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MULTINUCLEAR MAGNETIC RESONANCE, ELECTROCHEMICAL,
AND CALORIMETRIC STUDIES OF
SOME MACROCYCLIC COMPLEXES

presented by

Alfred J. Smetana

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

Major professor
Alexander I. Popov

Date August 10, 1979

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MULTINUCLEAR MAGNETIC RESONANCE, ELECTROCHEMICAL, AND CALORIMETRIC STUDIES OF SOME MACROCYCLIC COMPLEXES

By

Alfred J. Smetana

A DISSERTATION

Submitted to

Michigan State University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1979

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ABSTRACT

MULTINUCLEAR MAGNETIC RESONANCE, ELECTROCHEMICAL, AND CALORIMETRIC STUDIES OF SOME MACROCYCLIC COMPLEXES

By

Alfred J. Smetana

Since the introduction of synthetic macrocyclic ligands capable of forming stable complexes with the alkali ions, the popularity of this field of research has grown very rapidly. A large number of different physicochemical techniques has been used to study the thermodynamic and kinetic aspects of macrocyclic complexation.

Lithium-7 nuclear magnetic resonance studies have been carried out on lithium ion complexes of crown ethers 12-crown-4, 15-crown-5, and 18-crown-6 in water and in several nonaqueous solvents. Concentration formation constants of these complexes were determined from the variations of the ^{7}Li chemical shifts with the ligand/Li^{+} mole ratios. The stability of the complexes varied very significantly with the solvent. With the exception of pyridine, the stability varies inversely with the Gutmann donor number of the solvent. In general, the stability order of the complexes was found to be 15-crown-5·Li^{+} > 12-crown-4·Li^{+} > 18-crown-6·Li^{+}.

Since in this case the complexation reaction does not involve a separation or combination of charges, it has been generally assumed

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that at low ionic strength the concentration equilibrium constant is essentially equal to the thermodynamic value. To determine the validity of this assumption, concentration formation constants for the 18-crown-6·Na^+ complex in anhydrous methanol solutions were measured potentiometrically as a function of ionic strength of the solution. The concentration constant values remained reasonably close to the thermodynamic value at ionic strengths $\leq$ 0.05 M. At higher ionic strengths, the concentration value decreased significantly.

The thermodynamics of the complexation of the lithium ion by the three crown ethers was studied calorimetrically. Experimental values of $\Delta G°$, $\Delta H°$, and $\Delta S°$ indicate that in most cases, the lithium-crown complexes are both enthalpy and entropy stabilized. However, in few cases, the complexes were found to be either enthalpy or entropy destabilized. The results are explained in terms of electrostatic bond strengths, ligand configurational entropy, and solvent effects.

Oxygen-17 nuclear magnetic resonance studies in natural abundance have also been used to probe the chemical environment of the oxygen atoms in free and complexed crown ethers. This method has been shown to be qualitatively sensitive to the complexation of the crown ether by a metal cation. The ^{17}O resonance of the complexes was found to be $\sim$10 ppm upfield from the resonance of the free crown ethers.

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ACKNOWLEDGMENTS

The author wishes to thank Professor Alexander I. Popov for his guidance, encouragement, and friendship throughout this study.

He also wishes to thank Professor Andrew Timnick for his numerous helpful suggestions as second reader and especially for his resourcefulness.

Gratitude is extended to the Department of Chemistry, Michigan State University and the National Science Foundation for financial aid.

Deep appreciation is extended to my Mom, Dad, and sister for their prayers, encouragement, and constant support. Finally, I would like to thank my wife, Dianne, for her assistance in the preparation of this manuscript, her love, her patience, and especially for her deep understanding of the trials and tribulations of graduate studies in Chemistry. It is to Dianne that I dedicate this dissertation.

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CHAPTER 1

HISTORICAL REVIEW

A. Intro

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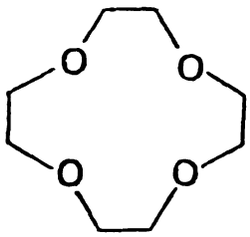
A. Introduction

Until 1967, the coordination chemistry of the alkali metal ions in solutions was virtually unexplored by chemists. It was believed that these ions were inert, unreactive, and therefore uninteresting. Consequently, it was a common practice to use alkali salts to maintain "high and constant" ionic strength of the solution, particularly for the studies of complexation reactions involving transition metal ions. Since the alkali ions are unreactive to most solvolysis and redox type reactions, workers assumed that the alkali salt did not participate in the complexation reaction. However, it has been shown that alkali ions do indeed form complexes in solution with ligands such as ethylenediaminetetraacetic acid (EDTA),(1) the transition metal complexes of which have received a considerable amount of attention. Some of these complexes, namely the sodium and lithium ion complexes with ℓ-trans-1,2-diaminocyclohexane N,N,N',N'-tetraacetic acid, an analog of EDTA, were very stable in aqueous solution, with stability constants reported as log K = 4.7 and 6.1, respectively.(2,3)

Studies directed toward the solution and coordination chemistry of the alkali ions became a particularly exciting field of research when Pedersen discovered a new type of synthetic ligands which he called crowns or macrocyclic polyethers.(4,5) The IUPAC nomenclature for these compounds is quite cumbersome, and these ligands have generally been discussed using their trivial names shown in Figure 1. Pedersen proposed that these ligands be identified by (a) the number and kind of substituent groups on the ring, (b) the total number of atoms in the ring, (c) the name crown (for the compound class), and



12-crown-4 (12C4)
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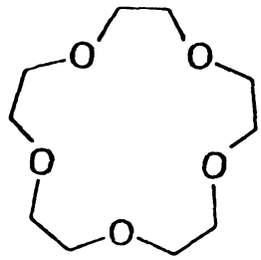

15-crown-5 (15C5)
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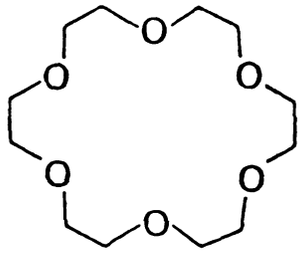

18-crown-6 (18C6)
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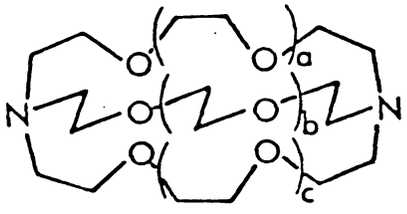

CRYPTAND

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a = b = 1, c = 0	C221
a = b = c = 1	C222

Figure 1. Synthetic macrocyclic polyether ligands.

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(d) the number of oxygen donor atoms in the ring. Figure 1 presents the molecular structures, trivial names, and approximate cavity sizes of the three crown ethers used in the study discussed in this dissertation. The structure of a cryptand is included in the family of synthetic macrocyclic ligands for completeness, and will be discussed shortly.

Macrocyclic polyether ligands have been shown to form remarkably stable complexes with alkali and alkaline earth ions, as well as some other ions (and molecules) in various solvents. Some of these complexes are of comparable stability to the EDTA·transition metal complexes. When the size of the cation and the ligand cavity are comparable, crown ether ligands form two-dimensional complexes in solution, where the metal ion "sits" in the center of the cavity to form the complex. This model of the complex utilizes the naive assumption that the ligand is a rigid ring. One particularly interesting observation made in the early days was that in the presence of some crowns, alkali salts can be solubilized in non-polar organic solvents; Pedersen observed that potassium permanganate could be solubilized in benzene by the crown ether dicyclohexyl-18C6.(5)

Shortly after Pedersen's publication on the synthesis of the first crown ethers, a logical extension to these ligands was introduced by Lehn and coworkers with the first reported syntheses of cryptands.(6,7) A cryptand (the name suggested by Lehn) is a macrobicyclic polyether containing three polyether strands joined at two nitrogen bridgeheads. The general formula for a cryptand is shown in Figure 1. These ligands are capable of forming three dimensional inclusive complexes (cryptates) with an ion of suitable size, where the ion is usually

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found in the center of the cavity, more or less insulated from the outside or bulk solution environment. The cavity size can be varied by increasing the number of ether oxygen groups in the bridging strands. The cryptand compound shown in Figure 1 is named cryptand-222 (a=b=c=1) or more simply C222 where the "C" stands for cryptand and "222" indicates that there are two oxygens in each of the strands. The cryptand C222 is a bicyclic ligand, hence it is called a [2]-cryptand. Ligands containing three and four macrocycles (called [3]- and [4]-cryptands) have also be synthesized.(8,9)

It should also be noted that macrocyclic ligands have also been synthesized in which some or all of the oxygen donor atoms have been replaced by sulfur or nitrogen. Such substitution has a dramatic effect on the stabilities of the complexes.

Numerous review articles have been published in recent years,(10-15) and at this time there exist also three books (16-18) on the chemistry of macrocyclic ligands. This historical review is not intended to be a comprehensive literature review. Specific references were selected to provide the necessary background information and to assess the significance of this study.

B. Cation Selectivity and Macrocyclic Complex Stability

Several factors have been shown to be of paramount importance in the determination of cation selectivity and macrocyclic complex stability. These include (a) the size relationship between the cation to be complexed and the ligand cavity, (b) the number, type, and arrangement of donor atoms in the ligand, (c) the type and charge

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of the cation, (d) substitution on the macrocyclic ring, and (e) since these complexes are formed in solution, the properties of the solvent must also be considered.

1. Size of Cation and Ligand Cavity

From the early days, Pedersen recognized that the strongest complexes between metal ions and crown ethers result when the size match is optimum. That is, when the crystal radius of the ion closely matches the radius of the crown cavity.(5) Workers reasoned that the strongest bonds between the metal ion and ligand donor atoms could be formed when all of the donors could participate equally in the bonding. If the cation is too large, it cannot fit inside the cavity, and therefore, the bonding interactions are weakened. Also, in some cases 2:1 (ligand to metal) sandwich complexes can be formed. If the metal ion is too small, the distance between the ion and the donor atoms is too large for effective bonding. It should be pointed out that other classes of macrocycles, namely cyclic tetraamine (19,20) and tetrathia (21) ligands also follow this general rule.

Thus far, the word "size" has been used rather arbitrarily, but the method of precise size determinations (particularly in solution) merits some discussion at this time. Molecular models have been used to determine ligand cavity sizes.(5) Corey-Pauling-Koltun (CPK) molecular models yield cavity diameters which are substantially smaller than the Fisher-Hirschfelder-Taylor (FHT) models. In general, there is better agreement between the CPK model measurements and the results obtained by X-ray crystallographic determinations of the structures

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of the complexed (with metal ions) ligands. The other size under consideration, of course, is that of the metal ion. Traditionally, the well accepted Pauling's radii for the alkali metal ions have been used to accurately describe their size. On the basis of Pauling's ionic sizes and the CPK molecular model measurements (see page 73), it is expected that the sodium ion forms the strongest complexes in solution with 15C5, but it has been experimentally determined that the cavity of benzo-15C5 is too small for the sodium ion,(22,23) and the strongest sodium crown complexes are formed consistently with 18C6,(24) which folds itself slightly to accommodate the sodium ion.(25) The results presented above as well as those presented in Chapter 3 correlate much better with the ionic sizes obtained from electron density measurements, from which the ionic diameters for the alkali ions are considerably larger than Pauling's values.

The above discussion applies strictly to crown ether ligands with cavity sizes as large as 18C6 (or perhaps even 21C7) where, although the ligand has many degrees of freedom, it may be conceptualized as a fairly rigid ring. The strongest complexes formed with larger crown ethers like dibenzo-27C9 and dibenzo-30C10 are with potassium ion and/or rubidium ion, the sizes of which are considerably smaller than the macrocyclic cavity (assuming a planar ligand configuration). The crystal structure of dibenzo-30C10·KI (26) shows that this large ligand folds on itself and forms a "wrap around" complex with K^+ so that all ten oxygen atoms participate in the bonding, and the ligand cavity diameter may not really be defined as previously. It has been pointed out, however, that crystal structures may differ significantly from

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the structures in solution, although it is likely that there will be similarities between the two conformations, particularly in the case of cation ordered complexes.(27,28)

The consonance between the size of the metal ion and macrobicyclic cavity is not unexpectedly of extreme importance in the determination of complex stability. Lehn and Sauvage (29) report cryptands selective for each of the alkali metal ions. As with the crowns, the selectivity is better with the smaller cryptands (∿C222) due to the increased flexibility of the larger cryptands.

2. Number, Type, and Arrangement of Donor Atoms

a. Number of donor atoms

Only a small amount of data is currently available on the influence of the number of donor atoms on complex stability. Cram and coworkers,(30) the originators of the so-called host-guest chemistry, found that 18C5 is a much poorer host than 18C6 for the t-butylammonium ion. For thia-substituted crown complexes with silver ion, increased complex stability is found as the number of sulfur atoms in the ring is increased.(31) However, it must be pointed out that this increased stability is due to the combination of two factors, the number and the type of donor atom, because the type of donor atom has also been changed upon increased substitution. In this case, the type of donor atom is probably the more important factor (see below). An excellent illustration of the effect of the number of donor atoms may be cited from the studies of Lehn and coworkers with cryptands C222 and $C22C_8$.

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In the latter case, the ether oxygens in one of the strands have been substituted by methylene groups. These two ligands are very similar in size, but the C222 complexes with metal ions are much more stable due to the increased number of binding sites.(29)

b. Type of donor atom

Considerably more data are available in the literature on systems studied in which sulfur or nitrogen atoms have been substituted for the oxygen atoms of the crown ethers. Substitution of nitrogen for oxygen drastically reduces the stabilities of the alkali metal and alkaline earth complexes, while enhancing the strength of the silver ion complexes.(31) When sulfur is substituted for oxygen, the same decrease in preference for the alkali metals, alkaline earths, and Tl^{+} and Pb^{2+} is observed, while the stabilities of the Ag^{+} and Hg^{2+} complexes are greatly enhanced.(24) This selectivity change may be explained by applying Pearson's concept of hard and soft acids and bases.(32) The alkali metal ions are hard acids which interact more strongly with hard bases such as oxygen, while metal ions such as Ag^{+} and Hg^{2+} are softer in character, and bond more strongly with nitrogen and sulfur, which are softer bases. It is also well known that silver ion interacts strongly with amines, and the general rule that the relative stability of the silver nonmetal bond increases in the order O<S<N (33) also seems to be applicable to the macrocyclic complexes.

Another complicating factor must be considered. If the sulfur atoms in the thia-crowns point into the ring, the cavity size is decreased. However, crystal structures show that the sulfur atoms

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are directed outward in the free ligands.(34) Although in the Cu^{2+} and Ni^{2+} tetrathia-14C4 crystal structures, the donor sulfurs point inward,(35,36) all the metal complexes may not be of the inclusive type as in the case of the $HgCl_2$ complex with 1,4-dithia-18C6 where the mercury lies outside the ring.(24) In the case of the tetraamine·Cu^{2+} complexes, the stability is also greatly reduced when the nitrogen atoms are substituted by sulfur atoms.(12,37)

c. Arrangement of donor atoms

The arrangement of the donor atoms in the ligand molecule is obviously of importance in complex formation, but it is difficult to evaluate this effect even semi-quantitatively. Stronger complexes are formed between the ammonium ion and 15C5 than with 18C6, probably because the smaller ligand provides a more favorable arrangement of donor atoms by way of hydrogen bonding.(38) However, consideration of relative sizes leads one to predict just the reverse, because NH_4^+ is too large to fit inside the cavity of even 18C6.(39) Cram et al.(30) have found that complexes of t-butylammonium ion with rigid cyclic crowns and their derivatives in chloroform solutions are more stable than with the corresponding open-chain ligands by several orders of magnitude. Frensdorff (31) observed the same behavior, but this also involves the effect of ring closure and leads to what has been termed the "macrocyclic effect" which is discussed later in this chapter.

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3. Type and Charge of Cation

The bonding of alkali (and alkaline earth) metal ions to macrocyclic ligands is believed to be electrostatic in nature.(40,41) In the complexes formed, the ligand donor atoms distribute themselves evenly over the spherical charge density of the metal cation. Therefore, one cannot really speak of a "coordination number" for these ions in macrocyclic complexes. The number of bonds formed between the metal ion and the ligand depends on the many factors under current discussion. There are no real stereochemical requirements of these cations.

The size of the ions in the above two families is perhaps the most important factor in the determination of the complex stability. Small ions like Li^+ and Mg^{2+} have large charge densities and are very strongly solvated compared to Cs^+ and Ba^{2+} so that in the former case more energy must be expended in the desolvation step of the complexation reaction. These differences in solvation provide for possible selectivity reversals. For example, among small cations, 18C6 forms stronger complexes with Na^+ than with Ca^{2+} (ions of similar sizes), while Ba^{2+} is preferred over K^+ in the case of larger cations in aqueous solutions.(12,38) Thallium(I) and lead(II) ions behave similarly to the alkali and alkaline earth ions, and their macrocyclic complexes have been shown to be stronger than the correspondingly sized ionic complexes of the alkali metal/alkaline earth ions.(38)

It has already been mentioned that the transition metal ions, Ag^+ and Hg^{2+}, prefer sulfur donors. Other ions such as Ni^{2+} and Cu^{2+}, have definite stereochemical preferences. For this reason, strong complexes between these ions and the cyclic tetraamines and their

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4. Substitution on Macrocyclic Ring

Substitution of benzo-groups on the macrocyclic or macrobicyclic ring usually changes the complex stability and can also change selectivity patterns. The addition of a benzene ring to one of the strands of cryptand C222 causes a rise in the sodium ion complex stability in 95% methanol and a drop in the stabilities of both the potassium and barium ion complexes. Addition of a second benzene ring to another strand results in a further decrease in the stability of the Ba^{2+} complex so that it becomes weaker than the K^+ complex.(42) Similar results were observed in methanol when 18C6 was compared with dibenzo-18C6. The K^+ and Ba^{2+} complexes of dibenzo-18C6 are both weaker than with the unsubstituted ligand, but the selectivity patterns have actually been reversed by substitution.(24) Such behavior has been explained in the following manner. Addition or substitution of aromatic rings tends to make the ligand more rigid and bulky while withdrawing some electron density from the main part of the macrocyclic ring so that the oxygen donors become less basic, thus decreasing the strength of the metal-ligand bonds. Substitution of cyclohexyl groups has a small effect as these groups change the properties of the macrocyclic ring only slightly.

Substitution of electron withdrawing groups onto the aromatic groups decreases the cation complex stability even further, while the substitution of electron donating groups increases the strength of

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the complex compared with the unsubstituted aromatic substituted macrocycles.(43) Other workers (44,45) even report selectivity reversals due to aromatic substitution. These results show that the apparently subtle aromatic substitutions can play an extremely important role in both complex stability and selectivity of benzo-crowns and benzo-cryptands toward cations.

5. Solvent Properties

The complexation of a metal ion by a ligand should be considered to be a competition between the ligand, the solvent molecules, and perhaps the counterion for the coordination sites around the metal ion. Therefore, it is obvious that the stability of the complex should vary inversely with the solvation energy of the cation or the solvating ability of the solvent.

Most of the early work on macrocyclic complexes was done in aqueous and methanolic solutions. It was recognized at that time that the solvent plays a very important role in the complexation reaction. Both crown ether complexes (31) and cryptates (29) were found to be more stable in methanol than in water by several orders of magnitude, because methanol solvates metal ions less strongly than water. This difference in solvating ability was discussed in terms of the much smaller dielectric constant of methanol.

Cahen *et al.* (46) correctly indicate that the dielectric constant is not the only solvent parameter which influences the stability of macrocyclic complexes. They report that there is little or no complex

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formation between the lithium ion and cryptands C222 and C221 in a strongly solvating solvent like dimethyl sulfoxide, while in a nearly equally polar but much less solvating solvent, nitromethane, rather stable complexes (log K > 4) are formed with these two cryptands. Mei et al. (47) studied cesium ion complexes with crowns and cryptands in various solvents and found that in general, the solvating ability as defined by Gutmann (48) agrees quite well with the behavior of these cesium ion complexes in nonaqueous solvents. Along these same lines, Shchori and Jagur-Grodzinski (43) found that with dibenzo-18C6 in dimethoxymethane and dimethylformamide solutions the complex stabilities were more similar than expected on the basis of polarity considerations alone, and may be attributed to the bidendate character of the less polar dimethoxymethane. Similar solvent effects have been observed by Dechter and Zink.(49)

From these selected references, it is seen that the solvent has a very significant effect on the stability of the complex. Likewise changes in selectivity patterns can also be induced by different solvents. Agostino et al. (50) studied alkali metal ion complexes with dicyclohexyl-18C6 in methanol, ethanol, and n-propanol. The dicyclohexyl-18C6 ligand is specific for K^+, but while the Cs^+ complex was more stable than the Na^+ complex in these alcohols, the Na^+ complex was found to be more stable in aqueous solution.(31) Similar reversals have been observed for the complexes of Ba^{2+} and K^+ with dibenzo-18C6 in methanol and water.(12,51) Solvent effects were also studied by Arnett and Moriarity.(52) They reported that the stabilities of the complexes of larger cations with dicyclohexyl-18C6 are less affected

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by changes in the solvent than those of smaller ions. It should be pointed out that these workers measured indirectly the enthalpy of complexation and discuss the stabilities in terms of enthalpy while totally neglecting the contribution of entropy to the free energy of complexation.

C. Thermodynamics of Macrocyclic Complexes

The previous section discussed the major factors which influence the thermodynamic stability of macrocyclic complexes. It was mentioned, only briefly however, that the cyclic polyethers form much more stable complexes than do their corresponding open chain analogs. The same effect has been observed for cyclic tetraamine ligands. It seems that ring closure is responsible for the increase in the complex stability constant, in some cases by several orders of magnitude. An even larger enhancement of complex stability is obtained by the addition of another connecting bridge onto the macrocyclic ring to form a macrobicyclic ligand or cryptand. Since the thermodynamic stability is comprised of two components (enthalpy and entropy) it was of considerable interest to determine the origin of this "macrocyclic effect" for the crowns and the cyclic tetraamines and the "cryptate effect" or "macrobicyclic effect" in the cases of the cryptands. The enthalpy changes associated with a complexation reaction are due to the energy changes associated with the formation/destruction of bonds, while the entropy change depends on the changes in the order of the system.

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1. Stepwise Complex Formation

The thermodynamics of the stepwise formation of metal ion complexes with halides and other anions in aqueous solution has been reviewed by Ahrland.(53) In general, reactions between hard acceptors and hard donors are most often endothermic particularly in the case of the first step.(53-56) In this case the stability of the complex is due almost exclusively to a large favorable entropy change. Soft/soft interactions are usually strongly exothermic while the entropy change is often negative or, if positive, it contributes only slightly to the complex stability.(53-55) For complexes formed between borderline hard/soft donors and acceptors, the entropy and enthalpy often contribute equally to the complex stability.(53)

In a later publication, Ahrland (57) examined the effect of solvent on the thermodynamic quantities by comparing complexes of Zn^{2+},(58) Cd^{2+},(59) and Hg^{2+} (60) with halides and thiocyanates in water and dimethyl sulfoxide (DMSO) solutions. He summarizes that the total entropy gain due to the desolvation of cations and anions upon complex formation is much larger in a relatively unstructured solvent, DMSO, than in the more highly structured water. In DMSO, the solvent molecules leave the well ordered solvates and enter into a fairly unordered bulk solvent upon complex formation. In water, they leave solvates which are either more or less ordered than in DMSO, but in either case, they enter a bulk solvent which is definitely much more ordered than DMSO. By enhancing the structure of the solvent via H-bonding between solvent molecules, the complexes in protic solvents become less stable. This view, of course, neglects consideration of any

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2. Chelate Effect

Based on the work of Schwarzenbach (54,61) and others,(62,63) it is generally agreed that the dramatic increase in metal ion complex stability for multidendate over unidendate ligand complexes is due almost entirely to favorable entropy changes, and this enhancement has been named the "chelate effect." Schwarzenbach (61) relates the increase in the entropy upon complex formation to the desolvation effect. For example, assuming that the solvation number of a given metal ion is six, the formation of a complex with a (hexadendate) ligand results in the release of six solvent molecules or five new particles in the complexation process. Thus, the overall entropy change contributes strongly to the complex stability.

In addition, Rasmussen (64) has shown that the use of some empirical equations for the entropy of dissolved species in aqueous solution can be used to calculate the magnitude of the chelate effect. There is at least one recent report (65) in which many more possible factors are considered. The author concludes that it is probably a coincidence that the standard enthalpy change for a chelation reaction turns out to be near zero and the entropy change is positive and near the theoretical value.

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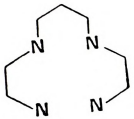
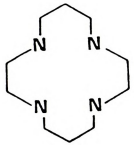
3. Macrocyclic Effect

Both thermodynamic and kinetic approaches have been proposed to elucidate the origin of the macrocyclic effect. Cabiness and Margerum (66) were the first to use the term "macrocyclic effect" to describe the greater stability observed for the complexes of Cu^{2+} with cyclic tetraamines over those of open-chain ligands of similar structure. However, their data do not support the same argument made for the chelate effect. They proposed that ligand solvation and configuration were more important than the entropy change. Later, Hinz and Margerum (67) reported data (Table 1) on the Ni^{2+} complexes with tetraamines in water and reached the same conclusion. The increased stability of the Ni^{2+} complex of cyclam (which is 14C4 with nitrogens substituted for all oxygens, also called 4N-14C4) over its linear counterpart was of enthalpic origin while the entropy change actually destabilized the cyclic complex.

