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Conformational study of cationic, zwitterionic, anionic species of aspartic acid, water-added forms and their protonation. A DFT method

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Abstract

The potential energy surfaces of various species of aspartic acid have been computed at the DFT/B3LYP/6-31G(d) level of theory. Conformations of 34, 11, 9 and 3 were found from 324, 162, 81 and 81 possible conformers for species H_3asp^+, H_2asp, $Hasp^-$ and asp^{2-}, respectively. The most stable conformation for species H_3asp^+, H_2asp, $Hasp^-$ and asp^{2-} are γ_D, α_L, ε_L and β_L conformers, respectively. Three protonation steps due to the tetrahydrated forms of species asp^{2-}, $Hasp^-$ and H_2asp of aspartic acid computed at the B3LYP/6-31+G(d, p) level of theory with zero-point vibrational energy corrections are exothermic reactions and their stabilization energies of the stepwise protonation are -244.68, -308.57 and -379.97 kcal mol^{-1}, respectively.
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1. Introduction

The conformational equilibria of cationic, zwitterionic and anionic species of aspartic acid were determined within the wide pH range of acidic to basic aqueous solutions [1,2]. Dianionic species of aspartic acid (asp^{2-}) found in the aqueous solution at high pH range was introduced and its reaction rates were reported [2,3]. At the wide pH range of aqueous aspartic acid solution, the structures of $[H_3^+N–CH(CH–COOH)(COOH)]^+$ for H_3asp^+, $[H_3^+N–CH(CH–COOH)(COO^-)]$ for H_2asp, $[H_3^+N–CH(CH–COO^-)(COO^-)]^-$ for $Hasp^-$ and $[H_2N–CH(CH–COO^-)(COO^-)]^{2-}$ for asp^{2-} have been found and their corresponding acidity constants were reported [1–5]. The zwitterionic form of zero net-charge species of aspartic acid was found that its local energy minima on the potential energy surface (PES) [6] of bare structure has not been similar to its hydrated structure. Many studies have been performed on aspartic acid and aspartate [7], N-acetyl-L-aspartic acid-N′-methylamide [8–11] and N-formyl-L-aspartic acid amide and N-formyl-L-aspartatamide [12] using ab initio MO and density functional methods. Thermodynamic quantities of conformational equilibria in the side chains of aspartic

acid in acidic, neutral and basic aqueous solutions were investigated using proton NMR method [13].

In solid state and aqueous solution, the neutral aspartic acid (H_2asp) is actually present as a zwitterionic α-aspartic acid as $[H_3^+N–CH(CH–COOH)(COO^-)]$ [3,6,14]. Nevertheless, the neutral aspartic acid as $[H_3^+N–CH(CH–COO^-)(COOH)]$ was also found as a β-carboxylate zwitterion. The stepwise deprotonation process of fully protonated species of aspartic acid (H_3asp^+) can be presented as a pH dependence diagram as shown in Fig. 1.

Definition of atomic numbering for H_3asp^+ as representation of aspartic acid and definition of dihedral angles ω (H1–O1–C1–C2), ψ (O1–C1–C2–N1), φ (H4–N1–C2–C1), χ_1(N1–C2–C3–C4), χ_2 (C2–C3–C4–O3) and χ_3 (C3–C4–O3–H2) are shown in Fig. 2. The dihedral angles χ_3 and ω were obtained from full optimizations and χ_3 is used to indicate the *endo* and *exo* conformational types of carboxylic group; the *endo* and *exo* forms are defined as $\chi_3=0$ and 180°, respectively. *E* and *Z* isomerism of the dihedral angle ω was applied for conformational nomenclature. Due to the *endo/exo* and *E/Z* definitions, all aspartic acid structures of various forms can be categorized into species (a) H_3asp^+-*endo-E*, (b) H_3asp^+-*endo-Z*, (c) H_3asp^+-*exo-E*, (d) H_3asp^+-*exo-Z*, (e) H_2asp-*endo*, (f) H_2asp-*exo*, (g) $Hasp^-$ and (h) asp^{2-} as shown in Fig. 3.

Due to the conformational convention for amino acid residues, [15,16] the number of possible conformations for each aspartic acid structures is 81 which is a combination

