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Isomerization versus Fragmentation of Glycine Radical Cation in Gas Phase

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The isomerization and fragmentation reactions of glycine radical cation, $[NH_2CH_2COOH]^{+\bullet}$, have been studied using the B3LYP density functional approach and the post-Hartree−Fock CCSD(T) method. The most stable isomer of glycine radical cation corresponds to $[NH_2CHC(OH)_2]^{+\bullet}$. The isomerization reaction from ionized glycine, $[NH_2CH_2COOH]^{+\bullet}$, to $[NH_2CHC(OH)_2]^{+\bullet}$ presents a high energy barrier due to large geometrical distortions at the transition state and important electronic reorganization. In contrast, the fragmentation processes arising from the C_α−R cleavage $NH_2CH_2COOH^{+\bullet} \rightarrow NH_2CH_2^{+} + COOH^{\bullet}$ and $NH_2CH_2COOH^{+\bullet} \rightarrow NH_2CHCOOH^{+} + H^{\bullet}$ appear to be more favorable. The effect of solvation on the isomerization and fragmentation reactions is discussed.

I. Introduction

Amino acid and peptides radicals are of great biological interest. The knowledge of their structure and reactivity is important to understand the role of transient species involved in protein radical catalysis[1] as well as the effects of oxidative damage in proteins.[2,3] Because of that, in the past few years, the properties of different amino acid-derived radicals have attracted considerable attention, both from an experimental[4−9] and theoretical point of views.[10−19]

Radicals derived from glycine, the simplest amino acid, have been widely considered.[4−5,7−9,11−16,18−23] However, most of the performed studies have focused their attention on the structure and magnetic properties of the C-centered glycyl $[NH_2CHCOOH]^{\bullet}$ radical,[4−5,12−16] one of the radiation products of glycine in solution. Recently, the glycyl radical has also been generated in the gas phase[20,21] by collisional neutralization of the stable glycyl cation $[NH_2{-}CH{-}COOH]^{+}$, which is obtained by dissociative ionization of several amino acids such as phenylalanine or serine. Unimolecular decompositions of the glycyl radical are then studied by ionization mass spectrometry experiments.

Fewer studies have been performed for the glycine radical cation $[NH_2CH_2COOH]^{+\bullet}$.[8−9,11,19,22,23] In solution, this cationic species does not appear to prevail in front of the glycyl radical even at pH = 1.[15] However, in gas phase these radical cations could be considered precursors of different derived radicals.[20−23] The knowledge of the different isomerization and fragmentation processes is, thus, important to understand its reactivity. In particular, mass spectrometry experiments have shown that the spectrum of glycine radical cation $[NH_2CH_2COOH]^{+\bullet}$ is very different from that of the isomeric enol ion $[NH_2CHC(OH)_2]^{+\bullet}$,[22,23] which is obtained via a McLafferty rearrangement of isoleucine. Therefore, even ions of high internal energy do not seem to interconvert prior to dissociation, indicating high isomerization energy barriers. Early calculations at the MNDO level of theory[23] determined that the barriers for interconverting the two isomers through different isomerization reactions were as high as 80−90 kcal/mol.

In the present work, the isomerization reactions of the glycine radical cation are evaluated by performing density functional and post Hartree−Fock calculations. In addition, we have analyzed the fragmentation reactions derived from various unimolecular decompositions. The transition states connecting the isomers have been localized in order to compare the efficiency of the different processes.

II. Methods

Molecular geometries and harmonic vibrational frequencies have been obtained using the nonlocal hybrid three parameter B3LYP density functional approach[24] and the conventional MP2 method, with the 6-31++G(d,p) basis set. The nature of the stationary points has been checked by vibrational frequency calculations. In all cases, intrinsic reaction coordinate (IRC)[25] calculations have been carried out to confirm that the located transition states link the proposed reactants and products.

Although for several radical cations the UB3LYP method has been shown to perform much better than the UMP2 one,[26,27] in certain very symmetrical cases, density functional methods have been proved to overestimate their stability.[28] Because of that, and in order to check the reliability of B3LYP and MP2 methods, we have also performed single point calculations at the coupled cluster level[29] with single and double excitations and a perturbative estimate of the triple excitations CCSD(T),[30] using the optimized B3LYP and MP2 geometries. Results show that CCSD(T) relative energies differ by less than 0.4 kcal/mol whether we use the B3LYP or MP2 geometries. Since optimized MP2 and B3LYP geometries show small differences we will report only the B3LYP and CCSD(T) results. On the other hand, photoelectron spectroscopy measurements for some of the species considered in this work, NH_2CH_2COOH, NH_2CH_2 and NH_2, have provided ionization potential (IP) values of 8.9, 6.3, and 11.5 eV, respectively,[31] which are in quite good agreement with those computed at the CCSD(T)//B3LYP level (8.8, 5.9, and 12.1 eV). Therefore, we expect the computed energetics of the considered processes to be reasonably accurate. Open shell

