An Ab Initio Investigation of the Structure and Alkaline Earth Divalent Cation Selectivity of 18-Crown-6

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Abstract: We present an ab initio, quantum mechanical study of 18-crown-6 (18c6) and its interaction with the alkaline earth dications Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, and Ru^{2+}. Geometries, binding energies, and binding enthalpies are evaluated at the restricted Hartree−Fock (RHF) and second-order Møller−Plesset perturbation (MP2) levels of theory using the 6-31+G* basis set and relativistic effective core potentials. The affinity of 18c6 for the dications is considerable, ranging from 150−300 kcal mol^{-1}. The cation−18c6 interaction arises principally from the electrostatic interaction of the dication with the nucleophilic ether backbone and from the polarization of the crown ether by the electric field of the dication. Whereas Ba^{2+} selectivity is observed for 18c6 in aqueous environments, our calculations clearly show that the crown ether in fact binds Mg^{2+} most strongly in gas phase. Thus, solvation effects appear to strongly influence cation selectivity. Indeed, Ba^{2+} selectivity is recovered when we consider the competition of the solvent and 18c6 molecules for the dications using a simple cation exchange reaction.

I. Introduction

Crown ethers bind alkali and alkaline earth cations to form remarkably stable and highly structured complexes.[1,2] In solution, crown ethers exhibit binding selectivities for specific cations based on the size of the crown ether cavity, the type of donor sites that line the cavity, and the polarity of the solvent.[3] These characteristics have been used to practical advantage in the design of novel materials for such diverse processes as isotope separations,[4−9] ion transport through membranes,[10] and transport of therapeutic doses of radiation to tumor sites.[11] Computational chemists have also focused their efforts on crown ethers as these molecules are perhaps the simplest that exhibit enzyme-like specificity. In particular, 18-crown-6 (18c6) has been the focus of a number of molecular mechanics,[12,13] molecular dynamics,[14−25] Monte Carlo,[26−28] and electronic structure investigations.[29−32]

Solvation strongly influences the cation selectivity of the crown ethers. In aqueous solution, 18c6, $(-OCH_2CH_2-)_6$, preferentially binds K^+ relative to the other alkali metals cations and Ba^{2+} relative to the other alkaline earth dications.[33] Since the ionic radii of K^+ and Ba^{2+} are nearly identical to the radius of the 18c6 cavity, cation size has generally been regarded as the primary factor that governs selectivity. Thus, macrocycles with small cavities favor small cations, while those with large cavities prefer large cations, as typically observed in the laboratory.[3] However, we recently reported *ab initio* calculations of 18c6 clearly revealing that cation size is not exclusively responsible for K^+ selectivity.[32] In the absence of any solvent molecules (*i.e.*, in gas phase), 18c6 in fact binds Li^+ most strongly, the smallest of the alkali metals cations. The K^+ selectivity is only recovered when solvation effects are considered.

To demonstrate the influence of solvation on selectivity, we examined the series of cation exchange reactions

$$K^+(18c6) + M^+(H_2O)_n \rightarrow M^+(18c6) + K^+(H_2O)_n \quad (1)$$

for $n = 0-4$, where M is an alkali metal (Li, Na, Rb, or Cs).[32] The competition of 18c6 and solvent water molecules for the cations K^+ and M^+ is reflected in the calculated enthalpies of

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reaction. These enthalpies were therefore used to judge the selectivity of 18c6. The $n = 0$ (*i.e.*, gas phase) result showed that 18c6 favors both Li^+ and Na^+ relative to K^+. Addition of just a few water molecules to eq 1 ($n = 3-4$) reversed the order of selectivity so that K^+ complexation was favored over all other cations.

We now turn our attention to the interaction of 18c6 with the divalent cations of the alkaline earth metals. The experimentally observed selectivity for the dications in aqueous solution is $Ba^{2+} > Sr^{2+} > Ca^{2+}$.[33] We show that this trend can be reproduced using *ab initio* methods with the analogous dication exchange reaction

$$Ba^{2+}(18c6) + M^{2+}(H_2O)_n \rightarrow M^{2+}(18c6) + Ba^{2+}(H_2O)_n \quad (2)$$

where the dication M^{2+} displaces Ba^{2+} from the 18c6 cavity as a function of n.

The present report focuses on the calculated binding energies, enthalpies, and structures for the M^{2+}(18c6) complexes of the dications Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, and Ra^{2+}. Details of the dication−water complexes have been presented elsewhere.[34] Structures and binding energies are calculated at the restricted Hartree−Fock (RHF) and second-order Møller−Plesset perturbation (MP2) levels of theory with split valence basis sets and effective core potentials (ECPs). These are the same theoretical methods and basis sets employed in recent work on monovalent and divalent cation−water and cation−ether studies.[32,34−36]

II. Methods

All calculations reported here employed ECPs and valence basis sets for the metals Ca, Sr, Ba, and Ra together with the 6-31+G* sets[37] for the lighter elements H, C, O, and Mg. Previous work on cation−ether interactions revealed that the diffuse *sp* ("+") functions of the 6-31+G* basis for C have only marginal influence on calculated energetic and structural properties.[32] Deleting these functions decreased the size of our basis for 18c6 by 48 functions (a significant number considering the respective n^4 and n^5 formal scalings of the RHF and MP2 methods). Hay and Wadt's 10-valence-electron ECPs[38] were employed for Ca, Sr, and Ba with (5*s*4*p*)/[3*s*2*p*] valence basis sets. The latter were augmented by six-term, *d*-type polarization functions with exponents (α_d(Ca) = 0.50, α_d(Sr) = 0.40, α_d(Ba) = 0.29) obtained from energy minimization of the $M^{2+}(H_2O)$ clusters.[34] For Ra, we used the 10-valence-electron, averaged relativistic ECP and (5*s*5*p*4*d*)/[3*s*3*p*1*d*] basis set reported by Ermler *et al.*[39] The potentials for Sr, Ba, and Ra were constructed from relativistic treatments of these atoms and, hence, should approximately treat the dominant mass-velocity and one-electron Darwin corrections that may contribute importantly for these atoms. For brevity, we shall simply refer to this hybrid basis set/ECP level as 6-31+G*, although this is not strictly the case. The 6-31+G* basis set for the M^{2+}(18c6) complexes consisted of a total of 357−365 basis functions.