Hinz and Margerum explained their results by assuming that the desolvation step of Ni^{2+} is the same in both reactions, and therefore considered the solvation of the ligand. They reasoned that since the cyclic ligand is much more compact, it is less solvated than the non-cyclic ligand, and therefore, less energy is expended in the desolvation step. Also, more entropy is expended to wrap the open-chain ligand around the metal ion, than to simply insert the ion into a preformed ligand cavity. They proposed that while this entropy term is undoubtedly the most important one toward the enhancement of the stability of macrocyclic complexes, it is outweighed by the enthalpy contribution in H-bonding solvents due to ligand solvation. In

Table 1. Thermodynamics of Some Tetraamine·Ni^{2+} Complexes in Aqueous Solution (67)

Table 1. Thermodynamics of Some Tetraamine·Ni^{2+} Complexes in Aqueous Solution (67)

	log K	$\Delta H°$ (kcal·mole^{-1})	$\Delta S°$ (cal·mole^{-1}·deg^{-1})
	15.3	-16.8	13.8
	22.2	-31	2.0
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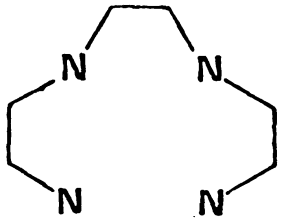
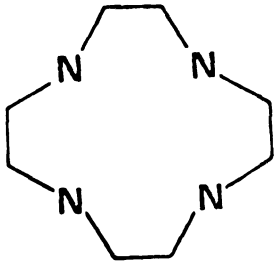
solvents where H-bonding is weak or absent, the changes in configurational entropy should be more dominant. Dei and Gori (68) also used the same ligand solvation enthalpy stabilization explanation in their studies of Cu^{2+} complexes with these same ligands in aqueous solution.

Paoletti et al. (69) presented some preliminary results on the thermodynamics of 4N-12C4·Cu^{2+} complexes in water and proposed that the macrocyclic effect results from a combination of favorable enthalpy and entropy changes. Later, after further studies, they concluded that only entropy contributions are important.(20) Their results (Table 2) as well as those of Kodama and Kimura (70-71) who studied the same systems, showed that the closed ring complexes are actually enthalpy destabilized and highly entropy stabilized. The results of Hinz and Margerum (4N-14C4·Cu^{2+} in water) and Paoletti et al. and Kodama and Kimura (4N-12C4·Cu^{2+} in water) are directly opposite. However, it really doesn't seem that the apparently small differences in ligand sizes and metal ions should produce such drastically different results. Space filling models show that Ni^{2+} or Cu^{2+} can fit into the cavity of the larger 4N-14C4, which has been confirmed by crystal studies,(72-74) but molecular models show that 4N-12C4 is too small to accommodate either of these ions. Therefore, assuming that the experimental results are correct, it is not clear what makes the results of these two systems so different.

In a more recent paper, Paoletti et al. (75) examined this contradiction in detail. They measured the enthalpy of complexation microcalorimetrically for complexes of Cu^{2+} and Zn^{2+} with the ligands 4N-12C4, 4N-13C4, 4N-14C4, 4N-15C4, and the corresponding linear

Table 2. Thermodynamics of Some Tetraamine·Cu^{2+} Complexes in Aqueous Solution (20)

Table 2. Thermodynamics of Some Tetraamine·Cu^{2+} Complexes in Aqueous Solution (20)

	log K	$\Delta H°$ (kcal·mole^{-1})	$\Delta S°$ (cal·mole^{-1}·deg^{-1})
	19.7	-25.2	5.7
	20.1	-21.6	19.5
 4N-12C4	24.8	-18.3	51.3

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counterparts in aqueous solution. The value of the entropy term was calculated by difference since the formation constants were known from other measurements. They summarized the macrocyclic effect as being due to a favorable entropy term and to a normally favorable enthalpy term. The magnitude of the latter critically depends on the size match between the cation and the ligand. They found that while the enthalpy went through a maximum with the best size match, ($4N\text{-}14C4 \cdot Cu^{2+}$) the entropy of the macrocyclic complexes decreased steadily with increasing size and decreasing rigidity of the macrocyclic ligands. They indicated that their enthalpy results are more trustworthy than the results of Hinz and Margerum (67) and Kodama and Kimura,(70,71) because the enthalpies were measured directly. In the work of the other groups, the thermodynamic quantities were determined from the temperature dependence of the formation constants, which is generally less accurate than the calorimetric method. A small error in equilibrium constants can result in a large error in $\Delta H°$, particularly if the reaction is studied over a narrow temperature range.

Frensdorff (31) noted similar behavior with cyclic polyethers. He determined stability enhancements of three to four orders of magnitude for Na^+ and K^+ complexes with 18C6 over those with the non-cyclic pentaglyme in methanol. He suggested that the decreased stability of the open chain ligands is due to the inability of the ligand to completely envelop the cation, due to the electrostatic repulsion between the terminal oxygens and the unfavorable change in entropy as a result of wrapping the ligand around the cation.

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been determined for some of the systems studied by Frensdorff.(24) Unfortunately, the thermodynamic values for the 18C6·Na^+, K^+, and Ba^{2+} systems in methanol do not yield reproducible trends in $\Delta H°$ or $\Delta S°$ to explain the macrocyclic effect. While the sodium complex is very much entropy stabilized, the potassium complex is enthalpy stabilized and entropy destabilized, and the barium complex is both enthalpy and entropy stabilized, but the enthalpy term is dominant. These results show that the macrocyclic effect depends very much on the systems studied and that different systems may be responding to different stabilizing factors. This may be the reason for the apparently contradictory results for the Cu^{2+} and Ni^{2+} complexes discussed earlier.

Ligands with mixed types of donor atoms do not seem to show a macrocyclic effect. Frensdorff (31) studied Ag^+ complexes with 1,10-diaza-18C6 and a similar linear analog with fewer donor atoms in aqueous solution and found no indication of a macrocyclic effect. The same ligands were studied by Anderegg (76) with Cd^{2+} and Hg^{2+} ions in aqueous solution, and again, no macrocyclic effect was observed. It must be pointed out however, that in these cases, the cyclic ligand and its linear counterpart are not strictly comparable as the non-cyclic ligand has fewer total atoms as well as fewer donor atoms.

Izatt et al. (24) also determined the absence of the macrocyclic effect for mixed donor crowns. They studied linear sulfur and oxygen containing crowns and their cyclic analogs with Hg^{2+} and Ag^+ in aqueous solution. These systems are complicated by the formation of both 1:1 and 2:1 (ligand to metal) complexes. The enthalpies for the first step in the complexation reaction with 2S-15C5 were nearly

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identical for the cyclic and noncyclic ligands. The 2:1 cyclic complexes were found to be less stable than the 2:1 linear complexes. As indicated previously, there is some doubt that the metal ions bind inclusively. In the crystal structures of both 1,10-dithia-18C6·$PdCl_2$ (77) and 1,4-dithia-18C6·$HgCl_2$ (24) the metal ions were bound externally. If similar structures exist in solution, then it is not at all surprising that the macrocyclic effect is absent, since only part of the ring participates in the complexation reaction.

The origin of the macrocyclic effect has also been examined from a kinetic viewpoint. The intriguing stabilities of macrocyclic complexes are due to the slow rate of the decomplexation reaction. Cabbiness and Margerum (78) found that the decomplexation rate of the Cu^{2+} cyclic tetraamine complex is much slower than that of its linear analog. The decomplexation rate was so slow that it overshadowed the slow formation rate of the cyclic complex.

The kinetic approach has also been supported by the data of Jones et al. (21) which illustrate that the slow decomplexation rate of the 4S-14C4·Cu^{2+} complex in 80% methanol compared to the linear ligand is responsible for the extra stability. The authors conclude that configurational effects in the dissociation step are responsible for the stability of the cyclic complex and that these effects should manifest themselves primarily in the entropy term. Furthermore, they hypothesize that solvation effects must be important only in the decomplexation step, and therefore, only for the complexed species and not for the free ligand.

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4. Cryptate Effect

Lehn and coworkers (29) have observed an even greater enhancement in complex stability over the macrocyclic effect by the addition of another strand onto the macrocyclic ring to form a macrobicyclic ligand. This enhancement has been named the "cryptate effect" or "macrobicyclic effect." When the added bridge is fully connected, the stability of the C222·K^+ complex in 95% methanol increases by five orders of magnitude compared with the ligand in which one end of the added arm remains unattached. Unfortunately, the thermodynamic quantities for these complexes have not been elucidated.

Kauffmann et al. (79) compared the thermodynamics of the C222·K^+ and dicyclohexyl-18C6·K^+ complexes in water and concluded that the cryptate effect is of enthalpic origin. However, these macrocycles cannot be compared directly due to the substitution on the crown. Anderegg (76) reached the same conclusion, but with ligands which are somewhat more comparable. He studied the 2N-18C6 and C222 complexes with metal ions. It should be noted, however, that C222 has two additional donor atoms. Anderegg's data for the Hg^{2+} and Cd^{2+} complexes with these ligands are contradictory, because the Hg^{2+} ion seems to show no cryptate effect while the Cd^{2+} bicyclic complex is entropy stabilized. Obviously, more data are needed to elucidate the origin(s) of the cryptate effect.

Kauffmann et al. (79) also report the results of a calorimetric study of alkali metal and alkaline earth cryptates in aqueous and 95% methanol solutions. From stability constants published previously, they also present the calculated entropies of complexation. The

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thermodynamics of complexation (for $\Delta G < 0$) may be divided into five classes (a) $\Delta H < 0$ and dominant, $\Delta S > 0$, (b) $\Delta H < 0$ and dominant, $\Delta S < 0$, (c) $\Delta H < 0$, $\Delta S > 0$ and dominant, (d) $\Delta H > 0$, $\Delta S > 0$ and dominant, and (e) $\Delta H < 0$, $\Delta S > 0$, and of equal importance. The results of Kauffmann et al. (79) are difficult to summarize, because each of the above cases has been observed for the various complexes. The trends in the enthalpies of complexation follow the same trends exhibited by the free energies of complexation, but the enthalpies are generally larger (more negative). Therefore, these complexes are mostly enthalpy stabilized. The entropies of complexation are much less positive (and frequently quite negative) than expected based on the release of solvent molecules upon complex formation. In general, the entropy term favors the complexes of small and bivalent cations over those of large and monovalent ones.

The many contributions to the overall entropy changes include solvation entropies of the metal cation and ligand, the changes in ligand internal entropy (due to orientation, rigidity, and conformational changes), the change in the total number of particles, and translational entropy. The two best explanations for the negative entropy changes (complex destabilization) seem to be the increase in the rigidity of the ligand upon complex formation, and the rearrangement of solvent (water) structure on cryptate formation. An alkali/alkaline earth ion in aqueous solution acts as a structure breaker, because solvation effects disturb the organization of the bulk solvent, but the complexed ion (inside an organic coat) acts as a structure maker since it is much less solvated. Therefore the overall effect

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Laszlo et al. (80) report a study of the Na^+ ion complex with a noncyclic heptadendate ligand in pyridine. They report $\Delta H° = -17$ kcal·mole^{-1} and $\Delta S° = -48$ cal·mole^{-1}·deg^{-1}. These results are not particularly surprising since unfavorable entropy changes are expected when the ligand is wrapped around the sodium ion. Mei et al. have reported a ^{133}Cs NMR study of cesium complexes with 18C6 in pyridine (81) and with C222 in various solvents.(82) In all cases, the complexes were enthalpy stabilized, but entropy destabilized, in some cases by nearly 20 entropy units. Since pyridine and the other nonaqueous solvents studied are relatively unstructured, these large negative changes in entropy must be attributed to increasing rigidity of the ligand upon complex formation.

It is clear that there is no one answer to the question of the macrocyclic/cryptate effect. Systems have been studied in which the effect is either a result of enthalpic stabilization, entropic stabilization, or a combination of both. At this time, despite the considerable amount of data available, more data on carefully selected systems must be obtained in a variety of solvents.

D. Lithium-Macrocyclic Complexes

Among the macrocyclic complexes of the alkali metal ions, the complexes of the Li^+ and Rb^+ ions have been neglected, especially in the case of the lithium crown complexes. Very few data exist on the stabilities of lithium crown complexes, and there appear to be no data

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on the thermodynamics of the lithium ion-crown interactions.

The lithium ion is the smallest of the alkali metal ions, has the highest charge density, and therefore, is the most strongly solvated. In nonaqueous solvents of low solvating ability, the lithium ion is preferentially solvated even by traces of water or other solvating solvents. Therefore, the lithium ion macrocyclic complexes are expected to be weaker than other alkali metal-macrocyclic complexes due to solvation effects alone, and extreme care must be taken in the drying and purification of nonaqueous solvents since small amounts of water can cause misleading results.

Based on the few data which are available, it is doubtful that strong lithium-crown complexes can exist in aqueous solution. It is for the above reasons, perhaps, that there is only a small amount of information on lithium-macrocyclic complexes.

The lithium ion is certainly an important one from several points of view. Lithium salts are used in the treatment of some nervous disorders,(83) and studies of lithium ion complexes with carrier/receptor type molecules may be of some help in understanding the antipsychotic effect of the lithium ion, which is a subject of current interest.(84) The lithium ion may interact with a modified central nervous system receptor which would normally function with a biological cation (Na^+, K^+, Mg^{2+}, or Ca^{2+}). In addition, nonaqueous solvents may be applied to mimic nonpolar membrane-type environments.

A large number of different physicochemical techniques have been used to study the thermodynamic and kinetic aspects of macrocyclic complexation.(85) Several years ago it was demonstrated that the

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nuclear magnetic resonance of alkali nuclei in solution offers a very sensitive probe for such studies. For example, Cahen et al. have used the ^{7}Li NMR technique to study the solvation of lithium ion,(86) the complexation of lithium ion by cryptands C211, C221, and C222,(46) and the kinetics of the C211·Li^{+} decomplexation reaction (87) in various solvents. The limiting chemical shift of the C211·Li^{+} complex was found to be solvent independent, indicating in this case, that the lithium ion is completely insulated from the solvent by this three-dimensional ligand. Lithium cryptates (with cryptands C211, C221, C222, C322, C332, and C333) have also been studied potentiometrically in water and in 95% methanol solutions by Lehn and Sauvage.(29)

Very little quantitative data are currently available in the literature on lithium complexes with crown ethers. Studies of extremely weak lithium ion complexes with dibenzo-18C6,(51) dicyclohexyl-18C6,(31) cyclohexyl-18C6,(31) di-(tert-butyl)dicyclohexyl-18C6,(88) and cyclohexyl-15C5 (31) have been reported in aqueous solutions. Matsuura et al. (89) studied conductiometrically dibenzo-18C6·Li^{+} complexes in dimethylformamide and propylene carbonate solutions, and reported the formation constants of 3.04 and 3.27 (log K), respectively. However, these results have been questioned.(90,91)

The quantitative data currently available on lithium crown complexes and lithium cryptates are presented in Table 3. All of the thermodynamic data which seem to be available are shown in Table 4. It is extremely difficult to draw any conclusions from the stability constant data, but it appears that the complex stability varies

Table 3. Reported Formation Constants for Lithium-Macrocyclic Complexes

Table 3. Reported Formation Constants for Lithium-Macrocyclic Complexes

Ligand	Solvent	log K	Method	Reference
Cyclohexyl-15C5	Water	< 1.0	Pot[a]	31
Cyclohexyl-18C6	Water	< 0.7	Pot	31
Dicyclohexyl-18C6	Water	0.6	Pot	31
Di-(t-butyl)-dicyclohexyl-18C6	Water	< 0.6	Con[b]	88
Dibenzo-18C6	Water	< 0	Spec[c]	51
	DMF	3.04	Con	89
	PC	3.27	Con	89
C211	Water	5.5	Pot	29
	Methanol (95%)	7.58	Pot	29
	Methanol	> 7.5	Pot	29
C221	Water	2.50	Pot	29
	Methanol (95%)	4.18	Pot	29
	Methanol	> 6.0	Pot	29
C222	Water	0.99	NMR[d]	46

Table 3. (cont'd.)

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Ligand	Solvent	log K	Method	Reference
C222	Water	< 2.0	Pot	29
	Methanol	2.65	Pot	29
	Pyridine	2.94	NMR	46
C322, C332, C333	Water	< 2	Pot	29
C322	Methanol	2.3	Pot	29
C222D[e]	Nitromethane	> 4	NMR	92
	Acetonitrile	3.23	NMR	92
	THF	3.12	NMR	92
	Pyridine	2.64	NMR	92
$C2_B11$[f]	Methanol	2.70	Pot	11
$C2_B21$	Methanol	5.0	Pot	11
$C2_B22$	Methanol	2.3	Pot	11
$C2_B2_B2$	Methanol	2.3	Pot	11
$C22C_8$	Methanol	2.2	Pot	29

Table 3. (cont'd.)

Table 3. (cont'd.)

Ligand	Solvent	log K	Method	Reference
$C2_O2_O2_S$[g,h]	Methanol	2.2	Pot	11
$C2_O2_OS2_S$	Methanol	2.3	Pot	11

[a]Potentiometry

[b]Conductance

[c]Spectrophotometry

[d]Lithium-7 nuclear magnetic resonance

[e]C222D is the dilactam of C222.

[f]Subscript "B" indicates benzo.

[g]Subscript "O" indicates oxygen donor.

[h]Subscript "S" indicates sulfur donor.

Table 4. Reported Thermodynamics of Lithium-Macrocyclic Complexes

Table 4. Reported Thermodynamics of Lithium-Macrocyclic Complexes

Ligand	Solvent	$\Delta H°$ (kcal·mole^{-1})	$\Delta S°$ (cal·mole^{-1}·deg^{-1})	Method	Reference
C211	Water	-5.1	8.05	Cal[a]	79
C221	Water	0.0	11.4	Cal	79
C222D	Acetonitrile	1.6	22	NMR[b]	93
	Nitromethane	6.1	38	NMR	93

[a]Calorimetry

[b]Lithium-7 nuclear magnetic resonance van't Hoff plot

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inversely with the solvating ability of the solvent. From the thermodynamic data in Table 4, it is seen that the lithium cryptates are entropy stabilized.

The stabilities, thermodynamics, and influence of solvent on lithium crown complexes remains virtually unexplored. Therefore, a considerable part of this dissertation addresses such a study.

CHAPTER 2

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A. Materials

1. Solvents

Acetonitrile (Matheson, Coleman, and Bell), acetone (Mallinckrodt), and methanol (Fisher or Mallinckrodt) were refluxed over calcium hydride (Fisher) for ~48 hours, then transferred by fractional distillation to another vessel containing freshly activated molecular sieves (Davison, 3 Å pore size, 8-12 mesh), allowed to stand for ~12 hours, and then redistilled. Molecular sieves were first washed with distilled water, oven dried at 200°C, and then activated at 500°C under a flow of dry nitrogen. Nitromethane (Aldrich), dimethyl sulfoxide (DMSO, Fisher), propylene carbonate (PC, Aldrich), and pyridine (PY, Fisher) were dried and purified in the same manner, except all operations were performed under reduced pressure. It was determined that the calcium hydride drying method was inadequate for acetone and methanol due to a reaction of calcium hydride with these solvents. Therefore, acetone was subsequently dried over calcium sulfate (W. A. Hammond Drierite, 8 mesh), and methanol was dried over magnesium turnings and then distilled. Tetramethylguanidine (TMG, Eastman) was refluxed over granular barium oxide (Fisher) for ~48 hours and purified by fractional distillation under reduced pressure. These drying methods produce solvents with water contents of less than 100 ppm determined (except for acetone) by an automatic Karl Fischer titration. The solvents were stored in brown glass bottles in a glove box under nitrogen atmosphere.

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2. Salts

Lithium perchlorate (K & K) and sodium perchlorate (G. F. Smith) were oven dried for several days at 180 and 150°C respectively. Silver perchlorate (Matheson, Coleman, and Bell) was dried for several days over P_2O_5 under vacuum at ambient temperature. Lithium iodide (K & K) was recrystallized from acetone and dried under vacuum over P_2O_5 at ambient temperature. Thallium perchlorate (K & K) was recrystallized from distilled water and dried under vacuum over P_2O_5 at ambient temperature. Potassium hexafluorophosphate (Pflaltz and Bauer) was recrystallized from water and dried for several days at 110°C under vacuum. Tetra-n-butylammonium perchlorate (TBAP, Eastman) was precipitated from acetone and then from methanol by the addition of water, and then precipitated from methanol by the addition of diethyl ether; the product was dried further under vacuum at ambient temperature. Tetra-n-butylammonium hydroxide (TBAH, Matheson, Coleman, and Bell) was obtained as a 25 mass percent solution in methanol and was used as received. Flame emission analysis showed that the concentration of the sodium and potassium ions in the TBAH solution was $< 10^{-6}$ molar.

3. Ligands

Twelve-crown-four (12C4, Aldrich) and fifteen-crown-five (15C5, Aldrich) were purified by fractional distillation under reduced pressure and dried under vacuum. Eighteen-crown-six (18C6, Aldrich or Parish) was purified by first forming the solid acetonitrile·18C6 complex.(94) The adduct was precipitated from an 18C6 solution in

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acetonitrile by cooling it in an ice-acetone bath. The solution was filtered rapidly and the weakly bound acetonitrile was removed under vacuum. The purified product had a melting point of 37-38°C in satisfactory agreement with the literature value of 39°C.(94)

B. Techniques and Instrumentation

1. Spectroscopy

a. Multinuclear magnetic resonance

Lithium-7 NMR measurements were made at 23.3180 MHz and at a field of 14.1 kgauss in the pulsed Fourier transform mode. The field was locked externally with a home-built probe (95) which used the Varian DP-60 console to lock on a proton resonance. This lock system holds the field within ±1 Hz which corresponds to less than ±0.05 ppm at this frequency. Therefore the errors on the chemical shifts are cited as ±0.05 ppm. The NMR spectrometer is interfaced to a Nicolet 1083 computer for time averaging and on-line Fourier transformation of data. The maximum computer memory available for data acquisition is 8192 data points. In order to obtain a relatively high degree of precision, a sweepwidth of 1000 Hz was selected, and all of the 8 K of memory was used for data acquisition. With these acquisition parameters, the optimum flip angle was determined to be ∿70°. In order to increase the signal to noise ratio (S/N), the lines were artificially broadened by 0.1-0.4 Hz by exponential multiplication of the free induction decay before Fourier transformation of the data. Using these acquisition and data manipulation parameters, and a

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lithium ion concentration of 0.02 M, a good signal (S/N ∿5) could be obtained with less than 50 scans (< 3.5 min). All ^{7}Li chemical shift measurements are referred externally to 4 M $LiClO_4$ in water, and are corrected for differences in bulk volume diamagnetic susceptibility of the solvents.(96,97) Equation 1 shows the relationship used to make these corrections.

$$\delta_{corr} = \delta_{obs} + \frac{2\pi}{3}(\chi_v^{\,r} - \chi_v^{\,s}) \qquad (1)$$

where δ_{corr} and δ_{obs} are the corrected and observed chemical shifts, respectively, and $\chi_v^{\,r}$ and $\chi_v^{\,s}$ are the bulk volume diamagnetic susceptibilities of the reference and sample solvents. Table 5 presents some properties of the solvents used in this investigation and the numerical values of the susceptibility corrections applied in this study. A positive value of the chemical shift indicates a shift to lower field. All ^{7}Li NMR measurements were made at 27 ± 1°C. The samples (2 ml) were contained in precision 10 mm o.d. Wilmad NMR tubes which were not spun.

Natural abundance oxygen-17 NMR measurements were made at 24.399 MHz and at a field of 42.3 kgauss in the pulsed Fourier transform mode on a Bruker WH-180 superconducting spectrometer. Due to the broadness of the resonances, only 1 K or 1024 data points were used for data acquisition with a sweep width of 20,000 Hz in the quadrature detection mode. In order to increase the S/N, the lines were artificially broadened by 50 Hz by exponential multiplication of the free induction decay before Fourier transformation of the data. A 50 μsec

Table 5. Some Solvent Properties and Diamagnetic Susceptibility Corrections

Table 5. Some Solvent Properties and Diamagnetic Susceptibility Corrections

Solvent	Dielectric Constant	Gutmann Donor[a] Number	Bulk Volume Diamagnetic Susceptibility x 10^6	Correction (ppm)
Nitromethane	35.9	2.7	-0.391	-0.689
Acetonitrile	37.5	14.1	-0.534	-0.390
Propylene carbonate	65.0	15.1	-0.634	-0.180
Acetone	20.7	17.0	-0.460	-0.545
Methanol	32.7	25.7	-0.515	-0.429
Pyridine	12.3	33.1	-0.612	-0.226
Dimethyl sulfoxide	46.7	29.8	-0.605	-0.241
Tetramethylguanidine	11.0	----	-0.590	-0.272
Water	78.5	$\sim$ 33[b]	-0.720	0.000

[a]Reference 48

[b]Predicted (98)

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radio frequency pulse was used with a pre-delay time of 500 μsec in order to avoid pulse feed through. Using these acquisition and data manipulation parameters, and a sample concentration of 0.5-1.0 M, (containing between four and six equivalent oxygen atoms per sample molecule) a good signal (signal to noise ratio ∿5) could be obtained with ∿500,000 pulses (∿4.3 hr.). The samples (5 ml) were contained in 15 mm o.d. NMR tubes which were fitted inside 20 mm o.d. NMR tubes which contained acetone-d_6 (Stohler). The acetone-d_6 served as both a lock compound and a secondary external reference. All ^{17}O NMR chemical shifts are referred to pure distilled water. A positive chemical shift indicates a shift to lower field. All measurements were made at ambient temperature (∿25°C). The sample NMR tubes were not spun.

b. Infrared

Infrared spectra were obtained using Perkin Elmer models 457 and 237B grating infrared spectrometers. Solutions and Nujol mulls of solid samples were placed between sodium chloride plates. Wavelength calibration was performed by using the standard polystyrene bands.

