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**The Synthesis and Complexation of Bis-crown Ethers
and Polymers Bearing Pendant Crown Ethers
and
The Study of Molecular Motion of Crown Ethers
in Solids using Solid State ^2H NMR**

by: John Kane Denike

A thesis submitted to
The Faculty of Graduate Studies and Research
in partial fulfillment of the requirements of
Doctor Of Philosophy

Carleton University
Ottawa-Carleton Chemistry Institute
Ottawa, Ontario
May 1992

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The undersigned hereby recommend to The Faculty of Graduate Studies and Research acceptance of this thesis by John Kane Denike in partial fulfillment of the requirements of Doctor Of Philosophy

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Abstract

The synthesis and characterization of a polymer bearing pendant benzo-12-crown-ether and its copolymer with styrene are reported. The crown ethers were synthesized starting with 3,4-dihydroxybenzaldehyde and 1,8-dichloro-3,6-dioxaoctane. A Wittig reaction was used to convert these to the 4'-vinylbenzo-12-crown-4 which was polymerized using azobisisobutyronitrile as a radical initiator. The 1:1 vinylbenzo-12-crown-4 / styrene copolymer was produced by the same method. Both of the polymers were characterized by their ability to extract picrates of lithium, sodium and potassium from an alkaline aqueous solution into a chloroform or dichloromethane solution of the polymer. These polymers have a tendency to form 2:1 crown to cation complexes due to their proximity on the polymer backbone. These properties are investigated and compared to those of their monomeric analogs. For all cations the homopolymer was found to extract the salts from the aqueous phase most effectively. The copolymer is slightly less effective than the homopolymer but more effective than either of the monomers by a factor of approximately 7, indicating that cooperative binding is likely. Na^+ is the most efficiently extracted cation, followed by K^+ and Li^+ .

The synthesis and complexation studies of bis-crown ethers is also reported. The bis-crown ethers consist of two crown ether rings connected by a four carbon bridge. The system under investigation here is 1,4-di(4'-benzo-12-crown-4)-2,3-dihydroxybutane. It is synthesized by the coupling of 4'-vinylbenzo-12-crown-4 using by conversion to the trialkyl borane followed by treatment with an alkaline aqueous silver

nitrate solution. The short carbon bridge serves to keep the two crown ether rings close together and predisposes the system to form 2:1 sandwich type complexes. This complexation is investigated by NMR in solution by comparing the spin-lattice relaxation times (T_1) of the crown ether alone in solution to its T_1 values while combined with various salts in solution.

Tetradeproterio-18-crown-6 ether was prepared and studied by solid state ^2H NMR. ^2H NMR lineshape measurements were used to confirm and refine a model for the large amplitude of motion in 18-crown-6 complexes previously identified from ^{13}C and ^1H NMR results. Reminiscent of the motion of a merry-go-round, the motion was shown to be a combined rotation and conformational adjustment of the macrocycle, in which individual $-\text{O}-\text{CH}_2-\text{CH}_2-$ units jump to adjacent sites in the crystal. Specifically, for the malononitrile complex, $18\text{-crown-6} \cdot 2\text{CH}_2(\text{CN})_2$, jump rates were obtained by modeling the intermediate rate lineshapes, yielding an activation energy of 47.6 ± 0.8 kJ/mole. Because this motion does not introduce disorder, it is invisible to X-ray diffraction.

Similar motions were investigated in complexes of 12-crown-4- d_4 by the same method. Two motions were identified in the $12\text{-crown-4} \cdot \text{LiSCN}$ complex. Analogous to the 18-crown-6 systems studied, the macrocycle undergoes a rotation with a simultaneous inversion of the conformation of the $-\text{CH}_2-\text{CH}_2-$ groups similar to the ring inversions of cyclohexane. As in the case of the $18\text{-crown-6} \cdot 2\text{CH}_2(\text{CN})_2$ complex, the rotation of the macrocycle is invisible to the X-ray diffraction, however

the inversion of the $-\text{CH}_2-\text{CH}_2-$ groups is not. It shows up as distortion or thermal vibrations in the crystal.

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Introduction

1.0 Crown Ethers and Their Complexes

The first macrocyclic polyethers were reported by Lüttringhaus¹ in 1937 but it was not until the pioneering work of Pedersen² thirty years later that the crown ethers, as he called them, were found to strongly bind to alkali and alkaline earth metals. While working for E. I. DuPont de Nemours and Company in the mid sixties Pedersen, in an attempt to find new ways of incorporation of vanadium with different ligands for potential use as a catalyst for alkene polymerization, isolated the crown ether, dibenzo-18-crown-6 (Figure 1) and demonstrated its complexing potential.

Figure 1: Dibenzo-18-crown-6

Since then, interest in crown ethers has increased markedly. These molecules have found a place in many facets of chemistry, especially synthetic organic and physical organic fields. An enormous amount of work has been reported using these ligands in catalyzing synthetic organic reactions and probing reaction mechanisms³. They are used extensively as phase transfer catalysts⁴ because complexation with alkali

and alkaline earth cations yields large lipophilic complexes which are readily extracted into organic solvents. Crown ethers show high selectivity in complexation because the macrocycles contain cavities of fixed sizes. This has resulted in a number of potential applications in ion transport⁵ and generation of strong bases by charge separation of ion pairs.⁶ The "naked" anions produced can then be used to catalyse and promote organic reactions and alter the direction of others.⁷ "The use of crown ethers as additives to organic reactions is limited solely by the chemist's imagination and will almost certainly continue to yield new and exciting results." (Baillargeon, 1974).⁷

Pedersen's work has lead to a new area of study referred to host-guest chemistry or inclusion chemistry. Since his original publication in 1967¹ hundreds of additional crown ethers and related compounds such as aza- and thio-crown ethers⁸, cryptands⁹, calixarenes¹⁰, hemispherands¹¹ and spherands¹² and have been prepared. The discovery has also generated a renewed interest in natural complexing agents such as cyclodextrins.¹³

The majority of crown ethers have been synthesized using Pedersen's procedures from glycol or catechol and a dihalide. Yields have been greatly improved by using an appropriately sized cation via a template effect.¹⁴ Pedersen observed that the ring closing step in the synthesis of 15-crown-5 was greatly facilitated by the use of a sodium ion, which by ion dipole interaction between the lone pairs on the oxygens and the positively charged cation, "wrapped" the three molecule intermediate around itself in a three-quarter circle and disposed it into ring closure.¹⁵ Greene¹⁶ examined the template effect in the synthesis of

18-crown-6 and was able to obtain a yield as high as 93%. According to the kinetic coordination template hypothesis, the geometric arrangement of ligands within the coordination sphere of the metal ion provides constraints that can be used to control the structure of a product formed by reactions of coordinated ligands. Specifically, the coordination sphere of the metal ion may serve as a template to hold reactive groups in proper position for sterically highly selective, multistep reactions.¹⁷ Lotta and collaborators¹⁸ have found that potassium, sodium and lithium act as suitable templates for 18-crown-6, 15-crown-5 and, 12-crown-4 respectively. Figure 2 shows the relationship between cavity size and ionic diameter for these species.

Figure 2: Selected Crown Ether Diameters and Cation Ionic Diameters³ (Å)

Crown ethers are neutral ligands which have the capacity of forming selective, stable complexes with both positively charged and in some cases neutral species. "The formation of a complex species by the association of two or more chemical entities (having, in general, electronic closed shells) is one of the most fundamental molecular processes in biology, in chemistry and in physics. Such a supramolecule represents the next higher level of physical complexity after the nucleus, the atom and the molecule. Its formation involves bonding interactions

which are much weaker than the usual well defined covalent bonds.”
(Lehn¹⁹)

The complexation process is attributed to an electrostatic attraction between the positive end of the cation-anion pair or polarized neutral molecule and the negative dipolar charge on the heteroatoms in the polyether ring.²⁰ The binding of the ligand with a ligand acceptor has been studied for such cases as the ethylenediamine and nickel²¹ with the conclusion that the complex formation is a stepwise process in which solvent molecules are consecutively replaced by the binding sites on the crown ether. The presence of more than one binding site on the ligand prevents dissociation.

Complexes of crown ethers and their derivatives are widely recognized as model systems for molecular recognition. The conformation of the crown can adapt for optimum complexation of the guest. 18-crown-6 is the archetypal macrocyclic ether and calculations on the isolated molecule show that it is very flexible with a large number of possible conformations having only slightly different energies.²² In solution the molecule rapidly interchanges between many conformations²³ and only a single ^{13}C or ^1H NMR signal is observable down to 143K.²⁴ In solid 18-crown-6 and its complexes, however, the molecule is usually locked into one of just a few conformations.²⁵ In the ideal case where all bond angles in the crown are taken as tetrahedral the C atoms and the C-H bonds can be placed on a “diamond lattice”.^{22a} Figure 3 shows solid 18-crown-6, which has a centre of symmetry^{25a}, and two conformations, with D_{3d} and C_1 symmetry on a diamond lattice.

Figure 3: Representations of the D_{3d} , C_1 and solid 18-crown-6 conformations on the grid of the "diamond lattice". Solid lines represent bonds of the macrocycle on the "zero" grid and dashed lines bonds on the first grid above. Connections between the grids are made by vertical bonds (parallel to the z-axis). The numbering scheme begins with an oxygen on the x-axis.

The most stable conformation has D_{3d} symmetry and the second most stable has C_1 . We will refer to the latter as C_1 since many of the other conformations also have C_1 symmetry. Both D_{3d} and C_1 are commonly found in solid complexes, though in the real world there is usually deviations from T_d angles and strict symmetry, so that only a pseudo- D_{3d} conformation is observed.

The correlation between the cavity size of the crown ether and the cationic diameter shown in Figure 2 above is useful in understanding the

selectivity of crown ethers to certain cations⁵ and is valid with the exception of some of the more flexible polyether systems.²⁶ Other factors, such as solvent effects and initial concentrations of reagents, also play an important role in determining the nature of the complexes obtained. 18-crown-6 is known to form both 1:1²⁷ and 2:1²⁸ complexes with benzene sulfonamide. The 2:1 complex exhibits C_1 symmetry in the macrocycle and has a melting point of 92°C while the 1:1 complex was found to have pseudo D_{3d} symmetry and have a melting point of 88-89°C. Both concentrations of reagents and the rate of crystal formation are important factors in the type of complex obtained. Unpublished results from this laboratory demonstrate that equimolar concentrations of reagents and slow crystal growth yields the 1:1 complex. Agitation of the solution, however, results in the rapid formation of the 2:1 complex.

The binding of a flexible ligand such as a crown ether to a ligand acceptor requires reorganization of the ether conformation as well as desolvation. However, the degree of reorganization required for a macrocycle to form a complex is significantly less than that for a linear analogue. The energy of complex formation is in part prepaid during the synthesis of the preorganized ligand in terms of conformation and dipole-dipole repulsion.²⁹

The $-\text{OCH}_2\text{CH}_2\text{O}-$ unit in the crown ethers demonstrates a preferred gauche conformation about the C-C bonds and an anti conformation about the C-O bonds³⁰ as shown in Figure 4.

Figure 4: Preferred gauche and anti conformations of the C-C and C-O bonds respectively in crown ethers.

Infrared studies on 1,2-dimethoxyethane have shown that the $-\text{OCH}_2\text{CH}_2\text{O}-$ system takes on a range of conformations in the liquid phase but adopts the gauche conformation in the crystals at $-195\text{ }^\circ\text{C}$.³¹ In the crystal form polyoxyethylene adopts gauche conformation around C-C bonds and anti conformation about the C-O axis.³² It has been shown that the $-\text{OCH}_2\text{CH}_2\text{O}-$ network is approximately $1.7\text{ kJ}\cdot\text{mol}^{-1}$ more stable when the oxygens are gauche rather than anti to each other.³³

A number of results describe the crystal structures of a number of structures of sandwich complexes between 12-crown-4 systems and sodium salts having a number of anions.³⁴ Results indicate that the 12-crown-4 ligand adopts a number of different conformations upon the formation of different complexes. The conformation of the parent 12-crown-4 has been characterized by low temperature crystallography³⁵ and the structure is shown in Figure 5.

Figure 5: Crystal structure of 12-crown-4 at -150°C

The compound adopts a pseudo square conformation in the crystal and has a two-fold symmetry. The notable aspect of this structure is the deviation from the normal gauche and anti orientations for the $-\text{O}-\text{C}-\text{C}-\text{O}-$ and $-\text{C}-\text{O}-\text{C}-\text{C}-$ units. The closest approach to the ideal gauche geometry for the two $-\text{O}-\text{C}-\text{C}-\text{O}-$ units is the $-\text{O}_4-\text{C}_5-\text{C}_6-\text{O}_1-$ segment which has a torsional angle of 74.5° while the $-\text{O}_1-\text{C}_2-\text{C}_3-\text{O}_4-$ has a value of -75.4° . Of the four $-\text{C}-\text{O}-\text{C}-\text{C}-$ structures, only the $-\text{C}_3-\text{O}_4-\text{C}_5-\text{C}_6-$ unit fits the anti geometry, with a torsional angle of 173.6° . The other three corresponding networks have dihedral angles of 140.2° , 102.7° and 85.2° . This deviation from the ideal geometry also occurs in complexes of 12-crown-4 and the geometries can deviate to a greater extent than for the free ligand.

An example of a 12-crown-4 complex is the 1:1 12-crown-4-lithium thiocyanate system which has been isolated and characterized by X-ray

crystallography.³⁶ The three dimensional structure is shown in Figure 6. with the LiSCN moiety directed into the page.

Figure 6: Three dimensional structure of the 12-crown-4•LiSCN complex

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

The molecular dynamics of crown ethers have also been studied. In fact a wide variety of ring systems have been investigated by NMR spectroscopy since the early sixties and the best documented example of conformational flexibility is for the chair-chair interconversion of cyclohexane³⁷ (Figure 7)

Figure 7: Cyclohexane chair to chair interconversions

NMR coalescence temperature analyses have shown conformational energy barriers exist in cyclooctane³⁸, cyclononane³⁹, as well as cyclodecane, cyclododecane and cyclotetradecane⁴⁰ systems. 12-Crown-4 and complexes of its lithium salts have been studied⁴¹ and were shown to exhibit two site exchange processes. ^1H resonances for the free ligand were found to coalesce at -126°C and the process has a free energy of activation of $28.5 \text{ kJ}\cdot\text{Mol}^{-1}$. This process is attributed to a stepwise movement at each corner of the rectangular conformation where the corner carbon is converted to a side carbon by passing through a high energy intermediate. Resonances for the LiSCN complex of 12-crown-4 were found to coalesce at -96°C and the process has a free energy of activation of $34.3 \text{ kJ}\cdot\text{Mol}^{-1}$. Similar mechanisms of interconversion are postulated for the free ligand and the complex.

Examination of the ^{13}C CP/MAS NMR spectra of several 18-crown-6 complexes⁴² showed that the ether carbon line was essentially invisible at room temperature and that for other complexes the spectrum was very broad. Temperature dependent ^{13}C CP/MAS NMR studies have shown that for many 18-crown-6 complexes the macrocycle resonance goes

through a fade-out region where the resonance is so broad that it becomes unobservable (see Table 1). This is illustrated for the malononitrile complex, where the fadeout occurs at ~ 250 K. Figure 8. Any fine structure observed at low temperatures collapses before fade-out occurs. In those cases where temperatures well above the fade-out region can be reached, the crown ether spectrum consists of a single sharp resonance; i.e. the chemical shift differences seen in the low temperature spectra have been averaged by exchange.

Figure 8: ^{13}C CP/MAS NMR spectra (45.28 MHz) of the 2:1 complex of malononitrile with 18-crown-6 as a function of temperature. Only the CH_2 resonances are shown and the spectra are normalized on the $\text{CH}_2(\text{CN})_2$ intensity.

Table 1: ^{13}C NMR fade-out temperatures and estimated activation energies for various 18-crown-6 complexes.

18-Crown-6 complex	Ring pseudo-symmetry	Fade-out temperature /K	Activation Energy /kJmol ⁻¹
1:1 Phenylsulphonamide	C_1	295	45.7
2:1 Phenylsulphonamide	D_{3d}	295	45.7
Dithio-oxamide	C_1	350	54.3
Nitromethane	D_{3d}	295	45.7
Formamide	D_{3d}	350	54.3
Malononitrile	D_{3d}	250	38.8
Perchloric acid	D_{3d}	205	31.8
Dimethyl sulphone	D_{3d}	340	52.7
N-Methylthiourea	$C_1 + D_{3d}$	340	52.7
Uncomplexed 18-crown-6	C_1	>295	>45.7

The authors postulated that this fade-out occurs due to a rapid reorientation of the entire macrocycle such that the $-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-$ units exchange positions around the ring and that each unit simultaneously readjusts to the local conformation at each site visited, thereby keeping the crystallographic data unchanged. The activation energy for this process was found to be $\approx 155 T_c \text{ J} \cdot \text{mol}^{-1}$, where T_c is the fade out temperature.

In this study, non deuteriated complexes of various crown ethers of known structure and conformation have been prepared and studied by variable temperature ^{13}C CP/MAS NMR as an initial test for molecular motion. Since only solid phase ^2H NMR can furnish details of the type and rates of motion, complexes that exhibit molecular motion in the CP/MAS spectra, have subsequently been prepared using deuteriated crown ethers and subjected to a detailed investigation. The utility of ^2H

NMR for such studies will be examined in greater detail in a subsequent section. But first the synthesis and properties of polymeric and dimeric species of benzo-12-crown-4 and some other crown ethers will be considered.

1.1 Polymers of Crown Ethers

Polymers bearing pendant crown ethers have generated a considerable amount of interest. Kopowal et al.⁴³ have found that these materials are considerably more effective in binding cations than their monomeric analogues but their selectivities were found to be identical. They demonstrated that these macrocycles strongly bind ions of different sizes including those with ionic radii exceeding the size of the polyether cavities. The difference in binding between these polymers and their monomeric analogues arises from the possibility of cooperative bonding between proximate crown ether residues on the polymer chain. Ionophoric polymers of this type are being examined in thin film sensors, transducers, ion exchange membranes, ion selective electrodes, and solid electrolytes.⁴⁴

The first polymers of crown ethers, linear condensation polymers containing the crown ether structure in the backbone, were first reported by Fiegenbaum and Michel.⁴⁵ An example is shown in Figure 9. Polymers of this sort have proven to be useful for ultrafiltration and reverse osmosis and are patented by Frost.⁴⁶

Figure 9: First reported polymer of a crown ether

Most of the polymers have molecular weights between 2000 and 4000 and contain between 5 and 10 ligands per chain. Ionic binding was studied by picrate salt extractions from water into a ligand-containing chloroform phase. By determining solubilities of picric salts in chloroform in the absence of ligand, the association constant of the crown ether with the picrate ion pair in the chloroform phase was determined. For a very similar polymer Gramain and coworkers⁴⁷ found that the association constants are comparable or slightly below those of the monomeric analogue, while cation selectivities remain essentially unchanged.

Ion binding properties of macrocyclic ligands incorporated into the polymer backbone structure do not differ much from their monomeric analogues except in some special cases, for example, where backbone flexibility permits the formation of 2:1 crown-cation complexes. Skinkai and coworkers⁴⁸ have reported a straight chain polymer containing a cis double bond which favours 2:1 crown-cation complexes. Polymers bearing pendant crown ethers, on the other hand, are more suited to the formation of 2:1 complexes.

In 1973 Smid and coworkers⁴³ developed the first polymers bearing pendant crown ether ligands, by the polymerization of 4'-vinylbenzocrown ethers. The monomers were synthesized by converting 3,4-dihydroxyacetophenone into 4'-acetobenzocrown ethers, followed by reduction to the alcohol and subsequent dehydration to the vinyl compounds. This sequence is shown in Figure 10.

Figure 10: Smid's synthesis of polyvinylbenzocrown ethers

Variations on the synthesis involved starting with 3,4-dihydroxybenzaldehyde, forming 4'-formylbenzocrown ethers and a subsequent formation of 4'-(1-hydroxyethyl)-benzocrown ether by a Grignard reaction followed by dehydration to the vinyl group⁴⁹ or by introducing directly a formyl group into a benzocrown ether.⁵⁰

The 4'-vinylbenzo crown ethers can be polymerized quantitatively to high molecular weight polymers using either radical or anionic initiators and the properties of the polymers seems to be essentially independent on the polymerization mechanism.⁴³ The polymers are amorphous with no signs of crystallinity as revealed by X-ray patterns and there is little difference between the binding efficiencies of the anionic and radical polymers. This indicates that the anionic polymerization apparently does not introduce any unusual regularities in the polymer chain, as has been observed for other monomers such as methyl methacrylate polymerized in THF at -80°C.⁵¹

The polymers of the various crown ethers have been evaluated by using optical spectroscopy, extraction equilibria, ion transport through low polarity bulk phases and electrolytic conductance.⁵² Here we will concentrate on the use of optical spectroscopy. This involves the extraction of a metal salt of a chromophore from an aqueous solution with an organic solution, usually dichloromethane or chloroform, containing the polymeric crown ether. The resultant organic solution is then analyzed to determine the amount of chromophore extracted from the aqueous solution.

For the extraction of cations larger than the cavity size of the crown ether, such as in the case of polyvinylbenzo-15-crown-5 and potassium, the ratio of cation to crown ratio rapidly approaches a maximum value of approximately 0.5 (actual value 0.42) strongly suggesting that a 2:1 complex is formed. Smid⁴³ found that in no cases, where a 2:1 complex is formed, did the ratio exceed 0.42. Since electrostatic repulsion and steric factors should be less important in polymers that form a 2:1 complex the most probable cause for the low ratio is a statistical factor. Flory⁵³ has calculated that in selecting, at random, pairs of consecutive constituents of a macromolecule made up of structural units CH_2CHX , 13.5% of unpaired substituents are left. This has been substantiated on a number of reactions on polymers.⁵⁴ The calculations apply strictly to irreversible reactions. The binding of cations to polyvinyl crown ethers is a reversible process with a continuous rearrangement of binding sites but a complete saturation, with a cation to crown ratio of 0.5, represents a less favourable distribution and a considerably lower entropy than the most probable distribution. The ratio that is eventually reached depends on the interaction energy between the cation and the crown. The observed ratio of 0.42 indicates that the statistical ratio of 0.43 is not exceeded.⁴³

In the case where the cation is smaller than the cavity size of the crown ether 1:1 complexes are prevalent. The ratio never reaches unity, likely due to the fact that a high degree of cation binding results in stronger repulsion between closely packed cations making additional binding more difficult. This however is not the case when the crown ethers are spaced sufficiently far apart. Smid⁵⁵ and coworkers have

produced several copolymers of vinylbenzo crown ethers with styrene. They found that the copolymer containing 20% vinylbenzo-18-crown-6 and 80% styrene complexes with potassium with a cation to crown ratio of approximately 1. Polymers with crown ether moieties separated by large distances are incapable of forming 2:1 complexes. Smid⁵⁶ and coworkers studied the binding of potassium tetraphenyl boron to styrene / benzo-15-crown-5 copolymers in methylethyl ketone. At molar crown content in polymers at more than 10% the complexation of potassium involves closely adjacent crown moieties on the same polymer chain. At crown content of 5% the chelating groups are getting so far apart that intermolecular 2:1 crown cation complexes are formed.

