Effect of Metal Ions (Li + , Na + , K + , Mg 2+ , Ca 2+ , Ni 2+ , Cu 2+ , and Zn 2+) and Water Coordination on the Structure of Glycine and Zwitterionic Glycine

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Effect of Metal Ions (Li⁺, Na⁺, K⁺, Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺) and Water Coordination on the Structure of Glycine and Zwitterionic Glycine

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Interactions between metal ions and amino acids are common both in solution and in the gas phase. Here, the effect of metal ions and water on the structure of glycine is examined. The effect of metal ions (Li⁺, Na⁺, K⁺, Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺) and water on structures of Gly·M^{n+}(H₂O)$_m$ and GlyZwitt·M^{n+}(H₂O)$_m$ ($m = 0, 2, 5$) complexes have been determined theoretically by employing the hybrid B3LYP exchange-correlation functional and using extended basis sets. Selected calculations were carried out also by means of CBS-QB3 model chemistry. The interaction enthalpies, entropies, and Gibbs energies of eight complexes Gly·M^{n+} (M^{n+} = Li⁺, Na⁺, K⁺, Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺) were determined at the B3LYP density functional level of theory. The computed Gibbs energies $\Delta G°$ are negative and span a rather broad energy interval (from −90 to −1100 kJ mol⁻¹), meaning that the ions studied form strong complexes. The largest interaction Gibbs energy (−1076 kJ mol⁻¹) was computed for the NiGly²⁺ complex. Calculations of the molecular structure and relative stability of the Gly·M^{n+}(H₂O)$_m$ and GlyZwitt·M^{n+}(H₂O)$_m$ (M^{n+} = Li⁺, Na⁺, K⁺, Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺; $m = 0, 2,$ and 5) systems indicate that in the complexes with monovalent metal cations the most stable species are the NO coordinated metal cations in non-zwitterionic glycine. Divalent cations Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺ prefer coordination via the OO bifurcated bonds of the zwitterionic glycine. Stepwise addition of two and five water molecules leads to considerable changes in the relative stability of the hydrated species. Addition of two water molecules at the metal ion in both Gly·M^{n+} and GlyZwitt·M^{n+} complexes reduces the relative stability of metallic complexes of glycine. For M^{n+} = Li⁺ or Na⁺, the addition of five water molecules does not change the relative order of stability. In the Gly·K⁺ complex, the solvation shell of water molecules around K⁺ ion has, because of the larger size of the potassium cation, a different structure with a reduced number of hydrogen-bonded contacts. This results in a net preference (by 10.3 kJ mol⁻¹) of the GlyZwitt·K⁺(H₂O)₅ system. Addition of five water molecules to the glycine complexes containing divalent cations Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺ results in a net preference for non-zwitterionic glycine species. The computed relative Gibbs energies are quite high (−10 to −38 kJ mol⁻¹), and the NO coordination is preferred in the Gly·M^{n+}(H₂O)₅ (M^{n+} = Mg²⁺, Ca²⁺, Ni²⁺, Cu²⁺, and Zn²⁺) complexes over the OO coordination.

1. Introduction

Glycine (Gly) is the simplest and smallest among the amino acids found in proteins and is of special interest as a model compound for theoretical and experimental studies of structure and reactivity of amino acids and peptides.[1] Experimental studies on gas-phase glycine demonstrate that it exists in a neutral form.[2−6] Calculations show no barrier to proton transfer and thus predict that the Gly zwitterion is not a stable species in the gas phase in the absence of other stabilizing forces.[7−11] The zwitterionic form of glycine (⁺H₃N−CH₂−COO⁻) can be stabilized by the presence of counterions and/or water molecules. To investigate the nature of the interaction between metal cations and glycine in the gas phase, a number of theoretical studies have been conducted.[10,12−26] The effect of water molecules on the stability of the zwitterionic structure of glycine, valine, and tryptophan was also investigated.[22,27−29] According to Gutowski et al.,[30] the zwitterion structure of glycine can be considerably

stabilized by the attachment of an excess electron. Previous studies[10,12−26] have been shown that the mode of metal ion complexation in the solvated structures changes with the size of M^{n+}. Small metal ions (Li⁺, Na⁺) interact with both the nitrogen and the carbonyl oxygen (NO coordination) in the lowest-energy conformers, while larger metal ions (K⁺, Cu²⁺, Zn²⁺) form Gly OO-coordinated salt bridges[10,15,24] with zwitterions. Zwitterions of amino acids can also be stabilized through interactions with solvent molecules such as water.[10] Calculations by Jensen and Gordon[29] indicated that two water molecules could make the zwitterionic form of Gly a local minimum on the potential energy surface. The three-water molecule cluster yields a Gly zwitterion minimum of about the same energy as the neutral form.[31] In these works, the relative affinities of different modes of binding of a given metal cation were studied using various levels of ab initio self-consistent field (SCF) and density functional theories, but none of them has attempted to investigate the binding role of different cations and solvent (water) in their interaction with the non-zwitterionic and zwitterionic forms of glycine. Here, we use several methods of

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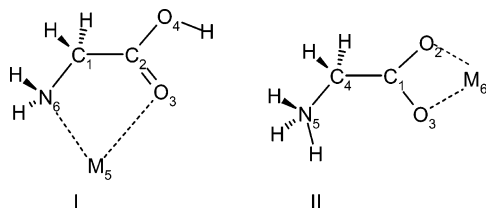
Figure 1. The structure of chelated glycine (**I**) and the zwitterionic form of glycine (**II**).

model chemistry to investigate structures of Gly·M^{n+}, Gly·$M^{n+}(H_2O)_2$, and Gly·$M^{n+}(H_2O)_5$ (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) systems. Further, we also studied GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) systems hydrated by two and five molecules of water. These metal cations have numerous and important biochemical functions in living systems. Their hydrated complexes with glycine should serve as the simplest models for more complex protein−metal systems in an aqueous environment.

2. Computational Details

All systems (Figure 1) were geometry-optimized with the *Gaussian 98* program[32] employing the B3LYP hybrid functional[33−37] with the 6-311+G(d,p) and 6-31+G(d) basis sets as implemented in the *Gaussian 98* package of computer codes.[32] For Ni, Cu, and Zn, we used the 6-311+G(d,p) Wachters−Hay[38,39] all-electron basis set. The calculations of smaller systems were also performed by means of the more accurate CBS-QB3 method.[40] The CBS-QB3 method uses B3LYP coupled to the CBSB7 defined basis set for all geometry optimizations and frequency calculations.

