 + y	125.8	0.9	119.2 + z	124.1	0.3
130	113.1 + y	124.1	0.0	118.3 + z	123.2	0.3
150	108.4 + y	120.0	0.6	117.0 + z	121.4	0.2
170	105.8 + y	117.5	0.7	116.3 + z	121.4	0.5
180	105.6 + y	117.9	0.7	116.3 + z	120.9	0.0

a: from best fit curve (Fig. 60)

b: from theoretical SCS values determined from benzene and anisole

c: x = 7.0 ppm, y = 11.0 ppm and z = 4.6 ppm

From the GIAO shielding calculations, upon rotating a methoxy group from 0° to 90° , the *ortho*-trans σ_{33} becomes shielded (by 4.7 ppm) in keeping with the expected inverse relation between σ and π density due to decreased mesomeric shielding⁽²⁶⁾. In contrast, for the *ortho*-cis carbon, the σ_{33} is deshielded by 9.4 ppm. If this 14.1 ppm difference in σ_{33} between these two sites is indeed a steric phenomenon, the experimental *ortho*-cis curve should reflect this where an initial sharp rise would level off after *ca.* 30° to resemble the *ortho*-trans. In fact the curve is the steepest from *ca.* 30° to 60° (Fig. 63). Therefore although not rigorously steric in origin, one can visualize the *ortho*-cis effect as arising through field interactions between the O-CH₃ bond and the σ system of the ring where a steady deshielding occurs up to 90° .

D- Conclusion

The theoretical anisotropic shielding trends for non-planar conformations need to be experimentally verified. Single crystal tensor measurement is a viable technique provided that the number of molecules per unit cell is not excessive, as such studies are very time consuming; in this respect benzo-10-crown-3 ($Z = 4$) would be a candidate. Finally, the theoretical investigations into the SCS dependence on dihedral angle should be extended into the 1,4-DMB system. Recall the 1,2-DMB and 1,4-DMB *ortho*-cis sites have been experimentally verified by variable spinning CP/ MAS to be anisotropically equivalent.

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CHAPTER 7

Unsymmetric *cis*-Cyclohexano-Crown EthersA- Introduction

The low temperature solution stereodynamics of unsymmetric *cis*-cyclohexano-crown ethers is of interest since the cyclohexyl ring inversion produces two conformations. Minor conformations could, in principle, also arise due to rotational isomerism in the macrocyclic ring⁽¹⁾. In this perspective, the *cis* isomers of cyclohexano-10-crown-3 (**5**) and cyclohexano-13-crown-4 (**8**) were synthesized.

In order to more fully comprehend the conformational mobility of these asymmetric bicycles, a comparison is made between **8** and the symmetric isomer **9**, which at low temperature undergoes a single degenerate conformational process.

1,4,7-Trioxecane, the parent compound of **5**, is unknown. The analogues shown below have only been investigated from a synthetic point of view^{(2),(4)}. The 8,8'-dimethyl moiety is the main product of the acid catalyzed insertion of isobutylene into 1,3,6-trioxocan⁽⁴⁾.

To the best of this author's knowledge there have been no studies on the conformational preferences of oxacyclodecanes.

B- cis-Cyclohexano-10-Crown-3

Dynamics of the process

The flipping of the cyclohexane ring converts the bridge O-C-C-O unit in the 1,4,7-trioxacyclodecane moiety from +g $\rightarrow$ -g. For symmetric *cis*-cyclohexano moieties, this inversion process is degenerate, but in the present case leads to two conformers. An investigation of the structural constraints imposed at the bridge in this bicyclic system shows an equatorial proton oriented *into* the crown cavity where it participates in unique *trans*-annular interactions for each of the major and minor isomers of **5**. It is well known

that such interactions play an important role in the conformational preferences of 10 membered rings. Indeed, the 2D-NOESY difference NMR spectrum for the major isomer shows correlations between an equatorial proton and both ethoxy and propoxy units.

Integration of the solution ^1H 210 K methine resonances for **5** (major and minor isomers), indicates the equilibrium constant K_{eq} is *ca.* 5. Based on the relative intensities of seven pairs of clearly resolved ^{13}C resonances (Fig. 65), good agreement is found with this value. This implies that the spin lattice relaxation times (T_1) and nuclear Overhauser enhancements (nOe's) for isomeric pairs of carbons are the same within error limits. The average of the ^1H and ^{13}C results based on nine measurements give $K_{\text{eq}} = 4.7 \pm 0.8$ with a free energy difference $\Delta G^\circ = -2.7 \pm 0.3$ kJ/mol between the two conformers.

Solution ^1H and ^{13}C Spectra

Assignment

To assist in the assignment of the 210 K solution spectra of **5**, the deuteriated analogues **6** and **7** were prepared.

At 210 K the methine proton signals of **5** (major isomer) can be assigned at 3.19 and 3.91 ppm on the basis of DEPT 135 (Fig. 66) and $^1\text{H}^{13}\text{C}$ HMQC (Fig. 67) experiments. The 3.19 ppm resonance has a wider linewidth reflecting a *trans* vicinal coupling, therefore is assigned as an axial proton. These assignments are supported in the literature for alkoxy substituted cyclohexanes, where axial methine protons resonate *ca.* 0.9 ppm upfield relative to equatorial^{(5),(7)}. Therefore the methine carbons bearing equatorial and axial oxygen resonate at 75.85 and 75.81 ppm respectively. Using the same procedure, the methine proton and carbon signals of the minor isomer are also assigned (Table 32).

The two most shielded cyclohexyl carbons are unambiguously assigned to C4, C5 on the basis of well known substituent effects. The γ site experiencing a *gauche* interaction with the axial oxygen is the most shielded at 19.0 ppm. The two β cyclohexyl resonances appear at 27.6 and 27.9 ppm.

Fig. 65 (a) Solution ^{13}C spectra of 5 at 298 K and 210K

Fig. 65 (b) Solution ^1H spectra of 5 at 298 K and 210 K

Fig. 66 DEPT 135 spectrum of 7 at 210 K

The 210 K $^1\text{H}^{13}\text{C}$ HMQC and $^1\text{H}^1\text{H}$ COSY spectra of 7 (Fig. 67, 68) verify that C7 is shielded 10.9 ppm relative to C9. Also, a comparison with the spectra of 6 allows for the assignment of C10 and C11 (Table 32). Because the 210 K long range HETCOR experiment failed to establish a connection between a methine carbon and C7, C11 through oxygen, the unambiguous NMR assignment of the major conformation of 5 remains elusive. A 210 K NOESY cross peak however is established between an equatorial cyclohexyl proton and those on C7 (Fig. 70). Therefore stereochemical shielding trends must be considered in the search for the major conformation.

Fig. 67 $^1\text{H}/^{13}\text{C}$ HMQC spectrum of 7 at 210 K

Fig. 68 $^1\text{H}/^1\text{H}$ COSY spectrum of 7 at 210 K

Fig. 69 Solution ^{13}C spectra of 5, 6 and 7 at 210 K

Fig. 70 NOESY spectra of 5 and 7 at 210 K

NMR singularities

A comparison of the corresponding cyclohexyl 210 K shifts between the major isomer of **5** (Table 33) and the related *cis*-cyclohexano-9-crown-3 (C9C3), shows close agreement to within 1 ppm, with the exception of the methine site bearing equatorial oxygen⁽⁵⁾. In **5** this site is quite shielded and resonates at 75.88 ppm, only 0.07 ppm from the axial. Usually, a cyclohexyl carbon bearing an equatorial alkoxy group resonates at *ca.* 80 ppm, downfield 5 ppm from the axial counterpart⁽⁸⁾⁻⁽¹¹⁾. Also noteworthy is the 10.9 ppm shielding of C7 over C9.

Table 32 Solution ¹³C shifts of **5**^a

	major, 210 K	minor, 210 K	298 K
C1	75.95	78.81	77.98
C2	75.88	77.20	77.71
C3	27.65	27.46	29.04
C4	23.79	23.79	23.43
C5	18.99	19.14	21.64
C6	27.95	28.95	29.14
C7	57.86	(67.88)	62.69
C8	29.30	30.09	30.70
C9	68.79	66.97	69.17
C10	71.18	(68.50)	71.59
C11	71.87	68.50	71.75

^a: $\delta_c \pm 0.01$ ref. from CD₂Cl₂ (53.80 ppm); brackets denote possible interchange due to spectral overlap

For C9C3, the close shift similarities (≤ 1.5 ppm) between the ^{13}C CP/ MAS and 210 K solution spectra reveals the solution conformation is very similar to the X-ray structure⁽⁵⁾, but **5** being an oil, precludes X-ray analysis. Therefore MM2 calculations were undertaken, in an attempt to identify the preferred conformation.

Conformational Analysis

The following constraints were considered in the MM2 minimization routine;

- (i) the O1-C11-C10-O3 torsion angle is *gauche* in keeping with the well established stereochemistry in similar systems.
- (ii) the 10.9 ppm deshielding of C9 over C7 originates from more non-ideal networks, intermediate between *gauche* and *anti*, involving the former.

Owing to the relative inflexibility of the 10-membered ring, only one minimum was found which satisfies these criteria, namely conformer A (Fig. 71). Considering the bulk macrocyclic conformation (O as CH_2), there is a C_2 axis connecting the mid-points of the C8-C9 and C1-O1 bonds, with a maximum symmetry-related torsion angle difference of 27.0° . Here the propoxy group is equatorial and the O1-C11-C10-O3 unit is *gauche* at -49.3° (Fig. 71). The g^-g^- O2-C7-C8-C9-O3 unit is a 1,3-diaxial type and carbons bonded to oxygen on the outside termini of such networks *i.e.*, C2, C10 are known to experience shielding⁽¹¹⁾. Compressed torsional networks $< 50^\circ$ also contribute an extra shielding to the terminal, over interior, carbons. In this regard, the relatively compressed C7-C8-C9-O3 = 45.9° network is expected to accentuate the shielding of C7 over C9, and this should also be transmitted to C2. Part of the extraordinary 5- 6 ppm shielding of C2 may also be due to a cyclohexane ring flattening associated with bridge strain, as was observed in dicyclohexano-12-crown-4⁽¹²⁾. In addition to that outlined above, the major factor accounting for the 10.9 ppm difference between C7 and C9 is the non-ideal deshielding C8-C9-O3-C10 = -113.0° torsional network. The close *trans*-annular H7...H1_{eq} distance of 2.16 Å is also in agreement with the NOESY spectra (Fig. 70).

O1-C1-C2-O2	-53.0	C8-C9-O3-C10	-113.0
C1-C2-O2-C7	-76.0	C9-O3-C10-C11	163.8
C2-O2-C7-C8	164.2	O3-C10-C11-O1	-49.3
O2-C7-C8-C9	-85.5	C10-C11-O1-C1	-70.4
C7-C8-C9-O3	45.9	C11-O1-C1-C2	142.9

Fig. 71 Conformer A; calculated to be the major isomer of **5** at 210 K

C- cis-Cyclohexano-13-Crown-4

For **8** two isomers are detected at 210 K with $K_{eq} = 2.2 \pm 0.4$ and $\Delta G^\circ = -1.7$ kJ/mol (Fig. 70). This is less than half of that found for **5**, possibly because the larger ring size results in decreased *trans*-annular interactions involving the equatorial proton. The two methine carbons are well separated by *ca.* 5 ppm, which is close to the normal value found in acyclic systems, and this might also reflect reduced strain at the bridgehead. The cyclohexyl assignments are based on established shielding trends for axial and equatorial alkoxy substituents, the other sites are assigned by $^1\text{H}/^{13}\text{C}$ HETCOR (Table 33). For **9** the inversion process is degenerate and the spectral results reflect this.

