J. Phys. Chem. A **2002,** *106,* 9359−9368

Reactions between Glycolic Acid and Cu^+ in the Gas Phase. An Experimental and Theoretical Study

Laurence Boutreau, Pierre Toulhoat, and Jeanine Tortajada*
Laboratoire Analyse et Environnement, UMR CNRS 8587, Université d'Evry Val d'Essonne, Institut des Sciences, Boulevard François Mitterrand, 91025 Evry CEDEX, France

Alberto Luna, Otilia Mó, and Manuel Yáñez*
Departamento de Química C-9, Universidad Autónoma de Madrid, Cantoblanco, 28049-Madrid, Spain

Received: June 25, 2002

The gas-phase reactions between glycolic acid and Cu^+ have been investigated by means of mass spectrometry techniques. The mass-analyzed ion kinetic energy (MIKE) spectrum reveals that the adduct ions [$HOCH_2$-COOH−Cu^+] decompose spontaneously by losing CH_2O_2, CO, and H_2O. A minor fragmentation corresponding to the loss of H_2 is also observed. The structures and bonding characteristics of the different complexes involved in the glycolic acid−Cu^+ potential energy surface (PES) have been theoretically studied by density functional theory (DFT) calculations carried out at the B3LYP/6-311+G(2df,2p)//B3LYP/6-31G* level. The attachment of Cu^+ to glycolic acid gives rise to two energetically degenerated structures: a chelated form in which Cu^+ interacts with the carbonyl oxygen and the hydroxyl oxygen atoms and another one in which the attachment of Cu^+ takes place exclusively at the carbonyl oxygen atom. The estimated glycolic acid−Cu^+ binding energy is 222 kJ/mol. Different mechanisms for the spontaneous fragmentations observed experimentally are proposed. The main conclusion is that the loss of 46 u should correspond dominantly to the loss of formic acid and in a lower proportion to the loss of CO + H_2O.

Introduction

The cationization of neutral molecules by association with metal cations is one of the most important topics in gas-phase ion chemistry, and it has received a great deal of attention both from the experimental[1−5] and the theoretical[6−9] points of view. Very often, metal cation association is accompanied by significant bond activation effects, which lead to specific fragmentations, that are very often of analytical utility.[10−14] On the other hand, these interactions are crucial in many biological processes, and as a consequence, many efforts have been also devoted to the investigation of the formation, intrinsic properties, and reactivity of organometallic complexes of biochemical relevance.[15−18] In this respect, it is worth noting that some metal cations, in particular, toxic elements or radioelements, and their gradual change in time constitute a main concern as far as the preservation of the environment is concerned. Indeed the migration and propagation of these elements (in traces) in natural surroundings can be widely facilitated by some organic macromolecules such as hydroxycarboxylic acids ($HOCH_2(CHOH)_n$-COOH), which can be produced by the alkaline degradation of cellulose. These acids are known to have strong complexing properties and could play a fundamental role in the transport of metal ions in aqueous media.

Although there are many studies devoted to investigating the reactivity of these systems from a macroscopic point of view, very little is known about the mechanisms at the molecular level, which are the ultimate responsible for the observed macroscopic behavior. A good knowledge of these mechanisms is essential to understand, in a subsequent step, the role of the medium and, what is more important, to predict the behavior of related compounds. In this context, the gas-phase reactions appear to be a well-suited alternative. However, the size of such hydroxycarboxylic acids is so large that it prevents a detailed analysis, mainly on theoretical grounds, for which their treatment at high levels becomes prohibited. A reasonably good alternative is to model the big molecules by smaller systems that present similar active sites within similar environments. Hence, for this purpose, glycolic acid ($CH_2OHCOOH$), which is the simplest α-hydroxycarboxylic acid, can be a good model. To investigate its complexing properties, we have chosen Cu^+ for several reasons: first, Cu^+ has a d^{10} closed-shell ground state with a low-lying empty 4s orbital, so it is reasonable to expect that the interaction of glycolic acid with this transition metal monocation would have important covalent contributions, as has been found in reactions of Cu^+ with small oxygen and nitrogen bases;[19,20] second, Cu^+ is a system of relevance from a biochemical viewpoint, and important efforts have been devoted to investigate its reactivity with α-amino acids from both the experimental[21] and the theoretical[22] points of view; third, we have recently started a systematic investigation[20,23−26] on the interaction between Cu^+ and small molecules that are suitable models of more complex biological species, and glycolic acid is also of interest in this particular context because it can be considered structurally analogous to glycine, which is the simplest α-amino acid. In fact, both compounds have three possible basic sites, which can lead to several kinds of complexations. In the case of glycine, Hoyau and Ohanessian[22,27] showed that different modes of complexation and several conformers are indeed possible, the most stable structure being a five-membered ring in which Cu^+ interacts simultaneously with the nitrogen and the carbonyl oxygen atoms.

