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## Explicit Solvent Effect on Cation– $\pi$ Interactions: A First Principle Investigation

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Sequential attachment of water molecules to cation– $\pi$  ( $\text{Li}^+$ –benzene,  $\text{K}^+$ –benzene, and  $\text{Mg}^{2+}$ –benzene) systems reveals that the cation– $\pi$  interaction strength varies in opposite direction depending on the site of solvation of the cation– $\pi$  system. Solvation of the metal ion decreases its interaction energy with the  $\pi$  system, while the solvation of the  $\pi$  system increases its interaction energy with the metal ion. The cation binding to benzene clearly enhances the ability of aromatic protons to participate in hydrogen bonding with water molecules. The distance between the metal ion and centroid of the benzene inherently varies with the position of water molecules in the vicinity of cation– $\pi$  complex. Reduced variational space (RVS) analysis on bare and solvated cation– $\pi$  complexes indicates that the major contributions to the total interaction energy are coming from the polarization and charge transfer energy terms of the  $\pi$  system. Topological atoms in molecules (AIM) analysis is performed to evaluate the nature of the cation– $\pi$  interaction. Good correlations are observed between interaction energies and charge density at the cage critical point of the cation– $\pi$  complexes.

### Introduction

The role of metal ions in regulating the structure and functions of small and large molecules is indisputable.<sup>1</sup> In last two decades several groups dedicated their time to study the cation– $\pi$  interactions and their relevance to several biological systems.<sup>2–13</sup> Alkali and alkaline earth metal ions are ubiquitous in biological systems with several cases of their central role in biological process.<sup>14</sup> The importance of cation– $\pi$  interaction in and their wide occurrence in biologically important systems is well documented.<sup>15–17</sup> The strength of cation– $\pi$  interactions is several times greater than other noncovalent interactions associated with molecular recognition such as hydrogen bonding and dispersive (van der Waals) interactions. Thus,  $\pi$  systems offer binding sites to the metal ion which compete with the traditional coordinating groups such as amines, alcohols, and ethers.<sup>18</sup> Thus, exploring the effect of aqueous solvent on cation– $\pi$  systems is interesting in its own right, and the current study is aimed to attempt a rigorous quantum mechanical approach to treat the effect of explicit water molecules.

Earlier studies on the effect of solvation on the cation– $\pi$  interaction energy reveal that the trends in the gas phase are quite different from that in solvent phase.<sup>19</sup> The disparity in binding energies was traced to the variations in the desolvation energy. Studies on the size selectivity in cation– $\pi$  interactions reveals that benzene could easily replace some of the water molecules to interact with  $\text{K}^+$ , whereas the first solvation shell of  $\text{Na}^+$  cannot be replaced by benzene.<sup>20</sup> A systematic computational study on cation– $\pi$ –anion interactions indicated that the anion in the vicinity of the  $\pi$  system leads to a large redistribution of electron density and hence leads to an inductive stabilization.<sup>21</sup> Competition between cation– $\pi$  interaction and aqueous solvation for the  $\text{Na}^+$  ion has been investigated using molecular dynamic simulations. This study shows that the  $\text{Na}^+$ –phenylalanine complex survives for a significant time in aqueous solution and that the free energy barrier

opposing dissociation of the complex is sizable.<sup>22</sup> A recent molecular dynamics study on the solvation of M–benzene (M =  $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Rb}^+$ , and  $\text{Cs}^+$ ) by using Ar atoms as solvent reveals that, even in the presence of Ar solvent, metal ions firmly bind to benzene.<sup>23</sup> A combined experimental and ab initio study on the interaction of solvated metal ions with N-methylacetamide (NMA) provided a good insight to the nature of M<sup>+</sup>…NMA (M<sup>+</sup> =  $\text{K}^+$  and  $\text{Na}^+$ ) interactions in an aqueous environment and showed how different ion…ligand pairwise interactions direct the extent of water…water and water…NMA hydrogen bonding.<sup>24</sup> The effect of aqueous medium on several nonbonded interactions has been studied by means of experimental and ab initio calculations.<sup>25</sup> An experimental study on cation– $\pi$  interactions between benzene and cations ( $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{Cs}^+$ , and  $\text{Ag}^+$ ) in aqueous solution are characterized via <sup>2</sup>H NMR relaxation times and calculations of molecular correlation times. This study indicates that the soft base cations and soft transition metals (e.g.,  $\text{Cs}^+$  and  $\text{Ag}^+$ ) have stronger cation– $\pi$  interactions compared with hard base cations (e.g.,  $\text{Li}^+$  and  $\text{Na}^+$ ).<sup>26</sup> Recently, our group has reported the effect of water molecules on solvating the metal ion in the cation– $\pi$  interaction; this study was able to address the apparent disparity between the structural parameters obtained using quantum chemical studies and X-ray crystallographic analysis.<sup>27</sup> Earlier study from our group examined the effect of  $\pi$  system size on the cation– $\pi$  interactions and revealed that the number of  $\pi$  systems in the conjugation may be taken as a general signature to estimate the cation– $\pi$  interactions.<sup>28</sup> The effect of water solvation on the interaction of quaternary ammonium ion with benzene shows that the interaction energy in the presence of solvent is reduced by about three-quarters when compared with gas-phase interaction energies.<sup>29</sup> Systematic post Hartree–Fock calculations on the solvation of the methylamine– $\pi$  system reveals that the solvation of the cation lengthens the cation– $\pi$  distance and lowers the cation– $\pi$  interaction energy.<sup>30</sup> A recent study on the interaction of a metal ( $\text{Na}^+$  and  $\text{K}^+$ ) to indole or phenol water clusters shows that the metal can strongly influence hydrogen bonding between water and phenol or indole.<sup>31</sup> The rate of solvent exchange around the divalent metal ions was studied by means of electrospray ionization Fourier-transform mass spectrometry; this study showed that  $\text{Ba}^{2+}$  and  $\text{Sr}^{2+}$  with four and

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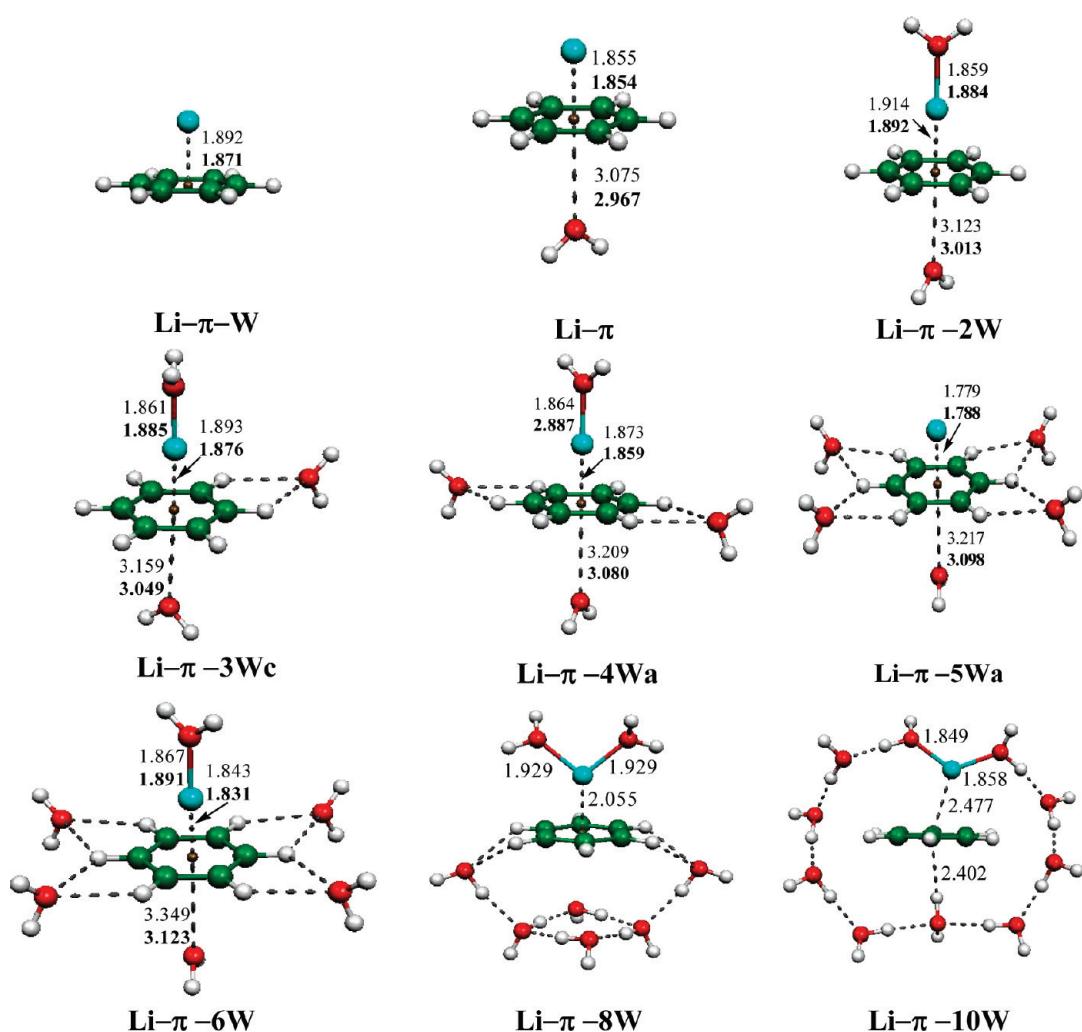
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seven water molecules, respectively, undergo rapid exchange with benzene, while the rate of exchange for  $Mg^{2+}$  and  $Ca^{2+}$  depend on the extent of solvation around it.<sup>32</sup>

