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Review

Structural aspects of the metal ion complexes of the conjugates of calix[4]arene: Crystal structures and computational models

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ABSTRACT

In this review, the structural aspects of the metal ion complexes of calix[4]arene and its derivatives have been discussed. Aspects, such as the coordination geometry about the metal ions and conformational mobility of the arms of the calix[4]arene as well as the calix[4]arene platform were discussed and compared appropriately. Structures derived based on the computational modeling of the metal ion complexes of the calix[4]arene derivatives have also been reviewed. The complexation of the metal ions with the derivatives was observed mainly through the heteroatoms which were further strengthened by cation$\cdots\pi$ interactions extended from the phenyl moieties of calix[4]arene. Solvent molecules play an important role in preorganizing the cavity to optimize the binding of metal ions. Conformational changes

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Abbreviations: XRD, X-ray diffraction; DFT, density functional theory; NMR, nuclear magnetic resonance; ORTEP, Oak Ridge Thermal-Ellipsoid Plot; Pic, picrate ion; Tert, Tertiary; THF, tetrahydrofuran; CD_3CN, deuterated acetonitrile; PLUTO, program for drawing crystal and molecular structures; HF, Hartree Fock; DMSO, dimethyl sulfoxide; MALDI, matrix assisted laser desorption ionization; Phos, phosphate; DMF, dimethyl formamide; Me, methyl; Ar, aromatic; Calix, calixarene.

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Coordination geometry
Computational modeling

were observed in the arms upon metal ion binding. However, conformational changes were also observed in the calix[4]arene moiety, particularly when no arms were built on these platforms for coordination. This review covers the structural information of ~125 metal ion complexes from a list of 145 literature references and thus covers the relevant literature in its entirety starting from the year 1989. Thus the present review covers the metal ion complexes of the calix[4]arene and its derivatives, *viz*., alkali and alkaline earth, transition (first, second and third row), main group and lanthanides, that may be of use in designing the conjugates of calix[4]arene for their possible applications.

1. Introduction

Calixarenes belong to a versatile group of macrocyclic compounds in supramolecular chemistry. These are well organized vase like molecular entities recognized for their utility in building units for molecular recognition [1–4]. Calixarenes have interesting applications as host molecules because of their preformed cavities. Although several calixarene based receptors have been reported and studied for their applicability in supramolecular chemistry, the more popularly studied one is the calix[4]arene [5–7]. Indeed, calix[4]arenes are the simplest and most common members of the calixarene family, with four phenolic residues being present in the macrocyclic ring. Because of these four phenoxy groups, reactions with transition metal ions or their complexes produces metal phenolates with the substitution of one to four hydrogen atoms [8–15]. Calix[4]arenes exhibit different conformations that may qualify these as ion and molecular hosts [1,7,16–20]. The preorganization of the benzene rings of calix[4]arene moiety assists the inclusion of solvent and or other guest species in the cavity [21–29] and thus acts as a molecular basket. Functionalization of calixarenes at the lower rim or at the upper rim often produces derivatives with reduced conformational mobility [30–36]. It is indeed possible to selectively introduce organic functionalities both at the lower rim as well at the upper rim. Synthetic calixarene conjugates contribute to the molecular recognition and thereby give new directions into nanotechnology, micro fabrication and molecular biology [4,37,38]. The nano cavities can be used for the encapsulation of drugs and their active transport through the cell membranes. In recent years, the conjugates of calix[4]arene received importance due to their versatility in exhibiting special features, as well applications that spans across several areas [39–52]. Therefore, appropriate derivatization of the calix[4]arene for the selective recognition of ions and molecules is a topic of current interest. During the past few years, several groups have been involved in synthesizing lower rim modified calix[4]arene derivatives and studying their ion and molecular recognition properties [53–56]. In recent years, several reviews have been published on biological applications, and ion and molecular recognition of the calix[4]arene derivatives [57–70] and a few reviews deal with computational studies of calixarene host–guest complexes [71–73]. Recently, our group contributed to a review article on the ion and molecular recognition of 1,3-di-derivatives of calix[4]arene as well as another on the nanostructual aspects of these derivatives [74]. Most of the literature reviews focuses on the synthesis and ion and molecular recognition studies of calix[4]arene derivatives. While few reviews have focused on the coordination chemistry, almost none focuses on the structural aspects of the metal ion complexes of the conjugates of calix[4]arene [75,76]. Therefore, the present review is aimed to focus at the structural aspects of the derivatives of calix[4]arene and their metal ion complexes, derived by single crystal XRD and computational calculations.