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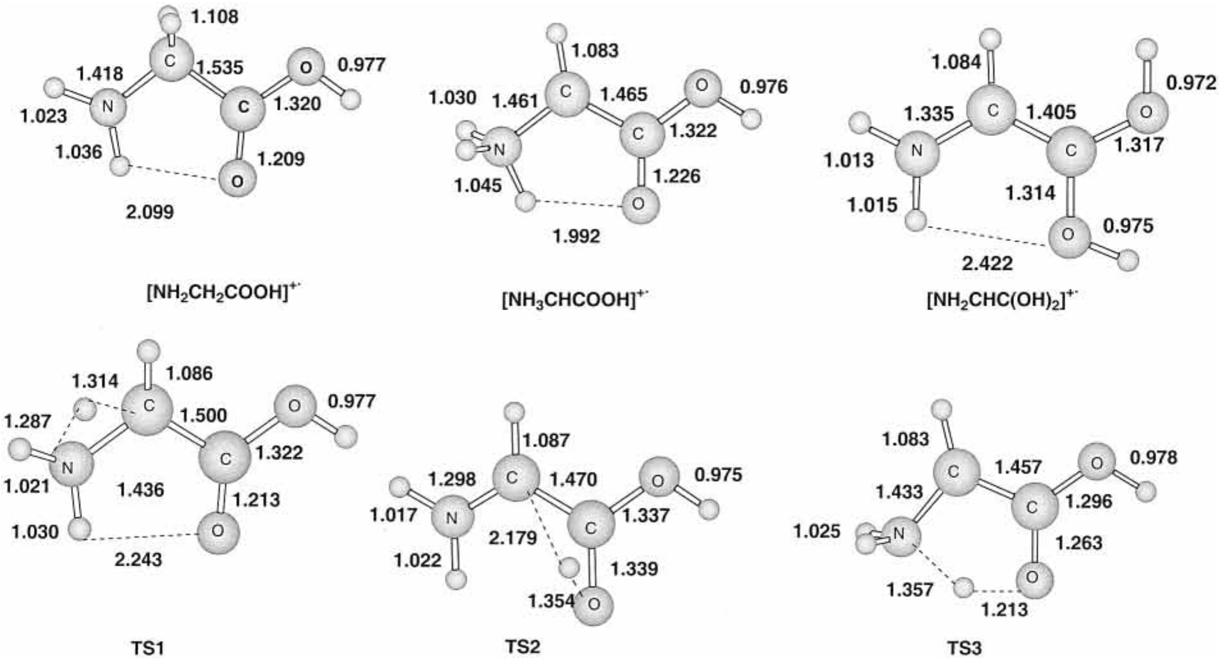

Figure 1. B3LYP main geometrical parameters of the minima and transition states (TS) of different isomers of ionized glycine. Distances are in Å.

systems have been computed considering an unrestricted formalism. For the CCSD(T) calculations we have correlated all the electrons except the 1s-like ones.

Moreover, to test the effect of further enlarging the basis set, we have also performed B3LYP calculations with the 6-311++G(2df,2pd) basis for the different stationary points corresponding to the isomerization processes. The results obtained show that the effect of enlarging the basis set is small at this level of calculation; the largest variation being about 2 kcal/mol.

Thermodynamic corrections have been obtained at the B3LYP level assuming an ideal gas, unscaled harmonic vibrational frequencies, and the rigid rotor approximation by standard statistical methods.[32] Net atomic charges and spin densities have been obtained using the natural population analysis of Weinhold et al.[33] All calculations have been performed with the Gaussian 98 package.[34]

III. Results and Discussion

First we will discuss the isomerization reactions of glycine radical cation. Second, we will consider all the fragmentation processes derived from the breaking of the different C_α-R bonds of glycine radical cation. We have considered both the loss of cationic and radical neutral fragments. Finally, the efficiency of the fragmentation reactions versus the isomerization ones will be discussed and compared to experimental results both in the gas phase and in solution. The B3LYP optimized parameters of the different stationary points corresponding to glycine radical cation and those corresponding to the unimolecular decomposition fragments are shown in Figures 1 and 2, respectively. The potential energy diagram of the considered reactions are shown in Figure 3.[35]