Fig. 72 ^{13}C NMR spectra of **8** and **9** at 210 K

Table 33 Solution ^{13}C shifts of **8** and **9**^a

	8			9	
	298 K	major, 210 K	minor, 210 K	298 K	210 K
C1	76.42	77.50	78.51	76.68	77.62
C2	76.75	72.00	71.86	76.68	72.08
C3	28.41	27.24	27.07	27.78	25.80
C4	27.65	23.99	23.99	22.41	23.97
C5	22.10	18.59	18.82	22.41	18.73
C6	22.90	25.68	67.75	27.78	27.34
C7	63.71	60.57	64.18	68.02	69.02
C8	31.12	29.86	29.75	(69.82)	(68.60)
C9	(71.0)	(69.97)	(69.77)	(66.40)	(66.73
C10	(70.41)	(64.69)	(66.84)	30.56	30.33
C11	(68.54)	(68.82)	(68.29)	(66.40)	(63.76)
C12	(66.23)	(68.82)	(68.29)	(69.82)	(68.37)
C13	69.13	68.97	68.65	68.02	63.59

^a: $\delta_{\text{C}} \pm 0.01$ ref. from CD_2Cl_2 (53.80 ppm)

brackets denote possible interchange

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CHAPTER 8

Experimental

Part I

Synthesis*

A- Esterification using Methanol and Thionyl Chloride**dimethyl 2,2'-oxydiacetate**

A 500ml 2-necked-RB-flask equipped with an isobaric dropping funnel (topped with a drying tube) and a thermometer was charged with diglycolic acid (13.4 g, 0.10 mol) and 120 ml of absolute MeOH. The reaction flask was cooled with an ice water bath. When all diglycolic acid was dissolved in MeOH, SOCl_2 (20 ml, 32.6 g, 0.27 mol) was added dropwise so that the temperature did not exceed 30°C . After 3 hr, the solvent was removed by rotory-evaporation and the material was dried on a vacuum pump, 97 % yield, mp $36\text{--}37^\circ\text{C}$ (lit. mp $36\text{--}38^\circ\text{C}^{(1),(2)}$).

50 MHz	$\text{C}=\text{O}$	$\text{O}-\text{CH}_2$	$\text{O}-\text{CH}_3$
^{13}C NMR in CDCl_3	170.00	68.00	51.9

B- Reactions using Ethyl Diazoacetate**ethyl 6-chloro-3-oxahexanoate**

All glassware was previously dried for 24 hr at 120°C . A 250 ml 2-necked-RB flask was flame dried under argon. The flask was charged with 3-chloro-1-propanol (4.72 g, 50 mmol), ethyl diazoacetate (5.70 g, 50.0 mmol) in 50 ml of CH_2Cl_2 (spectrograde solvent) under argon. The flask was cooled with an ice-water bath. With stirring 5 drops

*Abbreviations: room temperature (rt), anhydrous (anh.), hour (hr), minute (min.)

of the catalyst $\text{BF}_3 \cdot \text{Et}_2\text{O}$ were injected with a syringe through a septum where upon a violent exothermic reaction occurs with heavy N_2 release. After stirring 3 hr the reaction flask was allowed to come slowly to rt. The solvent was then removed by rotory-evaporation and the crude oil purified either by flash silica gel column chromatography (grade 60, 230-400 mesh) using EtOAc, 71% yield or by vacuum distillation (88 - 92°C / 4 mm Hg), 75% yield.

50 MHz	$\text{CH}_2\text{-O}$	$\text{O-CH}_2\text{-CH}_2$	$\text{CH}_2\text{-Cl}$	$\text{CH}_2\text{-CH}_2\text{-CH}_2$	$\text{O-CH}_2\text{-CH}_2$
^{13}C NMR in CDCl_3	68.34 68.00	60.74	41.57	32.54	14.07

^1H NMR in CDCl_3 , 200MHz	Multiplicity	Number of Hydrogens	Functional Group
4.22	q	2H	$\text{O-CH}_2\text{-CH}_2$
4.08	s	2H	$\text{O-CH}_2\text{-CO}$
3.68	t	4H	$\text{Cl-CH}_2\text{-CH}_2\text{-CH}_2$
2.07	q	2H	$\text{CH}_2\text{-CH}_2\text{-CH}_2$
1.28	t	3H	$\text{O-CH}_2\text{-CH}_2$

ethyl 6-chloro-3-oxahexanoate- d_2

50 MHz	$\text{CH}_2\text{-O}$	$\text{O-CH}_2\text{-CH}_2$	$\text{CH}_2\text{-Cl}$	$\text{CH}_2\text{-CH}_2\text{-CH}_2$	$\text{O-CH}_2\text{-CH}_2$	C=O
^{13}C NMR in CDCl_3	67.87	60.38	41.23	32.01	13.69	170.03

For the formation of the diester, 2 equivalents of ethyl diazoacetate are necessary. The workup similarly involves silica gel flash chromatography work (grade 60, 230- 400 mesh) using hexane:ether (1:1).

diethyl 3,7-dioxanonanodiate bp 144 - 146 °C/ 5 mm Hg

MS (CI); 248.9 (56.2%), 220.9 (87.5%), 175.0 (100%), 145.0 (100%),
143.0 (100%), 117.0 (49.3%)

50 MHz	$\text{C}=\text{O}$	$\text{O}-\text{CH}_2$	$\text{O}-\text{CH}_2-\text{CH}_2$	$\text{CH}_2-\text{CH}_2-\text{CH}_2$	$\text{O}-\text{CH}_2-\text{CH}_3$
^{13}C NMR in CDCl_3	170.34	68.36 68.23	60.61	29.67	14.01

^1H NMR in CDCl_3 , 200MHz	Multiplicity	Number of Hydrogens	3J (in Hz)	Functional Group
4.14	q	4H	7.13	$\text{O}-\text{CH}_2-\text{CH}_2$
4.00	s	4H	-	$\text{O}-\text{CH}_2-\text{CO}$
3.58	t	4H	6.25	$\text{CH}_2-\text{CH}_2-\text{CH}_2$
1.87	q	2H	6.25	$\text{CH}_2-\text{CH}_2-\text{CH}_2$
1.21	t	6H	7.13	$\text{O}-\text{CH}_2-\text{CH}_3$

diethyl 3,6-dioxaoctanedioate, silica gel column chromatography (grade 60, 230-400 mesh) using hexane: ether (1: 1), 74 % yield.

50 MHz	$\text{C}=\text{O}$	$\text{O}-\text{CH}_2$	$\text{O}-\text{CH}_2-\text{CH}_2$	$\text{O}-\text{CH}_2-\text{CH}_3$
^{13}C NMR in CDCl_3	169.85	70.39 68.09	60.25	13.70

^1H NMR in CDCl_3 , 200MHz	Multiplicity	Number of Hydrogens	Functional Group
4.20	q	4H	$\text{O}-\text{CH}_2-\text{CH}_2$
4.16	s	2H	$\text{O}-\text{CH}_2-\text{CO}$
3.78	dt	4H	$\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$
1.29	t	6H	$\text{O}-\text{CH}_2-\text{CH}_3$

diethyl 3,6-dioxaoctanedioate- d_4 , silica gel column chromatography (grade 60, 230-400 mesh) using hexane: ether (1: 1), 74 % yield.

50 MHz	$\text{C}=\text{O}$	$\text{O}-\text{CD}_2$	$\text{O}-\text{CH}_2-\text{CO}$	$\text{O}-\text{CH}_2-\text{CH}_2$	$\text{O}-\text{CH}_2-\text{CH}_3$
^{13}C NMR in CDCl_3	170.00	69.93 $^1J_{\text{CO}}=20.40$	68.02	60.20	13.67

¹ H NMR in CDCl ₃ , 200MHz	Multiplicity	Number of Hydrogens	Functional Group
4.22	q	4H	O-CH ₂ -CH ₃
4.17	s	2H	O-CH ₂ -CO
1.30	t	6H	O-CH ₂ -CH ₃

ethyl 9-chloro-3,6-dioxanonoate

50 MHz	Cl-CH ₂	Cl-CH ₂ -CH ₂	CH ₂ -CH ₂ -CH ₂ -O	O-CH ₂ -CH ₂ -O	CH ₂ -CO	C=O	O-CH ₂ -CH ₂	O-CH ₂ -CH ₃
¹³ C NMR in CDCl ₃	41.81	32.50	67.49	70.27 70.69	63.00	170.33	60.70	14.08

C- Reductions using LiAlX₄ (X = H, D)

6-chloro-3-oxa-1-hexanol

All glassware was previously dried for 24 hr at 120 °C. A 500 ml 3-necked-RB flask was flame dried under argon and equipped with a condenser, dropping funnel. The flask was cooled in an ice-salt water bath. A suspension of LiAlH₄ (800 mg, 21.07 mmol, 20% molar excess) in 250 ml anh.THF was introduced in the flask and stirred 15 min.. ethyl 6-chloro-3-oxahexanoate (6.34 g, 35.1 mmol) was added dropwise and the reaction let slowly come to rt overnight. Next the flask was heated gently at 40°C for 30 min., then cooled back to rt. The LiAlH₄ suspension was broken down by addition of 1.5 ml of distilled water followed by 10 ml of 10% H₂SO₄. The reaction was filtered by suction and the solvent removed by rotaryevaporation. The crude material was taken up in CH₂Cl₂ and partitioned into water. Rotory-evaporation of the water at 50°C followed by distillation (bp 78 - 82°C/ 4 mm Hg), leaves the product in 95 % yield.

MS (CI); (M+1)⁺ 138.9 (100%) and (M+3)⁺ 140.9 (100%), 123.0 (47.2%), 120.9 (100%), 106.7 (26.8%), 103.0 (34.6%).

50 MHz	$\underline{\text{CH}_2}\text{-CH}_2\text{-OH}$	$\text{HO-}\underline{\text{CH}_2}$	$\underline{\text{CH}_2}\text{-Cl}$	$\text{CH}_2\text{-}\underline{\text{CH}_2}\text{-CH}_2$	$\text{CH}_2\text{-}\underline{\text{CH}_2}\text{-O}$
^{13}C NMR in CDCl_3	71.92	61.17	41.57	32.22	67.20

6-chloro-3-oxa-1-hexanol- d_2 bp 60 - 65°C/ 9.5 mm Hg

50 MHz	$\underline{\text{CH}_2}\text{-CD}_2\text{-OH}$	$\text{HO-}\underline{\text{CD}_2}$	$\underline{\text{CH}_2}\text{-Cl}$	$\text{CH}_2\text{-}\underline{\text{CH}_2}\text{-CH}_2$	$\text{CH}_2\text{-}\underline{\text{CH}_2}\text{-O}$
^{13}C NMR in CDCl_3	72.03	61.08	41.83	32.57	67.61

^1H NMR in CDCl_3 , 200MHz	Multiplicity	Number of Hydrogens	Functional Group
3.55	s	1H	$\text{CD}_2\text{-OH}$
2.39	s	2H	$\text{CH}_2\text{-CD}_2\text{-OH}$
2.05	q	2H	$\text{CH}_2\text{-CH}_2\text{-CH}_2$
3.63, 3.65	dt	4H	$\text{CH}_2\text{-CH}_2\text{-CH}_2$

diethylene glycol- d_4 ⁽¹⁾

50 MHz	$\text{O-}\underline{\text{CD}_2}$	$\text{O-}\underline{\text{CH}_2}\text{-CH}_2$
^{13}C NMR in CDCl_3	61.12 $^1J_{\text{CO}} = 21.25$	73.12

triethylene glycol- d_8

50 MHz	$\underline{\text{CH}_2}\text{-CD}_2\text{-OH}$	$\underline{\text{CD}_2}\text{-O-CH}_2$	$\underline{\text{CD}_2}\text{OH}$
^{13}C NMR in CDCl_3	73.01	69.92 $^1J_{\text{CO}} = 21.10$	60.95 $^1J_{\text{CO}} = 21.10$

tetraethylene glycol- d_4 ⁽¹⁾

50 MHz	$\text{O-}\underline{\text{CH}_2}$	$\text{O-}\underline{\text{CD}_2}\text{-CH}_2$
^{13}C NMR in CDCl_3	72.37 70.16	60.85 $^1J_{\text{CO}} = 20.75$

3,7-dioxa-1,9-nonanediol-*d*₄

100 MHz	$\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O}$	$\text{O-CH}_2\text{-CD}_2$	$\text{CD}_2\text{-OH}$	$\text{CH}_2\text{-CH}_2\text{-CH}_2$
¹³ C NMR in CDCl ₃	68.36	72.02	61.12 ¹ J _{CD} = 21.5	29.59

3,7-dioxa-1,9-nonanediol lit. bp 105°C/ 0.2 mm Hg⁽³⁾

100 MHz	$\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O}$	$\text{O-CH}_2\text{-CH}_2$	$\text{CH}_2\text{-OH}$	$\text{CH}_2\text{-CH}_2\text{-CH}_2$
¹³ C NMR in CDCl ₃	68.36	72.02	61.59	29.59

¹ H NMR in CDCl ₃ , 400 MHz	Multiplicity	Number of Hydrogens	³ J (in Hz)	Functional Group
3.73	t	2H	4.56	CH ₂ -OH
3.62	AA'BB'	4H	6.10	CH ₂ -CH ₂ -CH ₂ -O
3.56	AA'BB'	2H	4.56	CH ₂ -CH ₂ -OH
2.66	bs	1H	3.06	CH ₂ -OH
1.88	q	2H	6.10	CH ₂ -CH ₂ -CH ₂

9-chloro-3,6-dioxa-1-nonanol bp 106 - 108°C/ 9.5 mm Hg

MS (CI); (M+1)⁺ 182.9 (100%) and (M+3)⁺ 185.0 (100%), 165.0 (71.7%), 123.0 (33.4%), 120.9 (75.0%), 103.0 (27.4%).

