



DFT Investigation of the Structure and Alkaline Earth Cation Selectivity of 1,4-Diazo-2,3,8,9-dibenzo-7,10-dioxacyclododecane-5,12-dione

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Quantum mechanical study of 1,4-diazo-2,3,8,9-dibenzo-7,10-dioxacyclododecane-5,12-dione and its interaction with the alkaline earth dications Be^{2+} , Mg^{2+} , Ca^{2+} are presented in this article. This compound is used for the construction of a potentiometric carbon paste modified electrode for calcium ion. All calculation is performed at density functional theory (DFT) level of the theory by using the 6-31G* basis set. Initially the geometry optimizations calculations are accomplished, then frequency and basis set superposition error are performed. The geometric optimization calculations are used to obtain the concerned information of geometric structures of the molecule and the HOMO-LUMO energy gap. The frequency calculations are used to obtain the data of thermo-chemistry such as the complex enthalpy and free Gibbs complex energy formation. Our calculations clearly show that the investigated molecule in fact binds Be^{2+} most strongly in gas phase. Whereas the best selectivity is observed for this molecule in experimental results is Ca^{2+} . Thus, solvation effects appear strongly influence cation selectivity.

Key Words: Macrocyclic compound, Density functional theory, Binding energies.

INTRODUCTION

Macrocyclic polyethers (or crown ethers) have received increasing attention from experimental and theoretical researchers since Pedersen first discovered them in 1967¹. High conformational flexibility of crown ethers allows them to act selectively as receptors to various guests (cations, anions and small organic molecules)². Regarding the host-guest complexation and molecular recognition properties crown ethers have been used practically in the design of novel compounds to be used in sensing, switching, phase-transfer catalysis, extraction, chromatography and they have also been used as membrane-forming amphiphiles, as biomimetic receptors and as model ion channels because of their ionophoretic properties³⁻⁸.

In solution, their ability to selectively bind various cations depends on the size of the crown ether cavity, the type of donor atoms (oxygen, nitrogen and sulfur) and the polarity of the solvent. Crown ethers bind alkali and alkaline earth cations to form remarkably stable and highly structured complexes. By changing these parameters the properties of crown ethers can be easily adjusted for example by substituting the oxygen atoms of the crown ether with amides a new compound have been designed that is used as ion carrier in construction of PVC-based selective electrodes for Cu(II) ⁹, Zn(II) ⁷, Hg(II) ⁷ and Sr(II) ⁷.

The most common techniques for studying cationized adducts in gas phase are electron ionization mass spectrometry (EI-MS), fast atom bombardment mass spectrometry (FAB-MS) and the kinetic method. However, only information about relative values of metal affinities can be obtained from these experiments⁸. The purposive investigations can facilitate finding the solution to the problems encountered in the experimental techniques that is allowing the determination of minima energy and optimal geometric structure⁹.

Computational chemists have focused their efforts on crown enzyme-like specificity and have investigated about a number of molecular mechanics, molecular dynamics, Monte Carlo and electronic structure¹⁰⁻¹².

There have been a number of computational studies of metal complexes with crown ethers that were used to predict several properties such as molecular structure, relative stabilities and NMR spectra¹³. These have provided a detailed description of the important conformations sampled in both gas- and condensed-phases and of the crown ether interactions with cations and solvent molecules¹¹. In recent years, theoretical investigations using density function theory (DFT) have become more common in academic researches. Developments in DFT have been resulted in considerable successes in determining binding energies, equilibrium structures and ground-

state vibrational frequencies for a wide range of molecular systems⁹. In this paper, the selectivity of a crown ether 1,4-diazo-2,3,8,9-dibenzo-7,10-dioxacyclododecane-5,12-dione (Fig. 1) with some alkaline earth dications is reported.

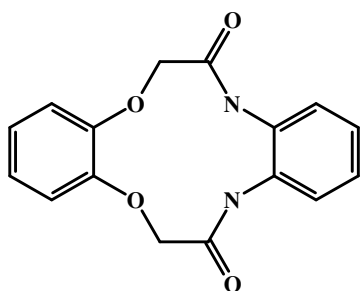


Fig. 1. Conformation of 1,4-diazo-2,3,8,9-dibenzo-7,10-dioxacyclododecane-5,12-dione

In this research, structures and binding energies have been calculated at density functional theory (DFT)^{14,15} level of theory with standard split valence basis set (6-31G*)¹⁶ for a comparative study on the Be²⁺, Mg²⁺ and Ca²⁺ complexes. The purpose of this research is to gain the lowest energy of the optimal geometric structure as accurate as possible. This research includes the calculations using the B3LYP/6-31G* method to determine the optimum geometric structures, molecular orbital energy and other thermodynamic properties of the complexes and these results have been compared to the experimental results at the end^{7,17,18}.