A. Glycine Radical Cation. Isomerization Reactions. The lowest energy conformer of $[NH_2CH_2COOH]^{+\bullet}$ presents C_s symmetry and a $^2A''$ ground electronic state. It shows an intramolecular hydrogen bond between the NH_2 group, which acts as proton donor, and the carbonylic oxygen, which acts as proton acceptor. The intramolecular H-bond is stronger than that observed for the analogous neutral parent molecule.[19] This is due to the fact that ionization of glycine is mainly located at the amino group, which produces an increase of its acidity and as a consequence a strengthening of the H-bond. Natural population analysis confirms that the radical character of $[NH_2CH_2COOH]^{+\bullet}$ is mainly located at the amino group since the charge and spin density on NH_2 are 0.61 and 0.87, respectively. The adiabatic ionization potential of glycine at the CCSD(T) level and including the B3LYP zero point energy is 8.8 eV, in very good agreement with the experimental value of 8.9 eV.[31]

Isomer $[NH_3CHCOOH]^{+\bullet}$ has also C_s symmetry and presents a $^2A''$ ground electronic state. Natural population analysis indicates that the radical character mainly lies on the C_α (0.89), whereas the positive charge is mainly located at the NH_3 group (0.65). Thus, this isomer shows an important degree of distonic character. The positively charged group NH_3^+ acts as proton donor in an intramolecular hydrogen bond with the carbonylic oxygen. The optimized distances shown in Figure 1 indicate that the H-bond in $[NH_3CHCOOH]^{+\bullet}$ is stronger than in $[NH_2CH_2COOH]^{+\bullet}$. The relative energy of this isomer with respect to $[NH_2CH_2COOH]^{+\bullet}$ at the B3LYP and CCSD(T) levels is −8.7 and −8.9 kcal/mol, respectively. Inclusion of the zero point correction at the B3LYP level, leads to a value of −6.8 (B3LYP) and −7.0 kcal/mol (CCSD(T)). These values are in quite good agreement with the one of −8.3 kcal/mol reported previously[11] at the G2(MP2) level.

The lowest energy conformer of the third isomer, $[NH_2CHC(OH)_2]^{+\bullet}$, presents also C_s symmetry and a $^2A''$ ground electronic state. In this case, the intramolecular H-bond is much weaker. Note that the computed NH—O distance (2.422 Å) in this isomer is significantly larger than the one obtained for $[NH_2CH_2COOH]^{+\bullet}$ (2.099 Å) or $[NH_3CHCOOH]^{+\bullet}$ (1.992 Å). This was to be expected considering that the hydroxylic oxygen is less basic than the carbonylic one. Despite that, this isomer is much more stable than the previous two. The relative energy of this isomer with respect to $[NH_2CH_2COOH]^{+\bullet}$ at the B3LYP and CCSD(T) levels is −26.4 and −20.8 kcal/mol, respectively. Inclusion of the zero point correction at the B3LYP level leads to a value of −24.6 (B3LYP) and −19.0 kcal/mol (CCSD(T)). This larger stability is due to the fact that the present structure corresponds to an α-carbon centered radical, as $[NH_3-CH-$