2. Electrochemistry

a. Potentiometry

Potentiometric titrations were done using the Corning NAS 11-18 sodium-ion electrode which was preconditioned to methanol as described

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by Frensdorff.(31) A methanolic silver-silver chloride reference electrode was used with saturated KCl as the supporting electrolyte; this electrode was constructed with a "thirsty quartz" junction (Corning Vycor brand 7930 acid-leached quartz) which seems to show a much lower transfer of potassium ion into the test solution than any other junction. The output from the electrodes was measured by means of a high-impedance operational amplifier voltage follower (input impedance greater than 10^{12} Ω) connected to an Analogic 2546 digital voltmeter. Potentials could be read in a range ±2.00 V with ±0.1 mV accuracy.

Titrations were carried out in an all-glass cell thermostated at 25.0 ± 0.1°C. The titrant was delivered from two or five ml microburets. In order to avoid solvent losses, the titration cell, while essentially airtight, was not purged with nitrogen. The titration assembly was enclosed in a grounded Faraday cage so as to reduce electrical noise. An air-driven magnetic stirrer was used for solution mixing since electrical stirrers introduced noise into the titration assembly.

The titrations were performed in the following manner. The electrodes were inserted into the cell and 20 ml of a methanolic TBAH solution (the supporting electrolyte and the solvent at a given ionic strength) was introduced and temperature equilibrated for 30 min. This solution was then titrated with a methanolic solution of sodium perchlorate (at the same ionic strength) to generate the electrode calibration curve. The resulting solution was then back titrated with a solution of the ligand, which was also of the same ionic strength, to generate the titration curve.

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b. Cyclic voltammetry

Cyclic voltammograms were obtained by using a Princeton Applied Research Model 174A polarographic analyzer and recorded on a Hewlett Packard 7040A x-y recorder. Voltage measurements were made with respect to an aqueous calomel electrode with 0.1 M NaCl as the supporting electrolyte; a platinum wire was used as the auxiliary electrode, and a hanging mercury drop as the working electrode. Tetra-n-butylammonium or tetraethylammonium perchlorate served as the supporting electrolyte. The solutions were degassed by passing a slow flow of pure dry nitrogen through them after first passing it through two fritted pre-saturators, one containing sulfuric acid and the other the solvent under study. The solution volumes were readjusted with degassed solvent after bubbling.

Both direct and indirect methods were used to study the complexation equilibria. In the direct method, the half-wave potential of Tl(I) ion was observed for various ligand concentrations while the metal concentration was held constant. In the indirect method, a competing metal salt was then added, and the Tl(I) half-wave potential was remeasured.

3. Calorimetry

a. Instrumentation

Enthalpies of complexation reactions were determined with a Guild Model 401-115 isoperibol solution calorimeter.(99) This system consists of a calorimeter cell, calorimeter insert (including

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thermistor, calibration heater, stirrer, and internal stainless steel cooling coil), stand, stirrer motor, temperature measurement and calibration control unit, stop clock, and an external cooling coil purged with a flow of nitrogen which is inserted in an ice bath to offset the heat of stirring. Two sizes of silvered glass dewar cells were fabricated in the Michigan State University glass shop,(100) which have an inner wall glass thickness of 0.4-0.6 mm and require either ∿35 or ∿55 ml of solution. A millivolt strip chart recorder was used to record the output of the thermistor-Wheatstone bridge circuit. The voltage applied to the calibration heater was measured with an Analogic 2546 digital voltmeter and an 8.5:1 voltage divider fabricated with 1% precision metal film resistors with temperature coefficients of 100 ppm. Potentials could be read in a range of ±2.00 V with ±0.1 mV accuracy. The entire system (control unit, recorder, and instrument stand) was grounded to a cold water pipe.

b. Experimental procedure

The actual experiment is performed in the following manner. A solution of one of the reaction components (the metal salt, in the case of complexation reactions) in the given solvent is allowed to equilibrate in the calorimeter cell for ∿1.5 hours while the flow rate of the cooling gas is carefully adjusted to maintain a horizontally straight baseline as close as possible to the initial temperature of the above mentioned solution. The system is then calibrated by electrically delivering a known quantity of heat into the calorimeter

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cell and measuring the recorder response. Since the resistance (R, ohms) of the calibration heater, the voltage (V, volts) across the calibration heater, and the time (t, sec) during which current flows are all known, the heat generated (Q, calories) may be easily calculated using Equation 2 (101)

$$Q = \frac{V^2 t}{4.184\ R} \qquad (2)$$

in which the factor 4.184 converts joules to calories. The response is traced by the recorder which is then calibrated in units of calories per division on the chart paper.

It is extremely difficult, if not impossible, to obtain perfectly adiabatic conditions even with a well designed/fabricated dewar cell. Therefore, some heat losses are observed. Also, since it requires a finite time period to generate electrically the heat of calibration, the final solution temperature is not reached instantaneously. A typical calibration response curve is shown in Figure 2. The curve is analyzed using a temperature extrapolation and time averaging procedure (Figure 2), in which the solid vertical line is used to represent the heat delivered by the calibration heater.

After this first calibration run, the system is brought back to the initial temperature by increasing the flow rate of the cooling gas for several seconds and re-equilibrating. Then the entire calibration procedure is repeated. In general, the precision of the calibration procedure has been determined to be better than ±1%.

Since the temperature of the solution inside the calorimeter

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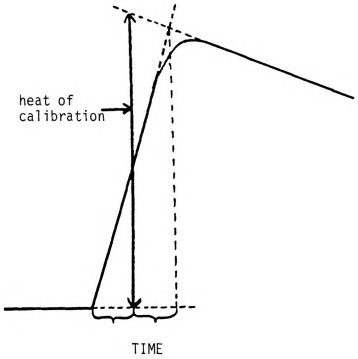

Figure 2. Calorimeter calibration response curve.

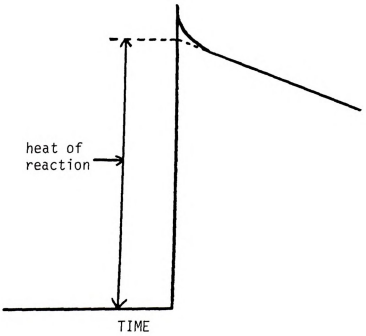

Figure 3. Calorimeter response curve for fast exothermic reaction.

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cell is not exactly equal to the initial temperature (the inside temperature is usually lower than the ambient temperature), a "blank" experiment is performed by adding a known volume (1 ml or less) of pure solvent to the calorimeter cell by means of a syringe and measuring the recorder response. This corrects for both temperature differences and any heat of dilution of the salt solution when the ligand solution is added. The system is brought back to the initial temperature as previously described, and the same volume of a solution of the other reaction component (the ligand) is added to the calorimeter cell by a syringe and the response is measured. After the chemical reaction has taken place, the system is brought back to the initial temperature, re-equilibrated, and re-calibrated twice.

A typical response curve for an exothermic reaction is shown in Figure 3. For fast reactions, the linear portion of the temperature decay is extrapolated back to the initial time of the reaction (Figure 3) to determine the heat involved. For slower reactions, the response curve looks more like a calibration response curve and is analyzed similarly.

The recorder deflection observed for the reaction is then corrected for any differences in temperature determined in the "blank" experiment by adding or subtracting the latter deflection as necessary. The enthalpy of reaction is calculated by comparing the corrected recorder deflection with the post-reaction calibration data. The calibration data obtained after the reaction are used, because the heat of reaction is released into/absorbed from the final resulting solution. Any differences in the calibration data obtained before vs. after the

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reaction are due to any change in the specific heat of the solution as a result of the reaction.

Since the system is calibrated directly in calories per division on the recorder chart paper, solution heat capacity measurements may be omitted. The standard enthalpy of reaction is calculated by dividing the heat of reaction by the number of moles of product formed. This may be done directly for reactions which go virtually to completion, but for incomplete reactions, the equilibrium constant must be known, or a large enough excess of one of the reaction components must be present in solution so as to drive the reaction completely to the right.

c. Testing of calorimeter

The accuracy and the precision of the calorimeter and experimental procedure were determined by using the standard reaction between perchloric acid and sodium hydroxide in aqueous solution.

The experimental procedure described previously was used and was begun with exactly 55 ml of 0.01405 M $HClO_4$ in the calorimeter cell. Various volumes of 0.6406 M NaOH (standardized against potassium hydrogen phthalate) were added during separate experiments to cover reaction conditions which ranged from excess base to excess acid. The results of six determinations were: -13.33, -13.75, -12.92, -13.34, -13.48, and -13.51 kcal·mole^{-1} which average to -13.4 ± 0.3 kcal·mole^{-1}. If the high and low values are omitted, the average would be -13.4 ± 0.1 kcal·mole^{-1}. The literature value for the heat of this reaction is -13.33 kcal·mole^{-1}.(102-104)

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It should be noted that these results have been corrected for the heat of dilution of the added sodium hydroxide solution. This heat was obtained separately by adding some of the NaOH solution to distilled water and determined to be 0.75 $kcal \cdot mole^{-1}$ under these experimental conditions.

The calorimeter and experimental procedure were also tested for a complexation reaction. The enthalpy of reaction for the complexation of sodium ion by 18C6 in anhydrous methanol was determined to be $-8.38\ kcal \cdot mole^{-1}$, in excellent agreement with the value of $-8.36\ kcal \cdot mole^{-1}$ reported by Izatt et al.(24)

4. Other Techniques

a. Data analysis

Use of a CDC 6500 computer system was made for data analysis. A nonlinear least squares curve fitting program KINFIT4 (105) was used to fit experimental data to mathematical equations to linearize ion-selective electrode calibration curve data and to calculate formation constants from NMR data.

The KINFIT4 program provides three checks on the "goodness of fit." A small standard deviation on the calculated value of an unknown is not in itself an indication of a good data fitting. The weights on the data points calculated and applied by the program should be all nearly equal, or this may indicate a systematic error in the data analysis. Lastly, in the case when two or more unknowns are calculated, the output contains a matrix of correlation coefficients.

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If the unknowns are coupled, the program experiences some difficulties in adjusting each unknown for its "best" value. The best data fitting results when one obtains small standard deviations, equal weights, and small correlation coefficients.

Formation constants from potentiometric titration data were calculated using a general equilibrium-solving program MINIQUAD76A.(106,107) Details on the use of these programs are given in the appendices.

b. Solution preparation

All samples were weighed out into volumetric flasks using an analytical balance and transferred to a nitrogen atmosphere glovebox for nonaqueous solution preparation. Solutions containing more than one solute were usually prepared by mixing appropriate volumes of more concentrated solutions followed by dilution to the mark with pure solvent. Unless otherwise noted, all concentrations are reported in molar units.

CHAPTER 3

STABILITIES OF LITHIUM COMPLEXES WITH SOME MACROCYCLIC POLYETHERS

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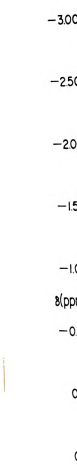
A. Introduction

As indicated previously in the historical review, lithium ion complexes with crown ethers have received a minimum of attention in the literature. The first part of this chapter reports the effects of complex formation on the ^{7}Li NMR spectra and the determination of the complex concentration formation constants with crown ethers 12C4, 15C5, and 18C6 in several solvents. In the second part of this chapter, the results of electrochemical studies on the same complexes are discussed.

B. Results and Discussion

1. Lithium-7 NMR

The variation of the ^{7}Li chemical shifts as a function of the 12C4/Li^{+} mole ratio in various solvents is shown in Figure 4. The lithium-7 NMR chemical shift - mole ratio data are shown in Table 6. It is immediately obvious that the solvent plays an important role in the complexation reaction. For example, the addition of 12C4 to a solution of lithium perchlorate in nitromethane results in a downfield shift with a sharp break at the 1:1 ligand/cation mole ratio followed by an upfield shift which gradually approaches a limiting value as the concentration of the ligand is increased. This behavior clearly indicates a two-step complexation reaction, i.e., the successive formation of a 1:1 and a 2:1 "sandwich" complex. Two complexes are also formed with 12C4 in propylene carbonate solution, but the exact location of the break is not certain due to the small change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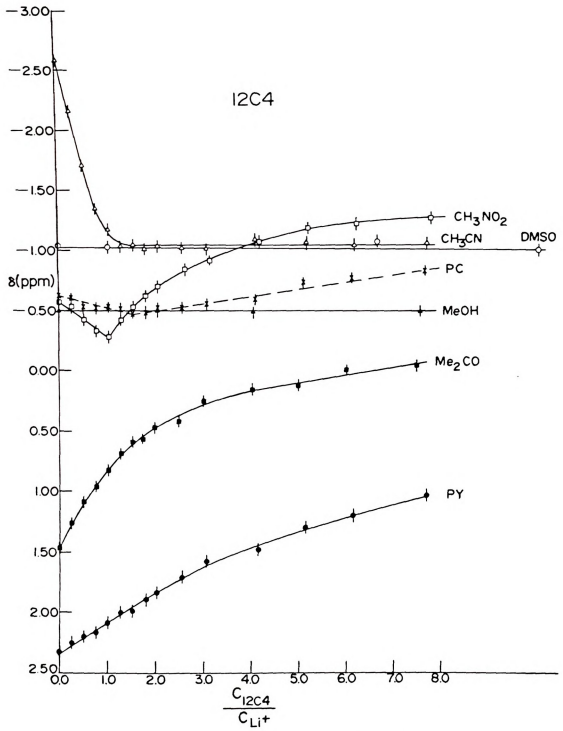


Figure 4. Lithium-7 chemical shifts vs. 12C4/Li^+ mole ratio in various solvents. The solutions were 0.02 M in $LiClO_4$.

Table 6. Lithium-7 NMR Chemical Shift-Mole Ratio Data at 27 ± 1°C

NITROMETHANE					
$\frac{C_{12C4}}{C_{Li^+}}$[a]	δ (ppm)	$\frac{C_{15C5}}{C_{Li^+}}$	δ (ppm)	$\frac{C_{18C6}}{C_{Li^+}}$[b]	δ (ppm)
0.00	-0.57	0.00	-0.54	0.00	-0.57
0.25	-0.53	0.10	-0.56	0.10	-0.63
0.51	-0.42	0.20	-0.68	0.19	-0.64
0.76	-0.33	0.30	-0.70	0.29	-0.69
1.02	-0.28	0.40	-0.80	0.39	-0.71
1.22	-0.42	0.51	-0.77	0.48	-0.72
1.53	-0.52	0.61	-0.89	0.57	-0.75
1.78	-0.62	0.71	-0.99	0.67	-0.76
2.03	-0.70	0.81	-1.10	0.77	-0.76
2.54	-0.85	1.01	-1.13	0.96	-0.77
3.05	-0.91	1.21	-1.19	1.16	-0.77
4.07	-1.07	1.62	-1.19	1.54	-0.82
5.09	-1.19	2.02	-1.23	1.93	-0.83
6.10	-1.22	2.43	-1.21	2.31	-0.79
7.63	-1.27	3.04	-1.23	2.89	-0.80
ACETONITRILE					
0.00	-2.58	0.00	-2.64	0.00	-2.67
0.25	-2.16	0.25	-2.35	0.26	-2.43
0.50	-1.70	0.49	-2.22	0.75	-1.99
0.76	-1.34	0.74	-1.97	0.93	-1.90

Table 6. (cont'd.)

$\frac{C_{12C4}}{C_{Li^+}}$[a]	δ (ppm)	$\frac{C_{15C5}}{C_{Li^+}}$	δ (ppm)	$\frac{C_{18C6}}{C_{Li^+}}$	δ (ppm)
1.01	-1.17	0.98	-1.81	1.06	-1.83
1.26	-1.03	1.23	-1.81	1.44	-1.70
1.51	-1.05	1.47	-1.79	1.86	-1.59
1.76	-1.01	1.72	-1.80	1.88	-1.59
2.02	-1.03	1.97	-1.78	2.14	-1.48
2.52	-1.02	2.21	-1.75	2.59	-1.43
3.02	-1.01	2.46	-1.77	3.50	-1.38
4.03	-1.09	2.70	-1.79	4.32	-1.32
5.04	-1.07	2.95	-1.80	5.22	-1.27
6.05	-1.05	3.93	-1.73	5.52	-1.40
7.56	-1.07	4.92	-1.81	7.94	-1.36
		PROPYLENE CARBONATE			
0.00	-0.62	0.00	-0.64	0.00	-0.66
0.25	-0.60	0.24	-0.85	0.25	-0.72
0.50	-0.53	0.49	-0.99	0.50	-0.80
0.75	-0.52	0.73	-1.23	0.75	-0.85
1.00	-0.54	0.97	-1.39	1.00	-0.90
1.25	-0.51	1.22	-1.39	1.25	-0.89
1.50	-0.47	1.46	-1.44	1.50	-0.94
1.75	-0.48	1.70	-1.40	1.75	-0.97
2.00	-0.52	1.95	-1.41	2.00	-0.99

Table 6. (cont'd.)

$\frac{C_{12C4}}{C_{Li^+}}$[a]	δ (ppm)	$\frac{C_{15C5}}{C_{Li^+}}$	δ (ppm)	$\frac{C_{18C6}}{C_{Li^+}}$	δ (ppm)
2.49	-0.52	2.19	-1.43	2.50	-0.98
2.99	-0.55	2.43	-1.38	3.00	-0.97
3.99	-0.59	2.68	-1.43	4.00	-0.99
4.99	-0.63	2.92	-1.41	5.00	-0.99
5.99	-0.67	3.89	-1.39	6.00	-1.00
7.48	-0.63	4.87	-1.41	7.49	-1.04
			PYRIDINE		
0.00	2.33	0.00	2.37	0.00	2.38
0.25	2.25	0.24	1.73	0.25	2.32
0.51	2.19	0.48	1.04	0.51	2.25
0.76	2.17	0.72	0.46	0.76	2.19
1.02	2.09	0.96	0.06	1.02	2.17
1.27	2.01	1.20	-0.24	1.27	2.13
1.53	1.99	1.44	-0.45	1.53	2.09
1.78	1.89	1.68	-0.59	1.78	2.03
2.03	1.84	1.92	-0.70	2.03	2.04
2.54	1.70	2.40	-0.84	2.54	1.89
3.05	1.58	2.88	-0.89	3.05	1.86
4.07	1.49	3.83	-0.95	4.07	1.70
5.09	1.31	4.79	-1.01	5.09	1.52
6.10	1.21	5.75	-1.07	6.10	1.48
7.63	1.03	7.19	-1.05	7.63	1.32

Table 6. (cont'd.)

$\frac{C_{12C4}}{C_{Li^+}}$[a]	δ (ppm)	$\frac{C_{15C5}}{C_{Li^+}}$	δ (ppm)	$\frac{C_{18C6}}{C_{Li^+}}$	δ (ppm)
		METHANOL			
0.00	-0.49	0.00	-0.49	0.00	-0.53
0.99	-0.53	0.26	-0.53	1.00	-0.51
1.97	-0.50	0.51	-0.57	1.99	-0.53
3.95	-0.48	0.77	-0.60	3.98	-0.53
7.40	-0.49	1.02	-0.64	7.47	-0.59
		1.28	-0.72		
		1.53	-0.72		
		1.79	-0.73		
		2.05	-0.75		
		2.56	-0.84		
		3.07	-0.84		
		4.09	-0.90		
		5.11	-0.99		
		6.14	-0.98		
		7.67	-1.01		
		DIMETHYL SULFOXIDE			
0.00	-1.04	0.00	-1.04	0.00	-1.04
0.98	-1.02	1.49	-1.01	0.95	-0.96
6.56	-1.07	7.46	-1.04	6.30	-0.97
9.84	-1.00			9.47	-1.07

Table 6. (cont'd.)

$\frac{C_{12C4}}{C_{Li^+}}$[a]	δ (ppm)	$\frac{C_{15C5}}{C_{Li^+}}$	δ (ppm)	$\frac{C_{18C6}}{C_{Li^+}}$	δ (ppm)
		TETRAMETHYLGUANIDINE			
0.00	0.44	0.00	0.36	0.00	0.44
10.65	0.42	0.99	0.40	8.73	0.46
		1.97	0.36		
		3.95	0.36		
		7.40	0.33		
		WATER			
0.00	0.06	0.00	0.03	0.00	0.06
9.80	0.05	0.87	0.05	9.67	0.01
		1.74	0.00		
		2.61	0.01		
		4.36	-0.02		
		8.71	-0.02		
		ACETONE			
0.00	1.47	0.00	1.43	0.00	1.46
0.25	1.26	0.25	0.90	0.24	1.31
0.49	1.09	0.50	0.33	0.48	1.11
0.74	0.97	0.75	-0.12	0.71	0.96
0.98	0.83	1.00	-0.51	0.95	0.82
1.23	0.69	1.25	-0.71	1.19	0.74
1.47	0.59	1.50	-0.74	1.43	0.66

Table 6. (cont'd.)

$\frac{C_{12C4}}{C_{Li^+}}$[a]	δ (ppm)	$\frac{C_{15C5}}{C_{Li^+}}$	δ (ppm)	$\frac{C_{18C6}}{C_{Li^+}}$	δ (ppm)
1.72	0.57	1.75	-0.77	1.67	0.59
1.96	0.47	2.00	-0.78	1.90	0.48
2.46	0.42	2.50	-0.83	2.38	0.37
2.95	0.26	3.00	-0.80	2.86	0.28
3.93	0.16	4.00	-0.78	3.81	0.11
4.91	0.12	5.00	-0.82	4.76	0.03
5.89	0.00	6.00	-0.79	5.71	-0.04
7.37	-0.05	7.50	-0.83	7.14	-0.16

$\frac{C_{18C6}}{C_{Li^+}}$[c]	δ (ppm)
0.00	1.25
0.25	1.09
0.50	0.92
0.74	0.83
0.99	0.75
1.24	0.65
1.49	0.59
1.74	0.51
1.98	0.44
2.58	0.34
2.98	0.23

Table 6. (cont'd.)

$\frac{C_{18C6}}{C_{Li^+}}$[c]	δ (ppm)
3.97	0.10
4.96	0.06
5.95	-0.04
7.44	-0.07

[a]The samples were 0.02 M in $LiClO_4$ unless otherwise noted.

[b]These samples were 0.01 M in $LiClO_4$.

[c]In this case only, the salt was LiI.

in the chemical shift. Similar behavior was observed by Mei et al. (47) with the 18C6·Cs^+ system in a number of nonaqueous solvents. Evidently, in both the cases the ligand cavity is too small to comfortably accommodate the metal ion.

On the other hand, the variation of the ^7Li chemical shift in pyridine, acetone, and acetonitrile solutions is monotonic. No variation in the chemical shift could be detected upon addition of 12C4 to $LiClO_4$ solutions in methanol, DMSO, TMG, and water. In the last four cases the solvation of the lithium ion must be strong enough to preclude the complexation reaction. It should be noted that in all cases reported in this chapter the ^7Li linewidth at peak half-height remained reasonably narrow (1-4 Hz) and independent of ligand concentration. Although the natural linewidth is less than 1 Hz, the lines observed in this study were somewhat broader due to the inhomogeneity created by the use of fairly wide bore (10 mm) sample tubes which were not spun.

The variation of the chemical shift with the ligand/Li^+ mole ratio was used as previously described (108) to obtain complex formation constants by means of a nonlinear least squares curve-fitting program, KINFIT4.(105) Equation 3 represents the equilibrium for the formation of a 1:1 complex,

$$M^+ + L \rightleftarrows ML^+ \qquad (3)$$

where M^+, L, and ML^+ represent the metal ion, ligand, and complex, respectively. The concentration equilibrium constant (K) is given

by Equation 4,

$$K = \frac{[ML^+]}{[M^+][L]} \tag{4}$$

where the brackets represent the molar concentrations of each specie. Using the mass balance equations, it can be shown that,

$$\delta_{obs} = [(KC_M - KC_L - 1) + (K^2C_L^2 + K^2C_M^2 - 2K^2C_LC_M + 2KC_L + 2KC_M + 1)^{1/2}]$$

$$[\frac{\delta_f - \delta_c}{2KC_M}] + \delta_c \tag{5}$$

where δ_{obs}, δ_f, and δ_c are the observed, free metal, and complex limiting chemical shifts, C_M and C_L are the metal and ligand analytical concentrations, and K is the equilibrium constant. When the complex is relatively unstable ($K < 100$) the value of δ_c cannot be determined directly from the chemical shift *vs.* mole ratio plot, and Equation 5 has two unknowns, K and δ_c. This method loses accuracy when the formation constant of a 1:1 complex is $\sim 10^4$ and becomes ineffective when $K \geq 10^5$.

The results of the analysis of these data are shown in Table 7. An upper limit for the value of K_2 for $(12C4)_2 \cdot Li^+$ in nitromethane was obtained by assuming that K_1 is so large that, in a solution with stoichiometric amounts of Li^+ and 12C4, the concentration of the free lithium ion is negligible. The small change in the ^7Li chemical shift in propylene carbonate solutions makes quantitative analysis of the data nearly impossible.

Table 7. Formation Constants for Some Lithium-Crown Complexes in Various Solvents

Solvent	Dielectric Constant	Donor[a] Number	log K 12C4	log K 15C5	log K 18C6
CH_3NO_2	35.9	2.7	$\log K_1 > 4$ $\log K_2 = 1.6$[b]	> 4	> 4
CH_3CN	38.8	14.1	4.25 ± 0.46[c]	> 4	2.34 ± 0.04
PC	65.0	15.1	-----	> 4	2.69 ± 0.11
$(CH_3)_2CO$	20.7	17.0	1.62 ± 0.03	3.59 ± 0.08	1.50 ± 0.02
$(CH_3)_2CO$	20.7	17.0	-----	-----	1.51 ± 0.02[d]
CH_3OH	32.7	25.7	~ 0	1.23 ± 0.06	~ 0
PY	12.3	33.1	0.70 ± 0.05	2.48 ± 0.02	0.62 ± 0.07
DMSO	46.7	29.8	~ 0	~ 0	~ 0
TMG	11.0	----	~ 0	~ 0	~ 0
H_2O	78.5	~ 33	~ 0	~ 0	~ 0

[a] Reference 48.

