

# Conformational analysis of alkali metal complexes of aspartate dianion and their interactions in gas phase

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## Abstract

The gas-phase geometry optimizations of mono and dinuclear complexes of dianionic species of aspartic acid,  $\text{asp}^{2-}$  with lithium, sodium and potassium cations were carried out using density functional calculation at the B3LYP/6-311++G(d,p) level. The metal ion affinities (MIAs) of  $\text{asp}^{2-}$  species and its complexes  $[\text{asp-M}]^-$ ,  $M = \text{Li}^+$ ,  $\text{Na}^+$  and  $\text{K}^+$  were determined using the vibrational frequency calculations at the same level of theory. The most stable complex conformer for aspartate complexes with  $\text{Li}^+$ ,  $\text{Na}^+$  and  $\text{K}^+$  alkali cations were found as a tri-coordinated form. All complexations of  $[\text{asp-M}]^-$  and  $[\text{asp-M}_2]$  complexes were found to be exothermic reactions. Relative bond distances between the alkali metal cation  $M^+$  and the binding atoms of aspartate ion in  $[\text{asp-M}]^-$  and  $[\text{asp-M}_2]$  complexes are in decreasing order:  $\text{K}^+ > \text{Na}^+ > \text{Li}^+$ .

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**Keywords:** Complexation; Aspartate dianion; Alkali cation; Lithium; Sodium; Potassium; Metal ion affinity

## 1. Introduction

The metalation of amino acids, peptides and nucleic acids plays a crucial role in several biological phenomena [1,2]. In particular, alkali metal cations: lithium, sodium and potassium have been found in biological systems. The cations interacting with proteins and peptides to control structural and regulating properties [3–6], transport process through transmembrane channels [7,8] were widely studied. The location of different metal ions in the hydrophobic cavity of a protein depends preferentially on the relative intrinsic bond strength between the metal ions and the various possible metal binding sites. The structures and energetics of gas phase cationized-amino acids have been investigated by a variety of methods. For instance, ion mobility [9,10], black body infrared radiative dissociation (BIRD) [11–16], kinetic method [17,18], H/D exchange [19,20], guided ion beam mass spectrometry [21–24], spectroscopy [25–29] and computational studies [30–41]. Not only cationized-amino acids but also cationized-peptide derivatives [42–48] have also been determined.

However, many studies have been focused on cationized adducts of neutral and zwitterionic forms of amino acids. The conformational preference between salt-bridge (SB) and charge solvated (CS) structures has been compared and discussed. Naturally, amino acids possess not only the zwitterionic form but also cationic and anionic forms in a wide pH range from acidic to basic aqueous solution. As well as aspartic acid, the conformational equilibria of cationic ( $\text{H}_3\text{asp}^+$ ), zwitterionic ( $\text{H}_2\text{asp}$ ), anionic ( $\text{Hasp}^-$ ) and dianionic ( $\text{asp}^{2-}$ ) species were presented within a wide pH range.

The conformational structures of various ionic species of gas-phase aspartic acid have been theoretically determined [49]. The lithium and sodium affinities of aspartic acid have been experimentally determined by Feng et al. [50] and Gapeev and Dunbar [37], respectively. The vanadium(III) complexes of various species of aspartic acid have been determined by Bukietyńska et al. [51]. Those cationized-structures were still unclear. The single crystal structures of aspartate dianion ( $\text{asp}^{2-}$ ) complexes with zinc(II), nickel(II) and copper(II) have been determined [52–54]. There are still no studies on  $\text{asp}^{2-}$  complexes with alkali cations in the literature. Thus, the present work is to elucidate the binding modes of interactions between alkali cations:  $\text{Li}^+$ ,  $\text{Na}^+$  and  $\text{K}^+$  and the aspartate dianion by means of a theoretical approach. The mononuclear  $[\text{asp-M}]^-$  as well as binuclear  $[\text{asp-M}_2]$  complexes can be expected.

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The conformational preferences and also metal ion affinities (MIA) of both types of complexes will be determined. Based on the gas phase conformations of  $\text{asp}^{2-}$  [49], the conformational changes between free and complex forms of the aspartate ligand will be also determined. The result is expected to predict the binding behavior of the aspartate ions or the side-chain aspartate at the C-terminus to these alkali cations.

## 2. Computational details

The geometrical structures of  $[\text{asp-M}]^-$  and  $[\text{asp-M}_2]$  ( $M = \text{Li}^+, \text{Na}^+, \text{K}^+$ ) were optimized using density functional theory (DFT). The DFT calculations have been performed with Becke's three parameter hybrid density functional using the Lee, Yang and Parr correlation functional (B3LYP) [55,56]. The B3LYP/6-311++G(d,p) level of theory has been employed for geometry optimizations of all complexes and their components. Counterpoise corrections were applied for energy improvement by eliminating the basis set superposition error (BSSE) [57,58] for the most stable complex conformers. All computations were performed with the GAUSSIAN 03 program [59]. The MOLDEN 4.2 program [60] was utilized to display the molecular structure, monitor the geometrical parameters and observe the molecular geometry convergence via the Gaussian output files. The molecular graphics of all related species were generated with the MOLEKEL 4.3 program [61].

As metal ion affinity (MIA) is defined as the negative of the reaction enthalpy ( $\Delta H^\circ$ ), the MIA for the complexations of  $[\text{asp-M}]^-$  and  $[\text{asp-M}_2]$  described by Eqs. (1) and (2) were computed using the following formulas.

$$\text{MIA}(1) = -[H_{[\text{asp-M}]^-}^\circ - (H_{\text{asp}^{2-}}^\circ + H_{M^+}^\circ)],$$

where the  $[\text{asp-M}]^-$  complex is formed from the  $\text{asp}^{2-}$  conformer as:



$$\text{MIA}(2) = -[H_{[\text{asp-M}_2]}^\circ - (H_{[\text{asp-M}]^-}^\circ + H_{M^+}^\circ)],$$

where the  $[\text{asp-M}_2]$  complex is formed from the  $[\text{asp-M}]^-$  complex conformer as:



As different complexes,  $[\text{asp-M}(p)]^-$  and  $[\text{asp-M}(q)]^-$  defined as the components based on the binding mode types p and q, the two possible MAI(2)s can therefore be evaluated from the following formulas:

$$\text{MIA}(2)_p = -[H_{[\text{asp-M}_2]}^\circ - (H_{[\text{asp-M}(p)]^-}^\circ + H_{M^+(q)}^\circ)] \quad (3)$$

$$\text{MIA}(2)_q = -[H_{[\text{asp-M}_2]}^\circ - (H_{[\text{asp-M}(q)]^-}^\circ + H_{M^+(p)}^\circ)] \quad (4)$$

The standard enthalpy  $\Delta H_{298}^\circ$  and Gibbs free energy changes  $\Delta G_{298}^\circ$  of complexation reactions were obtained by the thermodynamic analysis at 298 K, 1 atm. using the vibrational frequency calculations at the B3LYP/6-311++G(d,p) level of theory.