The formation of metal−glycine complexes can be described by reaction A

$$M^{n+} (g) + Gly (g) \rightarrow Gly \cdot M^{n+} (g) \qquad (A)$$

M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}. The gas-phase interaction enthalpy ΔH^{298} for reaction A is defined by eqs 1−3

$$\Delta H^{298} = \Delta E^{298} + \Delta(pV) \qquad (1)$$

$$\Delta H^{298} = [E^{298}_{M^{n+}\cdots Gly} - (E^{298}_{M^{n+}} + E^{298}_{Gly})] + \Delta pV \qquad (2)$$

$$\Delta H^{298} = E^{298}_{M^{n+}\cdots Gly} - E^{298}_{M^{n+}} - E^{298}_{Gly} - RT \qquad (3)$$

where $E^{298}_{M^{n+}\cdots Gly}$ is the energy of the complex, $E^{298}_{M^{n+}}$ the energy of the respective cation, and E^{298}_{Gly} the energy of the ligand at T = 298.15 K. In eq 3, the term ΔpV is substituted by $-RT$, as 1 mol of gas is lost with reaction A. The gas-phase Gibbs energy, ΔG^{298}, of the metal cation coordination reaction may be calculated from

$$\Delta G^{298} = \Delta H^{298} - T\Delta S^{298} \qquad (4)$$

The enthalpy of reaction A was calculated using expression 3. The entropy contribution is given by

$$-T\Delta S^{298} = -T[S(M^{n+}\cdots Gly) - S(M^{n+}) - S(Gly)] \quad (5)$$

The equilibrium geometry and tautomeric equilibria of Gly·M^{n+}, Gly·$M^{n+}(H_2O)_2$, and Gly·$M^{n+}(H_2O)_5$ (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) and corresponding zwitterionic forms were determined at the B3LYP/6-311+G(d,p)

and B3LYP/6-31+G(d) levels of theory. Open-shell calculations have been carried out using a spin-unrestricted formalism.

3. Results and Discussion

3.1. General Considerations. Structures of Gly·$M^{n+}(H_2O)_m$ (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}; m = 0, 2, and 5) ionic complexes were investigated. To account for the effect of metal cations and water on the relative stability and geometric structure of the neutral and zwitterionic species of glycine, we also studied the structures of GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) systems solvated by two and five molecules of water, respectively. Selected structural parameters of the fully optimized metallic complexes of glycine and the zwitterionic form of glycine are given in Tables 1 and 2, and the corresponding numbering scheme is presented in Figure 1. An analysis of the harmonic vibrational frequencies of the optimized species proved that all of them are minima (zero number of imaginary frequencies).

In the solid state and in solution, glycine is known to exist as a zwitterion. In contrast, all experimental evidence indicates that in the gas phase glycine exists in nonionized form.[2,6] Previous high-level theoretical studies have shown[7,8] that the gas-phase zwitterion transforms without barrier into the neutral isomer. Experimental evidence[2,6] and previous theoretical calculations[7−11,20,21] of the molecular structure of isolated glycine have shown that this molecule exists in several stable forms. The most stable structures are stabilized via intramolecular hydrogen bonds and/or hyperconjugation.[11] However, the extended structures represent the most realistic conformation of the glycine moiety in metal chelated systems.[12,41] Suitable starting geometries for glycine complexes with monovalent and divalent cations were generated from dicoordinated complexes of glycine (Figure 1). From experimental investigations,[42−44] it is known that the α-amino acids and their derivatives prefer to form five-membered chelate rings with metal cations. Previous investigations[9,13,15,16,41,45,46] have shown that the most stable structures for a metal cation and glycine are two, namely, the one where the cation binds to both the N6 and the O3 sites of the neutral glycine, and the other where it binds to both oxygen ends of the zwitterionic glycine. Structures **I** and **II** in Figure 1 illustrate the chelated metal ion complexes of glycine and zwitterionic glycine. To evaluate the effect of water on the reactivity of the complexes studied, we also examined di- and pentahydrated complexes of glycine and its zwitterionic form. For an illustration of the geometric structure of these complexes, the optimized coordinated and hydrated systems (represented by lithium species) are shown in Figures 2 and 3. Dihydrated tetrahedral complexes Gly·$M^{n+}(H_2O)_2$ and GlyZwitt·$M^{n+}(H_2O)_2$ (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) model frequently occurring tetracoordinated complexes of metal cations in biological systems.

The Gly·$M^{n+}(H_2O)_m$ and GlyZwitt·$M^{n+}(H_2O)_m$ (m = 0, 2, 5) clusters were generated starting from the low-energy conformers of the Gly·M^{n+} and GlyZwitt·M^{n+} complexes. The progressive hydration of the Gly·M^{n+}·$2H_2O$ and GlyZwitt·M^{n+}·$2H_2O$ complexes in systems with five molecules of water, represented by the Gly·$M^{n+}(H_2O)_5$ and GlyZwitt·$M^{n+}(H_2O)_5$ complexes is shown in Figures 2 and 3. Water molecules were added following the strategies used in our calculations on Gly·$M^{n+}(H_2O)_2$ and GlyZwitt·$M^{n+}(H_2O)_2$ complexes and related systems taken from the literature.[10,23,27,29] The fully optimized structures of the Gly·$M^{n+}(H_2O)_m$ and GlyZwitt·$M^{n+}(H_2O)_m$ (m = 5) systems converged to the energetically stable structures stabilized by both hydrogen bonds and strong electrostatic

TABLE 1: B3LYP/6-311+G(d,p) Optimized Relevant Bond Lengths (Å), Bond Angles (deg), and Dihedral Angles (deg) for the Metal-Coordinated and Hydrated Glycine Species

