Interaction of Co^+ and Co^{2+} with Glycine. A Theoretical Study

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Cobalt cations are open shell systems with several possible electronic states arising from the different occupations of the 3d and 4s orbitals. The influence of these occupations on the relative stability of the coordination modes of the metal cation to glycine has been studied by means of theoretical methods. The structure and vibrational frequencies have been determined using the B3LYP method. Single-point calculations have also been carried out at the CCSD(T) level. The most stable structure of Co^+−glycine is bidentate, with the Co^+ cation interacting with the amino group and the carbonyl oxygen of neutral glycine, and the ground electronic state being ^3A. For Co^{2+}−glycine, the lowest energy structure corresponds to the interaction of the metal cation with the carboxylate group of the zwitterionic glycine, the ground electronic state being $^4A''$.

Introduction

Interactions of metal cations with amino acids and peptides have attracted increasing attention in the past few years, which is reflected in the large number of publications devoted to this topic.[1−47] This interest arises for different reasons. On one hand, metal cation binding to peptides can induce activation effects which, under mass spectrometry conditions, can lead to specific fragmentations providing helpful information on the amino acid sequence of the peptide.[1−8,12,14] Interpretation of the mass spectra requires the accurate knowledge of the interactions between metal cations and amino acid residues. On the other hand, complexes of metal cations and amino acid residues are implicated in a great number of fundamental biological processes, such as dioxygen transport, electron transfer, or oxidation.[48] In particular, cobalt cations are essential for organisms as trace nutrients and are present in vitamin B_{12} in humans.[48,49] However, the excess concentration of different transition-metal cations such as cobalt, zinc, or nickel is toxic. As a response of metal toxicity, living systems have developed mechanisms of resistance based on the intracellular complexation of the toxic metal ion by peptides such as phytochelatins[50] or metallothioneins,[49] which involves the interaction of the cation with the amino acid residues.

These facts have motivated the experimental[16−27,43] and theoretical[21−27,35−47] study of the activation of different amino acids by metal cations. Theoretical methods allow us to study precisely the interaction of metal cations with amino acids and small peptides,[8,15,33,34] providing accurate determinations of some relevant magnitudes, such as complexation energies. However, till now most of the reported work has focused on the interaction of alkali and alkaline-earth metals with glycine,[25,36,38,39,41,42,45] the interaction of closed shell transition-metal cations with glycine,[35,37−40,42−44,46] or other metal−amino acid systems.[35,38,42,44,47] To the best of our knowledge, the interaction of cobalt cations with amino acids has not been considered from a theoretical point of view, and only some experimental work has been done on this topic.[7,20]

The aim of the present work is to provide a detailed analysis of the gas-phase binding chemistry between Co^+ and Co^{2+} cations and glycine, the simplest amino acid. The ground electronic states of Co^+ and Co^{2+} are $^3F(3d^8)$ and $^4F(3d^7)$, respectively.[51] Due to their open shell nature, the interaction of these cations with amino acids can lead to several low-lying electronic states arising from different metal d occupations. Moreover, depending on the degree of metal complexation, the relative stability of different spin electronic states could vary. Thus, in addition to the triplet states derived from the interaction of the $^3F(3d^8)$ ground state of Co^+, we have also considered the quintet and singlet states that arise from the $^5F(4s^13d^7)$ and $^1G(3d^8)$ excited states of Co^+.

Methods

Molecular geometries and harmonic vibrational frequencies of the considered structures have been obtained using the nonlocal hybrid three-parameter B3LYP density functional approach,[52−55] as implemented in the Gaussian 98 set of programs. Previous theoretical calculations have shown that the B3LYP approach is a cost-effective method for studying transition-metal−ligand systems.[56−60] However, to confirm the reliability of the B3LYP results for Co^+−L and Co^{2+}−L systems, we have performed calibration calculations for Co^+−H_2O and Co^{2+}−H_2O monohydrates. Different electronic states have been computed both with B3LYP and using the single and double coupled cluster method with a perturbational estimate of the triple excitations, CCSD(T).[61] In these calculations all valence electrons have been correlated.

Geometry optimizations and frequency calculations have been performed using the following basis set. The Co basis is based on the (14s9p5d) primitive set of Wachters[62] supplemented with one s diffuse function, two p diffuse functions, and one d diffuse function[63] and two f polarization functions,[64] the final contracted basis set being [10s7p4d2f]. For C, N, O, and H we have used the 6-311++G(2df,2p) basis set. Thermodynamic corrections have been obtained assuming an ideal gas, unscaled harmonic vibrational frequencies, and the rigid rotor approximation by standard statistical methods.[65] Net atomic charges and spin