Polymers of crown ethers are particularly useful for the formation of separated ion pairs. This loose ion pair formation is important in systems where the crown ethers are utilized for the purpose of enhancing the reactivity of the anionic species. This will be discussed in further detail in section 1.2.

No polymers of 12-crown-4 have been reported. In view of the current interest in the complexation of Li^+ by 12-crown-4 systems and the lack of information on binding properties of copolymeric species, the present study was undertaken. Accordingly, we have prepared 4'-vinylbenzo-12-crown-4, its homopolymer, and copolymer with styrene and compared the cation binding properties of these systems as well as 12-crown -4 and benzo-12-crown-4 with Li^+ , Na^+ and K^+ .

The vinyl crown ethers are synthesized by Pedersen's method V. The starting material for the crown ether is 3,4-dihydroxybenzaldehyde.

The crown is prepared by Williamson's ether synthesis using 1,8-dichloro-3,6-dioxaoctane to produce 4-formylbenzo-12-crown-4. This is converted to its vinyl counterpart by means of a Wittig reaction using triphenyl methyl phosphonium bromide. The vinylbenzo crown ether can then be polymerized using either radical or anionic initiators.⁴³ The synthetic sequence chosen is demonstrated in Figure 11.

Figure 11: Synthetic sequence for preparation of vinylbenzocrown ethers

This synthetic approach is investigated as an alternative to Smid's⁸ method, which uses 3,4-dihydroxyacetophenone as a precursor, because it is shorter and would allow for ^{13}C enrichment via the Wittig reaction as shown in Figure 12.

Figure 12: Isotopically Labeled 4'-Vinylbenzo-12-crown-4

This will subsequently allow for mobility studies of the labeled carbon in the polymer via ^{13}C spin lattice relaxation times (T_1 's) to be used as a probe for the study of binding between proximate crown ethers on the polymer chain.

1.2 Bis-crown ethers

Several studies have been reported on the complexation of cations to bis(crown ethers), compounds with ligands linked by a short chain.^{56,57} The data demonstrate that these compounds facilitate the formation of 2:1 crown-cation complexes, depending on the length, structure and flexibility of the connecting chain and, where ion pairs are concerned, on the nature of the counterion. The latter variable is especially important since a stable 2:1 crown-cation structure often requires increased charge separation between anion and cation. The process is generally easier with bulky or charge delocalized anions.⁵⁸

The first of these bis crown ethers was synthesized by Smid⁵⁶ and is shown in Figure 13. Several systems were produced with varying chain lengths connecting the two crown ether moieties. The extension of the chain from two to eight methylene groups lowered conductivity by 14%. Replacement of a methylene group by an oxygen had little or no effect.

The complex dissociation constant, K_a , also decreased with longer chain length.

Figure 13: 1,2-Bis[3',4'-(1'',4'',7'',10'',13''-pentaoxacyclopentadeca-2''-ene)-phenylcarboxyethoxy]ethane, one of the first bis crown ethers synthesized by Smid

The bis crown ethers are much more effective chelating agents than monocyclic polyethers, at least in the formation of separated ion pairs. Benzo-15-crown-5 has a comparable complexation constant to the bis crown ether but the bis crown ether leads to ion pair separation. With benzo-15-crown-5 loose ion pairs need a second crown ether molecule and this only occurs with a considerable excess of crown ether. When comparing chain lengths of 2, 5 and 8 groups the complexation constant, K_c , is highest for the five carbon bridge. Complexation is most effective when the oxygens of the two crown ethers are nearly coplanar with respect to each other. Too short of a chain would likely adversely affect the stability of the bis crown ether complex. Extending the chain too much results in a loss of conformational entropy resulting in a decrease in K_c .

Manabe and coworkers⁴⁸ have prepared and characterized bis crown ethers with cis and trans azo linkages. The first of these are shown in Figure 14.

Figure 14: Trans and cis azo-bis-crown ethers for photo control of ion extraction and ion transport

The trans system extracted sodium 5.6 times as effectively as did the cis, however, the cis extracts potassium 42.5 times better than the trans. The sodium fits directly into the cavity of the crown ether and is extracted as a 1:1 complex. The potassium is extracted as a 1:2 complex indicating that the cis system is sterically able to fold around the cation where the trans is not. The interesting aspect of these systems is that the two isomers can be isomerized by light allowing for the photocontrol of ion extraction and ion transport.

Laszlo and coworkers⁵⁹ have studied spiro bis crown ethers. An example is shown in Figure 15.

Figure 15: Spiro-bis crown ethers

Like other bis-crown ethers spiro bis-crown ethers form sandwich complexes, at high concentrations, having one cation between two ligand molecules. The distinct feature of these ligands, offered as cationic binding sites, is the formation of dicationic 1:2 complexes. These doubly occupied complexes are less disfavoured than could have been feared on the basis of strong electrostatic repulsions; furthermore entropy variations appear to be more favourable to double occupancy than to single occupancy of the two binding sites.

Weber and coworkers⁶⁰ have developed related crown compounds with two or three rings of various sizes and aromatic linkages (Figure 16).

Figure 16: Di- and tri-loop crown hosts having aromatic junctions

The complex formation of the di- and tri-loop hosts is not merely a simple coexistence of the compartmental coordination properties allocated by the individual crown ring. It can also involve cooperativity in complex formation depending on the cation. Multiple cation coordination, similar to the case found for the spiro-bis-crown ethers mentioned above is possible. Complexes of 1:2 and 1:3 ligand / cation with sodium thiocyanate were identified with the two and three loop systems respectively. In the tri-loop ligand the 22-crown-6 ring appears to function as a coordination site or a bridge between the two benzo-15-crown-5 molecules depending on the cation. In the case of an intramolecular sandwich complex the ring may not only function as shielding spacer bridges, but a portion of their oxygens may also be involved in coordination to the cation, thus stabilizing the complex.

Very little work has been reported on the synthesis and characteristics of bis-12-crown-4 systems. Wong and Ng^{57d} have reported the synthesis of one such system, shown in Figure 17, but its complexation properties have never been reported. Studies of the larger systems mentioned above indicate that if the bridge connecting the crown ethers is too large no intramolecular cooperative binding exists. The bridges on Wong's crown ethers range from nine to twelve atoms, probably disabling intramolecular sandwich-type complex formation.

Figure 17: 1,7-bis[3',4'-(1'',4'',7'',10''-tetraoxacyclododeca-2''-ene)-benzyl-1,4,7-trioxaheptane and 1,10-bis[3',4'-(1'',4'',7'',10''-tetraoxacyclododeca-2''-ene)-benzyl-1,4,7,10-tetraoxadecane, the first bis-12-crown-4 ethers

We chose to synthesize new bis-12-crown-4 ethers with much shorter bridges and study the cooperative binding of these systems.

Chapter 2: NMR Theory

The main interactions involving a nucleus with a magnetic moment which may occur in the solid are:

1. The Zeeman interaction with the magnetic field;
2. Direct dipole-dipole interactions with other nuclei;
3. Magnetic shielding by the surrounding electrons giving chemical shifts;
4. Spin-spin coupling to other nuclei;
5. Quadrupolar interactions which will be present for nuclei with spin $> 1/2$ only, and will often dominate the spectra of these nuclei.

A general Hamiltonian for the interactions experienced by a nucleus of spin I in the solid state may be written as follows⁶¹

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

2.1 The Quadrupolar Interaction

The nuclear quadrupole moment only exists for atoms with spins greater than $I = 1/2$ and usually dominates the NMR spectra of these nuclei. Its term in the Hamiltonian arises from the interaction of the nuclear charge with a non-spherically symmetric (lower than tetrahedral symmetry) electric field gradient.⁶¹ If we choose as axes of coordinates OXYZ the principal axis of the symmetrical electric field gradient tensor V_{ij} , so that

$$V_{xz} = V_{yz} = V_{xy} = 0 \quad (2)$$

and label these axes so that

$$|V_{zz}| \geq |V_{yy}| \geq |V_{xx}|, \quad (3)$$

and define the largest component of the electric field gradient, eq, to be along the Z-axis:

$$eq = V_{zz} \quad (4)$$

the asymmetry parameter is defined such that

$$\eta = \frac{|V_{yy}| - |V_{xx}|}{|V_{zz}|} \quad (5)$$

The quadrupolar Hamiltonian can be defined as in equation 5⁶²

$$\mathcal{H}_Q = \frac{e^2 q Q}{4I(2I-1)} [3I_z^2(I+1) + \frac{1}{2}\eta(I_+^2 + I_-^2)] \quad (6)$$

where eQ is the quadrupolar moment of the nucleus, I is the spin quantum number, I_z is the z component of the spin operator and I_+ and I_- are the "famous raising and lowering operators" respectively.⁶³

$$I_+ = I_x + iI_y, \quad I_- = I_x - iI_y, \quad (7)$$

The operators are called raising and lowering operators because of the effect they produce when they operate on a function $u_{I,m}$

$$I_+ u_{I,m} = \sqrt{I(I+1) - m(m+1)} u_{I,m+1} \quad (8)$$

$$I_- u_{I,m} = \sqrt{I(I+1) - m(m-1)} u_{I,m-1} \quad (9)$$

I_+ turns $u_{I,m}$ into a function whose m value has been raised by one unit and similarly I_- turns $u_{I,m}$ into a function whose m value has been lowered by one unit.

It is important to note that the relative signs of the electric field gradient tensors are traceless such that the relative signs of V_{xx} and V_{yy} are different from that of V_{zz} so that:

$$V_{xx} + V_{yy} + V_{zz} = 0 \quad (10)$$

In solution, since the tensor is traceless, the quadrupolar interactions average to zero and do not appear directly in solution NMR where there is rapid random motion of the molecules.⁶¹

In the case of nuclei with $I > 1/2$, the solid state NMR spectra are usually dominated by the nuclear quadrupole interaction. That is, the total Hamiltonian may be approximated as

$$\mathcal{H} = \mathcal{H}_Z + \mathcal{H}_Q \quad (11)$$

and terms such as the dipolar interactions, anisotropic chemical shifts and scalar spin-spin couplings may be neglected to a first approximation. The Zeeman Hamiltonian is given by

$$\mathcal{H} = \gamma \hbar I_z \cdot \mathbf{B}_0 \quad (12)$$

where γ is the gyromagnetic ratio for the nucleus. It is defined by the equation

$$\frac{\gamma}{2\pi} = \frac{\nu_0}{B_0} \quad (13)$$

ν_0 is the Larmor frequency. The Zeeman energy levels are given by

$$E_m = \gamma \hbar m B_0 \quad (14)$$

where m is the magnetic quantum number, which has a value of 0, ± 1 for deuterium. In the absence of a magnetic field the quadrupolar Hamiltonian for a spin $I = 1$ nucleus has three eigenstates:

$$E_m = \frac{e^2 q Q}{4I(2I-1)} [3m^2 - I(I+1)] \quad (15)$$

The $m = 1$ and $m = -1$ states are degenerate. If the quadrupolar interaction is treated as a perturbation on the Zeeman interaction (high field case) this leads to three energy levels. Substituting values of I (-1, 0, 1) and m (1) into equation (14) leads to three energy levels (Figure 18):

$$E_{-1} = \gamma \hbar B_0 + \frac{e^2 q Q}{4} \quad (16)$$

$$E_{+1} = -\frac{e^2 q Q}{4} \quad (17)$$

$$E_{+1} = -\gamma \hbar B_0 + \frac{e^2 q Q}{4} \quad (18)$$

Figure 18: Schematic Representation of the Energy Levels of a Spin $I = 1$ Nucleus Resulting from the Zeeman Interaction with the Magnetic field and with the Quadrupolar Moment of the Nucleus

The allowed transitions are $(m = -1) \leftrightarrow (m = 0)$ and $(m = 0) \leftrightarrow (m = 1)^1$ resulting in two transitions with frequencies given by ⁶⁴:

$$\nu = -\gamma \hbar B_0 \pm \frac{3}{4} \left(\frac{e^2 q Q}{h} \right) \quad (19)$$

These resonance lines only apply to a single deuterium atom fixed in a rigid molecule in a strong magnetic field where the largest component of the cylindrically symmetric electric field gradient tensor, eq , at the site of the nucleus is parallel to the magnetic field vector. Under certain conditions the transition $\Delta m = \pm 2$ may become partially allowed⁶⁵. This double quantum transition has been discussed for deuterium NMR by Wennerström, Persson and Lindman⁶⁶ and more recently by Pines and co-workers⁶⁷. It gives rise to a resonance line at the center of the two Δm

$= \pm 1$ transitions $h\nu(\Delta m = \pm 2) = \gamma\hbar B_0$. The double transition has been proposed to explain the occurrence of a sharp single line in the deuteron spectra of D_2O in liquid crystalline phases.

The collective term (e^2qQ/h) is known as the quadrupole coupling constant and may be evaluated directly from NMR studies of the spectra of single crystals. For deuterons attached to carbons, it has values between 170 and 200 kHz with the principal axis being the vector of the C-D bond. When eq is not parallel to the magnetic field, H_0 , we must rewrite the equation in reference frame where the magnetic field vector is the principal axis. When this is done an angular dependence between the magnetic field and eq arises. The first order perturbations on the Zeeman energy levels are given by:

$$E_m^{(1)} = \frac{3}{8} \left(\frac{e^2qQ}{h} \right) \left(m^2 - \frac{2}{3} \right) (3\cos^2\theta - 1) \quad (20)$$

where θ is the angle between eq and the magnetic field. Once again these perturbations give rise to two resonance lines:

$$\nu = -\gamma\hbar B_0 \pm \frac{3}{8} \left(\frac{e^2qQ}{h} \right) (3\cos^2\theta - 1) \quad (21)$$

with frequency separation:

$$\Delta\nu = \frac{3}{4} \left(\frac{e^2qQ}{h} \right) (3\cos^2\theta - 1) \quad (22)$$

Figure 19⁶¹ shows the variation of doublet peak separation with θ .

Figure 19: Variation of the Doublet Peak Separation with θ

Many studies have been done on single crystals. The analysis of the rotation pattern obtained with single crystals yields both the quadrupolar coupling tensor components and the orientation of these in the crystal.⁶⁸ Often single crystals are difficult to prepare and in many cases studies are limited to polycrystalline powder samples where the nuclear sites are randomly oriented with respect to the magnetic field, H_0 . The shape of this powder spectrum is then an average of the resonances of all possible orientations on the nuclear spins.

An analytical expression for the shape of the 'powder-type' spectrum is easy to derive when axial symmetry is present⁶⁵. If we assume uniform distribution of N nuclei over a surface of a sphere of radius r , the number of nuclei per unit area is $N/4\pi r^2$. The fraction, dN , of nuclei oriented between θ and $\theta + d\theta$ with respect to H_0 is given by the area of a zone of the sphere, $2\pi r^2 \sin \theta d\theta$, multiplied by the spin surface density:

$$dN = \left(\frac{N}{4\pi r^2} \right) 2\pi r^2 \sin\theta d\theta = \frac{1}{2} \sin\theta d\theta \quad (23)$$

The probability density $p(\theta)$ is thus given by

$$p(\theta) = \frac{1}{2} \sin\theta, \quad (24)$$

$$\int_0^\pi p(\theta) d\theta = 1. \quad (25)$$

According to equation (21) the resonance frequency shows the following dependence on the orientation angle θ :

$$\nu_{\pm} = -\gamma\hbar B_0 \pm \frac{3}{8} \left(\frac{e^2 q Q}{h} \right) (3\cos^2\theta - 1) \quad (26)$$

It is convenient to introduce a 'reduced' resonance frequency, $\xi_{\pm}$

$$\xi_{\pm} = \frac{\nu_{\pm} - \left(\frac{\gamma B_0}{2\pi} \right)}{\left(\frac{3}{4} \right) \left(\frac{e^2 q Q}{h} \right)} = \pm \frac{3\cos^2\theta - 1}{2}, \quad (27)$$

where $1 \geq \xi_{+} \geq -1/2$ and $-1 \leq \xi_{-} \leq 1/2$. Since NMR spectra are recorded as a function of frequency, we will define the probability function $p(\xi)$ so that $p(\xi)d\xi$ describes the fraction of the spins with the reduced resonance frequency between ξ and $\xi + d\xi$. The two probability densities $p(\theta)$ and $p(\xi)$ are related to each other according to

$$p(\xi) = p(\theta) \frac{d\theta}{d\xi} = \frac{1}{2} \sin\theta \frac{d\theta}{d\xi} = -\frac{1}{2} \frac{d\cos\theta}{d\xi}. \quad (28)$$

Now the deuterium spectrum contains two resonances, ξ_{+} and ξ_{-} , so that

$$p(\xi) = p(\xi_{+}) + p(\xi_{-}). \quad (29)$$

Combining equations (27) and (28) it then follows

$$p(\xi_{\pm}) \propto \frac{1}{\sqrt{\pm 2\xi_{\pm} + 1}}. \quad (30)$$

The probability densities $p(\xi_+)$, $p(\xi_-)$ and $p(\xi)$ are plotted in Figure 20. This line shape was first described by Pake⁶⁹ and is known as a Pake doublet. $p(\xi)$ diverges at frequencies $\xi = \pm 1/2$, which corresponds to nuclear sites inclined at $\theta = 90^\circ$ with respect to H_0 .

Figure 20: Theoretical powder pattern for a deuterium nucleus in a symmetric electric field gradient ($\eta = 0$). The fine lines show the individual components of the $m = -1 \leftrightarrow m = 0$ (ξ_+) and $m = 0 \leftrightarrow m = 1$ (ξ_-) transition, while the bold line indicates the sum of the two components.

To each resonance frequency $\xi_{\pm}$ there corresponds a transition probability $P(\xi_{\pm})$. As a first-order approximation we will assume that $I(\xi_{\pm})$

is equal for both deuterium transitions and independent of nuclear orientation. The total absorption intensity $S(\xi)$ is then simply

$$S(\xi) = Pp(\xi), \quad (31)$$

where P is a constant. The absorption intensity is thus linearly related to $p(\xi)$ and the shape of the powder type spectrum can be read off directly from Figure 20. For practical purposes the most important feature of Figure 20 is the frequency spacing of the two most intense peaks at $\xi = +1/2$ and $\xi = -1/2$, which is $\Delta\xi_{\text{powder}} = 1$ or

$$\Delta\nu_{\text{powder}} = \frac{3}{4} \frac{e^2 q Q}{h} \quad (32)$$

This indicates that the quadrupolar coupling constant can be determined directly from the powder pattern.

The previous discussion assumes that the electric field gradient tensor of C-D bonds have cylindrical symmetry. If this is not the case the perturbed eigenstates depend on both the polar angles, θ and ϕ , which describe the orientation of the magnetic field in the principal axis system of eq as shown in Figure 22⁶⁴

Figure 21: Diagram showing the polar angles θ and ϕ made by the magnetic field vector in the principal axis system of the electric field gradient tensor.

Equation (20) must be rewritten as:

$$E_m^{(1)} = \frac{e^2 q Q}{4h} (3m^2 - 2) \left(\cos^2 \theta - \frac{1}{2} \sin^2 \theta + \frac{1}{2} \eta \sin^2 \theta \cos 2\phi \right) \quad (33)$$

which yields frequency transitions:

$$\nu = \frac{\gamma B_0}{2\pi} \pm \left[\frac{3}{4} \left(\frac{e^2 q Q}{h} \right) \left(\cos^2 \theta - \frac{1}{2} \sin^2 \theta + \frac{1}{2} \eta \sin^2 \theta \cos 2\phi \right) \right] \quad (34)$$

This leads to a more complicated spectrum, with three pairs of discontinuities, as opposed to two in an axially symmetric case.^{70,71} Spectra with varying η values are shown in Figure 22. The principal components and the asymmetry parameter of the electric field gradient

can be read directly from the frequency separations of the pairs of singularities in the powder spectrum with:⁶⁴

$$\Delta\nu_{xx} \propto |V_{xx}| \quad (35)$$

$$\Delta\nu_{yy} \propto |V_{yy}| \quad (36)$$

$$\Delta\nu_{zz} \propto |V_{zz}| \quad (37)$$

$$\Delta\nu_{xx} \leq \Delta\nu_{yy} \leq \Delta\nu_{zz} \quad (38)$$

$$\eta = \frac{\Delta\nu_{yy} - \Delta\nu_{xx}}{\Delta\nu_{zz}} \quad (39)$$

Figure 22: ^2H NMR line shapes for (a) $\eta = 0$, (b) $\eta = 0.2$ and (c) $\eta = 1.0$, indicating the frequency separations ΔV_{xx} , ΔV_{yy} and ΔV_{zz} .¹

The calculation of the powder pattern is more complicated when the asymmetry parameter is not equal to zero. Detailed calculations have been carried out by Cohen and Reif.⁷²

Deuterium NMR has proven to be a valuable tool for determining types and rates of molecular motion in solids. It is well known that the magnetic resonance line shapes depend on the rate of the dynamic processes which modulate the anisotropic parts of the spin Hamiltonian. The line shape is particularly sensitive to the details of the microscopic model describing the dynamic processes when the modulation rate is on the order of the anisotropic interaction.⁷³ This is because the molecular motion induces a population weighted average of the tensor components over the different orientations visited during the motion and results in an effective tensor which may or may not have the same orientation as the static tensor. Molecular motions must be divided into three regimes, slow, intermediate or fast. Exchange rates in ^2H NMR of powder samples are analytically useful because of the characteristic line shape changes which occur as a function of exchange rate τ_c^{-1} . The large range of τ_c^{-1} over which the line shape effects occur is due to the size of the quadrupolar coupling constant, $\omega_q \sim 10^6$. In a powder sample the frequency separation, $\Delta\omega$, of two orientations between the exchange occurs can thus vary essentially from 0 to 10^6 s^{-1} , depending on the structural details of the dynamics. Whether the dynamics show the characteristic effects of slow, intermediate or fast exchange depends on whether $\Delta\omega\tau_c$ is much less than, approximately equal to or much greater than unity, respectively.⁷⁴

Slow molecular motions, with correlation times much longer than the transverse relaxation times will have little effect on the spectrum which will resemble the spectrum of the static molecule.⁷⁵ Pulse sequences have been developed which are sensitive to slow molecular motions⁷⁶ but these will not be considered here.