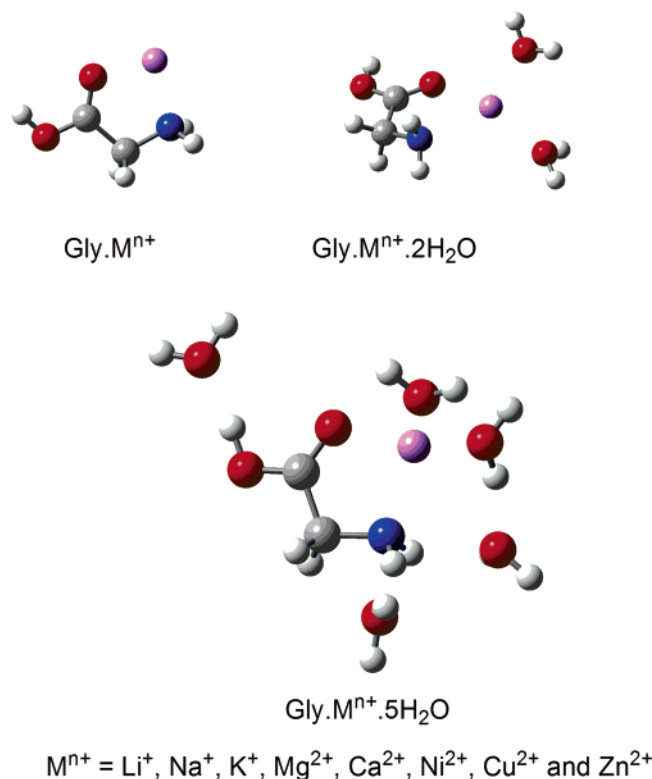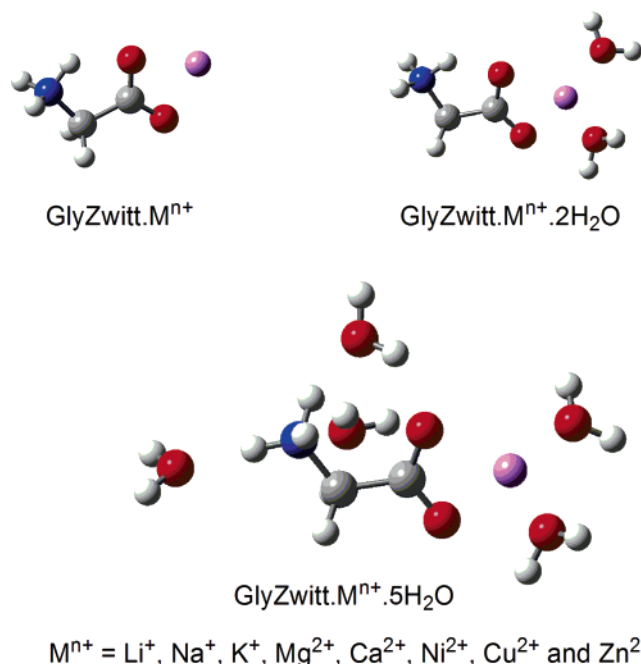| parameters	$(H_2O)_n$	Li$^+$	Na$^+$	K$^+$	Mg^{2+}	Ca^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
					$NH_2CH_2COOH \cdot M(H_2O)_n$				
d[C(1)−C(2)]	$n = 0$	1.517	1.520	1.518	1.518	1.512	1.497	1.506	1.526
	$n = 5$	1.520	1.522	1.521	1.521	1.520	1.505	1.515	1.521
d[C(2)−O(3)]	$n = 0$	1.226	1.219	1.217	1.253	1.248	1.273	1.267	1.256
	$n = 5$	1.226	1.222	1.220	1.250	1.241	1.264	1.254	1.246
d[C(2)−O(4)]	$n = 0$	1.312	1.321	1.326	1.279	1.286	1.267	1.271	1.276
	$n = 5$	1.312	1.318	1.321	1.277	1.288	1.267	1.273	1.280
d[C(1)−N(6)]	$n = 0$	1.483	1.477	1.471	1.511	1.499	1.521	1.514	1.508
	$n = 5$	1.469	1.466	1.465	1.492	1.486	1.494	1.489	1.486
d[N(6)⋯M(5)]	$n = 0$	2.062	2.464	2.916	2.123	2.494	1.902	1.988	2.031
	$n = 5$	2.114	2.467	2.904	2.145	2.566	1.913	2.037	2.153
d[O(3)⋯M(5)]	$n = 0$	1.859	2.234	2.584	1.939	2.181	1.790	1.878	1.934
	$n = 5$	1.958	2.295	2.656	1.986	2.292	1.857	1.966	2.044
Θ[C(1)−C(2)-O(3)]	$n = 0$	122.8	124.5	124.9	121.8	121.4	118.2	120.2	122.7
	$n = 5$	122.8	124.2	124.6	120.8	121.6	117.9	119.8	121.2
Θ[C(2)−C(1)-N(6)]	$n = 0$	110.2	111.7	111.9	111.1	110.8	106.7	109.1	111.9
	$n = 5$	111.3	112.8	112.9	111.3	111.8	107.5	109.1	111.1
Θ[C(1)−N(6)⋯M(5)]	$n = 0$	104.9	108.6	111.4	106.4	111.3	110.1	108.5	104.9
	$n = 5$	106.5	109.9	111.4	108.1	112.1	110.0	109.7	109.9
Θ[C(2)−O(3)⋯M(5)]	$n = 0$	113.9	119.4	126.3	115.8	125.7	117.2	115.3	111.0
	$n = 5$	114.2	118.7	123.6	117.1	125.4	115.9	115.9	116.9
Θ[O(3)⋯M(5)⋯N(6)]	$n = 0$	87.7	72.8	60.9	84.9	70.7	87.7	86.9	89.4
	$n = 5$	84.6	72.2	60.7	82.4	68.5	86.2	83.0	80.8
Φ[O(3)−C(2)-C(1)−N(6)]	$n = 0$	−5.0	−12.8	−13.7	−0.2	3.4	−0.3	−0.4	−0.9
	$n = 5$	−6.6	−10.7	−11.4	4.2	6.0	10.9	10.6	3.4
Φ[C(2)−C(1)-N(6)⋯M(5)]	$n = 0$	6.3	17.8	21.9	0.3	−4.2	0.4	0.4	1.1
	$n = 5$	7.8	15.6	25.0	−6.0	−8.2	−16.2	−16.0	−5.3
Φ[C(1)−C(2)-O(3)⋯M(5)]	$n = 0$	0.2	−1.4	−5.7	0.1	−0.3	0.1	0.1	0.2
	$n = 5$	1.1	−1.7	−12.3	0.3	0.2	0.3	0.9	0.7