## 3. Results and discussion

The possible binding modes shown in Fig. 1 are defined as six binding types. As the binding mode is defined as the ratio of the number of metal ions ( $N_M$ ) to the number of binding sites of the ligand ( $N_L$ ), the  $N_M:N_L$  ratios are 1:1 for binding mode types I and II, 1:2 for types III, VI and V and 1:3 for type VI. For a dinuclear complex, the type of the binding mode is defined as a combination of the types of the mononuclear complexes (types

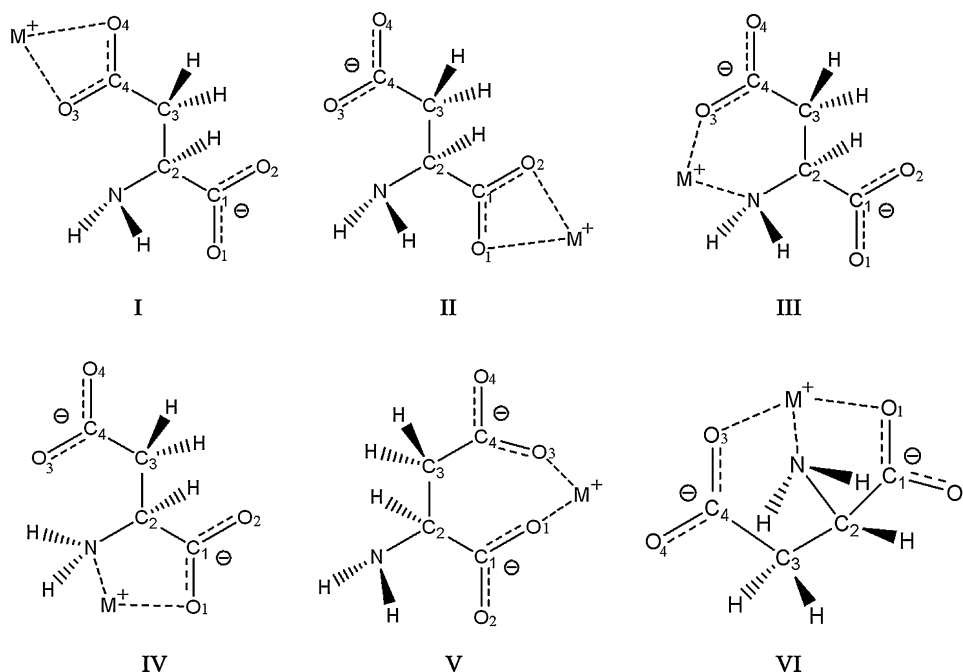


Fig. 1. The proposed possible sites for binding mode of interaction between cation and aspartate ( $\text{asp}^{2-}$ ) moiety.