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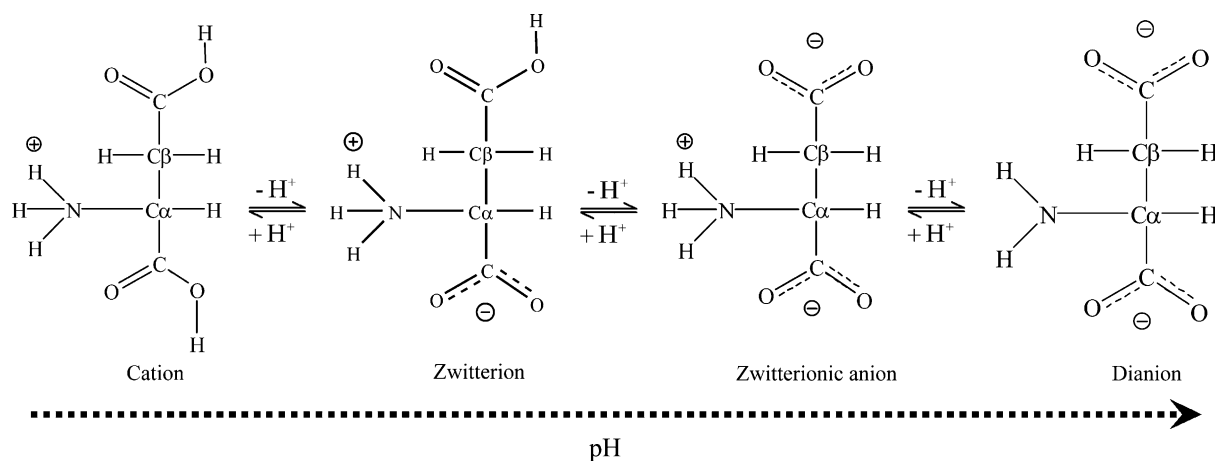*E-mail address:* vithaya.r@chula.ac.th (V. Ruangpornvisuti).

Fig. 1. pH dependence of four typical species of aspartic acid in aqueous solution and protonation reversible mechanism.

number of nine (γ_D, δ_D, α_L, ε_L, β_L, ε_L, α_D, δ_L, γ_L) back-bone (BB) and nine (g^+g^-, a g^-, $g^- g^-$, g^+a, a a, g^- a, g^+g^+, a g^+, $g^- g^+$) side-chain (SC) conformations. The nine BB conformations and nine SC conformations are located on Ramachandran map [17,18,19,20] and IUPAC [21] convention as shown in Fig. 4. To employ the Ramachandran and IUPAC conventions for the BB and SC conformations, respectively, the rotational conformation of aspartic acid notified as 'BB[SC]' has been therefore used to call the conformation of aspartic acid.

In present work, the conformations of species H_3asp^+, H_2asp, $Hasp^-$ and asp^{2-} of aspartic acid in gas phase have been located using the potential energy surface (PES) method. The water-added forms of the most stable conformation of each species of aspartic acid have been also studied. Protonation of tetrahydrated forms of the most stable conformation of species H_3asp^+, H_2asp, $Hasp^-$ and asp^{2-} of aspartic acid has been modeled and its reaction energies have been obtained.

2. Computational details

The PESs of all species (H_3asp^+-*endo-E*, H_3asp^+-*endo-Z*, H_3asp^+-*exo-E*, H_3asp^+-*exo-Z*, H_2asp-*endo*, H_2asp-*exo*, $Hasp^-$ and asp^{2-}) of aspartic acid were computed with 30° increments along four dihedral angles (ψ, ϕ, χ_1 and χ_2) using the hybrid density functional theory (DFT) at B3LYP/6-31G(d) [22,23,24] level of theory.

As the stabilities of bare structure of all species were examined, the species H_2asp and $Hasp^-$ are not stable without including three water molecules because their amino proton can transfer to their carboxylate oxygen. Therefore, their PESs were computed as trihydrated species by adding three water molecules to stabilize their molecular structures. The B3LYP/6-31G(d)-optimized structures of trihydrated and tetrahydrated forms of the most stable conformation of each species were fully reoptimized at the B3LYP/6-31+G(d, p) level of theory with the zero-point vibrational energy corrections. The stabilization energies of protonation of tetrahydrated form of aspartic acid were derived from their total energies computed at B3LYP/6-31+G(d, p) level of

theory. Therefore, the water-added structures are categorized into three models namely (1) bare, except for the species H_2asp and $Hasp^-$, (2) trihydrated and (3) tetrahydrated forms of various species of aspartic acid. All computations were performed using the GAUSSIAN 03 program package [25]. The MOLDEN 3.7 program [26] was utilized to observe molecular energies and geometries convergence via the Gaussian output files. The molecular graphics of all species were generated with the MOLEKEL program [27].

All geometric minima for each species of aspartic acid on the conformational PES are represented by Ramachandran and IUPAC maps as shown in Fig. 4. To combine the conformational convention and each species of aspartic acid, its full name has been therefore specified as 'species type-*endo/exo-Z/E*' of 'BB [SC]' such as conformer of H_3asp^+-*endo-Z* of γ_D [g^+g^-]. Energies for each structural conformers of H_3asp^+ and H_2asp species are therefore the functions of E (Ψ, ϕ, χ_1, χ_2, ω) and E (ψ, ϕ, χ_1, χ_2, χ_3), respectively. For the anionic species of $Hasp^-$ and asp^{2-}, their energies are a function of E (ψ, ϕ, χ_1, χ_2).