TABLE 2: B3LYP/6-311+G(d,p) Optimized Relevant Bond Lengths (Å), Bond Angles (deg), and Dihedral Angles (deg) for the Metal-Coordinated and Hydrated Zwitterionic Form of Glycine Species

parameters	$(H_2O)_n$	Li$^+$	Na$^+$	K$^+$	Mg^{2+}	Ca^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
					$GlyZwitt \cdot M^{n+}(H_2O)_n$				
d[C(1)−C(4)]	$n = 0$	1.536	1.544	1.550	1.515	1.519	1.504	1.508	1.517
	$n = 5$	1.534	1.538	1.542	1.513	1.518	1.503	1.505	1.512
d[C(1)−O(2)]	$n = 0$	1.241	1.237	1.235	1.264	1.260	1.274	1.271	1.267
	$n = 5$	1.243	1.242	1.241	1.268	1.267	1.273	1.271	1.269
d[C(1)−O(3)]	$n = 0$	1.272	1.272	1.272	1.275	1.270	1.276	1.269	1.269
	$n = 5$	1.277	1.275	1.273	1.271	1.267	1.273	1.268	1.267
d[C(4)−N(5)]	$n = 0$	1.514	1.513	1.512	1.509	1.510	1.509	1.510	1.508
	$n = 5$	1.495	1.496	1.497	1.486	1.487	1.484	1.485	1.486
d[O(2)⋯M(6)]	$n = 0$	1.928	2.284	2.621	2.001	2.238	1.843	1.958	1.992
	$n = 5$	1.987	2.369	2.732	2.020	2.264	1.873	1.963	2.018
d[O(3)⋯M(6)]	$n = 0$	1.985	2.346	2.723	2.032	2.297	1.870	2.005	2.050
	$n = 5$	2.092	2.418	2.853	2.057	2.325	1.904	2.016	2.080
Θ[C(1)−C(4)-N(5)]	$n = 0$	106.5	106.1	105.6	111.8	111.2	112.4	112.4	112.1
	$n = 5$	113.8	114.2	114.2	113.8	113.6	113.9	113.9	113.8
Θ[O(2)−C(1)-C(4)]	$n = 0$	119.5	118.3	117.9	119.2	118.4	122.5	121.3	118.8
	$n = 5$	116.2	115.2	114.7	118.0	117.0	120.5	119.3	118.0
Θ[O(3)−C(1)-C(4)]	$n = 0$	116.1	115.0	114.3	120.7	120.1	124.9	124.0	121.1
	$n = 5$	120.0	119.5	119.2	121.9	121.0	124.8	123.9	122.3
Θ[O(2)−C(1)-O(3)]	$n = 0$	124.4	126.7	127.8	120.1	121.5	112.6	114.8	120.1
	$n = 5$	123.8	125.3	126.1	120.1	121.9	114.7	116.8	119.7
Θ[C(1)−O(2)⋯M(6)]	$n = 0$	84.8	89.5	94.0	87.8	91.6	89.5	91.0	88.3
	$n = 5$	87.8	91.0	96.5	88.2	91.5	88.8	89.8	89.1
Θ[C(1)−O(3)⋯M(6)]	$n = 0$	81.6	85.9	88.4	86.1	88.6	88.2	88.9	85.7
	$n = 5$	82.5	88.0	90.1	86.5	88.8	87.4	87.5	86.4
Θ[O(2)⋯M(6)⋯O(3))]	$n = 0$	69.2	57.9	49.8	66.1	58.3	69.6	65.3	65.9
	$n = 5$	66.0	55.7	47.3	65.3	57.7	69.2	65.9	64.7
Φ[O(2)−C(1)-C(4)−N(5)]	$n = 0$	180.0	180.0	179.9	−179.9	−179.9	−179.8	180.0	180.0
	$n = 5$	176.7	179.3	−179.9	179.2	179.9	178.9	179.3	179.4
Φ[C(4)−C(1)-O(2)⋯M(6)]	$n = 0$	180.0	180.0	179.9	−179.9	−179.9	−179.9	180.0	180.0
	$n = 5$	179.7	−179.9	−179.9	−179.8	179.9	179.7	179.9	−179.9
Φ[C(4)−C(1)-O(3)⋯M(6)]	$n = 0$	180.0	180.0	−179.9	179.9	179.9	179.9	180.0	180.0
	$n = 5$	−179.7	179.9	179.9	179.9	−179.9	−179.6	−179.9	179.9
Φ[C(1)−O(2)⋯M(6)⋯O(3)]	$n = 0$	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	$n = 5$	0.0	−0.1	0.0	0.0	0.0	0.0	0.0	0.0

Gly.M^{n+} Gly.M^{n+}.2H$_2$O

Gly.M^{n+}.5H$_2$O

M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}

Figure 2. Overall structure of the B3LYP/6-311+G(d,p) optimized complexes of chelated glycine and its hydrates.

GlyZwitt.M^{n+} GlyZwitt.M^{n+}.2H$_2$O

GlyZwitt.M^{n+}.5H$_2$O

M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}

Figure 3. Overall structure of the B3LYP/6-311+G(d,p) optimized complexes of the chelated zwitterionic form of glycine and its hydrates.

interaction between water molecules and charged parts of the Gly·M^{n+} and GlyZwitt·M^{n+} complexes.

Systems Gly·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). Our previous calculations[20,21,26] have shown that metal coordination of the amino group nitrogen and oxygen of the carbonyl group of the glycine conformer results in changes of the optimum geometry of the parent compound. The effect of gradual hydration on the geometry of the Gly·M^{n+} and GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) systems indicates that hydration can also cause

observable changes in the geometry of the parent complexes. Selected structural parameters of the fully optimized metal complexes and their hydrated systems are given in Tables 1 and 2. General trends in changes of geometry of the metal complexes upon gradual hydration are the same. However, for simplicity, only the results for pentacoordinated systems (which represent the most complex first hydration shell studied) are discussed.