Most of the more detailed studies are performed by quantitative line shape analysis in the intermediate regime, i.e., when the rates are of the order of the frequency splitting in the NMR spectrum. These line shapes are often very sensitive to both the rate and mechanisms of the dynamic processes and to the detailed mechanistic pathways of the reaction.⁷⁷ Since the rates are of the order of the frequency splitting the spectra are very sensitive to changes of the echo delay time in the quadrupolar echo experiment. Several calculations have been carried out to simulate intermediate spectra^{73,74,78} but these will not be considered here.

The analysis of ^2H NMR lineshapes for very fast motions is typically dealt with in terms of order parameters, which are simply the averaged elements of the coupling tensors.⁷⁴ Although strictly rigorous, they provide no direct picture of the dynamics and no information on the time scale. However, if both static and motionally averaged spectra are available it is possible to obtain mechanistic information about the motion occurring. Activation energies of the motions occurring can be determined through the temperature dependence of the spin-lattice relaxation times, T_1 's.⁷⁹ The dependence arises through the relationship between T_1 's and correlation times shown in Figure 23.

Figure 23: Relationship between the spin-lattice relaxation time and the correlation time of molecular motion.

Following the assumption that molecular motions are thermally activated we can use the Arrhenius temperature dependence for the correlation time of the motion:

$$\tau_c = \tau_c^0 e^{(E_a/kT)} \quad (40)$$

where E_a is the activation energy of the process, k is the Boltzmann constant and τ_c^0 is a proportionality constant. In the extreme narrowing limit, when the product of the correlation time and the Larmor frequency is much less than unity, the relaxation rate at a specific frequency in the powder spectrum is linear with respect to τ_c ⁸⁰ resulting in an Arrhenius equation for T_1 :

$$\ln T_1 = C - E_a / kT \quad (41)$$

where C is a constant. A plot of $\ln T_1$ versus $1/T$ will have a slope of $-E_a / kT$. It is important to note that, because of an anisotropy in T_1 values across a powder⁷⁴ pattern all T_1 measurements must be made at the same position in the powder spectrum.

In a recent paper Wittebort, Olejniczak and Griffin⁷⁴ have elegantly described the basis for calculating motional averaging effects on ^2H NMR line shapes. For the fast motion limit, where the motion is fast compared to the static quadrupole coupling constant, the problem is relatively simple. The orientation of the static electric field gradient tensor is first described in a reference coordinate system in terms of the Euler angles.⁸¹ A weighted average of the tensor components over the different orientations visited during the motion gives an effective average tensor. Often it is possible to choose the initial reference system such that the average tensor is diagonal, otherwise a diagonalization must be carried out to determine the three principal components and their orientations.⁷¹

The Euler angles, α , β , and γ , shown in Figure 24 relate the axes of the electric field gradient tensor and the molecular motion to the rotational matrix, $\mathbf{R}(\alpha, \beta, \gamma)$.

Figure 24: Diagram illustrating the three successive rotations through the Euler angles, α , β , and γ .

$$R(\alpha\beta\gamma) = \overbrace{\begin{pmatrix} \cos\gamma & \sin\gamma & 0 \\ -\sin\gamma & \cos\gamma & 0 \\ 0 & 0 & 1 \end{pmatrix}}^{R_z(\gamma)} \overbrace{\begin{pmatrix} \cos\beta & 0 & -\sin\beta \\ 0 & 1 & 0 \\ \sin\beta & 0 & \cos\beta \end{pmatrix}}^{R_{y'}(\beta)} \overbrace{\begin{pmatrix} \cos\alpha & \sin\alpha & 0 \\ -\sin\alpha & \cos\alpha & 0 \\ 0 & 0 & 1 \end{pmatrix}}^{R_x(\alpha)} \quad (42)$$

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

$$\mathbf{V}(\alpha, \beta, \gamma) = \mathbf{R}(\alpha, \beta, \gamma) \mathbf{V}_{\text{PAS}} \mathbf{R}^{-1}(\alpha, \beta, \gamma) \quad (43)$$

The full description of the static tensor in the reference frame is given below since it is a useful starting point for all cases, although in

many instances great simplification can immediately be achieved by the appropriate choice of reference frame.⁷¹

$$V(\alpha, \beta, \gamma) = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix} \quad \text{where} \quad \begin{aligned} a_{12} &= a_{21} \\ a_{13} &= a_{31} \\ a_{23} &= a_{32} \end{aligned}$$

$$\begin{aligned} a_{11} = & (\cos^2 \alpha \cos^2 \beta \cos^2 \gamma + \sin^2 \alpha \sin^2 \gamma - 2 \sin \alpha \cos \alpha \cos \beta \sin \gamma \cos \gamma) V_{xx} \\ & + (\sin^2 \alpha \cos^2 \beta \cos^2 \gamma + \cos^2 \alpha \cos^2 \gamma + 2 \sin \alpha \cos \alpha \cos \beta \sin \gamma \cos \gamma) V_{yy} \\ & + (\sin^2 \beta \cos^2 \gamma) V_{zz} \end{aligned}$$

$$\begin{aligned} a_{22} = & (\cos^2 \alpha \cos^2 \beta \sin^2 \gamma + \sin^2 \alpha \cos^2 \gamma + 2 \sin \alpha \cos \alpha \cos \beta \sin \gamma \cos \gamma) V_{xx} \\ & + (\sin^2 \alpha \cos^2 \beta \sin^2 \gamma + \cos^2 \alpha \cos^2 \gamma - 2 \sin \alpha \cos \alpha \cos \beta \sin \gamma \cos \gamma) V_{yy} \\ & + (\sin^2 \beta \sin^2 \gamma) V_{zz} \end{aligned}$$

$$\begin{aligned} a_{33} = & (\cos^2 \alpha \sin^2 \beta) V_{xx} \\ & + (\sin^2 \alpha \sin^2 \beta) V_{yy} \\ & + (\cos^2 \beta) V_{zz} \end{aligned}$$

$$\begin{aligned} a_{12} = & (-\cos^2 \alpha \cos^2 \beta \sin \gamma \cos \gamma + \sin^2 \alpha \sin \gamma \cos \gamma + \sin \alpha \cos \alpha \cos \beta (\sin^2 \gamma - \\ & \cos^2 \gamma) V_{xx} \\ & + (-\sin^2 \alpha \cos^2 \beta \sin \gamma \cos \gamma + \cos^2 \alpha \sin \gamma \cos \gamma + \sin \alpha \cos \alpha \cos \beta (\cos^2 \gamma - \\ & \sin^2 \gamma) V_{yy} \\ & + (-\sin^2 \beta \sin \gamma \cos \gamma) V_{zz} \end{aligned}$$

$$\begin{aligned} a_{13} = & (\cos^2 \alpha \sin \beta \cos \beta \cos \gamma - \sin \alpha \cos \alpha \sin \beta \sin \gamma) V_{xx} \\ & + (\sin^2 \alpha \sin \beta \cos \beta \cos \gamma + \sin \alpha \cos \alpha \sin \beta \sin \gamma) V_{yy} \\ & + (-\sin \beta \cos \beta \cos \gamma) V_{zz} \end{aligned}$$

$$\begin{aligned}
 a_{23} = & (-\cos^2\alpha \sin\beta \cos\beta \sin\gamma - \sin\alpha \cos\alpha \sin\beta \cos\gamma) V_{xx} \\
 & + (\sin^2\alpha \sin\beta \cos\beta \sin\gamma + \sin\alpha \cos\alpha \sin\beta \cos\gamma) V_{yy} \\
 & + (\sin\beta \cos\beta \sin\gamma) V_{zz}
 \end{aligned}$$

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

$$V'(\alpha, \beta, \gamma) = \left(\frac{1}{n}\right) \sum_{i=1}^n V_i(\alpha, \beta, \gamma) \quad (44)$$

The procedure must one carried out for each deuteron affected by the motion. Figure 25 shows several ^2H NMR spectra resulting from different types of molecular motion.⁶⁴

Figure 25: The effect of molecular motion on ^2H NMR line shapes. a) Rigid C-D bond, b) Two fold flipping of a para-disubstituted deuterated aromatic ring about its long axis, c) The in plane rotation of a deuterated benzene ring, d) Rotation of a deuterated methyl group about its three-fold axis.

It is important to note that the appearance of the fast motional line shape depends on the mechanism of the motion, for example a continuous motion can sometimes be distinguished from a discrete jumping or flipping motion. For n -fold rotations, where $n \geq 3$, the averaged spectrum is always axial (i.e. $\eta = 0$).

Often deuterium powder spectra are very broad (up to $\sim 100 - 200$ kHz) implying that much of the information is contained in the early part of the free induction decay (FID). Since the dead time of most spectrometers is in the order of several microseconds, much of the information about these broad components is lost and can not be faithfully reproduced.⁸² The usual application of pulsed Fourier transform spectroscopy involves accumulation of the FID following a single $\pi/2$ pulse applied at a frequency, ω , close to the resonance frequency, ω_0 . The Fourier transform of this FID gives the frequency spectrum of the sample. If, however, a second pulse which rotates the magnetization by an angle θ and having a rf phase ϕ with respect to the first pulse is applied at time τ after the first pulse a "quadrupole spin echo" occurs at $t = 2\tau$ due to a refocusing of the nuclear magnetization. The echo is maximum when $\theta = \pi/2$ and $\phi = \pi/2$. Under these conditions it is possible to obtain a faithful reproduction of the spectrum by calculating the Fourier transform starting at $t = 2\tau$. The pulse sequence is known as the Quadrupolar Echo experiment⁸² and is illustrated in Figure 26.

Figure 26: Pulse sequence used in the quadrupolar echo experiments

In practice, the time τ_2 from the end of the second pulse to the top of the echo is slightly longer than τ_1 , for technical reasons associated with finite pulse widths and filter delays.⁸³

2.2 The Dipolar Interaction

The interaction between two nuclear spins depends on the magnitude and orientation of their magnetic moments and also on the length and orientation of the vector describing their relative positions. The effects of this interaction depends strongly on whether this vector is fixed in space or changes rapidly because of the relative motion of the nuclei.⁸⁴ We will first consider the static case and then move into the effects of molecular motion.

The dipolar Hamiltonian for a two spin system, I_1 and I_2 is given by:

$$\mathcal{H}_D = \frac{\hbar \gamma_1 \gamma_2}{r_{12}^3} [I_1 \cdot I_2 - 3 \frac{(I_1 r_{12})(I_2 r_{12})}{r_{12}^2}] \quad (45)$$

where $\mathbf{r}_{12}$ is the displacement vector between interacting spins and r_{12} is its magnitude. If the displacement vector is expressed in polar coordinates with the z direction being parallel to the magnetic field the Hamiltonian becomes:

$$\mathcal{H}_D = \frac{\gamma^2 \hbar^2}{r^3} (A + B + C + D + E + F), \quad (46)$$

where:

$$A = i_z i_z (1 - 3 \cos^2 \theta) \quad (47)$$

$$B = -\frac{1}{4}(1 - 3 \cos^2 \theta)(i_+ i_- + i_- i_+) = \frac{1}{2}(1 - 3 \cos^2 \theta)(i_z i_z + i \cdot i) \quad (48)$$

$$C = -\frac{3}{2} \sin \theta \cos \theta e^{-i\phi} (i_z i_+ + i_+ i_z) \quad (49)$$

$$D = C^* = -\frac{3}{2} \sin \theta \cos \theta e^{i\phi} (i_z i_- + i_- i_z) \quad (50)$$

$$E = -\frac{3}{4} \sin^2 \theta e^{-2i\phi} i_+ i_+ \quad (51)$$

$$F = E^* = -\frac{3}{4} \sin^2 \theta e^{2i\phi} i_- i_- \quad (52)$$

Only parts A and B contribute to the first order splitting of the Zeeman energy levels and should be retained for a perturbation calculation of the energy levels. In this case the total Hamiltonian becomes:

$$\mathcal{H}_T = \mathcal{H}_Z + \mathcal{H}_D \quad (53)$$

where

$$\mathcal{H}_Z = \gamma \hbar B_o (I_{1z} + I_{2z}) \quad (54)$$

and

$$H_D = \frac{\gamma_1 \gamma_2 \hbar^2}{r_{12}^3} \left[\left(\frac{3 \cos^2 \theta - 1}{2} \right) (I_1 I_2 - 3 I_{1z} I_{2z}) \right] \quad (55)$$

The Hamiltonian is now a diagonal matrix with four possible energy levels, which in the high field case interact with the Zeeman energy levels:

$$E_{-1} = \gamma \hbar B_o \quad (56)$$

$$E_0 = 0 \quad (57)$$

$$E_1 = -\gamma \hbar B_o \quad (58)$$

to produce new energy levels:

$$|s\rangle : 0 \quad (59)$$

$$|t_1\rangle : -\gamma \hbar B_o + \frac{\gamma^2 \hbar^2}{4} \left(\frac{1 - 3 \cos^2 \theta}{r^3} \right) \quad (60)$$

$$|t_0\rangle : -\frac{\gamma^2 \hbar^2}{2} \left(\frac{1 - 3 \cos^2 \theta}{r^3} \right) \quad (61)$$

$$|t_{-1}\rangle : \gamma \hbar B_o + \frac{\gamma^2 \hbar^2}{4} \left(\frac{1 - 3 \cos^2 \theta}{r^3} \right) \quad (62)$$

where s and t refer to the singlet and triplet states. The singlet state is not coupled to any component of the triplet states by either the Zeeman or dipolar interactions and can be ignored. The three remaining energy states lead to two possible transitions:⁸⁵

$$t_0 \leftrightarrow t_1: \nu = \frac{\gamma B_e}{2\pi} + \frac{3\gamma^2}{16\pi^2} \left(\frac{1 - 3\cos^2 \theta}{r^3} \right) \quad (63)$$

$$t_1 \leftrightarrow t_0: \nu = \frac{\gamma B_e}{2\pi} - \frac{3\gamma^2}{16\pi^2} \left(\frac{1 - 3\cos^2 \theta}{r^3} \right) \quad (64)$$

A static spectrum for a pair of spin $= 1/2$ nuclei would consist of a doublet with frequency separation:

$$\Delta\nu = \frac{3\gamma\hbar}{2} \left(\frac{1 - 3\cos^2 \theta}{r^3} \right) \quad (65)$$

It is clear that the peak separation depends on the orientation of the internuclear vector with respect to the magnetic field. Single crystals containing isolated spin pairs have been studied as a function of orientation in the magnetic field yielding structural information such as orientation of the line connecting the spins and internuclear distances.^{69,85}

Single crystals are not always available so one is often limited to working with powdered samples. In powdered samples all possible orientations of the crystal with respect to the magnetic field are possible and the resulting spectrum reflects a superposition of all possible doublets resulting in a Pake doublet. The inner singularities are the 90° orientations separated by $3\gamma_1\gamma_2\hbar/4\pi r_{12}^3$ and the outer shoulders are the 0° or 180° orientations separated by $3\gamma_1\gamma_2\hbar/2\pi r_{12}^3$. Although all orientational information is lost in the powder spectrum it is still possible to determine internuclear distances directly from the spectrum.⁶⁴

The dipolar powder spectra are sensitive to molecular motions, especially in the case of isolated spin pairs. The heteronuclear vector is treated in the same manner as the largest component of the electric field

gradient tensor of spin $I = 1$ systems to calculate an averaged spectrum. Isolated spin systems, however, are frequently unavailable. When many spins are present the static spectrum consists of one broad gaussian peak. These spectra are useful in the study of molecular motions and solid state phase transitions by means of moment analysis⁸⁶ or relaxation studies.⁸⁷

2.3 Spin Lattice Relaxation in Spin 1/2 Nuclei

In solids, the T_1 relaxation time of abundant homonuclear multispin systems is common to all spins present. All protons in a homogeneous organic solid relax at the same rate. The individual protons rapidly exchange energy with each other resulting in a common spin temperature. The common T_1 is sensitive to molecular motion and has been used in many studies.⁶¹ Another relaxation time frequently employed for abundant spin $I = 1/2$ nuclei is the relaxation time in the rotating frame, $T_{1\rho}$. In the case of T_1 relaxation, the time constant is characteristic of spins returning to the equilibrium state under the influence of a static magnetic field, B_0 . $T_{1\rho}$ is characteristic of the spins returning to their equilibrium under the influence of an applied magnetic field in the rotating frame in the form of a r.f. spin-locking pulse, H_1 . Since relaxation is most effective when relaxations occur at the Larmor frequency, $T_{1\rho}$ relaxation is sensitive to motions of a lower frequency than T_1 relaxation because $\gamma H_1 \ll \gamma H_0$.⁶⁴

Spin-lattice relaxation times can be obtained by a number of methods including inversion-recovery⁸⁸ and progressive saturation.⁸⁹ The inversion-recovery method will be discussed here since it is the method used in this thesis. A 180° pulse is applied in the z direction. At

any point in time the state of the magnetization may be monitored by applying a 90° pulse (sometimes referred to as the 'read' pulse). The pulse sequence is:

$$[180^\circ - \tau - 90^\circ(\text{FID}) - T_d]_n \quad (66)$$

where a delay time T_d , longer than the longest T_1 to be measured, must be left for Boltzmann populations to be reestablished between the 180° pulses. The accumulated FID is Fourier transformed, and the parameter τ is varied. The natural logarithm of the peak height, S , for each peak may be plotted against τ , and T_1 is found by the following equation:

$$\ln[S(\infty) - S(\tau)] = \ln 2 + \ln S(\infty) - \frac{\tau}{T_1} \quad (67)$$

At short recovery times τ the signal will appear negative, since in effect a 270° pulse has been applied. At long times, full recovery is obtained so that $S_0 \equiv S(\infty)$. At some intermediate time the signal will be zero; this time τ_{null} , can be used to give a measure (generally of low accuracy) for T_1 according to:

$$T_1 = \frac{\tau_{\text{null}}}{\ln 2} \quad (68)$$

2.4 The "Dipolar Washout" Phenomenon

Examination of ^{13}C CP / MAS NMR spectra of several 18-crown-6 complexes showed that the ether carbon line was essentially invisible at room temperature and that for other complexes the spectrum was very broad.⁴² Temperature dependent CP / MAS NMR studies showed that for many 18-crown-6 complexes the macrocycle resonance goes through a fadeout region where the line becomes so broad as to be unobservable.

Rothwell *et. al.*⁹⁰ have identified two mechanisms whereby a fade-out is expected. The first occurs for nuclei which have, as their main static broadening interaction, the anisotropic chemical shift. In this instance, incoherent averaging due to random molecular motion interferes with coherent averaging produced by slow magic angle spinning, and maximum broadening occurs when the motional jump rate and the spinning rate are equal. The second mechanism occurs for nuclei for which the principal line broadening is due to heteronuclear dipolar coupling. Excess line broadening occurs when incoherent averaging due to molecular motion interferes with the coherent averaging of the decoupling field. For CH₂ groups, dipolar coupling is by far the stronger interaction. Maximum broadening occurs when the motional correlation time is about equal to the inverse of the decoupling field amplitude, $\tau_c = 1/(2\pi\gamma H_1) \sim 2.5 \times 10^{-6}$ s in the present study.⁴² The magnetic field generated by the movement of atoms, hence electrons, effectively cancels the decoupling field resulting in a dipolar coupled signal which is on the order of hundreds of hertz broader than the decoupled signal.

2.5 The Chemical Shielding Interaction

An excellent review of the chemical shielding interaction has been given by Facey⁶⁴ and should be consulted if additional information is required. The application of a strong magnetic field causes the electrons around an atom to precess about the direction of **B₀** causing electron currents to flow. These currents give rise to secondary magnetic fields at the nucleus and lead to the chemical shift. The magnitude of this magnetic field is therefore dependent on the chemical environment of the atoms being studied. The chemical shielding interaction is defined in

terms of tensors and as such the chemical shift varies with orientation of the molecule in the magnetic field. The Hamiltonian expression for the chemical shielding interaction is :

$$\mathcal{H}_s = \frac{\gamma h}{2} \mathbf{I}_z \sigma B_0 \quad (69)$$

The chemical shielding interaction is not traceless, as is the electric field gradient tensor in the electric quadrupole interaction, and it may not be symmetric. It can however be broken down into two tensors, one symmetric and the other antisymmetric:⁹¹

$$\sigma_s = \frac{1}{2}(\sigma + \sigma^T) \quad (70)$$

$$\sigma_a = \frac{1}{2}(\sigma - \sigma^T) \quad (71)$$

where σ_s is the symmetric tensor, σ_a is the antisymmetric tensor and σ^T is the transpose of σ . The contributions of the antisymmetric tensor are negligible in the NMR spectrum and can be ignored.

In the absence of quadrupolar and dipolar effects the total Hamiltonian for a spin $1/2$ nucleus is given by:

$$\mathcal{H}_T = \mathcal{H}_Z + \mathcal{H}_Q \quad (72)$$

$$\mathcal{H}_T = \gamma h \mathbf{I}_2 \mathbf{B}_0 (\mathbf{E} \cdot \sigma) \quad (73)$$

where $\mathbf{E}$ is a second rank unit matrix. This yields two energy levels:

$$E_{\frac{1}{2}} = -\frac{\gamma h}{2} B_0 (1 - \sigma_{xx}) \quad (74)$$

$$E_{-\frac{1}{2}} = \frac{\gamma h}{2} B_0 (1 - \sigma_{xx}) \quad (75)$$

where σ_{zz} is the largest principal component of the chemical shielding tensor and it is assumed to be parallel to the magnetic field. These two energy levels give rise to a single transition with frequency:

$$\nu = \frac{\gamma}{2\pi} B_0 (1 - \sigma_{zz}) \quad (76)$$

If the principal component of the chemical shielding tensor is not parallel to the magnetic field it must be described in an axis system where it is. In this case the line has an orientational dependent position given by:

$$\nu = \frac{\gamma B_0}{2\pi} [1 - (\sigma_{xx} \cos^2 \theta_{xx} + \sigma_{yy} \cos^2 \theta_{yy} + \sigma_{zz} \cos^2 \theta_{zz})] \quad (77)$$

where σ_{ii} are the principal components and θ_{ii} are the angles between these components and the magnetic field vector. This indicates that the resonance frequency of each signal is dependent on its orientation in the magnetic field. Studies on single crystals, comparing the orientation in the magnetic fields have been done to determine the principal orientations of the shielding tensors as well as their orientation in the crystal lattice. The resultant spectrum, shown in Figure 27, resembles that of a single transition in ^2H NMR powder spectra. The shielding parameters can be read directly from the discontinuities.