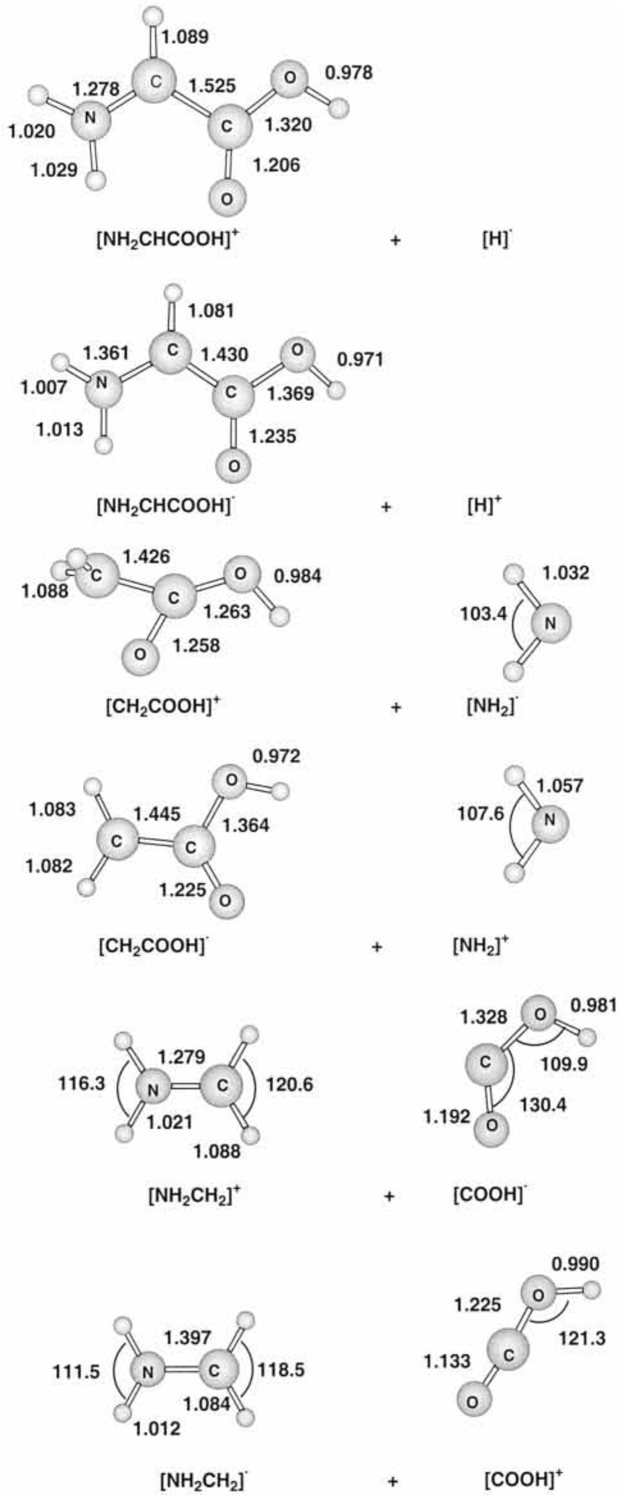

Figure 2. B3LYP main geometrical parameters of the unimolecular decomposition fragments of glycine radical cation. Distances are in Å and angles are in degrees.

COOH]$^{+\bullet}$, but with both a π donor (NH_2) and a π acceptor $C(OH)_2^+$ substituents. Such radicals present an extra stability due to the so-called captodative effect,[36] described as the combined resonance effect of the electron-withdrawing (capto) and electron-donating (dative) substituents at the radical center, which leads to a larger electron delocalization. Natural population analysis confirm this fact since the computed spin densities on the $C(OH)_2$, CH, and NH_2 groups are 0.42, 0.25, and 0.33, respectively.

TABLE 1: CCSD(T)/6-31++G(d,p) Adiabatic Ionization Potentials (in eV)[a]

radical	IP	radical	IP
$NH_2CHCOOH^\bullet$	6.7	$H^\bullet$	13.6
$CH_2COOH^\bullet$	8.8	$NH_2^\bullet$	12.1
$NH_2CH_2^\bullet$	5.9	$COOH^\bullet$	7.9

[a] Zero point energies are computed at the B3LYP/6-31++G(d,p) level.

Optimized geometries of the transition states connecting the different isomers are shown in Figure 1, whereas their relative energies with respect to the $[NH_2CH_2COOH]^{+\bullet}$ isomer are shown in Figure 3. It should be mentioned that intrinsic reaction coordinate (IRC) calculations show that TS2 and TS3 do not directly lead to the conformer of $[NH_2CHC(OH)_2]^{+\bullet}$ shown in Figure 1, but to another conformer of this isomer in which the two hydroxyl bonds are rotated. As found previously,[16] this isomer lies about 5 kcal/mol above the one reported in Figure 1.

It can be observed in Figure 3 that the two isomerizations arising from $[NH_2CH_2COOH]^{+\bullet}$ to $[NH_3CHCOOH]^{+\bullet}$ or $[NH_2CHC(OH)_2]^{+\bullet}$ present a quite high energy barrier, 39.5 and 44.8 kcal/mol, respectively, at the CCSD(T)/6-31++G(d,p) level. In contrast, the one corresponding to the $[NH_3CHCOOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$ isomerization is significantly much smaller (11.2 kcal/mol). This is mainly due to two factors. First, the $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_3CHCOOH]^{+\bullet}$ and $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$ processes correspond to 1,2 and 1,3 H-atom transfers, which require larger geometry distortions than the 1,4 transfer corresponding to the $[NH_3CHCOOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$ rearrangement. Second, the $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_3CHCOOH]^{+\bullet}$ and $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$ isomerizations transform a nitrogen-centered radical into two different carbon-centered radicals. This implies a much more important electronic reorganization than the one involved in the rearrangement between the two carbon-centered radicals, $[NH_3CHCOOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$, which mainly corresponds to π delocalization.

Natural population analysis seems to indicate that the $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_3CHCOOH]^{+\bullet}$ process corresponds to a hydrogen atom transfer, given that in the reactant the spin is mainly located on the nitrogen (0.91) whereas in the products the unpaired electron mainly lies at the carbon atom (0.89). At the transition state (TS1), the values of the spin density lie between those of the reactant and product: 0.42 at the nitrogen atom and 0.56 at the carbon atom.