3. Results and discussion

As the stabilities of bare structure of all species were examined, the proper zwitterionic structures of the species H_2asp and $Hasp^-$ are not stable because their amino proton can
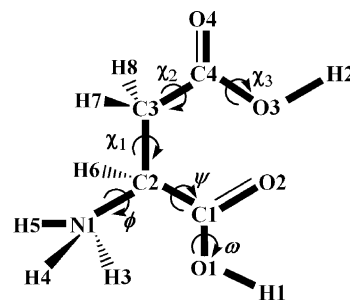

Fig. 2. Definition of atomic numbering for H_3asp^+ as representative of aspartic acid and definition of dihedral angles ω (H1–O1–C1–C2), ψ (O1–C1–C2–N1), ϕ (H4–N1–C2–C1), χ_1(N1–C2–C3–C4), χ_2 (C2–C3–C4–O3) and χ_3 (C3–C4–O3–H2).
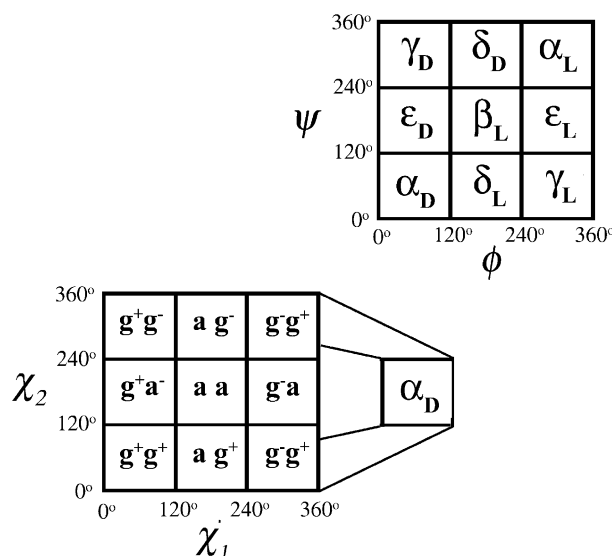
Fig. 3. Aspartic acid species (a) H_3asp^+-*endo-E*, (b) H_3asp^+-*endo-Z*, (c) H_3asp^+-*exo-E*, (d) H_3asp^+-*exo-Z*, (e) H_2asp-*endo*, (f) H_2asp-*exo*, (g) $Hasp^-$ and (h) asp^{2-} species.

easily transfer to their carboxylate oxygen. Due to the stability test of hydrated structures of the species H_2asp and $Hasp^-$, it was found that these two species are stabilized by at least three water molecules. The PESs for the species H_2asp and $Hasp^-$ were therefore computed as their trihydrated forms but for the species H_3asp^+ and asp^{2-}, their bare structures were employed.

3.1. PESs of various forms of aspartic acid and their geometrical conformations

Conformational structures of H_3asp^+-*endo-E*, H_3asp^+-*endo-Z*, H_3asp^+-*exo-E*, H_3asp^+-*exo-Z*, H_2asp-*endo*, H_2asp-*exo*, $Hasp^-$ and asp^{2-} species optimized at B3LYP/6-31G(d) level of theory are shown in Tables S1, S2, S3, S4, S5, S6, S7 and S8 as contained in the Supplementary material. Classification of the types of internal hydrogen bonding for aspartic acid are shown in Fig. 5. Two types of backbone/backbone (BB/BB) and five types of side-chain/backbone (SC/BB) hydrogen bonding were defined. The types and distances of existing hydrogen bonding for various H_3asp^+ forms of aspartic acid is shown in Table 1 and for various H_2asp, $Hasp^-$ and asp^{2-} forms are shown in Table 2. Bond distances of the internal hydrogen bonding of types 1a, 1b, 2a, 2b, 2c, 2d and 2e found in all conformations are within 1.768–1.949, 1.724–2.158, 1.875–1.910, 1.690–1.916 Å, at 2.010 Å and 1.706–1.760 Å, respectively. The numbers of stable conformers for H_3asp^+-*endo-E*, H_3asp^+-*endo-Z*, H_3asp^+-*exo-E*, H_3asp^+-*exo-Z*, H_2asp-*endo*, H_2asp-*exo*, $Hasp^-$ and asp^{2-} are 8, 13, 5, 8, 4, 7, 9 and 3 conformers and their conformational structures are shown in Figs. S1, S2, S3, S4, S5, S6, S7 and S8 as contained in Supplementary material, respectively. The landscape representations of the side-chain conformational PESs, $E=E(\chi_1, \chi_2)$ associated with the backbone conformations of H_3asp^+-*endo-E*, H_3asp^+-*endo-Z*, H_3asp^+-*exo-E*, H_3asp^+-*exo-Z*, H_2asp-*endo*, H_2asp-*exo*, $Hasp^-$ and asp^{2-} are shown in Figs. S9, S10, S11, S12, S13, S14, S15 and S16

(Supplementary material), respectively. The bottoms of the Figs. S9, S10, S11, S12, S13, S14, S15 and S16 show integrated scatter-plot diagrams of the existing conformations which correspond to the PESs located at the top of the figures.