Figure 27: The general powder NMR line shape for a proton decoupled, dilute spin $I = 1/2$ nucleus.

In solutions rapid isotropic motions average the $\cos^2\theta_{ij}$ term to a value of resulting in a single line at a frequency given by:

$$\nu = \frac{\gamma}{2\pi} B_c (1 - \sigma_i) \quad (78)$$

where σ_i has a value of one third of that of the trace of σ . It is this parameter that produces the chemical shifts observed in solution.

2.6 The Magic Angle Spinning (MAS) Technique

In order to obtain solution type spectra of solids, interactions such as the quadrupolar, dipolar and chemical shielding interactions must be removed. In the case of ^{13}C , a dipolar nucleus, quadrupolar interactions are not present. Heteronuclear dipolar interactions can be removed with the application of a high power r.f. field at the resonance frequency of the protons. Homonuclear dipolar interactions are insignificant for ^{13}C because it is isotropically dilute. The isotropic chemical shielding interaction is easily removed by a technique known as magic angle

spinning.^{91,92} The solid sample is spun at an angular velocity ω_r about an axis, β to the magnetic field, and angles χ_{ii} , θ_{ii} and ϕ_{ii} ($i = 1,2,3$) to the principal component of σ as shown in Figure 28.

Figure 28: A depiction of the motion of the principal components of a chemical shielding tensor as the sample is rotated macroscopically about an inclined axis at an angle β to the magnetic field vector.

The angle σ_{ii} becomes time dependent and can be expressed in terms of other angles in the system:

$$\cos \theta_{ii} = \cos \beta \cos \chi_{ii} + \sin \beta \sin \chi_{ii} \cos(\omega_r t + \psi_{ii}) \quad (79)$$

where ψ_{ii} are the azimuth angles of the principal components of σ at time $t = 0$. Substituting equation (79) into (77) and taking the time average yields the time averaged resonance frequency:

$$\nu = \frac{\gamma}{2\pi} B_0 \left[1 - \left(\frac{3}{2} \sigma_{ii} \sin^2 \beta + \frac{1}{2} (3 \cos^2 \beta - 1) \sum_{ii} \sigma_{ii} \cos^2 \chi_{ii} \right) \right] \quad (80)$$

If β is chosen such that the term $3\cos^2\beta - 1 = 0$, (i.e. $\beta = 54.7^\circ$) then equation (80) reduces to equation 76 which means that a solution like spectrum will be obtained for the solid. The angle 54.7° has been termed the "Magic Angle". The time dependent terms of $\cos\theta_{II}$ which are periodic in ω_r result in rotational echoes in the free induction decay and spinning side bands in the spectrum. The side bands occur at frequencies of $\pm n\omega_r$ from the isotropic peak where n is an integer. The side bands cover a range of frequencies on the same order as the static line width. In the limit of $\omega_r \rightarrow 0$, the side band envelope mimics the static spectrum. At a slightly higher rate this is not the case but one is still able to determine the principal components of the shielding tensor from it. Slow spinning experiments⁹³ or the use of pulses synchronized to the rotation period of the spinner⁹⁴ have been used to obtain such information. The spinning side bands are, however, in most cases more of a nuisance since they may overlap with other isotropic peaks. Pulse sequences have been designed to partially⁹⁵ or fully⁹⁶ suppress them in the spectrum.

The chemical shift observed in solids by using high resolution magic angle spinning are often different from those observed for the same compound in solution. Crystallographic effects or distortions as well as solvent effects in the solution cause this. In principle, every inequivalent atom will give rise to its own resonance. It is the crystallographic symmetry rather than molecular symmetry that determines the equivalence or nonequivalence of any group of atoms. Chemical shift values of the nuclei in solids can sometimes be used to study solid state phase transitions as the spectra of each phase may differ. The spectral

peaks of non crystalline or amorphous solids may be broadened as a result of the nuclei having a distribution of electronic environments.

2.7 The Cross Polarization (CP) Experiment

Even with the heteronuclear dipolar interaction removed by high power decoupling and the chemical shielding anisotropy interaction removed through magic angle spinning solid state ^{13}C NMR is still faced with a lack of sensitivity due to its long T_1 s. The problem has been solved with the development of a double resonance technique first introduced as proton enhanced nuclear induction spectroscopy⁹⁷ but now known as cross polarization. The sequence derives the ^{13}C magnetization from the ^1H spins in the rotating frame and is illustrated in Figure 29.

Figure 29: The pulse sequence used to obtain cross-polarization from the proton spin reservoir in ^{13}C spins for solids.

The first step is to apply a 90° pulse in the proton channel and to spin-lock the ^1H magnetization in the y direction by the application of a contact pulse, $B_{1\text{H}}$, phase shifted from the first pulse by 90° . While the protons are spin-locked, a pulse, $B_{1\text{C}}$, is applied at the resonance frequency of ^{13}C such that the Hartmann - Hahn condition⁹⁸ is fulfilled:

$$\gamma_{\text{H}}B_{1\text{H}} = \gamma_{\text{C}}B_{1\text{C}} \quad (81)$$

The gyromagnetic ratio of the proton is approximately four times that of ^{13}C so $B_{1\text{C}}$ must be four times as powerful as $B_{1\text{H}}$. Under these conditions both the ^1H and ^{13}C nuclei have the same energy and precess at the same rate in their rotating frame. Magnetization is then transferred from the protons to the ^{13}C by way of the B term in the heteronuclear Hamiltonian (see equations 46-52). Since protons are more abundant than ^{13}C only a small amount of magnetization is depleted from the proton reservoir. The magnetized ^{13}C nuclei are observed by turning off the $B_{1\text{C}}$ pulse and turning on the receiver. The spin-locking ^1H pulse is left on throughout the acquisition to remove the heteronuclear dipolar interaction. Cross polarization enhances the ^{13}C signal by a factor of four and also drastically reduces the acquisition time needed. The repetition rate of the experiment depends on the T_1 of the proton rather than that of the ^{13}C . Proton T_1 's are approximately an order of a magnitude less than that of ^{13}C making this a considerable advantage.

The CP/MAS experiment may be efficient at removing the dipolar coupling between protons and ^{13}C but it is often not enough to fully remove the dipole-dipole interaction between ^{13}C and quadrupolar

nuclei. Mixing between the quadrupolar and Zeeman Hamiltonians give rise to new terms in the dipolar Hamiltonian which are not removed by magic angle spinning.⁹⁹ As a result ^{13}C 's bonded to quadrupolar nuclei such as ^2H , ^{14}N , ^{35}Cl and ^{37}Cl are often quite broad. In some cases however, the relaxation between the eigenstates may be so fast that the dipolar interaction to ^{13}C is effectively averaged to zero¹⁰⁰ and very sharp lines are observed for the ^{13}C CP/MAS spectra of carbons attached to ^{19}Br , ^{81}Br and ^{127}I .

The magnetization of the ^{13}C nuclei is highly dependent on the contact time employed in the ^{13}C CP/MAS experiments. The relationship is shown in Figure 30.

Figure 30: The dependence of the intensity of a ^{13}C NMR line in a CP/MAS spectrum as a function of contact time. (A) $-\text{CH}_2-$ carbon, (B) carbonyl or quaternary carbon. The curves have been displaced from one another for clarity.

Carbons in different chemical environments polarize at different rates but they lose magnetization at the same rate as characterized by the common $T_{1\rho}$ of the proton reservoir. The contact time must be chosen long enough to allow all ^{13}C atoms in the sample to reach magnetization equilibrium but short enough to prevent significant loss of signal intensity. If the contact time is too short the spectral intensity will not quantitatively reflect the number of carbons on the sample. To prevent this a number of spectra are obtained as a function of contact time and an optimum value is obtained.

CP/MAS has been found to be a valuable tool for the investigation of molecular motion since the line widths are proportional to the correlation times, τ_c ,¹⁰¹ of the motions. For carbons with strong heteronuclear dipolar interactions the transverse relaxation rate ($1/T_2$) is proportional to the spectral density function, $J(\omega_1, \tau_c)$:

$$J(\omega_1, \tau_c) = \frac{\tau_c}{1 + \omega_1^2 \tau_c^2} \quad (82)$$

where ω_1 represents the strength of the decoupling field. When the decoupling field is on the same order as the reciprocal correlation time of the motion, the line width is at a maximum, and often too broad to be observed in the CP/MAS spectrum. In regions where the product of the decoupler field strength and the correlation time of the motion are either much greater or much less than unity, the line width obeys an Arrhenius relationship with temperature, and activation energies can be calculated.¹⁰¹

Results and Discussion

3.1.1 Synthesis and Characterization of Crown Ether Polymers

The present synthesis of polyvinylbenzocrown ethers (Figure 31) has several advantages over the method previously published by Smid⁴³. Smid uses a four step synthesis starting from catechol in which catechol is converted into its diacetate and subsequently to 3,4-dihydroxyacetophenone. The crown ether is formed and the methyl ketone is converted into the vinyl group with an overall yield of 13.1%. We wish to report a synthesis of 4'-vinylbenzo-crown ethers which involve only two steps and produce higher yields. In our scheme 4'-vinylbenzo-15-crown-5 is produced with an overall yield of 40.0% (with no attempts to maximize yields)¹⁰². The yield of 4'-vinylbenzo-12-crown-4 is somewhat lower due to the higher degree of difficulty in forming smaller ring sizes. This new synthesis also allows for easy labeling of the methylene carbon of the polymer chain with commercially available labeled Wittig reagent. Such labeling may be useful for ^{13}C T_1 studies since the methylene and methine carbons have essentially identical ^{13}C chemical shifts.

Figure 31: Synthesis of poly(vinylbenzo-12-crown-4)

It was our view at the start of this project that the aldehyde function might require protection from base catalyzed condensation to a Cannizzaro type product during the cyclization reaction. Such a protection was attempted using ethylene glycol in a reaction outlined by Daignault¹⁰³ for the protection of cyclohexanone but was unsuccessful. This failure can be attributed to a deactivation of the carbonyl carbon due to resonance donation from the para oxygen atom as shown in Figure 32.

Figure 32: Resonance stabilization of 3,4-dihydroxybenzaldehyde

The added stability of the aldehyde thus proves to be advantageous since cyclization to the crown ether can be performed in a mild base without affecting the aldehyde. Several cyclization reactions were successfully carried out producing low to moderate yields. The reaction of 3,4-dihydroxybenzaldehyde with 1,8-dichloro-3,6-dioxaoctane in 1-butanol with lithium hydroxide serving as both base and template was found to be the most practical of all methods attempted. It produced the highest yield and did not require an inert atmosphere. The reaction was repeated adding LiBr and LiClO₄ in attempt to provide a better template but this had no effect on either yield or reaction time. The major disadvantage is the long reaction time. In order to increase yields and decrease reaction time 4'-formylbenzo-12-crown-4 was prepared using the ditosylate instead of dichloride of triethylene glycol. Although the reaction did produce the desired product the yield was substantially lower and the reaction time was not much shorter. As a result this method was abandoned for the previous and more reliable synthesis.

The cyclization reaction produced two crown ethers, the desired product and its dimer, and an uncyclized mono addition product. Only one dimer was isolated as indicated by the single aldehyde peak present in the ¹H NMR spectrum. It has one of two possible structures as shown in Figure 33. We are unable to determine which of these compounds was isolated in the absence of X-ray data but believe the structure to be that of 33a.

Figure 33: Possible structures of dimer produced in the cyclization reaction,

If we consider the resonance stabilization depicted in Figure 32 we see that the 4-hydroxy proton is more acidic than the 3-hydroxy proton. This dictates that the uncyclized monoadduct will have the structure shown in Figure 34. The uncyclized monoadduct will then cyclize to form the desired product or combine with another to form dimer **33a**. No double addition product was isolated eliminating the possibility that a dimer is formed in the four step sequence shown in Figure 35 which would produce both of the dimers illustrated above.

Figure 34: Structure of uncyclized monoadduct formed in the cyclization reaction

Figure 35: Synthetic route to mixture of dimers

The ^1H NMR spectrum of 4'-formylbenzo-12-crown-4 is of interest and deserves some discussion. Figure 36 a shows the aromatic region of the ^1H NMR spectrum obtained on the Varian Gemini 200 MHz spectrometer. A first order analysis of the spectrum failed to produce the necessary coupling constants required to make spectral assignments of the three protons present. Tentative assignments can be made by using the additivity effects for the chemical shifts of substituted aromatics¹⁰⁴ for an analogous system. The ^1H NMR spectrum of 3,4-Dimethoxybenzaldehyde (Table 2) should be very similar to the aromatic region of 4'-formylbenzo-12-crown-4 so it will be used in this case.

Table 2: Calculated Chemical Shifts for the Aromatic Protons of 3,4-Dimethoxybenzaldehyde.

Proton	Calculated Chemical Shift
	(ppm)
H _a	7.61
H _b	7.65
H _c	7.27

Table 1 indicates that protons H_a and H_b have very similar chemical shifts and are substantially different from that of proton H_c. Because the difference in chemical shifts, $\nu_a - \nu_b$ is on the same order as the coupling constant, J_{ab} , an ABX spin system is expected. Under ideal conditions we would expect to see twelve major transitions for the aromatic protons in this spectrum. Unfortunately this is not the case (Figure 36a). The observed spectrum, like many other ABX spectra, show far less resolvable transitions either due to accidental overlap or because the transitions are too weak to detect. In these cases all coupling constants can not be determined making analysis difficult if not impossible. This problem was overcome by using approximate values for chemical shifts and coupling constants, both extracted from the spectrum shown in Figure 36a and estimated from the typical values for analogous systems, and simulating the expected spectrum. These parameters were adjusted until the simulated spectrum (Figure 36b) matched the observed spectrum. Chemical shifts and coupling constants are listed in Hertz with magnitudes chosen to simulate a 200 MHz spectrum. The values employed are $\nu_a = 1510$ Hz, $\nu_b = 1500$ Hz, $\nu_x = 1412$ Hz, $J_{ab} = 1.54$ Hz, $J_{bx} = 6.45$ Hz, and $J_{ax} = 0.40$ Hz. (N.B. For clarification, proton c above is proton X in the ABX spin system nomenclature)

Figure 36: 200 MHz ^1H NMR Spectrum of the Aromatic Protons of 4'-Formylbenzo-12-crown-4; a) Experimental, b) Simulated

A simple Wittig reaction on the 4'-formylbenzo-12-crown-4 afforded the vinylbenzo precursor to the polymer. Three sets of conditions were employed for this reaction. The first set of conditions involved the use of diethyl ether as a solvent and the reaction produced only a minimal yield. Diethyl ether was used as a solvent because triphenylphosphine oxide, a byproduct of the reaction, is not soluble in it and could be removed by filtration prior to workup. The low yield of the reaction was attributed to the extra stability of the aldehyde, a problem which we felt could be overcome by using a higher boiling solvent. This was proven to be the

case because changing the solvent to glyme (ethylene glycol dimethyl ether) increased the yield to 63%. In the final set of conditions the base was changed from lithium tertiary butoxide to sodium hydride, a stronger base and the yield was increased to 85%. Although the mechanism of the Wittig reaction is well known it is included here (Figure 37) both for completeness and for use as a future reference for a reaction with a similar mechanism.

Figure 37: Mechanism of the Wittig reaction used in synthesis of 4'-vinylbenzo-12-crown-4

The ^1H NMR spectrum of 4'-vinylbenzo-12-crown-4 is much simpler in the aromatic region than its formyl precursor. The splitting pattern appears to be that of an AMX system so all chemical shifts and coupling constants in this region can readily be extracted directly from the spectrum (Figure 38). The intensities of the peaks are slightly different than one would expect so the spectrum was simulated using the LAOCOON program using the chemical shifts and coupling constants extracted. The simulated spectrum is shown in Figure 38b. The

favourable comparison indicates that the chemical shifts and coupling constants are, in fact, correct.

Figure 38: a) 200 MHz ^1H NMR spectrum of the aromatic protons of 4'-vinylbenzo-12-crown-4; 7.045 δ (d), H_X ; 6.9803 δ (dd), H_B ; 6.8965 δ (d), H_A . $J_{\text{BX}} = 2.17$ Hz, $J_{\text{AX}} =$ not resolvable, $J_{\text{AB}} = 5.52$ Hz
 b) Simulated 200 MHz ^1H NMR spectrum of the aromatic protons of 4'-vinylbenzo-12-crown-4

The portion of the spectrum showing the vinylic protons is expanded and illustrated in Figure 39. It is representative of an AMX splitting pattern and all coupling constants are easily observed.

Figure 39: 200 MHz ^1H NMR spectrum of the vinylic protons of 4'-vinylbenzo-12-crown-4; 6.02 δ (dd), H_X ; 5.588 δ (dd), H_A ; 5.137 δ (dd), H_M , $J_{\text{MX}} = 10.8\text{ Hz}$, $J_{\text{AX}} = 17.53\text{ Hz}$, $J_{\text{AM}} = -0.87\text{ Hz}$.

As in the previous case there is too much overlap in the region of the protons on the ethereal protons to extract any valuable information from the ^1H NMR spectrum. At this point we will turn our attention to the ^{13}C NMR spectrum of 4'-vinylbenzo-12-crown-4 (appendix 2). The spectrum shows one less resonance in the aromatic region than one would expect to see. The APT (attached proton test) failed to resolve the problem. A calculation of the chemical shifts for the aromatic carbons of the analogous 3,4-dimethoxystyrene, below (Table 3), reveals that carbons 3 and 4 have resonances very close together. This suggests that the two signals for these carbons in our system also overlap and give rise to the resonance at 136.2 ppm. The resonance at 132.5 ppm was ruled

out because the attached proton test indicated that it is attached to a proton. It was labeled the vinyl methine signal because of this and its proximity to the shift of the analogous carbon of styrene, 135.5 ppm. All other resonances were assigned based on the APT results and their proximity to the calculated chemical shifts in Table 3.

Table 3: Calculated chemical shifts for the aromatic carbons of 3,4-dimethoxystyrene.

	Carbon	Calculated Chemical Shift
		(ppm)
1	129.3
	2	111.2
	3	143.2
	4	142.9
	5	113.4
	6	117.8

We chose to carry out the polymerization with a radical initiator as previously employed by Smid⁴³ because of the simplicity of the reaction and the availability of the necessary reagents. The polymer chains are much shorter than those previously reported. We used 0.5% initiator by weight and obtained a polymer with a mean mass number of 3,800. The weight is just over 10% of the values of those obtained by Smid even though we used less initiator by a factor of approximately 1.5. The polymerization properties of vinylbenzo-12-crown-4 are not expected to be significantly different from those of vinylbenzo-15-crown-5 and because the reaction time and temperature used were the same as those reported we must conclude that either our initiator was more active or that our degassing procedure was slightly less effective and that residual oxygen may also be acting as an initiator.

The identical procedure was carried out for the synthesis of the copolymer. ^1H NMR integration of the polymer obtained comparing the $\text{CH}_2\text{-O}$ and aromatic regions showed that both monomeric components were present in essentially equal amounts within the precision of the electronic integration ($\pm 3\%$).

On examining the NMR spectra of the polymers one can immediately see the lack of resolution relative to the spectra of the monomer. This loss of resolution is a result of very slow molecular motion (long correlation time, τ_c) caused by the pendant crown ethers restricting rotation about the polymeric chain. As shown in Figure 40 this long correlation time greatly reduces the spin-spin relaxation time, T_2 , which is inversely proportional to the resonance line width, $\delta\nu$.¹⁰⁵

Figure 40: Effect of the molecular correlation time (τ_c) on T_1 and T_2 .

We are unable to tell from the spectra if the polymers are isotactic or syndiotactic or a mixture of both because the lines are too broad. A mixture of both is expected. Because only two signals are present in the

high field region of the spectrum it is safe to conclude that all pendant crown ether substituents are equally spaced on the polymer chain as expected. When a substituted vinyl group is polymerized there are two possible structures formed depending on which end of the vinyl group is attacked. There is a slight difference in the stability of radicals with differing levels of substitution which is based on bond dissociation energies. If we compare the energy to break the primary C—H bond of propane (98 kcal/mol) with that required to break a secondary C—H bond of propane (95 kcal/mol), we find a difference of 3 kcal/mol. Since we are starting with the same reactant in both cases (propane), and since one of the products is the same in both cases ($\text{H}\cdot$), the 3 kcal/mol energy difference is a direct measure of the stability between the primary propyl radical and the secondary propyl radical. Similar differences are found in the energies of tertiary and secondary radicals. Thus the order of stability of radicals is as follows:

This is identical to the stability order of carbocations.¹⁰⁶

In the case of styrene the difference in the energy between the primary and secondary radicals is even greater due to the resonance stabilization of the secondary radical. As a result only one polymeric structure is formed.¹⁰⁷ Addition of an initiator to a styrene double bond produces a radical that can be stabilized by the phenyl ring (Figure 41a). If this radical adds to the methylene carbon of another styrene the new radical can also be stabilized by its phenyl ring (Figure 41b). On the other hand, if addition occurs at the methine carbon of the vinyl group of

the second styrene the product radical cannot be stabilized (Figure 41c). As a result the product having neighbouring groups is not formed.

Figure 41: Resonance stabilization of radicals in the polymerization of styrene; Both a) and b) show radical stabilization but c) can't be stabilized and the product is not found.

3.1.2 Polymer Complexation and Cation Extraction Studies

We repeated Smid's procedure for the extraction of metal picrates to compare the binding efficiencies of both polymers with benzo-12-crown-4 and unsubstituted 12-crown-4 ether. Benzo-12-crown-4 was chosen over vinylbenzo-12-crown-4 for a basis of comparison because we felt that it would give a better indication of the extraction capabilities of the monomer. Vinylbenzo-12-crown-4 has extended conjugation not found in the polymer which may have an effect on the solubility properties.