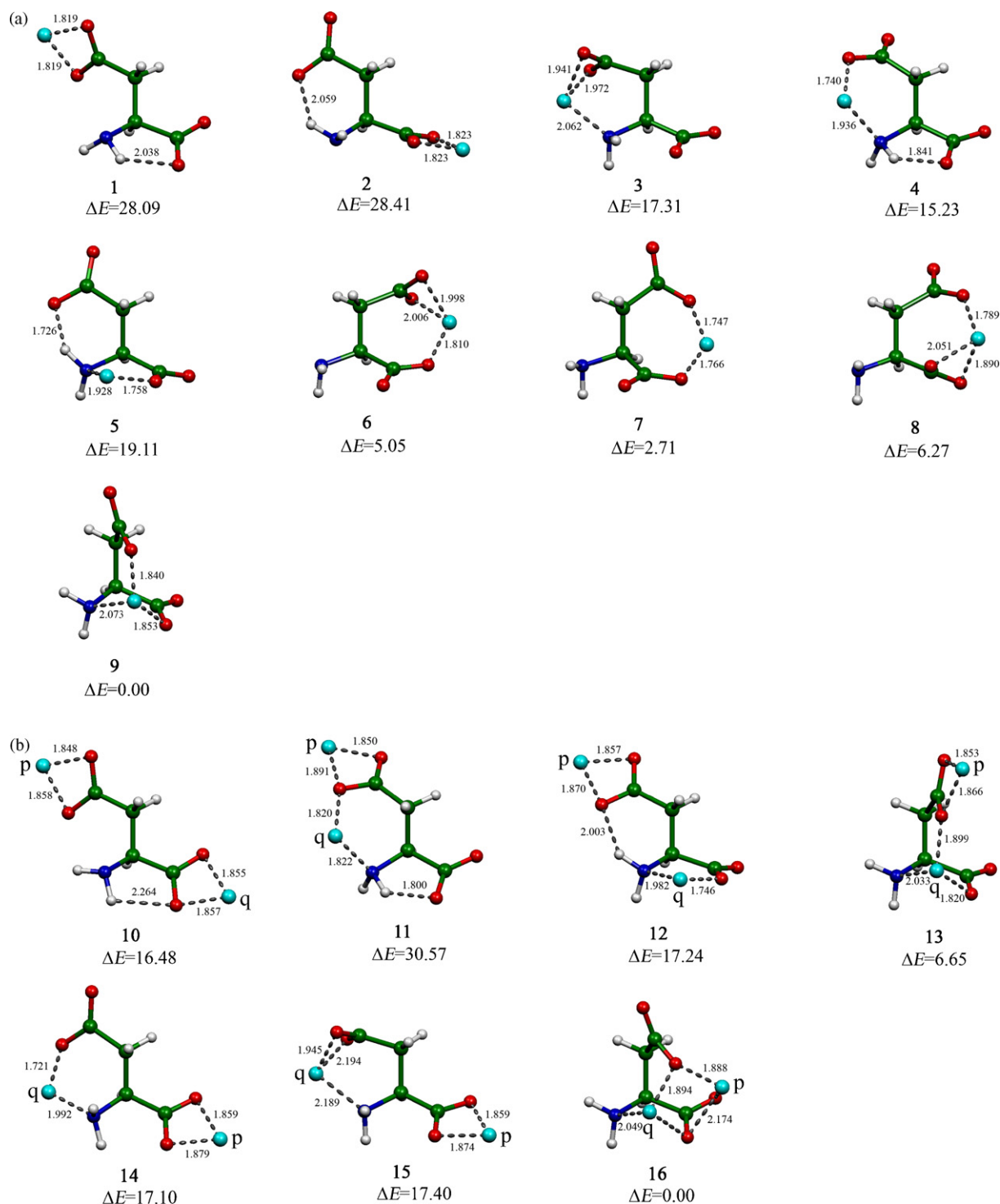


Fig. 2. The B3LYP/6-311++G(d,p)-optimized structures of (a) [asp-Li]<sup>+</sup> and (b) [asp-Li<sub>2</sub>] complexes. Bond distances are in Å and relative energies ( $\Delta E$ ) are in kcal/mol.

I, II, III, IV, V and VI). Therefore, the complex conformer **10** shown in Fig. 2 is therefore denoted as type I + II.

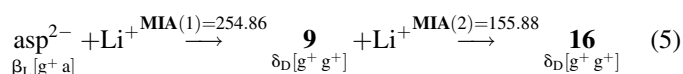
The optimized structures of mono and dinuclear complexes of lithium, sodium and potassium with aspartate dianion were obtained by the DFT computations with different basis sets. Data for the B3LYP/6-311++G(d,p)-optimized structures of all complex conformers were used for all calculations.

### 3.1. Lithium aspartate complexes

The B3LYP/6-311++G(d,p)-optimized structures of [asp-Li]<sup>+</sup> and [asp-Li<sub>2</sub>] complexes are shown in Fig. 2a and b, respectively. Nine and seven conformers of the mono and di-lithium complexes with aspartate anion, respectively, were found. The most stable structure for the [asp-Li]<sup>+</sup> and [asp-Li<sub>2</sub>]

complexes are the conformers **9** and **16**. The relative B3LYP/6-311++G(d,p)-computed energies of [asp-Li]<sup>−</sup> and [asp-Li<sub>2</sub>] complexes, respectively, compared to the complexes **9** and **16** are tabulated in Table 1. The monolithium complexes **1**, **2**, **4**, **5**, **7** and **9** are single mode of types I, II, III, IV, V and VI, respectively, but **3**, **6** and **8** are combination modes of types I + II, I + V and II + V, respectively. The di-lithium complexes **10**, **11**, **12**, **13**, **14**, **15** and **16** are all combination modes. The MIA(1)s of the lithium complexes with aspartate anion are shown in Table 1. Due to the most stable conformer **9**, the aspartate ligand prefers to bind with the lithium using its amino nitrogen and carboxylate oxygen atoms. For dinuclear complex **16**, a doubly tri-coordinated structure is formed by interaction between the asp<sup>2−</sup> ligand and the two lithium cations. The lithium cation firstly forms a tri-coordinated structure which is similar to **9**, then the second lithium cation forms a tri-coordinated structure using two α-carboxylate and one β-carboxylate oxygen atoms as shown in Fig. 2b. Comparing the asp<sup>2−</sup> complex with two lithium cations to the [asp-Zn·3H<sub>2</sub>O] [52] and [asp-Ni(im)<sub>3</sub>] [53] complexes, the N–M<sup>+</sup>, O<sub>1</sub>–M<sup>+</sup> and O<sub>3</sub>–M<sup>+</sup> bond lengths of both transition metal complexes are slightly longer than those of the lithium complexes.

The relative stabilities of the [asp-Li]<sup>−</sup> and [asp-Li<sub>2</sub>] complexes are in decreasing orders: **9** > **7** > **6** > **8** > **4** > **3** > **5** > **1** ≈ **2** and **16** > **13** > **10** > **14** ≈ **12** ≈ **15** > **11**, respectively. The MIA(1)s of the [asp-Li]<sup>−</sup> complexes are within 226.30–254.86 kcal/mol. The relative lithium ion affinities of the aspartate dianion are in decreasing order: **9** > **7** > **6** ≈ **8** ≈ **4** > **3** > **5** > **1** ≈ **2**. Based on the lower values of the MIA(2)s of the [asp-Li]<sup>−</sup> complexes, their relative lithium ion affinities are in decreasing order: **10** > **15** ≈ **16** ≈ **12** ≈ **14** > **13** > **11**. The most preferable feature of the conformational reaction of the lithium/asp<sup>2−</sup> complex can therefore be proposed as:



Due to Eq. (5), the aspartic acid conformations based on the Ramachandran nomenclature [62–65] of the free-form (asp<sup>2−</sup>), mono (**9**) and dinuclear (**16**) complexes are β<sub>L</sub>[g<sup>+</sup>a], δ<sub>D</sub>[g<sup>+</sup>g<sup>+</sup>] and δ<sub>D</sub>[g<sup>+</sup>g<sup>+</sup>], respectively. The aspartic acid features either in the complex **9** or **16** are the same conformation. The pre-organization energies of the aspartic dianions based on the structure changes from the isolated to **9** complex forms and from **9** to **16** complex forms are 28.44 and 14.21 kcal/mol, respectively (see Table 2).