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TABLE 1: Computed Excitation and Interaction Energies (kcal/mol)

system	state	open shell	d_{Co-O} (Å)	ΔE^a		
				B3LYP	CCSD(T)	exptl[b]
Co^+	$(d^8)\ ^3F$			0.0	0.0	0.0
	$(s^1d^7)\ ^5F$			17.3	11.5	9.9
	$(d^8)\ ^1G$			61.1	51.4	52.8
Co^+-H_2O	$^3B_1$	$d_{x^2-y^2}$, d_{xz}	1.970	0.0	0.01	
	$^3A_2$	d_{z^2}, d_{xy}	1.989	0.06	0.0	
	$^3A_1$	d_{z^2}, $d_{x^2-y^2}$	1.994	0.08	0.04	
	$^3B_2$	$d_{x^2-y^2}$, d_{yz}	2.006	2.3	2.1	
	$^5B_2$	d_{z^2}, d_{xz}, d_{xy}, s	2.064	23.0 (15.6)	16.0 (14.4)	
	(1) $^5B_1$	d_{z^2}, d_{yz}, d_{xy}, s	2.114	25.4 (18.0)	18.0 (16.4)	
	(2) $^5B_1$	d_{z^2}, d_{xz}, $d_{x^2-y^2}$, s	2.037	27.8 (20.4)	19.3 (17.7)	
	$^1A_1$	[c]	1.923	57.9 (49.6)	50.3 (51.7)	
$Co^{2+}-H_2O$	$^4B_2$	d_{z^2}, d_{xz}, d_{xy}	1.877	0.0	0.0	
	$^4B_1$	d_{z^2}, $d_{x^2-y^2}$, d_{xz}	1.868	3.3	2.4	

[a] In parentheses are given corrected values assuming errors on atomic excitation energies. [b] Reference 51. [c] The empty orbital corresponds to the d_{xz} orbital.

densities have been obtained using the natural population analysis of Weinhold et al.[66] Open shell calculations have been performed using an unrestricted formalism. All calculations have been performed with the Gaussian 98 package.[67]

Results and Discussion

Calibration Calculations. *$Co^{n+}-H_2O$ Systems*. The relative energies of different electronic states of Co^+-H_2O and $Co^{2+}-H_2O$ are given in Table 1. Following previous calculations reported in the literature,[68−71] we have selected the lower electronic states of each spin state.

As for the free metal ion, the triplet states of Co^+-H_2O are the most stable ones. However, the three lowest triplet states are almost degenerate, thus making it impossible to assign a unique ground electronic state, as pointed out in different previous published works.[68−71] Comparing the quintet with the triplet states, the former ones lie higher in energy. In fact, the energy difference between the quintet and triplet states in Co^+-H_2O increases compared to that of free Co^+. This is due to the occupation of the 4s orbital of Co^+ in the quintet states, which leads to a larger metal−ligand repulsion and, as a consequence, to larger Co^+-O distances. As for free Co^+, singlet states lie higher due to the loss of d−d exchange. However, the singlet−triplet separation in Co^+-H_2O is somewhat lower than the value found for Co^+, showing a slight decrease of the repulsion in the singlet state compared to the triplet ones, as reflected by the Co−O distances. For the $Co^{2+}-H_2O$ system, we only show the results of the two most stable quartet states. In this case we can assign unambiguously $^4B_2$ as the ground state of the system because the energy separation between the considered states is larger than in Co^+-H_2O.

The comparison between the CCSD(T) and B3LYP results shows that both methods predict almost the same order of electronic states. For Co^+-H_2O, however, a slight discrepancy is shown between both methods when the triplets are considered. Nevertheless, the difference is too small to ensure a ground state. Moreover, given a spin state, the computed relative energies are very similar at the two levels of theory. However, more important discrepancies are observed when states of different multiplicities are considered; that is to say, it seems that B3LYP tends to overestimate the energy differences between the triplet and the quintet or singlet states of Co^+-H_2O.

A similar behavior is observed when the B3LYP and CCSD(T) values of the $^5F-^3F$ and $^1G-^3F$ energy separations of free Co^+ cation are compared (see Table 1). At the CCSD(T) level, the computed $^5F-^3F$ and $^1G-^3F$ excitation energies are in very good agreement with the experimental values. However, at the B3LYP level, the energy differences are somewhat larger, which has been attributed to the known tendency of the DFT methods to overstabilize the d−d exchange.[60] As a result, the d^8 configuration is favored in front of the s^1d^7 one, the B3LYP $^5F-^3F$ excitation energy being larger than the CCSD(T) excitation energy and the experimental value. Similarly, the $^1G-^3F$ separation is overestimated at the B3LYP level compared to CCSD(T). These atomic deviations carry over to the molecular system and are responsible for the differences observed between CCSD(T) and B3LYP methods when relative energies between different spin states are computed. In fact, if relative energies are corrected considering the atomic errors, CCSD(T) and B3LYP methods provide quite close values (see Table 1). Finally, the B3LYP-computed binding energy, D_0, assuming the $^3B_1$ state of Co^+-H_2O (38.1 kcal/mol) is in good agreement with the CCSD(T) value (35.9 kcal/mol) and with the experimentally determined values (37−41 kcal/ mol).[72−74] Although differences are somewhat larger for $Co^{2+}-H_2O$, the B3LYP binding energy (98.5 kcal/mol) is also in quite good agreement with the CCSD(T) value (89.4 kcal/mol). Therefore, the B3LYP method appears to be a suitable enough method to study Co^+-L and $Co^{2+}-L$ systems, as long as deviations in the atomic excitation energies are taken into account.

