

A Molecular Mechanics Study of the Selectivity of Crown Ethers for Metal Ions on the Basis of Their Size

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Abstract. A molecular mechanics (MM) analysis is carried out on complexes of crown ethers $\text{CH}_2(\text{OCH}_2\text{CH}_2)_n\text{CH}_2\text{O}$, 12-crown-4 ($n = 3$), 15-crown-5 ($n = 4$), 18-crown-6 ($n = 5$), 24-crown-8 ($n = 7$), and 30-crown-11 ($n = 9$) to determine the nature of the selectivity shown by these ligands for metal ions on the basis of metal ion size. The MM program used is SYBYL, and M-O bonds are represented using a 'covalent' model, i.e. the M-O bonds are modelled with ideal M-O bond lengths and force constants. The previously used technique of calculating strain energy as a function of M-O bond length is used for all the complexes, and also the complexes of the non-macrocyclic polyethylene glycol analogues. It is concluded that the crown ethers fall into three groups with regard to selectivity for metal ions. Group one consists of the smaller macrocycles such as 12-crown-4 and 15-crown-5, where metal ions generally are too large to enter the cavity of the macrocycle, and the metal ion is coordinated lying outside the plane of the donor atoms of the ligand. Here factors that control selectivity are the same as in non-macrocyclic ligands, chiefly the size of the chelate ring. Group 2 contains only 18-crown-6 of the ligands studied here. 18-Crown-6 complexes have three important conformers, one of which, the D_{3d} , shows sharp size match selectivity, preferring metal ions with M-O bond lengths of about 2.9 Å. The other two conformers are adopted by metal ions too small for the D_{3d} conformer, and are more flexible, exerting little size-match selectivity. These other two conformers are of higher energy than the D_{3d} conformer for metal ions with M-O bond lengths greater than 2.55 Å. Thus, a genuine 'size match selectivity' is found for K^+ with 18-crown-6. With an ideal M-O bond length of 2.88 Å, K^+ fits the cavity of the D_{3d} conformer of 18-crown-6 very closely. The third group consists of very large macrocycles such as 24-crown-8 and 30-crown-10. These enfold the metal ion in extremely folded conformations, but may, as does 30-crown-10, exert considerable selectivity for metal ions on the basis of their size by virtue of the conformation resulting in a set of torsional angles in the ring atoms of the macrocycle which confer considerable rigidity on the ligand.

Key words: Crown ethers, molecular mechanics, macrocycles.

1. Introduction

One of the remarkable properties of crown ethers, as first discovered by Pedersen [1], is their ability to complex selectively with metal ions on the basis of metal ion size. The variation of $\log K_1$, the formation constant [2], of the complexes of crown ethers with Na^+ , K^+ , and Cs^+ , as a function of the size of the macrocyclic ring, is seen in Figure 1. The variation of $\log K_1$ for crown ethers with cavities of

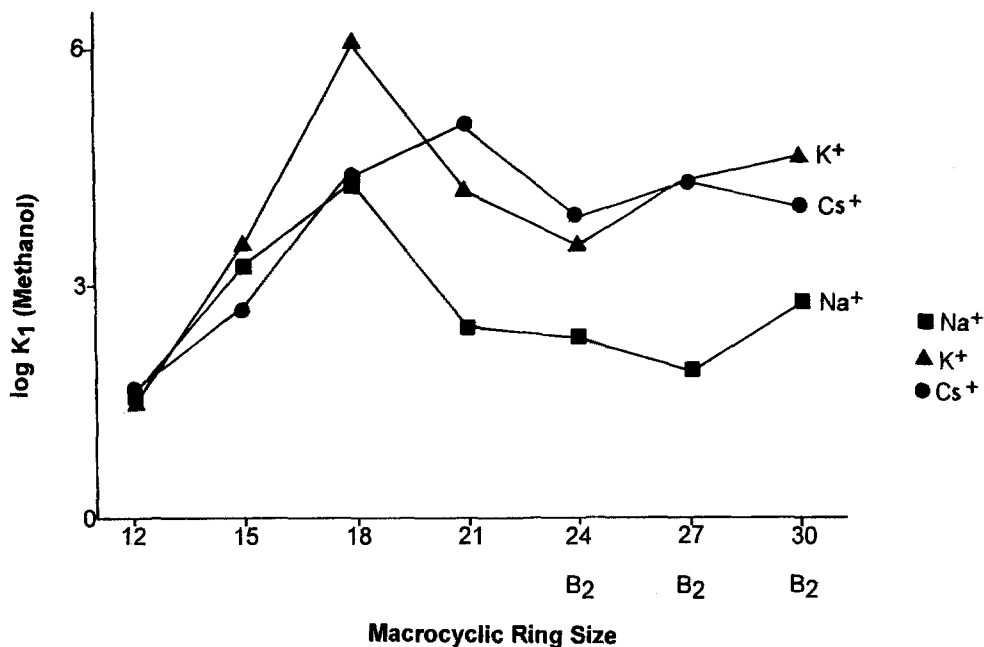


Fig. 1. Variation of $\log K_1$ for crown ether complexes of Na^+ , K^+ , and Cs^+ , as a function of size of the macrocyclic ring. Data in methanol at 25°C , from reference 2. The crown ethers are in simple unsubstituted forms, except for macrocyclic ring sizes 24, 27, and 30, which are dibenzo substituted.

different sizes with metal ions of different sizes has commonly been rationalized [3] in terms of the *size match selectivity* hypothesis. In this hypothesis the most stable complex will be formed where the match between the ionic radius of the metal ion and of the cavity in the macrocycle is the closest. Size match selectivity appears to operate for the complex of 18-crown-6 in Figure 1 (see Figure 2 for key to ligand abbreviations), since models show that K^+ fits the cavity in 18-crown-6 the best, and K^+ forms the most stable complex of the alkali metal ions with 18-crown-6. However, there are serious limitations [4] in terms of the ability of the hypothesis to account for the variation in $\log K_1$ seen in Figure 1. Thus, in Figure 1 the very large ring crown ether dibenzo-30-crown-10 forms a more stable complex with K^+ rather than the larger Cs^+ ion. The size match selectivity hypothesis would suggest that the larger cation would form the more stable complex with the larger crown ether. Similarly, with the very small ring 12-crown-4, the selectivity is still not significantly in favor of the small Na^+ ion.