Hence, the aim of this work is to carry out a study of the complexing ability of glycolic acid toward Cu^+, as well as an analysis of the unimolecular reactivity of the corresponding [glycolic acid, Cu^+] adducts by means of fast atom bombardment mass spectrometry (FAB/MS/MS) techniques. The ratio-

10.1021/jp026378w CCC: $22.00

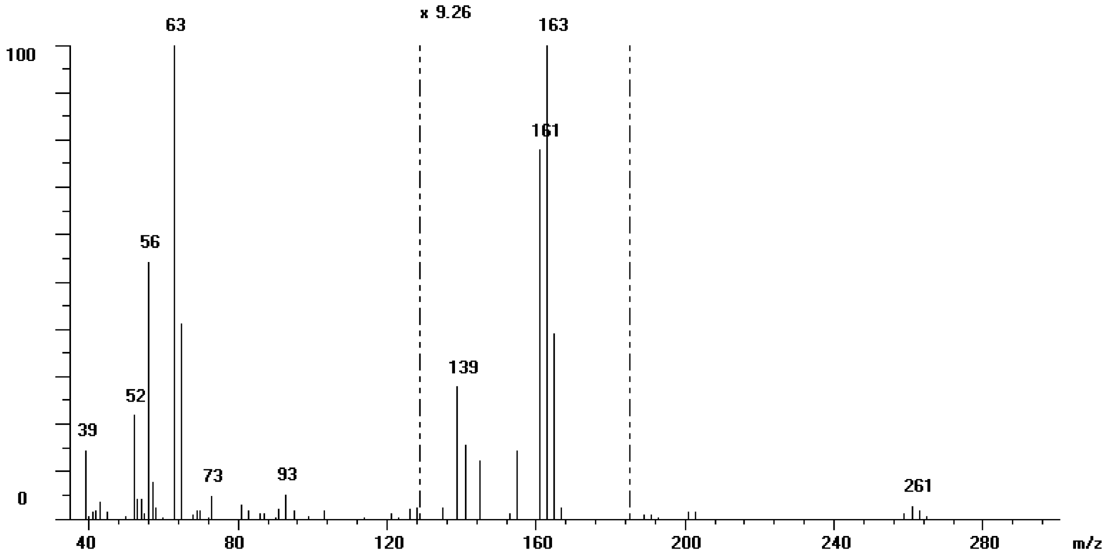


Figure 1. FAB Mass spectrum of the gas-phase reaction between glycolic acid and Cu$^+$.

nalization of the most important features of the FAB spectrum so obtained requires a reliable knowledge of the topology of the associated potential energy surface (PES), which will be obtained through the use of the density functional theory (DFT) B3LYP approach, which performs very well for this purpose when using flexible enough basis set expansions. These results will allow us to compare the behavior of glycolic acid and glycine when they react with Cu$^+$.

Experimental Section

The mass spectrometric measurements were recorded on a double-focusing ZAB-HSQ mass spectrometer (Fisons Instruments) of BEqQ configuration (B and E represent the magnetic and electric sectors, q is a collision cell consisting of a rf-only quadrupole, and Q is a mass-selective quadrupole). This mass spectrometer is equipped with a FAB ion source using the following conditions: accelerating voltage, 8 kV; neutral xenon beam of 7 keV; neutral current of ~10 A. The Cu$^+$ ions are likely formed from Cu^{2+} salt (e.g., $CuCl_2$ dihydrate) by oxidation/reduction processes as has been previously postulated.[28] Hence, glycolic acid was dissolved in a few drops of a saturated aqueous $CuCl_2$ solution. A few microliters of the resulting mixture was transferred onto the FAB probe tip. The unimolecular reactions of the mass-selected organometallic ions, corresponding to [glycolic acid, Cu$^+$] metastable ions, which take place in the second field-free region (second FFR) behind the magnet, were studied by mass-analyzed ion kinetic energy (MIKE) spectroscopy. This technique consists of focusing magnetically the relevant ion into the second FFR and detecting the products of spontaneous fragmentations by scanning the electrostatic analyzer, E. The MIKE spectra were recorded at a resolving power of ~1000.

Glycolic acid was purchased from Aldrich and used without further purification.

Computational Details

The geometries of the different species under consideration have been optimized by using the hybrid density functional B3LYP method,[29] which includes the Becke's three parameter nonlocal hybrid exchange potential[29] and the nonlocal correlation functional of Lee, Yang, and Parr.[30] All of these calculations were performed using the all electron basis of Wachters−Hay[31,32] (referenced as 6-311G*) for Cu and the 6-31G* basis set for the remaining atoms of the system. The harmonic vibrational frequencies of the different stationary points of the potential energy surface (PES) have been calculated at the same level. This allowed us to identify the local minima and the transition states (TS), as well as to estimate the corresponding zero-point energies (ZPE). To identify the minima connected by a given TS, we have also performed, for some cases, linear synchronous transit (LST)[33] calculations at the same level of theory.

The final energies of the different stationary points of the PES were obtained in DFT/6-311+G(2df,2p) single-point calculations using the aforementioned DFT-optimized geometries. For Cu, the basis set 6-311+G(2df,2p) corresponds to the (14s9p5d/9s5p3d) Wachters−Hay[31,32] basis supplemented with a set of (1s2p1d) diffuse functions and with two sets of f functions (rather than d) and one set of g functions (rather than f). All of these calculations have been carried out by using the Gaussian 98 suite of programs.[34]

To investigate the nature of the Cu−O bond and, in general, the bonding features of the complexes under consideration, we have used the natural bond orbital (NBO) analysis of Weinhold et al.[35] and the atoms in molecules (AIM) theory of Bader.[36] The first formalism allowed us to obtain the atomic natural charges and a description of the bonding in terms of the natural hybrids centered on each atom. Using the second approach, we have located the bond critical points (bcp's), that is, points where the electron density function, $\rho(\mathbf{r})$ is minimum along the bond path and maximum in the other two directions. The charge density at the bcp's is a good measure of the strength of the linkage. On the other hand, the energy density, $H(\mathbf{r})$, evaluated at these points gives information about the nature of the interactions. Negative values for $H(\mathbf{r})$ indicate that a stabilizing charge concentration takes place within the bonding region, which is a typical situation for covalent bonds. Conversely, positive values are associated with closed-shell interactions typically found in ionic linkages or hydrogen bonds.

