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Preferred conformations of the gas phase complex between Li^+ and a model macrocycle tetraamide

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Abstract

The gas-phase binding of Li^+ by a model macrocycle tetraamide, via its amide C=O groups, is investigated using ab initio methods. The macrocycle ligand contains four amide units linked by alternating phenyl and ethenyl groups. Geometries and vibrational frequencies for the complexes are obtained at the B3LYP/6-31G(d) level. Geometries are further optimized at the B3LYP/6-31+G(d) level. Interaction energies, corrected for basis set superposition error, are evaluated using the MP2 method with the 6-31+G(d) and 6-311+G(d) basis sets. It is found that the model tetraamide presents enough flexibility to bind the Li^+ metal ion in at least four different conformations characterized by their group symmetries C_s, C_2, C_{2h}, and C_{2v}. The respective interaction energies are close to one another with an average value of −79.40 kcal/mol at the MP2/6-311+G(d) level. Natural bond orbital analysis (NBO) is performed to investigate the extent of ligand polarization and charge-transfer (CT) interactions in the various conformations of the complex. Extended conformational searches for the free macrocycle tetraamide, and its Li^+ complex conformations are conducted using a Monte Carlo-based analysis with the PM3 semiempirical method and compared with the B3LYP results via similarity calculations.

Keywords: Ab initio; Gas-phase binding of metal ions; NBO analysis; Conformational search; Macrocycle tetraamides

1. Introduction

The development of ion receptors, also known as ionophores, is of great significance because of the fundamental role of ions in many chemical and biological processes [1]. A better understanding of ion-receptor interactions results in more efficient designs of ionophores with specific applications. For example, the increasing need of properly disposing of nuclear waste has led to the creative design of ionophores capable of binding radioactive ions to separate them from others [2]. Also, several other ion receptors have been designed for medicine [3], and pollution monitoring [4].

Macrocyclic ionophores are particular hosts capable of forming stable complexes with charged species by providing many binding sites directed toward the guest in a convergent manner. Perhaps the most widely known and extensively investigated macrocyclic ionophores are the so-called crown ethers and analogous which exhibit strong affinity and high selectivity for alkali and alkaline metal ions [5]. Some other widely investigated macrocyclic hosts include cryptands [6], starands [7,8], cyclodextrines [9], and calixarenes [10]. Macrocyclic polyamides form another group of ion receptors that have been given considerable attention [11]. The notable solubility in organic solvents usually accompanied by a diminished solubility in aqueous solution makes amides appealing for applications in the field of ion-selective electrodes and liquid–liquid separations. Additionally, the hydrogen bonding capabilities of amides are known to be crucial in many relevant systems including enzymes and proteins. Much effort has been devoted in the design of novel charged and neutral macrocycle tetraamides for anion recognition [11a,11b,11c,11d,11e,11f]. The complexation of

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alkali and transition metal ions by macrocyclic tetraamides has also been the subject of recent publications by several authors [11g,11h,11i,11j]. The important role played by proteins in the transportation of ions has prompted some researchers to study the binding properties of cyclic peptides [12]. Such studies demonstrated that the cyclic peptides are flexible enough to allow for either cation or anion binding despite the rigidity of the amide group. Thus, the amide group exhibits desirable amphiphilic properties with the carbonyl group serving as a suitable binding site for metal ions, and the N—H group serving as a binding site for anions [13,14].