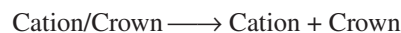
EXPERIMENTAL

As evidenced by the prior detailed *ab initio* theoretical studies of crown ether and its metal complexes^{10,11}, simple crown ethers present a significant computational challenge. At the heart of this challenges, are the number of atoms (43 in an alkali metal complex of 18c6) and the structural flexibility of macrocyclic backbone¹⁹. As in all complex systems, identifying the minimum-energy configuration is quite difficult because of the presence of several local minima on the energy surface. The molecular geometries with and without the metallic dications were determined by quantum mechanics methods, known to yield reasonable results and all of the calculations were performed in gas phase.

Initially, structures of the free molecule and complexes with dications were fully optimized by using additional step procedures at the density functional theory (DFT) of *ab initio* method and hybrid density functional B3LYP (Becke three-parameter-Lee-Yang-Parr)²⁰ level of theory with the standard split-valence 6-31g* basis set in the program package Gaussian98 (G98w)²¹.

After the optimizations, the harmonic vibrational frequencies calculations of free molecule and M²⁺/complexes were performed by using the B3LYP/6-31G level of theory in order to compute binding energies, Gibbs free energies and binding enthalpies^{10,11}. Binding energies for the M²⁺/complexes were evaluated at the B3LYP/6-31G* level of theory. The full counterpoise (CP) correction of Boys and Bernardi²² was applied to each binding energy to approximately account for basis set

superposition error (BSSE)^{10,11} run this program by used of "massage" key word in the output of the freq calculation^{23,24}. These quantities correspond to the gas phase dissociation energies with uncomplexed fragment for the below reaction:



To characterize the investigated inclusion complexes, the binding energy,

$$\Delta E_{\text{bind}} = E_{\text{comp}} - (E_{\text{Crown}} + E_{\text{Cation}})$$

was decomposed using the self-consistent charge and configuration method for subsystem. Here, E_{comp}, E_{crown} and E_{cation} denote the energies of the complex and its two noninteracting subsystems crown and cation. the subsystems cation and crown are an acid (electron cceptor) and a base (electron donor), respectively¹².

Enthalpy corrections at 298 K were evaluated using standard statistical mechanical expressions presented by Del Bene *et al.* with the DFT vibrational frequencies²⁵.

$$\Delta H_r(298\text{K}) = \sum_{\text{products}} \Delta_f H_{\text{prod}}(298\text{K}) - \sum_{\text{reactants}} \Delta_f H(298\text{K})$$

The reaction with lower enthalpy indicated that this macrocyclic select dication easier rather than the other dications. If the Gibbs free energies of a reaction is positive, the reaction is nonspontaneous and if the Gibbs free energies of a reaction is negative, the reaction is spontaneous. This parameter is calculated from the output of the freq calculation. The complex with the lowest gibbs free energy is the most stable form complex.

For all complexes, the following structural and electronic properties were determined: the ionization potential (IP) and the electron affinity (EA). The ionization potentials were calculated using the Koopman's theorem: IP = -ε_{HOMO} and EA = -ε_{LUMO}, where ε_{HOMO} and ε_{LUMO} are the HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) energies respectively. Koopman's theorem does not apply to DFT since the Kohm-Sham orbital energies do not have any physical meaning. However, using Janak's theorem and Perdew showed a connection between ionization potentials and electron affinitys to the HOMO and LUMO energies, respectively. On this basis, ε_g (HLG) values were obtained as the difference between the HOMO and LUMO energies, *i.e.* DFT calculations were carried out using the Gaussian 98 computer program²⁶.

$$\epsilon_g = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$$

Many modern programs use density functional theory (DFT). DFT is very attractive for calculation of finite systems because even the lowest level of DFT-the local spin density approximation (LSDA)-includes some electron correlation. This is extremely important in the design of organic molecular systems, which have extended π-systems^{27,28}.

Regarding to compare some *ab initio* methods used for the calculation in the previous research, DFT method is more powerful in the prediction of electron properties and optimized geometries of free molecule and its complexes. This method is time consuming since it involves evaluation of the two-electron integral.