Metal Cation−Glycine Complexes. Glycine is known to exist in neutral form in the gas phase, the zwitterionic form not being a minimum.[75−77] However, this form can be stabilized through the interaction with metal cations. Thus, we have considered the coordination of the metal cation to both forms of glycine. As starting points for geometry optimizations of the neutral form, we have considered different coordination modes that, according to previous works, maximize the metal cation−glycine interaction.[25,33,36−38,40−45] For the zwitterionic form only the interaction of the metal cation with CO_2^- has been considered. For each complexation mode the same spin states considered for the metal cation monohydrate systems have been computed.

Co^+-Glycine System. Figure 1 shows the obtained minima for Co^+-glycine. The computed relative energies are given in Table 2. It can be observed that all the structures involving the coordination of the metal atom to the amino group have C_1 symmetry while the structures involving only coordination to oxygen atoms show C_s symmetry. For those structures with C_s symmetry the lowest quintet and triplet states of both A′ and A″ symmetry have been computed.

For all three spin multiplicities the most stable structure, κ^2-N,O (1), corresponds to the metal cation interacting with the

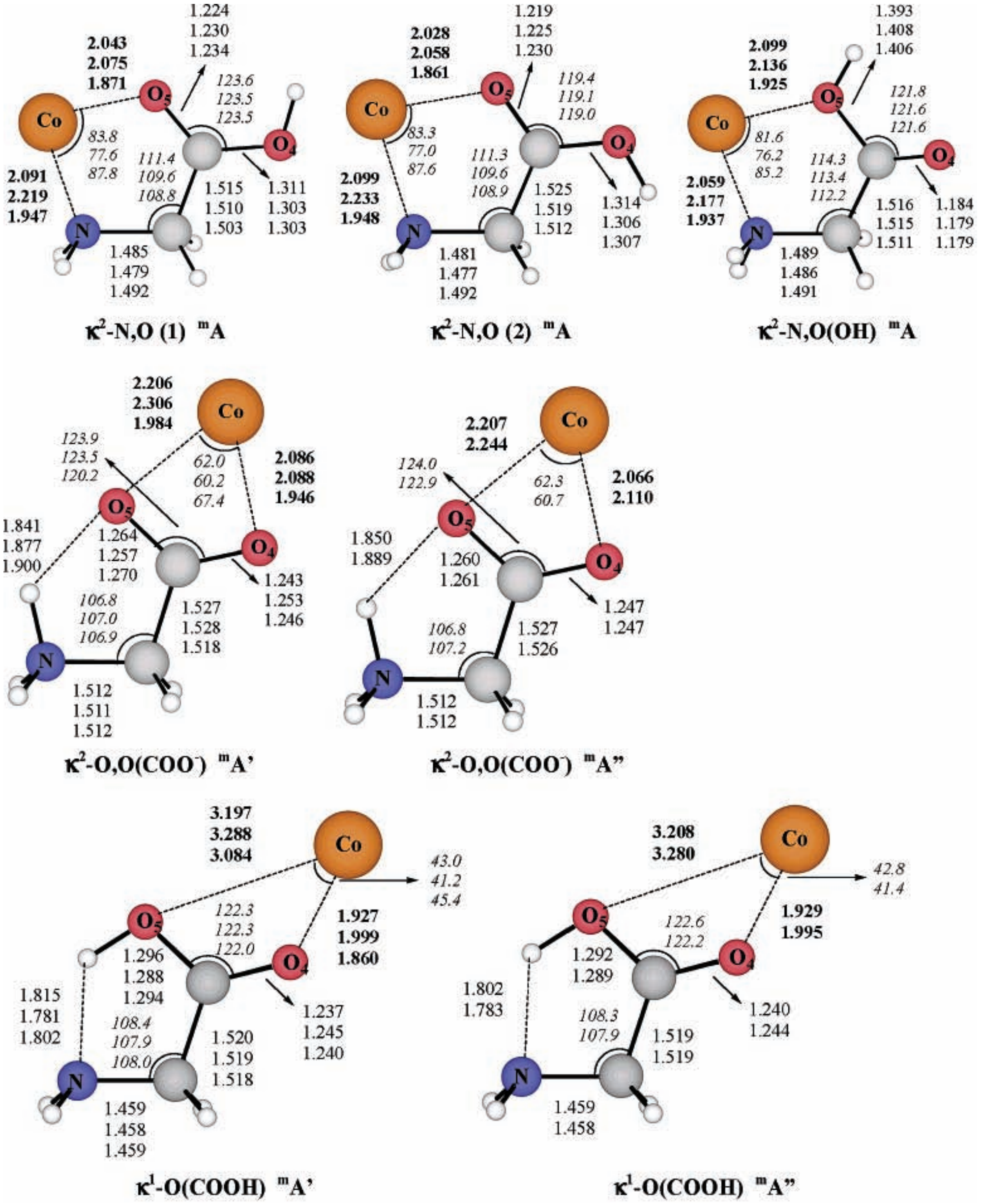


Figure 1. B3LYP-optimized geometries for the different minima of Co$^+$−glycine ($m = 3, 5, 1$ for triplet, quintet, and singlet states, respectively). Distances are in angstroms, and angles are in degrees.

nitrogen atom and the carbonyl oxygen of neutral glycine. However, the relative energies of the remaining structures vary depending on the spin state. In the triplet state, the energy order of the different coordination modes is κ^2-N,O (1) < κ^2-N,O (2) < κ^2-N,O(OH) $\approx$ κ^2-O,O(COO$^-$) < κ^1-O(COOH). This energy ordering is the same as that found previously for Ni$^+$ [43] and very similar to that found for Cu$^+$,[37] showing that the nature of the bond between the metal cation and glycine is essentially electrostatic.

The bonding in the triplet complexes arises from the interaction of triplet states of Co$^+$ with the ^{1}A′ state of glycine. The natural population analysis shows that the metal charge is in all cases larger than 0.86 and the spin density is almost entirely located over the metal atom. This fact implies that the charge transfer is not important for the description of the bonding in this complex or, at least, it