The hydration of the neutral Gly·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) systems results in different changes of the optimum geometry of the parent metal complexes (Table 1). The covalent bond lengths C(1)−C(4), C(1)−O(2), C(1)−O(3), and C(4)−N(5) of glycine are only slightly changed upon hydration. On the other hand, the M^{n+}···O and M^{n+}···N bonds in pentahydrated complexes are by about 0.01−0.09 Å longer. The M^{n+}···O bonds are always shorter (about 0.1−0.2 Å) than the analogous M^{n+}···N bonds (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}), indicating that all of these metal cations form stronger bonds to the oxygen atom of glycine. The equilibrium distances M^{n+}···O and M^{n+}···N decrease in the order K$^+$ > Ca^{2+} ≥ Na$^+$ > Mg^{2+} ≥ Li$^+$ ≥ Zn^{2+} > Cu^{2+} > Ni^{2+}. With regard to valence angles, larger changes (by about 1−3°) were observed only in the values of the valence angles C(1)−N(6)···M(5) and C(2)−O(3)···M(5) of the parent metal complexes in pentahydrated systems. The N···M^{n+}···O angle in the complexes of glycine extends relatively over a large interval (60−90°) and upon hydration slightly decreases. The chelate rings of the metallic complexes are almost planar (dihedral angles O(3)−C(2)−C(1)−N(6) and C(2)−C(1)−N(6)···M(5)), and the planarity of this moiety is also preserved in the pentahydrated complexes. Larger deviations from planarity upon hydration were only observed in complexes with the transition metals Ni^{2+}, Cu^{2+}, and Zn^{2+} (Table 1).

Systems GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). The interaction of inorganic cations with the anionic carboxylate group of zwitterionic glycine represents another category of complexes. Selected structural parameters of the isolated and pentahydrated GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) systems are presented in Table 2. An analysis of the directions in which metal ions approach a carboxyl group in crystal structures showed that the most likely arrangements of metal cations are syn, anti, and bidentate.[47] Bidentate (direct) bonding, in which the metal cation is oriented symmetrically to two oxygen atoms of the functional group (Figure 1), is preferred in the M^{n+}···O 2.3−2.6 Å separation range.[48] The complexes GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) represent an interaction of this type. For the GlyZwitt·M^{n+} complexes, the M^{n+}···O distances were found slightly shorter (1.9−2.6 Å), that those observed experimentally[48] (Table 2). This shortening of the M^{n+}···O length in our systems in comparison with the experimentally observed distances of the crystal structures of biomolecules could be partly because in real situations the equilibrium position of a metal cation is influenced by the stereochemical constraints of the biomolecule, the presence of other cations, and the effect of its environment.

The changes in geometry of zwitterionic glycine with hydration can be summarized as follows: The C(1)−C(4) and C(4)−N(5) bonds are slightly shortened and the C(1)−O(2) and C(1)−O(3) bonds are slightly elongated in most complexes. However, the C(1)−O(2) bond length was computed to be always about 0.01−0.03 Å shorter than the C(1)−O(3) distance. Thus, the metal coordination to the −COO$^-$ group of zwitterionic glycine is slightly asymmetric. The M^{n+}···O bonds are

TABLE 3: Calculated Gas-Phase Enthalpies, ΔH, Entropies, ΔS, and Gibbs Energies, ΔG, of the Ion−Glycine Systems

no	system		ΔH^{298} kJ mol^{-1}	ΔS^{298} J mol^{-1} K^{-1}	ΔG^{298} kJ mol^{-1}
1a	Gly···Li$^+$	A[a]	−250.0	−115.0	−215.7
		B[b]	−257.1	−115.5	−222.7
		C[c]	−236.0	−115.1	−201.7
		exp.[d]	−213.4		−176.1
1b	Gly···Na$^+$	A	−172.5	−116.1	−137.9
		B	−182.4	−113.4	−148.6
		C	−150.9	−116.3	−116.2
		exp.[d]	−153.1; −157.3; −154.4; −161.0		
1c	Gly···K$^+$	A	−119.7	−108.2	−87.4
		B	−124.2	−105.5	−92.8
		exp.[d]	−125.5		
1d	Gly···Mg^{2+}	A	−668.5	−130.6	−629.6
		B	−683.9	−125.8	−646.4
		C	−643.9	−130.7	−604.9
1e	Gly···Ca^{2+}	A	−470.0	−115.2	−435.7
		B	−430.7	−113.3	−396.9
1f	Gly···Ni^{2+}	A	−1114.6	−130.3	−1075.8
		B	−1147.3	−153.1	−1101.7
1g	Gly···Cu^{2+}	A	−972.9	−128.4	−934.6
		B	−1001.5	−119.7	−905.8
1h	Gly···Zn^{2+}	A	−846.6	−135.9	−806.1
		B	−872.3	−132.2	−832.9

[a] A − B3LYP/6-311+G(d,p) method. [b] B − B3LYP/6-31+G(d) method. [c] C − CBS-QB3 method. [d] Refs 52−54, 56, 57.

about 0.01−0.05 Å longer in pentahydrated complexes (Table 2). The equilibrium M$^+$···O distances decrease in the order K$^+$ > Na$^+$ > Ca^{2+} > Mg^{2+} > Zn^{2+} ≥ Cu^{2+} ≥ Li$^+$ > Ni^{2+}. The M^{n+}···O distances from the lithium to calcium cations can be approximately correlated to the ionic radii[49,50] for Li$^+$ (0.6), Na$^+$ (0.95), K$^+$ (1.33), Mg^{2+} (0.65), and Ca^{2+} (1.0), respectively. The O(2)−C(1)−C(4)−N(5) moiety of zwitterionic glycine is planar and becomes slightly nonplanar upon hydration. The O(2)···M^{n+}···O(3) angle of the "bifurcated" metal bond lies within the relatively narrow interval of 50−70°. The chelate rings of the complexes GlyZwitt·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) are almost planar in both isolated and pentahydrated systems.

3.2. Interaction Enthalpies, Entropies, and Gibbs Energies of the M^{n+}−Glycine complexes (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). Table 3 contains the interaction enthalpies (metal affinities), entropies, and Gibbs energies (metal acidities) of the metal ion−glycine systems computed by several theoretical methods. For comparison, the available experimental gas-phase thermodynamic data[51−53] are also included in this table. Thermodynamic parameters computed using the double-ζ 6-31+G(d) basis set are always by about 5−10 kJ mol^{-1} higher than the more accurate[54] calculations using the triple-ζ basis set. However, the relative trends in individual stability of glycine metallic complexes are equally reproduced by both methods. Table 3 also presents the available interaction enthalpies and Gibbs energies for selected complexes computed at the higher CBS-QB3 level of theory. The B3LYP/6-311+G(d,p) values are close to the CBS-QB3 results with an average absolute deviation of about 20 kJ mol^{-1}. The CBS-QB3 formalism approximates a high-level calculation with a very large basis set. The comparison of the B3LYP results with this method shows that density functional theory performs quite well and can be used as a relatively inexpensive alternative for investigations of larger metal complexes.