[b] Upper limit.

[c] The errors in the formation constants are the statistical standard deviations resulting from the non-linear least squares treatment of the data. In general the formation constants should be accurate to $\pm$ 0.1 log K unit.

[d] Lithium iodide was used in this case. In all other cases, the salt was $LiClO_4$.

The behavior of the ^7Li resonance as a function of 12C4/Li^+ mole ratio in pyridine and acetone solutions does not give an immediate indication of a step-wise complexation reaction. The monotonic change of the chemical shifts, however, does not preclude the possibility of formation of a 1:1 and a 2:1 complex in these solutions. In fact, similar monotonic curves were observed for the 18C6·Cs^+ system in dimethyl sulfoxide and acetonitrile solutions, but an analysis of the data showed the presence of two complexes.(47)

If only one complex is formed and the exchange between the two cationic sites is fast on the NMR time scale, then the resonance frequency of the cation is given by

$$\delta_{obs} = \delta_f X_f + \delta_c X_c \qquad (6)$$

where δ_f and δ_c are the ^7Li chemical shifts corresponding to the free and the complexed cation, and X_f and X_c are the populations of the lithium ion at each of the two sites. Since $X_f + X_c = 1$, Equation 6 can be rearranged to give

$$\delta_{obs} = (\delta_f - \delta_c)X_f + \delta_c \qquad (7)$$

A value of K_f, assuming a 1:1 reaction was obtained, the mole fraction of free Li^+ ion, X_f, was calculated, and δ_{obs} was plotted <u>vs.</u> X_f. The plots are shown in Figure 5. The data points fall on two very respectable straight lines with the predicted slopes and intercepts, indicating that the experimental data accurately fit the 1:1 complex

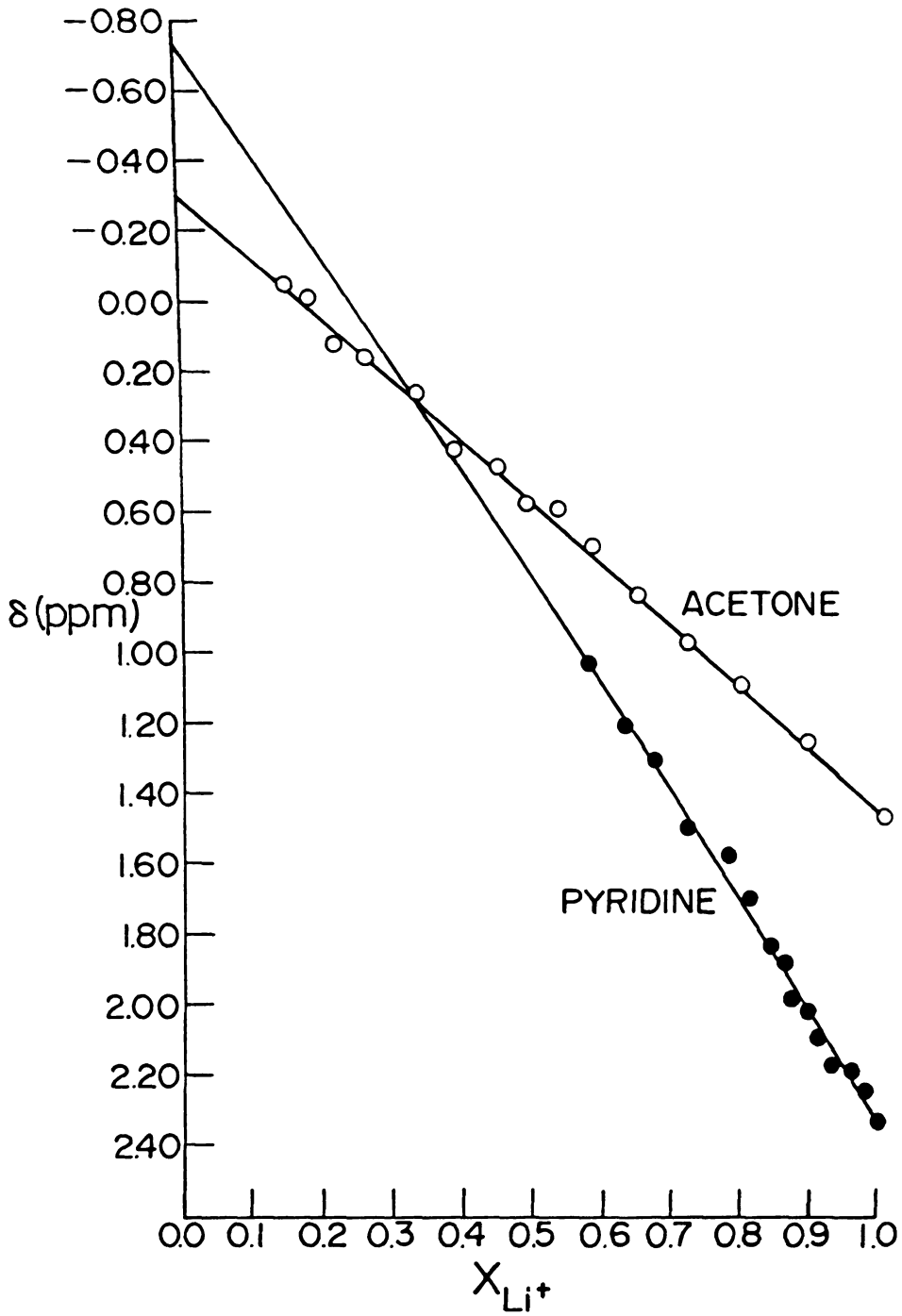


Figure 5. Observed chemical shift vs. mole fraction free lithium ion for 12C4·Li^+ in acetone and pyridine.

model. If a 2:1 complex is also formed, its concentration is negligible vis-a-vis the concentration of other species in solution.

No evidence for 2:1 complex formation is obtained when the lithium ion can comfortably fit inside the crown cavity. Figure 6 shows the mole ratio plots for the 15C5·Li^+ complex in various solvents. Sharp breaks in these plots at a 1:1 mole ratio in nitromethane, acetonitrile, and propylene carbonate solutions indicate the formation of a very stable (log K > 4) 1:1 complex.

On the other hand, such sharp breaks are not observed in the pyridine, acetone, and methanol solutions indicating that in these solvents the complex is much less stable. The addition of the ligand to a Li^+ salt in dimethyl sulfoxide, tetramethylguanidine, and water did not change the ^7Li chemical shift indicating, at best, only a very weak interaction between the ligand and the Li^+ ion.

A much weaker lithium complex is formed with a larger crown, 18C6. The mole ratio plots shown in Figure 7 indicate the formation of a stable complex only in nitromethane solutions where ion-solvent interactions are extremely weak. It is particularly interesting to note that the lithium ion does form a complex with a crown ether which is substantially larger than the ion. In fact, the cavity of 18C6 is substantially larger than the sodium ion.(25) No complexation reaction is observed in methanol, dimethyl sulfoxide, tetramethylguanidine or aqueous solutions.

Various scales of the solvating ability of solvents have been proposed. The scale proposed by Gutmann (48) seems to agree quite well with the behavior of alkali complexes in nonaqueous solvents.

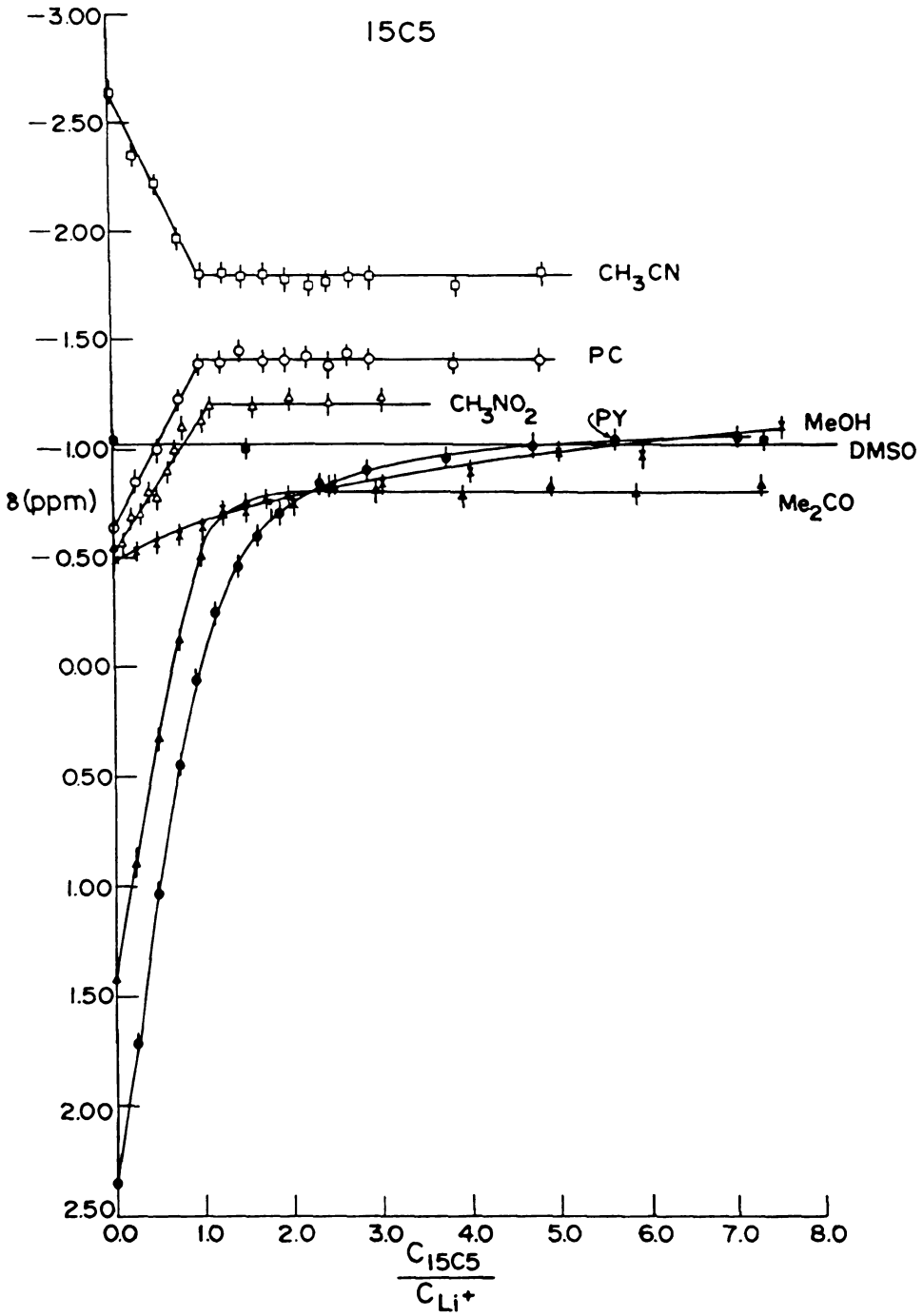


Figure 6. Lithium-7 chemical shifts vs. 15C5/Li^+ mole ratio in various solvents. The solutions were 0.02 M in $LiClO_4$.

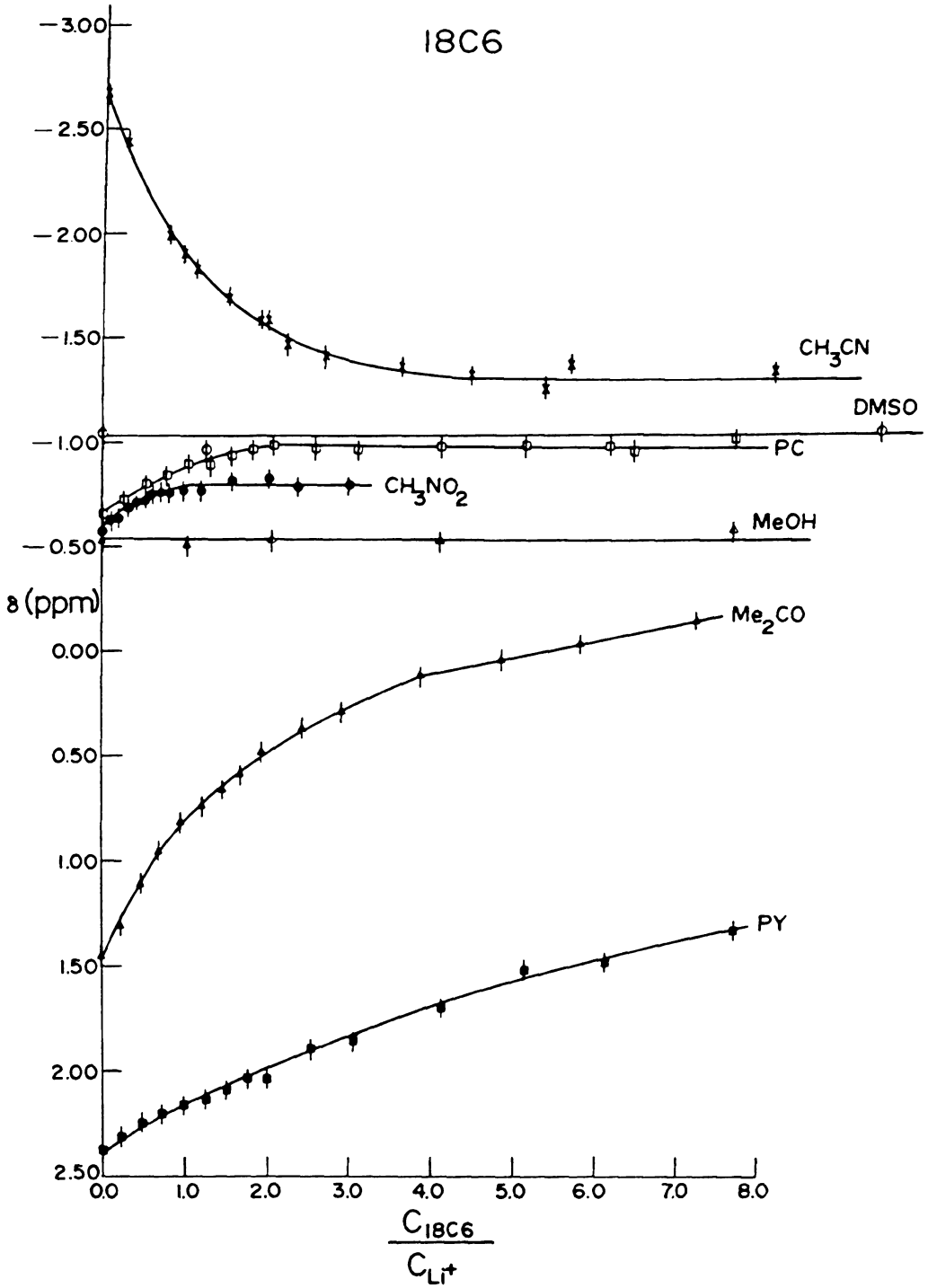


Figure 7. Lithium-7 chemical shifts vs. 18C6/Li^+ mole ratio in various solvents. The solutions were 0.02 M in $LiClO_4$ except in nitromethane where the concentration was 0.01 M.

The Gutmann donor number is defined as the negative enthalpy (in $kcal \cdot mole^{-1}$) of the reaction between a solvent molecule and antimony pentachloride in dilute 1,2-dichloroethane solution to form a 1:1 adduct.

$$S + SbCl_5 \xrightarrow[\text{dilute soln}]{\text{1,2-DCE}} S \cdot SbCl_5 \qquad (8)$$

$$\text{DONOR NUMBER} \equiv -\Delta H_{S \cdot SbCl_5}$$

It is seen from Table 7 that, in general, the stability of the complexes varies inversely with the Gutmann donor number of the solvent. Since the latter expresses the solvating ability of the solvent, this relationship is not unexpected. An obvious exception, however, is found in the case of pyridine solutions, where stable complexes are formed despite the very high donicity of this solvent. Similar behavior for pyridine solutions has been observed previously by Mei et al.(47) A possible reason for such an exception may be the relatively poor solvating ability of pyridine (a nitrogen donor, soft base) towards alkali cations (hard acids).

Another anamaly found in Table 7 is the stability reversal for the $18C6 \cdot Li^+$ complex in acetonitrile and propylene carbonate solutions. On the basis of both the donor numbers and the dielectric constants, it would be expected that this complex would be more stable in acetonitrile. However, ligand-solvent interactions should likewise affect the extent of the complexation reaction. Unfortunately, very little seems to be known about such interactions. It has been shown previously

that the crown ether 18C6 forms a relatively stable complex with acetonitrile which can be isolated in the solid state.(94) It is reasonable to assume that there is a considerable interaction between acetonitrile and 18C6 (and probably other crown ethers) in solution, which would obviously destabilize the 18C6·Li^+ complex.

In a given solvent the stabilities of the 12C4·Li^+ and 18C6·Li^+ complexes are nearly the same. It has already been shown that the 12C4 ligand is too small to accommodate the lithium ion, while the 18C6 ligand is too large for a tight fit inside the cavity. Both of these effects have been shown to destabilize the complex. Another consideration is the fact that the 12C4 ligand has only four donor atoms which would also tend to destabilize the resulting complexes compared to ligands with more donors.

The method used for the calculation of the formation constants does not take into account possible ionic association into solvent-separated, solvent-shared, or contact ion pairs. The literature indicates that in propylene carbonate (109) lithium perchlorate is essentially completely dissociated, while in acetonitrile and methanol solutions, ionic association is small since the ion pair formation constants have been reported to be K = 4 (110) or 68.4 (111) in acetonitrile, and K = 13.7 (112,113) in methanol. It is reasonable to expect that the same conditions will prevail in nitromethane which has a dielectric constant of 35.9. Therefore, in these four solvents, the competition from ion pairing should be negligible.

The situation is somewhat more complicated in the case of acetone solutions since it appears that the lithium salts undergo a considerable

amount of ion pairing in this solvent. The ion pair formation constants have been reported to be 5300 for $LiClO_4$ (114) and 145 for LiI.(115) As seen from Table 7 however, the same complexation constant for the 18C6·Li^+ complex is obtained with the perchlorate and iodide counterions. Also, the calculated limiting chemical shift of the complex is independent of the counterion (Table 8). It seems that if the ion pairing constants truely differ by more than one order of magnitude, the value of the "apparent" complexation constant should not be the same.

In the case of pyridine solutions it seems that the data on the ionic association in this solvent are not available. However, it would be expected that the low dielectric constant will favor ionic association and that in this case the complexation reaction competes with the ion pair formation. Therefore the values given in Table 7 represent relative complexing abilities of the three ligands in this solvent.

It is seen in Figures 4, 6, and 7 and Table 8 that the limiting chemical shifts of the lithium crown complexes approach the same general area, but the mole ratio plots do not converge to the same limiting value as was observed in the case of the C211·Li^+ complex in various solvents.(46) The limiting chemical shifts are somewhat solvent dependent, because the solvent molecules may still approach the complexed lithium ion from the open faces of the crown ethers.

It is well known, of course, that one of the main factors affecting the stability of macrocyclic complexes is the consonance between the size of the macrocyclic cavity and the ionic diameters. As seen

Table 8. Limiting Chemical Shifts of Some Lithium-Crown Complexes in Various Solvents

Solvent	Limiting Chemical Shift (ppm)			
		12C4	15C5	18C6
CH_3NO_2	-0.28[a] (1:1)	-1.51 ± 0.03[b] (2:1)	-1.21	-0.80
CH_3CN	-1.04		-1.79	-1.32
PC	-----		-1.41	-0.99
$(CH_3)_2CO$	-0.30 ± 0.03		-0.80	-0.52 ± 0.02
$(CH_3)_2CO$	-----		-----	-0.39 ± 0.03[c]
CH_3OH	-----		-1.25 ± 0.05	-----
PY	-0.74 ± 0.26		-1.15 ± 0.01	-0.44 ± 0.30

[a]Values cited without uncertainties were determined directly from the mole ratio plots and are accurate to ± 0.05 ppm.

[b]The errors cited in the calculated chemical shifts are the statistical standard deviations resulting from the nonlinear least squares data fitting. In general, these values are accurate to ± 0.05 ppm.

[c]Lithium iodide was used in this case. In all other cases, the salt was $LiClO_4$.

in Table 9, if the well accepted Pauling's ionic size of the lithium ion is assumed, the stability of the lithium complexes should be in

Table 9. Ionic Diameters of Alkali Ions and Ring Sizes of Some Crown Ethers

Cationic Diameters (Å)			Ring Size (Å)[b]		
Cation	Pauling	Electron[a] Density	Crown Ether	Corey-Pauling-Koltun	Fisher-Hirschfelder-Taylor
Li^+	1.20	1.86	12C4	1.2	1.5
Na^+	1.90	2.34	15C5	1.7	2.2
K^+	2.66	2.98	18C6	2.6	3.2
Rb^+	2.96	3.28			
Cs^+	3.38	3.66			

[a]Reference 116.

[b]Reference 117.

the order 12C4 > 15C5 > 18C6. Since the order is experimentally determined to be 15C5 > 12C4 ∿ 18C6, it seems that the ionic sizes obtained from the electron density measurements give better agreement with our results. It should also be noted that in all cases reported thus far, the sodium ion forms stronger complexes with 18C6 than with 15C5;(24) again, these results correlate better with the ionic sizes

obtained from electron density measurements.

The formation constants given in Table 7 were calculated in concentration units. Since in these cases, the complexation reaction does not result in a separation or combination of charges, we can assume that as long as the total ionic strength of a solution remains low, the values of the concentration constant will closely approximate the thermodynamic value. The validity of this assumption is investigated in Chapter 4.

2. Electrochemistry

Several strong lithium crown complexes (log K > 4) were encountered during this study. Due to the overall small range of lithium-7 chemical shifts and the method used to treat the NMR data, formation constants > 10^4 for 1:1 complexes could not be accurately determined. However, electrochemical techniques lend themselves quite well to the determination of very stable complexes. It should be noted that the intensity of a spectrometric signal (including NMR) is proportional to the concentration of the chemical species observed, while in potentiometric and polarographic studies, the signal is proportional to the logarithm of the concentration.

A considerable amount of time was spent trying to obtain a lithium ion-selective electrode, but without any success. Furthermore, the monovalent cation electrodes tested (Beckman 39137 and Corning 476220) yielded neither Nernstian nor reproducible response curves for the lithium ion. A competition method using a glass silver ion-selective electrode (Corning NAS 11-18) in methanol was successfully applied.

In this case, the ligand·Ag^+ equilibrium constants were determined, and then the system was titrated with a lithium salt solution. Since some ligand·Li^+ complex is formed, there is an increase in the Ag^+ ion concentration. With these data, the ligand·Li^+ formation constant can be calculated. Only very weak lithium crown complexes were observed in methanol. For studies in aprotic nonaqueous solvents, silver wire electrodes (Sargent, Catalog #S-30515C) were used to perform similar competitive experiments, but the silver wire electrode responses were neither Nernstian nor reproducible.

Cyclic voltammetry was then used to determine these large formation constants. The method used by Lingane (118) may be applied to the study of labile complexes provided the following assumptions are met. First, the electrode reaction must be reversible. The heterogeneous electron transfer at the electrode surface must be able to keep up with the potential sweep rate. Second, a large excess of ligand must be used so that the concentration of free ligand at the electrode surface may be assumed to be equal to that in the bulk solution, and also so that the change in the free ligand concentration upon complexation is small compared to its analytical concentration, and the free and analytical concentrations may be assumed to be equal. Lastly, it is assumed that the diffusion current constants for the free and complexed metal ions are nearly the same. Also, the experiment is performed at constant ionic strength.

With these assumptions applied to reaction 9

$$M + jL \rightleftarrows ML_j \qquad (9)$$

where

$$\beta_{ML_j} = \frac{[ML_j]}{[M][L]^j} \tag{10}$$

Lingane's equation is

$$\Delta E_{1/2} = (E_{1/2})_{free} - (E_{1/2})_{complex} \tag{11}$$

$$= \frac{2.303\ RT}{nF} \log \beta_{ML_j} + \frac{2.303\ RT}{nF}\ j \log C_L \tag{12}$$

where C_L is the analytical ligand concentration. This equation predicts that the measured half-wave potential of an electroactive cation should shift to a more negative potential in the presence of the ligand. A plot of $\Delta E_{1/2}$ *vs.* log C_L should yield a straight line from which the combining ratio, j, and the formation constant β_{ML_j} can be determined.

In many solvents, it is difficult to observe directly the reduction of the lithium ion, because it is too close to or beyond the solvent reduction wave. However, in acetonitrile, the lithium ion behaves fairly reversibly, but the addition of 15C5 resulted in irreversible behavior. Therefore, this direct method would not be applicable. Since the ligands used in this study have small cavity sizes, it is desirable to use a small electroactive cation to avoid higher order complexes in solution. Cadmium(II) perchlorate was then used to perform this experiment in an indirect manner. The Cd^{2+}-Cd^0 couple behaved reversibly, but this behavior became irreversible when 15C5 was added. While the $Cd(ClO_4)_2$ behaved irreversibly in the

presence of 15C5, the CdI_2 behaved partially reversibly, perhaps due to some specific adsorption of the iodide ion at the electrode surface.