The $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$ process is much more complex since the radical character in the reactant lies on the amino group, which is not involved in the 1,3 transfer whereas in the product the spin is delocalized all over the molecule. In contrast, the $[NH_3CHCOOH]^{+\bullet} \rightarrow [NH_2CHC(OH)_2]^{+\bullet}$ reaction could be viewed as a proton-transfer process between the NH_3^+ and the carbonylic oxygen accompanied with a certain π electronic reorganization that delocalizes the radical character. In this case, the spin density distribution of TS3 is very similar to that of the reactant. This was to be expected considering the orientation of the NH_2 group at the transition state.

B. Unimolecular Decompositions of the Glycine Radical Cation. Once the glycine radical cation is formed by irradiation it can evolve to different isomers via molecular rearrangements or it can also decompose into different fragments. Let us now consider the different unimolecular decompositions derived from the C_α−R breaking of $[NH_2CH_2COOH]^{+\bullet}$. Such cleavage can

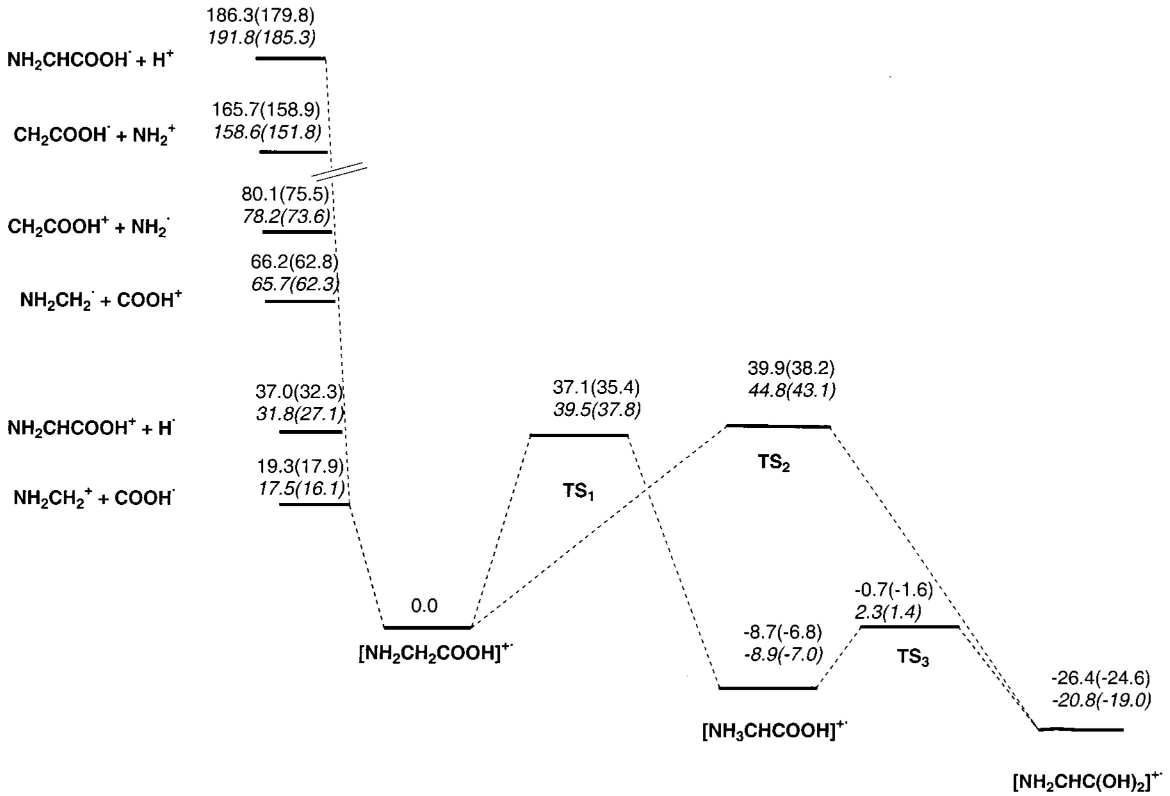

Figure 3. Potential energy diagram for the isomerization and fragmentation processes of glycine radical cation. B3LYP and *CCSD(T)* energies (in kcal/mol) relative to $[NH_2CH_2COOH]^{+\bullet}$.[35] In parentheses values including the zero point energy.