In all cases polyvinylbenzo-12-crown-4 extracted the metal picrate with the highest efficiency (Figures 42-44). At low concentrations, values for the copolymer were close but became slightly lower as the concentrations increased. The values used to calculate the extraction efficiencies of the polymers are plotted as concentrations of crown ether units to concentration of picrate. If however it was calculated on a basis of weight the homopolymer would be more efficient than the copolymer by an additional factor of 1.4, the ratio of molecular weight of repeating units. Both of the monomers were at least an order of magnitude less efficient than either of the polymers (Figures 45-48). In all cases sodium extractions were the most efficient. This is consistent with the known stabilities of 12-crown-4 complexes⁴¹. Lithium complexes of 12-crown-4 exhibit a 1:1 stoichiometry while analogous sodium complexes are 2:1. Van Remoortere reported a complex of sodium chloride/12-crown-4 in which the sodium had a coordination number of eight binding to all eight crown ether oxygens¹⁰⁸. Potassium complexes are known to be less stable⁴¹. Both of the polymers were also more than twice as effective when extracting potassium over lithium supporting the idea of cooperative binding between adjacent crown ether moieties on the polymer chain. Of the monomers benzo-12-crown-4 was the least effective. The benzo group increases the rigidity of the crown thus reducing its binding capabilities relative to free 12-crown-4 ether. In some of the graphs there appears to be a "cross-over" in extraction efficiencies of the various cations. This is the result of experimental error. An error of $\pm 2\%$ would be more than enough to cause the observed cross-overs.

Figure 42: Extraction of lithium picrate with polyvinylbenzo-12-crown-4 (□), Vinylbenzo-12-crown-4 / Styrene Copolymer (●), Benzo-12-crown-4 (■) and 12-Crown-4 Ether (○).

Figure 43: Extraction of sodium picrate with polyvinylbenzo-12-crown-4 (□), Vinylbenzo-12-crown-4 / Styrene Copolymer (●), Benzo-12-crown-4 (■) and 12-Crown-4 Ether (○).

Figure 44: Extraction of potassium picrate with polyvinylbenzo-12-crown-4 (□), Vinylbenzo-12-crown-4 / Styrene Copolymer (♦), Benzo-12-crown-4 (■) and 12-Crown-4 Ether (●).

Figure 45: Extraction of potassium (□), sodium (♦) and lithium (■) picrates with polyvinylbenzo-12-crown-4

Figure 46: Extraction of potassium (□), sodium (●) and lithium (■) picrates with vinylbenzo-12-crown-4 / styrene copolymer

Figure 47: Extraction of potassium (□), sodium (●) and lithium (■) picrates with benzo-12-crown-4

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Resolution test chart showing patterns of vertical and horizontal lines with numerical values ranging from 1.0 to 4.5.

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Figure 48: Extraction of potassium (□), sodium (◆) and lithium (■) picrates with 12-crown-4

In Figure 49 we compare the extraction capabilities of polyvinylbenzo-12-crown-4 with polyvinylbenzo-15-crown-5 and polyvinylbenzo-18-crown-6, reported by Smid⁴³. In the extraction of lithium and sodium picrates there are only slight differences in the binding efficiencies of the three polymers. In both cases polyvinylbenzo-15-crown-5 is the most efficient while polyvinylbenzo-12-crown-4 and polyvinylbenzo-18-crown-6 are only slightly less efficient and approximately equal to each other. This further supports the fact that sodium complexes are the most stable for these ring sizes. The benzo group on the smaller crown ether increases the rigidity of the system, effective¹ reducing the size of the cavity, preventing the lithium ion from easily fitting inside. This forces the complexes into a two to one stoichiometry making sodium the preferred anion. The extraction of

potassium does not follow the same trends. As would be expected, because of the small cavity size, polyvinylbenzo-12-crown-4 is by far the least efficient. Both polyvinylbenzo-15-crown-5 and polyvinylbenzo-18-crown-6 extract 43 to 45 times the potassium. The values for these two polymers are so close to each other that the binding mechanisms must be similar. Potassium does not fit into the cavity of 15-crown-5 suggesting that cooperative binding must be present. Distribution equilibria measurements have demonstrated that for 1:1 complexes the binding constant of the crown to cation is not significantly affected when the crown ligand is attached to the polymer chain.⁵⁵ However, it was observed that, while extracting potassium picrate from water into chloroform, the fraction of crown ligands complexed to K^+ never exceeded 0.5 for polyvinylbenzo-18-crown-6, while the fraction can approach unity for a copolymer with styrene containing 20% vinylbenzo-18-crown-6. Apparently, the complex formation constant for polyvinylbenzo-18-crown-6 depends on the fraction of crown ligands bound, and drops off rapidly when this fraction exceeds the value 0.5, either because of steric hindrance or increased electrostatic repulsion (when complex formation constants are very high, as for in tetrahydrofuran, the fraction of complexed crown units does approach unity for the homopolymer).⁵²

Figure 49: Comparison of the extraction of lithium, sodium and picrates with Polyvinylbenzo-12-crown-4 (■), Polyvinylbenzo-15-crown-5 (▨), and Polyvinylbenzo-18-crown-6 (■) [Picric acid] = 7×10^{-5} M; [crown units] = 35×10^{-5} M; [metal hydroxide] = 0.01 M. Based on total amount of picric salt.

3.2.1 Bis-Crown Ethers Synthesis

The next aspect of this project was the synthesis of the "dimer", i.e. two crown ethers separated by a three or four carbon bridge. Excess 4'-formylbenzo-12-crown-4 synthesized from the aforementioned polymer project seemed to make a fine starting point. The initial strategy outlined in Figure 50a was devised with the synthesis of a three carbon bridge in mind. The first three steps of the sequence were carried out with varied

levels of success when the synthesis was abandoned for the far shorter synthesis, illustrated in Figure 50b, producing a four carbon bridge.

Figure 50: Possible routes to the synthesis of bis-crown ether separated by a) three and b) four carbon bridges

The first new reaction in the synthesis of the dimers was the hydroboration / oxidation of 4'-vinylbenzo-12-crown-4. The first time the reaction was carried out commercial $BF_3 \cdot THF$ was used and the reaction

was not permitted to go above 20°C. DME was chosen as a solvent because of our success using it for other reactions. Because it is an ether it should still stabilize the borane. Unfortunately the reaction did not work and only starting material was recovered. The reaction was repeated in THF, again at room temperature. This time it did produce some product as determined by ^1H NMR but the yield was very poor. It was repeated a third time with refluxing for four hours prior to workup. The isolated yield of the desired product was increased to 60% and approximately 10% of the secondary alcohol was also isolated. The overall yield of the reaction was slightly lower than that reported for styrene¹⁰⁹ but the ratio of primary to secondary alcohols is about what is expected. Increasing the reflux time to eight hours produced some product that resembled the polymer and none of the desired material. The product was not characterized any further.

The alcohol (**9**) was brominated using a reaction developed by Ho¹¹⁰. This reaction was chosen because it is reported to give high yields with short reaction times. Ho reports chlorination of the analogous phenethyl alcohol with an isolated yield of 80% in a thirty minute reaction. Bromination of our alcohol was also complete in thirty minutes producing (**10**) with an isolated yield of 73%.

A proposed mechanism for the bromination reaction is shown in Figure 51. The reaction is believed to proceed through addition of triphenylphosphine to diethylazodicarboxylate giving a quaternary phosphonium salt. Protonation followed by attack of the alkoxy anion gives the ionic species (**1**).¹¹¹ Ho¹¹⁰ hypothesized that the use of a zinc halide will result in a partial covalent bond between the zinc metal and

the oxygen atom and lead to the formation of the reactive alkoxyphosphonium species (2). Subsequently, an S_N2 type displacement of the resulting alkoxyphosphonium species by a halide ion completes the reaction. The exact mechanism for the reaction is not clear. However, it is true that the reaction gave either no detectable amount of halide or poor yields when carried out under the same conditions using other inorganic halides with poorer covalent character of metal-oxygen bond such as sodium iodide, lithium bromide and magnesium chloride. Therefore, the use of zinc halide in this one step process is essential.¹¹⁰

Figure 51: Proposed mechanism for the bromination reaction

At this point a Grignard reaction was used in an attempt to couple 1-bromo-2-(4'-benzo-12-crown-4)-ethane to 4'-formylbenzo-12-crown-4. Attempts to generate the Grignard reagent with either magnesium turnings or powder were unsuccessful. The use of chemically activated magnesium, with iodine as outlined by Lai¹¹², prior to the reaction also failed. It is possible that the failure of this reaction is due to traces of

water that the drying procedures did not eliminate. The reaction was done on such a small scale that 2.7 mg of water would effectively quench it. Increasing the scale may have eliminated the problem but, with so many other options open, it seemed reasonable to try other avenues first.

A Wittig reaction followed by partial hydrogenation would also lead to the same product so this was attempted. To eliminate the possibility of contamination with atmospheric moisture the intermediate phosphonium salt was not isolated. When the formation of the salt was complete it was treated with phenyllithium to generate the ylide. Phenyllithium was used by Lambert¹¹³ on a similar system, 2-(4-methoxyphenyl)ethyltriphenylphosphonium bromide, because it is a stronger base than *n*-butyllithium, which is commonly used for Wittig reactions¹¹⁴. A mass spectrum of the reaction product indicated that some of the desired material had been prepared. The yield, however, was quite low and several attempts at chromatography failed to isolate any product.

It was at point that we decided to employ Brown's procedure for the coupling of olefinic derivatives and their conversion to saturated dimers.¹¹⁵ We chose to generate the borane solution in situ by standard procedures¹¹⁶ because of the age of our borane•THF reagent and the availability of borane trifluoride etherate and sodium borohydride in the laboratory. This caused additional complications because crown ethers readily form complexes with borane trifluoride¹¹⁷. Upon addition of the borane trifluoride etherate to the solution of 4'-vinylbenzo-12-crown-4 in diglyme a white gummy precipitate formed. Additional diglyme was added but failed to dissolve the precipitate. The problem was overcome by

refluxing the reaction mixture until the precipitate had dissolved. The elevated temperature served to break up the complex and allow the borane trifluoride to react with the sodium borohydride to form borane which does not form solid complexes with crown ethers¹¹⁷.

Two crown ethers were isolated from the reaction mixture, 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane ((15) in Figure 52, 42 %) and 4'-ethylbenzo-12-crown-4 ((16), 17 %). None of the expected product was obtained. For the coupling of 1-hexene Brown¹¹⁵ reported yields of 66% *n*-dodecane, 5% 5-methylundecane and a 20% mixture of 1-hexene and *n*-hexane. No alcohols or diols were obtained. The yield of the hydrogenated product was higher than expected. The high yield of 4'-ethylbenzo-12-crown-4 is a result of increased hydrogenation with sodium borohydride while the reaction mixture was refluxed to produce borane. The production of this undesired material may be substantially reduced with the use of commercial borane. The formation of the complex may also have been responsible for the formation of the diol. The use of commercial borane may also shed some light on the situation.

The reaction was repeated on a larger scale using $\text{BH}_3 \cdot \text{THF}$ in THF and resulted in the formation and isolation of several compounds. The most abundant of these was still 1,4-di-(4'-benzo-12-crown-4)-2,3-dihydroxybutane (15) followed by the expected product, 1,4-di-(4'-benzo-12-crown-4)-butane (14). This was mixed with a small amount (~ 10%) of 1,3-di-(4'-benzo-12-crown-4)-butane, (17), approximately the amount expected from the statistical data on the hydroboration of the methine carbon of the double bond. We were unable to separate these two compounds by chromatography because of their virtually identical rf

values in all solvents employed. A small amount of hydrogenated product ((**16**), 16%) and some 1-(4'-benzo-12-crown-4)-ethanol ((**18**) 6%) were also isolated.

Figure 52: Reaction products from coupling reaction

The mechanism for the coupling of olefins involves the formation of a trialkylborane followed by treatment with alkaline silver nitrate. The transalkylation from boron to silver is believed to generate an unstable alkyl silver intermediate, which decomposes to give radical species. Edwards and coworkers¹¹⁸ have shown that silver oxide rapidly oxidizes some amines to carbinoamines while being reduced to metallic silver. The radical species may then undergo normal radical coupling¹¹⁹. This mechanism is shown in Figure 53.

Figure 53: The reaction mechanism for the coupling of olefins using borane, silver nitrate and base.

This mechanism, however, does not account for the formation of the diol or any other oxidized material obtained from the reaction. In view of these products it is necessary to find another mechanism to explain the other products obtained. Silver nitrate in base may cause the formation of silver oxide, which has been used for the coupling and oxidation of silyl enol ethers in the formation of 1,4-diketones.¹²⁰ A possible mechanism is shown in Figure 54. The trialkyl borane is oxidized on a carbon α to the boron. A silver ion is responsible for an unstable alkyl-silver intermediate which forms a free radical. These free radicals will then couple producing the observed pinacol.

Figure 54: A possible mechanism for the coupling reaction to explain the formation of the diol.

3.2.2 Complexation of Blacrown Ethers

The complexation of 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane (**15**) was studied in solution by means of its ^{13}C spin-lattice relaxation time (T_1) alone and in the presence of LiClO_4 (1:1 and 1:2) and $\text{Ba}(\text{ClO}_4)_2$ (1:1). The results are shown in Table 4.

Table 4: T_1 Values for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane in methanol-OD, alone and complexed with LiClO_4 (1:1 and 1:2) and $\text{Ba}(\text{ClO}_4)_2$ (1:1 and 1:2)

Dimer			
Carbon	δ (ppm)	T_1 (s)	Error (s)
C5	125.17	1.12	0.01
C6	120.70	1.13	0.02
C3	120.41	1.30	0.02
C10'	73.82	0.80	0.01
C3'	73.25	0.81	0.01
C4'', C9''	72.63	0.76	0.01
C6'', C7''	71.61	0.80	0.01
C2	65.23	1.17	0.02
C1	40.67	1.06	0.01

Dimer + LiClO_4 (1 : 1)				Dimer + LiClO_4 (1 : 2)			
Carbon	δ (ppm)	T_1 (s)	Error (s)	Carbon	δ (ppm)	T_1 (s)	Error (s)
C5	125.34	0.77	0.02	C5	125.37	0.71	0.01
C6	120.76	0.88	0.02	C6	120.67	0.83	0.01
C3	120.49	0.87	0.01	C3	120.45	0.82	0.01
C10'	73.70	0.54	0.01	C10'	73.57	0.51	0.01
C3'	73.17	0.53	0.01	C3'	73.02	0.50	0.01
C4'', C9''	72.44	0.50	0.01	C4'', C9''	72.26	0.46	0.01
C6'', C7''	71.49	0.55	0.02	C6'', C7''	71.35	0.51	0.01
C2	65.38	0.85	0.02	C2	65.36	0.79	0.01
C1	40.71	0.74	0.02	C1	40.61	0.70	0.01

Dimer + $\text{Ba}(\text{ClO}_4)_2$ (1 : 1)				Dimer + $\text{Ba}(\text{ClO}_4)_2$ (1 : 2)			
Carbon	δ (ppm)	T_1 (s)	Error (s)	Carbon	δ (ppm)	T_1 (s)	Error (s)
C5	126.74	0.33	0.01	C5	127.25	.35	0.01
C6	121.53	0.38	0.01	C6	121.90	0.41	0.01
C3	121.17	0.7	0.01	C3	121.42	0.40	0.01
C10'	73.60	0.21	0.01	C10'	73.49	0.21	0.01
C3'	73.06	0.22	0.01	C3'	72.98	0.22	0.01
C4'', C9''	70.00	0.20	0.01	C4'', C9''	68.79	0.22	0.01
C6'', C7''	69.67	0.22	0.01	C6'', C7''	68.79	0.22	0.01
C2	65.12	0.51	0.01	C2	65.04	0.50	0.01
C1	40.55	0.40	0.01	C1	40.44	0.70	0.01

As molecules increase in size, they tumble less freely in solution, leading to an increase in correlation time and a corresponding decrease in the T_1 . Since most molecules lie either to the left of the T_1 minimum in Figure 55, this leads to a useful general rule that T_1 values decrease with increasing molecular weight.¹²¹

Figure 55: Relationship between correlation time of molecular motion and relaxation times

This assumption is only valid if the spin-lattice relaxation mechanism is dominated by the dipole-dipole mechanism. The amount of the relaxation by this mechanism can be determined by acquisition of an nOe suppressed spectrum and comparing it to the unsuppressed spectrum. The relaxation of all carbons with the exception of the quaternary aromatics is dominated by at least 90% dipole-dipole relaxation. The quaternary aromatic carbons, C1', C2' and C4', have very long T_1 's. The long delays necessary to study these carbons would cost too much in terms of spectrometer times so the T_1 's were not determined.

The addition of 1:1 LiClO_4 caused a significant decrease of all T_1 values of the molecule indicating an increase in the molecular weight of the molecule resulting in a longer correlation time. The addition of a second equivalent of LiClO_4 had very little effect on the T_1 s indicating that only a single lithium is bound to the two crown ether rings, probably in a sandwich type complex. The addition of $\text{Ba}(\text{ClO}_4)_2$ to the bis crown ether system caused a greater decrease in the T_1 s than did the LiClO_4 . This is in agreement of the expected results because $\text{Ba}(\text{ClO}_4)_2$ has a much higher molecular weight than LiClO_4 . The T_1 s are shown graphically in Figure 56.

Figure 56: Graphic depiction of T_1 values for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane alone (■) and complexed with LiClO_4 (1:2) (▒), LiClO_4 (1:1) (■), $\text{Ba}(\text{ClO}_4)_2$ (1:1) (▨) and $\text{Ba}(\text{ClO}_4)_2$ (1:2) (▩)

The T_1 experiments also served to answer the question as to whether the 1,2-diol on the bridge separating the two crown ether

moieties participates in the complexation process. As can be seen in Table 4 there is a significant difference in the chemical shift of the aromatic and ether carbons in the presence of the $\text{Ba}(\text{ClO}_4)_2$ showing that they are affected by the complexation of the neighboring oxygens. There is not a noticeable difference in the chemical shifts of the bridge carbons as would be expected if the diol was an active participant in binding to the barium. This is not terribly surprising based on their distance from the crown ether ring and the rigidity of the aromatic ring.

3.3.1 Synthesis of Deuteriated 18-crown-6 and 12-crown-4 Ethers

The details of the molecular motion of crown ethers in solids requires the use of deuteriated crown ethers. These previously unknown materials can be synthesized by existing methods for crown ether synthesis providing deuteriated starting materials are available. A convenient synthesis of 18-crown-6 involves the use of 1,8-dichloro-3,6-dioxaoctane and triethylene glycol¹²² (Figure 57).

Figure 57: Synthesis of 18-crown-6-d₄

In order to synthesize 18-crown-6-d₄ (**23**) one of these materials must be tetradeutero. Seeing that triethylene glycol is a precursor to 1,8-dichloro-3,6-dioxaoctane logic dictates that we prepare triethylene glycol-d₄. Glycols can easily be extended by -CH₂-CH₂-O- units by the treatment of ethylene oxide and base.¹²³ Ethylene oxide-d₄ (**16**) is commercially available (MSD Isotopes), making this a valuable method for our purposes. Diethylene glycol is converted into triethylene glycol-d₄ (**17**) by this method. As would be expected, however, this synthesis is not selective for just diethylene glycol and a mixture of glycols are produced. In order to statistically increase the amount of desired product a large excess of diethylene glycol is used. After the reaction this and any other glycols produced must be separated from the desired product. Seeing these glycols are liquids distillation would be the obvious choice for separation. Because the boiling points are fairly high, the distillation must be carried out under high vacuum. This, unfortunately, leaves a small difference in the boiling points of the materials and conventional fractional distillation failed to separate them. This problem was overcome by the use of spinning band distillation. The spinning band distillation apparatus has a fairly large volume so approximately 10 mL of the higher boiling tetraethylene glycol was added to ensure maximum recovery of the desired product. 18-crown-6-d₄ is then synthesized via the method of Gokel and coworkers¹²² for the protio analog.

Of the methods for the synthesis of 12-crown-4, two require the use of 1,8-dichloro-3,6-dioxaoctane and ethylene glycol. Liotta and coworkers¹²⁴ report a 13.2% yield for 12-crown-4 by the reaction of these starting materials in DMSO using sodium hydroxide as a base and

be placed on the diamond lattice as shown in Figure 59. As such, all bonds are considered to be tetrahedral. A reference frame is chosen for each case in which the z axis is parallel to one of the three fold axes on the diamond lattice and perpendicular to the molecular plane in the D_{3d} and solid 18-crown-6 conformations. The x axis is chosen as to pass through an oxygen atom, which then becomes O1 in the numbering scheme.

Figure 59: Representations of the D_{3d} , C_1 and solid 18-crown-6 conformations on the grid of the "diamond lattice". Solid lines represent bonds of the macrocycle on the "zero" grid and dashed lines bonds on the first grid above. Connections between the grids are made by vertical bonds (parallel to the z -axis). The numbering scheme begins with an oxygen on the x -axis.

In the case of C-D bonds it is generally a good approximation to place the principal ZZ axis of the electric field gradient tensor along the bond vector. This leads to a reasonable assumption that the YY or XX component of the tensor will be perpendicular to the CD₂ plane. We can then proceed to define the Euler angles necessary to rotate from the principal axis system of the tensor, for each C-D bond, to the reference frame. These are shown in Tables 4 to 6. The Euler angles are grouped in sets corresponding to the six sites which would be visited by a particular deuteron. There can be no exchange between the four sites within each of the six -O-CH₂-CH₂- units and hence there are four sets of six interchangeable deuteron positions. Furthermore the three conformations considered here all have a centre of symmetry, so these four sets fall into pairs of equivalent sets.