Previous work using Molecular Mechanics (MM) calculations [5–7] has shown that for tetraaza macrocycles, size match selectivity is not of major importance in controlling selectivity. In brief, a tetraaza macrocycle such as cyclam forms complexes with a variety of conformations. One of these, the *trans*-III or $++-$

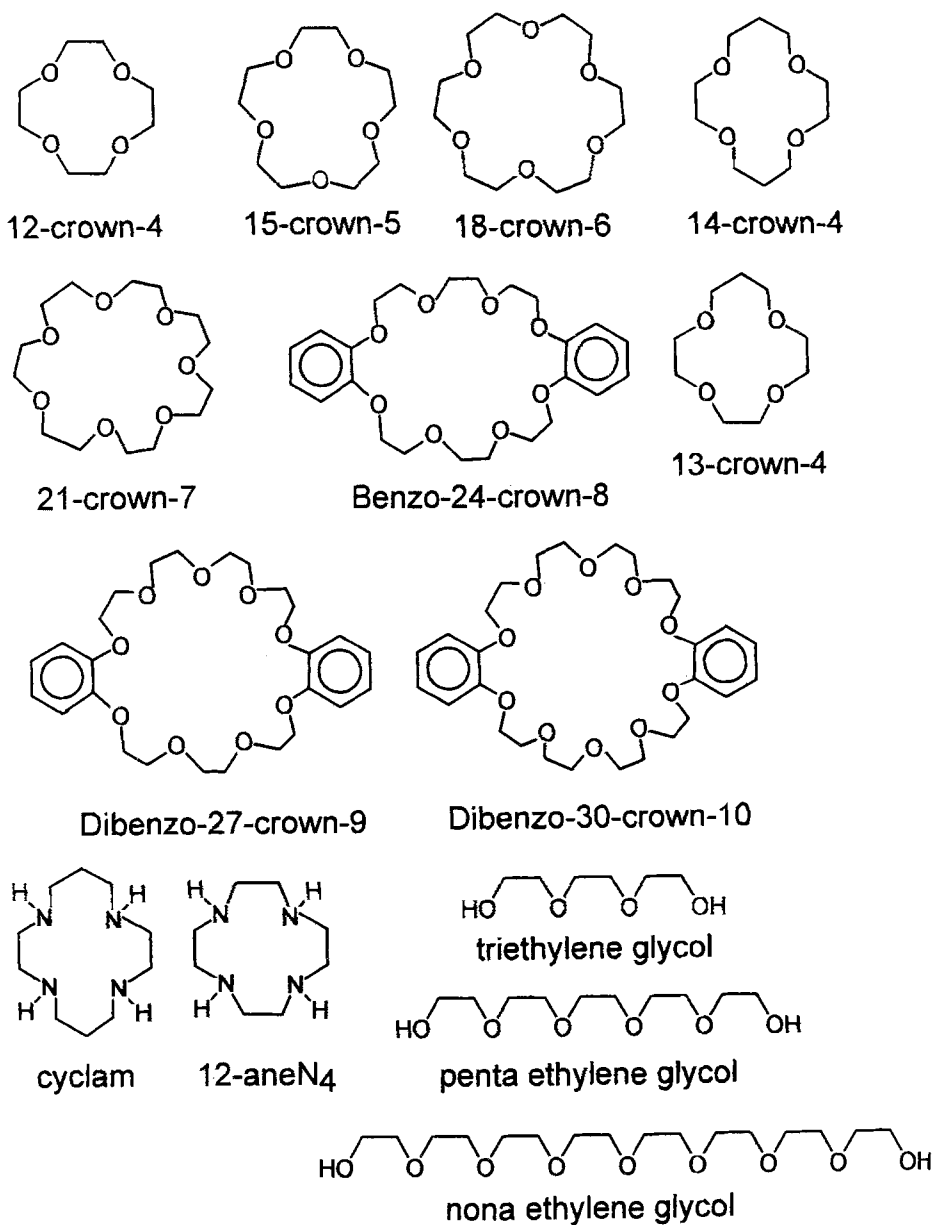
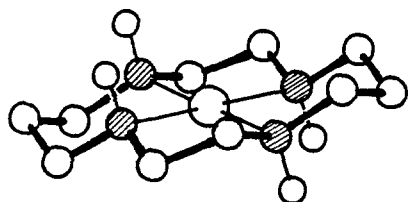


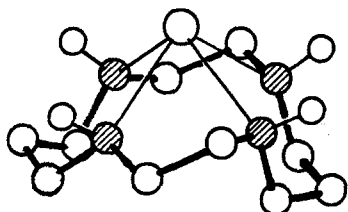
Fig. 2. Ligands discussed in this paper.

conformation (see Figure 3) holds the metal ion within the plane of the nitrogen donors, and on its own would exert considerable size match selectivity. However, where the metal ion is too large for the cavity in cyclam, either the *trans*-I or ++++ conformer, or the *cis*-V +-+ conformer is adopted, with the metal ion lying well out



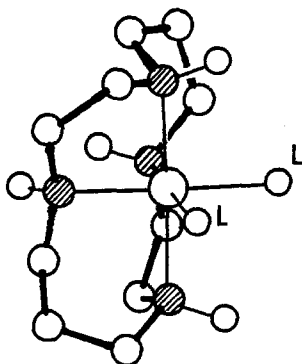
(a)

trans-III + + --
conformer, metal
ions of suitable
size [e.g. Cu(II)]
lie in plane
of donor atoms



(b)

trans-I + + + +
conformer, too-
large metal ions
[e.g. Hg(II), Cd(II)]
lie above plane
of donor atoms



(c)

cis-V + - + -
conformer allows
too-large [e.g. Pb(II)]
octahedral metal
ion to escape
compression.

Fig. 3. Common conformations of the complexes of the tetraaza macrocycle cyclam [5-7]. Structures generated with the program SYBYL [13].

of the plane. Here the factor that controls selectivity is the same as for open-chain ligands, namely, the size of the chelate ring.

The size of the chelate ring controls [3,6,7] selectivity for metal ions on the basis of metal ion size because the lone pairs on the donor atoms of a ligand that will form a five membered chelate ring are focussed on a point some 2.5 Å away, while the lone pairs on the donor atoms of a six membered chelate ring focus on a point 1.6 Å away. The presence of five membered chelate rings thus promotes selectivity for large metal ions, while six membered chelate rings promote selectivity for small metal ions. It has been found [8] that the presence of neutral oxygen donors in non-macrocyclic ligands promotes selectivity for large metal ions, provided, as is usually the case, the neutral oxygen donors are part of a five membered ring in the complex. This has led to speculation [3,6,8] that the metal ion selectivity of crown ethers is controlled by the fact that virtually all crown ethers form five membered chelate rings only. All metal ions that form stable complexes with crown ethers in aqueous solution have an ionic radius in excess of 1.0 Å, which corresponds to a M-O bond length of about 2.4 Å. The only crown ethers that complex well with small metal ions, such as 13-crown-4 and 14-crown-4 derivatives [2,9], which show strong selectivity for Li^+ , form six membered chelate rings on complex formation.