Based on the geometrical parameters of the conformations of species H_3asp^+, H_2asp or $Hasp^-$, their conformations are identical when their dihedral angles χ_1 and χ_2 are the same value and if their dihedral angles ϕ differ by 120° or ψ differ by 180°. In case of the species asp^{2-}, their conformations are identical when their dihedral angles χ_2 or ψ differ by 180°.

As the bare structures of the species H_3asp^+ and asp^{2-} and the trihydrated forms of the species H_2asp and $Hasp^-$ were employed in the PESs computations using the B3LYP/6-31G(d)
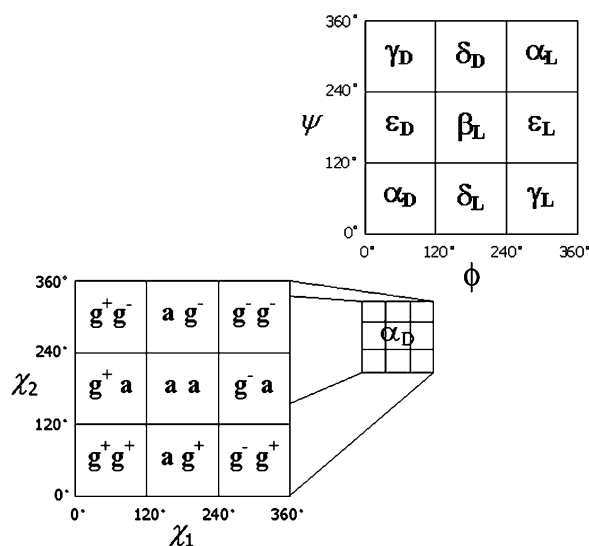

Fig. 4. A schematic representation of relation between a backbone (BB) conformation Ramachandran map (top) and a side-chain (SC) conformation map designated by IUPAC convention (bottom). The Ramachandran and IUPAC-SC conformation maps, defined as 'BB[SC]' conformational notation of aspartic acid.

Backbone/Backbone hydrogen bonding (BB/BB)

1a : (NH•••OC)   1b : (NH•••OH)

Side-chain/Backbone hydrogen bonding (SC/BB)

2a : (CO•••HN)   2b : (HO•••HN)   2c : (CO•••HO)
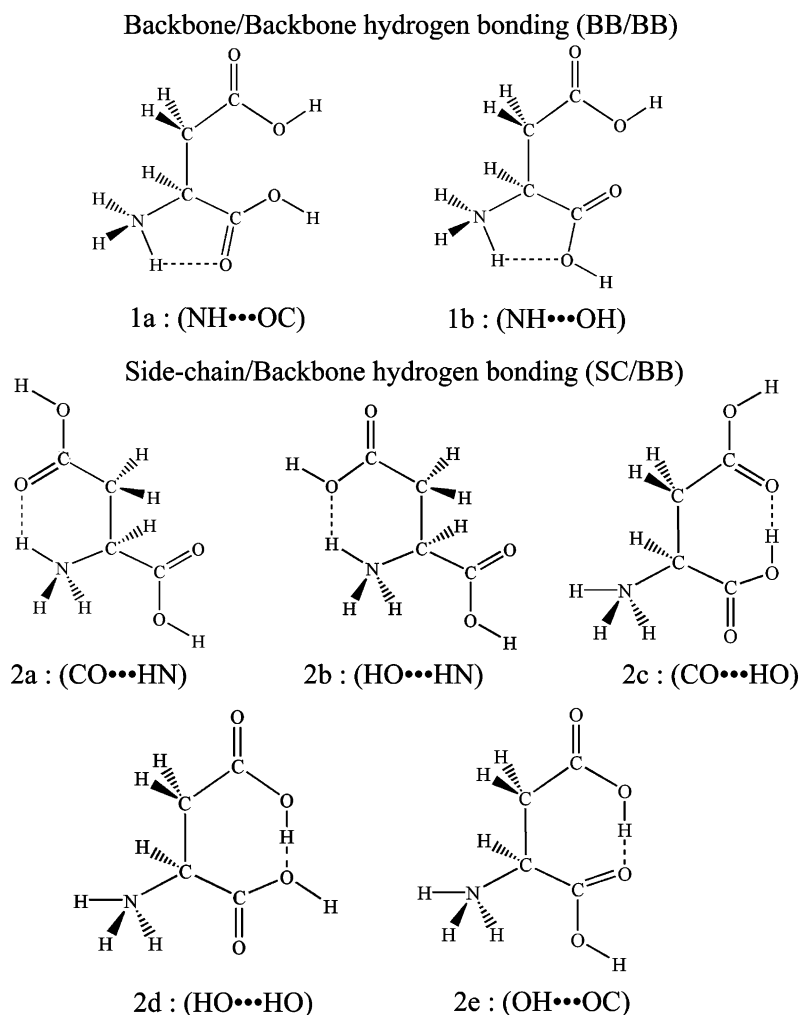
2d : (HO•••HO)   2e : (OH•••OC)