RESULTS AND DISCUSSION

The cation selectivity of chosen crown ether molecule depends on many parameters, such as bond length, bond angle, dihedral angle, binding energies, binding enthalpies, HOMO-LUMO gap and Gibbs free energies. Thus the calculations related to of these parameters, have been reported to demonstrate the cation selectivity behaviour of this molecule.

Geometries: The optimized DFT/6-31G* geometries for uncomplex molecule of the crown ether, shown in Fig. 2, are reported here in after for uncomplex and M^{2+} complexes. In the course of the study of the optimized free molecule whose structures are shown in Fig. 2, it has been found that the cavity size of the uncomplex molecule agree to 4.2318 Å at B3LYP/6-31G* method. The calculated COC and CCN bond angles are also 123.109.923° and 119.005° at B3LYP/6-31G* method. The OCCN dihedral angles agree to 135.2065° at B3LYP/6-31G* method. The calculated values related to the CCN and COC bond angles and OCCN dihedral angle have been illustrated and shown using an arrow in the Fig. 3.

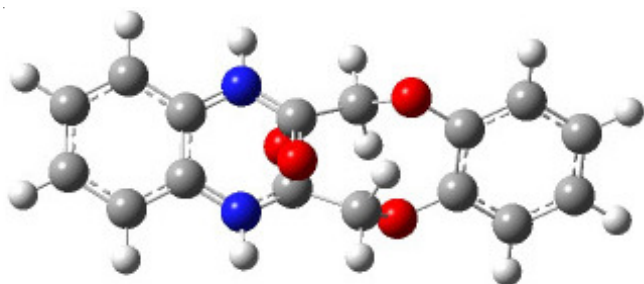


Fig. 2. Conformation of 1,4-diazo-2,3,8,9-dibenzo-7,10-dioxacyclododecane-5,12-dione optimized at DFT method

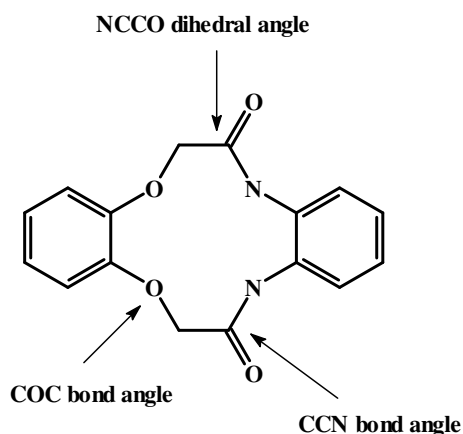


Fig. 3. COC and CCN bond angles and OCCN dihedral angle of 1,4-diazo-2,3,8,9-dibenzo-7,10-dioxacyclododecane-5,12-dione

In this step, the optimization of M^{2+} complexes has been performed and in each calculation, employed a starting geometry resembling the free structure that is shown in Fig. 2, with dications at the center of cavity. The optimized geometrical parameters for the Be^{2+} , Mg^{2+} and Ca^{2+} complexes are obtained and the related details are listed in Table-1. The Be^{2+} with ionic radius of 0.54 Å is smaller than the uncomplexed molecule and sits easily in the center of the free molecule as shown in Fig. 4. Besides the value resulted from DFT method

	Min	Mean	Max
M-O bond lengths			
Be^{2+} /complex	1.6868	1.6873	1.6879
Mg^{2+} /complex	1.9871	1.9871	1.9871
Ca^{2+} /complex	2.3500	2.3503	2.3507
M-N bond length			
Be^{2+} /complex	1.7086	1.7089	1.7092
Mg^{2+} /complex	2.0582	2.0582	2.0582
Ca^{2+} /complex	2.4563	2.4566	2.4569
COC bond angle			
Be^{2+} /complex	125.8398	125.8491	125.8584
Mg^{2+} /complex	121.7640	121.7655	121.7670
Ca^{2+} /complex	119.3470	119.3665	119.3860
CCN bond angle			
Be^{2+} /complex	109.3642	109.8441	110.3245
Mg^{2+} /complex	111.4610	113.5417	114.4710
Ca^{2+} /complex	118.3040	123.1102	127.9050
OCCN dihedral angle			
Be^{2+} /complex	–	0.0307	–
Mg^{2+} /complex	–	8.409	–
Ca^{2+} /complex	–	16.6997	–