be produced in two different ways; that is, by losing a cation (R^+) or a neutral radical ($R^\bullet$). Thus, we have considered the following reactions:

$$[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHCOOH]^+ + H^\bullet \tag{1}$$

$$[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHCOOH]^\bullet + H^+ \tag{2}$$

$$[NH_2CH_2COOH]^{+\bullet} \rightarrow [CH_2COOH]^+ + [NH_2]^\bullet \tag{3}$$

$$[NH_2CH_2COOH]^{+\bullet} \rightarrow [CH_2COOH]^\bullet + [NH_2]^+ \tag{4}$$

$$[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CH_2]^+ + [COOH]^\bullet \tag{5}$$

$$[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CH_2]^\bullet + [COOH]^+ \tag{6}$$

Figure 2 shows the optimized geometries of the different fragments whereas Figure 3 provides the reaction energies of the considered processes. First, it can be observed that the reaction energies (with the zero point energy included) corresponding to the loss of neutral radicals H (1), NH_2 (3), and COOH (5) (27.1, 73.6, and 16.1 kcal/mol at the CCSD(T) level) are significantly smaller than those that lead to the loss of H^+ (2), NH_2^+ (4), and $COOH^+$(6), (185.3, 151.8, and 62.3 kcal/mol, respectively). That is, reaction 1 is preferred over 2, reaction 3 over 4, and reaction 5 over 6. The preference for the loss of the neutral radical ($R^\bullet$) instead of the cation (R^+) can be understood from the ionization potentials of the radical fragments of the two reactions (see Table 1). That is, the more favorable process corresponds to the reaction that leaves the charge on the fragment with lower ionization potential.

The results obtained in the present work are in good agreement with gas-phase experimental studies[20,21] which, by dissociative ionization of several amino acids $NH_2CHRCOOH$, obtain the $NH_2CHCOOH^+ + R^\bullet$ products instead of the complementary ones $NH_2CHCOOH^\bullet + R^+$.

Among the three possible cleavages of the $C_\alpha-R$ bond in $[NH_2CH_2COOH]^{+\bullet}$ that lose neutral radicals ($R^\bullet$), the most favorable is the one corresponding to the breaking of the $C_\alpha-C$ bond (reaction 5). The second most favorable is the $C_\alpha-H$ one (reaction 1), whereas the most energetically is the breaking of the $C_\alpha-N$ bond (reaction 3). This order, $D_0(C_\alpha-C) < D_0(C_\alpha-H) < D_0(C_\alpha-N)$, nicely follows the order of IP of the fragments that support the positive charge. That is, the $IP(NH_2CH_2^\bullet) < IP(NH_2CHCOOH^\bullet) < IP(CH_2COOH^\bullet)$. Such behavior can be understood considering the following cycle:

$$\begin{tikzcd}
GR^{+\cdot} \arrow[r, "D_0(GR^{+\cdot})"] \arrow[d, "-IP(GR)"'] & G^+ + R^{\cdot} \\
GR \arrow[r, "D_0(GR)"] & G^{\cdot} + R^{\cdot} \arrow[u, "IP(G^{\cdot})"']
\end{tikzcd}$$

where $D_0(GR^{+\bullet}) = -IP(GR) + D_0(GR) + IP(G^\bullet)$. Table 2 shows the CCSD(T) values of the different terms of this equation for reactions 1, 3, and 5. Because the ionization potential of glycine, IP(GR), is the same term in the three reactions, the differences on the fragmentation energies arise from the D_0(GR) and IP(G) terms. However, it can be observed in Table 2 that the homolytic dissociation energies of $C_\alpha-C$, $C_\alpha-H$, and $C_\alpha-N$ bonds of neutral glycine, D_0(GR), are quite similar and thus, the differences between the reaction energies of reactions 1, 3, and 5 mainly arise from the changes on the $IP(G^\bullet)$.

TABLE 2: Decomposition of Fragmentation Energies of Glycine Radical Cation at the CCSD(T)/6-31++G(d,p) Level (in kcal/mol)[a]

$GR^{+\bullet} \rightarrow G^+ + R^\bullet$	$G^\bullet$	$R^\bullet$	$D_0(GR^{+\bullet})$	IP(GR)	D_0(GR)	$IP(G^\bullet)$
$[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHCOOH]^+ + H^\bullet$	$NH_2CHCOOH^\bullet$	$H^\bullet$	27.1	203.9	76.2	154.8
$[NH_2CH_2COOH]^{+\bullet} \rightarrow [CH_2COOH]^+ + [NH_2]^\bullet$	$CH_2COOH^\bullet$	$NH_2^\bullet$	73.6	203.9	75.6	201.9
$[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CH_2]^+ + [COOH]^\bullet$	$NH_2CH_2^\bullet$	$COOH^\bullet$	16.1	203.9	82.9	137.1

[a] $D_0(GR^{+\bullet}) = -IP(GR) + D_0(GR) + IP(G^\bullet)$. Zero point energies are computed at the B3LYP/6-31++G(d,p) level of theory.

