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The effect of ring annelation to benzene on cation-π interactions: DFT study

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ABSTRACT

Density functional theory (DFT) B3LYP/6-31G(d,p) calculations reveal that the binding affinity of alkali metal cations (Li^+, Na^+ and K^+) with benzene is enhanced by sequential ring annelation of six-membered aromatic ring or highly strained bicyclo[2.1.1]hexene moieties. The bicyclo[2.1.1]hexene annelation to benzene exhibits larger influence on cation-π interactions than six-membered ring annelation. The harmonic vibrational frequencies indicate that all complexes are minima on their respective potential energy surfaces. The extent of charge transfer values from π-systems to cations have been calculated and analyzed.

1. Introduction

Cation-π interactions represent quite strong intermolecular non-covalent interactions in supramolecular complexations and they are of considerable importance in chemistry as well as biology [1–6]. Participation of cation-π interactions in receptor–ligand complexes has been demonstrated by Mo et al. using quantum chemical calculations [6]. Theoreticians have given importance to understand the origin of cation-π interaction energies by contribution from different energy components such as electrostatic, polarization and charge transfer energies [5–7]. A detailed understanding of the interactions between alkali metal ions and different aromatic motifs is essential in both chemistry and biology because such interactions play vital role in protein structures and stability, protein–protein interactions, protein–enzyme interactions, and drug–receptor interactions [1,5,8]. Interactions of a range of cations with the aromatic motifs of naturally occurring amino acids have been the subject of theoretical interest [9]. Cation-π interactions are also useful in the areas of environmental science and mineral surface chemistry [10,11].

Recently, there has been significant interest in understanding of C—H···π, N—H···π, and O—H···π interactions involving benzene and substituted benzene systems [12–16], and the computed characteristic vibrational spectra for those complexes have been reported to be in a good agreement with the experimental results [13–16]. Modifications of host molecules by altering shapes have been used in designing of novel ionophores, new drug targets as well as in re-optimizing chemical agents that could be of medicinal value [1,17–19]. Designing of ionophores for capturing of alkali or alkaline earth metal ions is of widespread theoretical interest [17–19]. We have reported in our earlier study that ring annelation significantly enhances the binding affinity of Li^+ with the benzene ring and the strength of binding could be characterized using NMR spectroscopy [20]. Very recently, we have studied the cation-π interactions considering the cup-shaped molecules containing twin faces using quantum chemical methods. We have examined the face selectivity for cation binding in those cup-shaped molecules and found that vibrational spectra could be useful in characterizing the cation-π interactions and distinguish the face selectivity [21]. Computational studies indicated that multiple weaker non-optimal cation-π interactions contribute significantly to the overall binding strength of metal ion interactions with cage molecules [17,21]. Recently, Vijay and Sastry have investigated, using ab initio method, the binding of Li^+ and Mg^{2+} with the π-face of linear and cyclic unsaturated hydrocarbons to understand the size dependence on cation-π interactions [22]. Sastry and co-workers have provided new insights on cooperativity of cation-π and π–π interactions using quantum chemical calculations [23–25].

In this paper, we have investigated the effect of sequential ring annelation of mono-cyclic six-membered aromatic ring and bicyclo[2.1.1]hexene to the simplest aromatic benzene ring on the cation-π interactions considering the alkali metal cations: Li^+, Na^+ and K^+. The variation of binding affinities of these three metal ions with ring annelated benzenes has been examined. We have also explored the relationship between the extent of charge transfer from organic π-systems to metal ion and the interaction energies. The highly strained tris(bicyclo[2.1.1]hexeno)benzene was reported experimentally [26,27].

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2. Computational details

B3LYP functional in conjunction with 6–31G(d,p) basis set has been employed for optimizations of all the π-systems and complexes considered. Harmonic vibrational frequency calculations have been carried out to confirm whether the π-systems and complexes are minima or not. The zero-point vibrational energy (ZPVE) corrections were computed from frequencies evaluated at the B3LYP/6-31G(d,p) level. Basis set superposition error (BSSE) corrections were carried out for all complexes using the counterpoise (CP) method of Boys and Bernardi [28]. The values of electron charge transfer from organic species to cations have been calculated using Natural Population Analysis (NPA) and Mulliken charges obtained at the B3LYP/6-31G(d,p) level. All calculations were performed using Gaussian 03 program package [29].

3. Results and discussion

The model structures of cation-π complexes with principal geometric parameters are depicted in Fig. 1. In all of the cases, the metal ion was placed above to the central benzene ring. In the optimized geometries, the metal ion is not just exactly above to the centroid of considered ring. It is slightly displaced toward the edge in case of **2–M$^+$**, **3–M$^+$**, **5–M$^+$** and **6–M$^+$** complexes. As expected, the complexes containing Li$^+$ exhibit smaller ring centroid-M$^+$ distance than Na$^+$ and K$^+$ complexes. For all three alkali metal ions, the distance between the M$^+$ and ring centroid decreases with increasing number of ring annelation irrespective of mono- or bi-cyclic ring. However, bicyclo[2.1.1]hexene annelation shows slightly larger influence than mono-cyclic six-membered ring annelation.