is of the same magnitude in all the studied isomers. The open shell orbitals of three triplet-state structures are shown in Figure 2. The orbitals of the two remaining structures, κ^2-N,O (2) and κ^2-N,O(OH), are very similar to those of κ^2-N,O (1). In the case of the ^{3}A″ states the lowest monooccupied orbital is of π (a″) symmetry instead of σ (a′) symmetry (orbital 1 in Figure 2). It can be observed that in all cases the highest monooccupied orbital (2) corresponds to the antibonding combination of one dσ metal orbital with the nitrogen and oxygen lone pairs of glycine. The occupation of this orbital leads to the highest Pauli repulsion. To reduce the repulsion, orbital 2 polarizes through sd or pd hybridization depending on the metal coordination. While for the bicoordinated structures polarization takes place through 4p−3d mixing, in monocoordinated ones 4s mixing is also observed. The nature of the second monooccupied orbital, σ or π, does not have a fundamental influence on the stability of the complex, as revealed by the small energy difference between the ^{3}A′ and ^{3}A″ states in the complexes with C_s symmetry.

In the quintet complexes the interaction takes place between the quintet states (s^{1}d^7) of Co$^+$ and the ^{1}A′ state of glycine. As for the triplets, the two states of different symmetries, ^{5}A′ and ^{5}A″, of the C_s complexes κ^2-O,O(COO$^-$) and κ^1-O(COOH) lie very close in energy. However, in this case the A″ states are somewhat more stable than the A′ ones. Therefore, the energy

TABLE 2: Relative Energies of Co^+−Glycine (kcal/mol) and Population Analysis (Net Atomic Charges and Spin Densities of the Metal Atom) at the B3LYP Level

structure	state	ΔE^a	charge	spin
κ^2-N,O (1)	^{3}A	0.0	0.87	1.95
κ^2-N,O (2)	^{3}A	5.7	0.88	1.95
κ^2-N,O(OH)	^{3}A	11.6	0.88	1.95
κ^2-O,O(COO$^-$)	^{3}A′	11.8	0.87	1.96
	^{3}A″	12.1	0.86	1.95
κ^1-O(COOH)	^{3}A′	14.3	0.92	1.99
	^{3}A″	15.4	0.90	1.97
κ^2-N,O (1)	^{5}A	25.5 (18.1)	0.84	3.80
κ^2-O,O(COO$^-$)	^{5}A″	30.9 (23.5)	0.83	3.81
κ^2-N,O (2)	^{5}A	31.1 (23.7)	0.84	3.80
κ^2-O,O(COO$^-$)	^{5}A′	33.0 (25.6)	0.84	3.82
κ^1-O(COOH)	^{5}A″	36.1 (28.7)	0.89	3.86
	^{5}A′	36.9 (29.5)	0.89	3.87
κ^2-N,O(OH)	^{5}A	39.2 (31.8)	0.85	3.80
κ^2-N,O (1)	^{1}A	33.9 (25.6)	0.69	0.00
κ^2-N,O (2)	^{1}A	39.3 (31.0)	0.70	0.00
κ^2-N,O(OH)	^{1}A	48.5 (40.2)	0.70	0.00
κ^2-O,O(COO$^-$)	^{1}A′	51.7 (43.4)	0.72	0.00
κ^1-O(COOH)	^{1}A′	60.9 (52.6)	0.86	0.00

[a] In parentheses are given corrected values assuming errors on atomic excitation energies.