In real molecular complexes, the tendency to associate is described by Gibbs energies. It is, therefore, important to know the role of entropy in the processes studied. Table 3 also lists the differences in $S°$ values of the complexes and the isolated species. The formation of a single cationic metal−ligand complex from a pair of species necessarily involves a loss of entropy. In the case of the metallic complexes of glycine, the entropy change due to complexation is some −105 to −135 J mol^{-1} K^{-1}, and calculated enthalpies and Gibbs energies follow the same trend in the acidity of the metal cations studied. Slightly larger entropy changes are exhibited upon coordination of bivalent metal cations. The computed Gibbs energies $\Delta G°$ are negative and span a rather broad energy interval (from −90 to −1100 kJ mol^{-1}).

Glycine is a simple Lewis base, which involves a harder (O) and softer (N) basic center. The selectivity of the base glycine toward Lewis acids may be analyzed on the basis of hardness, charge, and ion size of cations studied. The coordination of individual metal cations can be also classified by the preferred ligand atoms. It is well-known that certain metal ions (hard Lewis acids) exhibit higher affinity for oxygen (O)-donor ligands, whereas metal ions acting as soft Lewis acids prefer to coordinate to nitrogen (or sulfur) donors.[49,54] Thus, the harder the Lewis acid, the stronger is the preference for O compared to N. For ionic complexes of the alkali metals, the following order of stability was found: Li$^+$ > Na$^+$ > K$^+$. The same stability order would be expected on the basis of their ionic radii[49,50] (for K$^+$ (1.33), Na$^+$ (0.95), Li$^+$ (0.6)). Bivalent cations, because of their higher positive charge of +2, are always bonded substantially more strongly to glycine than lithium, sodium, or potassium cations. The stability of the alkaline-earth metal Mg^{2+} and Ca^{2+} complexes of glycine also obeys the selection by ion size [Ca^{2+} (1.0), Mg^{2+} (0.65)] (magnesium complex of glycine is about 200 kJ mol^{-1} more stable than calcium complex). This indicates that effects such as covalence, steric hindrance, or other specific factors do not operate in complexes of glycine with alkali and alkaline-earth metals. A third category of species represents glycine complexes with Ni^{2+}, Cu^{2+}, and Zn^{2+} ions, respectively. The Gibbs energies of complexation reactions show an increasing binding affinity in the order Ni^{2+} > Cu^{2+} > Zn^{2+}. According to the highest interaction energies (Table 3), the transition metals Ni^{2+}, Cu^{2+} are most effectively recognized by the basic center of glycine.

Attachment of metal cations (Li$^+$, Na$^+$, K$^+$) to amino acids in the gas phase has been investigated experimentally.[51−53,56] Kebarle and co-workers[56] used the threshold collision-induced dissociation (CID) technique for determination of sodium and potassium binding enthalpies for glycine (−153.1 kJ mol^{-1} and −125.5 kJ mol^{-1}, respectively). Ohnanessian and co-workers used high-pressure mass spectrometric experiments for measurement of gas-phase sodium ion affinities for organic compounds.[52] On the basis of their experiments and by analysis available experimental and theoretical sodium ion affinities,[52] they recommended a sodium binding enthalpy for glycine to be 154.8 ± 8 kJ mol^{-1}. Wesdemiotis et al. used the collision-induced dissociation (CID) method for determination of the Na$^+$ affinities of α-amino acids.[53] The binding enthalpy for the glycine−Na$^+$ complex was estimated[53] to be 161 ± 8 kJ mol^{-1}. Gronert and co-workers via the kinetic method in a quadrupole ion trap mass spectrometer determined lithium cation binding energies of gaseous amino acids.[51] The binding Gibbs energy for the complex glycine−Li$^+$ was −176.1 ± 8 kJ mol^{-1}. Bojesen and co-workers determined lithium and sodium affinities[57] of glycine to be −213.4 and −158.6 kJ mol^{-1}.

A comparison of the CBS-QB3 computed enthalpies for the binding of sodium cation to glycine and available experimental values shows that CBS-QB3 and experimental data agree within

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TABLE 4: Relative Stability of Neutral and Zwitterionic Metal Ion Complexes of Glycine (Gly·M^{n+}) for Reactions GlyZwitt·M^{n+}·mH$_2$O → Gly·M^{n+}·mH$_2$O (m = 0, 2, 5)

cation (M^{n+})		GlyZwitt·M^{n+} → Gly·M^{n+}			GlyZwitt·M^{n+}·2H$_2$O → Gly·M^{n+}·2H$_2$O			GlyZwitt·M^{n+}·5H$_2$O → Gly·M^{n+}·5H$_2$O		
		ΔH^{298} kJ mol^{-1}	ΔS^{298} J mol^{-1} K^{-1}	ΔG^{298} kJ mol^{-1}	ΔH^{298} kJ mol^{-1}	ΔS^{298} J mol^{-1} K^{-1}	ΔG^{298} kJ mol^{-1}	ΔH^{298} kJ mol^{-1}	ΔS^{298} J mol^{-1} K^{-1}	ΔG^{298} kJ mol^{-1}
Li$^+$	A[a]	−24.2	2.0	−24.8	−26.5	−6.0	−24.7	−4.6	26.5	−12.5
	B[b]	−16.7	−3.3	−15.7	−19.6	−12.8	−15.8	5.4	21.8	−1.1
	C[c]	−20.7	1.7	−21.2						
Na$^+$	A	−12.7	0.3	−12.8	−18.3	13.4	−22.3	7.0	37.9	−4.3
	B	−4.9	−0.3	−4.8	−11.0	8.7	−13.6	17.5	48.3	3.1
	C	−11.6	0.0	−11.6						
K$^+$	A	−9.5	3.0	−10.4	−10.6	38.6	−22.1	21.6	37.9	10.3
	B	−1.6	2.0	−2.2	−2.5	36.9	−13.5	28.6	47.9	14.3
Mg^{2+}	A	25.3	−13.4	29.3	19.3	1.0	19.0	−16.9	−20.5	−10.8
	B	37.5	−7.4	39.7	30.6	−5.0	32.1	−5.5	−17.4	−0.3
	C	36.4	−14.4	40.7						
Ca^{2+}	A	45.5	−1.3	45.9	32.4	−1.3	32.8	−47.0	−61.7	−28.6
	B	53.4	−12.4	57.1	40.9	−4.7	42.3	−45.2	−64.1	−26.1
Ni^{2+}	A	4.8	−6.4	6.7	−8.0	−24.2	−0.8	−41.3	−55.7	−24.7
	B	12.8	−30.5	21.9	4.0	−13.4	8.0	−34.1	54.7	−17.8
Cu^{2+}	A	22.7	−8.1	25.1	9.6	−9.7	12.5	−29.7	−68.8	−9.2
	B	30.9	−0.3	31.0	20.6	−2.7	21.4	−25.1	−75.2	−2.7
Zn^{2+}	A	0.6	−14.8	5.0	−1.7	−32.9	8.1	−55.5	−59.7	−37.7
	B	12.1	−11.1	15.4	12.2	−10.4	15.3	−47.2	−67.8	−27.0