50 MHz	Cl-CH_2	$\text{Cl-CH}_2\text{-CH}_2$	$\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-O}$	$\text{O-CH}_2\text{-CH}_2\text{-O}$	$\text{O-CH}_2\text{-CH}_2\text{-OH}$	$\text{CH}_2\text{-OH}$
¹³ C NMR in CDCl ₃	41.87	67.64	32.60	70.30	72.60	61.61

3-chloro-1-propanol-*d*₂

All glassware was previously dried for 24 hr at 120 °C. A 500 ml 3-necked RB flask was flame dried under argon and equipped with a condenser, dropping funnel. The flask was cooled in an ice-salt water bath. A suspension of LiAlD₄ (2.50 g, 59.5 mmol; 20% molar excess) in 150 ml freshly distilled ether (over LiAlH₄) was introduced in the flask. The flask was warmed to rt and then ethyl 3-chloro-propionate (13.60 g, 100.0

mmol) was added dropwise to create a gentle reflux. After the addition was completed over a period of 1 hr the flask was gently warmed up to 35°C for 5 hr. The reaction over, the flask was cooled with an ice/ water bath and the LiAlH_4 suspension broken down by addition of distilled water followed by 10% H_2SO_4 solution until two clear phases formed. The aqueous layer was extracted three times with ether. The gathered organic layers were washed with saturated NaCl solution and dried over Na_2SO_4 . The solvent was removed by rotory-evaporation. The crude material was purified by distillation (bp 160-162°C/ 760 mm Hg) in near quantitative yield.

50 MHz	$\text{Cl}-\underline{\text{CH}}_2$	$\text{CH}_2-\underline{\text{CH}}_2-\text{CH}_2$	$\underline{\text{C}}\text{D}_2-\text{OH}$
^{13}C NMR in CDCl_3	41.30	34.55	58.42 $^1J_{\text{C}} = 21.3$

D- Tosylation Reactions⁽⁴⁾

Triethylene glycol ditosylate

In a 500 ml 2-necked RB flask equipped with an isobaric dropping funnel, argon in- and outlet was introduced triethylene glycol (6.70 ml; 50.0 mmol) in 80 ml anh. pyridine. The flask was cooled with an salted ice-water bath. TsCl (19.01 g; 50.0 mmol) was dissolved in 120 ml anh. pyridine and this solution added dropwise to the reaction flask upon stirring. The reaction was let upon stirring overnight. The reaction mixture was filtered by suction. The mother liquor was acidified with 6 M HCl until pH = 1. Upon standing formation of an heavy white precipitate that was filtered by suction and recrystallized from absolute EtOH in 80 % yield, mp 75- 76°C (lit mp. 78°C⁽⁵⁾).

50 MHz	i	o	m	p	$\underline{\text{C}}\text{H}_2-\text{O}$	$\underline{\text{C}}\text{H}_2$
^{13}C NMR in CDCl_3	144.84	129.83	127.93	132.92	70.66 69.18	21.63

Triethylene glycol ditosylate-*d*₈

MS (CI); (M+1)⁺ 466.8 (59.5%), 295.9 (40.6%), 294.9 (100%), 249.9 (28.7%), 248.9 (100%), 203.0 (89.8%), 202.0 (80.1%), 200.9 (100%), 155.0 (47.7%)

50 MHz	i	o	m	p	CH ₂ -O	CH ₃
¹³ C NMR in CDCl ₃	144.87	129.85	127.90	132.90	68.50	21.61

¹ H NMR in CDCl ₃ , 200MHz	Multiplicity	Number of Hydrogens	Functional Group
7.79	d	4H	aromatics
3.64	s	2H	CH ₂ -O
2.44	s	3H	CH ₃

Diethylene glycol ditosylate mp 95- 96 °C (lit. mp 98°C⁽⁵⁾)

50 MHz	i	o	m	p	CH ₂ -O	CH ₃
¹³ C NMR in CDCl ₃	145.84	130.85	128.70	134.20	70.40 69.18	21.53

E- Chlorination Reactions using Thionyl Chloride**1,6-dichloro-3-oxahexane**

A 25 ml 3-necked RB flask was equipped with a dropping funnel, condenser (topped with a drying tube) and the apparatus dried under argon. The flask was cooled with an ice-water bath and charged with 6-chloro-3-oxa-1-hexanol (3.20 g; 23.1 mmol). SOCl₂ (3.02 g, 25.4 mmol) was then introduced dropwise with stirring. The reaction is allowed slowly to come to rt then gently refluxed overnight. The crude material was purified taken up in CH₂Cl₂ and partitioned into H₂O. The organic layer was dried over

Na₂SO₄ and the solvent removed by rotaryevaporation to leave the product in 75% yield.

50 MHz	O-CH ₂	O-CH ₂ -CH ₂ -Cl	CH ₂ -Cl	CH ₂ -CH ₂ -CH ₂
¹³ C NMR in CDCl ₃	70.80 67.26	42.70	41.61	32.42

1,5-dichloro-3-oxapentane-d₄^{(1),(6)} bp 36 - 38°C/ 3 mm Hg, 84 % yield.

50 MHz	O-CH ₂ -CD ₂	CD ₂ -Cl
¹³ C NMR in CDCl ₃	71.07	42.03 ¹ J _{CO} = 22.80

¹H NMR in CDCl₃ δ: 3.69 (s, 4H)^{(1),(3)}

1,8-dichloro-3,6-dioxaoctane-d₈

50 MHz	O-CH ₂ -CD ₂ -Cl	CD ₂ -O	CD ₂ -Cl
¹³ C NMR in CDCl ₃	71.10	70.5	42.03 ¹ J _{CO} = 22.8

1,11-dichloro-3,6,9-trioxaundecane-d₄ bp 124 - 134 °C / 3 mm Hg, 86.5 % yield

50 MHz	O-CH ₂	O-CH ₂ -CD ₂ -Cl	CD ₂ -Cl	CH ₂ -CH ₂ -CH ₂
¹³ C NMR in CDCl ₃	70.69	67.77	42.32 ¹ J _{CO} = 22.80	29.84

dichloro-adducts; by-product of benzo-10-crown-3 in 23.60 % yield, as a mixture of isomers

GC/ MS (EI); M⁺ 351 (100 %).

¹³C NMR in CDCl₃ δ: MAJOR isomer: 148.9, 121.3, 114.2, 70.9, 7.8, 65.9, 42.8, 29.7 and MINOR isomer: ?, 121.7, 114.9, 69.6, 68.8, ?, 41.9, 32.7

F- Cyclization Reactions

Benzo-10-Crown-3 (2,3,5,6,7-5H-1,4,8-Benzotrioxacyclodecin)

To a 3-necked RB flask equipped with a condenser and a dropping funnel was introduced catechol (1.83 g; 16.6 mmol), 400 ml H₂O and LiOH·H₂O (1.39 g; 33.3 mmol). The reaction mixture was stirred for 1 hr at 40°C. Then 1,6-dichloro-3-oxahexane (2.61 g; 16.6 mmol) was added streamwise and the solution refluxed for 5 days. The reaction flask was cooled to rt and the medium was acidified (pH = 1- 2) with 6M HCl. The reaction mixture was extracted with CH₂Cl₂ (3 x 100 ml) then the organic layer washed carefully with 2 % KOH and dried over Na₂SO₄. The solvent was removed by rotary-evaporation and the crude oil purified by silica gel column chromatography (150 mesh, 58 Å) using hexane:acetone (9: 1). Recrystallization from cold pentane gives benzo-10-crown-3 in 12 % yield, mp 30- 31°C.

MS (EI); M⁺ 194.1 (53.6%) and the other peaks are 150.0 (71.7%), 121.0 (100.0%), 109.0 (49.5%), 79.9 (51.9%), 52.0 (30.0%), 40.9 (60.4%).

High resolution MS; C₁₁H₁₄O₃ (M⁺) m/z calc. 194.09429, found 194.09586

DSC measurement (1.4 mg); mp 31.38°C, no phase transition detected between - 50°C and the mp value.

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
¹³ C NMR in CDCl ₃	151.7	151.3	122.4	123.9	124.2	121.7	71.1	29.9	66.6	69.5	73.7
¹³ C CP/MAS	153.7	152.2	128.0	123.4	125.8	125.8	70.7	29.4	61.2	67.5	71.9

¹ H NMR in CDCl ₃ , 200 MHz	Spin System	² J (in Hz)	³ J (in Hz)	Identity
	ABCD			H6, H5, H4, H3
4.199	AA'BB'MM'	-14.35	5.07, 4.49	H7, H7'
1.885	AA'BB'MM'	-14.35	5.07, 4.49 5.41, 5.20	H8, H8'
3.897	AA'BB'MM'	-12.52	5.41, 5.20	H9, H9'
3.799	AA'BB'	-12.23	6.39, 2.29	H10, H10'
4.181	AA'BB'	-12.87	6.39, 2.29	H11, H11'

Two major by-products are formed during the reaction: the dimer (5 % yield; mixture of isomers) and the dichloro-adducts (see E-).

dibenzo-20-crown-6, mixture of isomers in a 3: 1 ratio.

GC/ MS (EI); M⁺ 388 (100 %), 121 (12.4 %)

¹³C NMR in CDCl₃ δ: MAJOR isomer: 149.5, 149.2, 121.6, 121.5, 115.3, 114.3, 70.1, 69.5, 68.7, 66.5, 30.3 and MINOR isomer: 149.5, 149.3, 121.6, 121.5, 115.0, 114.4, 70.2, 69.6, 68.6, 66.2, 30.3.

benzo-10-crown-3-d₂, recrystallized from pentane mp 30- 31 °C

MS (EI); M⁺ 196.0 (94.2 %), 149.4 (91.7 %), 138.0 (38.3 %), 122.0 (70.8 %), 120.9 (100 %), 109.9 (31.0 %), 79.9 (77.1 %), 52.0 (40.5 %), 40.9 (70.9 %).

High Resolution MS; C₁₁H₁₂O₃D₂ m/z calc. 196.10685, found. 196.10650

DSC measurement (3.8 mg); mp 31.0°C, no phase transition detected between - 100°C and the mp value.

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
¹³ C NMR in CDCl ₃	152.3	152.2	122.3	124.1	124.2	121.9	70.9	29.8	66.3	69.2	72.6
											¹ J _{CD} = 21.82
¹³ C CP/MAS	153.9	152.4	128.2	123.6	126.0	126.0	70.8	29.4	61.3	67.7	72.5
¹³ C Dip.Dep	153.9	152.4	-	-	-	-	71.5	-	-	-	-

¹ H NMR in CDCl ₃ , 200 MHz	Multiplicity	³ J (in Hz)	Identity
	ABCD		H6, H5, H4, H3
4.202	t	5.55	H7, H7'
1.887	q	5.42	H8, H8'
3.895	t	5.30	H9, H9'
3.793	s	-	H10, H10'

benzo-10-crown-3-*d*₂, recrystallized from pentane mp 30- 31 °C

MS (EI); M⁺ 196.0 (77.2 %), and the other peaks 152.0 (77.2 %), 136.0 (28.5 %), 122.0 (36.0 %), 120.9 (100 %), 109.9 (32.7.0 %), 109.0 (57.5 %), 79.9 (59.6 %), 52.0 (32.1 %), 43.1 (55.3 %).

High Resolution MS; C₁₁H₁₂O₃D₂ m/z calc. 196.10685, found. 196.10761

DSC measurement (3.7 mg); mp 31.8°C, no phase transition detected between - 100°C and the mp value.