The interaction energies, basis set superposition energy (BSSE) correction, BSSE and zero-point vibrational energy (ZPVE) corrected interaction energies for all of the complexes are provided in Table 1 along with the extent of charge transfer values (q_{CT}) calculated using Mulliken charges. The q_{CT} values were calculated by subtracting the residual charge of metal ion in the complex from the formal charge (+1 for alkali metal ions). Inclusion of the BSSE correction does not change the ordering of the stability of the complexes. The BSSE and ZPVE corrected interaction energies are taken for discussion unless otherwise noted. The computed values for benzene–metal ion interactions (**1–Li$^+$**, **1–Na$^+$** and **1–K$^+$**) of −38.0, −25.4 and −15.5 kcal/mol are in good agreement with the experimental values of −38.5 ± 3.2, −22.2 ± 1.4 and −17.5 ± 0.9 kcal/mol, respectively [3].

Sequential annelation of six-membered ring or bicyclo[2.1.1]-hexene to the benzene strengthens the cation-π interactions. The binding affinities of given metal ion with bicyclo[2.1.1]hexene annelated benzenes are considerably higher compared to six-mem-

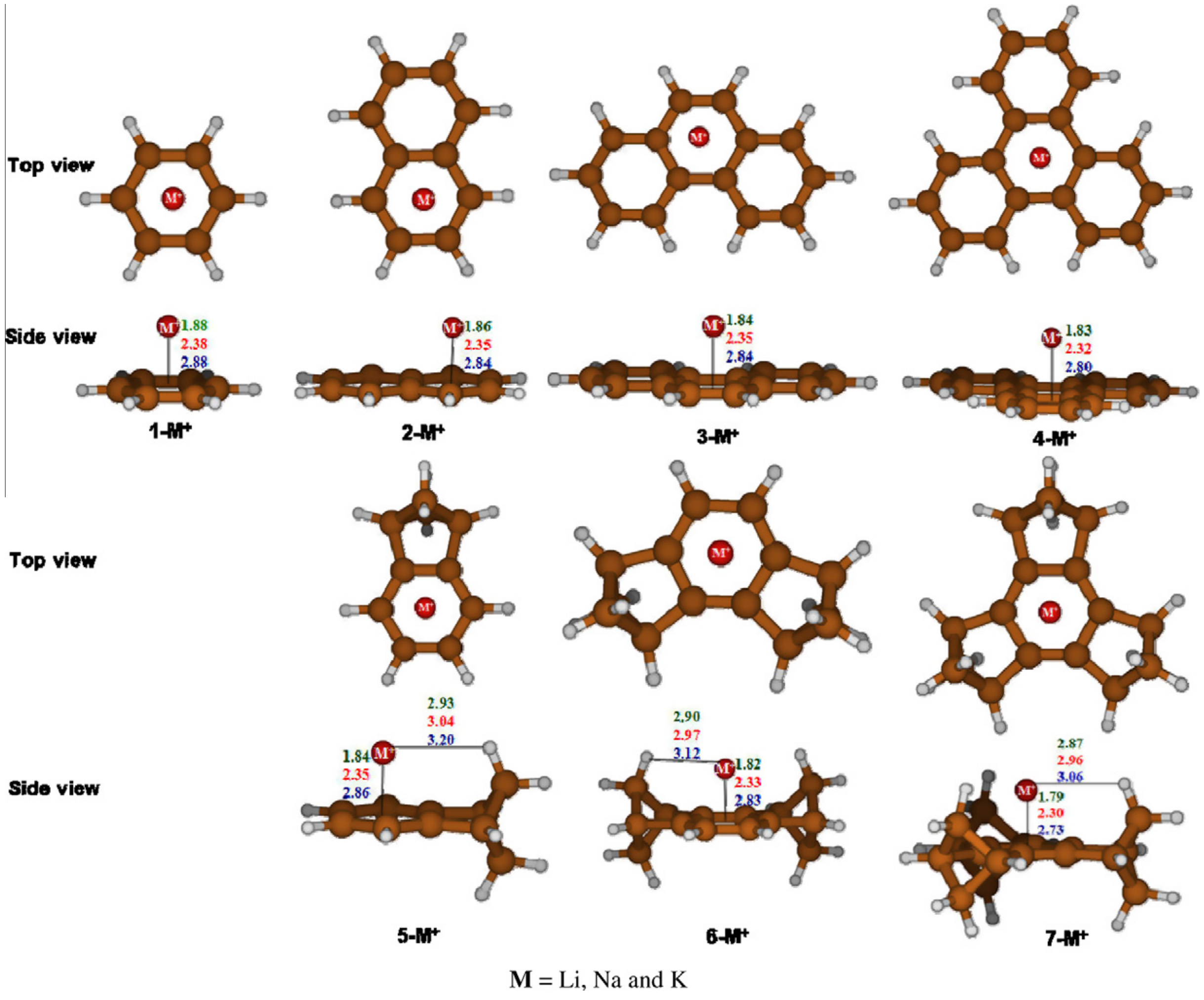

Fig. 1. Top and side views of the cation-π interaction complexes involving benzene, mono- and bi-cyclic annelated benzene ligands. Selected inter-moiety distances (in Å) obtained at the B3LYP/6-31G(d,p) level are given. The values in the top, middle and bottom are correspondingly for Li$^+$, Na$^+$ and K$^+$ metal ion complexes.