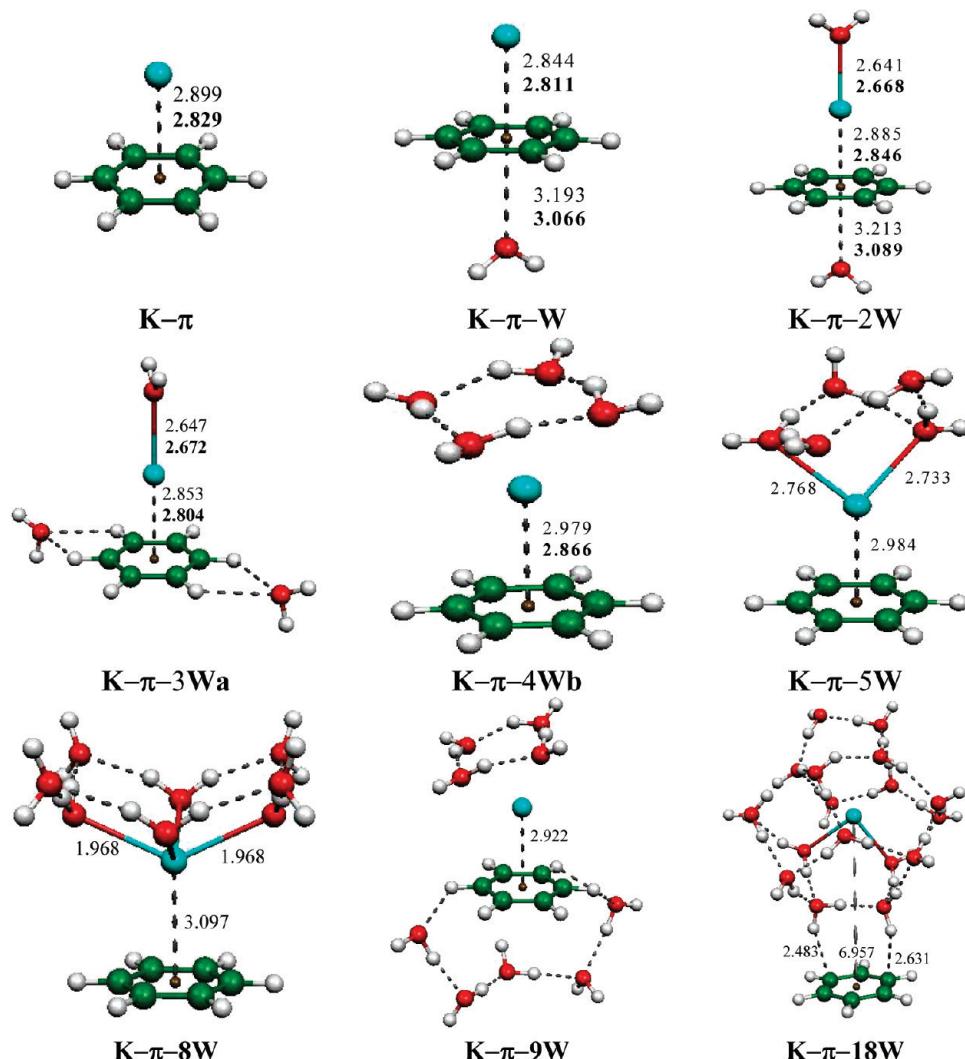
The current study aims at understanding the effect of solvent ( $H_2O$ ) on subtle interactions, such as cation– $\pi$ , and the structural changes that occur from gas phase to solvent phase.  $Li^+$ ,  $K^+$ , and  $Mg^{2+}$  ions are considered as cations, and high level ab initio and density functional calculations were performed to assess the effect of water on cation– $\pi$  interactions. The microscopic solvation of cation– $\pi$  systems (cation =  $Li^+$ ,  $K^+$ , and  $Mg^{2+}$ ;  $\pi$  = benzene) is done by keeping the metal and  $\pi$  system constant (except for  $K-\pi-12W$ ,  $K-\pi-18W$ ,  $Mg-\pi-12W$ ,  $Mg-\pi-15W$ ,  $Mg-\pi-18W$ , and  $Mg-\pi-19W$ ). Reduced variational space (RVS) analysis has been carried out to estimate the contribution of different energy components to the total interaction energy. AIM topological analysis of the electron density and electrostatic potential properties of different solvated cation– $\pi$  complexes are performed to understand the nature of cation– $\pi$  interactions in the presence of solvent. Certainly, molecular dynamics calculations are necessary to sample all the possible conformational space and depict the true picture of the solvation along with the effect of entropy, temperature, and pressure on the system. The quantum mechanical studies are expected to provide valuable insights into the microscopic details and also into the subtle variations in the structure and energetics of cation– $\pi$  interactions as solvent molecules are sequentially added along different orientations.

## Computational Procedure

All solvated cation– $\pi$  complexes are initially subjected to geometry optimization at B3LYP/6-31G(d,p) level, and the nature of the resultant stationary points has been ascertained with frequency calculations. Geometries obtained at B3LYP/6-31G(d,p) level are further refined at MP2/6-311+G(d,p) level. After consideration of the computational cost, the MP2/6-311+G(d,p) optimizations are carried out for the complexes containing up to seven water molecules only. Single point energy calculations have been performed at B3LYP/6-311++G(d,p) and MP2(FULL)/6-311++G(d,p) levels of theory using B3LYP/6-31G(d,p) optimized geometries. Single point calculations at MP2(FULL)/6-311++G(d,p) are repeated by using the optimized geometries of the MP2/6-311+G(d,p) level. Interaction energies obtained using the above-mentioned levels of theory have been corrected for basis set superposition error (BSSE) with “Counterpoise = N” option for all fragments in the complex using the Boys and Bernardi’s counterpoise method.<sup>33</sup> For example, for the system with ‘n’ water molecules  $N = n + 2$ . RVS energy decomposition analysis has been carried out for all solvated cation– $\pi$  systems at HF/6-31G(d,p) level.<sup>34</sup> RVS-SCF method uses the same definitions of the polarization and charge transfer terms as the Kitaura–Morokuma (KM) analysis. However, unlike the KM analysis, in which each component is considered independently, the RVS-SCF method is a sequential procedure in which the reference point for each



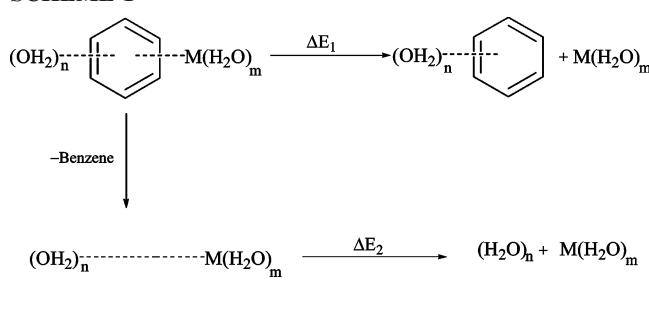
**Figure 1.** Geometrical parameters of bare and solvated  $Li-\pi$  complexes obtained at B3LYP/6-31G(d,p) (normal) and MP2/6-311+G(d,p) (bold) levels of theory. Bond lengths are in Ångströms.



**Figure 2.** Geometrical parameters of bare and solvated  $K-\pi$  complexes obtained at B3LYP/6-31G(d,p) (normal) and MP2/6-311+G(d,p) (bold) levels of theory. Bond lengths are in angstroms.

calculation is defined by solution of the monomer problem. Such a procedure avoids double counting of various interactions. To analyze the nature of cation- $\pi$  interaction in the presence of solvent, the atoms-in-molecules (AIM) theory of Bader is applied.<sup>35</sup> AIM calculations are performed based on the B3LYP/6-31G(d,p) level. The following scheme illustrates how the interaction energies are calculated in the current study.