Full geometry optimizations were performed at the RHF level of theory[37] using the GAUSSIAN 92[40] and GAMESS[41] programs. The "tight" gradient convergence threshold of GAUSSIAN 92 or a threshold of 0.000 03 au for GAMESS was used for all optimizations. These reduced thresholds insured the convergence of geometrical parameters to an acceptable level since the 18c6 complexes are rather floppy.

Harmonic vibrational frequencies were evaluated at the RHF level for each of the optimized M^{2+}(18c6) complexes. Normal mode calculations with the 6-31+G* basis set were judged to be too demanding for the available computational resources. The 18c6 complexes were, therefore, reoptimized at the RHF/3-21G level of theory followed by the evaluation of analytical second derivatives. The 3-21G basis sets[37] are available for all atoms included in this study except Ba and Ra. For Ba, we developed a 3-21G-type contraction (specifically, a (18*s*12*p*6*d*)/[7*s*6*p*2*d*] contraction) of Huzinaga's MIDI set.[42] All-electron basis sets are not available for Ra, so vibrational frequencies for the Ra^{2+}(18c6) complexes were calculated numerically (based on double-differencing of the gradients) with the 6-31+G* basis set. The numerical approach for the latter calculations was required since analytic second derivatives for ECPs are unavailable in the GAUSSIAN 92 and GAMESS programs.

Electron correlation effects were treated at the MP2 level of theory[37,43] using the RHF optimized geometries. Correlation of the inner shell 1*s* electrons of C and O and 1*s*, 2*s*, and 2*p* electrons of Mg was neglected in the frozen-core MP2 treatment. However, the ($n - 1$) outermost core electrons of Ca, Sr, Ba, and Ra were correlated in all calculations. Failure to correlate these electrons in our studies of cation−water complexes resulted in significant overestimation of M−O bond lengths and underestimation of the corresponding bond energies.[44,45] All MP2 calculations were performed by GAUSSIAN 92 with the semidirect approach.

Binding energies and enthalpies were evaluated at the RHF/6-31+G* and MP2/6-31+G* levels of theory. These quantities correspond to the energy (or enthalpy) change for the reactions

$$M^{2+} + 18c6 \rightarrow M^{2+}(18c6) \quad (3)$$

where the free 18c6 molecule is at the equilibrium RHF/6-31+G* geometry (C_i symmetry, cf. Figure 1).[32] The counterpoise (CP) correction of Boys and Bernardi[46] was applied to each binding energy to approximately treat basis set superposition error (BSSE). Benchmark calculations of cation−water and cation−dimethyl ether interactions suggest that CP-corrected 6-31+G* binding energies are in better agreement with estimated complete basis set limits than the corresponding uncorrected values.[32,44,45,47] Zero-point energies and enthalpy corrections (at 298 K) were evaluated using standard statistical mechanical expressions[48] with the RHF vibrational frequencies scaled by 0.9.[37]

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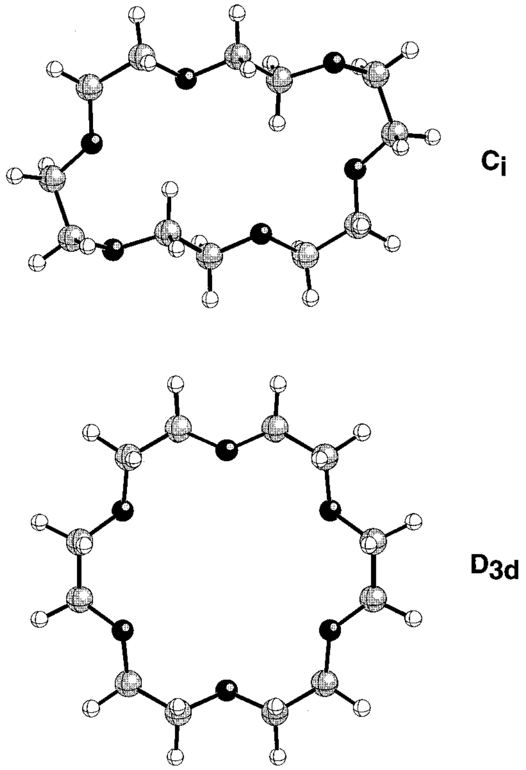

Figure 1. C_i and D_{3d} conformations of 18c6 optimized at the RHF/6-31+G* level. The C_i form is 4.4 kcal mol^{-1} more stable than D_{3d} at this level of theory. See ref 32 for additional details.

Cation−crown ether interactions were analyzed with the natural energy decomposition analysis (NEDA).[47,49] NEDA is a Hartree−Fock-based approach associated with Weinhold's natural bond orbital (NBO) method[50−53] that partitions the CP-corrected binding energy (ΔE) into electrostatic (ES), polarization (POL), charge transfer (CT), exchange (EX), deformation (DEF), and geometry distortion (DIS) components. The binding energies for the M^{2+}(18c6) complexes are therefore expressed as

$$\Delta E = \mathrm{ES} + \mathrm{POL} + \mathrm{CT} + \mathrm{EX} + \mathrm{DEF}(\mathrm{M}^{2+}) + \mathrm{DEF}(18\mathrm{c}6) + \mathrm{DIS}(18\mathrm{c}6) \quad (4)$$

A more complete description of the NEDA method can be found elsewhere.[47]

III. Structures

Two conformations of free (uncomplexed) 18c6 are frequently discussed in the literature, those of apparent lowest energy (the C_i form) and highest symmetry (the D_{3d} form). The optimized RHF/6-31+G* geometries for these two conformations, shown in Figure 1, were reported in our earlier communication of 18c6 and its alkali metal complexes.[32] Briefly, C_i 18c6 has four of its six oxygens directed inward from the ether backbone and the remaining two directed outward. It is the conformation observed in the X-ray analysis[54] of crystalline 18c6 and is the most frequently sampled conformation in both gas-phase simulations[16] and simulations of 18c6 in apolar solvents.[24,55]