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
¹³ C NMR in CDCl ₃	152.3	152.2	122.1	124.0	124.1	121.8	70.8	69.1	65.5 ¹ J _{CD} = 21.40	29.5	73.3
¹³ C CP/MAS	153.6	152.1	127.9	123.3	125.6	125.6	70.4	67.2	60.2	28.9	70.8
¹³ C Dip.Dep.	153.6	152.1	-	-	-	-	-	-	60.2	-	-

Benzo-9-Crown-3 (2,3,5,6-4H-1,4,7-Benzotrioxacyclononin)

The same procedure as for benzo-10-crown-3 was used using catechol (11 g; 0.1 mol), bischloroethylether (14.3 g; 0.10 mol), LiOH·H₂O (8.4 g; 0.20 mol) in water (2.2 L; 1225 factor of dilution). The crude material gained after acidic workup was put in the freezer in a small amount of Me₂CO. The mixture of benzo-9-crown-3 and dibenzo-18-crown-3 precipitates out. Washings with hot hexane dissolve benzo-9-crown-3. After rotary evaporation of the hexane the crude benzo-9-crown-3 solid was finally recrystallized from hexane:acetone (1:1), 27.2 % yield (mp 64- 66°C; lit. mp 67- 69°C^{(4),(7),(8)}).

MS (EI); M^+ 180 (68.6%) 136.1 (89.2%), 121.0 (91.8%), 79.9 (100%), 52.0 (43.7%)

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
^{13}C NMR in CDCl_3	151.4	151.4	122.9	123.9	123.9	122.9	74.0	72.3	72.3	74.0
^{13}C CP/MAS	151.0	148.7	127.2	121.8	124.6	119.0	76.1	72.9	70.4	68.2

^1H NMR in CDCl_3 , 200 MHz	Spin System	2J (in Hz)	3J (in Hz)	4J (in Hz)	5J (in Hz)	Identity
7.02	AA'BB'	-	9.00	2.00	0.50	H6, H3
6.98	AA'BB'	-	8.60, 9.00	2.00	-	H5, H4
4.33	AA'XX'	-11.01	2.19, 6.17	-	-	H7, H7' and H10, H10'
3.89	AA'XX'	-10.91	2.19, 6.17	-	-	H8, H8' and H9, H9'

Benzo-12-Crown-4 (2,3,5,6,8,9-6H-1,4,7,10-Benzotetraoxacyclododecin)^{(8),(9)}

The same procedure as for benzo-10-crown-3 was employed, using catechol (11 g; 0.10 mol), bischloroether (18.7 g; 0.10 mol), $\text{LiOH} \cdot \text{H}_2\text{O}$ (8.4 g; 0.20 mol) in water (1.5 L; 1225 factor of dilution). The crude material was purified by column chromatography (grade 60, 230-400 mesh) using ethyl acetate: ether (1: 1) followed by recrystallization from Me_2CO mp 45- 46°C in 39.80 % yield (lit. mp = 44- 46 °C^{(1),(6)}).

MS (EI); M^+ 224.1 (100%), 136.1 (94.7%), 121.0 (70.3%), 80.2 (36.6%)

High Resolution MS; $C_{12}H_{16}O_4$ m/z calc. 224.10486, found 224.10429

DSC measurement (2.3 mg); mp 45.03 °C

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12
^{13}C NMR in $CDCl_3$	150.5	150.5	118.0	122.5	122.5	118.0	71.5	69.7	71.0	71.0	69.7	71.5
^{13}C CP/MAS	152.0	151.5	117.0	121.9	121.9	117.0	74.2	69.0	72.5	70.8	68.0	74.2

Benzo-13-Crown-4 (2,3,5,6,7,9,10-7H-1,4,8,11-Benzotetraoxacyclotridecin)⁽³⁾

The same procedure as for benzo-10-crown-3 was employed, using catechol (2.93 g; 27.0 mmol), bischloroether (5.47 g; 27.0 mmol), $LiOH \cdot H_2O$ (2.24 g; 54.0 mmol) in water (2 L; 1250 factor of dilution). The crude material was purified by column chromatography (grade 60, 230-400 mesh) using ether or vacuum distillation (120- 165°C/ 5 mm Hg) followed by recrystallization from cold pentane, mp 53- 54 °C in 24 % yield (lit. mp 53°C⁽³⁾).

GC/ MS (EI); M^+ 238.0 (37.9%) 136.0 (100%), 120.9 (59.5%), 79.9 (45.0%), 40.9 (38.2%)

DSC measurement (1.7 mg); mp 53.0°C

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13
^{13}C NMR in $CDCl_3$	150.2	150.2	117.4	122.6	122.6	117.4	71.1	67.0	69.1	30.4	69.1	67.0	71.1
^{13}C CP/MAS	148.0	154.8	111.8	126.2	120.3	126.2	76.1	69.7	65.5	32.2	68.6	69.7	72.2

benzo-13-crown-4-*d*₄, recrystallized from cold pentane, mp 53- 55 °C.

MS (EI); M^+ 242.1 (39.0%), 138.0 (100%), 122.0 (44.7%), 79.9 (57.8%), 40.9 (39.9%)

DSC measurement (3.5 mg), mp , 54.11°C

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13
¹³ C NMR in CDCl ₃	150.1	150.1	117.3	122.5	122.5	117.3	70.3 ¹ J _{CO} = 21.5	68.8	67.0	30.3	67.0	68.8	70.3 ¹ J _{CO}
¹³ C CP/MAS	147.9	154.8	111.8	126.1	125.7	120.3	75.9	69.7	65.6	32.2	68.6	69.7	71.8
¹³ C Dip.Dep.	147.9	154.8	-	-	-	-	75.9	-	-	-	-	-	71.8

Benzo-13-Crown-4 (2,3,5,6,8,9,10-7H-1,4,7,11-Benzotetraoxacyclotridecin)

The same procedure as for benzo-10-crown-3 was employed, using catechol (1.70 g; 15.4 mmol), 1,9-dichloro-3,6-dioxanonane (3.11 g; 15.4 mmol), LiOH·H₂O (742 mg; 30.94 mmol) in water (900 mL; 1600 factor of dilution). The crude material was purified by column chromatography (grade 60, 230-400 mesh) using hexane: acetone (5: 1) and recover in a pure form as an oil 24.3 % yield.

MS (EI); M^+ 238.0 (20.8%), 182.0 (43.8%), 167.0 (100%), 151.0 (31.4%), 149.9 (33.0%), 139.0 (29.7%), 136.0 (30.8%), 135.0 (37.4%), 120.9 (35.1%), 79.9 (21.4%), 67.1 (21.4%), 45.1 (22.3%), 43.1 (67.2%), 40.9 (44.6%), 39.0 (24.2%)

High Resolution MS; C₁₃H₁₈O₄ m/z calc. 238.12051, found 238.11933

100 MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13
¹³ C NMR in CDCl ₃	149.6	150.6	120.0	121.8	123.2	115.3	68.92	30.12	66.55	68.52	68.59	68.99	70.84

15-Crown-5 (1,4,7,10,13-Pentaoxacyclopentadecane)⁽¹⁰⁾⁻⁽¹⁶⁾

In a 500 ml 3-necked RB flask equipped with mechanical stirrer, dropping funnel and reflux condenser containing 90 ml of dioxane was added crushed 98 % NaOH pellets (17.20 g; 0.43 mol), triethyleneglycol (18,75 g; 0.125 mol). The reaction mixture was heated gently for 30 min.. Then 1,5-dichloro-3-oxapentane (44.70 g; 0.31 mol, 2.2 molar excess) diluted in 30 ml of solvent were added streamwise upon violent stirring. The reflux was set up for 24 hours. The reaction mixture was then filtered by gravity, rinsed with CH₂Cl₂. The solvents were removed by rotoryevaporation. More salts precipitated out, so another filtration with CH₂Cl₂ was required before further purification by vacuum distillation leaves 10.10 g of 15-crown-5 in 36.7 % yield ,bp 130- 132 °C / 0.2 mm Hg (lit. bp 100- 135°C / 0.2 mm Hg⁽¹⁶⁾), .

MS (CI); M⁺ 220.9 (100%), 177.0 (3.6%), 133.0 (60.4%)

¹³C NMR in CDCl₃ δ; 70.37

¹H NMR in CDCl₃ δ; 3.65 (s, 20H)

15-crown-5-d₄

MS (CI); M⁺ 225.1 (100%), 151.0 (19.9%), 149.1 (54.4%), 137.0 (35.1%), 135.1 (33.2%), 133.0 (21.5%), 103.1 (24.7%)

21-Crown-7 (1,4,7,10,13,16,19-Heptaoxacycloheptacosane)⁽¹⁷⁾

In a 3-necked RB flask equipped with a condenser and a dropping funnel were introduced crushed KOH pellets (3.40 g; 61 mmol), tetraethylene glycol (3.88 g; 20 mmol) with 50 ml of 1,4-dioxane. Under violent stirring the reaction mixture was gently heated up. After 20 min. triethylene glycol ditosylate (9.16 g; 20mmol) dissolved in 150

ml of 1,4-dioxane was added streamwise to the reaction and reflux set up for 24 hr. The reaction mixture was filtered by gravity, washed with CH_2Cl_2 , and the solvents removed by rotary evaporation. 21-crown-7, a viscous colourless liquid (lit. bp 180- 200°C/ 0.1 mm Hg⁽¹⁸⁾), was recovered in pure form by column chromatography on neutral activated Al_2O_3 (150 mesh, 58 Å) with EtOAc as an eluant, 57.7 % yield.

MS (CI); M^+ 309 (68.5%), 221 (7.0%), 177 (16.3%), 133 (100%),
89 (35.8%), 73 (31.9%)

^{13}C NMR, 50 MHz, in CDCl_3 δ ; 70.46

^1H NMR, 200 MHz, in CDCl_3 δ ; 3.57

21-crown-7- d_{12}

MS (CI); $(\text{M}+1)^+$ 320.8 (72.4%), 187.0 (33.5%), 185.0 (34.2%), 181.9 (27.7%), 180.9 (23.7%), 142.0 (55.4%), 141.0 (100%), 138.0 (49.3%), 137.0 (89.0%), 136.0 (42.8%), 135.0 (86.2%)

50 MHz	C1	C2	C3	C4	C5	C6	C7
^{13}C NMR in CDCl_3	70.0 $^1J_{\text{C}} = 21.4$	70.6	70.0 $^1J_{\text{C}} = 21.4$	70.0 $^1J_{\text{C}} = 21.4$	70.7	70.8	70.8

^1H NMR, 200 MHz, in CDCl_3 δ ; 3.68

G- Complexation

(Benzo-10-crown-3) $_2$ · LiClO_4

Equimolar amounts of the ligand and the salt were dissolved in EtOAc. Evaporation and recrystallization from EtOAc gives the complex mp 188- 189 °C.

DSC measurement; mp 188.6 °C

Elemental analysis; %C found 52.81 calc 53.39
 %H found 5.60 calc 5.70
 %O found 32.89 calc 32.33

100 MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
¹³ C NMR in acetone-d ₆	153.7	153.4	122.9	124.6	124.7	122.8	71.4	30.8	66.7	70.0	74.3
¹³ C CP/MAS											
4A	148.1	146.9	117.1	127.5	126.3	119.3	71.5	23.1	63.9	74.0	74.0
4B	149.4	149.4	124.8	124.8	128.7	127.5	71.5	23.1	62.1	71.5	74.0

15-Crown-5 Complexes

15-crown-5 · NaI⁽¹⁹⁾

Equimolar amounts of 15-crown-5 and NaI were dissolved in EtOH: CH₂Cl₂ (7:3).
 Slow evaporation gave X-ray suitable crystals.