In order to understand the metal ion size based selectivity of crown ethers, an MM analysis of a selection of crown ether complexes has been carried out, and is reported here. There have been previous extensive MM calculations on crown ether complexes of alkali metal ions in aqueous solution [10,11]. These involved an electrostatic model of M-L bonding, which is in some ways the most realistic for the alkali metal ions. These papers provided a detailed analysis of the energetics involved in the crown-metal ion interaction. The questions being asked in this paper are more general, and are not primarily concerned with bond type, but rather the effect of metal ion size on selectivity. The approach here is to use force constants and ideal bond lengths to model the M-L bond. This serves in the first instance to hold the donor atoms at the appropriate distance from the metal ion. One then scans the strain of the complex as a function of M-O bond length, with a constant M-O force constant, a technique that has proved useful [5-7] in analyzing the selectivities of the tetraazamacrocycles. The minima in the curves obtained in Figures 5-7 indicate the best-fit M-O bond length for coordinating with the ligand. Different conformers of the complexes are examined in this way, and the regions of M-O bond length in which each is the most stable can provide considerable insight into the geometric factors affecting metal ion selectivity. Although it might be argued that the electrostatic model of bonding is more realistic for alkali metal ions interacting with crown ethers than a covalent model, the work here is not aimed only at the alkali metal ions, but is meant to be general. Further, the ionic model has some defects [12] which make it unsuitable in the present application. The most serious is that present purely electrostatic representations of the M-O bond are non-directional. Even in a purely electrostatic M-O bond, the negative charge on the oxygen donor atoms of a crown ether should be offset onto the lone pair of the oxygen, which is not the case in electrostatic models. The displacement of charge onto the lone pair of the donor atom gives even an ionic bond a directionality, which

is easily modelled in a covalent representation by having a M-O-C angle bending force constant. As discussed below, analysis of the structures of the Rb^+ and Cs^+ complexes with 18-crown-6 shows a small but definite M-O-C force constant, consistent with the M-O bond having directionality. A further problem [12] with a purely electrostatic representation of the M-O bond is that it produces the wrong shaped potential well for the bond. Thus, resistance to M-O bond elongation in the electrostatic model is produced by electrostatic attraction, which is a term in r^2 , where r is the M-O bond length. However, resistance to M-O compression arises from an exponential term in r , or a term in r^{12} , depending on the type of potential function used to model van der Waals repulsive forces between the metal ion and the oxygen donor atoms. Thus, in electrostatic models as presently formulated, bond extension is too easy, and bond compression too difficult, as seen in the poor ability of purely electrostatic models to reproduce M-O bond length details [12]. In contrast, bond compression and bond elongation by steric factors are of equal difficulty in a purely covalent model, and better reproduction of bond length features are found [12] even for complexes of K^+ in such a model. Since our primary concern here is the relationship between bond length and steric strain, not only is a covalent model simpler to apply and interpret, but for our purposes, it should give a better result. It should be emphasized, in any event, that *these calculations are not meant to apply specifically to alkali metal ions*, or any other type of metal ion. Rather, by their generality, they apply to all metal ions, and attempt to answer much broader questions than do calculations focussed only on alkali metal ions. Thus, the type of question that is addressed here is ‘why do only large metal ions – of whatever M-O bonding type – complex with crown ethers’, or ‘why does 12-crown-4 show so little discrimination amongst metal ions ranging in size from Na^+ to Cs^+ ?’ Thus, the present calculations apply to metal ions such as Tl^+ , Ag^+ , Pb^{2+} and Hg^{2+} , or even Cu^{2+} , where the M-O bonds would be much more covalent, just as much as to the more ionically bound alkali metal ions.

2. Experimental

2.1. MOLECULAR MECHANICS CALCULATIONS

These were carried out using the program SYBYL [13]. Sybyl models molecules by minimizing the total strain energy (ΣU) of the molecule, with contributions from bond length deformation strain energy (U_B), bond angle deformation strain energy (U_θ), torsional strain energy (U_ϕ), and van der Waals interactions between atoms not directly bonded to each other (U_{NB}).

$$\Sigma U = U_B + U_\theta + U_\phi + U_{NB} .$$

Charges on atoms can also be included, calculated by empirical, or semi empirical MO methods, although this was not done here for reasons mentioned above. The force constants and potential functions used in SYBYL are described fully elsewhere [14], and the interested reader is referred to this publication should

they wish to extend or examine the calculations reported here. SYBYL generates the geometry around the metal ion by use of van der Waals repulsion between the donor atoms, rather than by specifying O-M-O bond angles and angle bending force constants for the metal ion and its donor atoms. The calculations were therefore carried out using this approach of van der Waals repulsion between the donor atoms to generate the geometry around the metal ion, which has been suggested by Bernhardt and Comba [15] as a modification of our method [5-7]. All torsional constants involving the metal ion, and O-M-O angle bending constants were therefore set to zero, to allow van der Waals repulsion between the donor atoms alone to determine geometry. This has been demonstrated [16] to be a very satisfactory approach for generating coordination geometry for Co(III) complexes. The scans of strain energy as a function of metal ion radius were carried out as described previously [5-7]. A constant M-O bond stretching constant of $25.0 \text{ kcal mol}^{-1} \text{ \AA}^{-1}$ was used. The results of the calculations are not [5-7] particularly sensitive to the value of the force constant used. The preference of small metal ions for five membered chelate rings arises largely from bond angle and torsional requirements within the organic part of the chelate ring, so the M-O stretching force constants are not of great importance to the results obtained here, except to constrain the M-O bond to approximately the desired length. The angle bending constants of the organic part of the chelate ring are standard to the SYBYL force field, and are similar to those in other force fields. The results might be affected by angle bending constants involving the metal ion, and here one would say that these constants should be large in those complexes with more covalent M-O bonding, and smaller in those with less covalent M-O bonding. This is mimicked by the fact that as M-O bonds get longer, corresponding roughly to more ionic M-O bonds, so the oxygen atoms get further apart, and van der Waals repulsions become smaller, equivalent to weaker O-M-O bending constants. The effect of chelate ring size on complex stability depends on the orientation of the lone pairs of the donor atoms, which is in effect modelled by the M-O-C angle bending constant. The value of this constant is thus important here. The structures [17,18] of the Cs^+ and Rb^+ 18-crown-6 complexes provide sensitive determinations of the M-O-C force constant, since these metal ions lie more than 1 \AA out of the plane of the donor atoms of the macrocycle, with considerable distortion of the M-O-C angle away from 109.5° . It was found that with the M-O-C force constant set at $0.002 \text{ kcal mol}^{-1} \text{ radian}^{-1}$, the extent to which these metal ions lay out of the plane of the donor atoms could be modelled accurately. This value of the M-O-C force constant applies strictly only to Rb^+ and Cs^+ , but was used throughout for all the calculations. For more covalent metal ions, where this constant should be larger, the effects of chelate ring size should therefore become more marked. The results in Figures 5-7 are fairly rugged, and the overall conclusions cannot be altered by variation of the force constants involving the metal ion. All other parameters in the calculations were as contained in the TRIPOS 5.2 force field in SYBYL [14]. A validation of this force field is found in reference 14. The scans are presented as a function of M-O

bond length. The radius [19] of metal ions appears from the available data to be related quite well to M-O bond length by the approximation M-O bond length = ionic radius + 1.37 Å. The scans of strain energy versus M-O bond length seen in Figures 5 and 6 were thus drawn up using this approximation.