Fig. 5. Classification of the types of internal hydrogen bonding for various species of aspartic acid.

theoretical level. The most stable conformers of H_3asp^+, $H_2asp(3H_2O)$, $Hasp^-(3H_2O)$ and asp^{2-} of aspartic acid in gas phase are γ_D [g^- g^+] which is identical to δ_D [g^- g^+] (see Table S2 and Fig. S2), α_L [a g^-] (see Table S6 and Fig. S6), ε_L [g^+a] which is identical to β_L [g^+a] (see Table S7 and Fig. S7) and β_L [g^+a] which is identical to β_L [g^+g^-],?δ_L [g^+a] and δ_L [g^+g^-] (see Table S8 and Fig. S8), respectively.

3.2. Water-added structures and their protonation

The B3LYP/6-31+G(d, p)-optimized structures of various trihydrated and tetrahydrated species of aspartic acid and their selected geometrical data are tabulated in Table 3. The B3LYP/6-31G(d)-optimized structures of the bare molecule of species H_3asp^+ and asp^{2-}, trihydrated ($H_3asp^+(3H_2O)$, $H_2asp(3H_2O)$, $Hasp^-(3H_2O)$ and $asp^{2-}(3H_2O)$) and tetrahydrated ($H_3asp^+(4H_2O)$, $H_2asp(4H_2O)$, $Hasp^-(4H_2O)$ and $asp^{2-}(4H_2O)$) species were fully reoptimized at B3LYP/6-31+G(d, p) level. Conformations of the B3LYP/6-31G(d)-optimized geometries of all aspartic acid species are shown Table 4. The most stable conformation for each aspartic acid species existing as

trihydrated and tetrahydrated forms and their protonation and deprotonation schemes are shown in Fig. 6. The stabilization energies of protonation of tetrahydrated form of aspartic acid derived from their total energies computed at B3LYP/6-31+G(d, p) level of theory with zero-point vibrational energy (ZPVE)are listed in Table 5. Three protonation steps are exothermic reactions and their stabilization energies of the stepwise protonation are −244.68, −308.57 and −379.97 kcal mol⁻¹, respectively.

Based on the B3LYP/6-31+G(d, p) computations of different structural models (the bare, trihydrated and tetrahydrated structures), the conformation for the species H_3asp^+ γ_D [$g-$ $g+$]), H_2asp α_L [a $g-$]), $Hasp^-$ (ε_L [$g+a$]) and asp^{2-} (β_L [$g+a$]) are not changed as shown in Table 4. As compared to other species, the geometrical change of the species $Hasp^-$ has obviously occurred as shown in Fig. 7. Due to the change of trihydrated to tetrahydrated system, Fig. 7(c) illustrates that the side-chain carboxylic group of the species $Hasp^-$ is the main cause of its geometrical change; the change of its dihedral angles χ_1 and χ_2 are ∼4 and 9°, respectively.

Table 1
The present hydrogen bonding, its type and distance for conformations of the aspartic acid H_3asp^+ species