Results and Discussion

Experimental Results. Fast atom bombardment of glycolic acid dissolved in a aqueous solution containing $CuCl_2$ dihydrate produces [glycolic acid, Cu]$^+$ adduct ions at $m/z = 139$ and 141 with a weak intensity, as shown in the mass spectrum of Figure 1. Copper ions are seen in their natural abundance, that

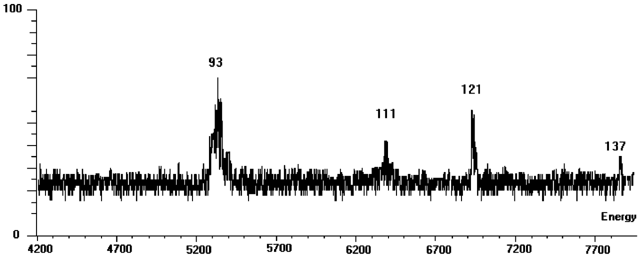


Figure 2. MIKE spectrum of $HOCH_2COOH-Cu^+$ ions produced in glycolic acid + Cu^+ reactions.

is, 69% ^{63}Cu and 31% ^{65}Cu. The existence of these two isotopes leads to an easy identification of copper-containing ions. We can also observe in our experimental conditions the formation of three ions at $m/z = 161$, 163, and 165 resulting from the association of two molecules of water with the Cu_2H^+ cluster. It is worth noting that the Cu_2H^+ ion was also detected[20] as a product in the reactions between formamide and Cu^+. The results presented hereafter will refer to the more abundant adduct ion at $m/z = 139$ containing the isotope ^{63}Cu.

As far as the unimolecular behavior of the [glycolic acid, Cu]$^+$ complex is concerned, the MIKE spectrum presented in Figure 2 shows that the $m/z = 139$ ion undergoes fragmentation by four distinct pathways. The major fragmentation is the elimination of 46 u leading to the ion at $m/z = 93$ assigned to the [H_2, C, O, Cu]$^+$ complex. Characteristic minor fragments at $m/z = 121$ and 111 are also observed and may be assigned, respectively, to the loss of H_2O and CO. The spectrum presents also a weak peak at $m/z = 137$ corresponding to a dehydrogenation process.

Theoretical Analysis. Among the eight different conformers that are local minima of the glycolic acid PES,[37] we have only considered the three most stable ones, which have been named as **A**, **B**, and **C** in Figure 3. Their corresponding energies are summarized in Table 1. Two of them, **A** and **C**, are stabilized by different intramolecular hydrogen bonds, which take place between the α-hydroxyl group and the oxo group or between both hydroxyl groups. A topological analysis of these hydrogen bonds (see Table 2) reveals that the strongest one is that of conformer **C**, which is however the less-stable form (see Table 1). In agreement with the experimental microwave studies,[38,39] which concluded that glycolic acid belongs to the C_s symmetry with the hydroxyl group pointing toward the carbonyl oxygen, our results show that the global minimum is conformer **A**. For conformer **B**, no bcp was found between both hydroxyl groups, so in this case, no intramolecular hydrogen bond seems to exist. The relative stabilities of conformers **A**, **B**, and **C** obtained at the B3LYP/6-31G* level are in good agreement with previous MP2/6-31G(d,p) theoretical estimates.[37] It is worth noting that the same trends were reported for neutral glycine.[40]

Glycolic Acid−Cu^+ Complexes. Structures and Bonding. Starting from the neutral species **A**, **B**, and **C**, we can envisage seven different [glycolic acid−Cu]$^+$ complexes (**1**−**7**, Figure 3). Complexes **1**, **4**, and **7** can be considered as the result of Cu^+ attachment to the three basic centers of the most stable conformer **A** of glycolic acid. Complexes **2**, **5**, and **6** are the result of Cu^+ association to either the carboxylic oxygen or the proton-donor hydroxyl group of conformers **B** and **C**. Finally, complex **3** is the result of Cu^+ attachment to the two OH groups of conformers **B** or **C**. The most stable complex corresponds to a chelated structure **1** in which the metal cation is bridging between the oxo-carboxylic oxygen and the hydroxyl group. However, complex **2** in which Cu^+ attaches exclusively to the oxo-carboxylic oxygen atom of conformer **C** is practically degenerate with the chelated form **1**, the energy gap between the two being smaller than 1 kJ/mol (see Table 1). This can be understood if one takes into account that while the formation of complex **1** from conformer **A** destroys the O−H···O intramolecular hydrogen bond (IHB) the formation of complex **2** from conformer **C** implies a significant reinforcement of the corresponding IHB. Consistently, the O−H···O bond distance decreases 0.104 Å, and the charge density at the bcp increases 0.004 e au^{-3} as can be seen in Table 2. Similarly, the attachment of Cu^+ to the donor OH group of conformer **B** to yield complex **6** leads to a significant reinforcement of the interaction between both hydroxyl groups. The result is that an IHB that does not exist in the neutral form appears and, as a consequence, the O−H··· distance decreases 0.359 Å. Conversely, attachment of Cu^+ to the carbonyl oxygen yielding complex **5** leads to a weakening of the aforementioned interaction. Accordingly, the O−H···O distance increases 0.432 Å, and the corresponding complex is found to be 40 kJ mol^{-1} less-stable than the global minimum. Hence, in general, the complexes in which Cu^+ is attached to one of the hydroxyl groups of glycolic acid are much less-stable than complexes **1** and **2** because of the low intrinsic basicity of these groups as compared with the carbonyl group. Only when Cu^+ interacts simultaneously with both groups an enhanced stability of the system is observed, but complex **3** is still about 27 kJ mol^{-1} less-stable than the global minimum. Consistently, both the NBO and the AIM analyses show that the C═O−Cu bonds in the complexes **1** and **2** have an important covalent character as compared to the HO−Cu ones. As illustrated in Table 2, the charge densities at the C═O−Cu bcp's of both complexes **1** and **2** are more than twice as large as those in typical ionic linkages,[41−43] while those associated with the Cu···O−H bcp's are much smaller. It can be also observed that the energy density, $H(\mathbf{r})$, is slightly negative indicating a nonnegligible covalent character of the interaction. Indeed, an inspection of the occupied molecular orbitals of complexes in which Cu^+ is attached to the carbonyl oxygen of the glycolic acid shows the existence of an orbital exhibiting a bonding interaction between a d_{z^2} orbital of Cu and a p orbital of oxygen (see Figure 4). Consistent with this analysis, the NBO method shows for complexes **2** and **5**, in which the Cu^+ is attached to the carbonyl oxygen, the existence of a bonding MO involving an almost pure p orbital of O and a sd hybrid of Cu^+. The dominant contribution (~92%) of the O-hybrid and the strong s character (~86%) of the sd hybrid of Cu^+ permit classification of this interaction as a dative bond, which involves the lone pair of the base and the initially empty 4s orbital of the metal cation.