The crown ethers, particularly the large members of the series, may form a very large number of different conformers in their complexes. Since our interest here is to gain insights into selectivity, rather than conduct an exhaustive investigation of the possible conformers of crown ether complexes, crystal structures of actual crown ether complexes were taken from the literature and used as starting structures for the MM calculations. Thus, for the different crown ethers, the following structures were used: 12-crown-4 complexes, the bismuth(III) complex [20]; 15-crown-5, the Na⁺ complex of benzo-15-crown-5 [21]; 18-crown-6, the K⁺ complex [22], Na⁺ complex [23], Rb⁺ complex [17], Cs⁺ complex [18], and Bi(III) complex [24] for the different conformers; 24-crown-8, the Ba²⁺ complex of dibenzo-24-crown-8 [25]; 30-crown-10, the K⁺ complex of the dibenzo ligand [26].

3. Results and Discussion

3.1. COMPLEXES OF 18-CROWN-6

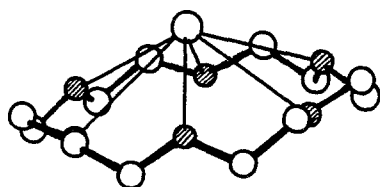
Figure 1 shows that 18-crown-6 is unusual in the sharp peak in complex stability experienced by the K⁺ complex with this size of macrocyclic ring. Examination of the literature suggests that when the metal ion does not fit the 18-crown-6 cavity, there may be three types of response:

(a) If the metal ion is too large for the cavity (Rb⁺, Cs⁺), then the metal ion will retain the D_{3d} conformer found in the K⁺ complex, but rise up out of the macrocyclic cavity [17,18] (Figure 4).

(b) For smaller metal ions (Na⁺) the macrocycle can assume a 'half-buckled' conformation in which five oxygen donors lie approximately in a plane containing the metal ion [23], while the sixth coordinates in an approximately axial position (Figure 4).

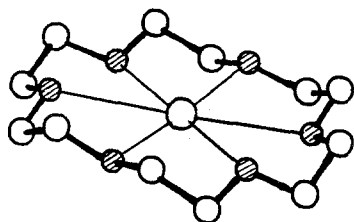
(c) For too-small metal ions such as Bi(III) [20] the ++-+- conformer is adopted (Figure 4). This is a widespread conformation in complexes of ligands which contain an 18-crown-6 like fragment, such as the BHE-18-aneN₂O₄ complex [24] of K⁺.

(The ++-+- designation of the conformer relates to the orientation of the non-coordinated lone pairs on the oxygen donor atoms in the complex. This corresponds to the convention for azamacrocycles [5,7] where the macrocycle is viewed from above, and a + indicates that the N-H hydrogen lies above the plane of the macrocycle, whereas a - indicates that it lies below. For crown ethers in this convention, the lone pair on the oxygen occupies the position of the N-H hydrogen of aza macrocycles).



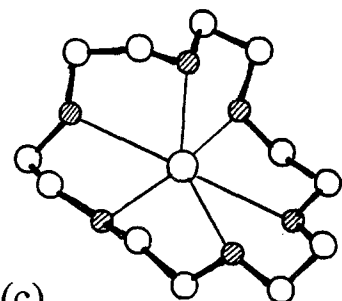
(a)

large Cs^+ ion
lies above plane
of donor atoms
in D_{3d} conformer



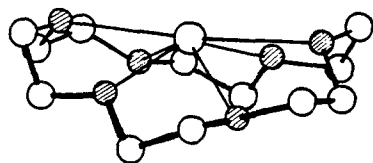
(b)

K^+ fits cavity
almost perfectly
in D_{3d} conformer



(c)

Na^+ too small for
 D_{3d} conformer, adopts
'half buckled'
conformer



(d)

smaller Bi^{3+} ion
adopts buckled
+-+- conformer

Fig. 4. Drawings of different conformers of the 18-crown-6 complex adopted as the metal ion becomes progressively smaller in (a) through (d). (a) is the D_{3d} conformer of Cs^+ with the too-large metal ion rising [18] up out of the plane of the ligand. (b) shows the D_{3d} conformer of K^+ which fits well into the cavity [22], (c) shows the 'half-buckled' conformer of the somewhat too-small Na^+ ion [19], and (d) shows the +++- conformer adopted by the much too small Bi(III) ion [24]. Structures generated with the program SYBYL [13].