Three interconversions of the complex conformer of lithium/aspartate systems namely reactions 3 ↔ 4 and 6 ↔ 7 for [asp-Li]<sup>−</sup> and 14 ↔ 15 for [asp-Li<sub>2</sub>] were found. The thermodynamic quantities of activation, equilibrium and rate constants of interconversion reactions 3 ↔ 4, 6 ↔ 7 and 14 ↔ 15 were determined via their transition states TSr3–4, TSr6–7 and TSr14–15, respectively, as shown in Table S1. The transition-state structures TSr3–4 and TSr6–7, and TSr14–15 are shown in Figs. S1 and S2, respectively. The B3LYP/6-311++G(d,p)-optimized structures of all [asp-Li]<sup>−</sup> and [asp-Li<sub>2</sub>] complex

Table 1

Relative B3LYP/6-311++G(d,p) energies and MIAs of minima for [asp-M]<sup>−</sup> and [asp-Mi<sub>2</sub>] complexes, M = Li<sup>+</sup>, Na<sup>+</sup> and K<sup>+</sup>

Complexes/ systems	Aspartate conformers	Binding mode	ΔE <sup>a</sup>	MIAs <sup>a</sup>
[asp-Li] <sup>−</sup>				
<b>1</b>	γ <sub>L</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>b</sup>	I	28.09	226.30
<b>2</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>c</sup>	II	28.41	226.07
<b>3</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>c</sup>	I + III	17.31	237.46
<b>4</b>	γ <sub>D</sub> [g <sup>−</sup> a] <sup>d</sup>	III	15.23	239.46
<b>5</b>	δ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>e</sup>	IV	19.11	235.69
<b>6</b>	γ <sub>D</sub> [a g <sup>−</sup> ] <sup>f</sup>	I + V	5.05	249.60
<b>7</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>g</sup>	V	2.71	251.93
<b>8</b>	γ <sub>D</sub> [a g <sup>+</sup> ] <sup>h</sup>	II + V	6.27	248.40
<b>9</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>i</sup>	VI	0.00	254.86
[asp-Li <sub>2</sub> ] <sup>j</sup>				
<b>10</b>	γ <sub>L</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>b</sup>	I + II	16.48	167.20 (167.43)
<b>11</b>	γ <sub>D</sub> [g <sup>−</sup> a] <sup>d</sup>	I + III	30.57	153.41 (140.25)
<b>12</b>	δ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>e</sup>	I + IV	17.24	166.69 (155.53)
<b>13</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>i</sup>	I + VI	6.65	177.50 (148.94)
<b>14</b>	γ <sub>D</sub> [g <sup>−</sup> a] <sup>d</sup>	II + III	17.10	153.55 (166.95)
<b>15</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>c</sup>	I + II + III	17.40	157.14 (166.75)
<b>16</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>i</sup>	II + V + VI	0.00	162.33 (155.88)
[asp-Na] <sup>−</sup>				
<b>1'</b>	γ <sub>L</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>k</sup>	I	21.73	197.10
<b>2'</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>l</sup>	II	21.97	197.43
<b>3'</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>l</sup>	I + III	12.51	206.80
<b>4'</b>	γ <sub>D</sub> [a g <sup>−</sup> ] <sup>m</sup>	I + V	3.34	219.00
<b>5'</b>	γ <sub>D</sub> [a g <sup>−</sup> ] <sup>n</sup>	V	0.26	215.84
<b>6'</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>o</sup>	VI	0.00	219.40
[asp-Na <sub>2</sub> ] <sup>p</sup>				
<b>7'</b>	γ <sub>L</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>k</sup>	I + II	20.51	145.76 (145.43)
<b>8'</b>	δ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>q</sup>	I + IV	24.85	141.50 <sup>r</sup>
<b>9'</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>o</sup>	I + VI	20.36	146.03 (123.73)
<b>10'</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>q</sup>	I + II + III	20.13	145.96 (136.59)
<b>11'</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>o</sup>	II + V + VI	0.00	148.02 (144.46)
[asp-K] <sup>−</sup>				
<b>1''</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>s</sup>	II	19.80	177.21
<b>2''</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>t</sup>	I + III	10.11	187.15
<b>3''</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>u</sup>	I + V	3.08	193.94
<b>4''</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>v</sup>	VI	0.00	197.09
[asp-K <sub>2</sub> ] <sup>w</sup>				
<b>5''</b>	γ <sub>L</sub> [g <sup>−</sup> g <sup>−</sup> ] <sup>x</sup>	I + II	16.90	− <sup>y</sup> (128.66)
<b>6''</b>	δ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>z</sup>	I + IV	22.31	− <sup>y</sup>
<b>7''</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>u</sup>	I + VI	19.65	− <sup>y</sup> (106.10)
<b>8''</b>	γ <sub>D</sub> [g <sup>−</sup> g <sup>+</sup> ] <sup>s</sup>	I + II + III	15.17	116.04 (− <sup>y</sup> )
<b>9''</b>	δ <sub>D</sub> [g <sup>+</sup> g <sup>+</sup> ] <sup>u</sup>	II + V + VI	0.00	130.54 (126.04)

<sup>a</sup> In kcal/mol with ZPVE corrections.

<sup>b</sup> Identical to δ<sub>L</sub> [g<sup>−</sup>g<sup>−</sup>].

<sup>c</sup> Identical to δ<sub>D</sub> [g<sup>−</sup>g<sup>+</sup>].

<sup>d</sup> Identical to α<sub>L</sub> [g<sup>−</sup>a].

<sup>e</sup> Identical to α<sub>L</sub> [g<sup>−</sup>g<sup>+</sup>].

<sup>f</sup> Identical to α<sub>L</sub> [a g<sup>−</sup>].

<sup>g</sup> Identical to α<sub>L</sub> [g<sup>−</sup>g<sup>−</sup>].

<sup>h</sup> Identical to α<sub>L</sub> [a g<sup>+</sup>].

<sup>i</sup> Identical to α<sub>L</sub> [g<sup>+</sup>g<sup>+</sup>].

<sup>j</sup> Based on the [asp-M]<sup>−</sup> complex components, type p and q in parenthesis, as reported in Fig. 2.

<sup>k</sup> Identical to δ<sub>L</sub> [g<sup>−</sup>g<sup>−</sup>].

<sup>l</sup> Identical to δ<sub>D</sub> [g<sup>−</sup>g<sup>+</sup>].

<sup>m</sup> Identical to α<sub>L</sub> [a g<sup>−</sup>].

<sup>n</sup> Identical to α<sub>L</sub> [g<sup>−</sup>g<sup>−</sup>].

<sup>o</sup> Identical to α<sub>L</sub> [g<sup>+</sup>g<sup>+</sup>].

<sup>p</sup> Based on the [asp-M]<sup>−</sup> complex components, type p and q in parenthesis, as reported in Fig. 3.

<sup>q</sup> Identical to α<sub>L</sub> [g<sup>−</sup>g<sup>+</sup>].

<sup>r</sup> No corresponding [asp-M]<sup>−</sup> complex components is found.

<sup>s</sup> Identical to δ<sub>D</sub> [g<sup>−</sup>g<sup>+</sup>].

<sup>t</sup> Identical to α<sub>L</sub> [g<sup>−</sup>g<sup>+</sup>].

