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Dipole-Bound Anions of Glycine Based on the Zwitterion and Neutral Structures

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Abstract: The instability of the zwitterion structure of glycine is significantly reduced by the attachment of an excess electron as a result of which a local minimum develops on the anionic potential energy surface for the zwitterion structure. However, the global anionic minimum, which is lower by 9 kcal/mol, corresponds to a singly hydrogen-bonded nonzwitterion structure. The vertical electron detachment energies for these two dipole-bound zwitterion and nonzwitterion structures are 3175 and 668 cm^{-1}, respectively.

1. Introduction

In aqueous solutions, the ionic form of amino acids predominates at pH 7, with the carboxyl deprotonated and one of the nitrogen atoms protonated. Therefore, most amino acids at neutral pH have no net charge, but they exist as zwitterions, usually in the $NH_3^+-CHR-COO^-$ form, which clearly have large dipole moments.[1] In contrast, in the gas phase the zwitterionic charge separation is not stabilized by the environment and a non-charge-separated configuration is likely to be more stable.

It was demonstrated in millimeter wave spectroscopy experiments[2] and by measurements of substituent effects on gas-phase basicity[3] that glycine is not a zwitterion in the gas phase. These results are consistent with ab initio calculations that indicate the nonionic tautomer is lower in energy.[4−10] On the basis of kinetic experiments, it was suggested that arginine, with its extremely basic guanidine group, might be stable as a zwitterion in the gas phase.[11] However, this result was not confirmed in later spectroscopic measurements,[12] although it was pointed out that there may be a significant barrier that separates the neutral

and zwitterion forms of arginine and the thermodynamically unstable form may have a sufficiently long lifetime to be observed experimentally.

Only recently, some progress has been achieved in preparation and characterization of gas-phase zwitterionic *ions*[13] and photoelectron spectra have been measured for the anions of two non-amino-acids: 1-methylpyridinium-3,5-dicarboxylate and its decarboxylated aryl.[14] The electron binding energies for carboxylate groups in different molecular environments were interpreted in terms of electrostatic interactions in the zwitterionic species.

With no experimental or theoretical proof of the thermodynamic stability of the zwitterion of an amino acid in the gas phase, newer efforts concentrated on hydrated,[10,15,16] protonated,[11,17,18] and alkali cationized[17−19] amino acids. For instance, it was found that two water molecules can stabilize the zwitterion of glycine sufficiently to render it geometrically stable.[9]

Of particular interest were experimental and computational studies of amino acids and peptides interacting with protons or alkali metal cations,[17−21] as the addition of an extra positive charge can stabilize a zwitterion structure via an intermolecular salt bridge system. The experimental and computational results indicated, however, that the complex of glycine with Na$^+$ has a charge solvation structure, in which a nonzwitterionic glycine binds Na$^+$ through the lone electron pairs of O and N, rather than a salt bridge structure.[17−19] The preference for the charge

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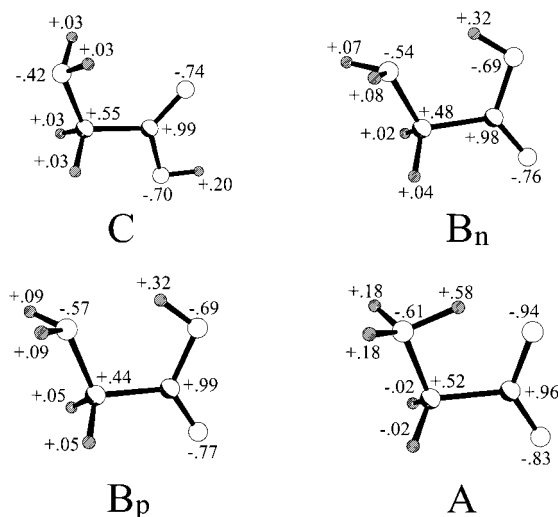(17) Wyttenbach, T.; Bushnell, J. E.; Bowers, M. T. *J. Am. Chem. Soc.* **1998**, *120*, 5098−5103.
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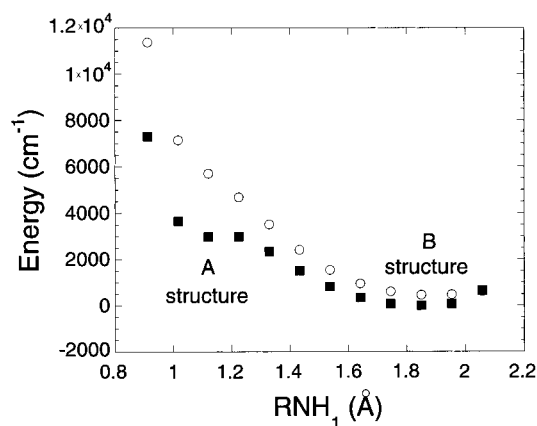
Figure 1. The structures of the neutral glycine at different stationary points on the MP2 potential energy surface supplemented with effective atomic charges. For the neutral **A**, the geometry of **A⁻** is used.