Conversely, no bonding orbital is found between the hydroxyl oxygen and Cu^+ in complexes **4** and **6**, reflecting a lower donor ability of the −OH groups with respect to the C═O ones. This would be consistent with the dominant electrostatic character of the interaction in this particular case, although polarization effects are also important, as reflected by a relatively large value of the charge density at the corresponding bcp (see Table 2).

It must be mentioned that, consistent with our findings, the most stable structure of [glycine,Cu^+][22,44,45] involves also the formation of a five-membered ring in which Cu^+ is bound simultaneously to the nitrogen and the carbonyl oxygen atoms. Equally important is the fact that structure **2** is essentially degenerate with **1** for [glycolic acid + Cu]$^+$ but significantly higher in energy for the analogous glycine complex.

At the highest level of theory used in this study, the estimated glycolic acid−Cu^+ binding energy is 222 kJ mol^{-1}. It is well-known that the B3LYP binding energies are generally larger

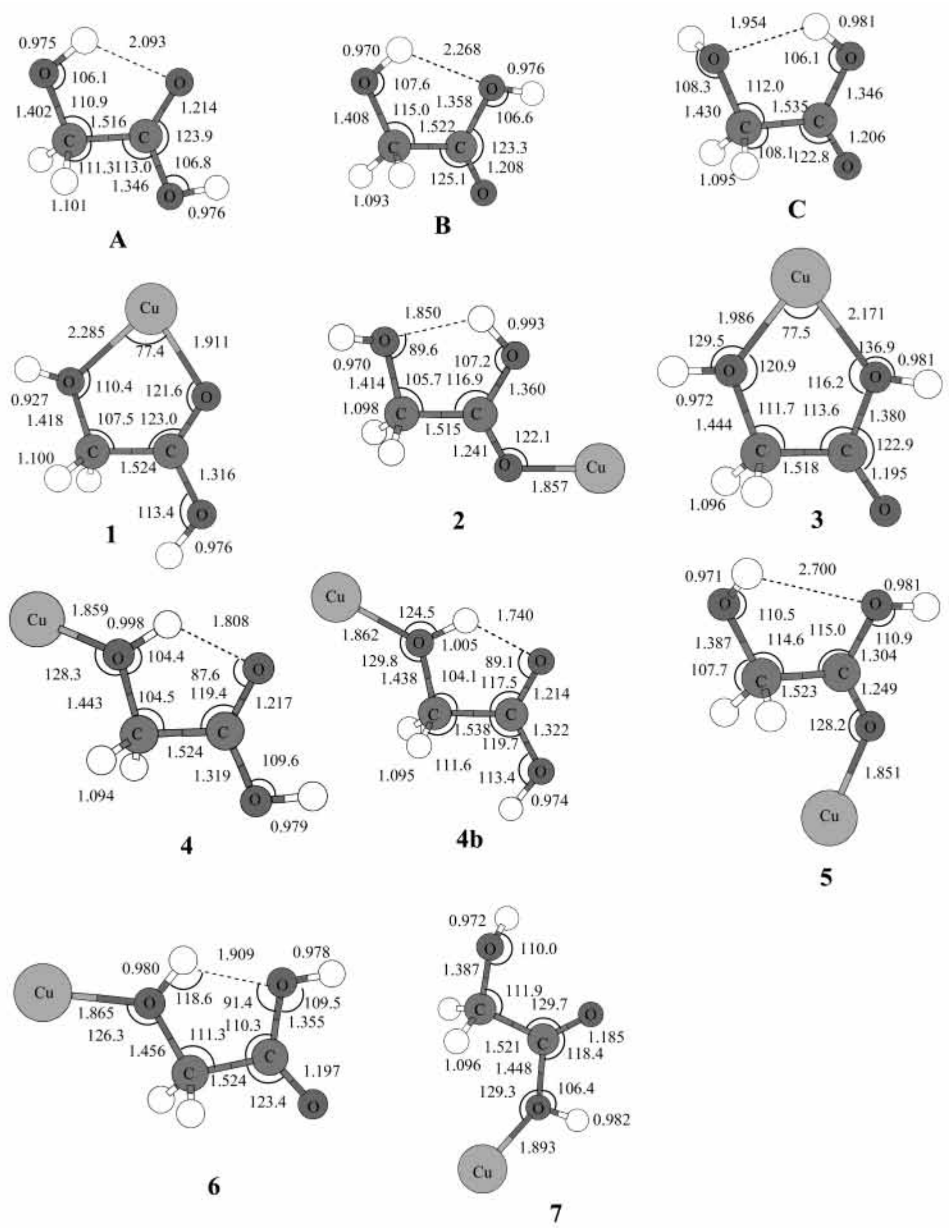


Figure 3. Optimized structures of the most-stable conformers of glycolic acid (**A**, **B**, **C**) and their Cu^+ adducts (**1**−**7**). Bond lengths are in Å and bond angles in deg.

than experimental ones, the average deviation being around 8 kJ mol^{-1}. Our calculated Cu^+ binding energy is 81 kJ mol^{-1} smaller than that estimated for glycine at a similar level of theory. This implies that, as expected, the substitution of a hydroxyl group by an amino group enhances significantly the basicity of the system. As we shall discuss in forthcoming sections, this difference will have a crucial importance as far as the different mechanisms of the unimolecular fragmentations of glycolic−Cu^+ complexes are concerned as compared with those involving glycine.

Glycolic Acid−Cu^+ Reactivity. The major unimolecular fragmentation of glycolic acid−Cu^+ corresponds to a loss of H_2CO_2. A brief report of the reactions of Cu^+ with some amino acids studied by different techniques of mass spectrometry (plasma desorption mass spectrometry (PDMS),[46,47] FAB/MS/MS,[48,49] laser desorption chemical ionization Fourier transform mass spectrometry (LD/CI/FTMS)[50]) show in all cases also the loss of 46 u. Several neutral fragments can be associated with this process including HCOOH and $C(OH)_2$ and also the combination of H_2O + CO and CO_2 + H_2. The authors concluded that all of these fragmentation pathways participate in the 46 u loss. This is also corroborated by neutralization-reionization mass spectrometry (NRMS) experiments recently reported.[51]