Conformer	Hydrogen bond			
	BB/BB types	BB/BB distances (Å)	SC/BB types	SC/BB distances (Å)
H_3asp^+-endo-E form				
γ_D [a a][a1]	1a	1.768	2d	1.780
γ_D [g⁻ a][b1]	1a	1.620	2b	1.910
γ_D [g⁻ g⁻]	1a	1.901	2c	1.820
γ_D [g⁻ g⁺][c1]	1a	1.949	2a	1.750
α_D [a g⁺]	1a	1.734	2c	1.694
α_D [g⁺a][d1]	–	–	2b	1.879
α_D [g⁺g⁻][e1]	–	–	2a	1.750
β_L [g⁻ g⁺]	–	–	2a	1.759
H_3asp^+-endo-Z form				
γ_D [a g⁻][a2]	–	–	–	–
γ_D [g⁻ a][b2]	–	–	2b	1.875
γ_D [g⁻ g⁺][c2]	–	–	2a	1.662
δ_D [a a][d2]	–	–	–	–
ε_D [g⁺a][e2]	–	–	2b	1.888
ε_D [g⁺ g⁻][f2]	–	–	2a	1.760
ε_D [a g⁻][g2]	1b	2.153	–	–
ε_D [g⁻ g⁺][h2]	–	–	2a	1.750
ε_D [g⁻ a]	1b	1.882	2b	1.882
ε_L [a a]	1b	2.158	–	–
α_D [a g⁺][i2]	–	–	–	–
α_D [g⁺a][j2]	1b	1.883	2a	1.868
α_D [g⁻ g⁻][k2]	–	–	2a	1.750
H_3asp^+-exo-E form				
γ_D [g⁻ g⁺][a3]	–	–	2a	1.688
ε_D [g⁻ g⁺]	–	–	2a, 2c	1.864, 1.867
α_D [g⁻ a][b3]	–	–	2d	2.010
α_D [g⁺ g⁻][c3]	–	–	2a	2.133
δ_L [a g⁺][d3]	1a	1.724	2c	1.690
H_3asp^+-exo-Z form				
γ_D [a g⁻][a4]	–	–	–	–
γ_D [g⁻ g⁺][b4]	–	–	2a	2.236
δ_D [g⁺ g⁻]	–	–	2a	1.722
ε_D [a g⁻][c4]	1b	1.724	–	–
ε_D [g⁻ g+][d4]	1b	2.156		2.156
β_L [g⁺ g⁻][e4]	–	–	2a	1.722
α_D [g⁻ a][f4]	–	–	2c	1.916
α_D [g⁺ g⁻][g4]	–	–	2a	1.712

[a1]Identical to δ_D [a a] and α_L [a a]. [b1]Identical to δ_D [g⁻ a] and α_L [g⁻ a]. [c1]Identical to δ_D [g⁻ g⁺] and α_L [g⁻ g⁺]. [d1]Identical to δ_L [g⁺a] and γ_L [g⁺a]. [e1]Identical to γ_L [g⁻g⁻]. [a2]Identical to δ_D [a g⁻] and α_L [a g⁻]. [b2]Identical to δ_D [g⁻ a] and α_L [g⁻ a]. [c2]Identical to δ_D [g⁻ g⁺]. [d2]Identical to α_L [a a]. [e2]Identical to ε_L [g⁺a]. [f2]Identical to β_L [g⁺g⁻] and ε_L [g⁺g⁻]. [g2]Identical to ε_L [a g⁻]. [h2]Identical to β_L [g⁻ g⁺] and ε_L [g⁻ g⁺]. [i2]Identical to δ_L [a g⁺]. [j2]Identical to δ_L [g⁺a] and γ_L [g⁺a]. [k2]Identical to δ_L [g⁺ g⁻] and γ_L [g⁺ g⁻]. [a3]Identical to δ_D [g⁻ g⁺] and α_L [g⁻ g⁺]. [b3]Identical to δ_L [g⁻ a] and γ_L [g⁻ a]. [c3]Identical to δ_L [g⁺ g⁻] and γ_L [g⁺ g⁻]. [d3]Identical to γ_L [a g⁺]. [a4]Identical to δ_D [a g⁻] and α_L [a g⁻]. [b4]Identical to δ_D [g⁻ g⁺] and α_L [g⁻ g⁺]. [c4]Identical to β_L [a g⁻] and ε_L [a g⁻]. [d4]Identical to β_L [g⁻ g⁺] and ε_L [g⁻ g⁺]. [e4]Identical to ε_L [g⁻ g⁻]. [f4]Identical to δ_L [g⁻ a] and γ_L [g⁻ a]. [g4]Identical to γ_L [g⁺g⁻].

Table 2
The present hydrogen bonding, its type and distance for conformations of species H_2asp, $Hasp^-$ and asp^{2-} of aspartic acid

Conformer	Hydrogen bond			
	BB/BB types	BB/BB distances (Å)	SC/BB types	SC/BB distances (Å)
H_2asp-endo form				
α_D [g⁺ g⁻]	1a	1.570	–	–
ε_D [g⁺g⁻]	1a	1.839	–	–
δ_D [g⁺g⁻]	1a	1.635	–	–
ε_L [g⁻ g⁺]	–	–	–	–
H_2asp-exo form				
ε_D [g⁺a]	–	–	–	–
ε_D [g⁺ g⁻]	1a	1.855	–	–
ε_D [a g⁻]	–	–	2e	1.760
ε_D [g⁻ g⁺]	1a	1.733	–	–
δ_D [g⁺g⁻]	1a	1.655	–	–
γ_L [g⁺g⁻]	1a	1.602	–	–
α_L [a g⁻]	–	–	2e	1.706
$Hasp^-$ form				
α_D [g⁺a][a1]	–	–	2a	1.407
δ_D [a g⁻]	–	–	–	–
ε_D [g⁺g⁺][b1]	–	–	2a	1.737
ε_D [g⁺a]	–	–	2a	1.532
ε_D [g⁻ g⁺]	1a	1.850	2a	1.438
γ_L [g⁺g⁺][c1]	–	–	2a	1.658
γ_L [g⁻ g⁺]	1a	1.801	2a	1.446
ε_L [g⁺a][d1]	–	–	2a	1.552
ε_L [g⁺g⁻]	–	–	2a	1.632
Asp^{2-} form				
γ_D [g⁺a][a2]	–	–	2a	2.25
α_L [g⁻ g⁺][b2]	–	–	2a	1.947
β_L [g⁺a][c2]	–	–	2a	2.027