#### SCHEME 1



$M = Li^+, K^+$  and  $Mg^{2+}$ ;  $n = 0 - 9$  and  $m = 0 - 18$

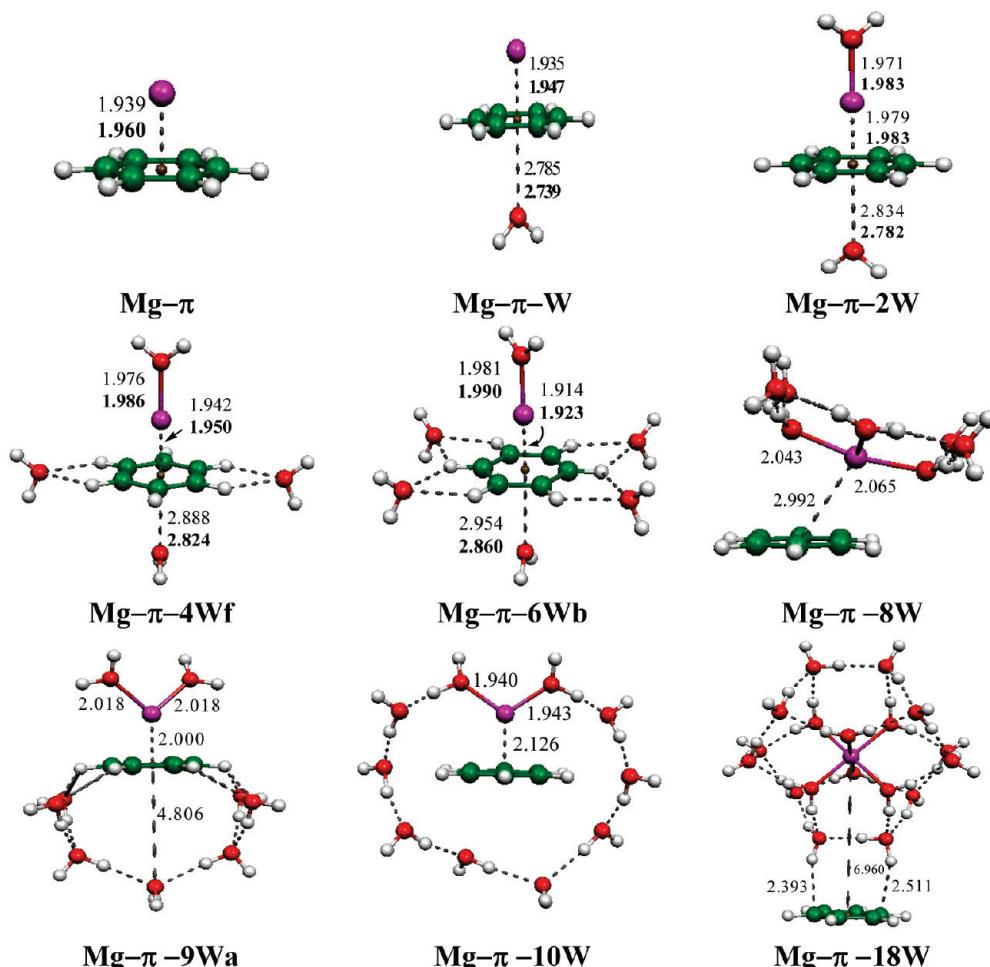
Here  $\Delta E_1$  is the cation- $\pi$  interaction energy in the presence of solvent molecules, and the  $\Delta E_2$  is the through-space interaction energy of solvated metal ion with the solvent molecules

present near the  $\pi$  system. All calculations have been performed using the Gaussian 03 suite of programs.<sup>36</sup>

#### Results and Discussion

**Geometries.** For each metal ion, a few important structures are depicted in the manuscript, and all complexes are provided in the Supporting Information. Figure 1 and Figure S1 show the geometrical parameters of bare and solvated  $Li-\pi$  complexes obtained at B3LYP/6-31G(d,p) and MP2/6-311+G(d,p) (for the complexes containing up to seven water molecules only) levels of theory. Initially all possible conformations are explored at the B3LYP/6-31G(d,p) level, searching the conformational space in the following way. Three putative sites are considered for introducing the solvent molecules in the vicinity of the cation- $\pi$  system: the first one is from the cation side, the second one is from the plane of benzene, and the third one is from below the plane of benzene. Unless otherwise mentioned, all geometries are discussed based on the B3LYP/6-31G(d,p) optimized geometries. Throughout the discussion, the distance between the centroid of benzene and the metal is referred to as cation- $\pi$  distance.

From Figure 1 and Figure S1, it is clear that when water molecules are present either in the plane or below the plane of benzene, the cation- $\pi$  distance is shorter compared to that in the bare cation- $\pi$  system. For example, the cation- $\pi$  distance



**Figure 3.** Geometrical parameters of bare and solvated  $\text{Mg}-\pi$  complexes obtained at B3LYP/6-31G(d,p) (normal) and MP2/6-311+G(d,p) (bold) levels of theory. Bond lengths are in angstroms.

in  $\text{Li}-\pi-\text{W}$  is 1.855 Å; this is 0.047 Å shorter than the cation– $\pi$  distance in bare (without solvent)  $\text{Li}-\pi$  complex. However, increasing the number of water molecules near the benzene further shortens the cation– $\pi$  distance. The shortest cation– $\pi$  distance (1.779 Å) is seen in the case of  $\text{Li}-\pi-5\text{Wa}$  complex, which contains five water molecules; out of these, four are connected to benzene protons through C–H…O hydrogen bonding and the fifth one is underneath the plane of benzene (see Figure 1). Expectedly, if water molecules directly coordinate with  $\text{Li}^+$  ion, then the cation– $\pi$  distance is elongated. For some of the considered complexes in this study, water molecules are present all around the cation– $\pi$  system ( $\text{Li}-\pi-3\text{Wc}$ ,  $\text{Li}-\pi-4\text{Wa}$ ,  $\text{Li}-\pi-6\text{W}$ ,  $\text{Li}-\pi-9\text{Wc}$ , and  $\text{Li}-\pi-10\text{Wc}$ ). The complex  $\text{Li}-\pi-3\text{Wc}$  has the cation– $\pi$  distance more or less equal to that in the bare  $\text{Li}-\pi$  system (without solvent), whereas for the complexes  $\text{Li}-\pi-4\text{Wa}$ ,  $\text{Li}-\pi-6\text{W}$ ,  $\text{Li}-\pi-9\text{Wc}$ , and  $\text{Li}-\pi-10\text{Wc}$ , the cation– $\pi$  distance is longer than that in the bare  $\text{Li}-\pi$  system. Except for a few complexes ( $\text{Li}-\pi-\text{W}$  and  $\text{Li}-\pi-4\text{W}$ ), it is observed that water molecules form a C–H…O (bridge) type of hydrogen bonding between the C–H of benzene and the oxygen atom of the water molecule. Earlier studies on benzene solvation reported no complexes having a C–H…O type hydrogen bonding,<sup>37</sup> however, the current study reports solvated cation– $\pi$  complexes that have a C–H…O type of hydrogen bonding between benzene and water. Thus, the presence of a metal ion ( $\text{Li}^+$ ,  $\text{K}^+$ , or  $\text{Mg}^{2+}$ ) may induce benzene protons to form a C–H…O type of hydrogen bonding. Earlier studies<sup>38</sup> clearly indicated that the range of C–H…O bond

length is 2.5–3.0 Å. The C–H…O interactions are confirmed with the bond critical points in topological AIM analysis. This has been discussed in AIM analysis in the subsequent section. The complexes  $\text{Li}-\pi-\text{W}$ ,  $\text{Li}-\pi-4\text{W}$ , and  $\text{Li}-\pi-6\text{W}$  are found to be first-order saddle points on the potential energy surface. For some complexes, water molecules are arranged in tetrahedral ( $\text{Li}-\pi-4\text{W}$ ), square planar ( $\text{Li}-\pi-4\text{Wa}$ ), and octahedral ( $\text{Li}-\pi-6\text{W}$ ) shape around the cation– $\pi$  system. For  $\text{Li}^+$  complexes, a maximum of three water molecules around the cation ( $\text{Li}^+$ ), and ten water molecules around the complete  $\text{Li}-\pi$  system, are observed in the current study. Geometrical parameters of all  $\text{K}^+$  complexes are depicted in Figure 2 and Figure 2S. From the bare  $\text{K}-\pi$  system to solvated complexes, a clear shortening of the cation– $\pi$  distance is observed. The shortest cation– $\pi$  distance is seen in  $\text{K}-\pi-4\text{Wa}$  (2.765 Å) complex. However, this complex is a higher order saddle point on the potential energy surface. Expectedly, as the ' $m$ ' value increases, the cation– $\pi$  distance lengthens. Comparison of the relative shortening of cation– $\pi$  distances for  $\text{Li}^+$  and  $\text{K}^+$  complexes reveals that  $\text{K}^+$  complexes have a higher reduction in cation– $\pi$  distance in the presence of solvent molecules near the  $\pi$  system. However, most of the  $\text{K}^+$  complexes with  $n = 1-5$  are found to be higher order saddle points on the potential energy surface. On the other hand,  $\text{K}-\pi$  solvation produces complexes up to the addition of eight water molecules around  $\text{K}^+$  ( $m = 8$ ). Similar complexes are not seen for  $\text{Li}^+$ ; a few complexes with  $m > 2$  are found, but they are not minima on the potential energy surface.