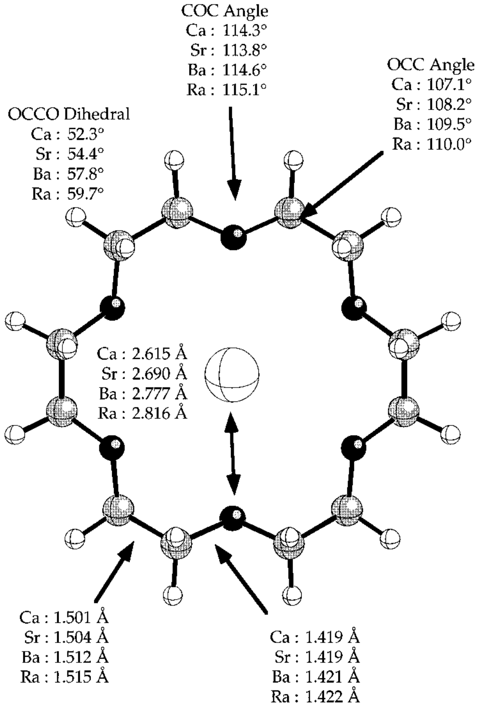

Figure 2. "Open" D_{3d} conformations of the M^{2+}(18c6) complexes for M = Ca, Sr, Ba, and Ra optimized at the RHF/6-31+G* level.

The D_{3d} conformation has all six of the oxygen centers directed inward from the ether backbone to form a preorganized, nucleophilic cavity that is optimal for cation complexation. RHF/6-31+G* calculations[32] revealed that gas-phase 18c6 in the D_{3d} conformation is 4.4 kcal mol^{-1} less stable than C_i 18c6 (5.4 kcal mol^{-1} at the MP2 level), in fair agreement with molecular mechanical force field results.[14,18] Simulations of 18c6 have suggested, however, that 18c6 favors "D_{3d}-like" conformations rather than C_i in polar solvents.[21,24,55] Molecular dynamics studies of 18c6 in water by Kowall and Geiger[21] and by Thompson[24] showed two water molecules strongly interacting with the ether oxygens to maintain this preorganized conformation.

Initial optimizations of the M^{2+}(18c6) complexes were performed with D_{3d} symmetry constraints. Each calculation employed a starting geometry resembling the D_{3d} 18c6 structure of Figure 1 with a cation at the center of the cavity. Optimized geometrical parameters for the Ca^{2+}, Sr^{2+}, Ba^{2+}, and Ra^{2+} complexes are shown in Figure 2. Optimization of the Mg^{2+} complex led to a structure that differs significantly from those obtained for the heavier dications. The optimized D_{3d} structure for Mg^{2+}(18c6) is shown in Figure 3. The crown ether binds the heavier dications in an "open" ring conformation in which the six oxygens coordinate the metal in an equatorial fashion. In contrast, the ether backbone of Mg^{2+}(18c6) has collapsed into a "folded" conformation in which the oxygens coordinate the metal in a quasi-octahedral arrangement. An attempt to optimize the open ring conformation of Mg^{2+}(18c6) was unsuccessful. We previously reported a D_{3d} structure for Li^{+}(18c6) having the open form.[32] Although Li^{+} (ionic radius = 0.76 Å)[56] and Mg^{2+} (0.72 Å) are of roughly the same size, a geometry optimization of Mg^{2+}(18c6) starting from the open Li^{+}(18c6) optimized structure (and replacing Li^{+} by Mg^{2+})

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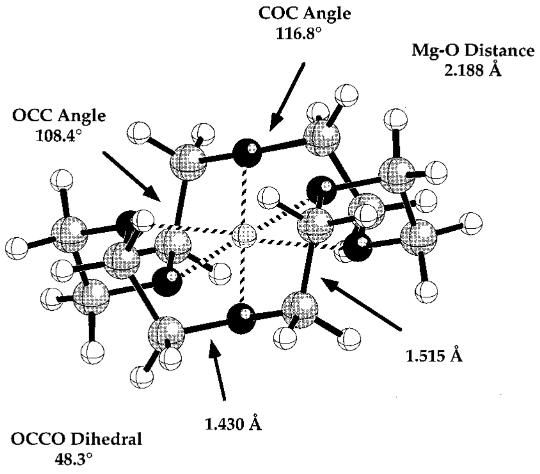

Figure 3. "Folded" D_{3d} conformation of Mg^{2+}(18c6) optimized at the RHF/6-31+G* level.

eventually reverted to the folded structure. This suggests that little or no energy barrier separates the open and folded forms of Mg^{2+}(18c6).

Complexation of the divalent cations causes the 18c6 cavity to contract somewhat. The oxygen to center-of-mass distance in the D_{3d} conformation of free 18c6 is 2.901 Å.[32] The corresponding distance (the M−O bond length) in the cation complexes is smaller, varying from 2.188 Å for Mg^{2+} to 2.816 Å for Ra^{2+}. Thus, it appears that each of the alkaline earth dications is somewhat smaller than the cavity of 18c6. Using a similar M−O distance criterion for the alkali metals, one would also judge the alkali cations Li^+, Na^+, K^+, and Rb^+ to be smaller than the 18c6 cavity.[32] Only Cs^+, which in the D_{3d} conformation has a Cs−O distance of 2.966 Å, appears to be larger than the cavity. The Ba^{2+} and Ra^{2+} cations are heavier than Cs^+, but based on their ionic radii, these two cations are more similar in size to K^+ and Rb^+ (1.38, 1.52, 1.67, 1.35, and ∼1.45 Å for K^+, Rb^+, Cs^+, Ba^{2+}, and Ra^{2+}, respectively.[56]

The optimized bond lengths and angles of the M^{2+}(18c6) complexes reveal fairly significant flexing of the crown ether backbone to accommodate cations of varying size. The OCCO dihedral angles in the open conformations decrease with decreasing cation size, from 59.7° in Ra^{2+}(18c6) to 52.3° in Ca^{2+}(18c6). These angles are significantly smaller than those of free 18c6 (75.4°), consistent with the strong electrical interactions that attract the ether oxygens inward toward the dication. The CC and CO bond lengths and COC and OCC bond angles decrease slightly with decreasing cation size, in accord with the smaller cavity sizes required by the smaller cations.