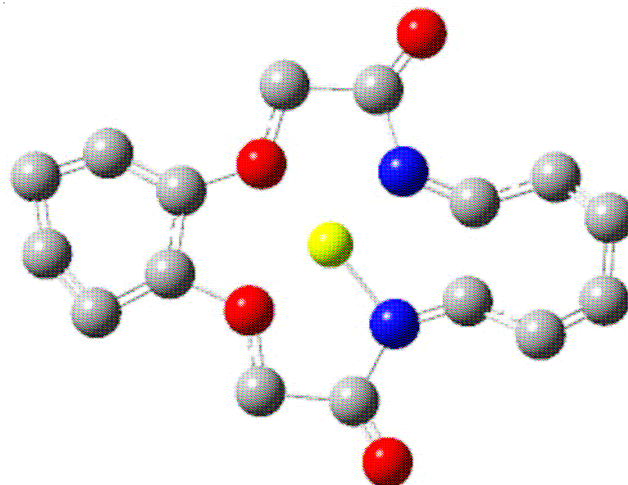
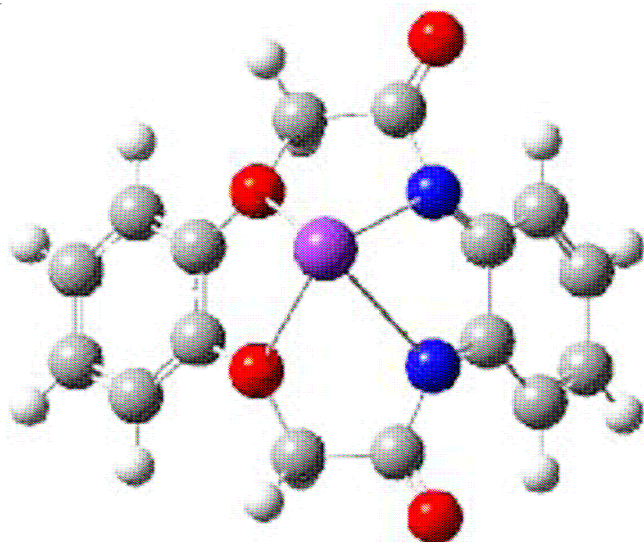
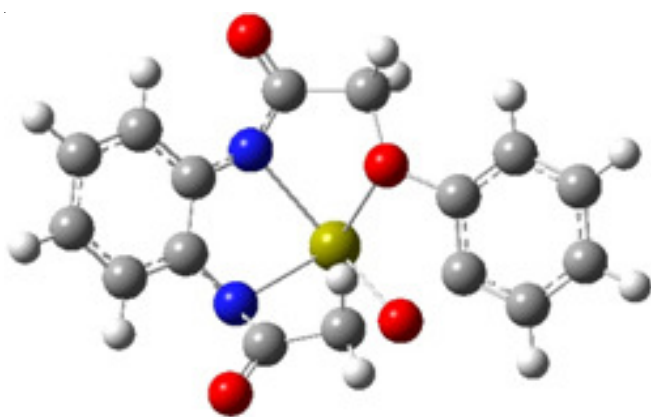


Fig. 4. Conformation of Be^{2+} /complex optimized at DFT method

for N-Be and O-Be bonds length of Be^{2+} /complex are equal to 1.7089 Å and 1.6873 Å, respectively. The CCN and COC bonds length are 109.8441° and 125.8491° of DFT method and OCCN dihedral angle is 0.0307°. In contrast to the previous cation the Mg^{2+} with ionic radius of 0.72 Å is slightly smaller than the uncomplexed molecule and so the Mg^{2+} cation sits in the center of host cavity as shown in Fig. 5. The values of Mg-N, Mg-O, COC, CCN and OCCN for DFT method are listed in Table-1. The Ca^{2+} with ionic radius 2.3 Å is as the same size of the uncomplexed molecule cavity and as shown in Fig. 6 and some bonds of the host molecule backbone breaks and the values of geometric parameters from DFT calculation are listed in Table-1.

The optimized bond lengths and angles of M^{2+} complexes reveal fairly significant flexing of the free backbone to accommodate cations of varying size. Regarding the above mentioned calculations, the OCCN dihedral angle size in the complex decreases with reducing the cation size. On the other hand C-C, M-N, M-O bond lengths, COC and CCN bond

Fig. 5. Conformation of Mg²⁺/complex optimized at DFT methodFig. 6. Conformation of Ca²⁺/complex optimized at DFT method

angles decrease slightly with reducing cation size, in accordance with smaller cavity sizes required by the smaller cations. As a result of the stronger polarization effects, M-N and M-O distances shorten and thus cause to form the stable complex. According to the table and results, in any complexes which dication is more willing to exposure in cavity of macrocyclic compound, caused to reduced the M-O and M-N bond lengths. In any complex which dication is more willing to exposure in cavity of macrocyclic compound, caused to take oxygen into the dication and as a result of COC bond angle is increased. In any complex which dication is more willing to exposure in cavity of macrocyclic compound, caused to take nitrogen into the dication and as a result of CCN bond angle is decreased.