[a] A − B3LYP/6-311+G(d,p) method. [b] B − B3LYP/6-31+G(d) method. [c] C − CBS-QB3 method.

the targeted range of 10 kJ mol^{-1}. A larger difference between theory and experiment was observed in the case of the GlyLi$^+$ complex. Our best (CBS-QB3 method) Gibbs energy value of 201.7 kJ mol^{-1} is about 25 kJ mol^{-1} larger than the experimental one. Similarly, our calculated lithium affinity (enthalpy) is about 23 kJ mol^{-1} larger than the experimental lithium affinity of glycine[57] measured by Bojesen et al. Calculations by Russo et al. gave glycine lithium and sodium affinities values[58] of −243.9 and −163.6 kJ mol^{-1} (B3LYP/6-311G(d,p) method) and are in good agreement with our calculations using the B3LYP/6-311+G(d,p) method (Table 3). The observed discrepancies between our theoretically computed and available experimental metal affinities of glycine could be partly due to some uncertainty in the interpretation of experimental data[52,53,56−58] which introduces larger errors in the absolute metal ion affinities. From the computational point of view, there is also some uncertainty in computations of metal ion affinities. With respect to the possible existence of several stable rotational conformers of glycine,[21,58] the enthalpy of complexation may be computed between two arbitrary species, but only the differences between the most stable species can have physical meaning and can be compared with experiments. Previous theoretical calculations indicate that the most stable conformer of glycine is that in which a hydrogen bond between the −NH$_2$ group (donor) and the carboxyl oxygen (acceptor) is formed.[21,58] In bicoordinated metal ion complexes of glycine, a rearrangement of the −NH$_2$ hydrogens is required in order to prepare the nitrogen lone pair for the interaction with the metal. This conformer of glycine is, according to the calculations,[21] some 6 kJ mol^{-1} less stable than the most stable structure stabilized by the intramolecular hydrogen bond −NH$_2$···O=C. Thus, the consideration of the thermodynamically most stable structure in our calculations (Table 3) introduces additional conformational stabilization to the interaction energy of the glycine−metal cation complexes studied.

3.3. Relative Stability of the of Gly·M^{n+}(H$_2$O)$_m$ and GlyZwitt·M^{n+}(H$_2$O)$_m$ (m = 0, 2, and 5) Complexes (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). As is well-known, the zwitterionic form of glycine does not exist in the gas phase.[2−6] However, the metal cations and/or water molecules may stabilize the zwitterionic structure of glycine.[10,15,24,29] In

that case, it appears as a minimum on the potential energy surface. The calculated relative enthalpies, entropies, and Gibbs energies of the fully optimized metal-coordinated and hydrated glycine and zwitterionic glycine species are given in Table 4. The B3LYP/6-311+G(d,p) method reproduces well the calculations of selected systems using the more accurate CBS-QB3 method. Thus, the results obtained by this method (method A, Table 4) will be used for the interpretation of results obtained for larger systems under study.

Reaction GlyZwitt·M^{n+} → Gly·M^{n+} (M^{n+} = Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). Relative enthalpies, entropies, and Gibbs energies for ion-coordinated glycine and zwitterionic glycine indicate that the coordination of the negatively charged carbonyl group of the zwitterionic glycine by certain metal cations can considerably stabilize GlyZwitt·M^{n+} complexes. Alkali metal cations of lithium, potassium, or sodium in the gas phase prefer to form bicoordinated metal complexes with glycine. The largest stabilizing effect is exhibited by lithium cation (about 20−25 kJ mol^{-1}). The net preference of GlyNa$^+$ and GlyK$^+$ complexes is the same and also large (about 10 kJ mol^{-1}). Russo et al. also found GlyLi$^+$ and GlyNa$^+$ systems more stable by 25.9 and 14.6 kJ mol^{-1} than the corresponding zwitterionic structures.[58] More interesting is the coordination of divalent cations. The coordination of the divalent alkaline-earth metal Mg^{2+} and Ca^{2+} cations to the two glycine species studied results in a pronounced stabilization of the zwitterionic form. The larger stabilization of the zwitterionic structure of glycine by these divalent ions could be explained on the basis of electrostatic effect. It is well-known that the adhesion of alkaline and alkaline-earth cations to basic centers is, because of their smaller polarizing effect, much lower and results in the formation of an essentially electrostatic bond.[59] On the basis of purely electrostatic effects, the strength of the binding of bivalent metal cations to the negatively charged carboxyl group of GlyZwitt should be considerably larger. The preference for GlyZwitt·M^{n+} complexes increases in the order Li$^+$ < Na$^+$ < K$^+$ < Mg^{2+} < Ca^{2+} (Table 4). For the glycine complexes with alkaline-earth cations Mg^{2+} and Ca^{2+}, the thermodynamically most stable species are zwitterionic ones. In the case of the transition metal Ni^{2+}, Cu^{2+}, and Zn^{2+} ions, the situation is slightly different. It is interesting that the M^{n+}···O

distances from nickel to zinc cation are varying within the relatively short interval of 1.85−2.0 Å, and they do not correlate with the ionic radii[49,50] for Ni^{2+} (0.72), Cu^{2+} (0.69), and Zn^{2+} (0.65), respectively. In the complexation of transition metal cations Ni^{2+}, Cu^{2+}, and Zn^{2+}, the charge transfer is important.[18,58] The largest stabilization Gibbs energy of 25.1 kJ mol^{-1} was computed for the open-shell system GlyZwitt·Cu^{2+}.