solvation structure results from a relatively low proton affinity of glycine of 211.9 kcal/mol, whereas Bowers et al. suggested that only amino acids with proton affinities larger than 217 kcal/mol can form salt bridge structures when sodiated.[18] It should be noted, however, that $(^{+}H_3 N-CH_2-COO-)Na^{+}$ has been theoretically characterized as a local minimum on the potential energy surface of sodiated glycine,[18] as opposed to the unsodiated glycine zwitterion $^{+}H_3 N-CH_2-COO^{-}$, which is not a stable structure.[4−10] The addition of a sodium ion stabilizes the zwitterion considerably relative to the nonzwitterion form (by more than 10 kcal/mol), but not sufficiently to make the salt bridge structure the global minimum.[17]

In the present contribution, we explore the stabilization of the zwitterion form of glycine by an excess electron. For this purpose, we perform highly correlated electronic structure calculations for anions formed by the zwitterion and nonzwitterion forms of glycine. We demonstrate that the instability of the zwitterion form of the neutral glycine is significantly reduced by the attachment of an excess electron and a local minimum develops on the anionic potential energy surface. These effects are related to the fact that the anionic states are dipole-bound and the dipole moment for the zwitterion structure is larger than that of the nonionic structure. The present study is a continuation of our previous works on electron attachment to model zwitterions: $^{-}HNNH_3^{+}$ [22] and $^{-}HPPH_3^{+}$.[23]

2. Methods

As demonstrated by others, the calculated relative energetics of different isomers of the neutral glycine are sensitive to the level of theory.[24] Moreover, electron correlation effects proved to be important for dipole-bound anions.[25] Therefore, the results reported in this study were obtained at the coupled cluster level of theory with single, double, and noniterative triple excitations.[26] We have used aug-cc-pVDZ basis sets[27] supplemented with additional even-tempered 5s and 5p symmetry

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Figure 2. The MP2 energy profile for the neutral (circles) and anionic (squares) glycine for proton transfer.

functions centered on the N atom. The robustness of the relatively small aug-cc-pVDZ basis set was earlier demonstrated for a variety of dipole-bound anions.[28,29] The geometric progression ratio for the extra 5s5p diffuse set was set to 3.2, and we started to build up the exponents from the lowest s and p exponents included in the aug-cc-pVDZ basis set designed for N. Stationary points on the potential energy surfaces of the neutral and the anion as well as harmonic vibrational frequencies were determined at the MP2 level. In calculations for the doublet anion, the value of $\langle S^2 \rangle$ never exceeded 0.7501 for the SCF wave function.

The vertical electron detachment energy (D) for the excess electron was first determined at the Koopmans' theorem level (D^{KT}) and then supplemented with orbital relaxation ΔD_{ind}^{SCF} and electron correlation effects estimated at the CCSD(T) level.[30] The second-order dispersion interaction between the loosely bound electron (lbe) and the neutral molecule (ΔD_{disp}^{MP2}) was extracted from the latter term[30]

$$\Delta D_{disp}^{MP2} = \sum_{a \in N} \sum_{r<s} \frac{|\langle \phi_a \phi_{lbs} || \phi_r \phi_s \rangle|^2}{e_a + e_{lbe} - e_r - e_s} \quad (1)$$

where ϕ_a and ϕ_{lbe} are spinorbitals occupied in the UHF wave function for the anion, ϕ_r and ϕ_s are unoccupied orbitals, and e's are the corresponding orbital energies. The remaining higher order correlation contribution to D, denoted ΔD^{HO}, is defined as

$$\Delta D^{HO} = D^{CCSD(T)} - D^{KT} - \Delta D_{ind}^{SCF} - \Delta D_{disp}^{MP2}$$