Taking as a reference the most stable conformer of glycolic acid **A**, these processes are also estimated to be exothermic in reactions with Cu^+ with the only exception of the loss of $C(OH)_2$.

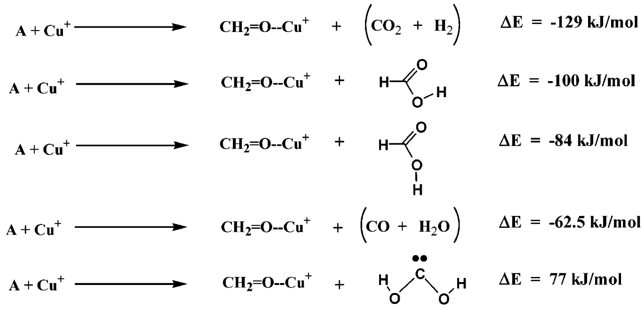


TABLE 1: Total Energies (E, hartree)[a], Zero-Point Energies (ZPE, hartree),[b] and Relative Energies (ΔE, kJ mol^{-1})[c] for the Stationary Points of the $[C_2, H_4, O_2, Cu]^+$ Potential Energy Surface

system	E	ZPE	ΔE
glycolic acid **A**	−304.418 504	0.066 960	0
glycolic acid **B**	−304.414 295 0	0.067 099	11
glycolic acid **C**	−304.412 942	0.067 609	16
Cu$^+$	−1640.176 694		
1	−1944.681 039	0.068 266	−222
2	−1944.681 012	0.068 625	−221
3	−1944.670 718	0.067 769	−196
4	−1944.667 843	0.069 052	−184
4b	−1944.657 15	0.068 52	−159
5	−1944.665 892	0.068 323	−182
6	−1944.658 149	0.068 473	−161
7	−1944.639 26	0.067 262	−115
TS14	−1944.657 01	0.069 20	−156
TS13	−1944.619 88	0.063 12	−75
TS44b	−1944.646 64	0.067 00	−135
TS3I2	−1944.587 92	0.065 40	15
I1	−1944.602 82	0.067 00	−20
I2	−1944.598 66	0.065 55	−13
I3	−1944.586 37	0.063 87	15
I4	−1944.557 83	0.062 62	87
TS1I1	−1994.589 46	0.065 52	11
TSI1I2	−1944.596 80	0.065 35	−8
TSI2I3	−1944.578 60	0.064 28	36
TSI1I4	−1944.533 80	0.061 06	146
TSI4C2	−1944.524 88	0.058 80	163
C1	−1944.671 18	0.066 00	−202
C2	−1944.666 77	0.066 34	−189
C3	−1944.663 40	0.065 06	−184
C4	−1944.647 02	0.066 76	−137
C5	−1944.630 37	0.067 61	−91
TSC1C2	−1944.644 80	0.064 00	−138
TSC1C3	−1944.646 77	0.063 49	−144
TSC1C5	−1944.624 92	0.066 877	−78
TSC4C5	−1944.607 77	0.065 47	−37
TSC1T1	−1944.598 81	0.059 28	−30
Ts4bC4	−1944.639 55	0.066 70	−134
TSC3H2	−1944.549 48	0.054 44	87
D1	−1944.699 531	0.067 620	−271
D2	−1944.699 596	0.066 095	−276
T1	−1944.702 809	0.061 376	−296
P1 + CO	−1944.673 25	0.059 78	−224
P1b + CO	−1944.214 43	0.056 455	55
P2 + H_2O	−1944.671 968	0.058 851	−223
P3 + H_2O	−1944.605 47	0.061 545	−41.2
P4 + H_2O	−1944.586 438	0.060 636	6.4
CH_2COCu^+ (P5) + HCOOH	−1944.566 29	0.063 04	−100
CH_2COCu^+ (P5) + CO + H_2O	−1944.607 64	0.055 62	−63
P6 + H_2	−1944.665 747	0.052 844	−222