<sup>u</sup> Identical to α<sub>L</sub> [a g<sup>−</sup>].

<sup>v</sup> Identical to α<sub>L</sub> [g<sup>+</sup>g<sup>+</sup>].

<sup>w</sup> Based on the [asp-M]<sup>−</sup> complex components, type p and q in parenthesis, as reported in Fig. 4.

<sup>x</sup> Identical to δ<sub>L</sub> [g<sup>−</sup>g<sup>−</sup>].

<sup>y</sup> No corresponding [asp-M]<sup>−</sup> complex component is found.

<sup>z</sup> Identical to α<sub>L</sub> [g<sup>−</sup>g<sup>+</sup>].

Table 2

Pre-organization energies of aspartate anions in the formation reaction of  $[\text{asp-M}]^-$  and  $[\text{asp-M}_2]$  complexes, computed at the B3LYP/6-311++G(d,p) level

Reaction	$\Delta E_{\text{preorg}}^a$	$\Delta E_{\text{ZPE, preorg}}^{a,b}$	$\Delta H_{298, \text{preorg}}^c$	$\Delta G_{298, \text{preorg}}^c$
$\text{asp}^{2-} \rightarrow [\text{asp}^{2-}]_9$	28.44	30.08	28.98	32.17
$\text{asp}^{2-} \rightarrow [\text{asp}^{2-}]_{6'}$	21.42	22.36	21.69	22.29
$\text{asp}^{2-} \rightarrow [\text{asp}^{2-}]_{4''}$	20.64	21.70	21.02	23.00
$[\text{asp}^{2-}]_9 \rightarrow [\text{asp}^{2-}]_{16}$	14.21	13.99	14.30	13.83
$[\text{asp}^{2-}]_{6'} \rightarrow [\text{asp}^{2-}]_{11'}$	16.39	16.68	17.18	17.49
$[\text{asp}^{2-}]_{4''} \rightarrow [\text{asp}^{2-}]_{9''}$	13.50	13.58	14.12	12.82

<sup>a</sup> In kcal/mol.<sup>b</sup> The ZPVE corrected energies.

conformers in cartesian coordinate system are listed in Table S2.

### 3.2. Sodium aspartate complexes

The B3LYP/6-311++G(d,p) optimized structures of  $[\text{asp-Na}]^-$  and  $[\text{asp-Na}_2]$  complex conformers are shown in Fig. 3a

and b, respectively. Six and five conformers for mono and dinuclear complexes of the  $\text{Na}^+/\text{asp}^{2-}$  system were found. The relative energies of  $[\text{asp-Na}]^-$  and  $[\text{asp-Na}_2]$  complex conformers, respectively, related to the complex conformers **6'** and **11'** are listed in Table 1. The monosodium complexes **1'**, **2'**, **5'** and **6'** are single mode of types I, II, V and VI, respectively, but **3'** and **4'** are combination modes of types I + II

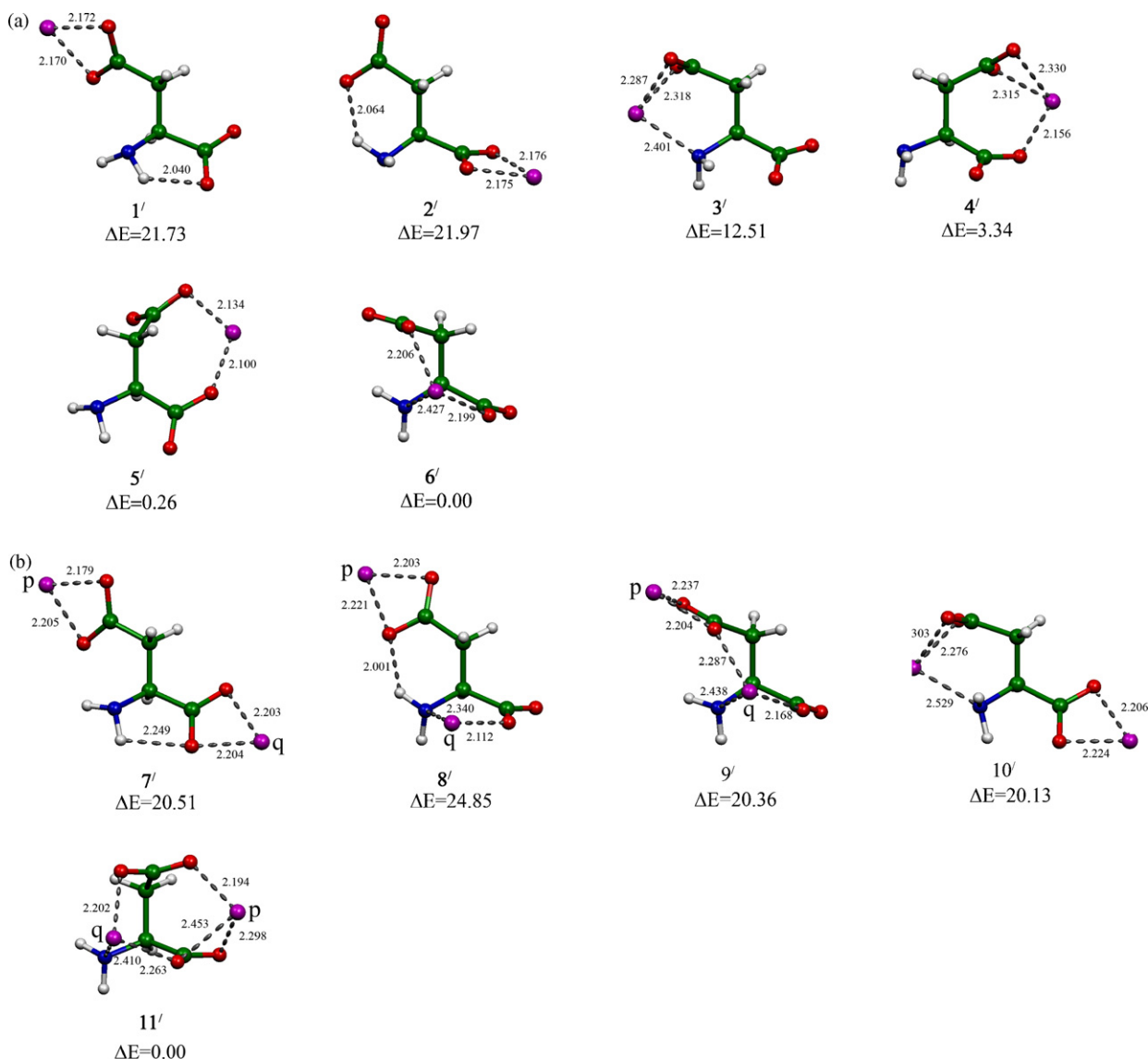
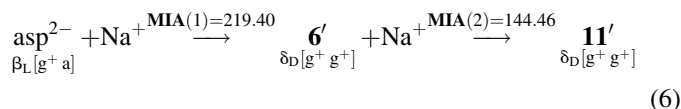