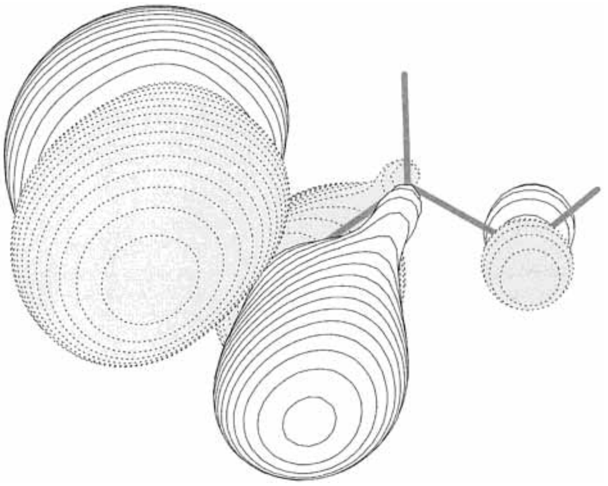

Figure 4. HOMO orbital of $[NH_2CH_2COOH]$.

These results agree well with the changes observed on the geometrical parameters of glycine upon ionization, which show that the C−N bond distance decreases by 0.04 Å, whereas the C−C and C−H bond distances increase by 0.02 Å and 0.01 Å, respectively. These changes are a consequence of the nodal properties of the HOMO orbital of glycine (see Figure 4). It can be observed that this orbital presents an antibonding character between N and C and a bonding character between the two carbon atoms and between the C and H.

C. Isomerization versus Fragmentation. Figure 3 shows that the energy barriers corresponding to the isomerization reactions of $[NH_2CH_2COOH]^{+\bullet}$ are significantly larger than the reaction energy of the most favorable fragmentation, $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CH_2]^+ + [COOH]^\bullet$ and similar to the second most favorable cleavage, $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CHCOOH]^+ + H^\bullet$. The other fragmentations appear at much higher energies and so they cannot be considered competitive. Therefore, from these results it can be concluded that the most probable process that glycine radical cation will undergo in gas phase will be the C_α−C fragmentation and not the isomerization rearrangements. The present calculations confirm the preliminary results obtained in an early study using the low level semiempirical MNDO method, which found high energy barriers for the isomerization reactions.[23]

The fact that the fragmentation of glycine radical cation is more favorable than its isomerization becomes more evident if one compares Gibbs free energies of the different species, in which the zero point energy, the thermal corrections, and the entropic effects have been taken into account (see Figure 5). As expected, the entropic effects favor the fragmentation processes, but slightly change the isomerization ones. In particular, the reaction free energy, ΔG_{298K}, of $[NH_2CH_2COOH]^{+\bullet} \rightarrow [NH_2CH_2]^+ + [COOH]^\bullet$ is 7.1 kcal/mol, much smaller than the activation free energy ($\Delta G^\ddagger_{298K}$) values of 35.8 and 38.8 kcal/mol computed for the two isomerizations of $[NH_2CH_2COOH]^{+\bullet}$. Because of that, the two fragmentations lower in energy are the ones to be expected in gas phase. Moreover, considering that ionization of glycine will provide the system with an excess of vibrational energy, such fragmentation may become spontaneous. The present calculations are in very good agreement with the experimental results which have shown that the spectrum of glycine radical cation $[NH_2CH_2COOH]^{+\bullet}$ is very