The degree to which the 18c6 cavity can contract for the smaller cations appears, however, to be somewhat limited. Comparison of the M−O distances in the M^{2+}(18c6) complexes to optimized M−O distances of the $M^{2+}(H_2O)_n$ cluster shows that Mg^{2+}, Ca^{2+}, and Sr^{2+} remain significantly farther from the oxygens of 18c6 than is perhaps optimal. For example, the ideal Mg−O distance is expected to lie within the range 1.94−2.11 Å, based on the optimized Mg−O distances of the monohydrate and octahedrally coordinated hexahydrate.[34] The folded D_{3d} form of Mg^{2+}(18c6) has, however, a relatively long Mg−O distance of 2.188 Å (Figure 3) that lies significantly outside this range. Thus, the 18c6 backbone appears unable to contract fully to yield an optimal cavity size for Mg^{2+}. Similarly, we judge the ideal M−O distances for Ca^{2+}, Sr^{2+}, Ba^{2+}, and Ra^{2+} to be approximately 2.30−2.44, 2.46−2.61, 2.66−2.83, and 2.78−2.92 Å, respectively.[34] Comparing these ranges to the M−O distances listed in Figure 2 suggests that Ca^{2+} and Sr^{2+} are significantly smaller than the cavities of their respective 18c6 complexes (by roughly 0.17 and 0.08 Å, respectively). The Ba^{2+} and Ra^{2+} cations, in contrast, appear to match the cavity size quite well.

The Ba^{2+}(18c6) complex is the only equilibrium structure of the D_{3d} geometries reported here. All others correspond to first- or higher-order saddle points according to vibrational frequencies analysis at the RHF/3-21G level [or RHF/6-31+G* for Ra^{2+}(18c6)]. The lowest vibrational frequency of Ba^{2+}(18c6) is 30 cm^{-1} and corresponds to the out-of-cavity motion of the cation along the C_3 symmetry axis of the crown ether. The Mg^{2+}(18c6) complex is a third-order saddle point characterized by three imaginary frequencies, one at 77i cm^{-1} and a degenerate pair at 37i cm^{-1}. Distorting the geometry along the 77i cm^{-1} mode followed by reoptimization led to an equilibrium structure of S_6 symmetry (Figure 4) that is 3.0 kcal mol^{-1} more stable than the D_{3d} form (at MP2/6-31+G*). The lowest frequency modes of the S_6 structure are a degenerate pair at 54 cm^{-1}. The D_{3d} structures for Ca^{2+}(18c6) and Sr^{2+}(18c6) are second-order saddle points characterized by a degenerate pair of frequencies at 23i and 22i cm^{-1}, respectively. Several attempts to optimize equilibrium structures of lower symmetry and energy failed, however, with the crown ether reverting to the D_{3d} conformation in each case. We initially suspected that the RHF/3-21G frequencies did not accurately reflect the curvature of the RHF/6-31+G* surface, but numerical evaluation of the frequencies for D_{3d} Ca^{2+}(18c6) with the full 6-31+G* basis still yielded a degenerate mode at 35i cm^{-1}. Our calculations clearly suggest that the potential energy surfaces are flat in the vicinity of the D_{3d} forms of Ca^{2+}(18c6) and Sr^{2+}(18c6). The D_{3d} structure for Ra^{2+}(18c6) is a first-order saddle point with an imaginary frequency of 33i cm^{-1} that corresponds to an out-of-cavity motion of the cation along the C_3 axis. Reoptimization of the Ra^{2+} complex led to a structure of C_{3v} symmetry (Figure 5) that is 1.3 kcal mol^{-1} more stable than the D_{3d} form (at MP2/6-31+G*). The lowest vibrational modes in the C_{3v} structure are a degenerate pair of 40 cm^{-1}.

Enhanced cation−ether interactions and an apparent reduction in eclipsing interactions act to stabilize the S_6 conformation of Mg^{2+}(18c6) relative to the D_{3d} form. The RHF/6-31+G* optimized S_6 geometry shown in Figure 4 is a twisted variant of the folded D_{3d} geometry of Figure 3. Distortion to S_6 shortens the Mg−O distances and leads to stronger polarization effects (*vide infra*). The S_6 conformation is further stabilized by diminished eclipsing interactions involving the crown ether. In the absence of Mg^{2+}, 18c6 in the S_6 geometry is 3.3 kcal mol^{-1} more stable (RHF/6-31+G*) than in the D_{3d} form. There are 12 nearly eclipsing CH/OC bond pairs in D_{3d} 18c6 (HCOC dihedral angles of 21.9°). Twisting the crown ether backbone into the S_6 conformation reduces the eclipsing interactions for six of these bond pairs as the dihedral angle increases to 36.3°. The other six pairs remain eclipsed at 9.6°.

The Ra^{2+} cation is sufficiently large that the Ra^{2+}(18c6) complex favors a geometry in which the cation is displaced 0.78 Å from the crown ether center of mass. This displacement lengthens the Ra−O distances somewhat (from 2.816 Å in the D_{3d} form to an average 2.865 Å in C_{3v}) and thereby weakens the electrostatic and polarization effects that act to stabilize the Ra^{2+}(18c6) complex. Similar effects were previously reported for the interactions of 18c6 with Rb^+ and Cs^+. These cations were respectively displaced from the crown ether center of mass by 1.01 and 1.60 Å.[32]

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[56] Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751.