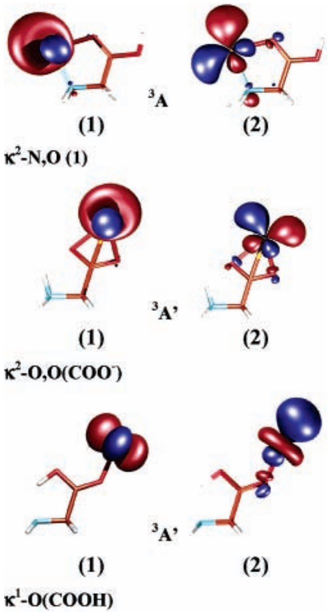


Figure 2. Open shell orbitals of the triplet states of the κ^2-N,O (1), κ^2-O,O(COO$^-$), and κ^1-O(COOH) structures of Co^+−glycine.

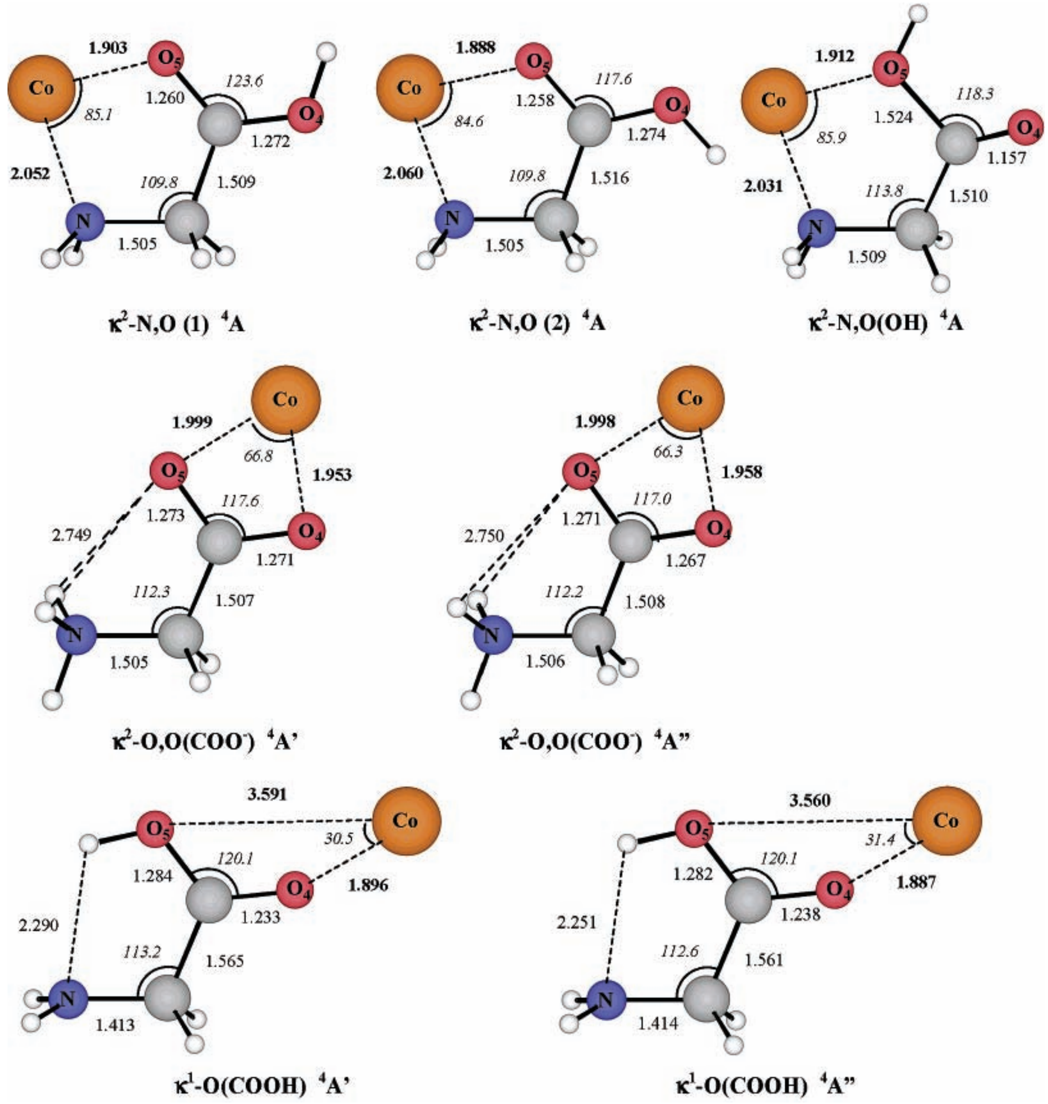
ordering of the different quintet coordinations is somewhat different from that found for the triplets, the most important variation being the larger stabilization of those structures coordinating through the carboxylic group with regard to the most stable conformer. This stabilization becomes remarkable for the κ^2-O,O(COO$^-$) (^{5}A″) coordination, which becomes only 5.4 kcal/mol less stable than the κ^2-N,O one. Thus, the energy order for quintet states is κ^2-N,O (1) < κ^2-O,O(COO$^-$) < κ^2-N,O (2) < κ^1-O(COOH) < κ^2-N,O(OH).