Table 5: Euler angles for the various sets of 6 exchanging C-D sites for 18-crown-6 complex with D_{3d} symmetry

Set 1				Set 2			
C* atom	α	β	γ	C* atom	α	β	γ
2	0	0	0	3	0	(180 + T _d)	60
5	0	(180 + T _d)	60	6	0	0	120
8	0	0	120	9	0	(180 + T _d)	180
11	0	(180 + T _d)	180	12	0	0	240
14	0	0	240	15	0	(180 + T _d)	300
17	0	(180 + T _d)	300	18	0	0	0

Table 6: Euler angles for the various sets of 6 exchanging C-D sites for 18-crown-6 complex with C_1 symmetry

Set 1				Set 2			
C* atom	α	β	γ	C* atom	α	β	γ
2	0	0	0	3	0	$(180 + T_d)$	60
5	120	$(180 + T_d)$	300	6	0	0	120
8	0	0	120	9	0	$(180 + T_d)$	180
11	0	$(180 + T_d)$	180	12	0	0	240
14	300	$(360 - T_d)$	240	15	0	$(180 + T_d)$	300
17	0	$(180 + T_d)$	300	18	0	0	0

Table 7: Euler angles for the various sets of 6 exchanging C-D sites for solid 18-crown-6

Set 1				Set 2			
C* atom	α	β	γ	C* atom	α	β	γ
2	0	0	0	3	0	$(180 + T_d)$	60
5	0	$(180 + T_d)$	60	6	0	0	120
8	0	T_d	180	9	0	$(180 + T_d)$	180
11	0	$(180 + T_d)$	180	12	0	0	240
14	0	0	240	15	0	$(180 + T_d)$	300
17	0	180	0	18	0	0	0

The values for the static tensor components derived from the low temperature spectrum of the malononitrile complex are: $\Delta\nu_{zz} = 246.1$ kHz, $\Delta\nu_{yy} = 131.8$ kHz, $\Delta\nu_{xx} = 114.3$ kHz, $\chi = 164.1$ kHz, and $\eta = 0.0711$ (Figure 60).

Figure 60: ^2H NMR spectrum of 18-crown-6- d_4 ·malononitrile complex at 198 K

Assuming these values the effective tensors averaged over the six sites can then be calculated for each of the sets in tables 4 to 6. In the Set 1 cases of C_1 and solid 18-crown-6 the averaged tensors were not diagonal in the chosen reference frame. In the special case of 3-fold reorientation of the D_{3d} molecule the exchanging sites must be subdivided into sets of three of which there are two distinct types: a) those with the C-D bond parallel to the rotation axis ($\beta = 0$) and b) those with the C-D bond at an angle of $\beta = (180 + T_d)$ where T_d is the tetrahedral angle of 109.5° . The resulting averaged spectral parameters are given in Table 8 and the corresponding lineshapes in Figure 61.

Table 8: Calculated fast motion limit lineshape components for the diamond lattice conformations. The calculations are based on the static lineshape components observed for the malononitrile complex.

	Spectrum Figure 61	$\Delta\nu_{zz}$ (kHz)	$\Delta\nu_{yy}$ (kHz)	$\Delta\nu_{xx}$ (kHz)	χ (kHz)	η
Static	A	246.1	131.8	114.3	164.1	0.0711
3-fold D _{3d} C + F $\Rightarrow$ B	F	246.1	123.05	123.05	164.1	0.0
6-site D _{3d}	C	78.14	39.07	39.07	52.1	0.0
6-site C _i C + G $\Rightarrow$ D	G	39.18	39.18	0.0	26.1	1.0
6-site solid 18-crown-6 C + F $\Rightarrow$ B	H	88.56	86.23	2.33	59.0	0.9474

Figure 61: Calculated static and fast motion limit ^2H NMR lineshapes. Parameters are given in Table 8. A: static, B: three-fold reorientation of D_{3d} conformation, C: six-site exchange of the D_{3d} , D: six-site exchange of C_1 , E: six-site exchange for solid 18-crown-6. B, D, and E are 1:1 composite lineshapes of C with F, G, and H respectively. The simulated spectra were convolved with Gaussian broadening function of halfwidth 5 kHz. The orientation of the static electric field gradient tensor with respect to the C-D bond is shown at the top right.

Clearly in most cases the two sets of sites average differently, which gives rise to the composite lineshapes B, D and E in Figure 61. For the six-site D_{3d} case Sets 1 and 2 average identically to give lineshape C, which is one component of all other cases. Three-fold reorientation of the D_{3d} conformation produces the very distinct lineshape B. In all of the other cases the lineshapes are considerably narrowed.

The ^2H NMR lineshape of non-complexed solid 18-crown-6- d_4 at ambient temperature, shown in Figure 62, appears to be unaveraged by molecular motion with $\chi = 157.6$ kHz and $\eta = 0.0661$. However, the observation that the intensity was rather low might be an indication that the lineshape is just beginning to show the effects of molecular averaging (jump rate about 10^3 to 10^4 Hz). Such motion was identified by a broadening of the ^{13}C resonances in the ^{13}C CP / MAS NMR spectrum.¹²⁶ The observed broadening must occur because the correlation time of the motion is approximately equal to the inverse of the chemical shift differences between the peaks leading to a jump rate of $\sim 7 \times 10^3$ Hz. Since the solid melts at about 312 K no further temperatures were investigated.

Figure 62: ^2H NMR lineshape of solid 18-crown-6- d_4 at 299 K.

For 18-crown-6• $2\text{CH}_2(\text{CN})_2$, a pseudo- D_{3d} case, however, fast motion limit lineshapes are clearly obtained by 350 K, as shown in Figure 63. From the static lineshape, which is observed below ~220 K, the intermediate lineshapes undergo pronounced changes in shape and intensity, narrowing to a single sharp line at room temperature, but then broadening up again and finally giving an axially symmetric line in the fast motion above 350 K. The 373 K lineshape shows that all of the deuterons are behaving in a similar manner, ruling out the three-site D_{3d} model but matching the prediction of the six-site D_{3d} model. However, the 373 K line is significantly narrower than predicted from the diamond-lattice model (see Table 9). This should not be surprising considering the distortions from the ideal symmetry. In fact, from the information given in the crystallographic study¹²⁷ one can calculate that, on average, the

C-D bonds are tilted off the diamond lattice bond by about 6° for the axial bonds and by about 4° for the equatorial bonds. Recalculating the average lineshape with these adjustments in the β Euler angles then produces an almost perfect match (Table 9)

Figure 63: ^2H NMR line shapes of 18-crown-6•2CH₂(CN)₂ as a function of temperature.

Table 9: Observed lineshape components for the 18-crown-6•2CH₂(CN)₂ complex compared with calculated values. The Euler angle $\beta = 0$ becomes 5.71° and $\beta = (180 + T_d)$ becomes 285.66°.

	$\Delta\nu_{zz}$ (kHz)	$\Delta\nu_{yy}$ (kHz)	$\Delta\nu_{xx}$ (kHz)	χ (kHz)	η
Static	246.1	131.8	114.3	164.1	0.0711
six-site D _{3d} diamond lattice calculated	78.14	39.07	39.07	52.1	0.0
Observed 373 K	69.6	34.8	34.8	46.4	0.0
Adjusted angles calculation	69.04	34.52	35.52	46.03	0.0

This is almost too good to be true, but further confirmation of the essential correctness of the model comes from a simulation of the intermediate rate lineshape. The calculations were performed using a considerably modified version of the program of Vega and Luz.⁷⁷ A jump matrix was constructed for jumps between adjacent sites and the adjusted β angles were used. The calculated lineshapes are shown in Figure 64.

Figure 64: Simulated ^2H NMR lineshapes for as a function of jump rate to adjacent $-\text{O}-\text{CH}_2-\text{CH}_2-$ sites.

The comparison between the simulation and experiment is again remarkable. Observed and calculated lineshapes were matched allowing a correlation of jump rate with temperature from which an Arrhenius plot (Figure 65) gives an activation energy, E_a , for the motion. An additional plot can be obtained for the temperature at which the echo amplitude is a minimum. A linear least squares fit gave $E_a = 47.6 \pm 0.8$ kJ/mole (correlation coefficient $R = 0.9986$). The rough estimate obtained from the ^{13}C CP/MAS fade-out temperature was about 39 kJ/mole.⁴²

Figure 65: Arrhenius plot of jump rate versus reciprocal temperature for 18-crown-6•2CH₂(CN)₂ obtained by matching experimental and simulated lineshapes. The point obtained for the echo intensity minimum is indicated by the circle.

The unusual narrowing and rebroadening of the line is reminiscent of the behaviour of the ^2H NMR spectra of cyclohexane C₆D₁₂ in a clathrate related to the Hofmann type clathrates,¹²⁸ where the

cyclohexane undergoes rapid n -fold reorientation followed by a slower inversion. In effect axial and equatorial deuterons exchange while the molecule reorients.

The results for the two C_1 cases, complexes with urea (5:1) and benzenesulphonamide (2:1), shown in Figures 66 and 67 respectively, also show considerable narrowing before melting, to widths less than those calculated for six-site exchange.

Figure 67: ^2H NMR lineshapes of 18-crown-6•5urea at low and high temperatures

Figure 67: ^2H NMR lineshapes of 18-crown-6•2phenylsulphonamide

Unfortunately detailed analysis of these lineshapes is not possible for a number of reasons:

- a) The urea complex has two inequivalent 18-crown-6 molecules¹²⁹, both C_1 , which is possibly a major complication responsible for our not being able to define the tensor components from the fast motion lineshape.
- b) The phenylsulphonamide complex lineshape is not quite in the fast motion limit at 360 K, indicated by a dependence of the lineshape on the quadrupole echo delay time.

c) Distortions from the ideal diamond lattice geometries are more severe in these cases. This may account for the observed lineshape not matching that predicted (See Figure 61 D)

d) The assumptions about the orientations of the quadrupole coupling tensor axes may not be strictly valid for the CD₂ groups at the site of the kinks in the C₁ conformation.

Nevertheless, it would be impossible for the degree of averaging observed to be brought about by any local site motion, so the lineshape still provide strong evidence for the reorientation of the whole macrocycle, complementary to the ¹³C NMR evidence.⁴²

In light of the low activation energies for the conformational changes in the free molecule,²² the activation energy for the motion in the solid complexes, some 40 - 50 kJ/mole, derive mainly from intermolecular contacts. The equilibrium structures therefore have individual O and CH₂ units librating in quite deep potential wells. On account of the Boltzman factor, molecules in the process of jumping (i.e. above the barrier) at any instant represent a very small fraction of the total and hence do not contribute significantly to diffraction. The librational motion in the potential wells does produce some elongation of the thermal ellipsoids along the ring, compare for example the structures of 18-crown-6•2CH₃NO₂ (pseudo-D_{3d}) at 123 K¹³⁰ and 295 K.¹³¹ For all purposes, therefore, the large amplitude of motion is invisible to diffraction methods.

A detailed analysis of solid 12-crown-4-d₄ could not be carried out because of the unusual absorbance in the centre of the doublet. This

absorbance may be due to water in the solid or some impurity which was invisible to the solution ^1H and ^{13}C NMR spectra. The ^2H NMR spectrum at 170 K is shown in Figure 68.

Figure 68: ^2H NMR of solid 12-crown-4- d_4 at 170 K

The 12-crown-4- d_4 - $\text{NaCl} \cdot 5\text{H}_2\text{O}$ complex exhibits a static lineshape at 242 K. As the temperature increases we begin to see a sharp isotropic line in the centre of the spectrum. At 377 K this peak dominates the spectrum. This indicates that the sample starts to melt or dissolve in the water of hydration before the fast motion limit is achieved preventing a detailed analysis of the motion. The ^2H NMR spectra as a function of temperature are shown in Figure 69.

Figure 69: ^2H NMR spectra of 12-crown-4- d_4 - $\text{NaCl}\cdot 5\text{H}_2\text{O}$ as a function of temperature

In the case of the 12-crown-4- d_4 -LiSCN complex we are able to obtain both static and fast limit motion spectra. A comparison of the calculated and observed electric field gradient tensors indicate the occurrence of two types of motion. These motions occur simultaneously so their effects cannot be distinguished. The macrocycle appears to rotate in a similar manner as did the 18-crown-6 and the $-\text{CH}_2-\text{CH}_2-$ groups flip such that the axial protons become equatorial and visa versa. The rotation of the ring is invisible to the X-ray diffraction but the flipping of the $-\text{CH}_2-\text{CH}_2-$ groups is not. It shows up as thermal vibrations or disorder in the crystal.³⁶ The ^2H NMR spectra as a function of temperature are shown in Figure 70.

Figure 70: ^2H NMR spectra of 12-crown-4- d_4 -LiSCN as a function of temperature

The spectra at 200.5 K (cooling) and 220 K (warming) correspond to a phase change. The fact that the phase change occurs at a different

temperature on cooling than on warming is indicative of a hysteresis. These results were confirmed by differential scanning calorimetry. Upon warming the phase change occurred at -57.1°C (218.4 K) accompanied by the absorption of 11.54 J/g (Figure 71). On cooling, however, the phase change did not occur until a temperature of -84.1°C (189.0 K) and it involved the release of 12.18 J/g (Figure 72). Both the absorption and release of energy should have the same values and the slight difference is due to experimental error. In both cases the temperature of the phase change occur at a slightly lower temperature than indicated by the ^2H NMR. This is likely due once again to experimental error in the determination of the temperature at which the spectra were obtained.

Figure 71: DSC plot of the phase change of 12-crown-4-d₄·LiSCN while heating

Figure 72: DSC plot of the phase change of 12-crown-4-d₄·LiSCN while cooling

Conclusions

The polymer of 4'-vinylbenzo-12-crown-4 and its copolymer with styrene are both far more effective at binding lithium, sodium and potassium than their monomeric analogues. The copolymer is slightly less effective than the homopolymer but more effective than either of the monomers by a factor of approximately 7, indicating that cooperative binding is likely. Sodium is the most efficiently extracted cation, followed by potassium and lithium. Polyvinylbenzo-12-crown-4 is approximately equal in its ability to extract lithium and sodium as are the polymers of vinylbenzo-15-crown-5 and vinylbenzo-18-crown-6 reported by Smid⁴³, however it is far less efficient for the extraction of potassium because of its size. The cooperative binding was confirmed for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane for both lithium and barium perchlorates supporting the idea that it exists in the polymer.

²H NMR has proven to be a useful tool for the study of molecular motion of crown ethers in solids. Both 18-crown-6 and 12-crown-4 rotate about the centre of the ring. In the complex with malononitrile the macrocycle experiences a 6-site exchange and the conformation of the -O-CH₂-CH₂- groups adjust to fit the conformation of the site visited, a motion analogous to that of a merry-go-round. In the case of the 12-crown-4·LiSCN complex the rotation of the macrocycle is accompanied by a rapid flipping of the -CH₂-CH₂- groups. These two motions occur simultaneously in the solid.

Experimental

4.1 General

^1H spectra were recorded on a Varian Gemini 200 spectrometer at 200 MHz. Unless stated otherwise samples were run in CDCl_3 with TMS used as an internal reference.

^2H NMR powder spectra were recorded on a Bruker CXP 180 spectrometer at 27.63 MHz, at various temperatures using a variable temperature N_2 gas-flow probe with a Bruker B-VT-1000 temperature controller. A phase alternated quadrupole echo pulse sequence⁸² was used with a delay time of 35 μs between X and Y pulses of 2.6 - 3.0 μs .

^{13}C solution NMR spectra were obtained on a Varian Gemini 200 spectrometer at 50.3 MHz. Unless stated otherwise samples were run in CDCl_3 with TMS used as an internal reference. ^{13}C spin-lattice relaxation times were determined using the inversion recovery method^{132,133} with delay times, τ , of 0.01, 0.5, 0.75, 1.0, 2.0, 3.0, 5.0 and 10.0 seconds

Solid state ^{13}C NMR were obtained on a Bruker CXP 180 spectrometer at 45.3 MHz, at various temperatures using high pressure dry N_2 gas, a dry ice heat exchanger and a Bruker B-VT-1000 temperature controller. The Cross Polarization / Magic Angle Spinning (CPMAS) technique was employed. Unless stated otherwise, cross polarization times were 1-5 ms and recycle times ranged from 1-20 seconds depending on sample and temperature. Samples were prepared in 7 mm sapphire or zirconium rotors with Kel-F caps in a Doty Scientific

Magic Angle Spinning Probe with spinning rates of 4-5.5 kHz. Chemical shifts were measured relative to external solid hexamethylbenzene (HMB) and converted to the TMS scale via the factor of 16.9 ppm, which is the chemical shift of the methyl group of HMB.

IR spectra were obtained on a Perkin Elmer 1600 Series Fourier Transform Infrared Spectrometer. Oils were analyzed neat on NaCl plates and solid materials were analyzed in KBr pellets.

Mass spectra 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.

Differential scanning calorimetry was performed using a DuPont DSC 10 differential scanning calorimeter model 10 couples to a DuPont 2100 Thermal Analyzer with a heating rate of 10 °C per minute from -145 °C to 20°C and a cooling rate of ~10 C per minute from -20 °C to -120 °C and a Nitrogen flow rate of 50 mL per minute. Samples were analyzed in crimped aluminum sample pans with an empty crimped pan used as a blank.

4.2 Monomers, Dimers and Polymers: Synthesis and Properties

Synthesis of 4'-Formylbenzo-12-Crown-4

A 3L, 3 neck round bottom flask, equipped with a magnetic stirrer and reflux condenser was charged with 1-butanol (2.0 L), 3,4-dihydroxybenzaldehyde (13.84g, 0.10 mol), 1,8-dichloro-3,6-dioxaoctane (18.76g, 0.10 mol), and lithium hydroxide (4.79g, 0.20 mol) and the

mixture was refluxed for 10 days. The solvent was removed by evaporation at reduced pressure and the resultant black slurry was dissolved in dichloromethane (500 mL). The water soluble salts were removed by filtration and subsequently washed with an additional 100 mL dichloromethane. The combined organics were washed with HCl (1 M, 3 x 100 mL), water (3 x 100 mL) and saturated sodium chloride (1 x 100 mL) then dried over anhydrous sodium sulfate. The solvent was removed by evaporation at reduced pressure and the resultant black slurry was purified by column chromatography on silica gel (grade 923, 100-200 mesh) with 40% ethyl acetate in hexane as eluent. Three products, as well as starting material, were isolated. These were the desired product, its dimer, and the uncyclized mono adduct.

4'-formylbenzo-12-crown-4 :

yield: 3.71 g, 14.72%. m.p: 81-82°C.

¹H NMR: 9.84 (1H s), CHO; 7.5 - 7.0 (3H m), aromatic H; 4.38 - 3.79 (12H m), CH₂. IR: 1685.2 cm⁻¹. CHO.

¹³C NMR: 190.6, CHO; 156.5, 150.7, 131.1, 127.3, 118.2, 116.1, aromatic C; 72.7, 71.3, 70.8, 70.7, 69.6, 69.4, O-CH₂-CH₂-O.

MS: M⁺, 252; other peaks at 164, 149, 45.

Elemental Analysis: Calculated; C: 61.90, H: 6.39, Found; C: 61.66, H: 6.64

Dimer:

Obtained as a byproduct in the preparation of 4'-formylbenzo-12-crown-4

yield: 0.63g, 5.0 %. m.p :134 - 136 °C.

^1H NMR: 9.84 (1H s), CHO; 7.5 - 7.0 (3H m), aromatic H; 4.38 - 3.79 (12H m), O-CH₂-CH₂-O. IR: 1685.2 cm⁻¹. CHO.

^{13}C NMR: 190.8, CHO; 154.1, 159.0, 130.1, 126.8, 111.7 110.8, aromatic C; 71.49, 71.40, 69.61, 69.44, 69.37, 69.30, O-CH₂-CH₂-O.

CIMS: M⁺, 505; other peaks at 149, 45.

Preparation of Triphenylmethyl Phosphonium Bromide

The triphenyl methyl phosphonium bromide was prepared by the method outlined by Vogel¹³⁴. Triphenyl phosphine (34.11 g, 0.13 mol) was dissolved in dry benzene (30 mL) in a stout walled jar and cooled in a salt water-ice bath. Methyl bromide in hexane (2.0 molar, 85 mL, 0.175 mol) was added dropwise via disposable syringe. The mixture was set aside for 44 hours, cooled in and ice bath then filtered. The product was washed with hot benzene, dried in an oven at 110°C and stored in a vacuum desiccator.

Yield: 44.98 g (98%) m.p. 231-233°C.

Preparation of 4'-vinylbenzo-12-crown-4

A dry 500 mL, 3 neck round bottom flask, equipped with a magnetic stirrer, reflux condenser and dropper funnel was charged with 1,2-dimethoxyethane (60 mL) and triphenyl methyl phosphonium bromide (6.32 g, 17.70 mmol). n-Butyllithium (1.6 M in hexane, 11.2 mL, 17.70 mmol) was added dropwise over a period of 10 minutes. The mixture turned orange and was stirred for an additional 90 minutes. 4'-Formylbenzo-12-crown-4 (2.98 g, 11.80 mmol) was dissolved in 100 mL of 1,2-dimethoxyethane and added dropwise over a period of 60 minutes.

The resultant suspension was refluxed for 20 hours, then cooled to room temperature. It was filtered and the filter cake was washed with ether (3 x 30 mL). The combined organics were washed with water (3 x 100 mL) followed by saturated sodium chloride (1 x 100 mL) then dried over anhydrous sodium sulfate and the solvent was removed by evaporation at reduced pressure. The resultant slurry was left at room temperature causing triphenylphosphine oxide to crystallize out as colourless prisms. The remaining oil was purified by flash chromatography on silica gel (grade 923, 100-200 mesh) using 40% ethyl acetate in hexane as the solvent.

4'-vinylbenzo-12-crown-4 :

yield 1.85g, 62.6%

^1H NMR: 7.045 δ (d), $\text{H}_{3'}$; 6.9803 δ (dd), $\text{H}_{5'}$; 6.8965 δ (d), $\text{H}_{6'}$; 6.02 δ (dd), H_a ; 5.588 δ (dd), H_c ; 5.137 δ (dd), H_b ; 4.194-4.142 δ and 3.855-3.766 δ (m), O-CH₂-CH₂-O. J_{ab} = 10.8 Hz, J_{ac} = 17.53 Hz, J_{bc} = 0.87 Hz, $J_{3'5'}$ = - 2.17 (1.95) Hz, $J_{3'6'}$ = not seen, $J_{5'6'}$ = - 5.52 (8.22) Hz

^{13}C NMR: 150.5, $\text{C}_{1'}$, $\text{C}_{2'}$; 136.2 δ , vinyl methine; 132.5 δ , C_4 ; 121.1 δ , C_5 ; 117.7 δ , C_6 ; 115.7 δ , C_3 ; 112.5 δ , vinyl methylene; 71.8 δ , 71.6 δ , 70.8 δ , 70.1 δ , 69.7 δ (relative intensity 2), OCH₂-CH₂O.

CIMS: $\text{M}+1$; 251 (100%), other peaks at 164, 149, 45.

Polymerization of 4'-Vinylbenzo-12-Crown-4⁴³

4'-vinylbenzo-12-crown-4 (1.00 g, 4.0 mmol) and ABIN (azobis(isobutyronitrile)) (0.0051 g), a radical initiator were dissolved in benzene (60 mL) and degassed using a high vacuum and four freeze-

pump-thaw cycles. The ampoule was sealed under vacuum and heated to 70° for 48 hours. The solution was then slowly added to approximately 20 times its volume of petroleum ether and the white precipitate was filtered off. The polymer was reprecipitated once again and dried under vacuum. The polymer had an M_n of 3,800 and a M_w of 5,500 as determined by gel permeation chromatography.