**TABLE 1: Counterpoise Corrected Interaction Energies  $\Delta E_1$  and  $\Delta E_2$  (in kcal/mol) for B3LYP and MP2 Methods**

complex	B3LYP/6-311++G(d,p) <sup>a</sup>	MP2(FULL)/6-311++G(d,p) <sup>a</sup>	$\Delta E_1$	$\Delta E_2$
Li- $\pi$	37.77	-	35.41	-
Li- $\pi$ -W	45.57	6.26	42.87	6.03
Li- $\pi$ -Wa	45.60	6.93	42.83	6.92
Li- $\pi$ -2W	35.46	5.23	34.81	5.39
Li- $\pi$ -2Wa	52.81	13.74	49.93	13.75
Li- $\pi$ -2Wb	52.70	13.11	49.87	13.13
Li- $\pi$ -2Wc	35.41	5.75	34.73	5.90
Li- $\pi$ -3W	23.85	4.26	25.47	4.46
Li- $\pi$ -3Wa	59.68	19.85	56.75	19.88
Li- $\pi$ -3Wb	41.53	11.40	40.82	11.66
Li- $\pi$ -3Wc	41.48	10.98	40.80	11.23
Li- $\pi$ -3Wd	59.70	20.52	56.75	20.55
Li- $\pi$ -4W	15.79	3.56	18.66	3.76
Li- $\pi$ -4Wa	47.38	16.76	46.71	17.10
Li- $\pi$ -4Wb	66.24	26.93	63.22	26.98
Li- $\pi$ -4Wc	66.32	26.42	63.31	26.47
Li- $\pi$ -4Wd	47.44	17.17	46.71	17.51
Li- $\pi$ -5W	52.92	13.74	52.21	23.07
Li- $\pi$ -5Wa	72.71	21.07	69.65	33.09
Li- $\pi$ -5Wb	55.14	22.66	52.14	13.70
Li- $\pi$ -5Wc	62.80	33.01	59.76	21.11
Li- $\pi$ -6W	58.37	27.70	57.67	28.18
Li- $\pi$ -6Wa	63.06	20.83	59.95	20.67
Li- $\pi$ -6Wb	49.09	17.27	48.26	17.71
Li- $\pi$ -7W	65.38	22.98	62.15	22.95
Li- $\pi$ -8W	41.21	18.12	39.60	17.07

<sup>a</sup> Single point calculations on B3LYP/6-31G(d,p)-optimized geometries.

Figure 3 and Figure S3 show the geometrical parameters of solvated and bare Mg- $\pi$  complexes obtained at B3LYP/6-31G(d,p) and MP2/6-311+G(d,p) (for the complexes containing up to seven water molecules only) levels of theory. For Mg<sup>2+</sup>, considered complexes comprise up to eighteen water molecules around the metal ion. For some of the complexes, the solvent molecules come in between the metal and  $\pi$  system. The addition of up to ten water molecules around the Mg- $\pi$  system complexes will not disturb the Mg- $\pi$  intact. Depending on the number of water molecules around the system, cation- $\pi$  distances vary between 1.939 Å (Mg- $\pi$ ) and 6.960 Å (Mg- $\pi$ -18W). Similar to Li<sup>+</sup> complexes, the cation- $\pi$  distance in Mg<sup>2+</sup> complexes depend on the position of water molecules around the Mg- $\pi$  system. The shortest cation- $\pi$  distance is seen in the case of Mg- $\pi$ -5Wc, wherein four water molecules are present in the plane of the  $\pi$  system and the fifth one is underneath the  $\pi$  system. On the other hand, the cation- $\pi$  distance in Mg- $\pi$ -18W is 6.960 Å; this complex comprises all eighteen water molecules in the first and second solvation shells of the Mg<sup>2+</sup> ion. For the complex Mg- $\pi$ -18W, some of the water molecules present in the second solvation shell are connected to the carbon atoms of benzene through a O-H $\cdots$ C type of hydrogen bonding. The complex Mg- $\pi$ -9Wb has nine water molecules around the metal ion, four in first solvation shell, and five in second solvation shell. In this complex, Mg<sup>2+</sup> is slightly distorted from the centroid of the benzene. For the complex Mg- $\pi$ -10W, all ten water molecules present in the system form a hydrogen bonding network around the Mg- $\pi$  system. Expectedly, the complexes which have water molecules directly coordinated to metal ions are lower in energy than the complexes which contain water molecules near the  $\pi$  system.

**Interaction Energies.** Interaction energies ( $\Delta E_1$  and  $\Delta E_2$ ) are calculated as shown in Scheme 1 and compiled in Tables 1, 2, and 3.  $\Delta E_1$  is the interaction energy of a metal ion with  $\pi$  system, and  $\Delta E_2$  is through-space interaction energy of solvent

**TABLE 2: Counterpoise Corrected Interaction Energies  $\Delta E_1$  and  $\Delta E_2$  (in kcal/mol) for B3LYP and MP2 Methods**

complex	B3LYP/6-311++G(d,p) <sup>a</sup>	MP2(FULL)/6-311++G(d,p) <sup>a</sup>	$\Delta E_1$	$\Delta E_2$
K- $\pi$	16.21	-	17.15	-
K- $\pi$ -W	21.46	4.17	22.50	4.18
K- $\pi$ -Wa	21.54	5.55	22.48	5.57
K- $\pi$ -2W	18.22	3.69	19.61	3.78
K- $\pi$ -2Wa	26.81	10.99	27.74	11.05
K- $\pi$ -2Wb	26.74	9.69	27.77	9.74
K- $\pi$ -2Wc	18.28	4.97	19.58	5.06
K- $\pi$ -3W	14.76	3.25	16.68	3.36
K- $\pi$ -3Wa	22.95	9.69	24.29	9.85
K- $\pi$ -3Wb	31.85	15.25	32.86	15.34
K- $\pi$ -3Wc	32.01	16.65	32.96	16.75
K- $\pi$ -3Wd	22.75	8.59	24.20	8.75
K- $\pi$ -4W	11.89	2.91	14.29	3.00
K- $\pi$ -4Wa	37.22	22.82	38.18	22.97
K- $\pi$ -4Wb	10.08	-	12.06	-
K- $\pi$ -4Wc	27.50	13.53	28.96	13.74
K- $\pi$ -4Wd	27.59	14.53	28.96	14.74
K- $\pi$ -4We	36.93	20.97	38.00	21.10
K- $\pi$ -5W	10.15	-	12.02	-
K- $\pi$ -5Wa	30.55	14.03	31.47	14.05
K- $\pi$ -5Wb	31.92	19.37	33.33	19.64
K- $\pi$ -6W	36.29	26.10	37.79	26.27
K- $\pi$ -6Wa	34.16	15.87	35.08	15.85
K- $\pi$ -7W	31.07	14.43	32.09	14.08
K- $\pi$ -8W	4.34	-	7.41	-
K- $\pi$ -8Wa	27.11	13.83	28.71	13.89
K- $\pi$ -8Wb	25.10	12.20	27.10	12.55
K- $\pi$ -9W	18.46	4.23	19.31	4.05
K- $\pi$ -12W	4.07	-	-	-
K- $\pi$ -18W	6.45	-	-	-

<sup>a</sup> Single point calculations on B3LYP/6-31G(d,p)-optimized geometries.

molecules present near the  $\pi$  system with the metal ion. Because the interaction energy trends obtained at the B3LYP/6-311++G(d,p)//B3LYP/6-31G(d,p) level are identical to those at the MP2/6-311++G(d,p)//B3LYP/6-31G(d,p) level, the discussion will center on the results of the MP2(FULL)/6-311++G(d,p)//B3LYP/6-31G(d,p) level. The complexes which have the highest metal- $\pi$  interaction energy ( $\Delta E_1$ ) are chosen and compared with the results of our previous work.<sup>27</sup> The plots are available in Figure 4 for Li<sup>+</sup>, K<sup>+</sup>, and Mg<sup>2+</sup> complexes. From the plots shown in Figure 4a, 4b, and 4c, it is clear that the position of water molecules in the vicinity of cation- $\pi$  complex plays an important role in altering the cation- $\pi$  interaction energy. Suppose that if water molecules are directly coordinated to the metal ion, the interaction energy decreases gradually with the increase in number of water molecules (if  $m \geq 1$ ). On the other hand, if water molecules are present near the  $\pi$  system (if  $n \geq 1$ ), interaction energy increases with the number of water molecules.