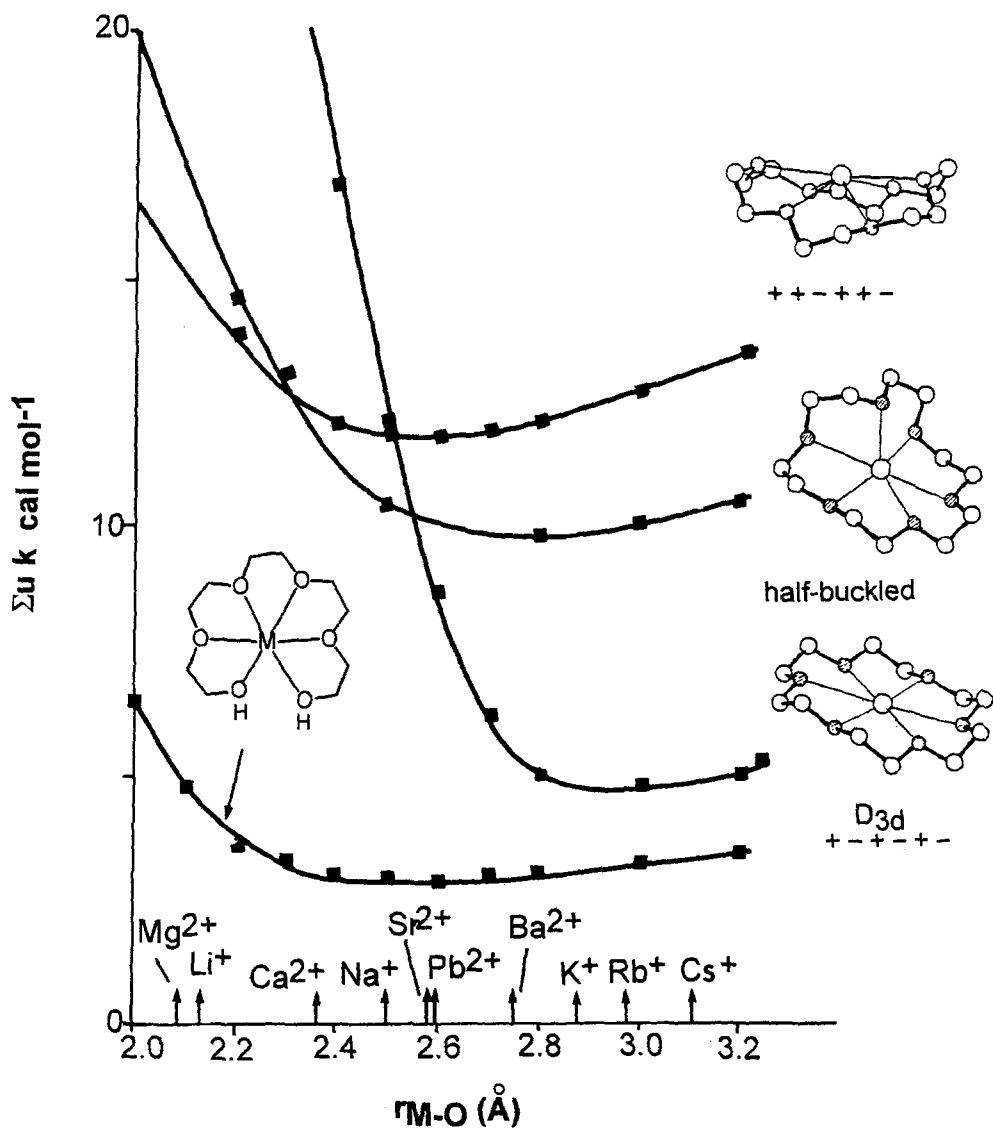


Fig. 5. The variation in strain energy of different conformers of complexes of 18-crown-6, calculated by Molecular Mechanics, as a function of M-O bond length, from coordinates for crystal structures [16,17,22-24] of the different conformers shown. The D_{3d} conformer is most stable for metal ions of M-O bond length more than 2.55 Å, while the 'half-buckled' and ++++- conformer, although of high energy, become more stable than the D_{3d} at short M-O bond lengths. Also shown is the plot of strain energy versus M-O bond length for the open-chain pentaethylene glycol complex, which indicates the metal ion size selective behavior of a non-macrocyclic analogue of 18-crown-6.

The scans of strain energy of the above three conformers of 18-crown-6 complexes as a function of M-O bond length are seen in Figure 5. It is seen that the D_{3d} conformer is that of lowest energy at M-O bond lengths above 2.55 Å. Below this there is a short region of M-O length from 2.55 to 2.30 Å where the most stable conformer is the 'half-buckled' conformer found in the Na^+ complex, in accord with the complex having a mean Na-O bond length [21] of 2.39 Å. At M-O bond lengths less than 2.30 Å, the ++-+- conformer is the most stable. Whether the 'half-buckled' or ++-+- conformer is adopted is not determined solely by strain energy as seen in the curves in Figure 5. The half-buckled conformer found in the Na^+ complex allows no space for coordination of an extra ligand such as a water molecule through the middle of the macrocyclic ring, as is found in the La^{3+} complex [26]. Thus smaller metal ions of coordination number more than seven cannot adopt the half buckled conformer, as this allows no room for coordination of the extra ligand through the macrocyclic ring. The Bi(III) 18-crown-6 complex does not have any additional unidentate ligands coordinated through its macrocyclic ring. Rogers *et al.* [20] have suggested that the lone pair of Bi(III) occupies this position, which might contribute to the adoption of the ++-+- conformer by Bi(III).

In Figure 5, in addition to the strain energy curves for the different conformers of crown ether complexes, the strain energy versus M-O bond length curve for pentaethylene glycol complexes is shown. The structure of the pentaethylene glycol complex was generated from the Na^+ 18-crown-6 structure by removing one ethylene bridge. The shape is typical of many generated here for open chain glycols. The extent to which the curve for a macrocyclic ligand is sharper than this typical curve for an open chain ligand is a measure of the extent to which the macrocyclic structure contributes to metal ion size based selectivity. The similarity of the shape of the curves for complexes of the open-chain ligand and the ++-+- conformer of 18-crown-6 complexes suggests that in this highly folded conformer the metal ion selectivity is not very different from that found in an open-chain ligand. The 'half-buckled' conformer shows a modest amount of size selectivity over and above that of an open chain ligand, in accord with the fact that this conformer holds the metal ion in the plane formed by five of the donor atoms. The D_{3d} conformer holds the metal ion within a rigid cavity, and shows strong selectivity against metal ions with radii less than 2.8 Å. The best-fit size for coordinating in the D_{3d} conformer, which is the minimum in the curve in Figure 5, is at an M-O bond length of 2.88 Å. This corresponds to an ionic radius of 1.51 Å, which is in good agreement with estimates based on models. The curve is rather flat at bond lengths above 2.88 Å, which suggests that the D_{3d} conformer has little selectivity resulting from purely steric considerations against metal ions with radii larger than 2.8 Å, i.e. Rb^+ and Cs^+ . This result is somewhat dependent on the size of the M-O-C force constant. If the latter is increased to the sort of value found for more covalent metal ions than those considered here, then there is a strong upturn in the curve for the D_{3d} conformer at longer M-O bond lengths. With a low M-O-C force constant there

is very little steric penalty for escaping compression by being extruded from the plane of the donor atoms, as happens with Rb^+ and Cs^+ complexes of 18-crown-6. However, it seems unlikely that the M-O-C force constants will be large for either Rb^+ or Cs^+ . Rather, the explanation advanced earlier [29] for the selectivity patterns of 18-crown-6 may be operative. In the gas-phase, inductive effects cause M-O bond strengths to increase [30–33] for sp^3 hybridized oxygens in the order $\text{H}_2\text{O} < \text{ROH} < \text{R}_2\text{O}$ ($R = \text{alkyl}$). The sum of the M-O bond energies of crown ethers should therefore be higher than for the water molecules displaced, assuming that these are the same in number in the two cases. Metal ions should thus respond to the increased donor strength of the ethereal oxygens of the crown ether in the order of their increasing Lewis acid strength. This accounts [34] for the fact that the post-transition ions, such as Tl^+ and Pb^{2+} with their greater electronegativity [35], and hence greater Lewis acidity, form more stable complexes with 18-crown-6 than do their alkali or alkaline earth analogues of the same ionic radius. It should be noted, in response to a comment from a referee, that this is in spite of the respective hydration enthalpies of Pb^{2+} and Tl^+ being higher than those for Sr^{2+} and Rb^+ . Pb^{2+} and Tl^+ are stronger Lewis acids than Sr^{2+} and Rb^+ respectively, and so have larger hydration energies, in spite of being the same size and charge as Sr^{2+} and Rb^+ respectively. However, stronger Lewis acids lead to even stronger interaction with the more basic donor atoms of the crown ether, and so Pb^{2+} and Tl^+ form more stable complexes with 18-crown-6, even though they are more strongly hydrated as free ions. In comparing ions of the same size but differing Lewis acidity, such as Pb^{2+} and Sr^{2+} , or Tl^+ and Rb^+ , the contribution of size is factored out, and we are left with the effect of greater Lewis acidity:

Metal ion	Sr^{2+}	Pb^{2+}	Rb^+	Tl^+
Ionic radius ^a	1.18	1.19	1.52	1.50
Electronegativity ^b	1.0	2.3	0.8	2.0
Heat of hydration ^c	-363.5	-371.9	-81.0	-87.0
$\log K_1$ (18-crown-6) ^d	2.84	4.23	1.55	2.44

^a In Å, for six coordination, from Ref. 19.