¹³C NMR in Me₂CO-d₆;

	C1	C2	C3	C4	C5
15-crown-5 · NaI	69.30	69.30	69.30	69.30	69.30
15-crown-5 -d ₄ · NaI	69.25	68.67 ¹ J _{CD} = 22.5	69.29	69.37	69.37
15-crown-5 -d ₄ · NaI	68.50 ¹ J _{CD} = 21.5	69.13	68.63 ¹ J _{CD} = 21.5	69.24	69.33
15-crown-5 · NaClO ₄	69.43	69.43	69.43	69.43	69.43
15-crown-5 -d ₄ · NaClO ₄	69.32	?	69.35	69.44	?
15-crown-5 -d ₄ · NaClO ₄	68.54 ¹ J _{CD} = 21.3	69.16	68.66 ¹ J _{CD} = 21.2	69.27	69.36

DSC measurements;

15-crown-5· NaI	phase transition at 343 K
15-crown-5-<i>d</i>₈· NaI	phase transition at 343.5 K
15-crown-5· NaClO₄⁽²⁰⁾	phase transitions at 356.5, 373.6 and 382.0 K
15-crown-5-<i>d</i>₈· NaClO₄	phase transitions at 357.4, 374.2 and 380.9 K

H- Hydrogenation Reactions

cis-Cyclohexyl-10-Crown-3

In 10 ml abs. EtOH was dissolved benzo-10-crown-3 (200 mg) and 40 mg of Rh on alumina catalyst. After 6 hr under 550-600 psi of H₂ (g) at 40°C the catalyst was filtered off and the ethanol was removed by rotaryevaporation yielding an oil. From ¹³C NMR there appears to be the *cis*-isomer along with 30% unwanted cleaved ether fragment. The hydrogenation apparatus was an American Instrument Co. 40,000 psi max, pressure high pressure apparatus. The isomer was separated successfully by plate chromatography on silica gel (1 mm plates) using benzene: acetone (5: 1), 70% yield.

High Resolution MS; C₁₁H₂₀O₃ (M⁺) m/z calc. 200.14124, found 200.14203

CD ₂ Cl ₂ , 100 MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
rt	77.98	77.71	29.04	23.44	21.64	29.14	62.68	30.69	69.16	71.59	71.74
MAJOR 210 K	75.95	75.88	27.65	23.79	18.99	27.95	57.86	29.30	68.79	71.18	71.87
MINOR 210 K	78.81	77.22	27.46	23.79	19.14	28.94	67.88	30.08	66.97	68.50	68.50

(a) LiAlX_2 ($\text{X} = \text{H, D}$), anh. THF, 95 % yield; (b) $\text{EtO}_2\text{CCHN}_2$, $\text{BF}_3 \cdot \text{Et}_2\text{O}$, CH_2Cl_2 , 75 % yield; (c) same as (a); (d) SOCl_2 (10 % molar excess), 75 % yield; (e) catechol (1 molar equivalent), $\text{LiOH} \cdot \text{H}_2\text{O}$ (2 molar equivalents), H_2O (factor of dilution 1335), reflux for 6 days, 75 % yield; (f) Rh on alumina, abs. EtOH, 550 - 600 psi of H_2 at 40°C for 6 hours, 70 % yield.

Fig. 73 Synthetic scheme for 10-crown-3 moieties

cis-cyclohexyl-10-crown-3- d_2

CD ₂ Cl ₂ , 100MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
π	77.88	77.74	29.03	23.45	21.64	29.17	62.69	30.69	62.69	71.62	-
MAJOR 210 K	76.07	75.93	27.73	23.92	19.09	28.11	58.07	29.39	68.89	71.17	-
MINOR 210 K	78.92	77.32	27.57	23.92	19.23	29.04	67.95	30.18	67.09	68.50	-

cis-cyclohexyl-10-crown-3- d_2

CD ₂ Cl ₂ , 100MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
π	77.88	77.74	29.03	23.45	21.64	29.17	-	71.62	-	30.69	9.17
MAJOR 210 K	76.00	75.92	27.68	23.83	19.03	27.99	57.90	29.13	-	71.16	71.92
MINOR 210 K	78.87	77.29	27.50	23.83	19.16	28.99	67.91	29.92	-	68.49	68.54

cis-Cyclohexyl-13-Crown-4 (cis-2,5,8,12-Tetraoxabicyclo-[11.4.0]-heptadecane)

The same procedure as that for cyclohexyl-10-crown-3 was employed, using 310 mg of benzo-13-crown-4 in abs. EtOH (15ml) with 62 mg of Rh catalyst. The product was recovered in 70% yield by plate chromatography using hexane: ether (1: 2).

MS (CI); (M+1)⁺ 245.0 (88.4%), 214.9 (27.7%), 173.0 (67.7%), 165.0 (45.3%), 160.9 (47.8%), 157.0 (37.4%), 147.0 (34.1%), 143.0 (94.2%), 117.0 (60.2%), 103.0 (100%)

CD ₂ Cl ₂ , 100MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13
π	76.68	76.68	27.78	22.41	22.41	27.78	68.02	69.82	66.40	30.56	66.40	69.82	68.02
210 K	77.62	72.08	25.80	23.97	18.73	27.34	69.02	68.60	66.73	30.33	63.76	68.37	63.59

***cis*-cyclohexyl-13-crown-4-*d*₄**

CD ₂ Cl ₂ , 100MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13
π	76.68	76.68	27.82	22.43	22.43	27.82	67.32	69.74	66.48	31.01	66.48	69.74	67.32
210 K	77.45	71.95	25.72	23.88	18.66	27.27	-	68.41	66.74	30.25	63.67	68.17	-

***cis*-cyclohexyl-13-crown-4 (*cis*-2,5,9,12-Tetraoxabicyclo-[11.4.0]-heptadecane)**

CD ₂ Cl ₂ , 100MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13
π	76.42	76.75	28.41	22.10	22.10	22.90	63.71	31.12	71.00	70.41	68.54	66.23	69.13
MAJOR 210 K	77.50	72.00	27.24	23.99	18.59	25.68	60.57	29.86	69.97	(64.69)	68.82	68.82	68.97
MINOR 210K	78.51	71.86	27.07	23.99	18.82	26.78	64.18	29.75	69.77	66.84	68.29	68.29	68.65

10-cyclohexyl-3,7,10-trioxa-1-decanol-*d*₂, cleavage product

100 MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11
¹³ C NMR in CD ₂ Cl ₂	-	72.18	68.47	32.65	68.47	70.87	-	78.11	30.35	26.24	24.55

I- Methylation Reactions using Dimethylsulfate**1,2-Dimethoxybenzene-*d*₆⁽²¹⁾**

In a 3-necked RB flask equipped with a condenser, a dropping funnel and an argon in and outlet, crushed NaOH 98 % pellets (1.51 g, 0.038 mol) dissolved in 12 ml of water is added catechol (2.08 g, 0.019 mol) freshly recrystallized from hexane: acetone (4:1). The reaction mixture was gently heated in order to form the dicarbanion, then it was cooled and (MeO)₂SO₂-*d*₆ (5.00 g; 0.038 mol) was added.

The reaction mixture was refluxed then for 15 min. then cooled, and extracted with ether. The organic layer was washed with 2 % KOH solution, dried over Na_2SO_4 . After removal of the solvent by rotary-evaporation, veratrole- d_6 was purified by distillation bp = $108^\circ\text{C}/18$ mm Hg in 73.6 % yield (lit. bp $88-90^\circ\text{C}/10$ mm Hg; lit. mp $15^\circ\text{C}^{(22)}$).

By acidification of the basic aqueous layer with 3M HCl, extraction with diethylether, drying over Na_2SO_4 , and removal of the solvent, guaiacol- d_3 was recovered, 24 % yield.

MS (EI); M^+ 144.1 (100%), 126.1 (49.2%), 98 (53.3%), 52.0 (24.5%), 28.1 (43.8%)

50 MHz	C1	C2	C3	C4	C5	C6	C7	C8
^{13}C NMR in CDCl_3	149.13	149.13	111.47	120.87	120.87	111.47	54.98 $^1J_{\text{CQ}} = 21.5$	54.98 $^1J_{\text{CQ}} = 21.5$

1,2-dimethoxybenzene

50 MHz	C1	C2	C3	C4	C5	C6	CM1	CM2
^{13}C NMR, in CDCl_3	149.12	149.12	111.46	120.88	120.88	111.46	55.77	55.77
^{13}C CP/MAS	149.40	149.40	110.40	121.10	122.80	112.00	56.90	55.00

2,3-Dimethoxynaphthalene ^{(23),(24)}

The same procedure as for veratrole was employed using 2,3-dihydroxynaphthalene (16.00 g, 0.10 mol), NaOH (4.30 g, 0.10 mol), $(\text{MeO})_2\text{SO}_2$ (12.60 g, 0.20 mol) in 65 ml H_2O to give 2,3-dimethoxynaphthalene recrystallized from EtOH mp $116-118^\circ\text{C}$ in 70 % yield (lit. mp $117-118^\circ\text{C}^{(25)}$).

MS (EI); M^+ 188.0 (100%), 173.0 (12.4%), 145.0 (30.1%), 127.0 (13.6%), 117.0 (11.3%), 115.1 (27.4%), 102.0 (27.1%).

50 MHz	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12
¹³ C NMR in CDCl ₃	106.24	149.39	149.39	106.24	126.24	124.15	124.15	126.26	129.13	129.13	55.8	55.8
¹³ C CP/MAS	105.77	150.40	150.40	106.72	126.79	123.78	123.78	127.99	129.72	129.98	54.96	54.81

J- Ortho-Metallation Reaction⁽²⁶⁾

1,2-Dimethoxybenzene-*d*⁽²⁷⁾

All glassware was flame dried. To a suspension of *t*BuOK (2.24 g, 20 mmol) in 40 ml of anh. THF (previously distilled over LiAlH₄) was added *n*BuLi (10.0 ml, 20 mmol; 2.0 M in pentane) at - 78°C. Then veratrole (1.38 g, 10 mmol) dissolved in 20 ml anh. THF was added with a syringe through a septum. After 15 min. of stirring at - 78 °C the reaction mixture quenched with D₂O. The reaction flask was warmed to rt. The reaction mixture was extracted partitioned between CH₂Cl₂/ H₂O and extracted into CH₂Cl₂. The organic layer was washed with 2 % KOH, saturated NaCl solution and dried over Na₂SO₄. The solvent was removed by rotaryevaporation. The crude material was purified by column chromatography on silica (grade 60, 230- 400 mesh) using hexane: ether (2: 1) to leave 0.89 g of product, 64 % yield and > 95 % deuterium incorporation.

	C1	C2	C3	C4	C5	C6	CM1	CM2
¹³ C NMR in CDCl ₃	149.06	149.06	111.16 ¹ J _{CD} = 24.0	120.77	120.86	111.41	55.81	55.81
¹³ C CP/MAS	149.30	149.30	110.40	121.00	122.70	111.90	56.90	54.90
¹³ C Dip.Diph.	149.30	149.30	110.40	-	-	111.90	56.90	54.90

400 MHz ¹H NMR δ; ABC spin system simulated by the LAOCOON program⁽²⁸⁾;

$$\delta_4 = \delta_5 = 6.91, \delta_6 = 6.88, {}^3J_{H4-H5} = {}^3J_{H5-H6} = 8.0 \text{ Hz}; {}^5J_{H4-H6} = 2.0 \text{ Hz}$$

Benzo-9-Crown-3-*d*

The same procedure as for the protio analogue was used; *t*BuOK (1.87 g, 16.67 mmol), *n*BuLi (8.33 ml, 16.67 mmol; 2.0 M in pentane), 1.5 g of benzo-9-crown-3 in 50 ml of anh. THF. The product was recovered by recrystallization from acetone to leave the product with 83.2 % incorporation, mp 64- 66°C.

MS (EI); M^+ 181.0 (71.8%), 137.1 (86.3%), 122.0 (99.0%), 81.0 (100%), 53.1 (44.8%).

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
^{13}C NMR in CDCl_3	151.45	151.41	122.62 $^1J_{\text{CO}} = 24.10$	123.87	123.98	122.88	74.11	72.36	72.36	74.11
^{13}C CP/MAS	151.70	149.30	119.9	125.30	122.60	128.00	76.90	73.80	71.20	68.90
^{13}C Dip. Diph.	151.70	149.20	119.7	-	-	127.9	-	-	-	-

K- Dehydration Reaction using Nafion-H⁽²⁹⁾**10-Crown-3**

A 50 ml RB flask was charged with 3,7-dioxa-1,9-nonanediol (8.10 g; 0.05 mol) and beads of Nafion H catalyst (2.30 g). The RB flask was equipped with a Claisen head and a receiver, which was cooled by an ice/ water bath. The reaction mixture was heated with an oil bath under reduced pressure (2.5 mmHg). The products were collected upon distillation. At $T = 122^\circ\text{C}$, the reaction mixture is characterized by a yellow-brownish color, indicative of polymerization conditions. The beads of Nafion H are darkened, indicative of inactivation. The reaction was stopped and the condensate that formed rinsed with acetone. Upon removing of the solvent by rotory-evaporation 6.90 mg of crude 10-crown-3 (0.1%) was recovered, bp 29- 31°C/ 2.5 mm Hg.