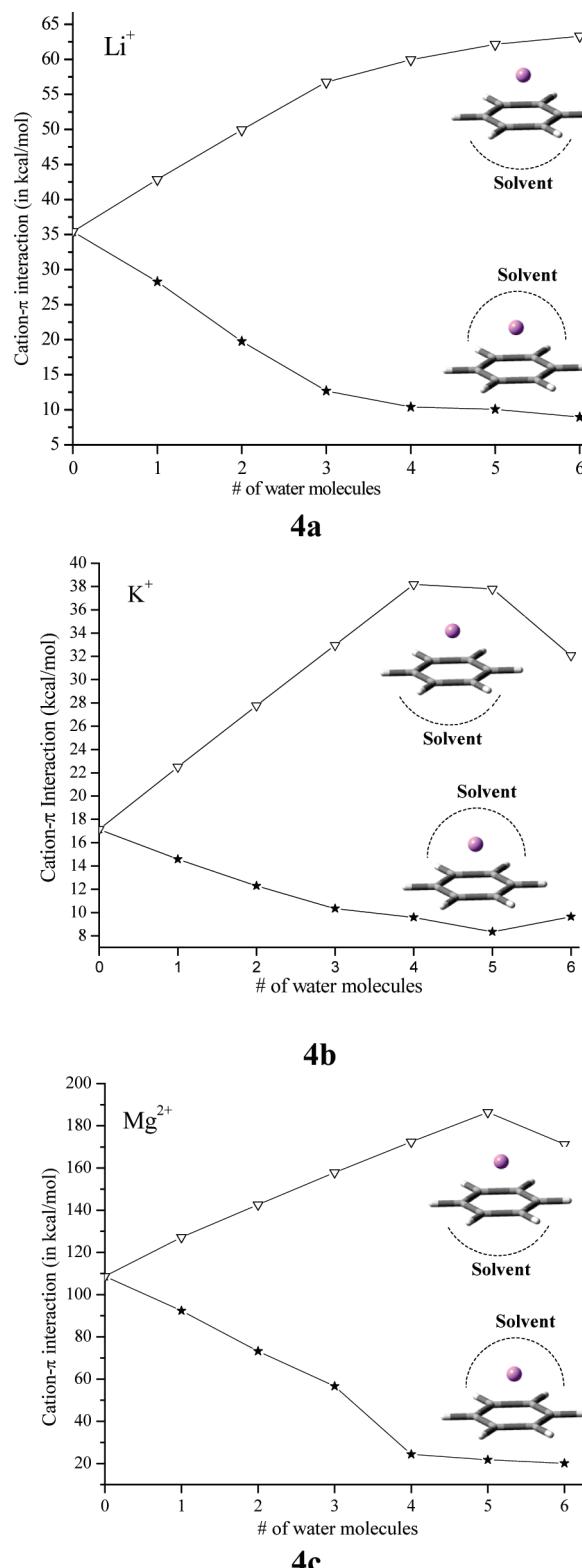
A quick perusal of interaction energies of these complexes reveals that the presence of the metal ion enhances the benzene protons to interact with solvent molecules through C-H $\cdots$ O hydrogen bonding; consequently, the cation- $\pi$  interaction energy gets strengthened. By taking the cation- $\pi$  interaction energy of a bare cation- $\pi$  system (without solvent) as reference, deviation of cation- $\pi$  interaction energies in the presence of solvent molecules was plotted. The plots for Li<sup>+</sup>, K<sup>+</sup>, and Mg<sup>2+</sup> complexes are depicted in Figure 5. From Figure 5 it can be understood that some of the complexes fall below the reference line, and some of them are above the reference line. Figure 5a, 5c, and 5e shows the deviation of  $\Delta E_1$  with respect to bare cation- $\pi$  interaction energy for all Li<sup>+</sup>, K<sup>+</sup>, and Mg<sup>2+</sup> complexes. To evaluate the effect of metal-water interaction on cation- $\pi$  interaction, through-space interaction energy ( $\Delta E_2$ )

**TABLE 3: Counterpoise Corrected Interaction Energies  $\Delta E_1$  and  $\Delta E_2$  (in kcal/mol) for B3LYP and MP2 Methods**

complex	B3LYP/6-311++G(d,p) <sup>a</sup>		MP2(FULL)/6-311++G(d,p) <sup>a</sup>	
	$\Delta E_1$	$\Delta E_2$	$\Delta E_1$	$\Delta E_2$
Mg- $\pi$	117.24	-	108.76	-
Mg- $\pi$ -W	136.76	27.57	127.19	14.40
Mg- $\pi$ -Wa	135.99	27.35	126.27	15.08
Mg- $\pi$ -2W	113.74	15.23	108.46	12.86
Mg- $\pi$ -2Wa	151.92	47.53	142.03	29.85
Mg- $\pi$ -2Wb	152.64	47.40	142.69	29.37
Mg- $\pi$ -2Wc	113.02	15.74	107.78	13.53
Mg- $\pi$ -3W	88.81	11.07	87.56	11.22
Mg- $\pi$ -3Wa	168.15	63.60	157.89	43.97
Mg- $\pi$ -3Wb	127.32	29.32	121.84	26.62
Mg- $\pi$ -3Wc	127.85	28.88	122.36	26.21
Mg- $\pi$ -3Wd	167.83	62.65	157.29	44.62
Mg- $\pi$ -4W	100.07	22.82	98.56	21.76
Mg- $\pi$ -4Wa	68.02	9.97	69.70	9.82
Mg- $\pi$ -4Wb	162.60	57.53	151.70	31.19
Mg- $\pi$ -4Wc	181.93	79.06	171.54	59.07
Mg- $\pi$ -4Wd	182.86	78.36	172.39	58.60
Mg- $\pi$ -4We	141.15	42.66	135.54	40.03
Mg- $\pi$ -4Wf	141.52	42.33	135.89	39.24
Mg- $\pi$ -5W	170.56	56.38	159.15	37.30
Mg- $\pi$ -5Wa	190.65	87.85	179.49	58.67
Mg- $\pi$ -5Wb	154.02	52.37	148.27	52.43
Mg- $\pi$ -5Wc	197.04	92.52	186.37	73.77
Mg- $\pi$ -6W	161.81	58.27	155.44	52.84
Mg- $\pi$ -6Wa	182.61	78.38	171.34	50.04
Mg- $\pi$ -6Wb	167.07	66.77	161.23	65.36
Mg- $\pi$ -7W	132.74	48.83	130.77	48.54
Mg- $\pi$ -7Wa	93.76	29.91	95.26	30.24
Mg- $\pi$ -7Wb	188.47	85.73	177.40	56.16
Mg- $\pi$ -8W	19.67	-	24.63	-
Mg- $\pi$ -8Wa	172.87	60.14	166.37	61.78
Mg- $\pi$ -8Wb	124.90	41.11	123.07	41.22
Mg- $\pi$ -9W	110.02	40.80	111.06	41.16
Mg- $\pi$ -9Wa	142.09	57.50	140.06	57.60
Mg- $\pi$ -9Wb	204.72	65.88	192.26	64.66
Mg- $\pi$ -9Wc	26.88	-	31.02	-
Mg- $\pi$ -12W	12.00	-	-	-
Mg- $\pi$ -15W	13.86	-	-	-
Mg- $\pi$ -18W	7.68	-	-	-
Mg- $\pi$ -19W	36.57	-	-	-

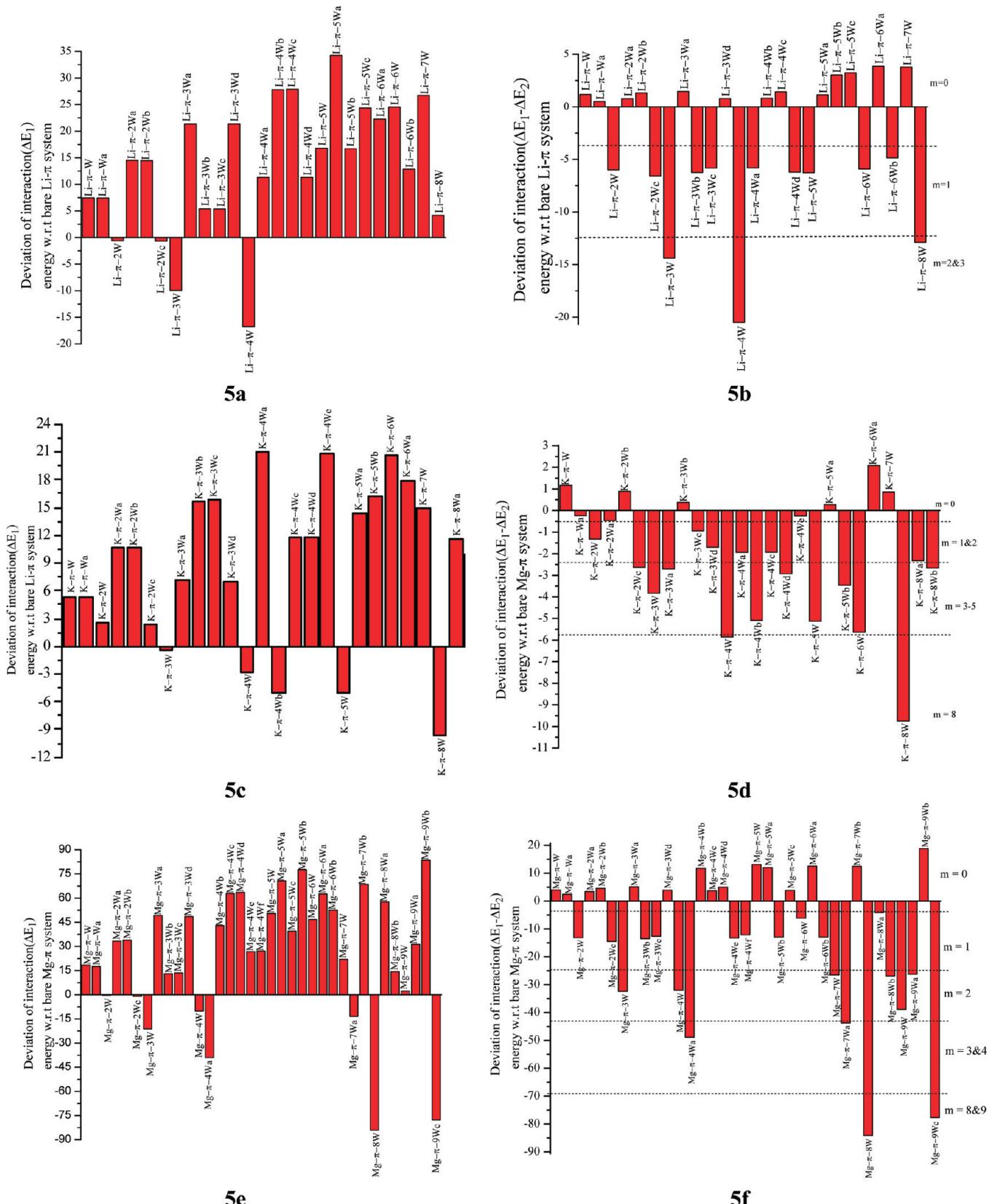
<sup>a</sup> Single point calculations on B3LYP/6-31G(d,p)-optimized geometries.