Reversible behavior has been found for Tl(I) with cryptand C222 in dimethylformamide and dimethyl sulfoxide.(119) This reversibility may be due to the partially covalent character of the Tl^+-O bonds. Thallium(I) perchlorate behaves fairly reversibly in acetonitrile and propylene carbonate solutions in the absence and presence of 15C5 as is apparent in the forward to backward peak separation of $\sim$80 mV (theoretical 57 mV) with potential sweep rates of 20 mV/sec or less. However, Tl^+ ion is much larger than Li^+ ion, and both 1:1 and 2:1 complexes can be formed with ligands 12C4 and 15C5. Therefore, many more solutions must be studied to define the plot of $\Delta E_{1/2}$ *vs.* C_L, because it would not be linear due to 1:1 and 2:1 complex formation. In principle, this does not present a problem, but practically, some difficulties were encountered. First of all, the aqueous SCE reference electrode with KCl as the supporting electrolyte could not be used due to the formation of a precipitate on the tip of the reference electrode. This was due to the low solubility of $KClO_4$ in nonaqueous solvents, where the ClO_4^- comes from the supporting electrolyte in the sample solution. Then saturated NaCl in H_2O was used as the fill solution, but NaCl is not soluble enough in certain nonaqueous solvents, and the above problem reappeared. Finally a 0.1 *M* NaCl in H_2O fill solution was used more successfully. The problem comes when many solutions are analyzed. It is preferable to leave the reference electrode in the solution so that the liquid junction

potential remains fairly constant. However, as the reference electrode remained in the solution over a period of time, a precipitate formed on the fiber at the tip of the reference electrode, which changed the reference potential. Furthermore, as this aqueous reference electrode is allowed to remain in the solution, water diffuses into the specifically dried and purified nonaqueous solvent. It should be possible to overcome these difficulties by the use of a reference electrode in the same solvent under study. This is more easily said than done, however.

Since two complexes exist between Tl^+ and 12C4 and 15C5, the equations of DeFord and Hume (120) must be applied for step-wise reactions

$$\Delta E_{1/2} = \frac{2.303\ RT}{nF} \log \beta_{ML_j} C_L^{\,j} \tag{13}$$

$$= \frac{2.303\ RT}{nF} \log(\beta_{ML} C_L + \beta_{ML_2} C_L^{\,2} + \ldots) \tag{14}$$

The data may then be analyzed using the Fronaeous equations.(121)

Should the ligand·Tl^+ equilibrium constant be quantitatively determined, a modification of the Ringbom and Eriksson (122,123) method can be applied to determine the ligand·Li^+ equilibrium constant. It was observed in this study that the addition of 15C5 to a solution of Tl^+ results in a shift of the half-wave potential to more negative values as the free ligand concentration is increased. The addition of another complexable metal ion should decrease the concentration

of free ligand, and the half-wave potential of Tl(I) reduction should revert to more positive values. From the equations given previously, the formation constants of the strong lithium crown complexes can then be evaluated.

CHAPTER 4

THE INFLUENCE OF IONIC STRENGTH ON THE CONCENTRATION FORMATION CONSTANT OF ION-MOLECULE COMPLEXES

A. Introduction

Experimental measurements of equilibrium constants of ionic reactions in solutions involve the vexing problem of activity corrections. A very common practice is to make the measurements at a "high and constant" ionic strength. It should be noted, however, that if alkali salts are used to maintain high ionic strength, they can sometimes participate in the reactions (particularly in complexation reactions) and, in addition, at high concentrations even in aqueous solution some ionic association can occur.

It is preferable (although more difficult) to measure the concentration constant at several ionic strengths and to extrapolate the results to an ionic strength of zero. Another procedure, although not as effective as the extrapolation method, is to calculate the activity coefficients using an appropriate form of the Debye-Hückel equation.

On the other hand, for ion molecule reactions of the type

$$M^+ + L \rightleftarrows ML^+ \tag{3}$$

where M^+ represents a metal ion and L some neutral ligand, the thermodynamic equilibrium constant is given by

$$K_t = \frac{a_{ML^+}}{a_{M^+}a_L} = K_c \frac{\gamma_{ML^+}}{\gamma_{M^+}\gamma_L} \tag{15}$$

where K_t, K_c, a's, and γ's represent the thermodynamic value,

concentration value, activities, and activity coefficients, respectively. It is generally assumed that $\gamma_{ML^+} = \gamma_{M^+}$ and that $\gamma_L = 1$. Thus the concentration equilibrium constant, K_c, is assumed to be essentially equal to the thermodynamic constant, K_t. However, it is obvious that the first approximation is valid only within the validity of the Debye-Hückel limiting law, i.e., for $I < 10^{-3}$ M in aqueous solutions and at much lower ionic strength in nonaqueous solvents with an intermediate or low value of the dielectric constant. At ionic strengths where the exact form of the Debye-Hückel equation,

$$-\log \gamma_i = \frac{AZ_i^2\sqrt{I}}{1 + Ba_i\sqrt{I}} \tag{16}$$

is valid, the activity coefficients of the free and complexed metal ions will not be equal since the size parameters (a_i) will be different, presumably with $a_{ML^+} > a_{M^+}$. This relationship predicts that $\gamma_{ML^+} > \gamma_{M^+}$ and therefore, $K_c < K_t$ at appreciable ionic strengths. In addition, at higher ionic strengths the activity coefficient of the neutral ligand γ_L will not be equal to unity.

In a saturated solution of the ligand, L, the chemical potential of dissolved L, is necessarily equal to that of solid L.

$$\mu^L_{solid} = \mu^{o,L}_{soln} + RT \ln a^L_{soln} \tag{17}$$

The addition of an electrolyte to the above solution may change the solubility of L, but not the chemical potential of the solid. As long as the solution remains saturated, the activity of L, a^L_{soln},

will also remain constant. Let

m_o = solubility (molal) of L in pure solvent

γ_o = activity coefficient of L in saturated solution

m_I = solubility (molal) of L in a solution of ionic strength I

γ_I = activity coefficient of L in the above solution

Then,

$$m_o\gamma_o = m_I\gamma_I \tag{18}$$

which may be rearranged to

$$\frac{\gamma_I}{\gamma_o} = \frac{m_o}{m_I} \tag{19}$$

It has been found experimentally (124) that

$$\log \frac{\gamma_I}{\gamma_o} \approx kI \tag{20}$$

which is of the exact same form as the well known empirical Setschenow equation,(125,126) where k is a constant which depends on the nature of L and of the electrolyte, and presumably on the solvent as well. For most electrolytes, $0 < k < 0.1$ so that the addition of an electrolyte decreases the solubility of the nonelectrolyte (salting out effect). Therefore, γ_L varies directly, but slightly with the ionic strength of the solution and tends to counteract the action of the

ion size parameter. However, Mohilner, et al. (127) have shown in aqueous solutions that for concentrations of a neutral molecule (2-butanol) up to 0.7 M, the activity coefficient of 2-butanol remained equal to unity in the presence of an electrolyte (sodium sulfate) whose concentration was 0.1 M, which corresponds to an ionic strength of $\sim$0.3 M. It is seen therefore, that in this work we assume that γ_L = unity.

For complexation reactions of the type shown in Equation 3, it is a common practice to report the thermodynamic formation constants in concentration units, which assumes that $\frac{\gamma_{ML^+}}{\gamma_{M^+}\gamma_L}$ = unity. It was of interest to us to test the validity of the above practice. Since the values of a_{M^+} and a_{ML^+} are generally unknown and since it is not possible at the present time to calculate precisely the variation of the activity coefficient of a neutral molecule as a function of the ionic strength of the solution, concentration formation constants were determined potentiometrically for the reaction

$$Na^+ + 18C6 \rightleftarrows 18C6 \cdot Na^+ \qquad (21)$$

in anhydrous methanol solutions at (25.0 $\pm$ 0.1)°C at various ionic strengths using tetra-n-butylammonium hydroxide as the supporting electrolyte.

B. Results and Discussion

The cell used in the potentiometric titrations was as follows:

Ag/AgCl//salt solution/glass electrode sensitive to Na^+

where the cell potential is given by

$$E = E^{\circ}_{glass} + \frac{RT}{nF} \ell n\, a_{Na^+} - E_{Ag/AgCl} + E_j \qquad (22)$$

$$= E^{\circ}_{cell} + \frac{RT}{nF} \ell n\, a_{Na^+} + E_j \qquad (23)$$

$$= E^{\circ}_{cell} + E_j + \frac{RT}{nF} \ell n\, \gamma_{Na^+} + \frac{RT}{nF} \ell n\, [Na^+] \qquad (24)$$

At constant ionic strength, γ_{Na^+} should remain constant. In the course of the titration, since the electrodes are not removed from the solution, and the solution composition changes very little, the liquid junction potential E_j should also remain constant. Therefore the expression for the cell potential may be rewritten as

$$E = E^{\circ\prime}_{cell} + \frac{RT}{nF} \ell n\, [Na^+] \qquad (25)$$

where E°' is the sum of the standard, liquid junction, and glass asymmetry potentials, and the activity coefficient term. Concentration electrode calibration removes the uncertainty involved in relating potentials of buffer solutions of known activity to measurements made at different ionic strengths.

This electrode calibration procedure gave calibration curves which deviated from linearity at $\sim 10^{-5}$ M. Midgley and co-workers (128) discussed the factors affecting the linearity of glass

ion-selective electrode calibration curves and concluded that the major contributions to nonideal calibrations fall in three classes: interfering contaminants, reagent blank, and dissolution of alkali metal ions from the glass membranes at or near the limit of detection. In this work, the contribution from the dissolution of the glass is considered to be negligible. Therefore, the calibration curves were linearized by fitting the experimental data to Equation 26

$$E = E^{\circ\prime} + m \log ([Na^+] + R) \qquad (26)$$

where $E^{\circ\prime}$, m (the Nernst slope) and R (the effective residual cation concentration contributed by the impurities in the solvent) are permitted to vary using a non-linear least-squares curve fitting procedure until the difference between the calculated and observed potentials is sufficiently small. Usually, the residual, R, was calculated to be $\sim 10^{-6}$ M which is in agreement with the concentration of sodium ions which may be experimentally realized in the reagent blank. A typical titration calibration curve is shown in Figure 8. The solid curve is the calculated calibration curve, and the solid circles are the experimental points.

After the calibration solution is back-titrated with the ligand, the value of the concentration complex formation constant can be calculated. Since the residual cation concentration is negligible compared to the total metal concentration, the amount of ligand used to complex this residual cation is also negligible. The concentration of the free sodium ion can be determined from Equation 27.

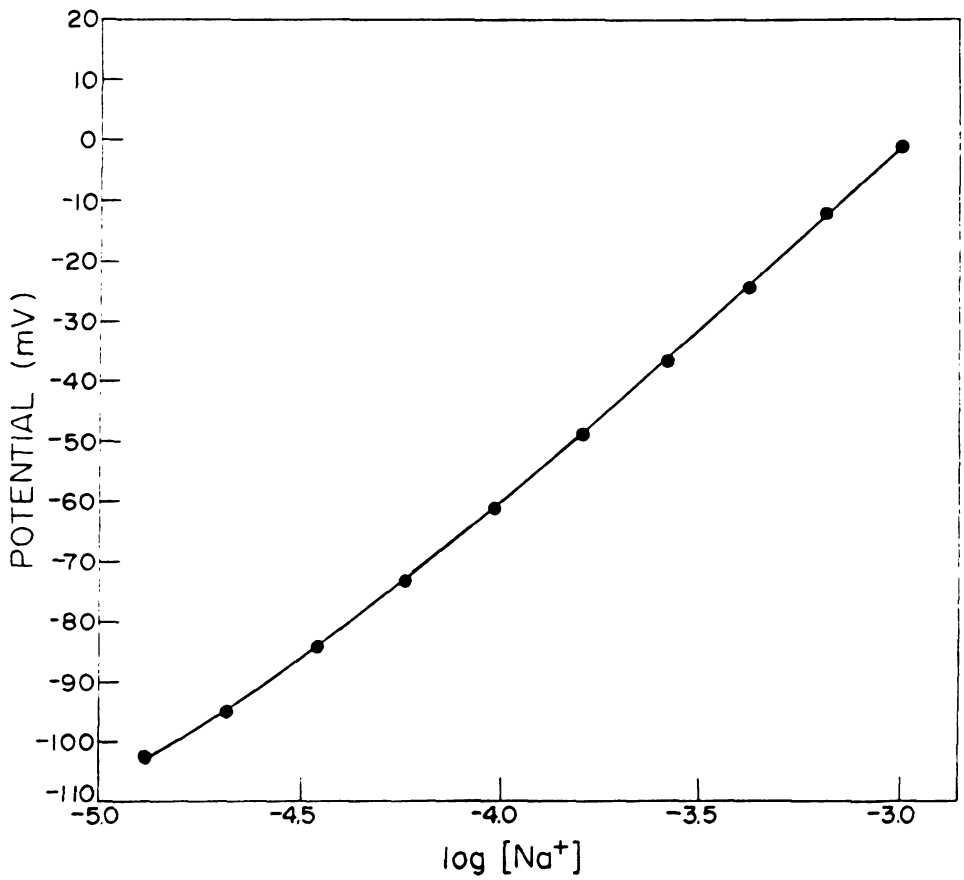


Figure 8. Calibration curve for the sodium-ion electrode in anhydrous methanol measured at I = 0.40 M.

$$[Na^+] = 10^{\left(\frac{E - E^{\circ\prime}}{m}\right)} \quad (27)$$

The mass balance equations are

$$[18C6 \cdot Na^+] = C_{Na^+} - [Na^+] \quad (28)$$

$$[18C6] = C_{18C6} - [18C6 \cdot Na^+] \quad (29)$$

where C_{Na^+} and C_{18C6} are the analytical concentrations of the sodium ion and the 18C6 ligand, respectively.

Before the equivalence point, the condition that $[18C6 \cdot Na^+] \approx C_{18C6}$, leads to large errors in the calculation of [18C6] by Equation 29. Therefore, only data after the equivalence point were used as input to the MINIQUAD76A general equilibrium solving program. A typical titration curve is shown in Figure 9. The agreement between the experimental and the calculated results was quite good, and the residuals on the calculated concentrations also showed little systematic error.

Concentration equilibrium constants for reaction 21 were obtained at various ionic strengths using TBAH as the supporting electrolyte. We assumed that TBAH was indeed an "inert" supporting electrolyte since the logarithms of the formation constants of 18C6 complexes with dimethylammonium and diethylammonium cations in methanol solutions are 1.76 and 0.85 respectively (129) and, therefore, one would not expect any complexation of the TBA ion by the 18C6 ligand. In addition, precise electrical conductance studies of ionic association

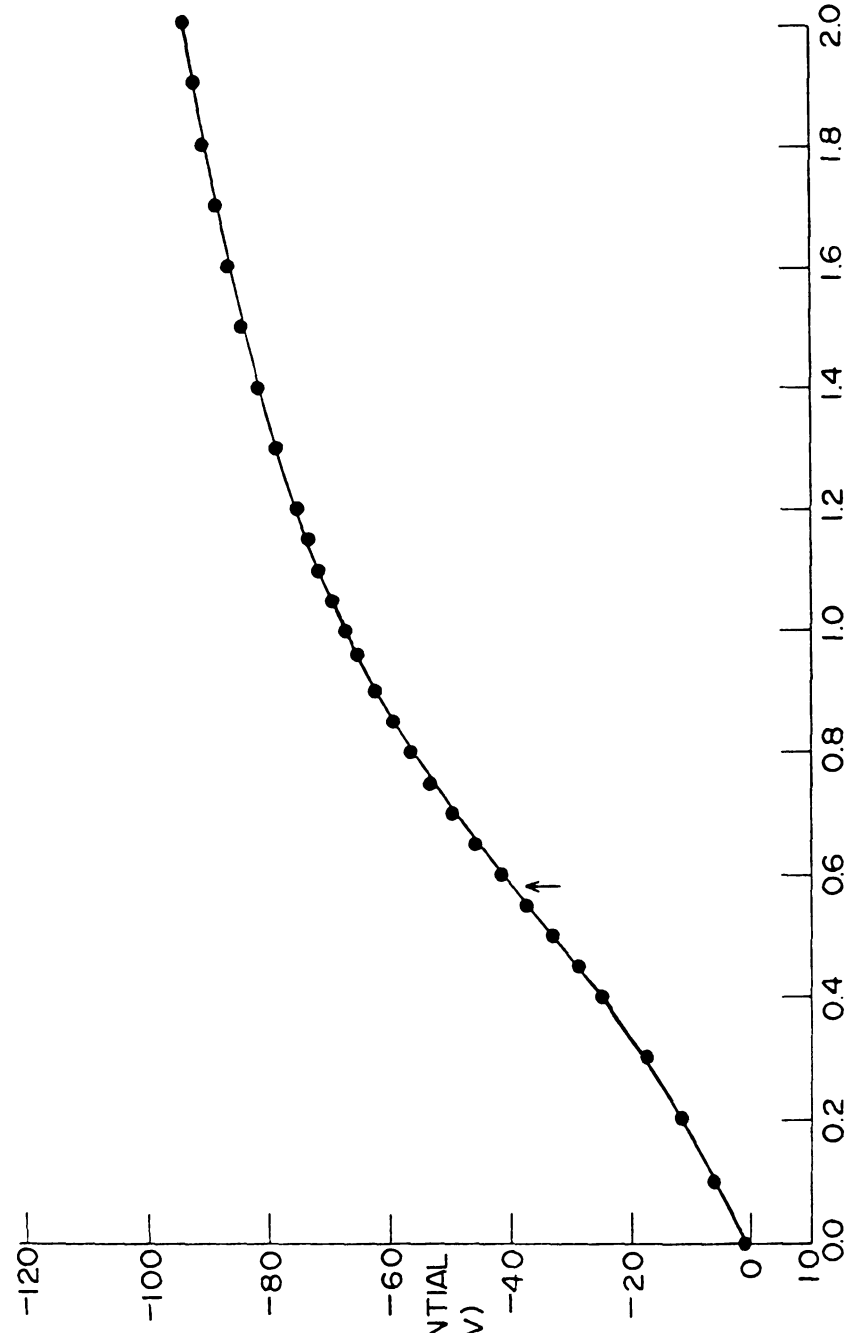


Figure 9. Titration curve of sodium perchlorate with 18C6 in anhydrous methanol measured at I = 0.40 M. The arrow indicates the equivalence point.

in anhydrous methanol solutions by Kay et al. (130) could not detect ion-pair formation in tetrabutylammonium chloride solutions. Data on the TBAH do not seem to be available in the literature, but it seems reasonable to conclude that in this case, the amount of ion pairing at best would be very small.

The results are shown in Table 10 and Figure 10. It is seen that for the ionic strength of 0.005 M to 0.05 M, the value of the concentration formation constant remains reasonably close to the extrapolated value at zero ionic strength (K_t). At higher ionic strengths however, the K_c value is somewhat further from the thermodynamic value. Since γ_L increases with increasing ionic strength (tending to increase the value of K_c), the decrease in K_c indicates that the variation in the ion-size parameter is the more important factor than the variation in γ_L.

Extrapolation of these results to infinite dilution yields a value of log K_t = 4.34 which is in good agreement with the value of 4.32 obtained by Frensdorff (31) also from potentiometric measurements, and a value of 4.36 obtained by Izatt, et al. (131) from calorimetric measurements.

The results plotted in Figure 10 illustrate that the influence of ionic strength on the concentration formation constant is measurable by our technique. However, the effect of the ionic strength on the ion-molecule reaction is rather small. The data given in Table 10 were used to fit the distance of closest approach for the complexed metal ion, a_{ML^+}, to the Debye-Hückel equation. Values of 4.0, 4.5, and 5.0 Å were assumed for the distance parameter of the

Table 10. Concentration Formation Constants, K_C, for the Reaction $Na^+ + 18C6 \rightleftharpoons 18C6 \cdot Na^+$ in Anhydrous Methanol at Various Ionic Strengths, I.

I (M)	log K_C [a]
0.005	4.33
0.01	4.32
0.03	4.30
0.05	4.29
0.08	4.27
0.10	4.28
0.20	4.22
0.30	4.17
0.40	4.13
0.50	4.09

[a] The uncertainty in log K_C is $\pm$ 0.02.

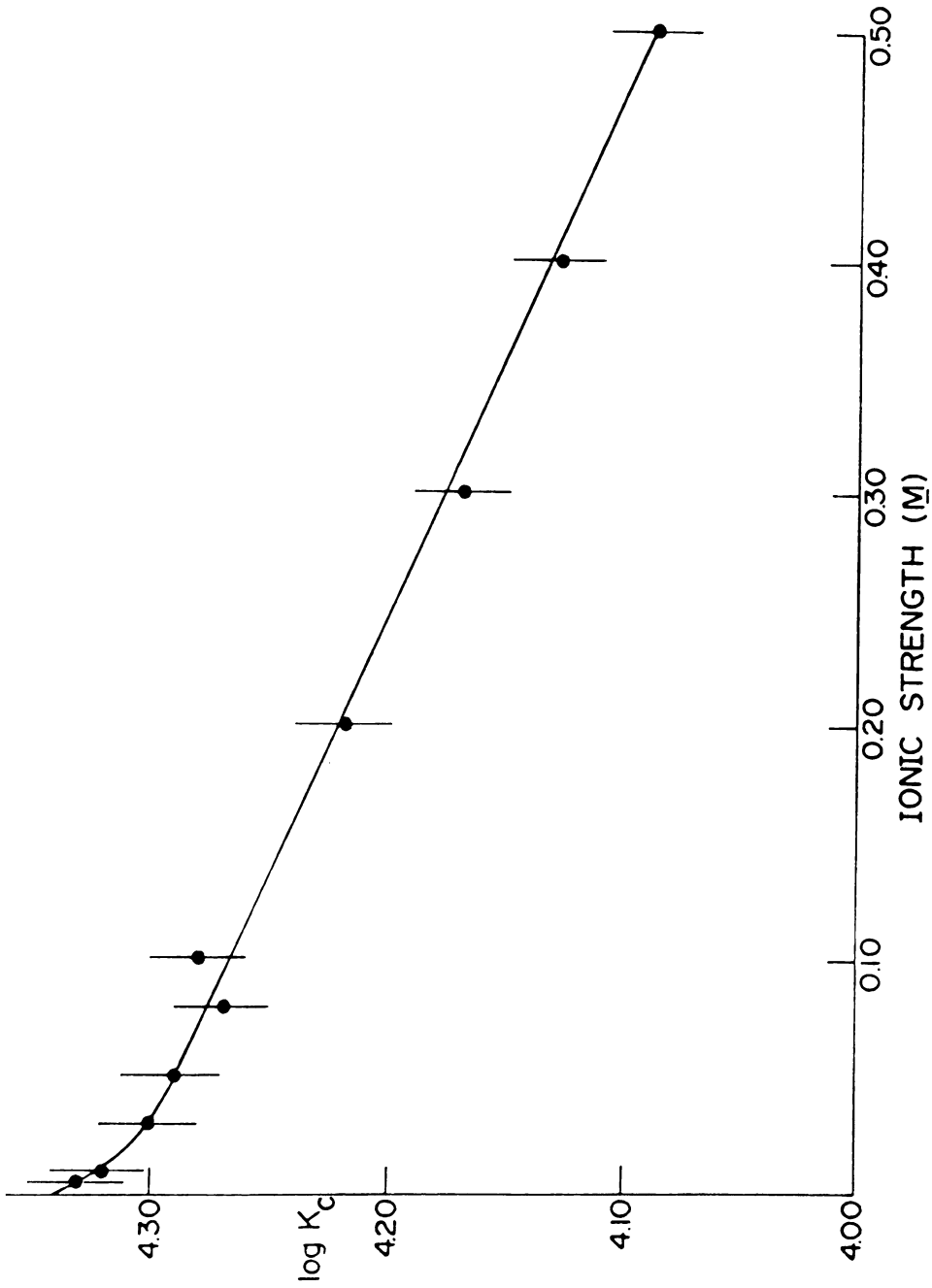


Figure 10. A plot of log K_c for the 18C6·Na^+ complex in anhydrous methanol against the ionic strength of the solution.

solvated sodium ion, and the KINFIT4 program was used to fit the data. The corresponding values of a_{ML^+} were calculated to be (8.0 ± 0.9), (9.2 ± 0.5), and (10.4 ± 0.7) Å respectively. Since the "small a" parameter in the Debye-Hückel equation is related to the distance of closest approach, these values are quite reasonable for the size of the solvated complex ion. Furthermore, these values should be considered to be at best only approximate, because the Debye-Hückel equation was used at ionic strengths where its usefulness is, at best, rather limited.

CHAPTER 5

ENTHALPY AND ENTROPY OF THE LITHIUM-CROWN COMPLEXES

A. Introduction

The thermodynamic stability ($\Delta G°$) of a complex is comprised of two components, the enthalpy ($\Delta H°$) and the entropy ($\Delta S°$) of complexation. The enthalpy changes are associated with the formation/destruction of bonds among the metal ion, ligand, and solvent molecules. The entropy changes depend on the overall changes in the order of the system. Although it is nearly impossible to separate the enthalpy and the entropy into their microscopic components, the macroscopic or overall quantities can be determined experimentally.

Two methods exist for the determination of these thermodynamic quantities. The temperature dependence of the stability constant can be determined, and the van't Hoff isotherm can be applied

$$\Delta G° = -RT \ln K + RT \Sigma \nu \ln C \qquad (30)$$

in which C is the concentration of the reactant/product and $\nu < 0$ for reactants and $\nu > 0$ for products. The abbreviated form of the van't Hoff isotherm is obtained by selecting the standard state as the hypothetical ideal 1 M solution of each specie.

$$\Delta G° = -RT \ln K \qquad (31)$$

Since

$$\Delta G° = \Delta H° - T\Delta S° \qquad (32)$$

then

$$-RT \ln K = \Delta H^\circ - T\Delta S^\circ \tag{33}$$

which may be arranged to

$$\ln K = -\frac{\Delta H^\circ}{R}\left(\frac{1}{T}\right) + \frac{\Delta S^\circ}{R} \tag{34}$$

A plot of $\ln K$ vs. $\frac{1}{T}$ should yield a straight line (provided ΔH° is independent of the temperature) from which ΔH° and ΔS° can be obtained.