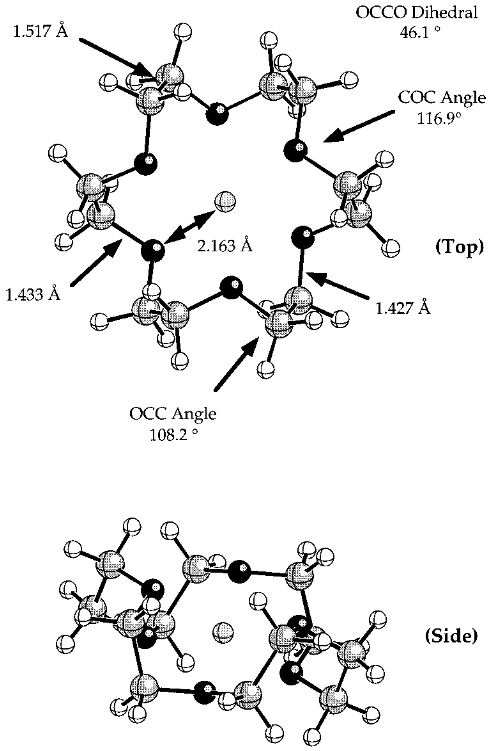

Figure 4. Top and side views of the S_6 conformation of Mg^{2+}(18c6) optimized at the RHF/6-31+G* level.

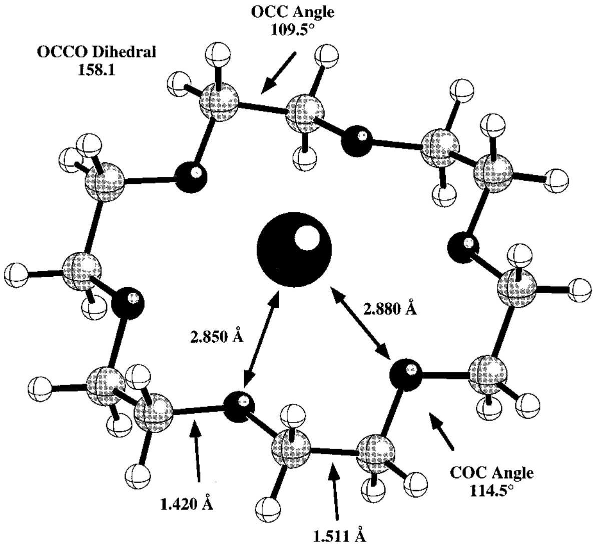

Figure 5. C_{3v} conformation of Ra^{2+}(18c6) optimized at the RHF/6-31+G* level. The metal cation sits on the C_3 rotation axis, 0.48 Å from the center-of-mass of the crown ether.

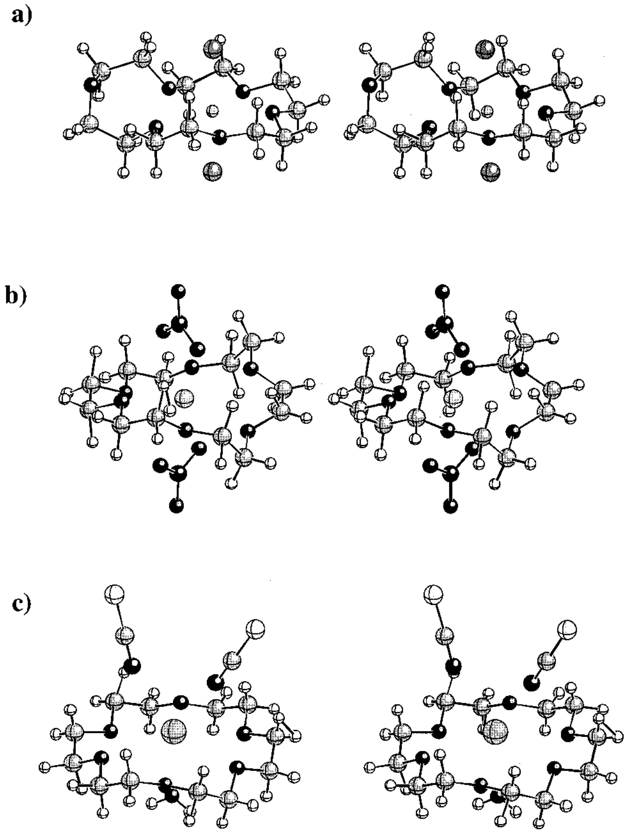

Figure 6. Stereoviews of the crystal structures for (a) $Mg^{2+}(18c6)\cdot 2Cl^-$, (b) $Ca^{2+}(18c6)\cdot 2NO_3^-$, and (c) $Ba^{2+}(18c6)\cdot 2NCS^-$ hydrate. Coordinates were taken from refs 53−55.

The RHF/6-31+G* optimized geometries differ fairly significantly from the crystal structures reported for Mg^{2+}(18c6),[57] Ca^{2+}(18c6),[58] and Ba^{2+}(18c6).[59,60] Coordinates for these structures were obtained from the Cambridge Structural Database and stereoviews are shown in Figure 6. Whereas the calculated D_{3d} and S_6 structures of Figures 3 and 4 show Mg^{2+} interacting with all six ether oxygens, the crystal structure reported by Strel'tsova *et al.*[57] has only five ether oxygens coordinating the metal. These five oxygens coordinate Mg^{2+} in an equatorial fashion with the two Cl^- counterions occupying axial positions, on either side of the crown ether cavity. The average M−O distance for the five oxygens is 2.254 Å, nearly 0.1 Å longer than that of the optimized S_6 conformation. These longer distances are consistent with the increased coordination of Mg^{2+} in the crystal (seven binding sites including the two Cl^-). The sixth ether oxygen lies 4.401 Å from the cation.

Tkachev and co-workers[58] reported the crystal structure for Ca^{2+}(18c6), a C_2 symmetry complex with two NO_3^- counterions. Four of the six $-CH_2OCH_2-$ linkages of the crown ether backbone are conformationally similar to those of D_{3d} 18c6. The other two linkages (on the back, left side of Figure 6) have buckled somewhat, presumably to decrease the Ca−O distances and thereby strengthen the Ca^{2+}−18c6 interaction. The Ca−O distances range from 2.559 to 2.678 Å with an average value (2.615 Å) that is fortuitously identical to that optimized for the Ca^{2+}(18c6) complex (Figure 2). The crystal structure for the Ba^{2+}(18C6) complex[59] includes two NCS^- counterions that coordinate the cation on one side of the cavity and a water molecule that coordinates the cation on the other. The crown ether exhibits a D_{3d}-like conformation with an average Ba−O distance of 2.835 Å that is slightly longer than the calculated value (2.777 Å, Figure 2). Rheingold *et al.*[60] more recently reported a structure for Ba^{2+}(18c6) in a D_{3d}-like conformation with average Ba−O distances of 2.823 Å.