is deducted from  $\Delta E_1$  and the resultant values are also plotted.  $\Delta E_2$  values are also tabulated along with cation- $\pi$  interactions ( $\Delta E_1$ ) in Table 1, 2, and 3 for  $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$  complexes, respectively. Figure 5b, 5d, and 5f shows the deviation of ( $\Delta E_1 - \Delta E_2$ ) with respect to the bare cation- $\pi$  interactions for  $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$  ions. In plots 5b, 5d, and 5f (see Figure 5) different areas are separated with dotted lines; here 'm' is the number of water molecules attached to the metal ion (see Scheme 1). The  $m = 0$  region for  $\text{Li}-\pi$  complexes (plot 5b) shows that if there are no water molecules on the metal ion, the  $\text{Li}-\pi$  interaction energies strengthen by about 1–5 kcal/mol. If  $m = 1$ , the  $\text{Li}-\pi$  interaction is reduced by about 5–8 kcal/mol, and for  $m = 2$  and 3 the decrease in the  $\text{Li}-\pi$  interaction is 3- to 4-fold higher than that of  $m = 1$ . For  $\text{K}-\pi$  complexes, as the 'm' value increases, the decrease in  $\text{K}-\pi$  interaction energy is relatively lower compared to  $\text{Li}^+$  complexes. For example, in the case of  $\text{K}-\pi$ -8Wa the decrease in  $\text{K}-\pi$  interaction energy is about 2.5 kcal/mol, whereas the  $\text{Li}-\pi$  interaction energy of a similar complex of  $\text{Li}$  ( $\text{Li}-\pi$ -8W) is reduced about 13.5 kcal/mol. From plot 5d, it is clear that the increase in  $\text{K}-\pi$  interaction energy is about 1–3 kcal/mol, and the decrease in the  $\text{K}-\pi$  interaction energy is about 10.5 kcal/mol for highest 'm' value. In the case of  $\text{Mg}-\pi$  complexes (plot 5f), for different 'm' values the regions are separated more clearly. The complex  $\text{Mg}-\pi$ -8Wa has two water molecules on the metal ion, and the interaction energy is reduced by about



**Figure 4.** Variation of cation- $\pi$  interaction energy with the position of the solvent molecule in the vicinity of the cation- $\pi$  system.

5 kcal/mol. In this complex there are six water molecules present near benzene with a hydrogen bonding network. As we can see from the plot 5f, increasing the 'm' value decreases the cation- $\pi$  interaction significantly (25–30 kcal/mol). The current study clearly reports the complexes which have higher cation- $\pi$  interaction energy than that of the bare cation- $\pi$  complex. In the case of  $\text{Li}^+$  and  $\text{K}^+$  complexes the enhancement in cation- $\pi$  interaction energy is about 1–4 kcal/mol, whereas for  $\text{Mg}^{2+}$



**Figure 5.** Deviation of cation- $\pi$  interaction energy in the presence of solvent with respect to bare cation- $\pi$  (without solvent) at the MP2(FULL)/6-311++G(d,p)//B3LYP/6-31G(d,p) level. Plots 5a, 5c, and 5e show the deviation of  $\Delta E_1$  with respect to bare cation- $\pi$  interaction energy. Plots 5b, 5d, and 5f show the deviation of  $(\Delta E_1 - \Delta E_2)$  with respect to bare cation- $\pi$  interaction energy.

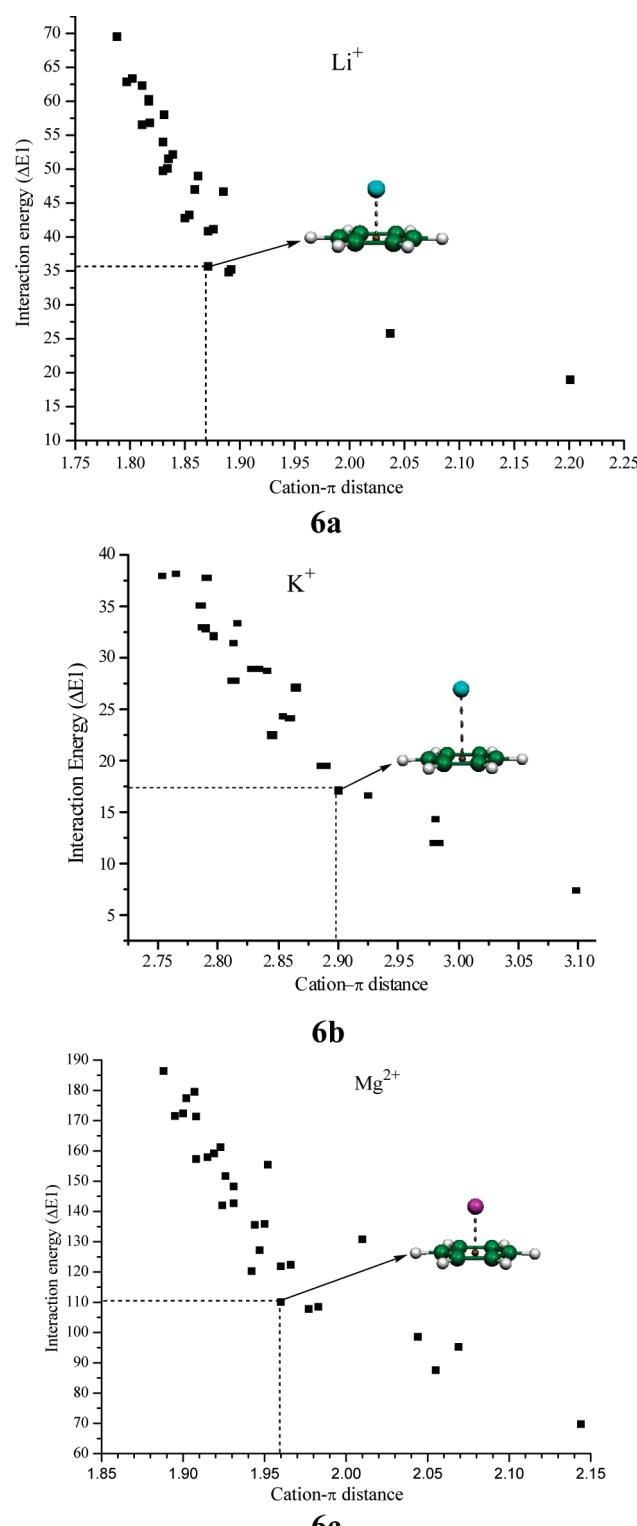
complexes, depending on the position of water molecules, the enhancement in the interaction energy goes up to 17.5 kcal/mol ( $Mg-\pi-9Wb$ ). It is observed that the increment in cation- $\pi$  interaction energy for  $Mg^{2+}$  complexes is 3–7 kcal/mol

higher than that of the corresponding  $Li^+$  and  $K^+$  complexes. Thus, the metal- $\pi$  interaction strongly depends on the charge and size of metal ion, and the position of the solvent molecules around the cation- $\pi$  system. Expectedly, the solva-

tion of the metal ion alone in the cation- $\pi$  system weakens the cation- $\pi$  interaction energy. However, the quantity of decrease depends on the number of water molecules directly coordinated to the metal ion. For example, the complex Li- $\pi$ -4W has three water molecules attached to the metal ion and a fourth present near the  $\pi$  system. The Li- $\pi$  interaction energy of this complex is 17 kcal/mol less than the Li- $\pi$  interaction energy of bare Li- $\pi$  system (without solvent). Results of K<sup>+</sup> complexes differ little from that of Li<sup>+</sup> and Mg<sup>2+</sup>. As the number of water molecules around the metal ion increases, Mg<sup>2+</sup> slowly distorts from the centroid of the  $\pi$  system (see Mg- $\pi$ -8W), whereas K<sup>+</sup> does not move from the centroid of the  $\pi$  system. On the other hand, the solvation of Li- $\pi$  system does not yield complexes with an '*m*' value greater than 3. From these observations it is clear that, compared to Li<sup>+</sup> and Mg<sup>2+</sup>, K- $\pi$  interaction is more competitive with K-water interaction. Interaction energies of solvated metal ion with the  $\pi$  system for the complexes (K<sup>+</sup> and Mg<sup>2+</sup>) containing 12, 15, 18, and 19 water molecules are estimated using the B3LYP/6-311++G(d,p) level and depicted in Tables 2 and 3. In all these complexes the metal ions are solvated with water molecules in their first and second solvation shells. Compared to bare metal- $\pi$  (without solvent) interaction energy, the solvated metal ion interaction energy with the  $\pi$  system is about 3–4 times lower for K<sup>+</sup> and 14 times lower for Mg<sup>2+</sup> complexes (M- $\pi$ -12W, M- $\pi$ -15W, M- $\pi$ -18W, and M- $\pi$ -19W; M = K<sup>+</sup> and Mg<sup>2+</sup>). It is also observed that this interaction is only due to the interaction of some of water molecules present in the first and second solvation shells of the metal ion with the  $\pi$  system. Thus, the current study shows that, depending on metal ion, if water molecules are directly coordinated to the metal ion, cation- $\pi$  interaction energies gets attenuated by about 70–80%.