[a1]Identical to γ_L [g⁺a]. [b1]Identical to β_L [g⁺g⁺]. [c1]Identical to δ_L [g⁺g⁺]. [d1]Identical to β_L [g⁺a]. [a2]Identical to γ_D [g⁺g⁻], ε_D[g⁺a], ε_D [g⁺g⁻]. [b2]Identical to α_L [g⁻a], ε_L [g⁻g⁺], ε_L [g⁻a]. [c2]Identical to β_L [g⁺g⁻], δ_L [g⁺a], δ_L [g⁺g⁻].

4. Conclusions

The potential energy surfaces for the bare structures of species H_3asp^+ and asp^{2-} and for the trihydrated structures of species H_2asp and $Hasp^-$ of aspartic acid have been performed at the DFT/B3LYP/6-31G(d) level of theory. Conformations of 34, 11, 9 and 3 were found from 324, 162, 81 and 81 possible conformers for species H_3asp^+, H_2asp, $Hasp^-$ and asp^{2-}, respectively. Based on the B3LYP/6-31+G(d,p) computations of different structural models (the bare, trihydrated and tetrahydrated structures), the conformation for the species H_3asp^+ γ_D [g− g+]), H_2asp α_L [a g−]), $Hasp^-$ (ε_L [g+a]) and asp^{2-} (β_L [g+a]) are not changed. In gas phase, the species H_2asp and $Hasp^-$ must be stabilized by at least three water molecules but the bare structures of the species H_3asp^+ and asp^{2-} are stable. Three protonation steps due to the tetrahydrated species of asp^{2-}, $Hasp^-$ and H_2asp of aspartic acid computed at B3LYP/6-31+G(d, p) level of theory with zero-point vibrational energy corrections are exothermic reactions and their stabilization energies of the stepwise protonation are −244.68, −308.57 and −379.97 kcal mol⁻¹, respectively.

Table 3

B3LYP/6-31+G(d, p)-optimized conformations of various species of trihydrated and tetrahydrated forms of aspartic acid, their selected geometrical data and total energies

Species	Conformations	Optimized parameters						
		ϕ	ψ	χ_1	χ_2	χ_3	ω	E_{total}(hartree)[a]
Trihydrated form								
H_3asp^+	γ_D [g⁻ g⁺]	25.36	−18.98	−50.18	27.13	0.68	0.76	−741.887223
H_2asp	α_L [a g⁻]	−72.92	−18.69	145.70	−106.50	166.30	−	−741.502018
$Hasp^-$	ε_L [g⁺a]	−36.74	−149.30	43.77	143.40	−	−	−741.001475
asp^{2-}	β_L [g⁺a]	−169.70	−163.70	58.26	167.41	−	−	−740.389035
Tetrahydrated form								
H_3asp^+	γ_D [g⁻ g⁺]	30.30	−34.67	−54.37	26.65	0.23	0.62	−818.311997
H_2asp	α_L [a g−]	−79.39	−19.14	148.89	−108.89	166.20	−	−817.922080
$Hasp^-$	ε_L [g⁺a]	−39.11	−150.30	47.78	134.33	−	−	−817.430348
Asp^{2-}	β_L [g⁺a]	−165.20	−153.60	58.87	157.00	−	−	−816.824823

[a] With ZPVE correction.

Table 4

B3LYP/6-31+G(d, p)-optimized conformations of various species of aspartic acid in gas phase

Species	Conformation		
	Bare	Trihydrated	Tetrahydrated
H_3asp^+	γ_D [g⁻ g⁺][a]	γ_D [g⁻ g⁺][a]	γ_D [g⁻ g⁺][a]
H_2asp	−[b]	α_L [a g⁻]	α_L [a g⁻]
$Hasp^-$	−[b]	ε_L [g⁺a]	ε_L [g⁺a][c]
Asp^{2-}	β_L [g⁺a][d]	β_L [g⁺a]	β_L [g⁺a]