[a] Values obtained at the B3LYP/6-311+G(2df,2p) level. [b] Values obtained using a 6-31G(d) basis set for first-row atoms and a 6-311G(d) basis set for Cu (see text). [c] Values realtive to the entrance channel (**A** + Cu$^+$) obtained at the B3LYP/6-311+G(2df,2p) level after including the corresponding ZPE corrections.

However, as we shall discuss later, the mechanisms that can be envisaged for the combined loss of $H_2 + CO_2$ involve activation barriers that are above the entrance channel. Hence, the observed loss of 46 u can be only associated with the loss of formic acid or the loss of H_2O + CO, which as we shall discuss later involve energy barriers below the entrance channel. As we have mentioned, the loss of carbenes ($C(OH)_2$), instead of formic acid, is predicted to be always endothermic, and therefore, it should be discarded.

TABLE 2: Charge Density, ρ, and Energy Density, $H(\mathbf{r})$, at Relevant Bond Critical Points of Glycolic Acid and Some of Its Cu$^+$ Complexes[a]

	OH···O IHB		CO−Cu		HO−Cu	
system	ρ	$H(\mathbf{r})$	ρ	$H(\mathbf{r})$	ρ	$H(\mathbf{r})$
A	0.022	0.001				
C	0.030	0.001				
1			0.093	−0.010	0.041	−0.006
2	0.034	0.007	0.106	−0.012		
3					0.051[b]	−0.005[b]
					0.076[c]	−0.007[c]
6	0.028	0.000			0.102	−0.006

[a] All values in au. [b] Values corresponding to the HO−Cu bond involving the hydroxyl group of the acidic function. [c] Values corresponding to the HO−Cu bond involving the hydroxyl group of the alcoholic function.

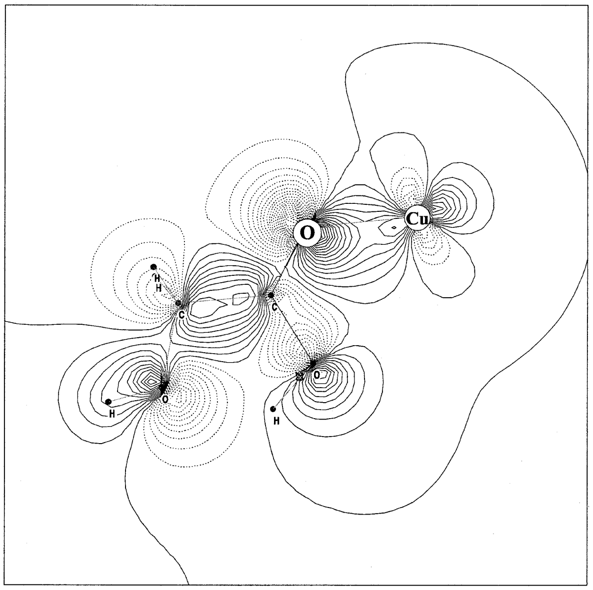


Figure 4. Density contour map of the 28th occupied canonical MO of complex **2** showing a bonding interaction between a d_{z^2} orbital of Cu and a p orbital of the carbonyl oxygen.

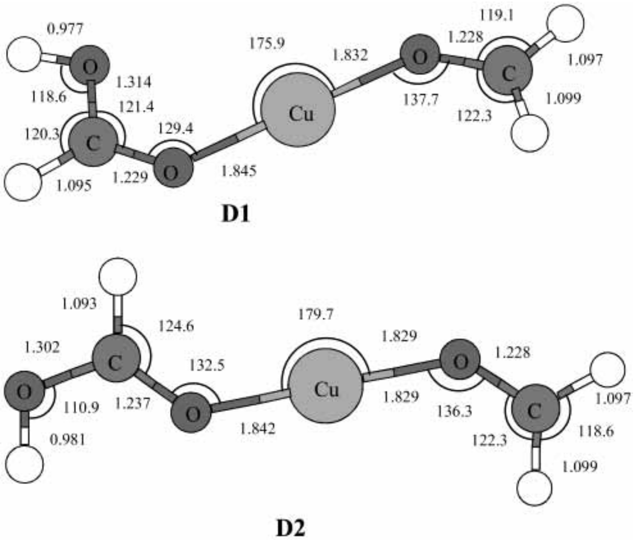


Figure 5. Optimized structures of the dicoordinated complexes between Cu$^+$, formaldehyde, and formic acid. Bond lengths are in Å and bond angles in deg.