Reaction GlyZwitt·M^{n+}·$(H_2O)_2 \rightarrow$ Gly·M^{n+}·$(H_2O)_2$ (M^{n+} = Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). The strongest interaction sites for water molecules should be the end of the metal ion of Gly·M^{n+} and GlyZwitt·M^{n+} systems because of their higher charge.

Hydration of the metal-coordinated complexes of glycine species by two water molecules was investigated for tetrahedral species (Figures 2 and 3). Our calculations indicate that the addition of two water molecules to the Gly·M^{n+} and GlyZwitt·M^{n+} systems does not significantly affect the relative energetics of structures containing glycine and zwitterionic glycine (Table 4). The largest changes in the relative stability of glycine and zwitterionic glycine complexes were computed for sodium and potassium compounds. In these systems, the addition of two water molecules caused further stabilization of the Gly·M^+ complexes. Among the divalent cationic complexes studied, the Gly·Ni^{2+}·$(H_2O)_2$ complex resulted, at the higher level of calculations, in 0.8 kJ mol^{-1} greater stability than the zwitterionic one. For all hydrated complexes (with the exception of the copper species), the stable species correspond to the nonplanar tetrahedral structures. On the other hand, the solvation unit in the Cu^{2+} complex is a planar glycine···Cu^{2+}(H_2O)$_2$ system. Planar [Cu···L$_4$]$^{2+}$ complexes have also been found by Ziegler and co-workers[60] using density functional theory, and the existence of [Cu···L$_4$]$^{2+}$ complexes has been experimentally confirmed by Stace and co-workers recently.[61]

Reaction GlyZwitt·M^{n+}·$(H_2O)_5 \rightarrow$ Gly·M^{n+}·$(H_2O)_5$ (M^{n+} = Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}). The complexes solvated by five water molecules were constructed from the fully optimized complexes solvated by two water molecules. Further, three molecules of water were located in the hydrogen bonding positions in the vicinity of the OH and NH$_2$ groups of the glycine. In zwitterionic glycine, another three molecules of water were bound by means of NH$^+$···O hydrogen bonds to the protonated NH$_3^+$ group of the zwitterionic glycine. Table 4 lists the relative energies for pentahydrated complexes. Our calculations at the B3LYP/6-311+G(d,p) level of theory indicate that addition of five water molecules to the Gly·M^{n+} and GlyZwitt·M^{n+} complexes leads to change of the relative stability of Gly·M^{n+} and GlyZwitt·M^{n+} species for individual cations (Table 4). For M^{n+} = Li^+ and Na^+, the addition of five water molecules does not change the relative order of stability. Structures containing non-zwitterionic glycine are 12.5 and 4.3 kJ mol^{-1} more stable. In the Gly·K^+ complex, the solvation shell of water molecules around K^+ ion has, owing to the much larger size of potassium cation in comparison with lithium and sodium cations, a different structure with a reduced number of hydrogen-bonded contacts. This results in lower energetic stability of the Gly·K^+(H_2O)$_5$ complex and net preference (by 10.3 kJ mol^{-1}) for the GlyZwitt·K^+(H_2O)$_5$ system. Even more interesting is the situation with the glycine complexes containing the divalent cations Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}. The net stabilizing effect of the addition of five water molecules to the metal ion complex of glycine is always larger than the stabilizing effect of three intermolecular hydrogen bonds NH$^+$···O of water molecules bound to the protonated −NH$_3$ group of the zwitterionic glycine. The computed relative Gibbs energies are quite high (−10 to −38 kJ mol^{-1}), and the NO coordination is preferred over the OO coordination in the Gly·M^{n+}(H_2O)$_5$ (M^{n+} = Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) complexes.

Summary and Conclusions

Our model calculations of the molecular structure and relative stability of the Gly·M^{n+}(H_2O)$_m$ and GlyZwitt·M^{n+}(H_2O)$_m$ (M^{n+} = Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}; m = 0, 2, and 5) systems indicate that in the complexes with monovalent metal cations the most stable species are the NO-coordinated metal cations with non-zwitterionic glycine. The divalent cations Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} prefer coordination via the OO group of the zwitterionic glycine. Stepwise addition of two and five water molecules leads to considerable changes in the relative stability of the individual hydrated species studied. Addition of two water molecules at the metal ion in both Gly·M^{n+} and GlyZwitt·M^{n+} complexes reduces the observed relative stability of individual metallic complexes of glycine. For M^{n+} = Li^+ and Na^+, the addition of five water molecules does not change the relative order of stability. In the Gly·K^+, complex the solvation shell of water molecules around K^+ ion has, because of the larger size of potassium cation, a different structure with reduced hydrogen-bonded contacts. This results in a net preference (by 10.3 kJ mol^{-1}) for the GlyZwitt·K^+(H_2O)$_5$ system. Addition of five water molecules to the glycine complexes containing the divalent cations Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} results in a net preference for non-zwitterionic glycine species. The computed relative Gibbs energies are quite high (−10 to −38 kJ mol^{-1}), and NO coordination is preferred over the OO coordination in the Gly·M^{n+}(H_2O)$_5$ (M^{n+} = Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) complexes. The interaction enthalpies, entropies, and Gibbs energies of eight complexes Gly·M^{n+} (M^{n+} = Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}) were determined at the B3LYP density functional level of theory. The computed Gibbs energies $\Delta G°$ are negative and span a rather broad energy interval (from −90 to −1100 kJ mol^{-1}). For ionic complexes of the alkali metals and the alkaline-earth metals, the following order of stability was found: Mg^{2+} > Ca^{2+} > Li^+ > Na^+ > K^+. The same stability order would be expected according to ionic radii. A third category of species represents glycine complexes with the metal ions Ni^{2+}, Cu^{2+}, and Zn^{2+}. The Gibbs energies of complexation reactions show an decreasing binding affinity in the order Ni^{2+} > Cu^{2+} > Zn^{2+}. The transition metal ions Ni^{2+} and Cu^{2+} are most effectively bound by the basic center of glycine. The largest interaction Gibbs energy (−1076 kJ mol^{-1}) was computed for the NiGly^{2+} complex.

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