^b From reference 31.

^c Enthalpy of transfer of ion from gas to aqueous phase, in kcal mol^{-1} , from H.L. Friedman and C.V. Krishnan, in *Water, a Comprehensive Treatise*, Vol. 3, F. Franks (ed.), Plenum, New York, 1973, p. 55.

^d In water at 25°C, mean of values reported in Ref. 2.

The order of Lewis acid strength for the alkali metal ions increases in the gas-phase [32] $\text{Cs}^+ < \text{Rb}^+ < \text{K}^+ < \text{Na}^+ < \text{Li}^+$. This should be the order of complex stability with crown ethers, *even considering that hydration energies of these ions increase in this order*, since the ethereal oxygen donor of the crown ether is a stronger base than water. Thus, with no major increase in steric strain for the D_{3d}

conformer above a M-O bond length of 2.88 Å, the order of decreasing complex stability of 18-crown-6 complexes $K^+ > Rb^+ > Cs^+$ will have a contribution from the Lewis acidity of the cations, which decreases in the same order. For the lighter alkali metal ions, the order of $\log K_1$ $Li^+ < Na^+ < K^+$ is the opposite of what would be expected from the Lewis acidity of the cations, and is controlled by the increasing strain energy of the complexes formed by the lighter members of the series. One should note that the K^+ ion M-O bond length occurs at exactly the energy minimum for the D_{3d} complex in Figure 5.

The alkali earth metal ion M-O bond lengths are also indicated on Figure 5. The Ba^{2+} ion occurs close to the energy minimum for the D_{3d} conformer, which accounts for the high stability of the complex. The high strain energy for the conformers adopted by the smaller metal ions accounts for the stability order $Ba^{2+} > Sr^{2+} > Ca^{2+} > Mg^{2+}$. Again, the greater stability of complexes of alkali earth metal ions than those of alkali metal ions of the same size relates to the greater response of the stronger Lewis acid divalent ions to the greater basicity of the ethereal oxygen donor than of water.

3.2. THE COMPLEXES OF 12-CROWN-4 AND 15-CROWN-5

The ligand 12-crown-4 does not have a cavity large enough for any metal ion to lie within the plane of the donor atoms. All metal ions must thus coordinate lying out of the plane of the donor atoms, and by analogy with 18-crown-6 complexes, should not show any sharp selectivity effects. The curve of strain energy versus M-O length for 12-crown-4 complexes is seen in Figure 6. Also included is the curve for the complex of the open chain ligand triethylene glycol. This was generated by removing one ethylene bridge from the structure of the 12-crown-4 complex. The curve for the 12-crown-4 complex is very similar to that for its open-chain analogue, suggesting that in out-of-plane coordination of the metal ion, 12-crown-4 exerts virtually no size-match selectivity, as supported by the results in Figure 1. Also included in Figure 6 is the comparable curve for the *trans*-I conformer of the 12-aneN₄ complex. The much sharper curve for the 12-aneN₄ complex is due to the much larger M-N-C angle bending force constants as compared to the M-O-C constants applicable to 12-crown-4. The flat curve for 12-crown-4 would resemble that for 12-aneN₄ complexes as the M-O-C angle bending constant becomes larger. Smaller metal ions tend to be more covalent, with correspondingly larger M-O-C angle bending force constants, so that many smaller metal ions with more covalent M-O bonds would be excluded from forming complexes with 12-crown-4. This would arise, by analogy with the analysis of 12-aneN₄ [5-7], because of the higher strain involved in coordinating small metal ions in five membered chelate rings.

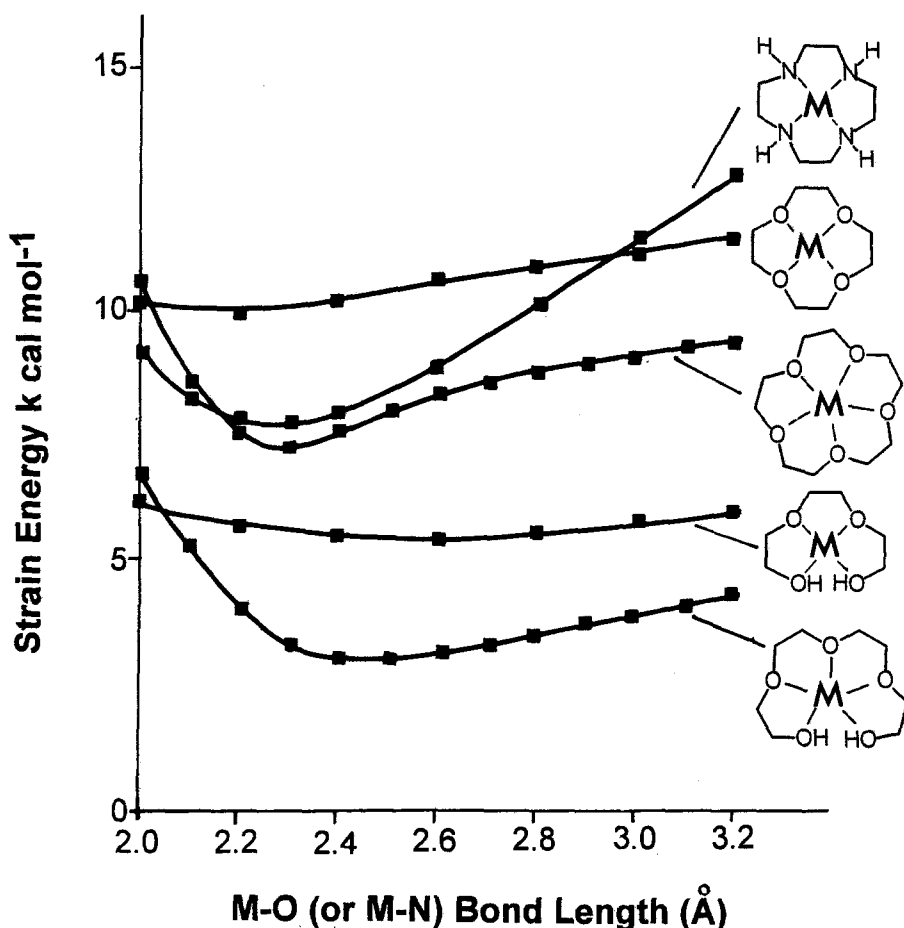


Fig. 6. The variation in strain energy of complexes of 12-crown-4 and 15-crown-5, calculated by Molecular Mechanics, as a function of M-O bond length, from coordinates for crystal structures [20,21] of the complexes. Also shown is the variation in strain energy as a function of M-N bond length for the 12-aneN₄ complex, showing the much sharper size selectivity of the nitrogen donor macrocycle. Also shown is the plot of strain energy versus M-O bond length for the complexes of the open-chain triethylene glycol and tetraethylene glycol, which indicate the metal ion size selective behavior of non macrocyclic analogues of 12-crown-4 and 15-crown-5.