It is also important to note that no fragmentations leading to HCOOH−Cu$^+$ + CH_2O (loss of 30 u) are observed in the MIKE

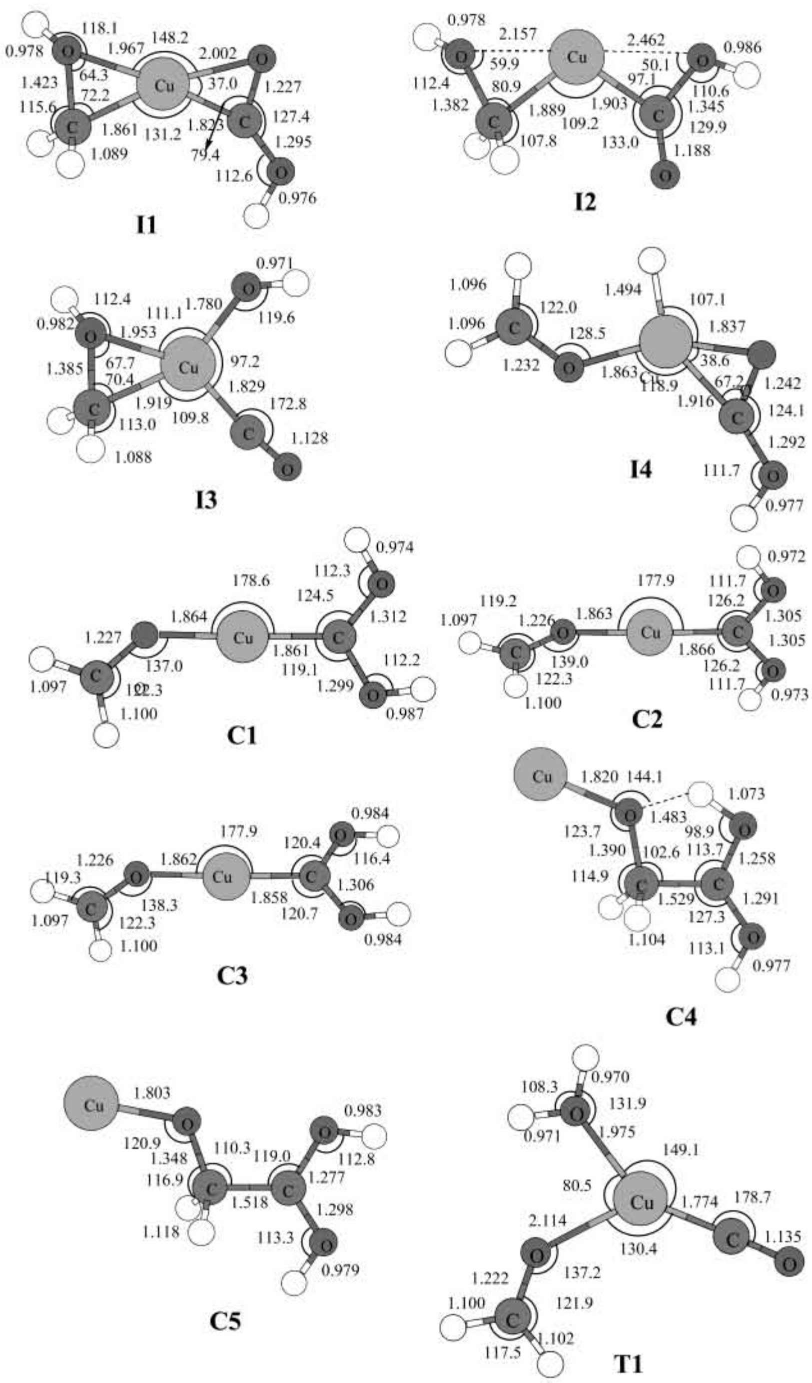


Figure 6. Optimized structures of the relevant stationary points of the $[H_4, C_2, O_3, Cu]^+$ PES. Bond lengths are in Å and bond angles in deg.

spectrum. This is, in principle, a quite surprising result because the calculated Cu^+ binding energy of formic acid is 17 kJ mol^{-1} higher than the Cu^+ binding energy of formaldehyde. Therefore, the loss of 30 u should be thermodynamically favored with regards to the loss of 46 u, in clear contrast with the experimental evidence. Indeed, the complexes between Cu^+ with formic acid and formaldehyde, **D1** and **D2** (see Figure 5), are very stable reflecting the well-established ability of Cu^+ to form linear or nearly linear dicoordinated complexes between two neutral moieties.[20,23,25] Despite that, these complexes cannot play any significant role in glycolic$-Cu^+$ reactions because they would lead to a preferential loss of formaldehyde, which is not observed. There are, however, alternative dicoordinated complexes between formaldehyde and the carbenic isomers of formic acid. These complexes, **C1**$-$**C3**, together with **C4** and **C5** in which Cu^+ is attached to the carbenic isomer of glycolic acid (see Figure 6), are appropriate precursors for the loss of formic acid. Furthermore, they are also very stable. In fact, because of their high stability with respect to both the entrance and the exit channels, if they dissociate into H_2COCu^+ + $C(OH)_2$, the carbene formed has enough energy to isomerize to yield formic acid (the estimated barrier for this isomerization being only 129 kJ mol^{-1} in agreement with previous theoretical[52−54] and experimental[55,56] results), and this overall process is more exothermic than the dissociation into H_2CO + $(OH)_2C-Cu^+$ by 57 kJ mol^{-1}. On the other hand, any attempt to shift one of the hydroxyl hydrogens of the carbenic moiety in complexes **C1**$-$**C5** toward the carbon atom leads directly to the dissociation into H_2COCu^+ + formic acid. Therefore, the next question to be solved is what are the possible