[a] Identical to δ_D [g⁻g⁺].
[b] Unstable species.
[c] Identical to β_L [g⁺a].
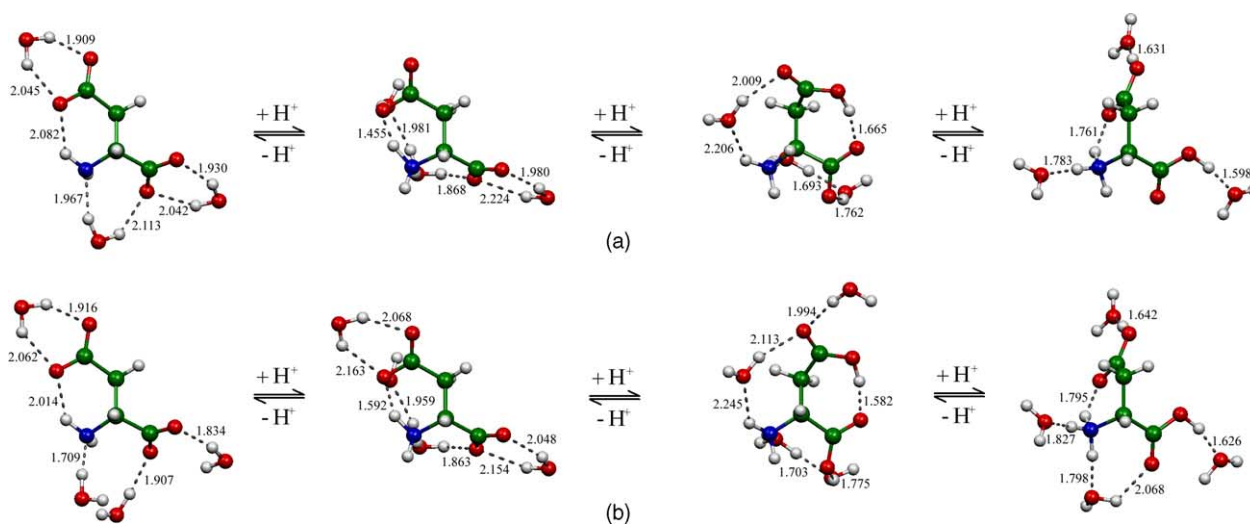[d] Identical to β_L [g⁺g⁻], δ_L [g⁺a] and δ_L [g⁺g⁻].

Fig. 6. The B3LYP/6-31+G(d,p) optimized structures of the most stable conformers of four species of aspartic acid as (a) trihydrated and (b) tetrahydrated forms and their protonation schemes. The hydrogen bond distances are in Å.

Table 5

Stabilization energies of protonation reaction of tetrahydrated forms of species asp^{2-}, $Hasp^-$ and H_2asp of aspartic acid, computed at B3LYP/6-31+G(d, p) level of theory

Protonation/reaction steps	$\Delta E^{a,b}$
ΔE_1:$asp^{2-}(4H_2O) + H^+ \rightarrow Hasp^-(4H_2O)$	−244.68
ΔE_2:$Hasp^-(4H_2O) + H^+ \rightarrow H_2asp(4H_2O)$	−308.57
ΔE_3:$H_2asp(4H_2O) + H^+ \rightarrow H_3asp^+(4H_2O)$	−379.97

[a] In kcal mol^{-1}.
[b] With ZPVE corrections.
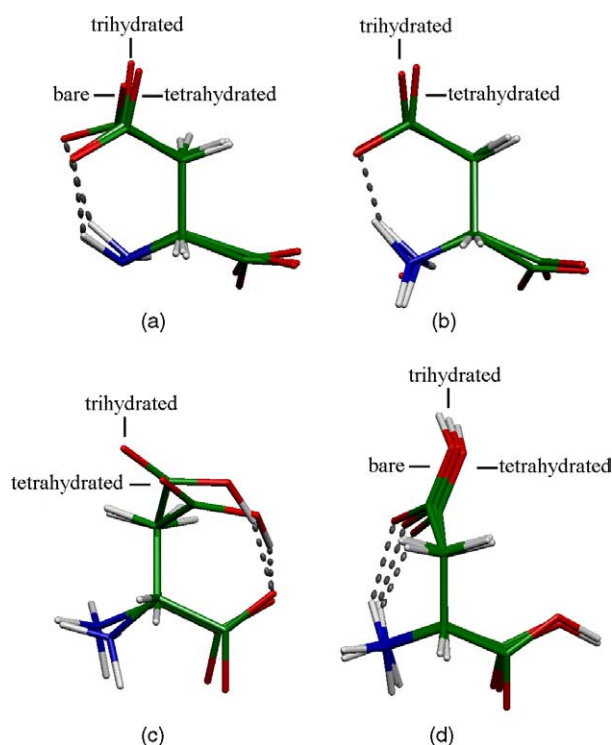

Fig. 7. Superimpose pictures of the geometrical changes of the most stable conformers of species (a) asp^{2-}, (b) $Hasp^-$, (c) H_2asp and (d) H_3asp^+. For clarity, water molecules are not displayed.

Acknowledgements

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.theochem.2005.10.036

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