Interaction energy values of K<sup>+</sup> complexes are consistently lower (1–2 kcal/mol) at B3LYP/6-311++G(d,p) than at MP2(FULL)/6-311++G(d,p), whereas for Li<sup>+</sup> and Mg<sup>2+</sup>, the MP2(FULL)/6-311++G(d,p) level produces interaction energies which are lower (1–3 kcal/mol) than that for B3LYP/6-311++G(d,p). The current authors have recently reported the benchmark analysis on metal ion (Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Be<sup>2+</sup>, Mg<sup>2+</sup>, and Ca<sup>2+</sup>) solvation using MP2 and B3LYP levels.<sup>39</sup> This study shows that B3LYP and MP2 performs equally good for K<sup>+</sup> solvation, and for other alkali and alkaline earth metals, the MP2 method with a triple  $\zeta$  basis set has shown promising results. Similarly, the observed differences in interaction energies of the current study shows that for K<sup>+</sup> the results are competitive at B3LYP and MP2, whereas for Li<sup>+</sup> and Mg<sup>2+</sup> MP2 seems to be good. It is well-known that basis set super position errors are relatively minimal at B3LYP, compared to MP2. The current study displays similar trends in interaction energies at B3LYP and MP2. Thus, BSSE values at MP2 do not change observed trends (or magnitude) of cation- $\pi$  interaction energies.

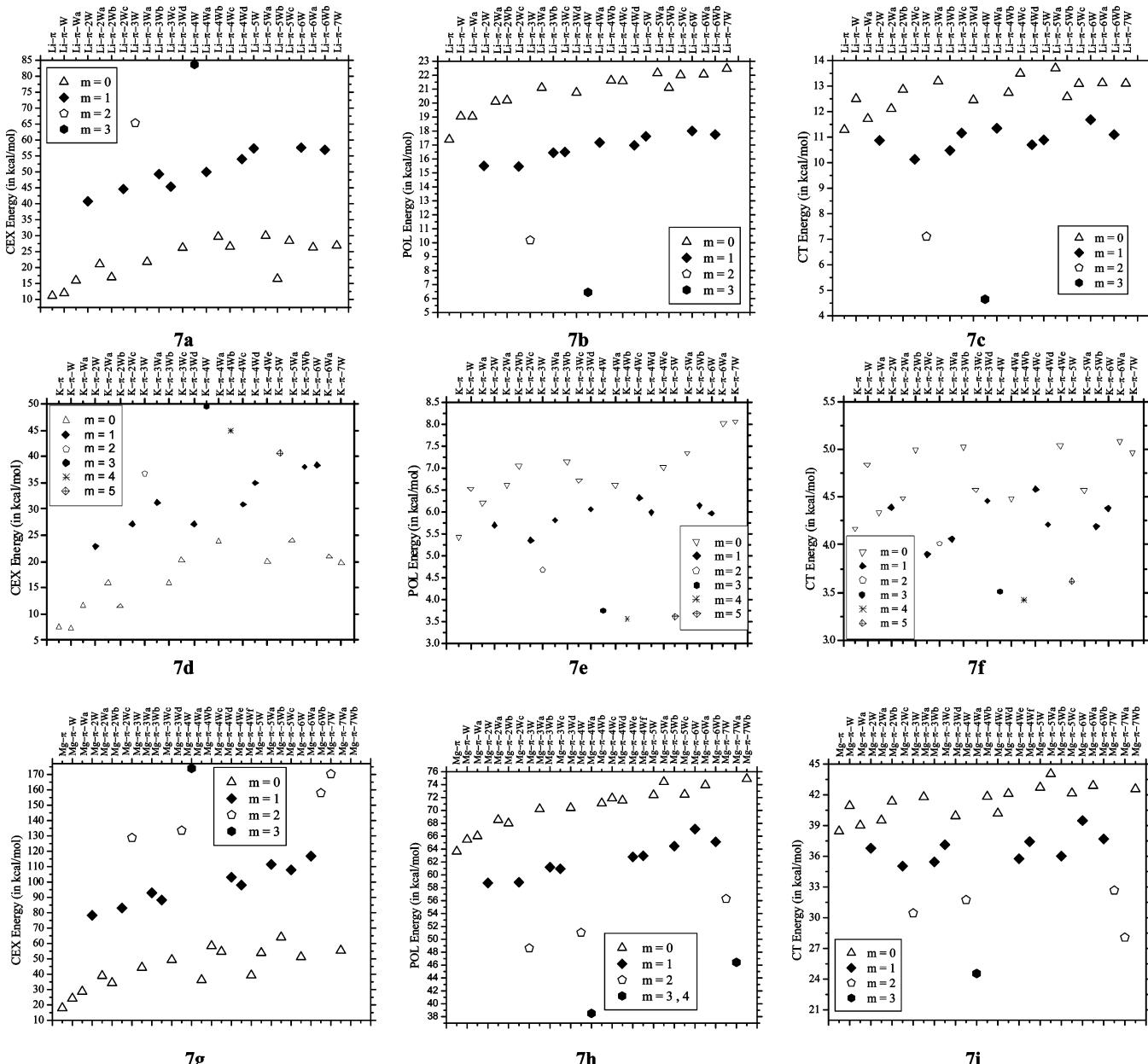
Through-space interaction energy ( $\Delta E_2$ ) values obtained at various levels are listed in Tables 1, 2, and 3 for Li<sup>+</sup>, K<sup>+</sup>, and Mg<sup>2+</sup>, respectively. Expectedly, as the number of water molecules increases ( $m \geq 1$ ) on the metal ions, through-space interaction energy gets lower. We know that the water molecules which directly coordinate metal ions neutralize the charge of the metal ions, which automatically suppresses the interaction of metals with either the  $\pi$  system or with other water molecules present near the  $\pi$  system. On the other hand, if we keep the number of water molecules on the metal as zero ( $m = 0$ ) and increase the number of water molecules near benzene ( $n = 1$ ,



**Figure 6.** Correlation of interaction energy (in kcal/mol) [MP2(FULL)/6-311++G(d,p)//B3LYP/6-31G(d,p)] versus cation- $\pi$  distance (in Å) [B3LYP/6-31G(d,p)]. Dotted line indicates bare cation- $\pi$  complex (without solvent).

2, 3..., etc.),  $\Delta E_2$  increases by about 10–15 kcal/mol for each water molecule added.

Figure 6 shows the correlation of cation- $\pi$  interaction ( $\Delta E_1$ ) versus cation- $\pi$  distance. From the plot it is clear that the cation- $\pi$  distance is inversely proportional to the cation- $\pi$  interaction energy. For the sake of clarity, the snapshot of the bare cation- $\pi$  system was provided in the correlation graph. The discussions in previous sections suggested that the position

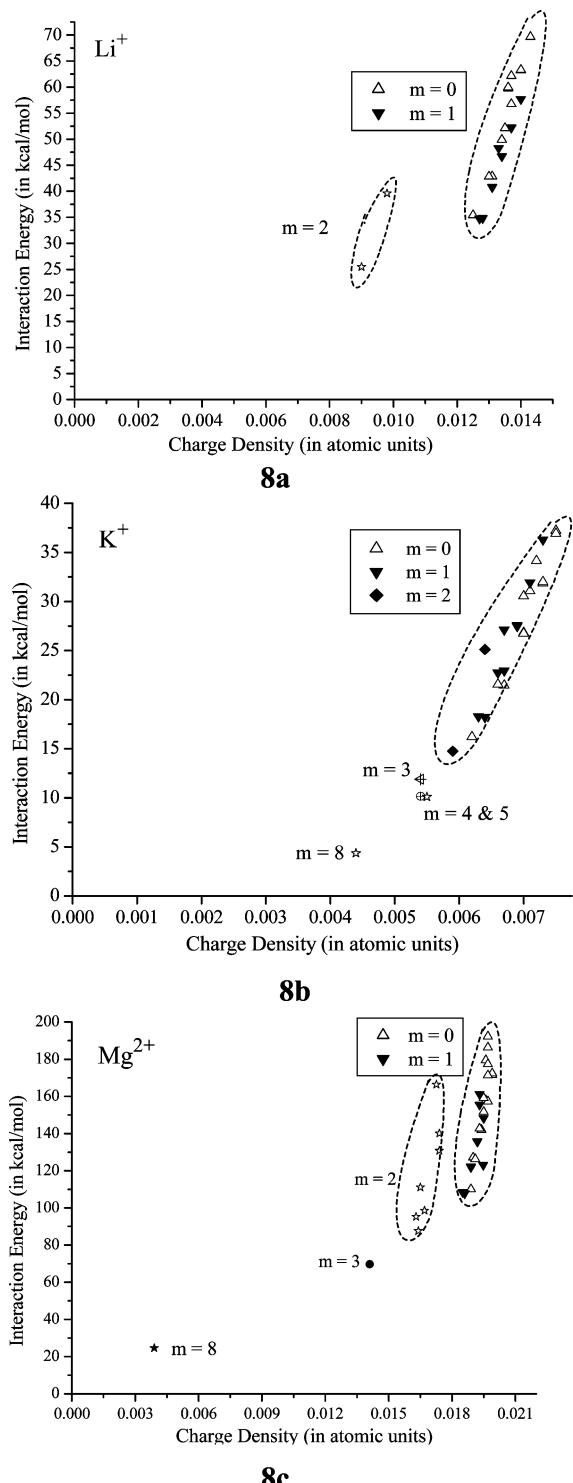


**Figure 7.** Correlation of energy components (CEX, POL, and CT) in RVS analysis with respect to different cation- $\pi$  complexes. Polarization and charge transfer energies are taken only for benzene. Plots 7a, 7b, and 7c are for  $\text{Li}^+$ , the plots 7d, 7e, and 7f are for  $\text{K}^+$ , and the plots 7g, 7h, and 7i are for  $\text{Mg}^{2+}$  complexes.

of water molecules plays an important role in altering the cation- $\pi$  distance. Increasing the number of water molecules near the metal ions increases the cation- $\pi$  distance. For the three metals considered if  $m > 1$ , then the cation- $\pi$  distance is similar or higher than that of the bare cation- $\pi$  complex. On the other hand if  $m = 0$  and  $n > 1$ , then the cation- $\pi$  distance is shorter than that of the bare cation- $\pi$  system (without solvent). The complexes having the water molecules near the metal ion are found to be more stable than the complexes wherein the solvent molecules are present around the whole cation- $\pi$  system.