HOMO-LUMO gap: The energy gap between the highest occupied and the lowest unoccupied orbital (HOMO and LUMO respectively), known as the HOMO-LUMO gap or simply HUMO-LUMO gap, is a critical parameter in determining molecular electrical transport properties because it is a measure of electron conductivity^{21,22,28}. Values of HUMO-LUMO gap ($\epsilon_g = \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$) for the M/complexes are reported in Table-2.

Table-2 shows that the HUMO-LUMO gap values increase in going from Be²⁺ to Mg²⁺ and Ca²⁺. Since HUMO-LUMO gap is a measure of electrical conductivity, the decreasing trend

TABLE-2
TOTAL ENERGIES, BINDING ENTHALPIES, GIBBS
FREE ENERGIES AND HLG OF M²⁺/COMPLEXES

	ΔE_{comp} (kcal/mol)	ΔG (kcal/mol)	ΔH^{298} (kcal/mol)	ϵ_g (HLG)
Be ²⁺ /complex	449.9243	341.3651	335.4766	0.0481
Mg ²⁺ /complex	576.9199	504.5176	498.1509	0.0521
Ca ²⁺ /complex	598.5088	598.6165	591.9297	0.0692

in the HUMO-LUMO gap value means that electrical conductivity increases and hence, HUMO-LUMO gap values for Ba²⁺ with lowest size is increased and Ba²⁺/complex has the highest electrical conductivity among the mentioned cations.

Binding energies: The CP-corrected binding energies were used because of basis set superposition error (BSSE) in M²⁺/complexes at DFT method. These quantities have been calculated using the following equation:

$$\Delta E_{\text{bind}} = E_{\text{comp}} - E_{\text{Crown}} - E_{\text{Cation}}$$

And the results have been reported in Table-2. According to this table, the most stable complex is one with the lowest binding energy.

Binding enthalpies: The results of enthalpy corrections at 298 K were evaluated using standard statistical mechanical expressions presented in Table-2. According to the results the binding enthalpy for the Be²⁺/complex is 333.4766 kcal/mol. The binding enthalpies for the other dications are considerably weaker and diminish monotonically from 498.1509 kcal/mol for the Mg²⁺/complex to 591.9297 kcal/mol for Ca²⁺/complex with increasing the dication size.

Gibbs free energies: If the Gibbs free energies of a reaction is positive, the reaction is nonspontaneous and if the Gibbs free energies of a reaction is negative, the reaction is spontaneous. This parameter is calculated from the output of the freq calculation. According to the result of calculation, Gibbs free energy for Be²⁺/complex is 341.3651 kcal/mol and for Mg²⁺/complex and Ca²⁺/complex are 504.5176 kcal/mol and 598.0165 kcal/mol respectively and Be²⁺/complex with the minimum Gibbs free energy is the most stable form. The result are shown in Table-2.

Conclusion

We have presented a detailed *ab initio* study of the structure of free molecule and its interaction. Geometries were optimized for the uncomplex molecule and for each of its M²⁺/complex. In gas phase, the radius of the Ca²⁺ is 2.3 Å and as the same as the cavity size of the free molecule that was expected the most stable complex should be formed. The radius of the Be²⁺ and Mg²⁺ are smaller than the cavity size of the free molecule that was expected that do not form stable complexes. Ca²⁺ is perfect size to fit into cavity of free molecule but the backbone of the host molecule collapses. The Mg²⁺ with 0.72 Å radius forms a complex that the cation sits in the center of free molecule. Be²⁺ with 0.54 Å radius forms a Be²⁺/complex that the cation sitting easily at the center of the host cavity.

Here, it should be mentioned that cation size alone cannot fully be taken into account as observed selectivity and some other parameters such as binding energy, Gibbs free energies and binding enthalpy are more important parameter

than geometric results. Indeed, while Ca^{2+} perfect size to fill the cavity but Ca^{2+} /complex because of the highest ΔE_{bind} and ΔG do not form a stable complex and the backbone of free molecule collapses. The lowest binding energy and enthalpy for the Be^{2+} /complex show that the free molecule forms a stable complex with Be^{2+} rather than the other cations and so Be^{2+} easily sits in the center of free molecule.

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