As for triplets, the natural population analysis shows that the metal charge and the spin density are mainly located at the metal atom, the open shell monooccupied orbitals being the 4s and three 3d orbitals. These 3d orbitals correspond to the same open shell orbitals found for the triplets plus another dσ or dπ orbital depending on the symmetry of the state. As in the previous case, for the quintets, the orbitals whose occupation leads to the highest Pauli repulsion (4s and orbital 2 of Figure 2) are always monooccupied, while the nature of the other two open shell orbitals does not cause significant energy differences. Singlet states show the same energy ordering of the different coordination modes as that found for the triplet states. As expected, the empty 3d orbital corresponds to orbital 2 shown in Figure 2 for the triplet complexes.

The interaction with the metal cation induces the activation of the glycine bonds. However, it is worth noting that the values of the geometrical parameters of the glycine moiety do not vary considerably from one spin state to another of the same coordination. In all the considered structures having one of the oxygen atoms of neutral glycine interacting with the metal cation, the corresponding C−O distance increases compared to the values of free glycine (1.203 Å for the carbonyl oxygen and 1.353 for the carboxylic one) due to the polarization of the σ electron density. Conversely, the other C−O distance is shortened. The lengthening of the C−N distance compared to the value of free glycine (1.446 Å) can also be observed, while the C−C one remains almost unaffected (1.522 Å). The most important variations among different spin states are observed for the metal−ligand distances. That is, the singlets show the strongest bond between the metal cation and glycine, while the quintets exhibit the weakest interaction as demonstrated by their larger metal−ligand distances. The reason for this behavior is the different occupations of the metal orbitals in each state. In the quintets the occupation of the 4s orbital leads to an increase of the metal−ligand repulsion, which is reflected in a lengthening of the distances compared to those of the most stable triplets. However, in the singlets not only the s orbital is empty but also orbital 2 in Figure 2 is empty, resulting in the reduction of the repulsion and the decrease of the metal−ligand distances. Because of that, although the relative stability of the three spin states, triplets, quintets, and singlets, follows the same trend as found in the free metal cation and in the metal cation monohydrate system (see Tables 1 and 2), the variations of metal−ligand repulsion lead to significant changes in energy differences between different spin states. If we focus on the most stable coordination of each spin state, κ^2-N,O (1), it can be observed in Table 2 that the quintet−triplet separation increases about 8.2 kcal/mol compared to that obtained for the metal cation. On the contrary, the singlet−triplet energy difference decreases enormously (about 27.2 kcal/mol). This result might be very relevant when the coordination of Co^+ to larger biological systems is considered where the presence of additional ligands could produce a further reduction of the singlet−triplet separation or even an inversion of the relative stability of the different spin multiplicities, due to the larger strength of the ligand field.

Co^{2+}−Glycine System. Figure 3 and Table 3 show the obtained minima and the computed relative energies for Co^{2+}−glycine, respectively. As in the case of Co^+, structures involving the coordination of the metal atom to the amino group are C_1 while the structures where the metal cation interacts only with oxygen atoms exhibit C_s symmetry. Again, for these latter cases the lowest A′ and A″ states have been considered. For this system only the quartet spin state (d^7) has been computed since the doublet states of Co^{2+} lie much higher in energy and coordination is not expected to reverse the doublet−quartet relative stability.

Table 3 shows that the energy ordering of the different structures obtained for Co^{2+}−glycine is different from that determined for Co^+−glycine. As in the case of other divalent metal cations,[37,39−42] the ground-state structure is the zwitterionic one, κ^2-O,O(COO$^-$), mainly due to the large electrostatic interaction between the divalent metal cation and the CO_2^-



κ^2-N,O (1) ^{4}A

κ^2-N,O (2) ^{4}A

κ^2-N,O(OH) ^{4}A

κ^2-O,O(COO$^-$) ^{4}A'

κ^2-O,O(COO$^-$) ^{4}A"

κ^1-O(COOH) ^{4}A'

κ^1-O(COOH) ^{4}A"

Figure 3. B3LYP-optimized geometries for the different minima of Co^{2+}−glycine. Distances are in angstroms, and angles are in degrees.