3.3. THE COMPLEXES OF 24-CROWN-8 AND 30-CROWN-10

The dibenzo-30-crown-10 ligand [24] folds around K⁺ much like the seam on a tennis ball. This is shown in Figure 8 as the MM generated structure with the benzo groups removed. The curves of strain energy versus M-O bond length for [M(30-crown-10)]ⁿ⁺ complexes are seen in Figure 7. The coordinates of the [M(30-crown-10)]ⁿ⁺ cation used for the MM calculations were taken from the crystal structure [26] of the dibenzo complex, omitting the benzo groups. The 30-crown-10 structure

with its 'tennis ball seam' conformation does exert a fairly strong size preference for metal ions of the size of K^+ , as is shown in calculations where the K^+ ion is deleted from the complex. The free ligand thus generated maintains almost exactly the same structure with the K^+ ion removed. The curve of strain energy versus M-O bond length for $[M(30\text{-crown-}10)]^{n+}$ complexes seen in Figure 7 shows the preference for K^+ to have a strong steric contribution, with the minimum in the curve being at 2.92 Å, close to the ideal length of 2.88 Å for K^+ . Also included in Figure 7 is the curve for the nonaethylene glycol complexes, which was generated from the 30-crown-10 complex by removal of one ethylene bridge. The curve for the complexes of the open-chain nona-ethylene glycol complexes is similar to that for the 30-crown-10 complexes. The size selectivity for metal ions displayed by 30-crown-10 is due to the torsional angles in the ligand which maintain the tennis ball seam structure, and is not primarily dependent on the presence of a macrocyclic structure. The curve of strain energy versus M-O length for 24-crown-8 complexes, also shown in Figure 7, is flatter than that for 30-crown-10 complexes, indicating that 24-crown-10 does not produce the same elegant structure as 30-crown-10, with a loss of rigidity and hence of sharper size selectivity for metal ions.

4. Conclusions

The crown ethers fall into three separate groups with respect to selectivity for metal ions:

Group one consists of the smaller macrocycles such as 12-crown-4 and 15-crown-5 where metal ions generally are too large to enter the cavity of the macrocycle, and the metal ion is coordinated lying outside of the plane of the donor atoms of the ligand. Here factors that control selectivity are largely the same as in non-macrocyclic ligands, chiefly the size of the chelate ring.

Group two contains only 18-crown-6 of the ligands studied here. 18-Crown-6 complexes have three important conformers, one of which, the D_{3d} , shows sharp size match selectivity, preferring metal ions with M-O bond lengths of about 2.9 Å. The other two conformers are adopted by metal ions too small for the D_{3d} conformer, and are more flexible, exerting little size match selectivity. This resembles the behavior of tetraazamacrocycles in that there is one conformer of high rigidity which would, if it were the only energetically attainable conformer, exert considerable size match selectivity. For both 18-crown-6 and tetraazamacrocycles there exist, however, other conformers that can accommodate metal ions which do not fit this more rigid conformer, the rigid D_{3d} conformer of 18-crown-6, or the rigid *trans*-III conformer for the tetraazamacrocycles. There is, however, an important difference between 18-crown-6 and the tetraaza macrocycles. For the tetraaza macrocycles, the more flexible *trans*-I and *cis*-V conformers are of similar energy to the rigid *trans*-III conformer, whereas for 18-crown-6 complexes, the more flexible 'half-buckled' and ++-+- conformers are of considerably higher energy than the D_{3d} conformer. Thus something more closely approaching size

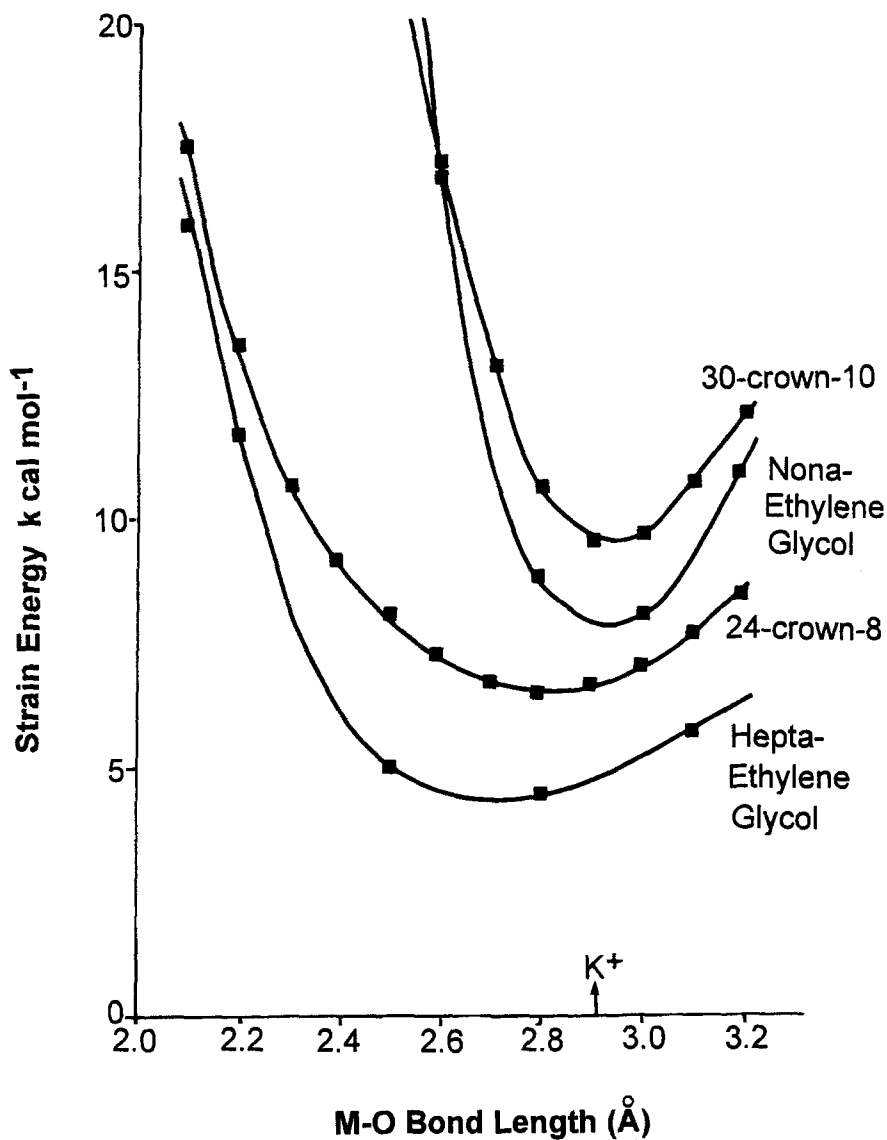


Fig. 7. The variation in strain energy of complexes of 24-crown-8 and 30-crown-10, calculated by Molecular Mechanics, as a function of M-O bond length, from coordinates for crystal structures [25,26] of the complexes. Also shown is the plot of strain energy versus M-O bond length for the complexes of the open-chain heptaethylene glycol and nonaethylene glycol, which indicate the metal ion size selective behavior of non macrocyclic analogues of 24-crown-8 and 30-crown-10.