Fig. 3. The B3LYP/6-311++G(d,p)-optimized structures of (a)  $[\text{asp-Na}]^+$  and (b)  $[\text{asp-Na}_2]$  complexes. Bond distances are in Å and relative energies ( $\Delta E$ ) are in kcal/mol.



and I + V, respectively. The disodium complexes, **7'**, **8'**, **9'**, **10'** and **11'** are all the combination modes. The relative stabilities of the [asp-Na]<sup>−</sup> and [asp-Na<sub>2</sub>] complex conformers are in decreasing order: **6'** > **5'** > **4'** > **3'** > **1'** ≈ **2'** and **11'** > **10'** ≈ **9'** ≈ **7'** > **8'**, respectively. The MIAs of the [asp-Na]<sup>−</sup> and [asp-Na<sub>2</sub>] complex conformers are within the narrow ranges of 195.62–17.92 and 124.91–55.58 kcal/mol, respectively. The most preferable feature of the conformational reaction of the Na<sup>+</sup>/asp<sup>2−</sup> complex system can therefore be proposed as:

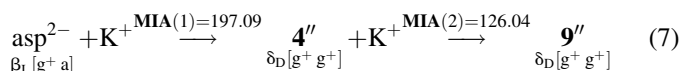


The B3LYP/6-311++G(d,p)-optimized structures of all [asp-Na]<sup>−</sup> and [asp-Na<sub>2</sub>] complex conformers in cartesian coordinate system are listed in Table S3.

### 3.3. Potassium aspartate complexes

The B3LYP/6-311++G(d,p) optimized structures of [asp-K]<sup>−</sup> and [asp-K<sub>2</sub>] complex conformers are shown in Fig. 4. All mono and di-potassium complexes except **1''** and **4''** are combination modes. The relative stabilities of [asp-K]<sup>−</sup> and [asp-K<sub>2</sub>] complex conformers are in decreasing order: **4''** > **3''** > **2''** > **1''** and **9''** > **8''** > **5''** > **7''** > **6''**, respectively. The relative energies of [asp-K]<sup>−</sup> and [asp-K<sub>2</sub>] complex

conformers, respectively, related to the complex conformers **4''** and **9''** are listed in Table 1. The MIAs of the [asp-K]<sup>−</sup> and [asp-K<sub>2</sub>] complex conformers are within the narrow ranges of 177.21–197.09 and 106.10–130.54 kcal/mol, respectively. The most preferable feature of the conformational reaction of the K<sup>+</sup>/asp<sup>2−</sup> complex system can therefore be proposed as:



The B3LYP/6-311++G(d,p)-optimized structures of all [asp-K]<sup>−</sup> and [asp-K<sub>2</sub>] complex conformers in cartesian coordinate system are listed in Table S4.

### 3.4. Binding energies of aspartate complexes

Relative binding energies of the complexation reactions of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] are in decreasing order: [asp-Li]<sup>−</sup> > [asp-Na]<sup>−</sup> > [asp-K]<sup>−</sup> and [asp-Li<sub>2</sub>] > [asp-Na<sub>2</sub>] > [asp-K<sub>2</sub>], respectively. The relation of the Gibbs free energy changes of the complexation of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] against sizes of alkali metal cations are shown in Fig. 5. Thermodynamic quantities of the formation reaction of the most stable complex conformers of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes computed at the B3LYP/6-311++G(d,p) level are shown in Table 3. The BSSE-corrected energies of the most stable complex conformers were obtained and shown that they are not