3. Results

In agreement with earlier studies,[4−10] we find that the zwitterion structure of the neutral glycine **A** (see Figures 1 and 2) is not even a minimum on the electronic ground-state potential energy surface. Rather, geometry optimization based on ab initio calculated forces moves downhill in energy from **A** and collapses to the nonionic structure **Bₙ**. This is visualized in Figure 2, where the energies of the neutral and anionic glycine are displayed as functions of the distance between the nitrogen atom and the H₁ hydrogen atom that is displaced as tautomerization occurs. The stationary point **Bₙ** of the neutral glycine is separated from a symmetry-equivalent **Bₙ** structure by a small barrier (19 cm⁻¹) at the top of which is a C_s-symmetry structure **Bₚ**. The **Bₙ** minimum is only 1 kcal/mol higher in energy than the neutral global minimum, **C**, which is geometrically quite distinct[24] (see also Figures 1 and 3). Moreover, there is a

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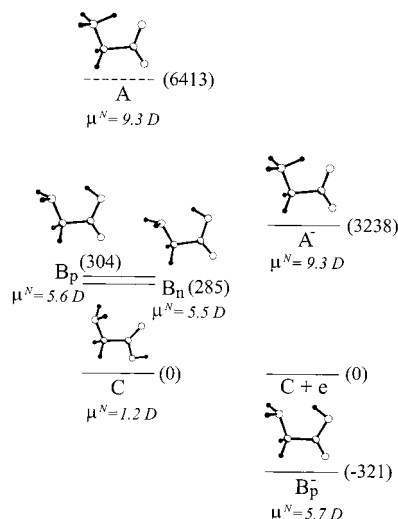
Figure 3. The equilibrium structures, relative CCSD(T) energies without zero-point vibrational energies (in parentheses, given in cm^{-1}), and MP2 dipole moments of the neutral glycine (in Debyes). For the neutral **A**, the geometry of **A**$^-$ is used and the energy level is indicated by a dashed line since it does not correspond to a stationary point on the potential energy surface of the neutral.

significant difference in the polarity of **B**$_n$ and **C** (Figure 1); the MP2 dipole moment of **B**$_n$ is 5.52 D, whereas that of **C** is only 1.18 D.

To the best of our knowledge, the glycine molecule does not form a valence-type anion in the gas phase because it has no vacant or half-filled valence orbital available. However, the dipole moment of **B**$_{n,p}$ is more than sufficient to support a dipole-bound anionic state and the dipole moment of the zwitterion structure **A** is expected to be even larger than that of **B**$_{n,p}$. On the other hand, structure **C** has such a small dipole moment that it cannot bind an electron. Let us therefore turn to our study of the stability of dipole-bound anions of glycine derived from the nonionic (**B**$_p$ or **B**$_n$) and zwitterion (**A**) structures.

The MP2 energy profile for the transition between the zwitterion (**A**) and neutral (**B**) structures of the glycine anion is displayed in Figure 2. A broad plateau develops for R_{NH_1} in the 1.0−1.3 Å range. Specifically, a local MP2 minimum is present at R_{NH_1} =1.12 Å, but the depth of this minimum with respect to the barrier at R_{NH_1} =1.13 Å is only 1 cm^{-1}. Higher order CCSD(T) single point calculations performed at the stationary point on the MP2 potential energy surface led to a deeper minimum (27 cm^{-1}), but this stability is so weak that we do not expect this zwitterion form of the anionic glycine to exist in the gas phase at any but the lowest temperatures. On the other hand, the presence of a broad plateau for the anion and the lack of such for the neutral glycine clearly demonstrates that the dipole-based electron binding can be used to express and stabilize very interesting regions of the potential energy surface.