**Reduced Variational Space (RVS) Analysis.** Energy decomposition analysis is performed to inspect the contribution of various energy components to total interaction energy of the cation- $\pi$  complex. Reduced variational space analysis for many fragment systems are performed as implemented in the GAMESS program package.<sup>34</sup> Correlation plots are made by taking the CEX (coulomb exchange) of all systems, POL (polarization),

and CT (charge transfer) of benzene against different complexes. The plots are shown in Figure 7. For the sake of clarity, different symbols are given to the complexes with different ' $m$ ' values. From plots 7a, 7d, and 7g one can see that a series of complexes fall within the range of 10–30 kcal/mol for  $\text{Li}^+$  complexes, 5–20 kcal/mol for  $\text{K}^+$  complexes, and 20–60 kcal/mol for  $\text{Mg}^{2+}$  complexes. From the plots it is clear that all these complexes have zero water molecules on the metal atom ( $m = 0$ ). Another series of complexes ( $m = 1$ ) fall within the range of 30–60 kcal/mol for  $\text{Li}^+$  complexes, 20–40 kcal/mol for  $\text{K}^+$  complexes, and 60–120 kcal/mol for  $\text{Mg}^{2+}$  complexes. These results clearly indicate that the energy term CEX represents a major contribution of metal–water interaction than to the metal– $\pi$  interaction. Dissimilar results are observed in the case of other energy components such as POL and CT. Complexes that have two or three water molecules on metal ions have minimum contributions to the total interaction energy. For  $\text{Li}^+$  complexes when  $m = 0$ , the contribution of the POL energy term is about 17–23

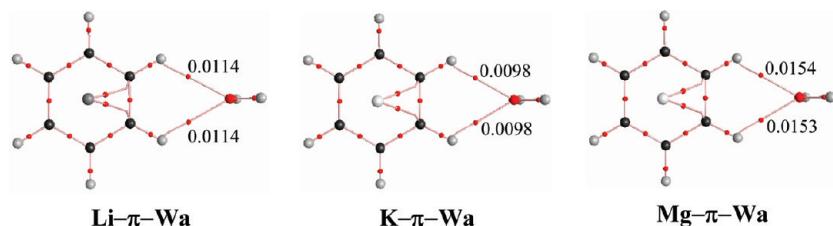


**Figure 8.** Correlation of MP2/6-311++G(d,p) interaction energy ( $\Delta E_1$ ) versus the charge density at cage critical points ( $\rho$ ) for  $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$  complexes.

kcal/mol. Contribution of POL energy in the case of  $\text{K}^+$  is about 6–8 kcal/mol for  $m = 1$  and it is less than 5 kcal/mol for higher ‘ $m$ ’ values. For  $\text{Mg}^{2+}$  complexes, the contribution of POL energy is about 65–75 kcal/mol. If we compare the contributions of POL and CT terms to total interaction energy, the contribution of the POL term is 2-fold to the CT term. From these results it is clear that the energy terms POL and CT have more contribution to the metal– $\pi$  interaction energy than to the metal–water interaction energy. The CEX term in RVS analysis is the sum of the electrostatic and Pauli exchange energies. Thus, it is important to note that the significant Pauli repulsion term is set to offset the electrostatic attractions significantly.

**AIM Analysis.** To evaluate the nature of cation– $\pi$  interactions and C–H $\cdots$ O type hydrogen bonding, topological analysis of the electron density distribution within Bader’s atoms in molecules theory (AIM) was performed. Variation of charge density at cage critical points with respect to interaction energy ( $\Delta E_1$ ) is given in Figure 8. The cage critical points (3, +3) are characterized by a rank of 3 and a signature of +3, and they are located in the interior of a volume enclosed by two or more ring surfaces. The cage critical point (3, +3) is a local minimum with electron density rising in all three directions of space. For the characterization of C–H $\cdots$ O hydrogen bonding, the electron density at bond critical points was taken into account. According to AIM theory, any chemical bond including hydrogen bonding is characterized by the presence of so-called bond critical points (BCP). This means that the electron density at this point has a minimal value along the line of the bond and a maximal value in two orthogonal directions.

We can see that the charge densities at cage critical points for the solvated complexes are directly proportional to its interaction energy. For all three metals considered, different areas are separated with different symbols in Figure 8. As we can see from the plots for  $m = 0, 1$ , and  $2$ , higher charge densities are found at cage critical points. As the ‘ $m$ ’ value increases, the charge densities are lowered. If we compare the results of  $\text{Li}^+$  and  $\text{Mg}^{2+}$  with  $\text{K}^+$ , in the case of  $\text{K}^+$ , complexes with  $m = 0, 1$ , and  $2$  are mixed in the same region, whereas for  $\text{Li}^+$  and  $\text{Mg}^{2+}$ , only the complexes with  $m = 0$  and  $1$  are mixed and the charge densities of the complexes with  $m = 2$  are clearly separated in the plots. These results clearly indicate that the solvation of  $\text{K}^+$  with one or two water molecules does not reflect much on the  $\text{K}^+–\pi$  interaction energies. For the complexes having ten water molecules ( $M-\pi-10W$ ), because of their complex structures we could not estimate the cation– $\pi$  interactions. The cage critical points of these complexes are much lower compared to other similar complexes considered. The molecular graphs obtained from AIM theory for cation– $\pi$  complexes solvated with one water molecule are given in Figure 9. Though we have several complexes having C–H $\cdots$ O type of hydrogen bonding, we have taken only one complex for each metal to simplify the discussion. For hydrogen bonding, the electron density ( $\rho$ ) at BCP should be between 0.002 and 0.035.



**Figure 9.** Molecular graph obtained from AIM theory for cation– $\pi$  complexes solvated with one water molecule. The electron charge density (in atomic units) at bond critical points of C–H $\cdots$ O hydrogen bonding obtained at the B3LYP/6-31G(d,p) level.

All charge density values shown in Figure 9 are clearly within the range of hydrogen bonding. This observation confirms the C-H $\cdots$ O type of hydrogen bonding in the presence of metal cation ( $\text{Li}^+$ ,  $\text{K}^+$ , or  $\text{Mg}^{2+}$ ).

## Summary

The current study demonstrates how the aqueous solvent can alter the subtle (cation- $\pi$ , cation =  $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$ ) interactions. The cation- $\pi$  interaction energy is sensitive to the site of solvation of cation- $\pi$  systems, and size and charge of the metal ion. Compared to  $\text{Mg}^{2+}$  and  $\text{Li}^+$ ,  $\text{K}-\pi$  interaction energies are more competitive with metal-water interaction energies. The approach of the water molecules determines how the cation- $\pi$  strengths are altered upon solvation, the strength is attenuated when water molecules selectively surround the metal ion while it is exalted upon selectively solvating the  $\pi$  system. Thus, solvation of metal ions lowers the interaction energy and causes lengthening of the cation- $\pi$  distance, while when water molecules selectively approach the  $\pi$  system a starkly contrasting effect results, i.e., exaltation of interaction energy and shortening of the cation- $\pi$  distance. Although the qualitative observation is virtually similar in the three cations ( $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$ ) studied, the solvent-assisted exaltation and attenuation of the cation- $\pi$  strength depending on the face of metal ion attack is more dramatic in the case of  $\text{K}^+$  ion. The trends of geometrical parameters obtained at B3LYP/6-31G(d,p) and MP2/6-311+G(d,p) levels shows that the conformational search for model systems can be performed with the more economical B3LYP method. RVS analysis indicates that the major contributions to the cation- $\pi$  interaction energy are coming from the POL and CT energy terms of benzene. The topological analysis of electron density distribution within Bader's atoms in molecules theory (AIM) shows that, depending on the site of solvation, cation- $\pi$  interaction energy becomes stronger or weaker. The electron density values at BCPs confirm the C-H $\cdots$ O bridge type hydrogen bonding between the oxygen atom of water and the C-H group of benzene.

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**Supporting Information Available:** Geometrical parameters of  $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$  complexes at B3LYP/6-31G(d,p) and MP2/6-311+G(d,p) levels, O-H stretching frequencies of water molecules in  $\text{Li}^+$ ,  $\text{K}^+$ , and  $\text{Mg}^{2+}$  complexes at the B3LYP/6-31G(d,p) level, interaction energies calculated at the MP2/6-311+G(d,p)//MP2/6-311+G(d,p) level, and the total energies of all complexes at MP2 and B3LYP levels. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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