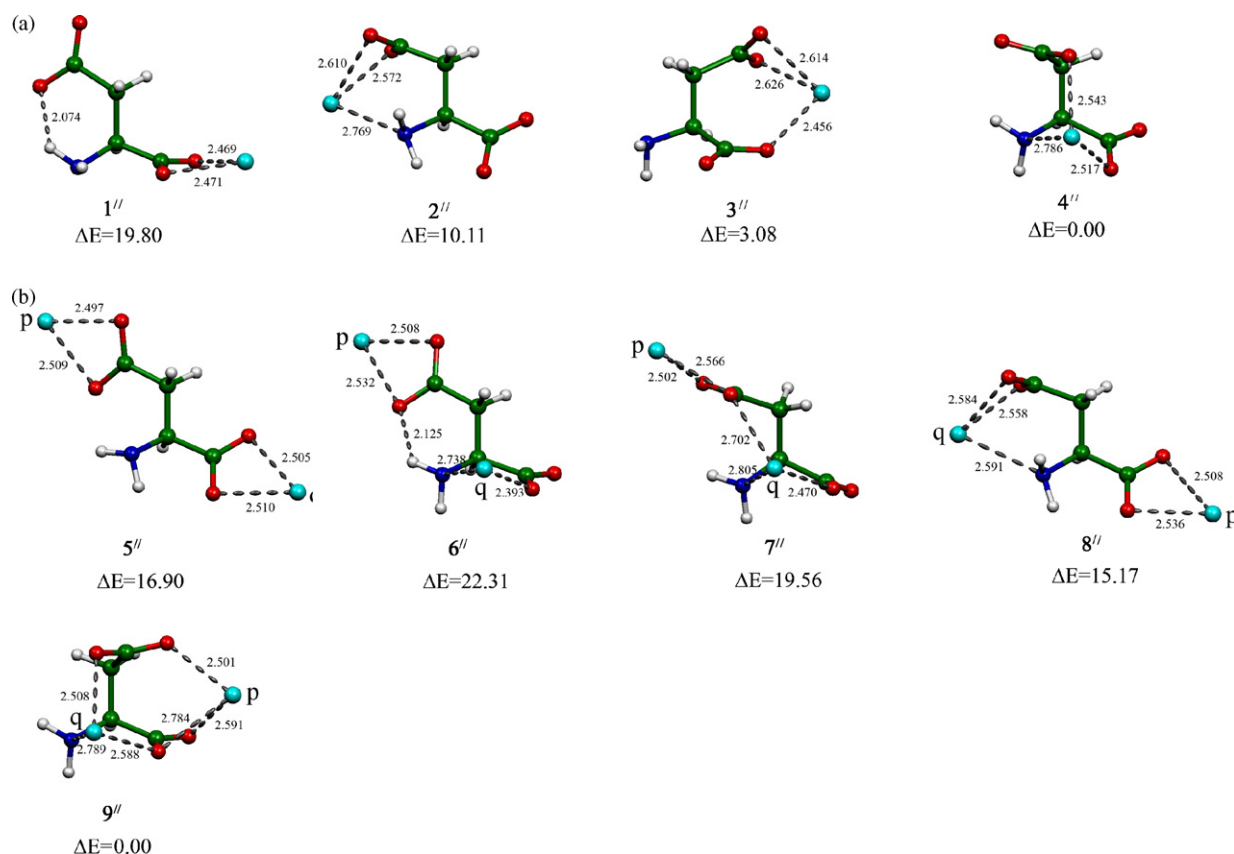


Fig. 4. The B3LYP/6-311++G(d,p)-optimized structures of (a) [asp-K]<sup>−</sup> and (b) [asp-K<sub>2</sub>] complexes. Bond distances are in Å and relative energies (ΔE) are in kcal/mol.

Table 3  
Thermodynamic quantities of the formation reaction of the most stable complex conformers for [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes computed at the B3LYP/6-311++G(d,p) level of theory

Reaction	$\Delta E^a$	BSSE <sup>a</sup>	$\Delta E_{BSSE}^a$	MIA <sup>b</sup>	$\Delta G_{298}^{\circ}$ <sup>a</sup>
asp <sup>2−</sup> + Li <sup>+</sup> → [asp-Li] <sup>−</sup>	−253.76	1.79	−251.97	254.86	−245.46
asp <sup>2−</sup> + Na <sup>+</sup> → [asp-Na] <sup>−</sup>	−218.76	2.35	−216.41	219.40	−210.25
asp <sup>2−</sup> + K <sup>+</sup> → [asp-K] <sup>−</sup>	−193.55	1.50	−192.05	197.09	−185.45
[asp-Li] <sup>−</sup> + Li <sup>+</sup> → [asp-Li <sub>2</sub> ]	−154.77	2.65	−152.12	155.88	−146.57
[asp-Na] <sup>−</sup> + Na <sup>+</sup> → [asp-Na <sub>2</sub> ]	−143.79	0.70	−143.09	144.46	−135.12
[asp-K] <sup>−</sup> + K <sup>+</sup> → [asp-K <sub>2</sub> ]	−125.52	2.61	−122.91	126.04	−117.32

<sup>a</sup> In kcal/mol.

<sup>b</sup> MIA(1) =  $-(H_{[asp-M]}^{\circ} - (H_{asp^{2-}}^{\circ} + H_{M^+}^{\circ}))$  for [asp-M]<sup>−</sup> complexation and MIA(2) =  $-(H_{[asp-M_2]}^{\circ} - (H_{[asp-M]}^{\circ} + H_{M^+}^{\circ}))$  for [asp-M<sub>2</sub>] complexation.

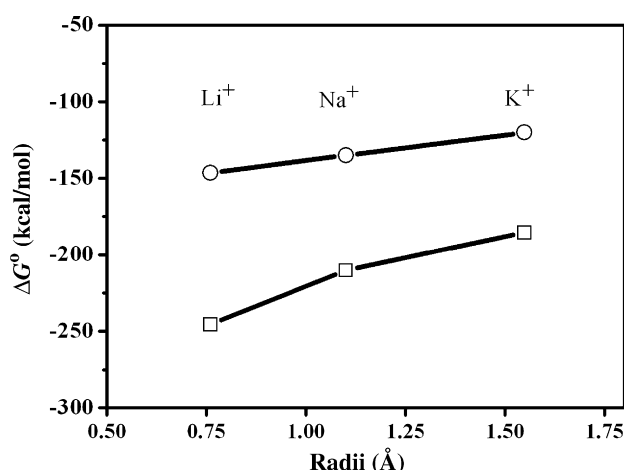


Fig. 5. Plot of complexation free energies of the (a) [asp-M]<sup>−</sup> (□–□–□–□) and (b) [asp-M<sub>2</sub>] (○–○–○–○) against sizes of the alkali metal ions M (M = Li<sup>+</sup>, Na<sup>+</sup> and K<sup>+</sup>).

very different from their non-corrected energies. The pre-organization energies of aspartate anion based on the structure changes from the isolated to the [asp-M]<sup>−</sup> complex forms and [asp-M]<sup>−</sup> to [asp-M<sub>2</sub>] complexes forms computed at the B3LYP/6-311++G(d,p) level are reported in Table 2. The  $E_{HOMO}$ ,  $E_{LUMO}$  and Frontier molecular orbital energy gap,

$\Delta E_{HOMO-LUMO}$  of the alkali cations, free ligand, and all the most stable complex conformers for [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes computed at the B3LYP/6-311++G(d,p) level are shown in Table 4. Relative reactivities of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes are in order: [asp-K]<sup>−</sup> > [asp-Na]<sup>−</sup> > [asp-Li]<sup>−</sup> and [asp-K<sub>2</sub>] > [asp-Na<sub>2</sub>] > [asp-Li<sub>2</sub>], respectively, but their absolute values are not very different. As the energy gap for K<sup>+</sup> and Na<sup>+</sup> cations are, respectively, lower than Na<sup>+</sup> and Li<sup>+</sup> cations by 0.38 and 0.88 eV, their relative reactivities are correspondingly in decreasing order: K<sup>+</sup> >> Na<sup>+</sup> >> Li<sup>+</sup>. The B3LYP/6-311++G(d,p)-computed NBO and Mulliken charges on the selected atoms of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes for lithium, sodium and potassium complex systems are tabulated in Tables S5–S7, respectively.