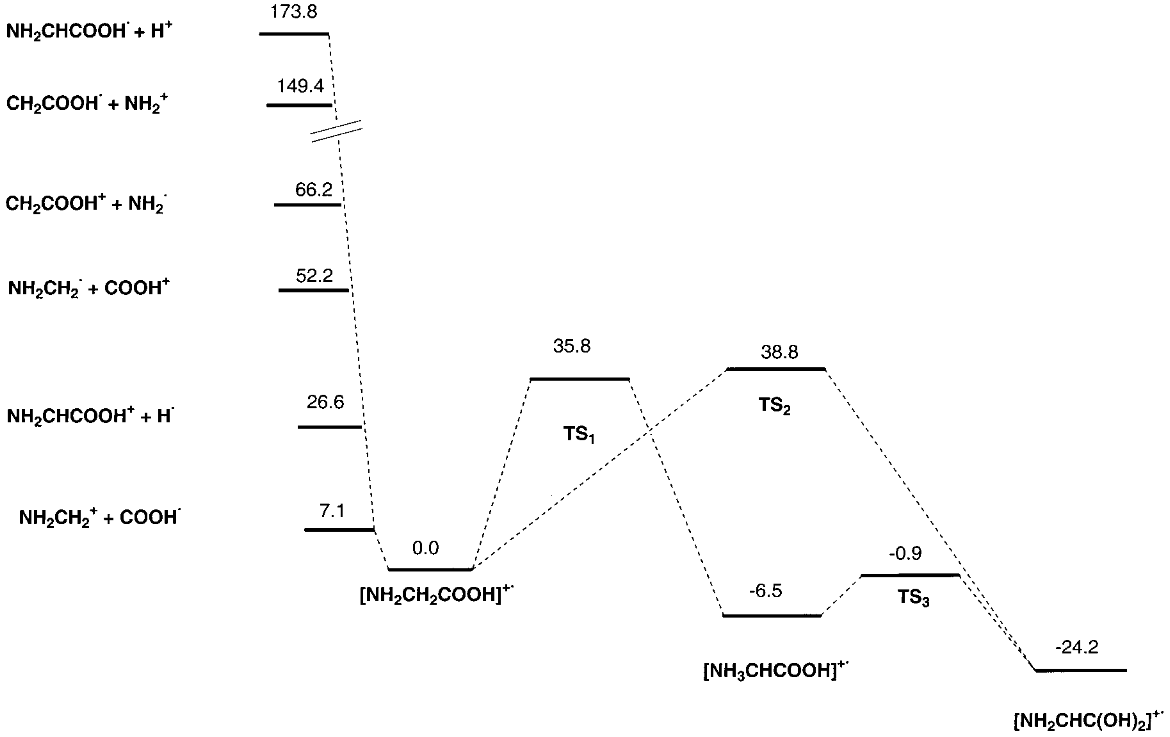

Figure 5. B3LYP Gibbs free energies (in kcal/mol) relative to $[NH_2CH_2COOH]^{+\bullet}$.

different from that of the isomeric enol ion $[NH_2CHC(OH)_2]^{+\bullet}$,[22,23] indicating that the two isomers do not interconvert prior to dissociation. Moreover, the mass spectrum of $[NH_2CH_2COOH]^{+\bullet}$ is dominated by the loss of $NH_2CH_2^+$ (m/z 30), in agreement with the most favorable cleavage predicted by theory.[22]

Finally, let us discuss the effect of solvation on the studied reactions. As mentioned in the Introduction, the C-centered glycyl $[NH_2CHCOOH]^\bullet$ radical, is one of the products obtained upon irradiation of glycine in aqueous solution. However, from our results in the gas phase, such radical will not be produced since the reaction energy of the corresponding fragmentation process, reaction 2, is the most costly in energy. Nevertheless, it must be mentioned that the solvation of the proton is much more important than that of the other cations. In solution the proton will associate with a water molecule to lead to the hydronium H_3O^+ cation. This association energy at the B3LYP level is 171.8 kcal/mol, which would make this fragmentation reaction the most favorable one. Moreover, if one considers the effect of solvation on the different cations using the continuum model, the formation of glycyl radical would even be more efficient than the other reactions, given that the stabilization of the cations by the solvent becomes more important as the size of the cation decreases, and hydronium is the smallest one. Therefore, it is not surprising that the glycyl radical is the species experimentally observed in solution.[9,14-16] In contrast, given the similar size of all the isomers of glycine radical cation, solvation is not expected to affect significantly the isomerization processes, unless the water molecules catalyze the intramolecular H atom transfers leading to much smaller energy barriers. Solvent-assisted catalysis has been observed in previous studies for different isomerization of radical cations.[37]

IV. Conclusions

The isomerization and fragmentation reactions of glycine radical cation, $[NH_2CH_2COOH]^{+\bullet}$, have been studied using the B3LYP density functional approach and the post-Hartree−Fock CCSD(T) method. The most stable isomer of glycine radical cation corresponds to $[NH_2CHC(OH)_2]^{+\bullet}$. The isomerization reaction from ionized glycine $[NH_2CH_2COOH]^{+\bullet}$ to $[NH_2CHC(OH)_2]^{+\bullet}$ presents a high energy barrier due to large geometrical distortions at the transition state and important electronic reorganization. In contrast, the $C_\alpha-C$ and $C_\alpha-H$ fragmentation reactions of $[NH_2CH_2COOH]^{+\bullet}$, in which a neutral radical is lost, appear to be more favorable. The relative energies of the different decomposition processes arising from the $C_\alpha-R$ cleavage have been rationalized according to the ionization potentials of all possible generated radical fragments. It has been shown that the preferred processes are those that leave the positive charge on the fragment with lower ionization potential. Such relation is expected to hold also for other amino acids and so could be used to predict which unimolecular decomposition processes would be the most favorable ones and to interpret mass spectrometry experiments.

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