This method has been criticized because it assumes that ΔH° is temperature independent. Furthermore, the determination of the thermodynamic quantities from the temperature dependence of the formation constant is generally less accurate than the calorimetric method, because a small error in the equilibrium constants can result in a large error in ΔH°, particularly if the reaction is studied over a narrow temperature range. Also, this method was ineffective when the lithium-7 NMR technique was used, because the change in the resonance as a function of the temperature was extremely small.

The more accurate and direct method is to obtain ΔH° calorimetrically and calculate ΔS° by difference using the value of the equilibrium constant determined by a complementary technique. It should be noted that formation constants for 1:1 complexes up to $\sim 10^4$ can also be determined calorimetrically,(132) provided that ΔH°

is measurable.

This chapter presents the results of a calorimetric study in which the enthalpies of complexation for the lithium-crown complexes have been determined. The entropies of complexation are also discussed.

B. Results and Discussion

Table 11 shows the results of this calorimetric study. In general, the lithium-crown complexes are both enthalpy and entropy stabilized, but sometimes slightly entropy destabilized. It is immediately obvious that the enthalpy of complexation is strongly solvent dependent. As the solvating ability of the solvent increases, the complexation reaction becomes less exothermic for the formation of the 12C4·Li^+ and the 15C5·Li^+ complexes. For these two complexes, the favorable enthalpy term follows the same trend as the overall complex stability. This trend does not seem to be followed in the case of the 18C6·Li^+ complex in these solvents. In fact, just the opposite trend is observed. However, in all cases, the enthalpy term is the most negative (the most stabilizing) for the 15C5·Li^+ complex, in which the cation-ligand cavity size consonance is the closest.

In the case of the 18C6·Li^+ complex, as the donicity of the solvent increases, the entropy term becomes increasingly negative (destabilizing). In propylene carbonate and acetone solutions the entropy term generally becomes increasingly negative (less positive) with increasing ligand cavity size. This observation may be

Table 11. Thermodynamic Quantities for Some Lithium-Crown Complexes in Various Solvents.[a]

	12C4		15C5		18C6	
Solvent	$\Delta H°$[b]	$\Delta S°$[c]	$\Delta H°$	$\Delta S°$	$\Delta H°$	$\Delta S°$
CH_3NO_2	- 8.8	--- [d]	-10.4	--- [d]	$\sim$ 3 [h]	> 0
	- 4.6[e,f]	- 8.2[e,g]				
CH_3CN	- 3.9[e]	6.5[e]	- 5.1	> 1.5[j]	$\sim$ 0	10.7[e]
PC	- 2.6[e]	>10. [j]	- 4.0	> 5.0[j]	- 3.8[e]	- 0.6[e]
$(CH_3)_2CO$	- 3.2[i]	- 3.4[e]	- 4.7[i]	---	- 3.5[i]	- 4.9[e]
			- 4.6[e]	1.0[e]		
CH_3OH	- 0.8[i]	--- [d]	- 2.7[i]	- 3.4[e]	- 2.8[i]	--- [d]

[a] 0.02 M in $LiClO_4$

[b] $\pm$ 0.2 kcal·mole^{-1}

[c] cal·mole^{-1}·deg^{-1}

[d] Unknown because log K is not precisely known

[e] Calculated using formation constant (Chapter 3)

[f] $\Delta H_2°$

[g] $\Delta S_2°$

[h] $\pm$ 1 kcal·mole due to limited solubility of 18C6

[i] 0.50 M in $LiClO_4$

[j] Lower limit calculated for log K = 4

explained by the consideration of the ligand configurational entropy. The free uncomplexed crown ether in solution is flexible, but when it is complexed by the lithium ion, it becomes more ordered. The larger free ligands are more flexible than the smaller ones, and consequently have more degrees of freedom to lose in the complexation process. With respect to the ligand configurational entropy alone, it is expected to be the most negative for the 18C6·Li^+ complex, because the ligand must contract and/or fold to bring the donor ether oxygen atoms within bonding distance of the lithium ion. Consequently, in acetone solutions, the entropies of complexation fall in the order 18C6·Li^+ < 15C5·Li^+ < 12C4·Li^+. In propylene carbonate solutions the order is 18C6·Li^+ < 12C4·Li^+ < 15C5·Li^+.

While the entropies of complexation in propylene carbonate and acetone solutions are the most negative for 18C6·Li^+, the enthalpies for the formation of this complex are consistently more stabilizing than in the case of 12C4·Li^+. Even though the 18C6·Li^+ complex is less stable than 12C4·Li^+ in these two solvents, there is more heat associated with the participation of six ligand donor atoms (18C6) than with the formation of four bonds (12C4).

Since several of the lithium-crown complexes have stability constants greater than 10^4 which could not be determined quantitatively in this study, some of the calculated entropies of complexation in acetonitrile and propylene carbonate solutions are reported in Table 11 as the lower limits of $\Delta S°$ for log K = 4.

In nitromethane the 12C4·Li^+, $(12C4)_2$·Li^+, and 15C5·Li^+ complexes are enthalpy stabilized, while 18C6·Li^+ is enthalpy destabilized.

The stability of the 18C6·Li^+ complex in nitromethane is due totally to favorable entropy changes. This complexation reaction is endothermic, but in the actual experiment, a heat change of only 0.2 calories was obtained due to the low solubility of 18C6 in nitromethane (<0.05 M) and the small amount of the complex which is formed in the solution. Therefore, this enthalpy is the least certain of all of the values reported in Table 11.

Even though the bonding interactions in the 18C6·Li^+ complex occur at larger distances than in the cases of the two smaller ligands, it is difficult to explain the enthalpy destabilization of 18C6·Li^+ in nitromethane. In acetonitrile, there is a substantial interaction between the solvent molecules and the 18C6 molecules which causes the heat of ligand-cation bond formation to be very small. Similar enthalpy destabilization of a lithium macrocyclic complex (C222-dilactam·Li^+) has been reported (93) in acetonitrile and nitromethane solutions. Both 12C4·Li^+ and 15C5·Li^+ are both enthalpy and entropy stabilized in acetonitrile solutions.

In propylene carbonate solutions, the three lithium-crown complexes are both enthalpy and entropy stabilized except for the 18C6·Li^+ complex which is very slightly entropy destabilized.

In the acetone solutions, the use of the formation constants determined by the ^7Li NMR mole ratio method and the calorimetric data for the 12C4·Li^+ and 18C6·Li^+ complexes (incomplete reactions) led to unreasonably large negative enthalpies and large negative entropies of complexation. This indicates that the formation constants are probably too small, which is probably due to the ion pair formation in this solvent. Therefore, the enthalpies of complexation

in acetone solutions were determined under two sets of experimental conditions. The heats of reaction were determined at high ionic strength (0.5 M in $LiClO_4$) to provide a sufficiently large excess of the lithium ion to complex essentially all of the ligand. This was done because the lithium-crown complexes in acetone solutions are relatively unstable. Since only a small fraction of the ligand is complexed, small heat changes result. These same determinations were also carried out at low ionic strength (0.02 M in $LiClO_4$) under conditions of an incomplete complexation reaction.

The standard enthalpy of reaction, $\Delta H°$ (obtained under conditions of a large excess of the lithium ion), can be used with the heat associated with partial complexation, q (obtained at low ionic strength), to calculate the value of the complex formation constant. The number of moles of the complex, ML^+, formed in the solution at low ionic strength can be calculated by Equation 35

$$\text{\# moles } ML^+ = \frac{1}{\Delta H°} \cdot q \tag{35}$$

The concentration of the complex is obtained by dividing by the volume of the solution. The value of the concentration formation constant is then calculated according to Equation 4

$$K = \frac{[ML^+]}{[M^+][L]} = \frac{[ML^+]}{(C_M - [ML^+])(C_L - [ML^+])} \tag{4}$$

where C_M and C_L are the analytical concentrations of the metal ion and the ligand respectively. This provides a complementary method and a check on the formation constants obtained by the lithium-7 NMR mole ratio method.

It should be noted that in the actual experiment, a concentrated solution of the ligand (~0.5 M) in the given solvent was added to the salt solution. It was determined that the heat of dilution of the ligand solution was negligible, but at high ionic strength, the enthalpy of complexation values had to be corrected for the heat of dilution of the salt solution when the ligand in pure solvent was added.

The formation constants for the 12C4·Li^+, 15C5·Li^+ and 18C6·Li^+ complexes in acetone were determined calorimetrically (Table 12) to be log K = 2.1, 3.3, and 2.2 respectively, compared with the values reported in Chapter 3, log K = 1.62, 3.59, and 1.50 respectively. The agreement between the two methods is satisfactory considering that data from only two calorimetric experiments were used in each calculation.

The results in methanol are similar to those observed in acetone solutions. However, within experimental error, the enthalpies for the formation of 15C5·Li^+ and 18C6·Li^+ in methanol are identical. The formation constants for the 15C5·Li^+ and 18C6·Li^+ complexes in methanol were also determined calorimetrically, and were found to be equal. In both cases log K is equal to 1.1 (Table 12). While the 18C6·Li^+ complex is expected to be weaker than the 15C5·Li^+ complex (the NMR method could not detect any complex formation), these

Table 12. Calculation of Formation Constants From Calorimetric Data.

Complex / Solvent	ΔH° (kcal·mole^{-1})	q (cal)	Solution Volume (ℓ)	C_M ($\underline{M} \times 10^2$)	C_L ($\underline{M} \times 10^2$)	log K Calorimetry	log K NMR
12C4·Li^+ acetone	- 3.2	1.76	0.058	1.96	1.62	2.1	1.62
15C5·Li^+ acetone	- 4.7	2.64	0.057	1.93	1.03	3.3	3.59
18C6·Li^+ acetone	- 3.5	1.39	0.057	2.09	1.00	2.2	1.50
15C5·Li^+ methanol	- 2.7	0.25	0.058	1.90	0.992	1.1	1.23
18C6·Li^+ methanol	- 2.8	0.30	0.057	1.94	0.967	1.1	$\sim$ 0

results are in good agreement with the 15C5·Li^+ stability constant determined by NMR (log K = 1.23). The small quantity of heat released upon the formation of 12C4·Li^+ in methanol, prevented the calculation of the formation constant. This small enthalpy is in agreement with the NMR results, in which complex formation could not be detected.

The many contributions to overall entropy changes include the solvation entropies of the metal ion and the ligand, the changes in the ligand internal entropy (due to orientation, rigidity, and conformational changes), and the change in the total number of particles and the translational entropy. The negative entropy change for the formation of 15C5·Li^+ in methanol can certainly be attributed to possible increased ligand rigidity upon complex formation, but since methanol is a structured solvent, the rearrangement of the solvent structure during the complexation process should also be considered. The lithium ion which is strongly solvated in methanol acts as a structure breaker, because solvation effects disturb the organization of the bulk solvent, but the complexed ion (inside of the crown ether organic coat) acts as a structure maker, because it is much less solvated. The overall effect is a loss in entropy.

CHAPTER 6

NATURAL ABUNDANCE OXYGEN-17 NMR STUDY OF SOME MACROCYCLIC COMPLEXES

A. Introduction

Cation-ligand interactions in macrocyclic complexes can be examined by observing the magnetic resonance of the nuclei of the ligand and/or of the cation. In the first case, ^{1}H and ^{13}C NMR measurements were widely used since the "early" days of macrocyclic complexes. While the resonance frequency of both nuclei are usually sensitive to the complexation reaction, these nuclei do not participate directly in the formation of the complex. The immediate chemical environment of the lithium ion in the lithium-crown complexes was probed directly by observing the lithium-7 NMR resonance (Chapter 3). Obviously, it would be interesting to examine the influence of complexation on the NMR spectra of the ligand atoms which directly form the ligand-cation bond(s). Evidently, oxygen-17 NMR would be a good candidate for such a study.

The properties of the oxygen-17 nucleus are given in Table 13. It has a large range of chemical shifts (~1000 ppm), and despite the low natural abundance and low sensitivity, a number of NMR studies have been carried out on reactions involving oxygen compounds, albeit of enriched samples.(133,134) The resonance of the ^{17}O nucleus seems to be a very sensitive probe of chemical environment and structure. For example, the two ether oxygens of propylene carbonate (propanediol-1,2-carbonate) show two separate ^{17}O resonances, while the differences in the corresponding chemical environments are quite subtle. There appears to be only one report of an oxygen-17 NMR study involving metal complexes with acetate and citrate ions (135) where the carboxylate groups were enriched to ~5% ^{17}O. The addition of calcium(II)

Table 13. Some Properties of the Oxygen-17 Nucleus

Spin	5/2
Electrical Quadrupole Moment	-2.6×10^{-26} (e x cm^2)
Natural Abundance	0.037%
NMR Sensitivity vs. ^1H (at constant field)	2.91×10^{-2}
Resonance Frequency (at 42.3 kgauss)	24.399 MHz
Magnetic Moment	-1.8930 Nuclear magnetons

to a solution of these anions did not induce any changes in the ^{17}O resonance. However, large shifts were induced by the addition of dysprosium(III) ion which was used as a (paramagnetic) model for the calcium(II) ion.

It was of interest to us, therefore, to investigate the possible use of oxygen-17 NMR as a probe of the complexation reaction of macrocyclic polyethers with alkali metal cations.

B. Results and Discussion

The ^{17}O NMR chemical shifts for the free and complexed 12C4 in various solvents are shown in Table 14. Neat 12C4 is a viscous liquid which produces a very broad resonance with a linewidth of ~1200 Hz. Introduction of this compound into a solvent of lower viscosity drastically decreases the linewidth. The chemical shifts of the free

Table 14. Oxygen-17 NMR Study of Macrocyclic Polyether 12C4 and Its Li^+ Complex

	Free Crown		Crown + $LiClO_4$[b]		
Solvent	δ (ppm)[a]	$\Delta\nu_{1/2}$ (Hz)[a]	Li^+/12C4	δ (ppm)	$\Delta\nu_{1/2}$ (Hz)
Neat Ligand	$\sim$ 0	$\sim$ 1200	---	---	---
Nitromethane	- 8	500	2.0	- 18	600
			1.0	- 21	625
			0.5	- 15	500
			0.33	- 14	625
Acetonitrile	- 7	250	1.0	- 17	400
Pyridine	- 5	725	1.0	- 13	625
Acetone	- 5	250	1.0	- 13	650
			1.0[c]	- 14	375

[a]Due to the broadness of the lines, chemical shifts are accurate to $\pm$ 2 ppm and linewidths to $\pm$ 25 Hz.

[b]The addition of an equimolar amount of tetrabutylammonium perchlorate to nitromethane and pyridine solutions of 12C4 resulted in chemical shifts of -5 and -6 ppm with linewidths of 575 and 400 Hz, respectively.

[c]In this case only, the salt is $NaClO_4$.

crown in the four solvents investigated (Table 14) are several ppm upfield from the resonance of the neat ligand. The addition of an equimolar amount of $LiClO_4$ to the solution of the crown shifts the ^{17}O resonance upfield by ~10 ppm. A complexable cation decreases the electron density from the oxygen atoms via ion-dipole and ion-induced dipole interactions so that the population average signal shifts upfield. Since the addition of a salt with a large uncomplexable cation, tetrabutylammonium perchlorate, does not change the chemical shift of the ligand, the observed shift must be due to the complexation reaction.

The overall effect of the complexation on the ^{17}O chemical shift is disappointingly small. It seems that with the present state of the art only a qualitative indication of the ligand-cation interaction can be obtained by this technique. The lithium-7 NMR study discussed in Chapter 3 showed that the 12C4·Li^+ complex is quite stable (log K > 4) in nitromethane and acetonitrile solutions and weak in acetone and pyridine solutions. It is seen that this distinction cannot be observed by the ^{17}O NMR.

In nitromethane solutions, lithium-7 NMR showed the existence of 12C4·Li^+ and $(12C4)_2$·Li^+ complexes. A similar conclusion can be obtained from the ^{17}O NMR measurements. The addition of the Li^+ ion to a solution of 12C4 in nitromethane results in an upfield shift of the ^{17}O signal, but after the 1:1 mole ratio of Li^+/12C4 is reached, further addition of the lithium ion reverses the direction of the chemical shift.

The chemical shift of the 12C4·Na^+ complex in acetone was found

to be -14 ppm (Table 14). The chemical shift of $(12C4)_2 \cdot Na^+$ could not be obtained, because the preparation of 2:1 solutions in these solvents always resulted in the formation of a precipitate.

Similar studies were carried out on crown ethers 15C5 and 18C6 (Table 15). In general, the results are similar to those observed for 12C4. Here again, the complexation produces a ∿10-16 ppm upfield shift. A somewhat different behavior is observed for the $18C6 \cdot K^+$ and the $18C6 \cdot Ag^+$ complexes in acetonitrile. In these cases, the addition of the metal ion to the ligand solution resulted in a much smaller change in the ^{17}O resonance frequency. In the case of the silver ion, the complex may be quite unstable in acetonitrile solutions due to the strong $CH_3CN \cdot Ag^+$ interaction.(136) On the other hand, it seems difficult to explain the insensitivity of the ^{17}O chemical shift of 18C6 towards the formation of a potassium complex since it is quite stable in both acetone and acetonitrile solutions.(137)

The chemical shifts of the oxygen atoms of the solvent molecules remain constant and independent of the solution composition. The resonance of the perchlorate anion is split into a quadruplet by the ^{35}Cl nucleus. The center of the quadruplet is at 291 ppm, in excellent agreement with the literature value of 290 ppm.(138) Such constancy is not at all surprising, because the solvent molecules are in large excess, and the perchlorate anion is known to be quite inert.

It was of obvious interest to us to extend this investigation to several other common solvents such as alcohols, ethers, sulfoxides, and water. However, in these cases the crown ether ^{17}O resonance was totally masked by the solvent oxygen resonance. In pyridine

Table 15. Oxygen-17 NMR Studies of Crown Ethers 15C5 and 18C6 and Their 1:1 Complexes

		Free Crown		Complex		
Ligand	Solvent	δ (ppm)	$\Delta\nu_{1/2}$ (Hz)	M^+	δ (ppm)	$\Delta\nu_{1/2}$ (Hz)
15C5	Neat Ligand	∿+10	∿ 1700	---	---	---
	Nitromethane	- 3	675	Li^+	-13	500
	Acetonitrile	- 3	500	Li^+	-13	475
	Pyridine	- 2	575	Li^+	-18	425
	Acetone	- 3	375	Li^+	-13	375
				Na^+	-13	450
18C6	Acetonitrile	+ 3	550	---	---	---
				Li^+	-14	425
				Na^+	- 9	600
				K^+	+ 2	1050
				Ag^+	+ 6	750

Table 15. (cont'd.)

		Free Crown		Complex		
Ligand	Solvent	δ (ppm)	$\Delta\nu_{1/2}$ (Hz)	M^+	δ (ppm)	$\Delta\nu_{1/2}$ (Hz)
18C6	Acetone	0	525	---	---	---
				Li^+	-16	400
				Na^+	-12	575
				K^+	+ 3	775
				Ag^+	-13	750

solutions the ^{17}O resonance of the complexed 18C6 was so broad so as to preclude the observation of the ^{17}O resonances of even 0.5 M solutions of the ligand (3 M in equivalent oxygens) with very long scanning periods (more than 10^6 scans). The solubility of 18C6 in nitromethane was so low that its signal could not be detected under our experimental conditions.

Since the overall range of ^{17}O chemical shifts is so large it was anticipated that the shifts upon complexation would be more significant. However, the interaction between the oxygens of a crown ether and a metal ion is predominantly electrostatic,(40,41) consequently the change in the environment of a single oxygen atom upon complexation should be small. It should be noted that the large ^{17}O chemical shifts are usually observed when a change occurs in the covalent bonding of an oxygen atom. Therefore, it seems the ^{17}O NMR is not a sensitive probe of the immediate chemical environment of a macrocyclic polyether. Similar results were obtained by Foster and Roberts with a ^{15}N NMR study of cryptates (139) where the ^{15}N resonance also seems to be quite insensitive to complexation.

CHAPTER 7

SUGGESTIONS FOR FUTURE STUDIES

A. Strong Lithium-Macrocyclic Complexes

The stability constants for the very stable lithium-crown complexes (log K > 4) could not be quantitatively determined due to the reasons described in Chapter 3. The preliminary data indicate that the cyclic voltammetric method is applicable, and the necessary quantitative data are obtainable by utilizing the thallium(I) competition method. The main problem remaining deals with the reference electrode in nonaqueous solvents (see Chapter 3). The applicability of this technique should also be examined for the strong lithium cryptate complexes observed by Cahen et al.(46) These data can then be used with complementary calorimetric data to obtain the thermodynamic quantities for the complexation reactions.

B. The 12C4-18C6 Interaction

Crown ether 18C6 is a solid at 25°C with a melting point of 39°C, while 12C4 is a liquid with a boiling point of ∿70°C at ∿0.05 mm Hg. Eighteen-crown-six and 12C4 were dried separately under vacuum, but when they were placed together under a common vacuum, 18C6 absorbed 12C4. Similar behavior was not observed with 15C5, which is also a liquid at 25°C. This is a particularly interesting observation from both kinetic and thermodynamic view points. Twelve-crown-four was absorbed in a more than 1:1 but less than 2:1 mole ratio. Examination of infrared spectra was inconclusive as no new bands were observed.

The vapor pressure of 12C4 in and of itself is not large enough for 12C4 to distill over into the container of 18C6 under vacuum.

Therefore, there must be some "complex" formation. This complex would be interesting to study, but the method of instrumental analysis is not obvious at this time as the two compounds are very similar in structure.

C. Microprocessor Control Solution Calorimeter

The calorimeter used for the determination of enthalpies of reaction in Chapter 5 and described in Chapter 2 is of the adiabatic (more correctly isoperibol) design. The experience of this author with this particular system has indicated the necessity of equilibration periods consisting of several hours in some cases. In addition, the temperature of the calorimeter contents cannot be precisely measured with the present apparatus. This equilibration time could be shortened considerably by electronic modification of the instrument so that the temperature of the calorimeter contents is automatically held constant (isothermal) by intelligent instrument control. This modification is also attractive from another point of view, because, since the temperature is held constant, heat capacity measurements may be totally omitted.

Several types of isothermal calorimeter designs have been described.(140-144) The recent advances in applications of microprocessor control of analytical instrumentation makes this problem particularly amenable to such control. It is out of the scope of this discussion to treat this project in any detail, but rather to mention the importance of its implementation. The calorimeter cell, insert, and stirrer assembly would remain unchanged. In the actual experiment,

the flow rate of cooling gas would be increased so that the heat of stirring is more than offset, and the heater would cycle for very well defined short periods of on time (heat pulses) to maintain constant temperature. With well defined heating periods, it is then necessary to count the heat pulses. The rest of the experiment may be performed in virtually the same manner. It should be pointed out however, that this method requires constant cooling throughout the entire experiment which may present some difficulty with the present apparatus. Commonly, Peltier thermoelectric coolers with constant current sources have been employed for constant cooling.(141-144)

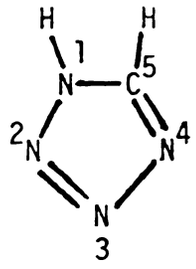
APPENDICES

APPENDIX A

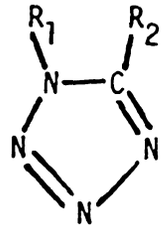
THE CRYSTAL AND MOLECULAR STRUCTURES OF THREE CYCLOPOLYMETHYLENE TETRAZOLE COMPOUNDS

A. Introduction

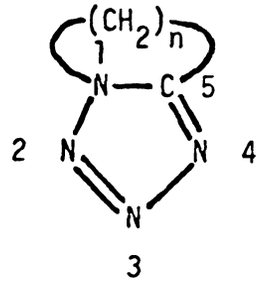
Cyclopolymethylenetetrazoles are known for their strong stimulating effect on the central nervous system. In sufficient doses, they are capable of inducing epileptic convulsions. The formula for tetrazole (I), a 1,5-disubstituted tetrazole (II), and a cyclopolymethylenetetrazole (III) are shown below. The activity increases



I



II



III

with the length of the hydrocarbon chain and varies from 1000 mg/kg for trimethylenetetrazole (TMT, n=3) to 30 mg/kg for heptamethylenetetrazole (n=7).(145)

As expected, the aqueous solubility decreases with increasing length of the hydrocarbon chain. Trimethylenetetrazole is soluble to the extent of 1.4 molal, while the solubility of heptamethylenetetrazole is 0.18 molal. A glaring exception is pentamethylenetetrazole (PMT, n=5) which is soluble to the extent of 5.0 molal.(146)

Crystallographic studies of the PMT complex of iodine monochloride (147) showed that PMT acts as a monodendate ligand and

coordinates through N(4) of the tetrazole ring. In the silver complex $AgNO_3 \cdot (PMT)_2$,(148) monodendate tetrazoles are coordinated to the silver atom via N(4) and bridging tetrazoles are linked to silver atoms via N(3) and N(4). It was of interest to determine the crystal structure of the free ligand to see if there were any changes in the configuration of the molecule upon complexation.