The relative energies of the neutral and anionic glycine structures calculated at the CCSD(T) level of theory and corrected for the MP2 zero-point vibrational energies are collected in Table 1, see also Figure 3. In agreement with previous studies for the neutral glycine,[24] the low-dipole-moment **C** structure is lower in energy than the high-dipole-moment structure **B**$_n$, but the difference is only 394 cm^{-1}. Geometry optimization for the *anion* starting from the **B**$_n$ structure of the neutral converged to a structure with C_s symmetry denoted **B**$_p^-$, which is the lowest energy stationary point that we found on the potential energy surface of the anion. It is even lower than
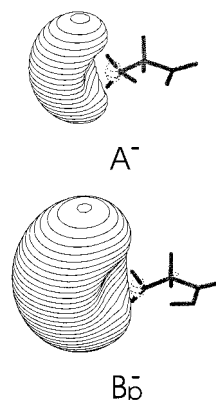
Figure 4. Singly occupied molecular orbital of the anionic glycine at the **A**$^-$ (contour spacing 0.021) and **B**$_p^-$ (contour spacing 0.0087) stationary points.

Table 1. The CCSD(T) Energies (E in cm^{-1}) of the Neutral and Anionic Species Calculated with Respect to the C Tautomer of the Neutral (the energies, also in cm^{-1}, corrected for the MP2 zero-point vibrational energies, are denoted $E + E_{vib}^o$)

system	E	$E + E_{vib}^o$
neutral (**C**)^{a,b}	0	0
neutral (**B**$_p$)	304	368
neutral (**B**$_n$)	285	394
anion (**B**$_p^-$)	−321	−279
anion (**A**$^-$)	3238	2888

^{a} The CCSD(T) energy is −283.79681153. ^{a} The MP2 value of E_{vib}^o is 50.051 kcal/mol.

Table 2. The Components of the Vertical Electron Detachment Energy (in cm^{-1}) Calculated for the Anion of Glycine at Its **B**$_p^-$ and **A**$^-$ Structures

structure	B$_p^-$	A$^-$
D^{KT}	290	1920
ΔD_{ind}^{SCF}	33	284
ΔD_{disp}^{MP2}	287	1199
ΔD^{HO}	58	−229
$D^{CCSD(T)}$	668	3175

the **C** structure of the neutral, by 279 cm^{-1}. In addition to the **B**$_p^-$ species, we found, as noted above, a shallow local minimum structure **A**$^-$ having zwitterionic type bonding. The **A**$^-$ structure is 2888 cm^{-1} higher than the **B**$_p^-$ structure.

The vertical electron detachment energies for the anion of glycine at the **B**$_n^-$ and **A**$^-$ stationary points are collected in Table 2. The values of the MP2 dipole moments of the neutral at the anionic **B**$_n^-$ and **A**$^-$ stationary points are 5.7 and 9.3 D, respectively. As expected, the larger the dipole moment of the neutral, the larger the value of D^{KT} and the more compact the charge distribution of the excess electron is (Figure 4).

The SCF orbital polarization term, ΔD_{ind}^{SCF}, does not exceed 15% of D^{KT}. The ΔD_{disp}^{MP2} contribution describes dynamical correlation between the excess electron and the electrons of the neutral molecule. This stabilizing effect is as large as D^{KT} for **B**$_p^-$ and it represents 62% of D^{KT} for **A**$^-$. The higher order correlation term, ΔD^{HO}, contributes less than 9% to $D^{CCSD(T)}$, but this relatively small contribution results from a cancellation of different electron correlation components. The vertical electron detachment energies calculated at the CCSD(T) level for the **B**$_p^-$ and **A**$^-$ structures are 668 and 3175 cm^{-1}, respectively, and the errors are expected to be less than 10%.[25]

4. Conclusions

We conclude that the binding of an excess electron considerably stabilizes the zwitterion of glycine relative to the nonzwitterion form (by ca. 8 kcal/mol) but not sufficiently to render this the lowest energy structure of the anion. The issue of whether electron attachment can offset the instability of the zwitterion form of amino acids with more significant proton affinities (such as arginine) will be explored in a future study. The lowest energy $\mathbf{B}_p^-$ anion of glycine is vertically stable with respect to the neutral by 668 cm^{-1} and is adiabatically stable with respect to the global minimum $\mathbf{C}$ of the neutral by 279 cm^{-1}.