TABLE 3: Relative Energies of Co^{2+}−Glycine (kcal/mol) and Population Analysis (Net Atomic Charges and Spin Densities of the Metal Atom) at the B3LYP Level

structure	state	ΔE	charge	spin
κ^2-O,O(COO$^-$)	^{4}A″	0.0	1.57	2.73
	^{4}A′	3.0	1.58	2.74
κ^2-N,O (1)	^{4}A	6.3	1.59	2.75
κ^2-N,O (2)	^{4}A	11.1	1.60	2.75
κ^2-N,O(OH)	^{4}A	30.7	1.61	2.76
κ^1-O(COOH)	^{4}A″	35.4	1.39	2.44
	^{4}A′	36.5	1.35	2.39

group. A decomposition analysis shows that not only the electrostatic interaction with glycine is larger in the zwitterionic than in the neutral form, but also Pauli repulsion is smaller, which overcompensates for the larger deformation energy of glycine in the zwitterionic structure. The other four structures follow the same order as the triplet and singlet states of Co$^+$−glycine.

In the C_s complexes the lowest electronic states are of A″ symmetry as in the case of the quintet of Co$^+$. In fact, the open shell orbitals of Co^{2+}−glycine are similar to those found in the corresponding quintet-state structures of Co$^+$−glycine, but removing the s electron. The main difference found is that in Co^{2+}−glycine the σ orbital equivalent to orbital 2 of Figure 2 has a more important contribution of the glycine fragment. As a result, the spin density and the charge are more delocalized all over the system, indicating that the glycine fragment of the complex exhibits a partial radical character as found for Cu^{2+}−glycine.[37] This is especially noticeable in the case of the κ^1-O(COOH) structure, as shown in Table 3. This behavior is confirmed by the geometrical parameters of this coordination where an important increase of the C−C bond and of the intramolecular hydrogen bond takes place compared to those of Co$^+$−glycine. This fact can be observed in Figure 3. A deeper analysis of the population shows that the spin density on glycine mainly lies on the nitrogen atom (about 0.45), which means that the amino group becomes less basic after cationization, resulting in the weakness of the intramolecular hydrogen bond. All these facts are in agreement with the computed parameters of glycine radical cation, 1.70 Å for the C−C bond and 2.31 Å for the intramolecular hydrogen bond.[78]

For the remaining structures some other differences compared to Co$^+$−glycine should be pointed out. The metal−ligand distances are in all cases shorter than the corresponding ones of the triplet and quintet states of Co$^+$−glycine due to the enhanced electrostatic interaction and to the smaller metal−ligand repulsion. However, the Co^{2+}−glycine metal−ligand distances are somewhat larger than the distances found for the singlet state, due to the occupation of orbital 2 in the Co^{2+}−glycine system, which leads to an enhancement of the Pauli

TABLE 4: Interaction Energies (D_e, D_0, ΔH_{298}°, and ΔG_{298}°) (kcal/mol) of Co^+−Glycine and Co^{2+}−Glycine

		Co^+, ^3A	Ni^+, $^2A^a$	Cu^+, $^1A^b$	Co^{2+}, $^4A''$	Cu^{2+}, $^2A'^{\,b}$
D_e	B3LYP	74.2	84.6	75.2	203.3	243.0
	BHLYP	68.8			188.7	215.2
	CCSD(T)	72.4		67.1	190.5	210.5
$D_0{}^c$		70.4		66.2	188.0	212.7
ΔH_{298}° ^{d}		71.2		66.9	188.7	213.4
ΔG_{298}° ^{d}		62.5		58.7	180.1	203.4

[a] Reference 43. [b] Reference 37. [c] Determined using the CCSD(T) value and the B3LYP unscaled harmonic frequencies. [d] After taking into account thermal corrections determined at the B3LYP level.

repulsion. In general, the Co^{2+}−glycine system shows a larger activation of the adjacent bonds of the metal cation, as can be observed in Figures 1 and 3; see the C−N and the C−O bonds interacting with the metal in the κ^2-N,O, κ^2-N,O(OH), and κ^2-O,O(COO^-) structures as examples. For the κ^2-O,O(COO^-) structure another difference should be noted. The NH_3 group rotates and the O−HN distance increases significantly compared to those of Co^+−glycine, causing the disappearance of the hydrogen bond established in Co^+−glycine. The population analysis shows that this is due to the reduction of the electron density over the proton acceptor oxygen atom upon ionization, which decreases its proton acceptor character, and to the electrostatic repulsion between the $NH_3{}^+$ group and Co^{2+}.