Previous studies have indicated that TMT (146) and PMT (149) form dimers in aqueous solution which may be related to the high solubility of these two compounds. When a tert-butyl group is substituted for a hydrogen in the 8-position of PMT (Figure 13, page 124), the solubility in water decreases tremendously to $\sim 3 \times 10^{-3}$ molal.(146) Solvation of these compounds is expected to be due primarily to dipole-dipole interactions of the tetrazole with the solvent molecules, but the dipole moments of substituted tetrazole compounds are found to be near 6D,(150) and reside in the tetrazole ring itself. Therefore, one would expect similar solvation effects for substituted tetrazoles. Therefore, it was of interest to us to examine the crystal structures of these compounds for features which can help to explain the unusual solubility characteristics of these compounds.

B. Experimental Part

Trimethylenetetrazole (Aldrich) was recrystallized from a 5:1 mixture of carbon tetrachloride and ethanol, m.p. 110°C, lit. 110°C;(151) PMT (Aldrich) was recrystallized from diethyl ether and dried under vacuum, m.p. 60°C, lit. 59°C;(152) and 8-tert-butylpentamethylenetetrazole (8-t-butyl PMT) was prepared (146) according to the method

of D'Itri,(153,154) m.p. 133°C, lit. 132.5-133.0°C.(155)

Crystals of these three compounds were grown from covered dilute solutions of the tetrazoles (∿0.05 molal) in ether (TMT and PMT) or in acetone (8-t-butyl PMT) from which the solvent was permitted to evaporate slowly to dryness. Single crystals were mounted for each compound. Both PMT and 8-t-butyl PMT were mounted on glass fibers, and TMT was mounted in a glass capillary under vacuum to minimize the apparent air decomposition.

The diffraction data were measured with a Picker FACS-I automatic diffractometer using zirconium-filtered (PMT) or graphite-monochromatized (TMT and 8-t-butyl PMT) Mo Kα radiation.

C. Structure Solution and Refinement

The three crystal structures were determined by Wei and Ward.(156) The structures were refined to convergence by full-matrix least-squares calculation. The molecules are symmetrical except for N(1) and C(5) of the tetrazole ring. Since the thermal parameters for these atoms were unusual, and since the final difference maps showed the largest positive densities to be near C(5) and the largest negative densities near N(1), the refinements were continued after reversing the identities of atoms (1) and (5). The results of these "reversed" refinements corresponded closely to the earlier refinements indicating that atoms (1) and (5) refine equally well as C and N or as N and C, and therefore these two atoms are disordered by approximately 50% occupancy of each atom-type at each location. Further refinements, using composite "NC" atoms (1/2 N + 1/2 C in their scattering factors)

for (1) and (5), gave much better agreement without increasing the number of refined parameters.

D. Discussion

As shown in Figures 11-13, the cyclopolymethylenetetratetrazole molecules each contain a planar tetrazole ring. Table 16 presents some of the crystallographic data. The polymethylene ring in TMT is planar to within ±0.02 Å and lies 0.5° from the plane of the tetrazole ring. The polymethylene rings in PMT and 8-t-butyl PMT are planar only to within ±0.36 Å (seven-membered rings in chair form) and lie approximately 24° from the planes of the tetrazole rings.

The bond distances in the tetrazole rings range from 1.307 to 1.340 Å (Table 17). The digit in parentheses following the bond length is the estimated standard deviation as it applies to the least significant digit. The relative average lengths of these bonds are in agreement with the disordered model in which all bonds, except NC(1)-NC(5), are averages of single and double bonds. The average angles (Table 17) indicate that N(3) is displaced towards the NC(1)-NC(5) bond thereby increasing the bond angle at N(3) and decreasing the bond angles at N(2) and N(4) from the overall average of 108°. The bond angles differ significantly from those in the unsubstituted tetrazole (157) in which the angles at N(2), N(3), N(4) are all approximately 108°. Except for the N(2)-N(3) bond length (reported at 1.30(1) Å), the tetrazole ring average bond lengths in TMT, PMT, and 8-t-butyl PMT agree with those in tetrazole.

The bond lengths in the polymethylene rings appear to be normal

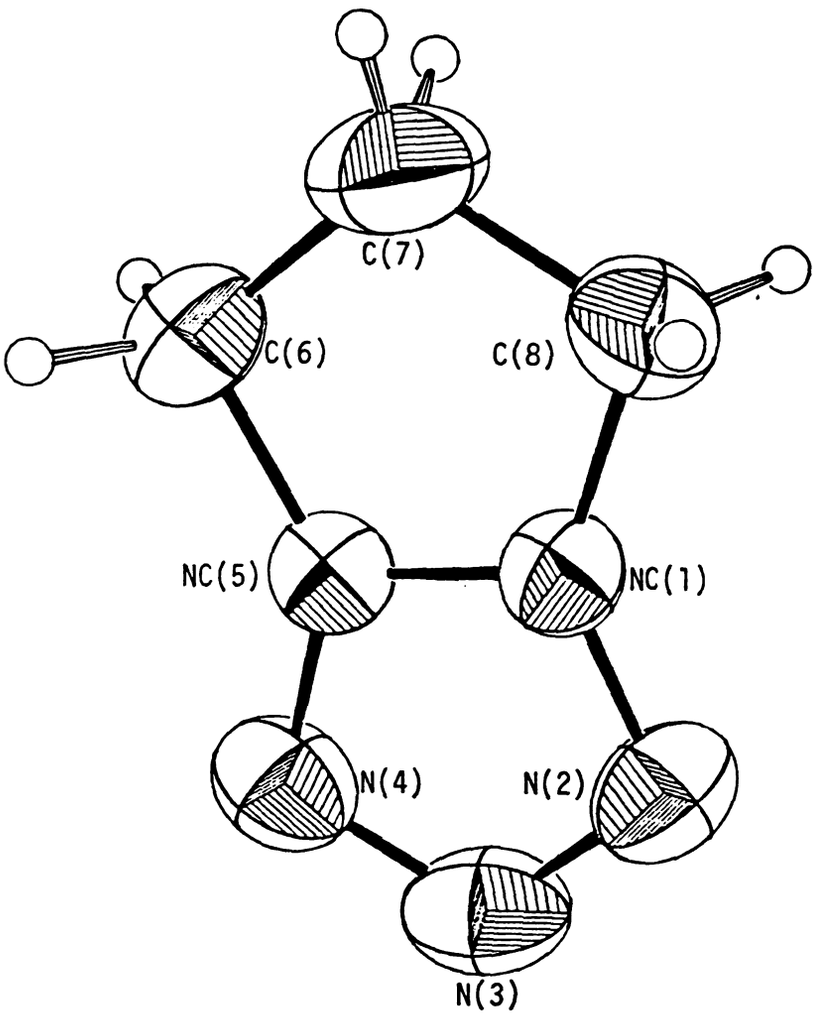


Figure 11. Molecular structure of TMT.

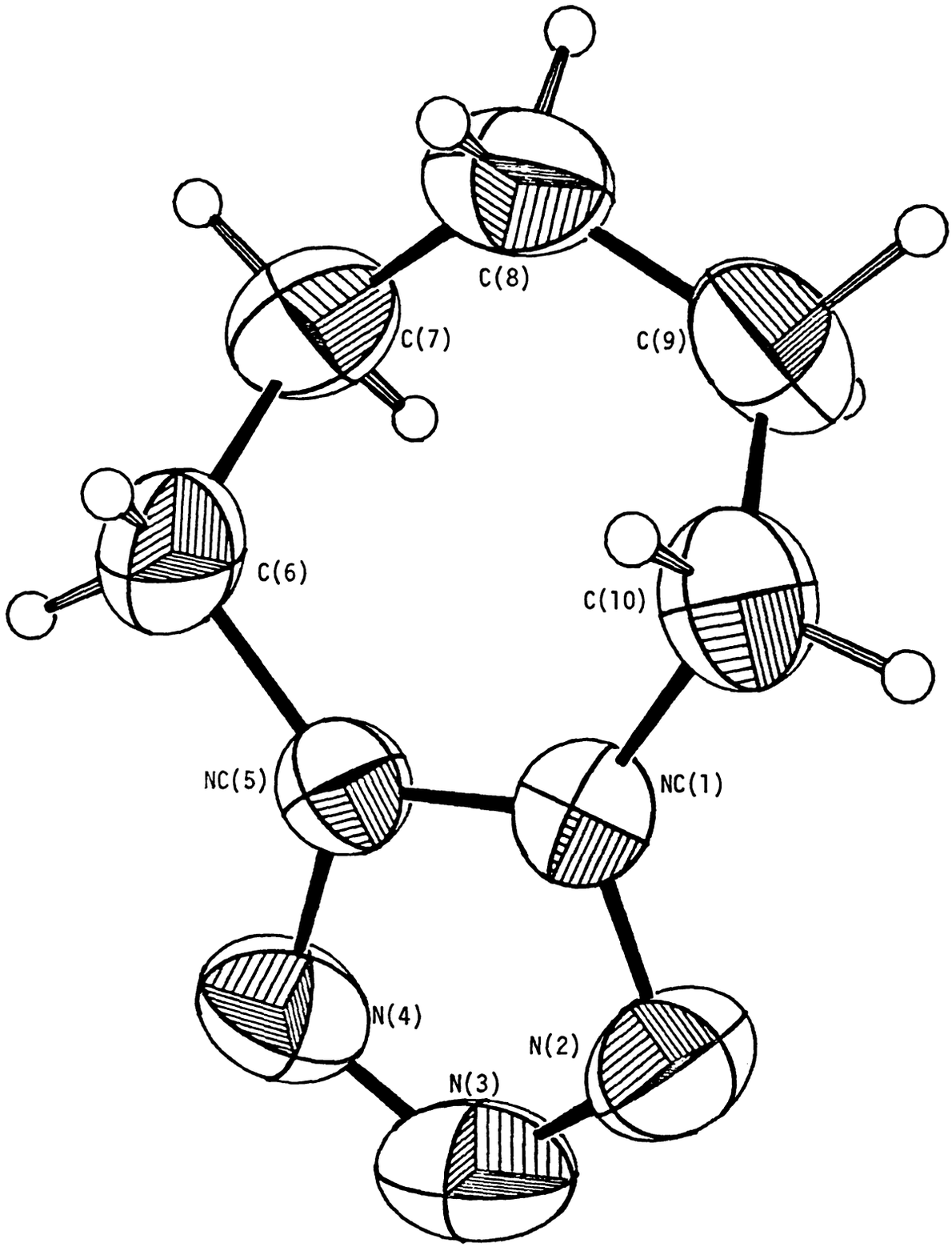


Figure 12. Molecular structure of PMT.

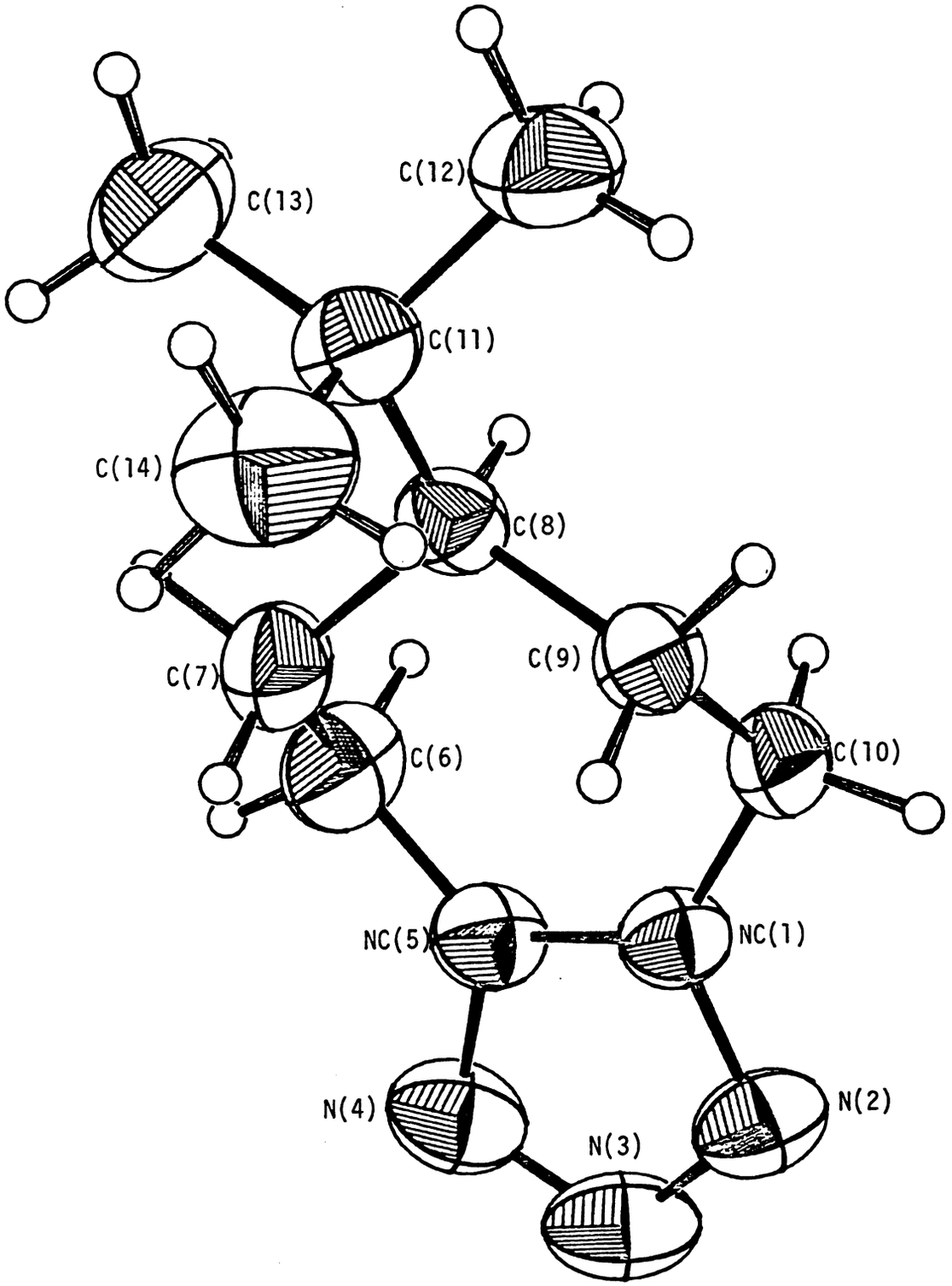


Figure 13. Molecular structure of 8-t-butyl PMT.

Table 16. Cyclopolymethylenetetrazole Crystallographic Data

	TMT	PMT	8-t-butyl PMT
Formula	$C_4H_6N_4$	$C_6H_{10}N_4$	$C_{10}H_{18}N_4$
Molecular Weight	110.12	138.17	194.28
a (Å)	7.758(5)	13.310(6)	12.881(4)
b	10.367(6)	8.409(3)	6.614(2)
c	6.694(2)	6.6589(2)	14.132(6)
β (°)	102.02(4)	94.72(3)	111.52(2)
V ($Å^3$)	526.6	735.0	1120.0
Space Group	$P2_1/n$	$P2_1/n$	P_21/C
Density (g/cm^3)	1.389	1.249	1.152

Table 17. Cyclopolymethylenetetrazole Interatomic Distances (Å) and Angles (°)

	TMT	PMT	8-t-butyl PMT
NC(1)–N(2)	1·329 (3)	1·340 (3)	1·337 (2)
NC(1)–NC(5)	1·307 (3)	1·326 (2)	1·322 (2)
NC(1)–C(8)	1·473 (4)	–	–
NC(1) C(10)	–	1·475 (3)	1·469 (3)
N(2)–N(3)	1·332 (3)	1·322 (3)	1·325 (2)
N(3)–N(4)	1·324 (3)	1·309 (3)	1·324 (3)
N(4)–NC(5)	1·335 (3)	1·336 (3)	1·338 (2)
NC(5)–C(6)	1·473 (3)	1·471 (3)	1·462 (3)
C(6)–C(7)	1·517 (5)	1·511 (4)	1·524 (3)
C(7)–C(8)	1·500 (5)	1·516 (4)	1·527 (3)
C(8)–C(9)	–	1·503 (4)	1·528 (3)
C(8)–C(11)	–	–	1·558 (3)
C(9)–C(10)	–	1·514 (5)	1·525 (3)
C(11)–C(12)	–	–	1·531 (3)
C(11)–C(13)	–	–	1·526 (3)
C(11)–C(14)	–	–	1·530 (3)
N(2)–NC(1)–NC(5)	109·4 (2)	108·3 (2)	108·9 (2)
N(2)–NC(1)–C(8)	137·2 (3)	–	–
N(2)–NC(1)–C(10)	–	125·0 (2)	124·7 (2)
NC(5)–NC(1)–C(8)	113·4 (2)	–	–
NC(5)–NC(1)–C(10)	–	126·6 (2)	126·3 (2)
NC(1)–N(2)–N(3)	104·8 (3)	105·7 (2)	106·0 (2)
N(2)–N(3)–N(4)	111·6 (3)	111·3 (2)	110·5 (2)
N(3)–N(4)–NC(5)	104·5 (3)	106·1 (2)	106·3 (2)
NC(1)–NC(5)–N(4)	109·7 (2)	108·6 (2)	108·3 (2)
NC(1)–NC(5)–C(6)	113·5 (2)	127·2 (2)	127·4 (2)
N(4)–NC(5)–C(6)	136·9 (3)	124·2 (2)	124·3 (2)
NC(5)–C(6)–C(7)	101·0 (3)	112·0 (2)	113·9 (2)
C(6)–C(7)–C(8)	110·6 (3)	115·2 (3)	115·3 (2)
C(7)–C(8)–NC(1)	101·4 (3)	–	–
C(7)–C(8)–C(9)	–	115·5 (3)	111·6 (2)
C(7)–C(8)–C(11)	–	–	113·3 (2)
C(9)–C(8)–C(11)	–	–	112·5 (2)
C(8)–C(9)–C(10)	–	114·9 (3)	115·8 (2)
C(9)–C(10)–NC(1)	–	112·7 (2)	113·5 (2)
C(8)–C(11)–C(12)	–	–	110·0 (2)
C(8)–C(11)–C(13)	–	–	110·8 (2)
C(8)–C(11)–C(14)	–	–	111·4 (2)
C(12)–C(11)–C(13)	–	–	106·5 (2)
C(12)–C(11)–C(14)	–	–	109·3 (3)
C(13)–C(11)–C(14)	–	–	108·8 (3)

with average NC-NC distances of 1.335 Å, average NC-C distances of 1.471 Å, and average C-C distances of 1.516 Å. The angles in the polymethylene ring of TMT are quite different from those in PMT and 8-t-butyl PMT and reflect the differences between a planar five-membered ring (TMT) and the chair form seven-membered rings (PMT and 8-t-butyl PMT). The only major angular difference between PMT and 8-t-butyl PMT is C(7)-C(8)-C(9) which in 8-t-butyl PMT is decreased by the substitution of the t-butyl group at C(8).

The major differences in the molecular structures of the free ligand (PMT) and the $AgNO_3$ (148) and ICl (147) complexes are due to the disorder of atoms (1) and (5) in the tetrazole ring of PMT. The tetrazole ring bond-lengths in PMT relative to those in the two complexes show the averaging of double and single bonds by the disordered structure. The bond angles are essentially the same in the three determinations. The pentamethylene rings are all in the chair form, the average C-C bond lengths are shorter by 0.030 Å in PMT, and the bond angles agree rather well except for those at NC(1), NC(5), and C(7) which average 3.1° larger in PMT.

The cyclopolymethylenetetrazole molecules pack together without hydrogen bonding as shown in Figures 14-16. The tetrazole rings of TMT and PMT, in adjacent molecules related by a center of symmetry, overlap significantly to produce "dimers," presumably by dipole-dipole interactions. The distances between the least-squares planes of the tetrazole rings are 3.408 Å for TMT and 3.705 Å for PMT compared with 3.226 Å for tetrazole.(157) The overlaps are illustrated in Figures 17 and 18. The 8-t-butyl PMT does not crystallize with

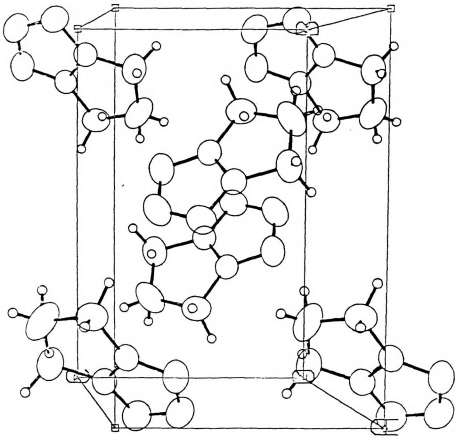


Figure 14. Packing diagram for TMT.

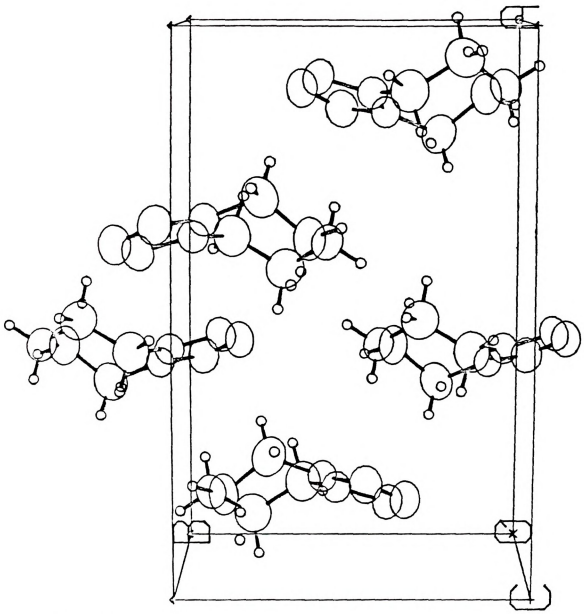


Figure 15. Packing diagram for PMT.

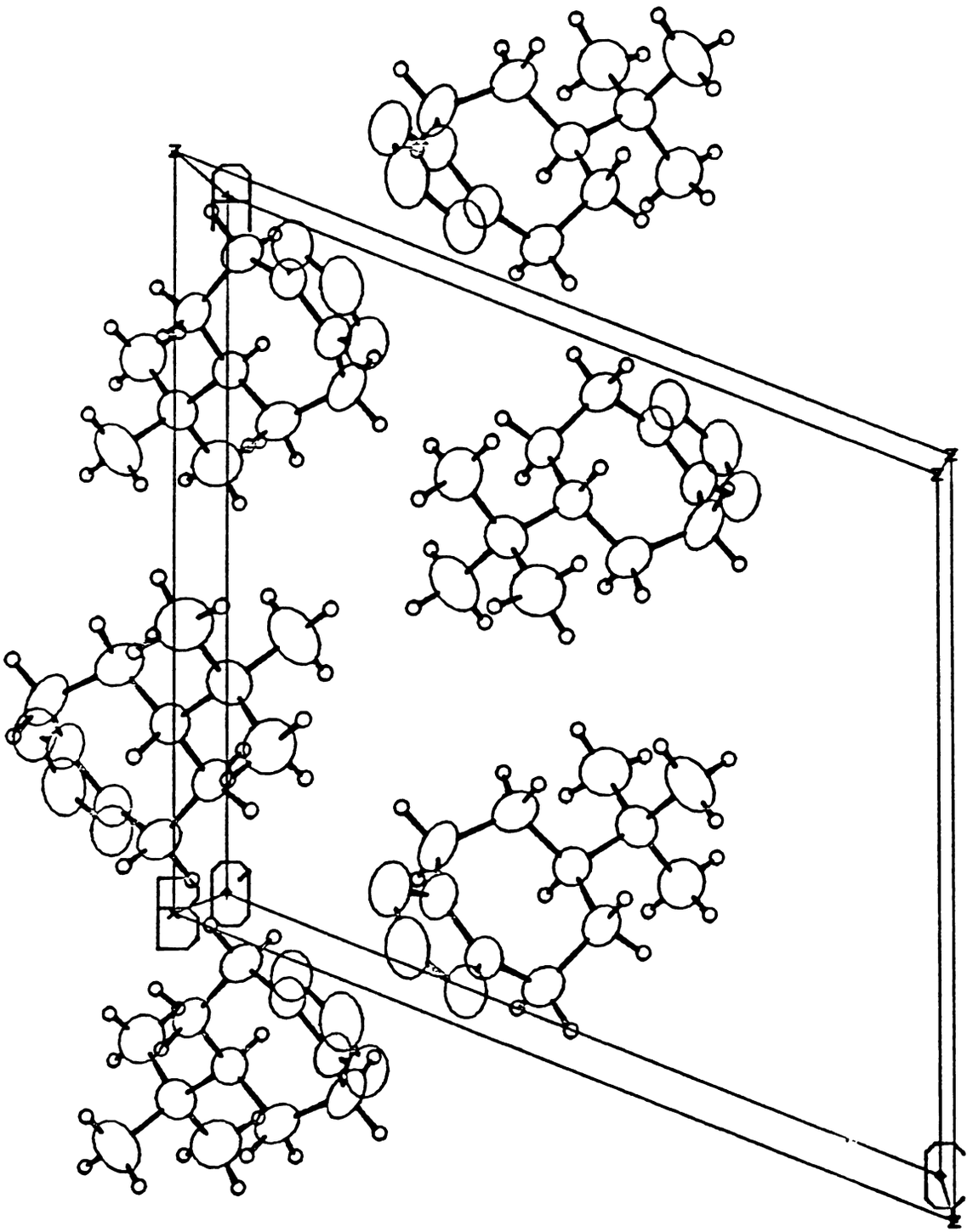


Figure 16. Packing diagram for 8-t-butyl PMT.