Bond distances between the alkali metal cation and the amino-nitrogen atom of the aspartate ion of the most stable complex conformers of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] are 2.073 and 2.049 Å for the lithium, 2.427 and 2.410 Å for sodium and 2.786 and 2.789 Å for potassium complex systems, respectively (see Table 5). Bond distances between the alkali metal cations and the oxygen atoms of the aspartate ions are within 1.804–1.909 Å for the lithium, 2.199–2.453 Å for sodium and 2.501–2.784 Å for potassium complex systems. Relative bond distances between the alkali metal cation M<sup>+</sup> and the binding atoms of the aspartate ion in [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes are in decreasing order: K<sup>+</sup> > Na<sup>+</sup> > Li<sup>+</sup>.

Table 4  
The  $E_{HOMO}$ ,  $E_{LUMO}$  and Frontier molecular orbital energy gap,  $\Delta E_{HOMO-LUMO}$  of cations, free ligand, and various most stable complex conformers for [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] computed at the B3LYP/6-311++G(d,p) level of theory

Species	$E_{HOMO}^a$	$E_{LUMO}^a$	$\Delta E_{HOMO-LUMO}^a$	$\eta^{a,b}$	$\mu^{a,c}$	$\chi^{a,d}$
Li <sup>+</sup>	−2.031	−0.005	2.026	1.013	−1.018	1.018
Na <sup>+</sup>	−1.161	−0.019	1.142	0.571	−0.590	0.590
K <sup>+</sup>	−0.816	−0.062	0.754	0.377	−0.439	0.439
asp <sup>2−</sup>	0.065	0.226	0.161	0.080	0.146	−0.146
[asp-Li] <sup>−</sup>	−0.252	−0.015	0.237	0.118	−0.134	0.134
[asp-Na] <sup>−</sup>	−0.241	−0.014	0.227	0.114	−0.128	0.128
[asp-K] <sup>−</sup>	−0.238	−0.018	0.220	0.110	−0.128	0.128
[asp-Li <sub>2</sub> ]	−0.265	−0.015	0.250	0.125	−0.140	0.140
[asp-Na <sub>2</sub> ]	−0.253	−0.017	0.236	0.118	−0.135	0.135
[asp-K <sub>2</sub> ]	−0.242	−0.024	0.218	0.109	−0.133	0.133

<sup>a</sup> In eV.

<sup>b</sup> Chemical hardness,  $\eta = \Delta E_{HOMO-LUMO}/2$ .

<sup>c</sup> Electronic chemical potential,  $\mu = (E_{HOMO} + E_{LUMO})/2$ .

<sup>d</sup> The Mulliken electronegativity,  $\chi = -(E_{HOMO} + E_{LUMO})/2$ .

Table 5

Bond distances of alkali metal cations and binding atoms of aspartate ions in the most stable complex conformers [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>], computed at the B3LYP/6-311 + +G(d,p) level

Bonds	Complex/distances <sup>a</sup>					
	[asp-Li] <sup>−</sup>	[asp-Na] <sup>−</sup>	[asp-K] <sup>−</sup>	[asp-Li <sub>2</sub> ]	[asp-Na <sub>2</sub> ]	[asp-K <sub>2</sub> ]
M <sup>+</sup> –N <sup>b</sup>	2.073	2.427	2.786	2.049	2.410	2.789
M <sup>+</sup> –O <sub>1</sub> <sup>b</sup>	1.853	2.199	2.517	1.909	2.263	2.588
M <sup>+</sup> –O <sub>3</sub> <sup>b</sup>	1.804	2.206	2.543	1.894	2.202	2.508
M <sup>+</sup> –O <sub>1</sub> <sup>c</sup>	–	–	–	1.959	2.453	2.784
M <sup>+</sup> –O <sub>2</sub> <sup>c</sup>	–	–	–	2.174	2.298	2.591
M <sup>+</sup> –O <sub>3</sub> <sup>c</sup>	–	–	–	1.888	2.194	2.501

<sup>a</sup> In Å.

<sup>b</sup> Refers to the M<sup>+</sup><sub>q</sub> of complex [asp-M<sub>2</sub>], see Fig. 1.

<sup>c</sup> Refers to the M<sup>+</sup><sub>p</sub> of complex [asp-M<sub>2</sub>], see Fig. 1.

#### 4. Conclusions

The B3LYP/6-311++G(d,p)-optimized structures of mono and dinuclear complexes of dianionic species (asp<sup>2−</sup>) of aspartic acid with Li<sup>+</sup>, Na<sup>+</sup> and K<sup>+</sup> cations were obtained. The most stable conformers mono- and dinuclear complexes of asp<sup>2−</sup> with Li<sup>+</sup>, Na<sup>+</sup> and K<sup>+</sup> are **9** and **16**, **6'** and **11'** and **4''** and **9''**, respectively. The metal ion affinities of the most stable complex conformers are MIA(1) = 254.86 and MIA(2) = 155.88 kcal/mol for the asp<sup>2−</sup>/Li<sup>+</sup> complex system, MIA(1) = 219.40 and MIA(2) = 144.46 kcal/mol for the asp<sup>2−</sup>/Na<sup>+</sup> complex system, and MIA(1) = 197.09 and MIA(2) = 126.04 kcal/mol for the asp<sup>2−</sup>/K<sup>+</sup> complex system. The asp<sup>2−</sup> complex components of the most stable complex conformer exist as δ<sub>D</sub>[g<sup>+</sup>g<sup>+</sup>] conformation. Relative energies of complexation reaction of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] are in decreasing order: [asp-Li]<sup>−</sup> > [asp-Na]<sup>−</sup> > [asp-K]<sup>−</sup> and [asp-Li<sub>2</sub>] > [asp-Na<sub>2</sub>] > [asp-K<sub>2</sub>], respectively. The relative reactivities of [asp-M]<sup>−</sup> and [asp-M<sub>2</sub>] complexes are in order: [asp-K]<sup>−</sup> > [asp-Na]<sup>−</sup> > [asp-Li]<sup>−</sup> and [asp-K<sub>2</sub>] > [asp-Na<sub>2</sub>] > [asp-Li<sub>2</sub>], respectively, but their absolute values are not very different. As the energy gap for K<sup>+</sup> and Na<sup>+</sup> cations are, respectively, lower than Na<sup>+</sup> and Li<sup>+</sup> cations by 0.38 and 0.88 eV, their relative reactivities are correspondingly in decreasing order: K<sup>+</sup> ≫ Na<sup>+</sup> ≫ Li<sup>+</sup>.

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#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jmgm.2007.01.001.

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