Interaction Energies. The interaction energies (D_e) of Co^+−glycine and Co^{2+}−glycine computed at different levels of calculations are given in Table 4. As it is usually found, the obtained B3LYP interaction energies are somewhat larger than the CCSD(T) ones, especially for the divalent cation. However, in the case of Co the agreement between B3LYP and CCSD(T) interaction energies is much better than in the previous calculations of Cu. The large difference found in the case of Cu^{2+} was attributed to the nature of the Cu^{2+}−glycine bond.[37] This system shows a three-electron interaction with an important delocalization, which manifests itself in the value of the spin density over the metal cation (0.47 for the most stable κ^2-O,O(COO^-) coordination). These kinds of situations are known to be overstabilized by density functional methods due to a bad cancellation of the self-interaction part by the exchange functional, the error decreasing the larger the amount of exact exchange included in the functional. Because of that, we have also performed calculations using Becke's half and half exchange functional.[52] The computed BHLYP binding energy is smaller than the B3LYP one and in better agreement with the CCSD(T) value. For Co^{2+}, the observed variation (15 kcal/mol) is, however, significantly smaller than that observed for Cu^{2+} (28 kcal/mol). This is due to the fact that for Co^{2+}−glycine the delocalization is less pronounced (the value of the spin density for the metal is 2.73), and therefore, the overestimation of the B3LYP value is smaller.

To our knowledge no experimental data on the Co^+/Co^{2+}−glycine interaction energies have been reported. On the other hand, doubly charged M^{2+}−L complexes are difficult to generate due to charge-transfer dissociation processes and proton-transfer reactions.

When the D_e values of Co^+−glycine, Ni^+−glycine,[43] and Cu^+−glycine are compared,[37] it can be observed that the binding energy increases from Co^+ to Ni^+ and then decreases from Ni^+ to Cu^+, the Co^+−glycine and Cu^+−glycine interaction energies being very similar. This trend has been previously described for other ligands such as H_2O,[68,70,71,73,74,79] NH_3,[79,80] or adenine[81] and is correlated with the size of the metal cation and the metal−ligand repulsion. That is, from $Co^+(d^8)$ to $Ni^+(d^9)$, metal−ligand distances decrease ($d_{Ni-O} = 1.981$ Å and $d_{Ni-N} = 2.018$ Å for the most stable structure of Ni^+−glycine at the B3LYP level),[43] paralleling the decrease of the atomic radii, so the electrostatic interaction energy increases. However, for $Cu^+(d^{10})$, having the smallest ionic radius of the three, metal−ligand distances increase ($d_{Cu-O} = 2.057$ Å and $d_{Cu-N} = 2.050$ Å for the most stable structure of Cu^+−glycine at the B3LYP level)[37] and, consequently, the interaction energy decreases. This is due to the fact that the metal 3d orbital interacting with the lone pairs of N and O (orbital 2 in Figure 2) becomes doubly occupied, which significantly increases the metal−ligand repulsion. This does not occur for divalent M cations for which this 3d orbital remains singly occupied. Because of that and because of its smaller size, Cu^{2+} shows a larger interaction energy than Co^{2+}.

Conclusions

A computational study of the binding of cobalt cations Co^+ and Co^{2+} to glycine is presented in this paper. Several coordination modes as well as different electronic states arising from the triplet, singlet ($3d^8$), and quintet ($4s^13d^7$) states of Co^+ and quartet states ($3d^7$) of Co^{2+} have been considered. To ensure the reliability of the B3LYP for this kind of system, we have performed calibration calculations for the Co^+/Co^{2+}−H_2O monohydrates. The B3LYP method appears to reproduce well the CCSD(T) energy differences among electronic states having the same spin state but not among electronic states of different spin multiplicities. However, deviations can easily be corrected considering the errors on the atomic excitation energies.

For Co^+−glycine, the ground-state structure is found to be bidentate with the amino group and the carbonyl oxygen of neutral glycine, the ground electronic state being ^3A. The interaction of Co^+ with the zwitterionic form of glycine is about 12 kcal/mol less favorable, as found for other monovalent metal cations such as Ni^+ and Cu^+. The valence shell occupation of Co^+ has a crucial importance as it can lead to an enhancement or decrease of the metal−ligand repulsions, which affects the cobalt−glycine distances and thereby the strength of the electrostatic interaction. In this sense, quintet states, arising from $4s^1d^7$ electronic configuration, present larger metal−glycine distances and a weaker interaction than the singlet or triplet (d^8) states. In all considered structures the d orbital with a larger overlap with glycine is found to be monooccupied or empty (in the singlet states). The binding of Co^+ to glycine leads to an increase of the quintet−triplet difference and to a decrease of the singlet−triplet difference with respect to the naked atom and to the cobalt−water system.

In the case of Co^{2+}, the larger electrostatic interaction established with the zwitterionic conformation of glycine makes the bidentate coordination with the carboxylate group the most stable structure. The ground electronic state is $^4A''$. As found for Cu^{2+}, the energy difference between the zwitterionic and neutral structures is found to be about 6 kcal/mol. Compared to that in the Co^+−glycine system, the bonding in the Co^{2+}−glycine system becomes more complex since some charge transfer from cobalt to the glycine moiety takes place. On the other hand, whereas for Co^+−L systems the computed B3LYP binding energies are in good agreement with the CCSD(T) ones, they seem to be somewhat overestimated for Co^{2+}−L systems, especially when the cation is bound to glycine, for which the spin density is more delocalized over the system.

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