MS (CI); M^+ 147 (100 %)

50 MHz	$\text{CH}_2\text{-}\underline{\text{C}}\text{H}_2\text{-CH}_2$	$\text{CH}_2\text{-CH}_2\text{-}\underline{\text{C}}\text{H}_2$	$\text{O-}\underline{\text{C}}\text{H}_2\text{-}\underline{\text{C}}\text{H}_2\text{-O}$
^{13}C NMR in acetone- d_6	32.60	68.81	72.03 67.25

^1H NMR in acetone- d_6 , 200MHz	Multiplicity	3J (in Hz)	Functional Group
1.97	q	6.20	$\text{CH}_2\text{-}\underline{\text{C}}\text{H}_2\text{-CH}_2$
3.79	t	6.20	$\text{CH}_2\text{-CH}_2\text{-}\underline{\text{C}}\text{H}_2$
3.70	AA'BB'	-	$\text{O-}\underline{\text{C}}\text{H}_2\text{-}\underline{\text{C}}\text{H}_2\text{-O}$
3.65	AA'BB;	-	$\text{O-}\underline{\text{C}}\text{H}_2\text{-CH}_2\text{-O}$

Part II**Processing Techniques****A- Nuclear Magnetic Resonance****Solution NMR*****¹H and ¹³C solution NMR***

The ¹³C solution spectra were recorded on Varian Gemini XL-200, Bruker AMX-400 and AMX-500 spectrometers at 50.3, 100.6 and 125.8 MHz respectively. The concentrations of the samples for the normal 50.3 MHz ¹³C and 200 MHz ¹H spectra were approximately 0.2 and 0.1 M in CDCl₃ respectively. TMS was used as an internal reference in 5 mm o.d. tubes. Routinely ¹³C spectra were obtained with complete ¹H noise decoupling. Normal operating conditions for ¹³C at 50.3 MHz were as follows: pulse width 16 μs (90°) and 30K data points with a repetition rate of 1.0 s. The number of accumulations for the low temperature spectra was typically 1000- 2000 and the temperatures were calibrated using a copper-constantan thermocouple in a dummy NMR tube. Normal operating conditions for the ¹³C and ¹H spectra at 100.6 and 125.8 MHz, 6 and 7 μs (45°) and 30 to 32K data points, respectively.

2D-NMR experiments***a- NOESY experiment***

The ¹H¹H nOe experiments were performed with a 0.5 M CDCl₃ solution at 200 MHz using a delay time of 6 s, 6000 accumulations and a mixing time selected to be consistent with the 1/T₁ criterion⁽³⁰⁾ (usually 0.3 s for the series of benzo-crown-ethers investigated).

b- HETCOR (HMQC) experiment

For the ¹H¹³C HETCOR experiment, the free induction decays were acquired over 1024 data points for each of the 512 values of the evolution time, with a

digital resolution of ca 8 Hz/ point in F2 and 4 Hz/ point in F1. The raw data were zero filled in F1 prior to the transformation using the qsine window function for both F1 and F2. The proton relaxation delays were set to 1 s. Delays were chosen to emphasize J values of 135- 140 Hz. For the long range HETCOR (HMBC) experiment, delays were chosen to emphasize a coupling of 7.5 Hz.

c- COSY experiment

The ^1H - ^1H COSY experiments were run using the N-type cycling with a 45° mixing pulse. The free induction decays were acquired over 1024 data points for each of the 256 values of the evolution time, with a digital resolution of ca. 5 Hz/ point. The raw data were zero filled in F1 prior to the transformation using the qsine window function for both F1 and F2. The data were symmetrized about the diagonal.

^{13}C spin-lattice relaxation time

^{13}C spin-lattice relaxation times were determined at 50.3 MHz via the inversion recovery method⁽³¹⁾ with typical delay times $D_1 = 20$ s and the array $D_2(1) = 0.01, 0.05, 0.1, 0.25, 0.5, 0.75, 1.0, 2.0, 4.0, 8.0, 12.0, 16.0, 20.0, 25.0$ s. The standard XL-200 software was employed to process the data obtained. The samples were degased under vacuum prior to measurement by bubbling with N_2 .

Solid state NMR experiments

^{13}C CP/MAS spectra

The ^{13}C CP/MAS spectra were acquired at 50.32 MHz on a Bruker ASX-200 solid state NMR spectrometer, equipped with a Bruker 7 mm triple resonance MAS probe. The magic angle was accurately set using the ^{79}Br resonance of KBr by maximizing the number of rotational echoes in the free induction decay. The ^1H 90° pulse lengths were typically 4.2 μs with a delay time dependent on the relaxation of the ^1H nuclei under investigation. The chemical shifts were externally referenced to the ^{13}C resonance of tetrakis(trimethylsilyl)silane $\text{Si}(\text{Si}(\text{CH}_3)_3)_4$, which was assigned a chemical shift of 3.7 ppm

(wrt TMS). The spin rates were typically between 4 and 6 kHz and were stable to within *ca.* 5 Hz. The experiments achieved at various temperatures were conducted by driving the spinner with cold N₂ gas.

Specific cases

Delay times were of 60.0 s for 1,2-DMB at 260 K; 5 s for 1,4-DMB and 1,3,5-TMB at rt; 2 s for MB at 210 K.

¹³C CP/ MAS spectra of 1,3-DMB were recorded at 45.3 MHz on a Bruker CXP-180 with 3.6 μs for the 90° pulse, a delay of 2- 4.0 s and a contact time of 3.5 ms at *ca.* 150 K. Chemical shifts were measured relative to hexamethylbenzene (HMB) and converted to TMS scale *via* the factor of 16.9 ppm, which is the chemical shift for the CH₃ group of HMB.

¹³C CP/MAS dipolar dephased spectra

The ¹³C CP/MAS Dipolar Dephased spectrum of *ortho*-d 1,2-DMB was recorded with a dephasing delay of 40 μs.

²H solid state NMR experiment

²H NMR powder spectra for deuterated 15-crown-5 and 21-crown-7 complexes were recorded on a Bruker AMX 300 spectrometer at 46 MHz at various temperatures by using a variable N₂ gas flow probe with a EURO THERM temperature controller. A phase alternated quadrupole echo sequence⁽³²⁾ was used with a delay time of 35 μs between X and Y pulses of 2.6 to 3.0 μs.

The solid state ²H NMR powder spectra were recorded on a Bruker ASX-200 NMR spectrometer, equipped with a Bruker 7 mm triple resonance MAS probe at 30.72 MHz. The quadrupole echo pulse sequence⁽³²⁾ with phase cycling was used to record the spectra of deuterated 1,2-DMB derivatives (*ortho*-d 1,2-DMB and 1,2-DMB-*d*₆). The delay between the two 90° pulses were typically 30- 35 μs and the echo delays 28- 30 μs. The 90° pulses were 3.0 to 4.0 μs long. The delay time was 60.0 s for *ortho*-d 1,2-DMB and 5.0 to 10.0 s for 1,2-DMB-*d*₆.

B- Mass Spectrometry Techniques

Electron impact or chemical ionization

The MS spectra of all samples were recorded on A VG 7070E mass spectrometer by either electron impact at 70 eV, 6 kV accelerating or chemical ionization, using diethyl ether as the reagent gas.

High resolution

The new compounds were analyzed on a KRATOS CONCEPT II H with the resolution of 8000 and ionization of 70 eV. The samples were scanned by 10 sec./dec., with ac voltage of 8 kV using perfluorokerosene as reference.

C-Differential Scanning Calorimetry (DSC) and Thermogravimetry/ Differential Thermal Analyzer (TG/ DTA).

DSC

The DSC plots were recorded on a Seiko instrument SSC/ 5200 equipped with a DSC220C head with a heating rate of 10°C/ min. from -100 to 160°C and a nitrogen flow rate of 50 ml/ min. The cooling rate was 5°C per minute. Samples (amount of substance used for each run about 4- 10mg) were analyzed in a crimed aluminium sample pan with an aluminum lid as reference.

TG/ DTA

The TG/ DTA plots were recorded on a Seiko instrument thermal analysis system SSC/ 5200 equipped with a TG/ DTA220 head with a heating rate of 10°C/ min. and a nitrogen flow rate of 200 ml/ min.

D- Crystallographic Data

General procedure

Single crystals of 15C5· NaI, 2,3-dimethoxynaphthalene, B10C3 and (B10C3)₂· LiClO₄ were mounted on a glass capillary and measured on a Rigaku diffractometer with MoK α radiation. Cell constants and intensity data were collected at - 80°C using the $\theta/2\theta$ scan technique to a maximum 2θ value of 49.9°. The structure was solved by direct methods. All the atoms were refined anisotropically except the hydrogens, which were refined isotropically. Weights based on counting statistics were used and all calculations were performed using the NRC/VAX crystallographic software package^{(33),(34)}.

X-ray structure of 1,2-DMB

1,2-DMB (lit. mp 15°C⁽³⁵⁾) was purchased from Aldrich and purified by distillation. Suitable crystals in the form of needles were obtained by slow crystallization from anhydrous pentane in a freezer at - 5°C. Further work was achieved in a cold room at + 4°C where the crystals were filtered by suction, washed with aliquots of cold pentane and kept sealed under nitrogen in a freezer. The mounting on the X-ray axis was achieved using epoxy glue which was first allowed to harden in the cold room for 5 minutes. The intensity data were obtained at - 120°C with a Nonius diffractometer using the $\theta/2\theta$ scan mode. All atoms were refined anisotropically except hydrogens, which were refined isotropically. The protons HM1B and HM2A were found and the other methoxy hydrogen positions calculated. Weights based on counting statistics were used and all calculations performed using the NRC/VAX crystallographic software package^{(33),(34)}.

E- Computations

LORG

The X-ray coordinates were used as input into the QUANTA/ CHARMM⁽³⁶⁾ molecular modelling program and where necessary hydrogen atoms were added using CHARMM force field parameters. The resulting Z-matrix was then used as input for an *ab initio* RH SCF calculation in the program GAMESS⁽³⁷⁾ using the D95V basis set. The post SCF NMR shielding tensor calculations were done using the RPAC⁽³⁸⁾ program using

the nosort option for the localization of orbitals.

GIAO

The theoretical NMR chemical shifts were calculated using the Gaussian 94 program⁽³⁹⁾. The basis sets used were 6-31G* and cc-pVTZ. The calculations methods were the Continuous Set of Gauge Transformations (CSGT) and the Gauge Independent Atomic Orbitals (GIAO) methods. The length of time required for the calculations ranges from 39' to 23 hrs and 55'. The calculations with the cc-pVTZ basis set proved to be extremely time consuming (in the case of 1,2-DMB, taking 10 days and 16 hrs) while the 6-31G* calculations took only 7 hrs and produced the same trends throughout the various carbons (Table 34). So, these test calculations using much larger basis sets show the 6-31G* basis set is adequate in providing relative chemical shifts. The ground state wavefunctions were computed within the gradient corrected local density (LDA) functional B3LYP approximation. A recent study has shown that a combination of B3LYP and GIAO using 6-31G* basis set is able to provide reasonable chemical shifts for a variety of molecules (CH₄, C₂H₄, C₂H₂, C₆H₆,...)⁽⁴⁰⁾.

The calculations were performed on the X-ray determined structure for 1,2-DMB. In case of anisole (MB) the structure was optimized using the Gaussian Program with 6-31G* basis set.

Table 34 Calculations of the ^{13}C tensors of 1,2-DMB with various basis sets.

		C1	C2	C3	C4	C5	C6	CM1	CM2
cc-pTVZ	σ_{11}	237.8	232.6	209.2	241	235.2	205	69.6	71.6
	σ_{22}	161.2	164.2	127.7	128.6	125.5	128.5	62.7	66.5
	σ_{33}	63.1	63.9	-2.1	1.1	-5.6	-6.3	-1.2	4.5
	σ_{iso}	154.0	153.5	111.6	123.5	118.4	109.0	43.7	47.5
6-311G*	σ_{11}	231.7	227.8	183.6	241.1	236.2	206.4	90.0	90.8
	σ_{22}	180.9	183.5	118.1	136.8	133.6	134.9	79.6	84.3
	σ_{33}	84.1	85.1	4.3	15.5	7.7	5.4	5.6	12.3
	σ_{iso}	165.5	165.5	102.0	131.1	125.8	115.6	58.4	62.5
6-31G*	σ_{11}	200.3	196.7	210.4	207.5	202.9	180.3	77.1	77.1
	σ_{22}	158.3	161.0	134.2	122.6	119.0	118.5	67.1	71.8
	σ_{33}	70.1	71.1	9.6	9.6	2.1	-0.2	2.2	8.0
	σ_{iso}	142.9	142.9	118.0	113.2	108.0	99.5	48.8	52.3

The results on the ^{13}C shifts are presented relative to tetramethylsilane (TMS) computed using a similar procedure ($\delta = 191.1$ ppm relative to the bare nucleus) (Table 35).