IV. Binding Energies and Enthalpies

Table 1 lists the CP-corrected binding energies and enthalpies (298 K) for the M^{2+}(18c6) complexes. These quantities are evaluated with respect to the free 18c6 molecule in its equilibrium C_i conformation. CP corrections are sizable but generally a small percentage of the total binding energy. For

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(57) Strel'tsova, N. R.; Ivakina, L. V.; Storozhenko, P. A.; Bulychev, B. M.; Bel'skii, V. K. *Dokl. Akad. Nauk. SSSR* **1986**, *291*, 1373.

(58) Tkachev, V. V.; Atovmyan, L. O.; Zubareva, V. E.; Raevskii, O. A. *Koord. Khim.* **1987**, *13*, 264.

(59) Wei, Y. Y.; Tinant, B.; Declercq, J.-P.; Meersche, M. V.; Dale, J. *Acta Cryst., C-Cryst. Struct. Commun.* **1988**, *44*, 77.

(60) Rheingold, A. L.; White, C. B.; Haggerty, B. S.; Kirlin, P.; Gardiner, R. A. *Acta Crystallogr.* **1993**, *C49*, 808.

example, the CP correction for S_6 Mg^{2+}(18c6) at the MP2 level is 13.6 kcal mol^{-1}, or about 5% of the total binding energy of −295.6 kcal mol^{-1}. The binding energies evaluated at the MP2/6-31+G* level tend to be about 3−6% (or 7−12 kcal mol^{-1}) stronger than the RHF values. Since the MP2 energies should be more reliable than the corresponding RHF values, we focus the following discussion on the MP2 values only.

In gas phase, 18c6 binds Mg^{2+} more strongly than any of the other alkaline earth dications. The binding enthalpy for the S_6 conformation of Mg^{2+}(18c6) complex is −293.6 kcal mol^{-1}. The binding enthalpies for the other cations are considerably weaker and diminish monotonically with increasing cation size from −223.7 kcal mol^{-1} for Ca^{2+}(18c6) to −167.8 kcal mol^{-1} for Ra^{2+}(18c6). A similar trend was previously reported for complexes of 18c6 with the monovalent alkali metal cations.[32] The binding enthalpies for these complexes ranged from −95.4 kcal mol^{-1} for Li^+(18c6) to −48.7 kcal mol^{-1} for Cs^+(18c6), the cation−crown ether interaction weakening with increasing cation size.

While we anticipate that the calculated binding energies and enthalpies for the M^{2+}(18c6) complexes are reasonably accurate, there exist no experimental or higher level theoretical data for direct comparison. Calculations of $M^{2+}(H_2O)_n$ clusters has revealed, however, that RHF and MP2 binding energies calculated with the 6-31+G* basis are somewhat (2−5%) weaker than values calculated at higher levels of theory and with larger basis sets.[34] The source of this discrepancy is likely the inability of the 6-31+G* basis to describe the severe polarization effects experienced by water in close proximity to a dication. Similar effects can be expected for the 18c6 complexes. Thus, we speculate that the binding energies and enthalpies reported here are somewhat weaker than experiment or higher levels of theory would indicate. Higher level calculations of the M^{2+}(18c6) complexes are not currently feasible and an experimental determination of the binding energies may be impossible due to the competing reaction channels

$$M^{2+}(18c6) \rightarrow M^{+} + 18c6^{+} \qquad (5)$$

that involve electron transfer from the ligand to the metal. Similar reactions are observed for the dissociation of $M^{2+}(H_2O)_n$ clusters.[61]

NBO analysis of the 18c6 complexes reveals strong polarization of the crown ether by the dication. Results are listed in Table 2. Comparison of the oxygen and methylene charges in the M^{2+}(18c6) complexes to the corresponding charges for free 18c6 indicates considerable polarization of the electron distribution from the methylenes toward the oxygen centers that line the crown ether cavity. Polarization effects are clearly the strongest in Mg^{2+}(18c6). The charge on the methylene groups in the S_6 structure is +0.416, significantly larger than the average charge on methylene (+0.355) in uncomplexed C_i 18c6. The difference of these values (0.416−0.355) reflects a transfer of 0.061*e* from each methylene to the adjacent oxygen. Somewhat weaker transfers of electron density are found for the larger dications. Additional evidence of polarization is found in the ionic character of the crown ether CO bonds (also reported in Table 2). The average ionic character of a CO bond in free 18c6 is 38.40%, polarized in the sense C^+O^-. In contrast, the ionic character of the bonds in the M^{2+}(18c6) complexes ranges from 41.24% for Ra^{2+}(18c6) to 42.82% for Mg^{2+}(18c6), each clearly reflecting the polarization of these bonds toward oxygen by the dication.

Table 1. Total Energies, Binding Energies, and Binding Enthalpies of Free and Complexed 18c6[a]

	sym	method	energy	ΔE	ΔH^{298}
free[b]	C_i	RHF	−917.500 35		
		MP2	−920.127 97		
	D_{3d}	RHF	−917.493 31		
		MP2	−920.119 42		
Mg^{2+}	S_6	RHF	−1116.779 29	−286.5	−284.5
		MP2	−1119.433 26	−295.6	−293.6
	D_{3d}	RHF	−1116.776 38	−284.6	−282.1
		MP2	−1119.428 41	−292.8	−290.3
Ca^{2+}	D_{3d}	RHF	−953.461 05	−217.8	−217.0
		MP2	−956.158 34	−224.5	−223.7
Sr^{2+}	D_{3d}	RHF	−947.363 71	−200.3	−199.0
		MP2	−950.084 56	−209.3	−208.0
Ba^{2+}	D_{3d}	RHF	−942.165 31	−171.8	−171.0
		MP2	−944.894 95	−183.3	−182.5
Ra^{2+}	C_{3v}	RHF	−940.992 50	−159.3	−157.3
		MP2	−943.683 32	−169.7	−167.8
	D_{3d}	RHF	−940.989 81	−157.4	−155.8
		MP2	−943.681 27	−167.8	−166.1