In a recent ab initio study, the equilibrium geometries and relative stabilities of four clearly distinct conformations of a model macrocycle tetraamide were reported [15]. The four amide groups are found in the general sequence —L1—[NHCO]—L2—[CONH]—L1—[NHCO]—L2—[CONH]—, where the phenyl group was chosen for L1 and the ethenyl group for L2. Here, L1 links two amide groups trough covalent bonding of the nitrogen atoms specifically in the positions 1 and 3 of the phenyl group. Similarly, L2 links two amide groups by covalent bonding to the carbonyl carbon atoms. It is noteworthy that macrocycle tetraamides with the above general sequence, with different linkers L1 and L2, have been experimentally studied by other researchers [11]. The most relevant study is that of Singh et al. [11l], who reported the synthesis and biochemical activity of manganese and iron complexes with macrocycle tetraamides; for one of these macrocycles the L1 used, a phenyl group, was the same as the L1 used in our model system, and the L2 was a phenyl group binding the carbonyl carbons in the 1 and 2 positions, which is therefore very close to our L2. Other experimental and closely related studies are those by Jurczak et al. [11a], where $L1 = (CH_2)_n$ ($n = 2$–5), and L2 = pyridine (binding the C=O groups in the 1 and 3 position of pyridine); Still et al. [11k], where L1 = cyclohexane (binding the NH groups in positions 1 and 2), and L2 = phenyl (binding the C=O groups in positions 1 and 3). The present study expands on the previous work by investigating, via ab initio calculations, the structural transformations and accompanying electron density redistribution of the model macrocyclic tetraamide upon gas-phase binding of an alkali metal ion, more specifically the Li^+ ion. It should be noted that in the tetraamide complexes with iron and manganese reported by Sing et al. [11l], the metal ions are proposed to have octahedral coordination with four coordination sites provided by the tetraamide via its amide nitrogens, and two Cl^- bonded to the metal ions. In this study, we evaluate the ability of the tetraamide model to bind metal ions via its carbonyl oxygen atoms, and thus expand its potential usefulness. Natural bond orbital analysis (NBO) is performed to investigate the energetic importance of ligand polarization and charge-transfer (CT) interactions. Conformational searches are also performed for both the free macrocycle and its Li^+ complexes using a Monte Carlo-based analysis and the PM3 semiempirical method.

2. Methods of calculations

Ab initio calculations were carried out with the GAUSSIAN 03 program [16]. Geometry optimizations and frequency calculations were first performed at the B3LYP [17] level using the 6-31G(d) [18]. The geometries were further optimized using the 6-31+G(d) basis set [19]. Single-point energy calculations were performed using the 6-31+G(d), and 6-311+G(d) [20] basis sets at the MP2 level [21]. The optimized geometries were subjected to natural bond orbital (NBO) analysis performed on wave functions calculated at the HF/6-31+G(d,p) level [22]. The interaction energies reported here were corrected for basis set superposition error (BSSE) using the counterpoise method of Boys and Bernardi [23]. Conformational searches were carried out using a Monte Carlo-based analysis with the PM3 semiempirical method as implemented in Spartan'04 and Spartan'06 for Windows [24]. Initial geometries were taken from Parra et al. [15], which were the results of geometry optimizations using density functional theory (B3LYP) with the 6-31+G(d) basis set. These geometries were also used as initial guess geometries for geometry optimization under the PM3 semiempirical method. Similarity calculations were carried out to quantify the extent of similarity of the results obtained from the expanded conformational searches and the DFT results.

3. Results and discussion

3.1. Uncomplexed macrocycle tetraamide

In a previous study [15], a limited B3LYP/6-31+G(d) search for stable conformations of the model macrocycle tetraamide resulted in the identification of four clearly distinct minimum-energy structures that were labeled AA_1, AA_2, BC_1, and BC_2. In this work, these labels are respectively replaced by the more compact labeling M1, M2, M3, and M4. The relative electronic energies at the MP2/6-31+G(d,p) level were reported to be M1 (0.00 kcal/mol) < M2 (0.86 kcal/mol) < M3 (2.09 kcal/mol) << M4 (9.17 kcal/mol). We decided to expand the conformational search of the free macrocycle using a Monte Carlo-based analysis with the PM3 semiempirical method as implemented in Spartan'04 and '06 for Windows [24]. The DFT minimum-energy structures were used as initial guess geometries for both PM3 geometry optimizations and conformationals searches. The main purpose of the optimization under PM3 conditions is to carry out a broader search for minima. Geometry optimizations using the PM3 semiempirical method resulted in conformations fairly close to those obtained using DFT for the M1 (C_i), M2 (C_2), and M3 (C_s) ligands. The similarities are above 90% with small differences found mostly on the tilt angle of the benzene rings relative to the ethylene moieties. In contrast, the M4 (C_s) geometry was notoriously different, only 76% similar to the DFT geometry. The difference is