Table 35 ^{13}C tensors of TMS.

	Si	C1	C2	C3	C4
σ_{11}	415.4	189.6	189.6	189.6	189.6
σ_{22}	415.4	189.6	189.6	189.6	189.6
σ_{33}	415.4	194.0	194.0	194.0	194.0
σ_{iso}	415.4	191.1	191.1	191.1	191.1

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Conclusion and Future Work

A- Motion Study in Crown Ethers

For $3n$ -crown- n complexes ($n = 4, 5, 6$) a *merry-go-round* motion is a common solid state dynamic at high temperature. It can be thought of as an axial n -fold rotation combined with conformational readjustment to keep the X-ray structure unchanged.

Table 38 Static lineshape features of $3n$ -crown- n complexes

	T(K)	$\Delta\nu_{zz}^a$	$\Delta\nu_{yy}^a$	$\Delta\nu_{xx}^a$	χ_{eff}	η
$18C6-d_4 \cdot 2 CH_2(CN)_2^{(1)}$	198	246.1	131.8	114.3	164.1	0.0711
$12C4-d_4 \cdot LiSCN^{(2)}$	218	238.3	119.15	119.1	158.9	0
	175	250.0	125.0	125.0	166.7	0
$15C5-d_8 \cdot NaI$	238	242.7	113.3	113.3	161.8	0.0659
$15C5-d_4 \cdot NaClO_4$	225	242.7	113.3	113.3	161.8	0.0659
$21C7-d_{12} \cdot KI$	184	244.9	131.5	131.5	163.3	0.0737

a : in kHz

A number of phase transitions complicate the interpretation of the dynamics of the $15C5$ complexes, necessitating a high temperature X-ray structure. For $21C7 \cdot KI$, no X-ray structure could be obtained due to excessive dynamic disorder, however the f m l at 340 K (Table 39) shows all deuterons to be equivalent due to up-down flips of the $O-CH_2-CH_2-O$, without n -fold rotation ($\eta = 1$).

Table 39 f.m.l. lineshape features of 3*n*-crown-*n* complexes

	T(K)	$\Delta\nu_{zz}^a$	$\Delta\nu_{yy}^a$	$\Delta\nu_{xx}^a$	χ_{eff}	η
18C6- <i>d</i> ₄ · 2 CH ₂ (CN) ₂ ⁽¹⁾	373	69.6	34.8	34.8	46.4	0
12C4- <i>d</i> ₄ · LiSCN ⁽²⁾	242	-	-	-	56.97	0.226
		-	-	-	12.02	1
15C5- <i>d</i> ₈ · NaI	345	50.7	25.3	25.3	33.8	0
15C5- <i>d</i> ₄ · NaClO ₄	380	50.1	25.0	25.0	33.4	0
21C7- <i>d</i> ₁₂ · KI	339.5	36.0	36.0	0	24.0	1
	389	24.0	24.0	0	16.0	1

a: in kHz

In view of the problems experienced with 15C5 and 21C7 complexes, a new approach is necessary in the motional study of oxiranes via solid state ²H NMR. Owing to the scarcity of well characterized models, one should seek more symmetric analogues, preferably close to a "diamond lattice" conformation. From a literature survey, the following potential candidates were found; 12C3, 12C3· Li⁺, 14C4 (symmetric isomers), 16C4 and 16C4· Li⁺. For 12C3· LiSCN, a non-angular diamond lattice conformation is encountered with C-C-C-O and C-O-C-C dihedral angles of *ca.* 73° and 168° respectively⁽³⁾. All known X-ray structures containing 14C4 adopt the "rectangular" diamond lattice conformation⁽⁴⁾⁻⁽⁷⁾. Also 16C4 has been found as the major crystalline tetrahedric by-product (lit. mp 70.7°C⁽⁸⁾, 67.5°C⁽⁹⁾) when oxetane and 3,3-dimethyloxetane are polymerized with BF₃⁽⁸⁾ and has been shown to adopt the "square" diamond lattice conformation both in solution⁽¹⁰⁾ and in the crystalline state⁽¹¹⁾, with C-C-C-O and C-O-C-C dihedral angles of *ca.* 64° and 173°, respectively.

It would be of interest to determine whether the f.m.l. *merry-go-round* motion is also sustained in these macrocyclic ethers which contain propyleneoxy moities. A promising candidate is 16C4, where the motion of the free ligand could be investigated. Other candidates include thio- and aza-crown ethers as well as totally saturated cyclic alkanes. For example, the crystal structure of cyclotetradecane reveals a "rectangular" diamond lattice conformation⁽¹²⁾.

B- X-ray, ¹³C solid state NMR and *ab initio* shielding tensor analyses

The use of 1,2-dimethoxybenzene as a model for 1,2-dialkylbenz-annelated crown ethers proved to exhibit additivity with respect to a planar methoxy substituent, with the exception of the *ipso* sites⁽¹³⁾. Determination of the X-ray structures and tensors for a series of simple methoxybenzenes gives, for the first time, enough additive sites with which to calculate the static tensor of benzene without any approximations. In benzo-crown ethers, a negative sinusoidal correlation was observed between the torsion about the C_{ipso}-O bond and the aromatic electronic density, related through the ¹³C shifts of the *para* and *ortho* sites. This is justified theoretically by the decrease of mesomeric and steric contributions of a methoxy group rotated out of the aromatic plane. Experimental determination of the tensors in simple benzo-crown ethers such as B10C3, is needed to better understand the dihedral angle dependence of aromatic isotropic shifts.

C- Conformational analysis of cyclohexyl-crown analogues

Prior to this work, conformational analysis of *cis*-1,2-cyclohexano-crown ethers was limited to the 15C5⁽¹⁴⁾ and 9C3⁽¹⁵⁾ systems. Here, cyclohexane ring inversion produces degenerate conformations due to the inherent symmetry of the crown appendages. For the asymmetric *cis*-cyclohexano-10C3 and *cis*-cyclohexano-13C4, cyclohexyl ring inversion leads to two conformers at 210 K where the value of the equilibrium constant is attributed to preferred *trans*-annular interactions involving the equatorial bridgehead proton. This effect is most striking with the ten-membered cavity,

therefore synthesis of the parent 10C3 is proposed in order to better understand this behavior.

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Appendix

Appendix A

1- Experimental ^{13}C shielding tensors of 1,2-DMB

	σ_{11}	σ_{22}	σ_{33}	σ_{iso}
C1, C2	209 ± 1	168 ± 1	71 ± 3	149.4
C3	185 ± 3	137 ± 1	14 ± 2	112.0
C4	210 ± 1	134 ± 7	19 ± 6	121.1
C5	215 ± 10	139 ± 2	14 ± 12	122.8
C3	184 ± 5	134 ± 0	13 ± 5	110.4
M1	82	68	15	55.0
M2	84	68	19	56.9

2- Calculated and experimental ^{13}C shift tensors for 1,4-DMB

		σ_{11}	σ_{22}	σ_{33}	σ_{iso}
C_1	s	232	159	70	
	m1	230 ± 5	162 ± 5	74 ± 5	
	exp.	230 ± 1	159 ± 1	73 ± 1	154.0
C_2	s	200	131	22	
	m1	198 ± 5	136 ± 5	23 ± 5	
	exp.	194 ± 2	131 ± 0	28 ± 1	117.7
C_3	s	193	137	6	
	m1	193 ± 5	134 ± 5	12 ± 5	
	exp.	186 ± 2	138 ± 2	13 ± 3	112.0
M_1	s	80	72	13	
	m1	80 ± 5	71 ± 5	16 ± 5	
	exp.	82 ± 5	67 ± 2	16 ± 1	54.8

s: ref.(32) Chapter 3
m1: ref.(28) Chapter 3
exp.: this study

3- Calculated^a and experimental^b ¹³C shift tensors for 1,3,5-TMB

		σ_{11}	σ_{22}	σ_{33}	σ_{iso}
C1, C5	calc.	240	168/169	73/74	161/161
	exp.	241	168	77	162
C2		155	108	29	97
		154	107	34	99
C3		238	169	73	160
		241	168	77	162
C4		152	105	17	91
		152	107	21	93
C6		151	107	1	86
		151	110	3	88
M1, M5		80/80	69/69	11/9	53/53
		87	65	12	55
M3		80	70	11	54
		87	65	12	55

a: ref. (32) Chapter 3

b: this study

Appendix B

Principal elements of the shielding tensors of anisole upon rotation of C2-C1-O1-CM1 (with optimization) by the GLAO method using the 6-31G level basis set.*

		C1	C2	C3	C4	C5	C6	CM1
θ 0	σ_{11}	220.2	178.7	216.6	203.4	215.7	186.4	73.9
	σ_{22}	158.7	115.7	132.9	120.9	134.0	120.6	65.5
	σ_{33}	65.5	8.2	14.3	10.8	14.3	22.3	10.0
	σ_{iso}	148.1	100.8	121.3	111.7	121.3	109.8	49.8
10	σ_{11}	220.0	180.8	218.1	204.9	217.2	188.3	76.0
	σ_{22}	160.0	118.5	134.4	122.7	135.5	122.3	66.9
	σ_{33}	62.8	4.6	11.4	7.8	11.4	19.5	6.7
	σ_{iso}	147.6	101.3	121.3	111.8	121.4	110.0	49.9
20	σ_{11}	222.8	182.3	217.9	204.8	217.0	189.2	77.2
	σ_{22}	159.5	121.3	134.4	123.5	135.6	122.9	67.3
	σ_{33}	63.7	3.2	11.4	7.8	11.5	19.9	5.9
	σ_{iso}	148.7	102.3	121.2	112.0	121.4	110.7	50.1
30	σ_{11}	224.0	185.1	217.7	205.0	216.9	190.7	78.2
	σ_{22}	159.0	124.4	134.4	124.6	135.8	123.6	69.2
	σ_{33}	63.9	2.3	11.3	7.8	11.5	20.3	5.0
	σ_{iso}	149.0	103.9	121.1	112.5	121.4	111.5	50.8
40	σ_{11}	225.5	188.7	217.3	205.6	216.8	192.4	78.9
	σ_{22}	158.8	126.8	134.6	125.9	136.0	124.3	73.0
	σ_{33}	64.4	2.7	11.3	7.8	11.6	20.6	4.4
	σ_{iso}	149.6	106.1	121.1	113.1	121.4	112.5	52.1
50	σ_{11}	227.0	192.5	217.0	206.6	216.9	194.1	79.7
	σ_{22}	159.0	128.4	135.0	127.2	136.2	125.1	78.1
	σ_{33}	64.6	4.8	11.3	7.6	11.6	20.7	4.2
	σ_{iso}	150.2	108.6	121.1	113.8	121.6	113.3	54.0

Principal elements of the shielding tensors of anisole upon rotation of C2-C1-O1-CM1 (with optimization) by the GIAO method using the 6-31G level basis set.*

		C1	C2	C3	C4	C5	C6	CM1
θ 60	σ_{11}	228.4	195.8	216.8	207.9	217.0	195.7	83.7
	σ_{22}	159.5	129.2	135.5	128.3	136.4	125.8	80.4
	σ_{33}	64.3	8.1	11.3	7.4	11.6	20.5	4.4
	σ_{iso}	150.8	111.0	121.2	114.6	121.7	114.0	56.1
70	σ_{11}	229.7	198.0	216.8	209.3	217.2	197.1	87.8
	σ_{22}	160.1	129.3	136.0	129.2	136.6	126.7	81.7
	σ_{33}	63.9	11.9	11.3	7.2	11.5	20.0	4.7
	σ_{iso}	151.2	113.1	121.4	115.2	121.8	114.6	58.1
80	σ_{11}	230.5	199.1	217.0	210.3	217.3	198.3	90.0
	σ_{22}	160.5	129.0	136.5	129.8	136.7	127.5	82.9
	σ_{33}	63.5	15.2	11.4	7.0	11.5	19.2	5.0
	σ_{iso}	151.2	114.4	121.6	115.7	121.8	115.0	59.3
90	σ_{11}	230.8	199.0	217.2	210.7	217.2	199.0	90.6
	σ_{22}	160.7	128.3	136.7	130.0	136.7	128.4	83.5
	σ_{33}	63.3	17.6	11.5	6.9	11.5	17.6	5.1
	σ_{iso}	151.6	115.0	121.8	115.9	121.8	115.0	59.7