[a] Total energies (in au) calculated with 6-31+G* basis set at the RHF/6-31+G* optimized geometries. Total energies (in au) of the dications are (MP2 values in parentheses): $E(Mg^{2+}) = -198.81213(-198.81213)$; $E(Ca^{2+}) = -35.61099(-35.66382)$; $E(Sr^{2+}) = 29.54106(-29.61220)$; $E(Ba^{2+}) = -24.38717(-24.46085)$; $E(Ra^{2+}) = -23.23553(-23.24673)$. Counterpoise corrected binding energies and enthalpies (in kcal mol^{-1}) evaluated relative to the free dication and 18c6 (C_i). Enthalpy corrections determined using RHF/3-21G harmonic vibrational frequencies, except for Ra^{2+}(18c6). [b] Free 18c6 values from Glendening, Feller, and Thompson, ref 32.

Table 2. Atomic and Group Charges and Ionic Character of the CO Bonds of Free and Complexed 18c6[a]

	sym	$q(M^{2+})$	q(O)	$q(CH_2)$	$\Delta q(CH_2)$[b]	C^+O^- [c]
free	C_i		−0.710	0.355	0.000	38.40
	D_{3d}		−0.694	0.347	−0.008	37.66
Mg^{2+}	S_6	1.835	−0.804	0.416	0.061	42.82
	D_{3d}	1.831	−0.802	0.415	0.060	42.86
Ca^{2+}	D_{3d}	1.934	−0.796	0.404	0.049	41.86
Sr^{2+}	D_{3d}	1.939	−0.792	0.401	0.046	41.64
Ba^{2+}	D_{3d}	1.946	−0.790	0.400	0.045	41.46
Ra^{2+}	C_{3v}	1.944	−0.785	0.397	0.042	41.24
	D_{3d}	1.944	−0.787	0.398	0.043	41.36

[a] RHF/6-31+G* values. Values averaged over atoms or groups for low symmetry structures. [b] Average charge of the methylene group relative to that of free 18c6 (C_i). [c] Percentage ionic character of the CO bonds.

Polarization effects in the dication complexes of 18c6 are considerably stronger than those previously reported for the monovalent cation complexes.[32] The Mg^{2+}(18c6) and Li^+(18c6) complexes serve to illustrate this point. Both have similar structure, S_6 symmetry in the lowest energy conformation, and the two cations Mg^{2+} and Li^+ are of nearly identical size. Whereas the atomic and group charges suggest a transfer of 0.061*e* from methylene to oxygen in Mg^{2+}(18c6), the corresponding transfer in Li^+(18c6) is only 0.025*e*. Furthermore, the percentage ionic character of the CO bonds in the latter (39.90%) is significantly less than that of the Mg^{2+} complex (42.82%). Clearly, a dication polarizes the crown ether more strongly than a monocation of similar size.

Polarization of 18c6 contributes significantly to the calculated binding energies. Table 3 reports NEDA results for the M^{2+}(18c6) complexes. In each case, the leading attractive contribution to ΔE is either the electrostatic (ES) or polarization (POL) component. Charge transfer (CT) is also important but somewhat weaker than ES and POL. Thus, for example, the RHF binding energy for Ba^{2+}(18c6) is −171.8 kcal mol^{-1}. The Ba^{2+}−18c6 interaction is dominated by ES (−173.8 kcal mol^{-1}), but POL also contributes importantly (−159.8 kcal mol^{-1}). CT

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[61] Blades, A. T.; Jayaweera, P.; Ikonomou, M. G.; Kebarle, P. *J. Chem. Phys.* **1990**, *92*, 5900.

Table 3. Natural Energy Decomposition Analysis of Complexed 18c6[a]

	sym	ΔE	ES	POL	CT	EX	DEF(M^{2+})	DEF(18c6)	DIS(18c6)
Mg^{2+}	S_6	−286.5	−224.6	−342.1	−126.2	−11.6	34.5	327.7	55.8
	D_{3d}	−284.6	−225.2	−325.3	−120.8	−10.3	30.3	307.6	59.1
Ca^{2+}	D_{3d}	−217.8	−187.0	−174.8	−51.9	−9.3	25.6	147.4	32.2
Sr^{2+}	D_{3d}	−200.3	−179.6	−167.1	−46.2	−14.1	40.3	142.9	23.5
Ba^{2+}	D_{3d}	−171.8	−173.4	−159.8	−39.2	−20.4	64.2	139.2	17.7
Ra^{2+}	C_{3v}	−159.3	−162.1	−146.6	−41.5	−18.6	58.8	132.9	17.8
	D_{3d}	−157.4	−168.9	−152.8	−45.1	−21.7	70.8	143.9	16.4

[a] RHF/6-31+G* values. Energies in kcal mol^{-1} (ES = electrostatic interaction; POL = polarization; CT = charge transfer; EX = exchange; DEF = deformation; DIS = geometric distortion).

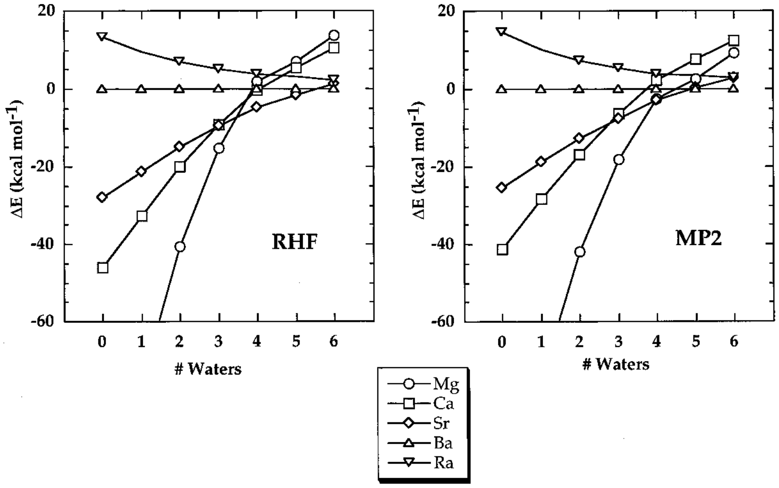

Figure 7. Reaction enthalpies for the exchange reactions of eq 2 at the RHF/6-31+G* (left) and MP2/6-31+G* (right) levels of theory.

strengthens the interaction by an additional −39.2 kcal mol^{-1}, arising principally from the delocalization of the oxygen lone pair electrons into the proximal 6*s* orbital of Ba^{2+}. The transfer of electrons from 18c6 to the metal is reflected in the atomic charge at Ba (+1.946, cf. Table 2), which is 0.054*e* less than the formal +2 charge of a dication.