The present review is been divided into five parts. While the first part deals with the complexes of alkali and alkaline ions, the second and third part deals with the transition ions. The fourth and fifth parts focus on the main group metal and lanthanide complexes respectively. Each part has been further divided into subgroups based on the nature of the derivatives used for complexation. The main focus in this has been given to the mode of binding of calix[4]arene and their derivatives and the type of coordination geometries formed about the metal ions. The conformational changes observed upon complexation with metal ions have also been discussed and compared appropriately.

2. Alkali and alkaline earth ion complexes

2.1. Crown ether derivatives

DFT computational studies of the formation of the Na^+, K^+ and Rb^+ complexes of 1,3-alternate-bis(1-methoxyethyl) calix[4]-arene-azacrown-5 {[**1**·Na^+]; [**1**·K^+]; [**1**·Rb^+]}, 1,3-alternate-bis(1-methoxyethyl)calix[4]arene-N-phenyl-azacrown-5 {[**2**·Na^+]; [**2**·K^+]; [**2**·Rb^+]} have been performed. The interatomic distances of oxygen atoms on the upper crown loop of **1** and **2** decreases by 0.3–2.3 Å upon complexation (Fig. 1). This is due to the inductive effect arising from the crown O···M^+ interactions. The interatomic distances observed between the carbon atoms in the phenyl rings facing downward {labeled as (i)} increases while some of them decrease. This facilitates the inward rotation of the inverted phenyl units which brings the unshared electron pairs of the oxygen center to be directed into the cavity and thereby enhances the strength of the O···M^+ interactions. However, with these phenyl rings, the interatomic distances observed between some of the carbon atoms increases when compared with the free ligand. The results are explainable by the trapping of M^+ in a cavity composed of phenolic, polyether oxygen atoms and two π-basic benzene rings, via metal-oxygen and cation–π interactions [77]. While Na^+ is trapped in the center of the polyether fragment, K^+ and Rb^+ move closer to the two phenolic oxygen atoms (O1 and O4) owing to their larger ionic radii.

Thus the binding selectivity of a conjugate of the calix[4]arene seems to be associated both with the size of the alkali ion as well as the nature of the cavity. The Na^+ is too small to coordinate to all the heteroatoms of the N-azacrown-5 fragment. Therefore, the large-cavity azacrown-5 undergoes considerable changes to bring the binding moieties into close proximity in order to bind to the cation. In the case of K^+ and Rb^+ complexes, the metal ions fit well within the cavity and have strong interactions with heteroatoms in the azacrown. The complexes of **2** showed strong interactions when compared with that of **1** suggesting that the phenyl group attached to the nitrogen of azacrown promotes metal complexation by 3D encapsulation.

The structure of the Na^+ complex of tetra-(benzo-l5-crown-5) substituted calix[4]arene (**3**) has been derived based on ^1H NMR and the K^+ complex of bis-(benzo-l5-crown-5) substituted calix[4]arene (**4**) has been determined by single crystal XRD. ^1H NMR studies showed that Na^+ is bound to four crown ether moieties of **3** as well as all four lower rim amide groups as shown in Fig. 2(a). The X-ray structure of the potassium complex of **4** showed that one of the two amide NH groups is directed toward an oxygen atom at 3.39 Å, while the other NH moiety is directed away from the cavity as can be seen from Fig. 2(b). The O_{ca1ix}—C—C—N linkage is *trans*-, rather than the usual *cis*-. This arrangement facilitates