Appendix C

Principal elements of the shielding tensors of 1,2-DMB upon rotation of C3-C2-O2-CM2 by the GLAO method using the 6-31G level basis set.*

		C1	C2	C3	C4	C5	C6	CM1	CM2
θ 0	σ_{11}	197.8	201.5	180.6	204.7	210.0	185.2	78.8	78.4
	σ_{22}	162.1	159.5	119.7	120.6	123.6	119.7	73.7	68.2
	σ_{33}	68.2	66.9	-3.7	-1.3	6.2	0.8	5.3	-0.17
	σ_{iso}	142.7	142.6	98.9	108.0	113.3	101.9	52.6	48.8
10	σ_{11}	197.9	201.6	181.4	204.6	209.8	185.3	78.9	78.6
	σ_{22}	162.5	159.1	120.8	120.6	123.9	119.8	73.6	68.0
	σ_{33}	68.2	67.1	-4.8	-1.3	6.2	0.8	5.3	-0.4
	σ_{iso}	142.8	142.6	99.1	108.0	113.3	102.0	52.6	48.7
20	σ_{11}	198.3	202.0	183.1	204.5	209.7	185.4	78.9	79.1
	σ_{22}	163.4	158.6	123.0	120.7	124.6	120.0	73.5	69.1
	σ_{33}	68.1	67.6	-6.2	-1.3	6.1	0.8	5.3	-0.9
	σ_{iso}	143.3	142.8	100.0	108.0	113.5	102.1	52.6	49.1
30	σ_{11}	199.4	202.6	185.8	204.41	209.9	185.5	78.9	79.3
	σ_{22}	164.5	158.2	125.1	120.8	125.5	120.2	73.5	72.2
	σ_{33}	67.9	68.2	-6.8	-1.3	6.1	0.9	5.3	-1.6
	σ_{iso}	149.0	143.0	101.3	112.5	113.8	102.2	52.5	50.0
40	σ_{11}	201.1	203.3	188.7	204.2	210.6	185.7	78.9	79.4
	σ_{22}	165.8	158.1	126.7	121.1	126.6	120.4	73.5	76.9
	σ_{33}	67.7	68.6	-6.0	-1.3	6.0	0.9	5.3	-2.1
	σ_{iso}	144.9	143.3	103.1	108.0	114.4	102.3	52.5	51.4
50	σ_{11}	203.3	204.0	191.2	204.0	211.6	185.8	78.8	82.1
	σ_{22}	166.9	158.1	128.1	121.4	127.7	120.6	73.5	79.4
	σ_{33}	67.6	68.6	-4.2	-1.2	6.0	1.0	5.3	-2.4
	σ_{iso}	145.9	143.5	105.0	108.10	115.1	102.5	52.5	53.0

Principal elements of the shielding tensors of 1,2-DMB upon rotation of C3-C2-O2-CM2 by the GLAO method using the 6-31G level basis set.*

			C1	C2	C3	C4	C5	C6	CM1	CM2
θ	60	σ_{11}	205.6	204.5	192.9	203.9	212.9	186.0	78.8	86.1
		σ_{22}	167.8	158.0	129.3	121.7	128.8	120.71.	73.5	79.6
		σ_{33}	67.6	68.3	-1.8	-1.1	6.0	1.0	5.3	-2.5
		σ_{iso}	147.0	143.6	106.8	108.2	115.9	102.5	52.5	54.4
	70	σ_{11}	207.8	204.9	193.8	203.9	214.0	186.2	78.8	88.4
		σ_{22}	168.3	157.9	130.2	122.0	129.6	120.6	73.6	79.8
		σ_{33}	67.8	67.8	0.4	-1.1	5.9	1.0	5.3	-2.5
		σ_{iso}	148.0	143.5	108.1	108.3	116.5	102.6	52.6	55.2
	80	σ_{11}	209.7	205.0	193.8	203.8	214.9	186.3	78.8	88.6
		σ_{22}	168.4	157.8	130.7	122.2	130.2	120.4	73.7	79.8
		σ_{33}	68.1	67.3	2.3	-1.0	5.9	1.1	5.2	-2.5
		σ_{iso}	148.7	143.3	108.9	108.3	117.0	102.6	52.6	55.3
	90	σ_{11}	211.0	204.7	193.0	203.8	215.3	186.4	78.8	87.3
		σ_{22}	167.8	157.7	130.7	122.4	130.3	120.1	73.7	79.5
		σ_{33}	68.7	66.8	3.4	-1.0	5.9	1.2	5.2	-2.7
		σ_{iso}	149.2	143.1	109.1	108.4	117.2	102.6	52.6	54.7

ethyl 6-chloro-3-oxahexanoate

201

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200MHz in CDCl_3

ethyl 6-chloro-3-oxahexanoate- d_2

202

^{13}C NMR, 50 MHz in CDCl_3

diethyl 3,7-dioxanonanedioate

203

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200MHz in CDCl_3

diethyl 3,6-dioxaoctanedioate

204

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200MHz in CDCl_3

diethyl 3,6-dioxaoctanedioate- d_4

205

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200 MHz in CDCl_3

3-chloro-1-propanol-d₂

206

¹³C NMR, 50 MHz in CDCl₃

diethylene glycol-*d*₄

207

¹³C NMR, 50 MHz in CDCl₃

6-chloro-3-oxa-1-hexanol

208

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200MHz in CDCl_3

6-chloro-3-oxa-1-hexanol-*d*₂

209

¹³C NMR, 100 MHz in CDCl₃

¹H NMR, 400MHz in CDCl₃

¹³C NMR, 50 MHz in CDCl₃

triethylene glycol- d_8

211

^{13}C NMR, 50 MHz in CDCl_3

3,7-dioxa-1,9-nonenediol

212

^{13}C NMR, 100 MHz in CDCl_3

^1H NMR, 400MHz in CDCl_3

3,7-dioxa-1,9-nonanediol-*d*₄

213

¹³C NMR, 50 MHz in CDCl₃

¹H NMR, 200 MHz in CDCl₃

tetraethylene glycol-*d*₄

214

¹³C NMR, 50 MHz in CDCl₃

9-chloro-3,6-dioxa-1-nonanol

215

^{13}C NMR, 100 MHz in CDCl_3

^1H NMR, 400MHz in CDCl_3

1,5-dichloro-3-oxapentane-*d*₄

216

¹³C NMR, 50 MHz in CDCl₃

1,6-dichloro-3-oxahexane

217

^{13}C NMR, 50 MHz in CDCl_3

1,6-dichloro-3-oxahexane-*d*₂

218

¹³C NMR, 50 MHz in CDCl₃

¹H NMR, 200 MHz in CDCl₃

1,9-dichloro-3,7-dioxanonane-*d*₄

219

¹³C NMR, 50 MHz in CDCl₃

¹H NMR, 200 MHz in CDCl₃

220

Chemical structure of the monomer 1,4-bis(4-methylphenyl)-1,3-bis(2,2,4,4-tetrahydroxybutyl)benzene. The structure shows a central benzene ring with a methyl group at position 1 and a sulfonate group at position 4. The sulfonate group is linked to a butane chain at position 5, which has hydroxyl groups at positions 2 and 3. The butane chain is further linked to another sulfonate group at position 6, which is linked to another benzene ring at position 1, which has a methyl group at position 4. The butane chain has hydroxyl groups at positions 2 and 3. The structure is labeled with numbers 1 through 8 and letters DD, DDDD, and DD above the corresponding groups.

benzo-10-crown-3

221

^{13}C NMR, 100 MHz in CDCl_3

^{13}C CP/ MAS, 50 MHz

COSY 45

222

^1H NMR, 400 MHz in CDCl_3

223

DSC

224

High resolution MS

Mass	Int%	Dev mmu	C	H	O
195.09701	0.7	-5.11	11	15	3
194.09586	7.3	1.56	11	14	3

benzo-10-crown-3-*d*₂

225

¹³C NMR, 100 MHz in CDCl₃

¹³C CP/ MAS, 50 MHz

Dipolar Dephased

^1H NMR, 400 MHz in CDCl_3

226

DSC

227

High resolution MS

Mass	Int%	Dev mmu	C	H	O	2 H
198.11124	0.2	6.78	14	14	1	0
		8.32	14	12	1	1
		9.87	14	10	1	2
		0.90	7	18	6	0
		2.45	7	16	6	1
		4.00	7	14	6	2

^{13}C NMR, 100 MHz in CDCl_3 ^{13}C CP/ MAS, 50 MHz

Dipolar Dephased

DSC

229

High resolution MS

Mass	Int%	Dev	C	H	O	2
198.11479	0.4	-9.26	11	16	3	1
		-7.71	11	14	3	2
		4.45	7	18	6	0
		6.00	7	16	6	1
		7.54	7	14	6	2

benzo-12-crown-4

230

^{13}C NMR, 50 MHz in CDCl_3

^{13}C CP/ MAS, 50 MHz

^1H NMR, 400 MHz in CDCl_3

231

COSY 45

232

HMQC

DSC

233

High resolution MS

Mass	Int%	Dev mmu	C	H	O
225.10905	6.3	-3.63	12	17	4
224.10429	48.7	-0.57	12	16	4

benzo-13-crown-4

234

^{13}C NMR, 100 MHz in CDCl_3

^{13}C CP/ MAS, 50 MHz

COSY 45

235

HMQC

DSC

236

MS

benzo-13-crown-4-*d*₄

237

¹³C NMR, 100 MHz in CDCl₃

¹H NMR, 400 MHz in CDCl₃

Dipolar Dephased

DSC

239

MS

^1H NMR, 400 MHz in CDCl_3

15-crown-5

241

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200 MHz in CDCl_3

21-crown-7

242

X = H

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200 MHz in CDCl_3

X = D

^{13}C NMR, 50 MHz

^1H NMR, 200 MHz

¹³C NMR, 100 MHz acetone-d₆

¹H NMR, 400 MHz acetone-d₆

^{13}C CP/ MAS, 50 MHz

244

3

Dipolar Dephased

DSC and TGA

15-crown-5 · NaI

246

^{13}C NMR, 50 MHz in CDCl_3

^1H NMR, 200 MHz in CDCl_3

DSC

15-crown-5 · NaClO₄

247

¹³C NMR, 50 MHz in CDCl₃

DSC

15-crown-5-*d*₈ NaI

248

¹³C NMR, 50 MHz in CDCl₃

DSC

15-crown-5-*d*₈ · NaClO₄

249

¹³C NMR, 50 MHz in CDCl₃

DSC

cyclohexyl-10-crown-3

250

^{13}C NMR, 100 MHz in CD_2Cl_2

^1H NMR, 400 MHz in CD_2Cl_2

COSY 45

251

HMQC

DEPT, 100 MHz

252

High resolution MS

Mass	Int%	Dev mmu	C	H	O
200.14203	9.2	0.79	11	20	3
199.98967	0.2	-0.16	14	0	2
		-6.03	7	4	7

cyclohexyl-13-crown-4

254

^1H NMR, 400 MHz

in CD_2Cl_2

^{13}C NMR, 100 MHz in CD_2Cl_2 ^1H NMR, 400 MHz in CD_2Cl_2

COSY 45

256

HMQC

^{13}C NMR, 100 MHzin CD_2Cl_2 ^1H NMR, 400 MHz in CD_2Cl_2

1,2-dimethoxybenzene

258

^{13}C NMR, 100 MHz in CDCl_3

^{13}C CP/ MAS, 50 MHz

1,2-dimethoxybenzene-*d*

260

^{13}C NMR, 100 MHz in CDCl_3

Dipolar Dephased

benzo-9-crown-3-*d*

262

^{13}C NMR, 100 MHz in CDCl_3

^{13}C CP/ MAS, 50 MHz

263

Dipolar Dephased

^{13}C NMR, 50 MHzin CDCl_3 ^1H NMR, 200MHzin CDCl_3

MS