Yield: 96%. m.p.: 115-133°C.

^1H NMR: 6.62d-6.11δ (3H), aromatic H; 4.2-3.6δ (12H), O-CH₂-CH₂-O; 1.16-2δ (3H), benzylic CH, CH₂.

^{13}C NMR: 149.9, 148.2, 140.2, 128.3, 121.7, 117.9δ; aromatic C; 71.6-69.8δ, O-CH₂-CH₂-O; 40.2δ; benzylic CH, CH₂.

Copolymer

The copolymer was also prepared by the same procedure using equimolar quantities of 4'-vinylbenzo-12-crown-4 and styrene with the same ratio of initiator. The polymer had an M_n of 2,700 and a M_w of 3,500 as determined by gel permeation chromatography.

Yield: 92%. m.p.: 118-134 °C.

^{13}C NMR (APT): 152.2δ, 149.4δ, 147.6-144.8δ, 142.5-139.6δ, quaternary aromatic; 127.9, 125.6δ, 121.7δ, 118.8δ, tertiary aromatic; 71.6-69.8δ, O-CH₂-CH₂-O; 40.5-40.1δ, benzylic CH, CH₂.

Extractions

A metal hydroxide solution (0.01 M) containing a small amount of picric acid ($7 \times 10^{-5}\text{M}$) was vigorously shaken with an equal volume of methylene chloride solution of the crown ether. Molar ratios of 0, 1, 3, 5, 7, 10, 15, 20, and 25 of crown ether to picrate were employed. The layers

were separated and filtered to remove cloudiness. The concentration of picrate was determined by visible spectroscopy using the extinction coefficients reported by Pedersen¹³⁵ (λ_m 357 nm, ϵ 1.5×10^4 in water and λ_m 378 nm, ϵ 1.8×10^4 in CH_2Cl_2). The results are shown in Tables 10 - 13.

Table 10: Polyvinylbenzo-12-crown-4 Extractions

[Crown] / [Picrate]	Picrate Extracted (%)		
	Potassium	Sodium	Lithium
0	0	0	0
1	0.98	1.58	0.91
3	3.33	6.41	1.90
5	5.22	9.65	3.19
7	6.21	12.97	4.10
10	7.27	17.27	5.09
15	10.75	23.08	6.76
20	14.46	27.25	7.21
25	21.80	33.64	9.04

Table 11: Copolymer Extractions

[Crown] / [Picrate]	Picrate Extracted (%)		
	Potassium	Sodium	Lithium
0	0	0	0
1	1.29	2.32	0.52
3	3.42	6.22	1.33
5	4.86	9.52	1.78
7	6.68	12.36	2.59
10	8.13	15.66	3.33
15	10.33	21.36	4.22
20	13.14	26.08	5.7
25	14.28	29.82	6.36

Table 12: Benzo-12-crown-4 Extractions

[Crown] / [Picrate]	Picrate Extracted (%)		
	Potassium	Sodium	Lithium
0	0	0	0
1	0.16	0.18	0.25
3	0.24	0.27	0.50
5	0.40	0.46	0.66
7	0.48	0.73	0.75
10	0.64	1.10	0.91
15	0.81	1.19	1.00
20	1.13	1.64	1.08
25	1.45	2.10	1.16

Table 13: 12-Crown-4 Extractions

[Crown] / [Picrate]	Picrate Extracted (%)		
	Potassium	Sodium	Lithium
0	0	0	0
1	0	0.30	0.08
3	0.15	0.90	0.33
5	0.30	1.57	0.42
7	0.53	2.02	0.58
10	0.61	2.85	0.66
15	0.76	3.75	0.83
20	0.91	4.72	1.58
25	1.06	5.92	1.74

Synthesis of 2-(4'-benzo-12-crown-4)-ethanol (9)

A dry 100 mL three-neck round bottom flask equipped with a magnetic stirrer, reflux condensor and septum inlet was charged with 4'-vinylbenzo-12-crown-4 (1.0 g, 3.995 mmol) and dry THF (25 mL). The solution was stirred and kept under a steady flow of argon. Borane•THF

(1.0 M, 2.0 mL, 2.0 mmol) was added through the septum via a disposable syringe over a period of twenty minutes. The solution was kept at 20°C and stirred for 1 hour, refluxed for four hours then cooled to 0°C with an ice water bath. Sodium hydroxide (0.5 mL, 3M) and hydrogen peroxide (30%, 0.5 mL) were added and the reaction was stirred at 0°C for one hour. The mixture was added to a separatory funnel containing water (50 mL) and extracted with dichloromethane (3 x 50 mL). The combined organics were dried over sodium sulfate and the solvent was removed at reduced pressure by rotary evaporation. The remaining oil was purified by flash chromatography on silica gel (grade 923, 100-200 mesh) using 40% ethyl acetate in hexane as the solvent.

2-(4'-benzo-12-crown-4)-ethanol (9):

yield: 1.85g, 30.8%

¹H NMR (Varian EM 360, 60 MHz): 7.0-6.64δ (d), Aromatic H; 4.3-4.0δ and 3.93-3.61δ (m), O-CH₂-CH₂-O and PhCH₂CH₂OH; 2.83δ (bs), PhCH₂CH₂OH; 2.72δ (t, J = 7 Hz), PhCH₂CH₂OH

¹³C NMR: 151.51, 148.96, 133.52, 121.11, 118.42, 118.14 C_{1'}, C_{2'}, C_{4'}, C_{5'}, C_{6'}, C_{3'}; 72.06, 71.49, 71.14, 71.03, 69.93δ (relative intensity 2), OCH₂-CH₂O; 63.47δ, PhCH₂CH₂OH; 38.65δ, PhCH₂CH₂OH.

CIMS: M+1; 269 (68%), other peaks at 251, 149.

Synthesis of 1-bromo-2-(4'-benzo-12-crown-4)-ethane (10)¹³⁶

2-(4'-benzo-12-crown-4)-ethanol (.549 g, 2.10 mmol) and triphenylphosphine (1.65 g 6.3 mmol) were dissolved in dry THF (25 mL) in a 50 mL three neck round bottom flask equipped with a magnetic

stirrer and reflux condensor and kept under a steady flow of argon. Zinc bromide (0.472 g, 2.1 mmol) and Diethylazodicarboxylate (DEAD) (1.1 g, 6.3 mmol) were dissolved in dry THF (5 mL) and added to the reaction vessel. The solution, originally transparent orange, started turning translucent (opaque) yellow. It was stirred at room temperature for 30 minutes, added to a separatory funnel containing 150 mL of water and extracted with dichloromethane (4 x 50 mL). The combined organics were dried over sodium sulfate and the solvent was removed at reduced pressure by rotary evaporation. The remaining oil was purified by flash chromatography on silica gel (grade 923, 100-200 mesh) using 40% ethyl acetate in hexane as the solvent.

1-bromo-2-(4'-benzo-12-crown-4)-ethane (10):

yield: 1.81g, 87.3%. m.p. 56-58°C

¹H NMR: 6.804d (d), **H_{3'}**; 6.767d (dd), **H_{5'}**; 6.897d (d), **H_{6'}**; 3.071δ (t), PhCH₂CH₂Br; 3.320δ (t), PhCH₂CH₂Br; 4.194-4.137δ and 3.875-3.788δ (m), O-CH₂-CH₂-O. $J_{ab} = 7.7$ Hz, $J_{3'5'} = \sim 2.06$ Hz, $J_{3'6'}$ = not seen, $J_{5'6'} = 8.04$ Hz

¹³C NMR: 151.01, 149.37, **C_{1'}**, **C_{2'}**; 133.97, **C_{4'}**; 123.16, **C_{6'}**; 118.18, 118.66, **C_{3'}**, **C_{5'}** 72.3δ, 72.1δ, 71.6δ, 71.5δ, 70.3δ (relative intensity 2), OCH₂-CH₂O; 39.34δ, PhCH₂CH₂Br; 33.45δ, PhCH₂CH₂Br.

CIMS: M+1; 331 (68%), other peaks at 251, 149.

Synthesis of 1,4-di(4'-benzo-12-crown-4)butane (14)¹¹⁵

A 50 mL neck round bottom flask equipped with a magnetic stirrer, heating mantle and reflux condensor was charged with diglyme (5 mL)

and sodium borohydride (0.106 g 20% excess over 2.2 mmol) and stirred until the sodium borohydride dissolved. 4'-vinylbenzo-12-crown-4 (2.34 g, 9.23 mmol) was added in one portion followed by a dropwise addition of boron trifluoride•etherate. This caused the formation of a white gummy precipitate, likely a crown ether / BF₃ complex. Additional diglyme (5 mL) was added and the mixture was refluxed until the precipitate dissolved (~ 4 hrs.). The reaction was cooled to 0°C using an ice bath. Aqueous potassium hydroxide (2.0 M, 11.2 mL) and aqueous silver nitrate (5.0 M, 2.24 mL) were added in succession turning the mixture black. It was allowed to reach room temperature and stirred for 12 hours. The mixture was filtered by gravity, added to a separatory funnel containing H₂O (300 mL) and extracted with CH₂Cl₂ (4 x 100 mL). The combined organics were dried over sodium sulfate and the solvent was removed at reduced pressure (aspirator) by roto-evaporation. The remaining oil was purified by flash chromatography using 30% ethyl acetate in dichloromethane to remove the first compound (4'-ethylbenzo-12-crown-4) and 100 % ethyl acetate to elute the rest.

Two products were isolated from this reaction, 4'-ethylbenzo-12-crown-4 and 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane.

4'-ethylbenzo-12-crown-4 (16):

yield: 0.24 g, 9.57%.

¹H NMR: 7.88d (d), H_{6'}; 6.72δ (dd), H_{5'}; 6.67d (d), H_{6'}; 2.49δ (t), PhCH₂CH₃; 1.12δ (t), PhCH₂CH₃; 4.11-4.05δ and 3.80-3.72δ (m), O-CH₂-CH₂-O J_{ab} = 7.65 Hz, J_{3'5'} = ~ 2.1 Hz, J_{3'6'} = not seen, J_{5'6'} = 7.88 Hz

^{13}C NMR: 150.58, 148.48, 139.21, 121.76, 118.46, 118.18, 117.57 C_2' , C_1' ; C_4' , C_5' , C_3' , C_6' ; 71.57 δ , 71.42 δ , 71.6 δ , 71.28 δ , 70.06 δ (relative intensity 2), $\text{OCH}_2\text{-CH}_2\text{O}$; 28.37 δ , PhCH_2CH_3 ; 15.64 δ , PhCH_2CH_3 .

CIMS: $\text{M}+1$; 253 (34.4%), other peaks at 149.

1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane(15):

yield: 0.56 g, 22.4%.

^1H NMR: 6.91d (d), H_6' ; 6.82 δ (dd), H_5' ; 6.77d (d), H_6' ; 4.11-4.05 δ and 3.80-3.72 δ (m), $\text{O-CH}_2\text{-CH}_2\text{-O}$ and $\text{PhCH}_2\text{CHOH-}$; 2.77 δ (t), $\text{PhCH}_2\text{CHOH-}$; 1.89 δ (bs), $\text{PhCH}_2\text{CHOH-}$.

^{13}C NMR: 150.56, 149.07, 133.35, 123.01, 118.59, 118.48, 117.57 C_2' , C_1' ; C_4' , C_5' , C_3' , C_6' ; 73.81, 73.27, 72.67 (relative intensity 2), 71.61 δ (relative intensity 2), $\text{OCH}_2\text{-CH}_2\text{O}$; 63.60 δ , $\text{PhCH}_2\text{CHOH-}$; 38.65 δ , $\text{PhCH}_2\text{CHOH-}$.

FTIR: 3382.1 cm^{-1} R-OH

CIMS: $\text{M}+1$; 537 (68%), other peaks at 295, 269 (100%), 149(100%).

Analysis: Calculated; C-62.9%, H-7.62%, O-25.42%, Found; C-59.48%, H-7.50%

The reaction was repeated on a slightly larger scale using the commercially available borane•THF complex (Aldrich) instead of generating this reagent in situ. 4'-Vinylbenzo-12-crown-4 (5.0 g, 20.0 mmol) was dissolved in THF (25 mL) under a steady flow of argon in a 250 mL three neck round bottom flask equipped with septum gas inlets, a magnetic stirrer and reflux condensor. The reaction vessel was cooled to 0 °C in an ice bath and borane•THF in THF (1.0 M, 7.33 mL, 7.33 mmol, 10% excess) was added dropwise via a disposable syringe. The

solution was stirred at 0 °C for 1 hour, warmed to room temperature and stirred for an additional hour. The reaction was cooled to 0 °C. Potassium hydroxide (2.0 M, 24 mL) and silver nitrate (5.0 M, 4.8 mL) were added and the reaction was stirred for one hour at 0 °C and one hour at room temperature. The mixture was filtered by gravity and the residue was washed with CH₂Cl₂ (3 x 50 mL) and water (2 x 50 mL). The phases were separated and the aqueous phase was washed with additional CH₂Cl₂ (3 x 50 mL). The combined organics were dried over sodium sulfate and the solvent was removed at reduced pressure (aspirator) by roto-evaporation. The remaining oil was purified by flash chromatography. The polarity of the solvent was gradually increased from 30% ethyl acetate in dichloromethane to 100 % ethanol. Four products and some polymeric material were isolated and identified. Two of the products were identical to those isolated in the previous reaction and the other two were 1,4-(4'-benzo-12-crown-4)-butane and 1-(4'-benzo-12-crown-4)-ethanol

4'-ethylbenzo-12-crown-4 (16):

Yield: 0.80 g. 16 %

Spectral Data: See Above

1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane (15):

Yield: 1.63 g. 30.5 %

Spectral Data: See Above

1,4-(4'-benzo-12-crown-4)-butane (14):

Yield: 0.47 g. 18.8 %

^1H NMR: 6.88d (d), H_6 ; 6.77 δ (d), H_5 ; 6.73 (d), H_6 ; 4.11-4.05 δ and 3.80-3.72 δ (m), $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$; 2.54 δ (m), $\text{PhCH}_2\text{CH}_2-$; 1.60 δ (m), $\text{PhCH}_2\text{CH}_2-$; $J_{3'5'} = 1.97$ Hz, $J_{3'6'}$ = not seen, $J_{5'6'} = 7.88$ Hz

^{13}C NMR: 150.42, 148.62, 137.41, 122.31, 118.59, 118.28, 117.94 $\text{C}_{2'}$, $\text{C}_{1'}$; $\text{C}_{4'}$, $\text{C}_{5'}$, $\text{C}_{3'}$, $\text{C}_{6'}$; 72.08, 71.11, 70.97, 69.89 δ (relative intensity 2), $\text{OCH}_2-\text{CH}_2\text{O}$; 35.23 δ , $\text{PhCH}_2\text{CH}_2-$; 30.99 δ , $\text{PhCH}_2\text{CH}_2-$.

CIMS: $\text{M}+1$; 503 (17.4%), other peaks at 149(100%).

Analysis: Calculated; C-66.91%, H-7.16%, O-29.93%, Found; C-65.33%, H-7.62%

1-(4'-benzo-12-crown-4)-ethanol (18):

Yield: 0.32 g, 6.0 %

^1H NMR: 7.01 - 6.89 δ Aromatic H ; 4.22-4.10 δ and 3.85-3.70 δ (m), $\text{O}-\text{CH}_2-\text{CH}_2-\text{O}$; 4.80 δ (q, $J = 6.45$ Hz), PhCHOHCH_3 ; 2.39 δ (bs), PhCHOHCH_3 ; 1.44 δ (d, $J = 6.45$ Hz), PhCHOHCH_3

^{13}C NMR: 150.63, 149.68, 140.88, 119.52, 118.10, 118.48, 115.03 $\text{C}_{2'}$, $\text{C}_{1'}$; $\text{C}_{4'}$, $\text{C}_{5'}$, $\text{C}_{6'}$, $\text{C}_{3'}$; 72.02, 71.53, 71.21, 71.10, 69.93 δ (relative intensity 2), $\text{OCH}_2-\text{CH}_2\text{O}$; 69.85 δ , PhCHOHCH_3 ; 25.15 δ , PhCHOHCH_3 .

FTIR: 3416.9 cm^{-1} R-OH

CIMS: $\text{M}+1$; 269 (36.4%), other peaks at 251(100%), 149(100%).

In order to study the complexation of 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane T_1 values were obtained by the inversion recovery method for the crown ether alone and combined with LiClO_4 (1 : 1).

LiClO_4 (1 : 1) and $\text{Ba}(\text{ClO}_4)_2$ (1 : 1). In all cases the crown ether (~100 mg) was dissolved in CH_3OD (~0.2 mL) and the appropriate amount of perchlorate was added. The solutions were degassed by bubbling argon through them. τ values of 0.01, 0.5, 0.75, 1.0, 2.0, 3.0, 5.0 and 10.0 seconds were used. The T_1 data are shown in Tables 14-18.

Table 14: T_1 data for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane in methanol-OD.

Peak #1 $T_1 = 21.186$ s		Peak #2 $T_1 = 18.7$ s		Peak #3 $T_1 = 11.4$ s		Peak #4 $T_1 = 1.1$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-17.3	0.00	-16.5	0.00	-25.7	0.00	-50.7
0.50	-16.0	0.50	-14.7	0.50	-22.0	0.50	-8.2
0.75	-13.2	0.75	-13.7	0.75	-20.2	0.75	7.3
1.00	-14.0	1.00	-12.8	1.00	-18.4	1.00	19.6
2.00	-9.7	2.00	-9.3	2.00	-11.7	2.00	49.1
3.00	-7.2	3.00	-5.9	3.00	-5.5	3.00	61.1
5.00	0.74	5.00	0.28	5.00	5.5	5.00	68.0
10.00	14.0	10.00	13.2	10.00	25.3	10.00	69.4
Peak #5 $T_1 = 1.342$ s		Peak #6 $T_1 = 1.298$ s		Peak #7 $T_1 = 0.802$ s		Peak #8 $T_1 = 0.808$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-49.6	0.00	-48.7	0.00	-45.2	0.00	-43.4
0.50	-12.0	0.50	-10.5	0.50	6.1	0.50	7.0
0.75	2.6	0.75	3.62	0.75	22.5	0.75	22.6
1.00	13.9	1.00	15.2	1.00	33.5	1.00	34.2
2.00	44.0	2.00	44.1	2.00	56.6	2.00	56.4
3.00	57.1	3.00	56.9	3.00	63.3	3.00	62.8
5.00	68.7	5.00	67.4	5.00	66.3	5.00	65.9
10.00	72.0	10.00	70.8	10.00	66.5	10.00	67.5
Peak #9 $T_1 = 0.765$ s		Peak #10 $T_1 = 0.795$ s		Peak #11 $T_1 = 1.174$ s		Peak #12 $T_1 = 1.062$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-66.6	0.00	-49.6	0.00	-41.2	0.00	-40.7
0.50	13.4	0.50	-12.0	0.50	-5.3	0.50	-1.6
0.75	37.3	0.75	2.6	0.75	7.1	0.75	12.7
1.00	54.9	1.00	13.9	1.00	17.1	1.00	24.4
2.00	87.6	2.00	44.0	2.00	43.5	2.00	49.4
3.00	97.3	3.00	57.1	3.00	53.2	3.00	58.8
5.00	100.5	5.00	68.7	5.00	60.7	5.00	65.1
10.00	102.3	10.00	140.6	10.00	62.0	10.00	66.0

Table 15: T_1 data for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane complexed with LiClO_4 (1:1) in methanol-OD.

Peak #1 $T_1 = 14.8$ s		Peak #2 $T_1 = 14.0$ s		Peak #3 $T_1 = 8.3$ s		Peak #4 $T_1 = 0.77$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-22.3	0.00	-20.9	0.00	-29.5	0.00	-45.9
0.50	-19.6	0.50	-18.7	0.50	-24.8	0.50	7.3
0.75	-18.7	0.75	-17.1	0.75	-22.0	0.75	23.4
1.00	-16.9	1.00	-16.0	1.00	-20.1	1.00	34.9
2.00	-11.7	2.00	-11.6	2.00	-11.2	2.00	56.0
3.00	-7.3	3.00	-7.1	3.00	-3.9	3.00	61.7
5.00	4.3	5.00	3.8	5.00	14.8	5.00	65.8
10.00	21.3	10.00	18.9	10.00	34.8	10.00	66.6
Peak #5 $T_1 = 0.9$ s		Peak #6 $T_1 = 0.9$ s		Peak #7 $T_1 = 0.5$ s		Peak #8 $T_1 = 0.5$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-49.4	0.00	-47.9	0.00	-42.5	0.00	-42.1
0.50	2.8	0.50	3.8	0.50	22.2	0.50	23.3
0.75	19.2	0.75	20.9	0.75	37.2	0.75	38.8
1.00	31.9	1.00	33.2	1.00	47.1	1.00	48.8
2.00	57.4	2.00	58.8	2.00	60.4	2.00	61.8
3.00	64.9	3.00	67.0	3.00	62.5	3.00	63.4
5.00	70.9	5.00	71.4	5.00	64.9	5.00	66.8
10.00	71.4	10.00	72.1	10.00	65.5	10.00	66.4
Peak #9 $T_1 = 0.5$ s		Peak #10 $T_1 = 0.6$ s		Peak #11 $T_1 = 0.8$ s		Peak #12 $T_1 = 0.7$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-64.1	0.00	-86.8	0.00	-37.2	0.00	-38.0
0.50	37.8	0.50	45.9	0.50	4.5	0.50	12.1
0.75	61.6	0.75	78.7	0.75	18.8	0.75	26.9
1.00	75.4	1.00	99.2	1.00	29.3	1.00	37.4
2.00	94.0	2.00	128.4	2.00	48.3	2.00	56.7
3.00	96.2	3.00	132.6	3.00	53.9	3.00	61.0
5.00	100.2	5.00	139.4	5.00	58.9	5.00	64.8
10.00	101.7	10.00	140.5	10.00	59.0	10.00	65.4

Table 16: T_1 data for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane complexed with LiClO_4 (1:2) in methanol-OD.