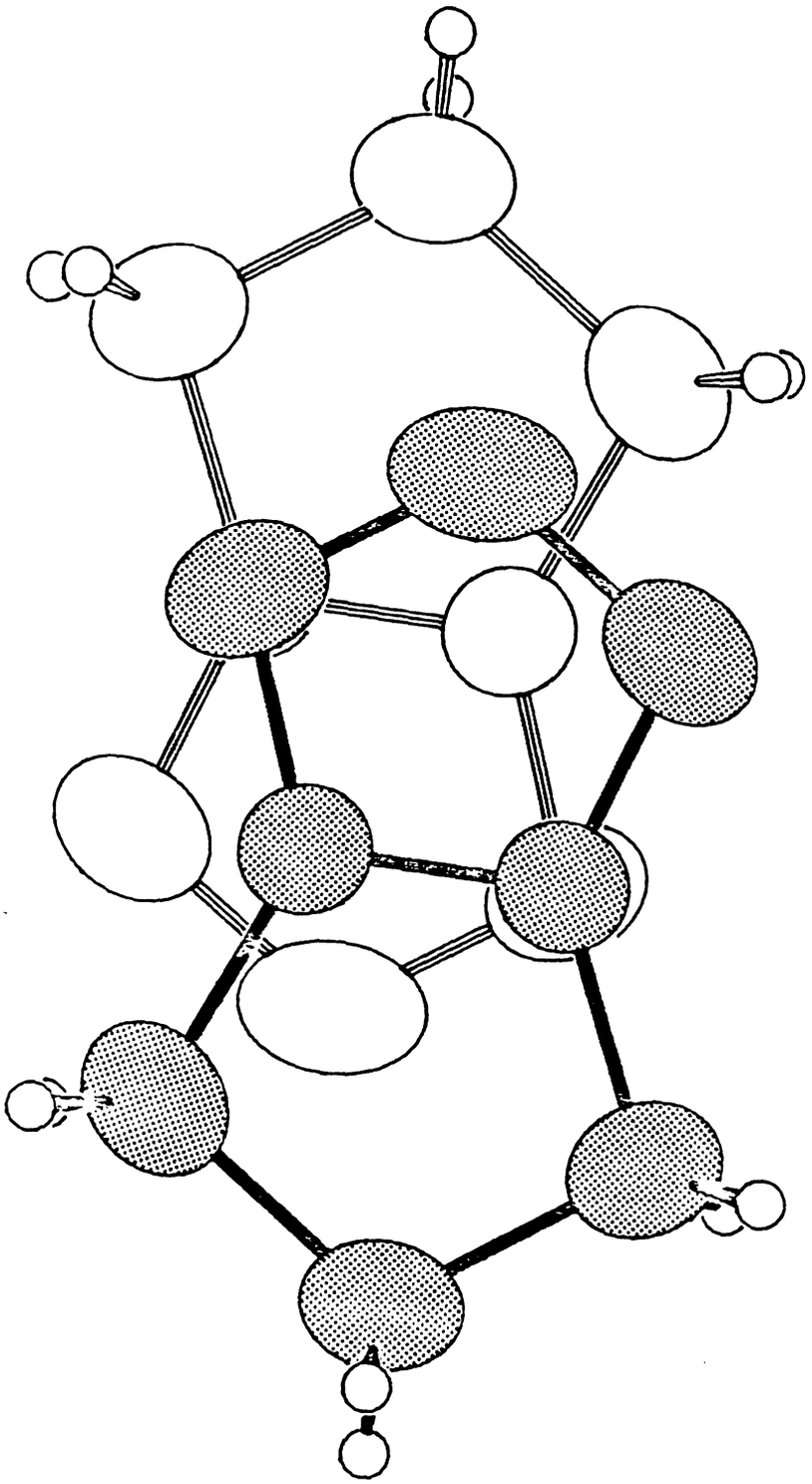


Figure 17. Overlap of molecules in TMT.

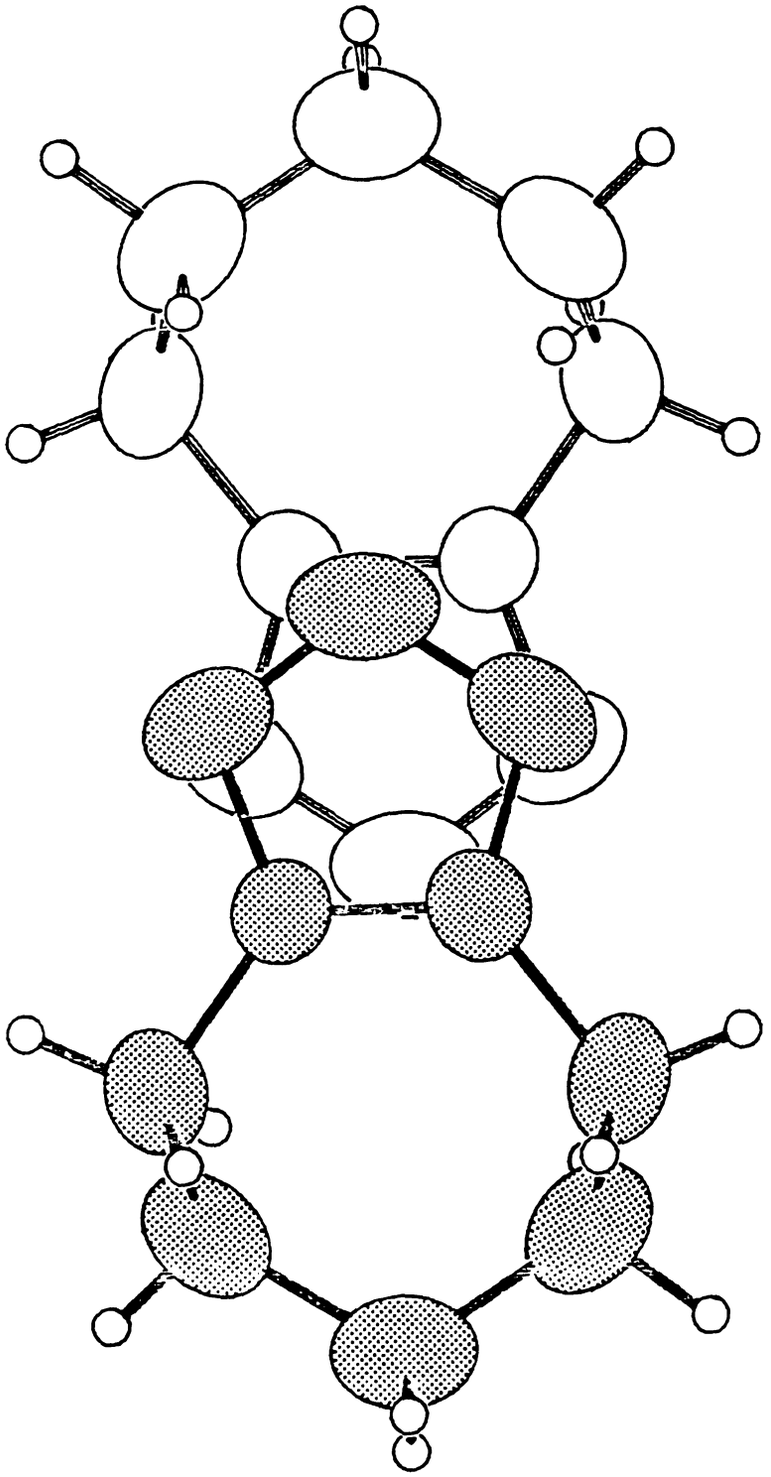


Figure 18. Overlap of molecules in PMT.

the tetrazole rings of adjacent molecules parallel to each other. It appears that adjacent molecules, related by twofold screw axes, form "chains" in which N(3) of one molecule is directed towards the center of the tetrazole ring of the next molecule.

The distances between the centers of the tetrazole rings of the two molecules forming "dimers" are 3.481 Å for TMT and 3.741 Å for PMT, which indicate fairly strong dipole-dipole interactions. The "dimers" themselves do not interact strongly with each other as indicated by the distances between tetrazole ring centers of 5.401, 5.902, and 6.694 Å for TMT and 5.863, 6.589, and 8.072 Å for PMT. Thus, the forces between "dimers" are weak and this may account for the large solubilities of TMT and PMT.

The distances between the centers of the tetrazole rings of individual molecules of 8-t-butyl PMT are 4.390 Å along the "chains" and 6.132, 6.614, and 7.557 Å to other adjacent molecules. It would be expected that the lattice energy of 8-t-butyl PMT would be higher (interactions at 4.390 Å between individual molecules) than those of TMT or PMT (interactions at 5.4 Å minimum between "dimers"), and consequently, the solubility of 8-t-butyl PMT would be less than that of TMT or PMT.

APPENDIX B

APPLICATION OF COMPUTER PROGRAM KINFIT4 TO THE CALCULATION OF FORMATION CONSTANTS FROM NMR DATA AND THE CALIBRATION OF ION-SELECTIVE ELECTRODES

A. Calculation of Formation Constants from NMR Data

1. Program Function

The KINFIT4 computer program is a nonlinear least squares curve fitting routine. The equation to which the data are fitted is inserted by the user into the SUBROUTINE EQN. This program was used to fit the lithium-7 NMR chemical shift vs. mole ratio data to Equation 5. In many cases, the limiting chemical shift of the complex,

$$\delta_{obs} = [(KC_M - KC_L - 1) + (K^2C_L^2 + K^2C_M^2 - 2K^2C_LC_M + 2KC_L + 2KC_M + 1)^{1/2}]$$

$$[\frac{\delta_f - \delta_c}{2KC_M}] + \delta_c \qquad (5)$$

δ_c, was obtained directly from the mole ratio plot. However, when the complex is relatively unstable ($K < 100$), the value of δ_c cannot be determined directly from the mole ratio plot, and Equation 5 has two unknowns, δ_c and K, designated U(1) and U(2) respectively, in the FORTRAN CODE. The input variables are the analytical concentration (M) of the ligand (XX(1)) and the observed chemical shift (XX(2), ppm).

The data input includes the usual control cards and the NMR data. The first control card gives the number of data points, the maximum number of iterations to be performed, the number of constants to be read, and the convergence tolerance. The subsequent cards include a title card, a card containing the values for the constants (if any),

a card containing the initial estimates for the unknown parameters, and data cards. Each data entry is followed by its estimated variance.

The SUBROUTINE EQN and a sample data listing are given for the case when two unknowns are calculated. If the value of δ_c is already known, U(1) is replaced by its value.

2. SUBROUTINE EQN

```
      SUBROUTINE EQN
      COMMON KOUNT,ITAPE,JTAPE,IWT,LAP,XINCR,NOPT,NOVAR,NOUNK,X,U,ITMAX,
     1WTX,IEST,I,AV,RESID,IAE,EPS,ITYP,XX,RXTYP,DX1I,FOP,FO,FU,P,ZL,TO,E
     2IGVAL,XST,T,DT,L,M,JJJ,Y,DY,VECT,NEST,CONST,NDAT,JDAT,MOPT,LOPT,
     3YYY,CONSTS
      COMMON/FREQT/IMETH
      COMMON/POINT/KOPT,JOPT,XXX
      DIMENSION X(4,300),U(20),WTX(4,300),XX(4),FOP(300),FO(300),FU(300)
     1,P(20,21),VECT(20,21),ZL(300),TO(20),EIGVAL(20),XST(300),Y(10),
     2DY(10),CONSTS(50,16),NEST(50),ISMIN(50),RXTYP(50),DX1I(50),IRX(50)
     3,MOPT(50),LOPT(50),YYY(50),CONST(16),XXX(15)
      GO TO (2,3,4,5,1,7,8,9,10,11,12)  ITYP
    1 CONTINUE
      ITAPE=60
C     METAL NMR EQUATION FOR K1.  FIT K1 AND DELTA ML.  NO ION PAIRING.
      NOUNK=2
      NOVAR=2
C     CONST(1)=METAL CONCENTRATION, M
C     CONST(2)=CHEMICAL SHIFT OF FREE METAL, PPM
C       XX(1)=LIGAND CONCENTRATION, M
C       XX(2)=OBSERVED CHEMICAL SHIFT, PPM
C        U(1)=LIMITING CHEMICAL SHIFT OF COMPLEX, PPM
C        U(2)=FORMATION CONSTANT FOR 1 TO 1 COMPLEX
      JTAPE=61
      RETURN
    7 CONTINUE
      RETURN
    8 CONTINUE
      RETURN
    2 CONTINUE
      IF(IMETH.NE.-1) GO TO 35
      RETURN
   35 CONTINUE
      A=(U(2)**2)*(XX(1)**2)
      B=(U(2)**2)*(CONST(1)**2)
      C=-2.0*(U(2)**2)*(XX(1))*CONST(1)
      D=2.0*(U(2))*(XX(1))
      E=2.0*(U(2))*(CONST(1))
      AA=(U(2))*(CONST(1))
      BB=-(U(2))*XX(1)
      CC=(CONST(2)-U(1))/(2.*(CONST(1))*(U(2)))
      S=(((AA+BB-1.)+SQRT(ABS(A+B+C+D+E+1.)))*CC)+U(1)
      RESID=S-XX(2)
      RETURN
    3 CONTINUE
      RETURN
    4 CONTINUE
      RETURN
    5 CONTINUE
      IF(IMETH.NE.-1) GO TO 20
      RETURN
   20 CONTINUE
      RETURN
    9 CONTINUE
      RETURN
   10 CONTINUE
      RETURN
   11 CONTINUE
      RETURN
   12 CONTINUE
      RETURN
      END
```

3. Sample Data Listing

```
   15        100                              2.0001
 LI-7 NMR KF OF 15C5LICLO4 IN ACETONE AT 25 DEG C I=0.02 M DATA III-14.
0.02073    -1.43
0.80       1000.
0.0           1.0E-06-1.43        2.5E-030.005185     5.0E-06-0.90        2.5E-03
0.01037       5.0E-06-0.33        2.5E-030.01555      5.0E-060.12         2.5E-03
0.02074       5.0E-060.51         2.5E-030.02592      5.0E-060.71         2.5E-03
0.03111       5.0E-060.74         2.5E-030.03629      5.0E-060.77         2.5E-03
0.04148       5.0E-060.78         2.5E-030.04665      5.0E-060.83         2.5E-03
0.05222       5.0E-060.90         2.5E-030.06296      5.0E-060.78         2.5E-03
0.1037        5.0E-060.82         2.5E-030.1244       5.0E-060.79         2.5E-03
0.1555        5.0E-060.83         2.5E-03
```

B. Calibration of Ion-Selective Electrodes

1. Program Function

The KINFIT4 program was also used to linearize the sodium ion-selective electrode calibration data by fitting these data to Equation 26.

$$E = E^{\circ\prime} + m \log ([Na^+] + R) \qquad (26)$$

Initially, the unknowns used were m, $E^{\circ\prime}$, and R. Although the calculated value of m, the Nernst slope, was always in excellent agreement with the theoretical value, it was coupled to the intercept, and a statistically superior data fitting resulted when the value of the slope was inserted as a constant. The input variables are the logarithm of the sodium ion concentration (XX(1)) and the observed potential (XX(2), mV).

2. SUBROUTINE EQN

```
      SUBROUTINE EQN
      COMMON KOUNT,ITAPE,JTAPE,INT,LAP,XINCR,NOPT,NOVAR,NOUNK,X,U,ITMAX,
     1ETX,TEST,I,AV,RESID,IAE,EPS,ITYP,XX,XXTYP,DX11,FOP,FO,FU,P,ZL,TO,E
     2IGVAL,XST,T,DT,L,M,JJJ,Y,DY,VECT,NEST,CONST,NDAT,JDAT,MOPT,LOPT,
     3YYY,CONSTS
      COMMON/FREDT/IMETH
      COMMON/POINT/KOPT,JOPT,XXX
      DIMENSION X(4,300),U(20),WTX(4,300),XX(4),FOP(300),FO(300),FU(300)
     1,P(20,21),VECT(20,21),ZL(300),TO(20),EIGVAL(20),XST(300),Y(10),
     2DY(10),CONSTS(50,16),NEST(50),ISMIN(50),XXTYP(50),DX11(50),IRX(50)
     3,MOPT(50),LOPT(50),YYY(50),CONST(16),XXX(15)
      GO TO (2,3,4,5,1,7,8,9,10,11,12)  ITYP
    1 CONTINUE
      ITAPE=60
      NOUNK=2
      NOVAR=2
C     U(1)=VOLTAGE - PNA INTERCEPT
C     U(2)=RESIDUAL CATION CONCENTRATION
C     CONST(1)=REACTION TEMP. IN DEG. C.
      JTAPE=61
      RETURN
    7 CONTINUE
      RETURN
    8 CONTINUE
      RETURN
    2 CONTINUE
      IF(IMETH.NE.-1) GO TO 35
      RETURN
   35 CONTINUE
      SODIUM=10**(XX(1))*U(2)
      S=ALOG10(SODIUM)
      POT=0.1984*(273.15+CONST(1))*S+U(1)
      RESID=POT-XX(2)
      RETURN
    3 CONTINUE
      RETURN
    4 CONTINUE
      RETURN
    5 CONTINUE
      IF(IMETH.NE.-1) GO TO 20
      RETURN
   20 CONTINUE
      RETURN
    9 CONTINUE
      RETURN
   10 CONTINUE
      RETURN
   11 CONTINUE
      RETURN
   12 CONTINUE
      RETURN
      END
```

3. Sample Data Listing

```
  10       100                                1.0001
STANDARDIZATION OF NAS 11-18 WITH NACL04 IN MEOH AT 25.0 DEG C. I=0.10 11-34.
     25.0
     200.    1.0E-06
  -4.6673    1.0E-06    -90.40    4.0E-02    -4.6638    1.0E-06    -81.50    4.0E-02
  -4.4221    1.0E-06    -70.40    4.0E-02    -4.2094    1.0E-06    -59.40    4.0E-02
  -3.9825    1.0E-06    -47.10    4.0E-02    -3.7651    1.0E-06    -35.20    4.0E-02
  -3.5546    1.0E-06    -23.10    4.0E-02    -3.3473    1.0E-06    -11.10    4.0E-02
  -3.1487    1.0E-06     0.2000   4.0E-02    -2.9631    1.0E-06     10.700   4.0E-02
```

APPENDIX C

APPLICATION OF COMPUTER PROGRAM MINIQUAD76A TO THE DETERMINATION OF EQUILIBRIUM CONSTANTS FROM POTENTIOMETRIC DATA

A. Program Function

The MINIQUAD76A program is a general equilibrium solving routine for the calculation of equilibrium constants from potentiometric data. Up to 20 equilibria involving five reactants can be considered, and a maximum of three electrodes can be used to determine the concentrations of free species.

The equilibrium constant for reaction 21

$$Na^+ + 18C6 \rightleftharpoons 18C6 \cdot Na^+ \qquad (21)$$

was calculated as

$$K = \frac{[18C6 \cdot Na^+]}{[Na^+][18C6]} \qquad (36)$$

As indicated in the data input instructions which follow, the user specifies the number of formation constants to be used in the calculation. The formation constants can be either held constant or refined in the calculation. The stoichiometries, initial solution volume, reaction temperature, initial number of millimoles of each reactant, and the titrant concentration and temperature are specified by the user. The electrode calibration parameters are entered as the slope and intercept of the calibration plots. The titration data are entered as the measured electrode potentials as a function of the volume of the titrant added. The data input instructions and a sample data listing are presented in the following sections.

B. Data Input Instructions

1. 1 card /20A4/ : descriptive title

2. 1 card /8I5/ : LARS, NK, N, MAXIT, IPRIN, NMBEO, NCO, ICOM.

LARS is an indicator for the data points to be considered in the refinement: with LARS=1 all the data points are used, with LARS=2 alternate points, with LARS=3 every third point, etc. (last points on all titration curves are always used).

NK is the total number of formation constants.

N is the number of formation constants to be refined.

MAXIT is the maximum number of iteration cycles to be performed: with MAXIT=0 and according to the values of JPRIN and JP (see below) the residuals on mass balance equations and/or the species distribution are evaluated for the given formation constants and conditions.

IPRIN=0 is normal; IPRIN=1 monitors the progress of the refinement at each cycle; IPRIN=2 produces an additional listing of the experimental data at each titration point.

NMBEO is the total number of reactants (mass balance equations) in the system under consideration.

NCO is the maximum number of unknown concentrations of free reactants; if NCO=0 the whole job is abandoned before refinement.

ICOM=0 is normal; with ICOM=1 data points are eliminated before the refinement if the corresponding block of the normal equation matrix is found to be not positive-definite.

3. 1 card /3F10.6, 8X,I2/ : TEMP, ADDTEMP, ALPHA, NOTAPE

TEMP is the reaction temperature in °C.

ADDTEMP is the titrant temperature in °C.

ALPHA is the coefficient of cubical expansion for the solvent used, $°C^{-1}$.

NOTAPE=0 is normal; NOTAPE=1 reads values for EZERO and SLOPE (see below) from device TAPE3. This allows calibration curve data to be calculated and used in the same computer run.

4. NK cards /F10.6,7I5/ : BETA(I), JPOT(I), JQRO(J,I) (NMBEO values), KEY(I)

The formation constants are expressed in exponential notation

$$\beta_i = \text{BETA(I)} \cdot 10^{\text{JPOT(I)}} .$$

JQRO(J,I) (J=1, NMBEO) are the NMBEO stoichiometric coefficients of the ith species with formation constant β_i. The order of coefficients is arbitrary, except that those referring to reactants, of which the free concentration is determined potentiometrically, must come last. Such a choice implies that a progressive integer number (from 1 to NMBEO) is assigned to each reactant.

KEY(I) is the refinement key of the ith formation constant: with KEY=0 the formation constant is not refined and with KEY=1 the formation constant is refined.

5. The following set of cards for each titration curve:

1 card /12I5/ : NMBE, JNMB(I) (NMBE values), NC, JP(I)

NMBE is the number of reactants (mass balance equations) involved in the titration curve.

JNMB holds the integer numbers previously assigned to the NMBE reactants involved.

NC is the number of unknown free concentrations at each point of the titration curve; the number of concentrations experimentally determined (i.e., the number of electrodes) is NEMF=NMBE-NC.

JP contains integer numbers corresponding to selected reactants: in the subroutine STATS the formation percentages relative to these reactants will be calculated, depending on the value of JPRIN.

1 card /5A10/ : REACT(I) (NMBE values)

REACT contains the names of the reactants, listed in the same order as JNMB.

1 card /4I5/ : JEL(I) (NEMF values), JCOUL

JEL holds the number of electrons transferred at each electrode. If the decimal cologarithm of concentration (e.g., pH) is to be read in, put JEL(I)=0.

JCOUL=0 is normal; JCOUL=1 if the total volume of the solution does not change during the titration (e.g., coulometric experiments).

1 (or 2) card(s) /8F10.6/ : TOTC(I) (NMBE values),
EZERO(I) (NEMF values),
ADDC(I) (NMBE values),
VINIT

TOTC contains the initial number of millimoles of reactants in solution; the order of reactants is the same as in JNMB.

EZERO(I) holds the standard potential of the ith electrode (mV); the value is ignored if JEL(I)=0.

ADDC contains the molar concentrations of titrant solutions (there is one for each reactant); the order of the reactants is the same as in JNMB.

VINIT is the initial volume of the solutions (cm^3), and should correspond to the volume expected at the temperature of the TITRANT.

1 card /8F10.6/ : SLOPE (NEMF values).

SLOPE contains the slopes of the calibration curves for the species measured, in units of mV per decade of concentration, the value is ignored if JEL(I)=0.

cards /I5,8F8.3/ one for each point of the
titration curve: LUIGI, TITRE(I)
(NMBE values), EMF(I) (NEMF values)

LUIGI=0 is normal, LUIGI=1 indicates the end of a titration curve, LUIGI < 0 indicates the end of all titration curves, LUIGI=2 indicates that, for coulometric titration, current (mA) and fractional

current efficiency are read instead of a data point.

TITRE contains the volumes of titrant solutions (cm^3) added in volumetric titrations or time of current passage (sec) in coulometric experiments.

EMF contains the potentials (mV) measured on each electrode with non-zero JEL value (otherwise the decimal cologarithms of concentration).

6. 1 card /I5/ : JPRIN

JPRIN controls the amount and type of output produced by STATS:

JPRIN	Statistical Analysis	Tables	Graphs
0	no	no	no
1	yes	no	no
2	yes	yes	no
3	yes	no	yes
4	yes	yes	yes

If JPRIN > 1, the amount and type of tables and/or graphs is determined by the values contained in JP for each titration curve.

7. 1 card /I5/ : NSET

NSET=1 for another set of formation constants - items 1-4, 6, and 7, only -; NSET=0 for another complete set of data, NSET=-1 for the termination of the run.

C. Sample Data Listing

```
KE DF 1PCGMA IN MEDM AT 25.0 DEGREES C.  I=0.10  II=34.25.
   1     1     1    25     2     2     1     0
     25.0          25.0     0.0012           1
 2.0             4     1     1     1
   2     1     2     1     1     2
     1826     SODIUM
   1     0
         0.  0.02722      156.37  0.04216          0.0         25.
  59.155
   0    0.700    0.000    -35.1
   0    0.750    0.000    -39.3
   0    0.800    0.000    -43.7
   0    0.850    0.000    -47.0
   0    0.900    0.000    -50.7
   0    0.950    0.000    -53.6
   0    1.000    0.000    -56.3
   0    1.050    0.000    -59.0
   0    1.100    0.000    -61.5
   0    1.170    0.000    -64.4
   0    1.200    0.000    -65.7
   0    1.250    0.000    -67.6
   0    1.330    0.000    -70.5
   0    1.400    0.000    -72.9
   0    1.500    0.000    -75.8
   0    1.600    0.000    -78.5
   0    1.700    0.000    -80.8
   0    1.800    0.000    -83.1
   0    1.900    0.000    -85.2
  -1    2.000    0.000    -87.3
   4
  -1
```

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