match selectivity is found for K⁺ with 18-crown-6, since metal ions too small for the *D*_{3d} conformer cannot form complexes of equal stability by adopting other conformers, as is the case with tetraaza macrocycles. With an ideal M-O length

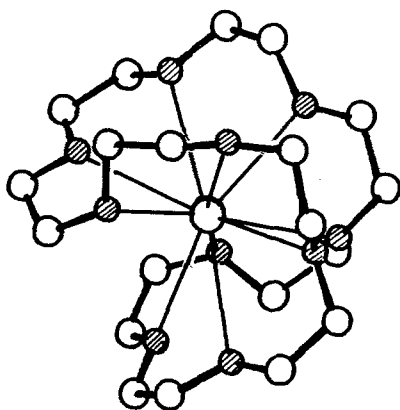


Fig. 8. The structure of the 30-crown-10 complex of K^+ generated by molecular mechanics calculation (SYBYL [13] program) with coordinates from the crystal structure of the dibenzo-30-crown-10 complex as trial coordinates.

of 2.88 Å, K^+ fits the cavity of the D_{3d} conformer of 18-crown-6 very closely. Even so, if 18-crown-6 could not form the half buckled and $++-+-$ conformers in its complexes, it would show much sharper size match selectivity, and would not complex at all with metal ions smaller than K^+ .

The third group consists of very large macrocycles such as 24-crown-8 and 30-crown-10. These enfold the macrocycles in extremely folded conformations, but may, as does 30-crown-10, exert considerable selectivity for metal ions on the basis of their size by virtue of the conformation adopted resulting in a set of torsional angles in the ring atoms of the macrocycle which confer considerable rigidity on the ligand.

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References

1. C.J. Pedersen: *J. Am. Chem. Soc.* **89**, 2459 (1967).
2. R.M. Izatt, K. Pawlak, J.S. Bradshaw, and R.L. Bruening: *Chem. Rev.* **91**, 1721.
3. R.D. Hancock: *J. Chem. Educ.* **69**, 615 (1992).
4. G.W. Gokel: *Crown Ethers and Cryptands*, The Royal Society of Chemistry, 1991.
5. V.J. Thom, C.C. Fox, J.C.A. Boeyens, and R.D. Hancock: *J. Am. Chem. Soc.* **106**, 5947 (1984).
6. R.D. Hancock: *Acc. Chem. Res.* **23**, 253 (1990).
7. R.D. Hancock: *Progr. Chem.* **37**, 187 (1989).

8. R.D. Hancock: in *Perspectives in Coordination Chemistry*, A.F. Williams, C. Floriani, and A.E. Merbach, Eds., Verlag Helvetica Chimica Acta, Basel, 1992, pp. 129–151.
9. R.A. Bartsch, B.P. Csech, S.I. Kang, L.E. Stewart, W. Wolkowitz, W.A. Charewicz, G.S. Heo, and B. Son: *J. Am. Chem. Soc.* **104**, 3249 (1982).
10. G. Wipff, P. Weiner, and P.A. Kollman: *J. Am. Chem. Soc.* **104**, 3249 (1982).
11. P.D.J. Grootenhuis, and P.A. Kollman: *J. Am. Chem. Soc.* **111**, 2152 (1989).
12. K.V. Damu, R.D. Hancock, P.W. Wade, J.C.A. Boeyens, D.G. Billing, and S.M. Dobson: *J. Chem. Soc., Dalton Trans.* 293 (1991).
13. SYBYL program, available from TRIPOS associates, 1699 South Hanley Road, St Louis, MO 63144, U.S.A.
14. M. Clark, R.D. Cramer, and N. van Opdenbosch: *J. Comput. Chem.* **10**, 982 (1989).
15. P.V. Bernhardt and P. Comba: *Helv. Chim. Acta* **74**, 1834 (1991).
16. A.M. Bond, T.W. Hambley, and M.R. Snow: *Inorg. Chem.* **24**, 1920 (1985).
17. M. Dobler and R.P. Phizackerley: *Acta Crystallogr., Sect B* **B30**, 2746 (1974).
18. M. Dobler and R.P. Phizackerley: *Acta Crystallogr., Sect B* **B30**, 2748 (1974).
19. R.D. Shannon: *Acta Crystallogr., Sect A* **A32**, 751 (1976).
20. R.D. Rogers, A.H. Bond, and S. Aguinaga: *J. Am. Chem. Soc.* **114**, 2960 (1992).
21. M.A. Bush and M.R. Truter: *J. Chem. Soc., Perkin Trans. 2*, 341 (1972).
22. P. Seiler, M. Dobler, and J.D. Dunitz: *Acta Crystallogr., Sect B* **B30**, 2744 (1974).
23. M. Dobler and J.D. Dunitz, and P. Seiler: *Acta Crystallogr., Sect B* **B30**, 2741 (1974).
24. N.W. Alcock, M. Ravindran, and G.R. Willey: *J. Chem. Soc., Chem. Commun.* 1063 (1989).
25. (a) D.L. Hughes and J.N. Wingfield: *J. Chem. Soc., Chem. Commun.* 804 (1977). (b) D.L. Hughes, C.L. Mortimer, and M.R. Truter: *Acta Crystallogr., Sect B* **B34**, 800 (1978).
26. M.A. Bush and M.R. Truter: *J. Chem. Soc., Perkin Trans. 2*, 345 (1972).
27. R.D. Gandour, F.R. Fronczek, V.J. Gatto, C. Minganti, R.A. Schultz, B.D. White, K.A. Arnold, A.D. Mazzochi, S.R. Miller, and G.W. Gokel: *J. Am. Chem. Soc.* **108**, 4078 (1986).
28. R.D. Rogers and K.L. Kurihara: *Inorg. Chem.* **26**, 1498 (1987).
29. M.S.B. Munson: *J. Am. Chem. Soc.* **87**, 2332 (1965).
30. R.W. Taft, J.F. Wolf, J.L. Beauchamp, G. Scorrano, and E.M. Arnett: *J. Am. Chem. Soc.* **100**, 1240 (1978).
31. J.S. Uppal, and R.H. Staley: *J. Am. Chem. Soc.* **104**, 125 (1982).
32. M.M. Kappes, and R.H. Staley: *J. Am. Chem. Soc.* **104**, 1813 (1982).
33. R.M. Izatt, R.E. Terry, B.L. Haymore, L.D. Hansen, N.K. Dalley, A.G. Avondet, and J.J. Christensen: *J. Am. Chem. Soc.* **98**, 7620 (1976).
34. B. Douglas, D.H. McDaniel, and J.J. Alexander: *Concepts and Models of Inorganic Chemistry*, 2nd Edition, Wiley, New York, 1983, p. 74.