Peak #1 $T_1 = 14.7$ s		Peak #2 $T_1 = 14.7$ s		Peak #3 $T_1 = 7.2$ s		Peak #4 $T_1 = 0.7$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-30.0	0.00	-28.5	0.00	-40.4	0.00	-62.6
0.50	-26.1	0.50	-24.7	0.50	-33.8	0.50	10.7
0.75	-24.1	0.75	-21.8	0.75	-31.0	0.75	31.8
1.00	-23.0	1.00	-21.0	1.00	-26.8	1.00	42.3
2.00	-16.4	2.00	-15.4	2.00	-15.1	2.00	75.6
3.00	-10.9	3.00	-10.1	3.00	-5.1	3.00	82.0
5.00	4.9	5.00	3.2	5.00	18.4	5.00	84.2
10.00	26.2	10.00	23.4	10.00	42.7	10.00	83.9
Peak #5 $T_1 = 0.8$ s		Peak #6 $T_1 = 0.8$ s		Peak #7 $T_1 = 0.6$ s		Peak #8 $T_1 = 0.5$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-66.2	0.00	-68.1	0.00	-53.3	0.00	-54.4
0.50	4.0	0.50	5.9	0.50	28.9	0.50	30.3
0.75	26.4	0.75	28.1	0.75	47.9	0.75	50.3
1.00	44.2	1.00	45.8	1.00	61.1	1.00	63.0
2.00	79.2	2.00	81.5	2.00	77.6	2.00	78.8
3.00	87.4	3.00	90.6	3.00	80.2	3.00	81.0
5.00	91.0	5.00	94.4	5.00	78.5	5.00	81.6
10.00	91.4	10.00	93.5	10.00	78.5	10.00	60.3
Peak #9 $T_1 = 0.5$ s		Peak #10 $T_1 = 0.5$ s		Peak #11 $T_1 = 0.8$ s		Peak #12 $T_1 = 0.7$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-84.0	0.00	-115.0	0.00	-50.0	0.00	-51.2
0.50	53.3	0.50	61.9	0.50	7.4	0.50	15.1
0.75	81.2	0.75	106.2	0.75	25.6	0.75	35.1
1.00	100.4	1.00	131.8	1.00	38.8	1.00	49.5
2.00	124.1	2.00	169.2	2.00	65.5	2.00	74.5
3.00	125.3	3.00	172.8	3.00	71.6	3.00	79.7
5.00	125.2	5.00	173.5	5.00	74.2	5.00	80.5
10.00	123.7	10.00	173.0	10.00	74.4	10.00	82.1

Table 17: T_1 data for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane complexed with $\text{Ba}(\text{ClO}_4)_2$ (1:1) in methanol-OD.

Peak #1 $T_1 = 6.5$ s		Peak #2 $T_1 = 6.5$ s		Peak #3 $T_1 = 3.7$ s		Peak #4 $T_1 = 0.3$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-29.3	0.00	-28.1	0.00	-33.3	0.00	-34.9
0.50	-23.1	0.50	-22.8	0.50	-22.6	0.50	33.7
0.75	-20.3	0.75	-20.2	0.75	-18.2	0.75	44.6
1.00	-18.0	1.00	-18.7	1.00	-14.0	1.00	49.0
2.00	-8.0	2.00	-8.1	2.00	1.5	2.00	53.6
3.00	0.5	3.00	1.0	3.00	12.4	3.00	53.9
5.00	18.2	5.00	17.2	5.00	33.4	5.00	54.1
10.00	36.7	10.00	35.5	10.00	46.3	10.00	54.1
Peak #5 $T_1 = 0.4$ s		Peak #6 $T_1 = 0.4$ s		Peak #7 $T_1 = 0.2$ s		Peak #8 $T_1 = 0.2$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-35.3	0.00	-35.0	0.00	-29.1	0.00	-28.6
0.50	28.6	0.50	30.4	0.50	42.5	0.50	47.8
0.75	40.6	0.75	42.4	0.75	47.2	0.75	42.5
1.00	46.3	1.00	48.3	1.00	49.4	1.00	50.3
2.00	52.5	2.00	53.9	2.00	51.1	2.00	50.4
3.00	52.9	3.00	54.3	3.00	49.6	3.00	50.7
5.00	53.0	5.00	54.1	5.00	49.8	5.00	50.5
10.00	52.5	10.00	54.0	10.00	49.8	10.00	50.5
Peak #9 $T_1 = 0.2$ s		Peak #10 $T_1 = 0.2$ s		Peak #11 $T_1 = 0.5$ s		Peak #12 $T_1 = 0.4$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-48.1	0.00	-56.9	0.00	-31.8	0.00	-30.4
0.50	74.0	0.50	84.7	0.50	19.9	0.50	30.5
0.75	81.9	0.75	96.0	0.75	32.8	0.75	41.9
1.00	84.3	1.00	99.5	1.00	40.6	1.00	47.8
2.00	85.6	2.00	101.6	2.00	50.5	2.00	54.3
3.00	85.5	3.00	101.3	3.00	52.5	3.00	54.8
5.00	85.4	5.00	100.7	5.00	52.3	5.00	55.0
10.00	84.8	10.00	101.2	10.00	52.0	10.00	55.6

Table 18: T_1 data for 1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane complexed with $\text{Ba}(\text{ClO}_4)_2$ (1:2) in methanol-OD.

Peak #1 $T_1 = 7.8$ s		Peak #2 $T_1 = 6.9$ s		Peak #3 $T_1 = 4.2$ s		Peak #4 $T_1 = 0.4$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-14.4	0.00	-14.7	0.00	-16.7	0.00	-18.1
0.50	-11.9	0.50	-11.8	0.50	-11.8	0.50	15.6
0.75	-10.3	0.75	-11.5	0.75	-10.1	0.75	21.8
1.00	-9.7	1.00	-9.3	1.00	-8.3	1.00	24.2
2.00	-5.2	2.00	-5.0	2.00	-1.2	2.00	26.9
3.00	-1.6	3.00	-1.1	3.00	4.7	3.00	27.5
5.00	7.4	5.00	6.4	5.00	14.5	5.00	26.8
10.00	16.8	10.00	16.0	10.00	22.0	10.00	26.9
Peak #5 $T_1 = 0.41$ s		Peak #6 $T_1 = 0.40$ s		Peak #7 $T_1 = 0.21$ s		Peak #8 $T_1 = 0.22$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-19.4	0.00	-20.1	0.00	-15.0	0.00	-15.2
0.50	13.7	0.50	14.2	0.50	21.1	0.50	20.94
0.75	21.0	0.75	20.0	0.75	24.2	0.75	24.3
1.00	23.9	1.00	24.8	1.00	25.2	1.00	25.6
2.00	28.3	2.00	28.3	2.00	25.8	2.00	25.6
3.00	28.3	3.00	28.3	3.00	25.1	3.00	25.2
5.00	28.6	5.00	28.5	5.00	24.7	5.00	24.8
10.00	27.7	10.00	28.7	10.00	25.1	10.00	25.3
Peak #9 $T_1 = 0.22$ s		Peak #10 $T_1 = 0.22$ s		Peak #11 $T_1 = 50$ s		Peak #12 $T_1 = 70$ s	
τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height	τ (s)	Peak Height
0.00	-45.9	0.00	-45.9	0.00	-16.8	0.00	-15.0
0.50	66.0	0.50	66.0	0.50	10.0	0.50	14.1
0.75	75.5	0.75	75.5	0.75	16.1	0.75	20.1
1.00	78.3	1.00	78.3	1.00	19.6	1.00	23.6
2.00	79.4	2.00	79.4	2.00	25.1	2.00	26.9
3.00	79.8	3.00	79.8	3.00	26.4	3.00	27.3
5.00	79.2	5.00	79.2	5.00	25.6	5.00	27.0
10.00	79.0	10.00	79.0	10.00	25.6	10.00	26.8

4.3 Deuteriated Crown Ethers: Synthesis and Properties

(i) Materials

The previously unknown 18-crown-6-d₄ was prepared via reaction of triethylene glycol-d₄ with the commercially available (Aldrich) 3,6-dioxo-1,8-dichlorooctane. The following procedures were employed.

Triethylene glycol-d₄ (17)

Method was adapted from that reported for unlabelled material¹¹⁸. A 100 mL 3 neck round bottom flask, equipped with a dry ice condenser, magnetic stirrer and a septum gas inlet was charged with diethylene glycol (22.07 g, 0.208 mol) and pulverized KOH (1.00 g, 0.018 mol). To this was added, via the septum, gaseous ethylene oxide-d₄ (MSD isotopes), (5.0g, 0.104 mol), at room temperature while the mixture was being stirred. Stirring was continued at ambient temperature for 1h. Subsequently, the mixture was slowly heated to 50 °C and stirred for 6 h. Following cooling to room temperature, the mixture was neutralized with 3N HCl and slowly distilled at reduced pressure on a spinning band column. To maximize recovery of the desired product, 10 mL of the higher boiling tetraethylene glycol was added to the crude product prior to the spinning band distillation.

Yield of **1**, b.p. 120-125 (0.4 mm Hg) was 9.0 g (56%).

Mass spectrum (CI), M+1, 155.0.

18-crown-6-d₄ (23)

Again the method was adapted from that used for unlabelled material.¹²² A 250 mL 3 neck round bottom flask, equipped with a magnetic stirrer, reflux condenser and an addition funnel, was charged with **1** (9.0 g, 54.8 mmol) and 60 mL of THF. An aqueous solution of KOH (7 mL of 60% solution) was added and the mixture was stirred for 15 minutes after which time it had darkened considerably. Subsequently, 3,6-dioxo-1,8-dichlorooctane (10.9 g, 58.4 mmol) in 10 mL THF was added over a 5 minute period. The resulting solution was stirred vigorously and refluxed for 24 h. Following cooling and solvent removal at reduced pressure, the resulting thick brown slurry was diluted with dichloromethane (50 mL) and filtered to remove insoluble salts. These salts were washed with dichloromethane (3x25 mL) and the combined organics were dried over sodium sulfate. Following solvent removal the crude product was distilled under reduced pressure (0.1 mm) and all fractions with b.p. 130-200 °C were combined. This material (8.5 g) was stirred with acetonitrile and heated to dissolve all solids. Cooling generated crystals of the 18-crown-6-d₄•acetonitrile complex which were collected by filtration. Subsequent dissolution of this complex in 30 mL of dichloromethane and solvent removal at reduced pressure (15 mm) up to 70°C, yielded as residue, pure 18-crown-6-d₄, (3.72 g, 24%) which solidified upon cooling, m.p. 38-39°C (reported 39-40°C). Mass spectrum (CI), (M+1) 268.9.

12-Crown-4-d₄ (25)

A 1L three neck round bottom flask was charged with *t*-butyl alcohol (450 mL) and lithium metal (1.6 g, 0.23 mol). This was stirred mechanically for one hour. Ethylene glycol (4.46 g, 0.073 mol) was added

dropwise causing the formation of a white suspension. Lithium bromide (6.34 g, 0.073 mol) and 1,8-dichloro-3,6-dioxaoctane (13.75 g, 0.073 mol) were added in succession and the mixture was refluxed for 12 days. After a few hours of refluxing the entire contents formed a thick white suspension which remained for five days. After this time a translucent beige solution remained. When reflux was discontinued the solution was cooled and neutralized with 3M hydrochloric acid. The solvent was removed by roto-evaporation at reduced pressure (aspirator). The residue was added to a separatory funnel containing 500 mL of water and extracted with dichloromethane (4 x 125 mL). The combined organics were dried over sodium sulfate and the solvent was removed by roto-evaporation at reduced pressure (aspirator). The remaining brown residue was distilled under high vacuum (0.2 mm Hg) yielding 12-crown-4 (3.62 g, 20.5 mmol, 28.1 %)

4.4 Complexes: Synthesis and Properties

12 crown-4 / calcium chloride¹³⁷

Calcium chloride (1.11g, 100 mmol) was dissolved in water (5.1 mL) 12-crown-4 (2.0g, 11.4 mmol) was added forming a copious yellow precipitate. The mixture was heated to dissolution and allowed to cool forming needle like crystals.

elemental analysis: expected: **H**; 7.48, **C**; 22.28, **O**; 44.51, **Cl**; 16.44, **Ca**: 9.29, found: **H**; 7.33, **C**; 23.33, **O**; 36.23, **Cl**; 20.04.

12 crown-4 / sodium chloride¹⁰⁸

Sodium chloride (0.33 g, 5.7 mmol) was dissolved in water (1.5 mL) 12-crown-4 (2.0 g, 11.4 mmol) was added forming a white precipitate. The mixture was heated to dissolution and allowed to cool forming colourless plates $\approx 3 \text{ mm}^2$.

elemental analysis: Calculated: **H**; 8.45, **C**; 38.36, **O**; 20.60, **Cl**; 22.82,
found: **H**; 8.33, **C**; 37.89, **O**; 20.63, **Cl**; 22.83.

12 crown-4 / sodium hydroxide¹³⁸

Sodium hydroxide (0.29 g, 5.7 mmol) was dissolved in water (1.5 mL) 12-crown-4 (2.0 g, 11.4 mmol) was added forming a white precipitate. The mixture was heated to dissolution and allowed to cool forming slightly yellow plates .

elemental analysis: Calculated: **H**; 9.13, **C**; 35.82, **O**; 50.69, **Na**; 4.28,
found: **H**; 2.36, **C**; 9.91, **O**; could not determine due to O interference,

12 crown-4 / Magnesium Chloride

Magnesium Chloride hexahydrate (0.93 g, 5.7 mmol) was dissolved in water (1.5 mL) 12-crown-4 (1.0 g, 5.7 mmol) was added forming a colourless solution. Evaporation of some of the water caused the formation of colourless prismatic crystals.

12 crown-4 / Lithium Thiocyanide³⁶

12 Crown-4 (1.0 g, 5.6 mmol) and lithium thiocyanide (0.37 g, 5.6 mmol) were combined and dissolved in methanol (5.0 mL). The solution

was evaporated to 2.5 mL then stored overnight at -10°C in a freezer producing colourless crystals. m.p.: $249-251^{\circ}\text{C}$

12 crown-4 / Lithium Bis(trimethylsilyl)amide¹³⁹

Lithium bis(trimethylsilyl)amide was obtained from Aldrich and used directly from the bottle. The crown ether was obtained from Aldrich, dried by refluxing and distilling over molten sodium at reduced pressure. All solvents were obtained from Aldrich, degassed with a steady flow of argon and dried over sodium wire. The complex was formed in an argon atmosphere in a dry box. Lithium Bis(trimethylsilyl)amide (1.68 g, 10.0 mmol) was dissolved in hexane (5.0 mL). 12-crown-4 (1.8 g, 10 mmol) was added causing the formation of a light green precipitate. The product was filtered by gravity, recrystallized in a 1:1:1 mixture of tetrahydrofuran, diethyl ether and hexane and dried under high vacuum yielding 2.13 g, 60.17%. No melting point was reported for this complex in the original publication nor could one be obtained here because it is too unstable.

12 crown-4 / Lithium Diphenyl Phosphine¹⁴⁰

The same conditions employed for the formation of 12 crown-4 / lithium bis(trimethylsilyl)amide were used for this complex. Diphenyl phosphine was obtained from Aldrich and used directly from the bottle. Diphenyl phosphine (0.93 g, 5.0 mmol) was dissolved in diethyl ether (5.0 mL). *n*-Butyl lithium in hexane (2.4 mL, 2.0 M) was added dropwise and the resultant solution was stirred at room temperature for 1 hour causing it to turn yellow. 12-Crown-4 (1.8 g, 10 mmol) was added forming an orange precipitate. The product was filtered, recrystallized in a 4:1

mixture of THF and ether and dried under high vacuum. No melting point was reported for this complex in the original publication nor could one be obtained here because it is too unstable.

12-crown-4 / Lithium Diphenylamide¹⁴¹

The same conditions employed for the formation of 12 crown-4 / lithium bis(trimethylsilyl)amide were used for this complex. Diphenyl amine was obtained from Aldrich and used directly from the bottle. Diphenyl amine (0.85 g, 5.0 mmol) was dissolved in diethyl ether (5.0 mL). *n*-Butyl lithium in hexane (2.4 mL, 2.0 M) was added dropwise and the resultant solution was stirred at room temperature for 1 hour causing it to turn green. 12-Crown-4 (1.8 g, 10 mmol) was added forming a light yellow precipitate. The product was filtered, recrystallized in a 4:1 mixture of THF and ether and dried under high vacuum. No melting point was reported for this complex in the original publication nor could one be obtained here because it is too unstable.

18-crown-6 / Benzene sulfonamide (1:2)

Benzene sulfonamide (0.595 g, 3.96 mmol) and 18-crown-6 (0.5 g, .1.98 mmol) were dissolved in hot ethanol (1.0 mL). The solution was allowed to cool to room temperature and formed rhombohedron crystals overnight.

yield 0.47 g, 43%; m. p.: 91-92°C (lit: 92)²⁸; integration of the ¹H NMR spectrum showed that the complex is in fact 1:2.

18-Crown-6 / Malononitrile (1:2)¹²⁷

Malononitrile was recrystallized in chloroform by making a saturated solution at room temperature then cooling in a dry ice / acetone bath. This was repeated three times for optimum purity.

A solution of malononitrile (0.66 g, 10 mmol) in diethyl ether (7.0 mL) was added dropwise to a solution of 18-crown-6 (1.32 g, 5.0 mmol) in diethyl ether (10 mL) causing the immediate formation of a white precipitate. The precipitate was filtered and washed with ether (4 x 20 mL) and dried in a vacuum dessicator at reduced (aspirator) pressure.

18-crown-6 / urea (1:5)¹²⁹

18-crown-6 (0.264 g, 1. mmol) and urea (0.300 g 5.0 mmol) were dissolved in a 1:2 methanol-chloroform mixture . Ether was added dropwise until precipitation occurred. The mixture was heated to dissolution and allowed to recrystallize at room temperature.

yield 0.41 g 73%; m.p.: 148-150°C (lit. 148-150°C). Integration of the ¹H NMR spectrum indicated a 5 : 1 complex, **NH₂** 4.43δ 20 H, **CH₂** 3.55δ 24 H.

Appendix 1

^1H NMR Spectra

All ^1H NMR spectra except for 2-(4'-benzo-12-crown-4)-ethanol were recorded on the Varian Geemini 200 spectrometer at 200 MHz. The spectrum for 2-(4'-benzo-12-crown-4)-ethanol was recorded on a Varian EM 360 spectrometer at 60 MHz. All samples were run in CDCl_3 with TMS used as an internal reference.

4'-Formylbenzo-12-crown-4

Uncyclized monoadduct from the cyclization of 4'-Formylbenzo-12-crown-4

4',4''-di(formylbenzo)-24-crown-8

4'-vinylbenzo-12-crown-4

START OF SWEEP 2-(4'-benzo-1,2-crown-4)-ethanol

↑
H
A

154
END

2-(4'-benzo-12-crown-4)-bromoethane

156

4'-ethylbenzo-12-crown-4

1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane

157

1,4-(4'-benzo-12-crown-4)-butane

1-(4'-benzo-12-crown-4)-ethanol

18-crown-6-d₄

12-crown-4-d₄

161

Appendix 2

^{13}C NMR Spectra

All ^{13}C NMR spectra except for 2-(4'-benzo-12-crown-4)-ethanol were recorded on the Varian Geemini 200 spectrometer at 50.3 MHz. The spectrum for 2-(4'-benzo-12-crown-4)-ethanol was recorded on a Varian XL 200 200 MHz spectrometer at 50.3 MHz. All samples were run in CDCl_3 with TMS used as an internal reference.

4'-Formylbenzo-12-crown-4

163

Uncyclized monoadduct form the cyclization of 4'-Formylbenzo-12-crown-4

4,4'-di(formylbenzo)-24-crown-8

165

4'-vinylbenzo-12-crown-4

166

Polyvinylbenzo-12-crown-4

4'-vinylbenzo-12-crown-4 / Styrene Copolymer

2-(4'-benzo-12-crown-4)-ethanolSPECTRAL LINES FOR TH- 20.00
REF. 260.0 REF. 0

INDEX	FREQ.	PPM	INTENSITY
01	7574.1	150.531	35.304
02	7493.9	148.958	38.283
03	6717.4	133.523	53.140
04	6186.5	122.971	84.253
05	6093.0	121.112	28.240
06	5966.7	118.602	94.918
07	5957.5	118.432	93.120
08	5943.3	118.137	31.075
09	5917.0	77.876	59.161
10	5905.6	77.633	182.797
11	5899.0	77.509	41.903
12	5892.2	77.364	61.632
13	5905.0	77.240	74.022
14	5873.8	77.000	187.841
15	5866.4	76.854	43.243
16	5840.2	76.730	41.092
17	5854.2	76.612	77.187
18	5841.9	76.366	185.350
19	5835.2	75.233	43.856
20	5830.3	74.136	30.989
21	5828.3	74.095	33.372
22	5825.8	74.047	25.567
23	5425.2	72.058	98.588
24	5426.5	71.965	39.432
25	5576.7	71.492	97.638
26	5579.1	71.143	129.763
27	5573.2	71.025	124.017
28	5517.9	69.927	200.000
29	5247.0	64.542	31.619
30	5193.3	63.474	90.720
31	1944.4	38.650	62.081
32	1.44E-4	4.83E-4	46.002
33	-0.1	-0.083	45.435

2-(4'-benzo-12-crown-4)-bromoethane

170

4'-ethylbenzo-12-crown-4

1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane

1,4-(4'-benzo-12-crown-4)-butane

173

1-(4'-benzo-12-crown-4)-ethanol

12-crown-4-d₄

31 of/de 3

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Appendix 3

Mass Spectra

4'-Formylbenzo-12-crown-4

Uncyclized monoadduct form the cyclization of 4'-Formylbenzo-12-crown-4

4,4'-di(vinylbenzo)-24-crown-8

4'-vinylbenzo-12-crown-4

2-(4'-benzo-12-crown-4)-bromoethane

4'-ethylbenzo-12-crown-4

1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane

1,4-(4'-benzo-12-crown-4)-butane

1-(4'-benzo-12-crown-4)-ethanol

186

18-crown-6-d₄

12-crown-4-d₄

Appendix 4

IR Spectra

PERKIN ELMER

92/03/11 16:08
X: 1 scan, 4.0cm-1

PERKIN ELMER

2-(4'-benzo-12-crown-4)-ethanol

80.21
ST

191

92/03/11 15:55
X: 1 scan, 4.0cm-1

1,4-(4'-benzo-12-crown-4)-2,3-dihydroxybutane

192

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