V. Cation Selectivity

The binding enthalpies of Table 1 suggest that 18c6 binds Mg^{2+} more strongly that any of the other alkaline earth dications in gas phase. In contrast, 18c6 is observed to selectively bind Ba^{2+} in aqueous solution.[33] Clearly, the Ba^{2+} selectivity of 18c6 is not an intrinsic property of the crown ether itself. The selectivity instead results from a delicate balance as the crown ether and solvent molecules compete for the cation in solution.

To examine the role of the solvent molecules more closely, we modeled the competition of 18c6 and H_2O for the cation using the simple exchange reactions of eq 2. Note that these reactions only involve clusters of the form M^{2+}(18c6) and $M^{2+}(H_2O)_n$, $n = 0-6$. Thus, we only consider limited hydration of the cation and ignore hydration of the cation−crown ether complex entirely. The latter effect was examined in our study of the alkali cation selectivity of 18c6. While fairly important, calculations of clusters such as $M^+(18c6)\Sigma H_2O$ proved exceedingly expensive but did not influence the calculated selectivity.

The exothermicity of the exchange reactions can be considered an approximate measure of the selectivity of 18c6. Reaction enthalpies

$$\Delta H(n) = \Delta H[M^{2+}(18c6)] + \Delta H[Ba^{2+}(H_2O)_n] - \Delta H[Ba^{2+}(18c6)] - \Delta H[M^{2+}(H_2O)_n] \qquad (6)$$

were evaluated as a function of *n* using the binding enthalpies for the M^{2+}(18c6) complexes in Table 1 together with the $M^{2+}(H_2O)_n$ enthalpies reported elsewhere.[34] In general, the water molecules of the $M^{2+}(H_2O)_n$ clusters coordinate the dication in highly symmetric arrangements (*i.e.*, linear, trigonal, tetrahedral, square pyramidal, and octahedral) that tend to minimize repulsions between proximal ligands. Figure 7 shows $\Delta H(n)$ as a function of *n* for the various cations at the RHF and MP2 levels of theory.

Figure 7 clearly reveals the essential contribution of cation−solvent interactions to the selectivity of 18c6. For a particular degree of hydration, *n*, 18c6 favors the cation that corresponds to the most exothermic of the exchange reactions. In the absence of any solvent ($n = 0$), the selectivity is

$$Mg^{2+} > Ca^{2+} > Sr^{2+} > Ba^{2+} > Ra^{2+} \quad \text{(RHF, MP2)}$$

simply reflecting the strength of the intrinsic cation−18c6 interactions listed in Table 1. This sequence is, however, strongly influenced by the addition of water molecules to the $M^{2+}(H_2O)_n$ clusters. At the highest degree of hydration considered here, $n = 6$, we find the following selectivity sequences

$$Ba^{2+} > Sr^{2+} > Ra^{2+} > Ca^{2+} > Mg^{2+} \quad \text{(RHF)}$$

$$Ba^{2+} > Ra^{2+} > Sr^{2+} > Mg^{2+} > Ca^{2+} \quad \text{(MP2)}$$

Hence, our calculations recover the Ba^{2+} selectivity of 18c6 is recovered even when considering relatively few water molecules.

VI. Summary

We have presented a detailed *ab initio* investigation of the complexation of divalent alkaline earth cations by 18c6 that augments our earlier study of the monovalent alkali cations. Geometries were optimized for the complexes of 18c6 with the cations Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, and Ra^{2+}. In gas phase,

Ba^{2+}(18c6) is the only complex that favors the open D_{3d} structure with the cation residing at the center of the crown ether cavity. The Mg^{2+} cation is sufficiently small that the crown ether collapses into a tightly bound, folded structure of S_6 symmetry. A similar structure was previously reported for Li^+(18c6). The Ca^{2+} and Sr^{2+} cations also appear to be somewhat smaller than the 18c6 cavity such that a structure of lower symmetry than D_{3d} is favored. We were, however, unable to identify any lower energy structures. The Ra^{2+} cation is sufficiently large that the metal favors a position of 0.78 Å outside the crown ether cavity. Similar structures were previously found for the Rb^+(18c6) and Cs^+(18c6) complexes.

The calculated binding enthalpies for the M^{2+}(18c6) complexes are significantly stronger than those involving the alkali cations. In addition to the stronger electrostatic interaction of the crown ether with a dication, compared to that with a monocation, we find evidence of enhanced polarization effects. Natural energy decomposition analysis evaluates a polarization contribution to the binding energy is nearly as strong as the electrostatic component. Weaker polarization effects were previously found in the M^+(18c6) complexes. This suggests that force fields that explicitly treat polarization will be required to reliably simulate the complexation of strongly charged metals in solution.

Solvation strongly influences the cation selectivity of 18c6. Previously, we demonstrated that gas-phase 18c6 binds Li^+ more strongly than the other alkali metal cations. The K^+ selectivity observed in aqueous solution is recovered using a simple cation exchange reaction that reflects the competition of the solvent molecules and 18c6 for the cation in solution. Likewise, we have shown in the present work that gas-phase 18c6 binds Mg^{2+} more strongly than the other alkaline earth dications. The Ba^{2+} selectivity observed in aqueous solution is again recovered using the cation exchange reaction.

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