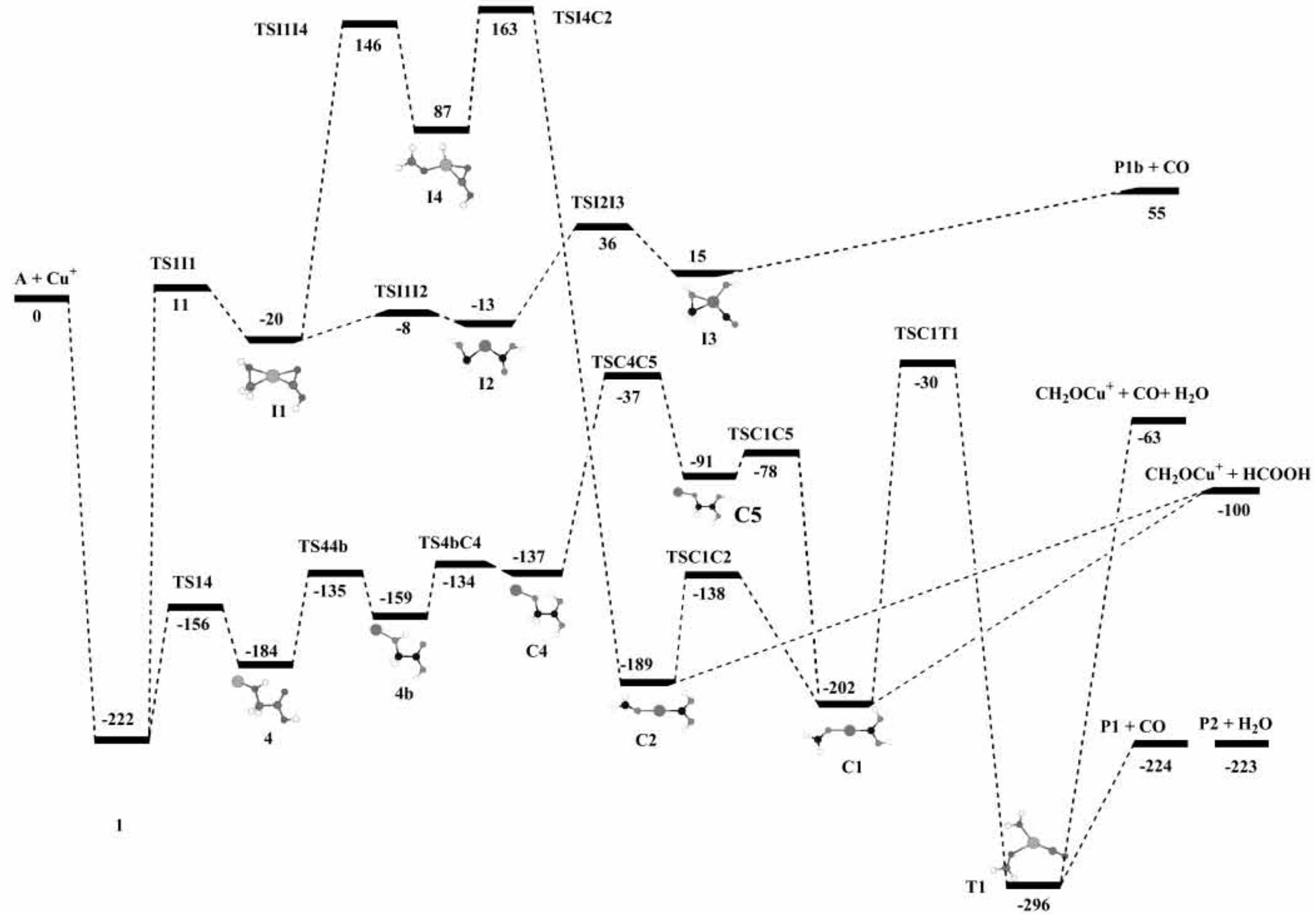
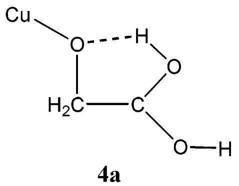


Figure 7. Energy profile of the [H$_4$, C$_2$, O$_3$, Cu]$^+$ PES. All values are in kJ mol^{-1}.

mechanisms leading to the formation of these [H$_2$CO$-$Cu$-$(OH)$_2$C]$^+$ complexes.

Unimolecular Reactivity through Complexes C1$-$C5. Loss of 46 u. Let us consider in the first place the possible mechanisms with origin in the most stable glycolic$-$Cu$^+$ complex **1**, the energy profiles of which are given in Figure 7. The structures of the different local minima have been included in Figure 6. The geometries of the corresponding transition states are provided as Supporting Information. The insertion of Cu$^+$ into the C$-$C bond of glycolic acid, which is a necessary step to form dicoordinated complexes involving formaldehyde and the carbenic isomers of formic acid, leads to complex **I1** in a slightly exothermic process. Complex **I1** may evolve through the transition state **TSI1I4** to complex **I4**, which in turn leads, through a 1,2-H shift, to a very stable complex, **C2**. Once complex **C2** is formed it can either dissociate into CH$_2$OCu$^+$ + HCOOH or isomerize yielding complex **C1**, the latter process being the most favorable one. Complex **C1** can be also an appropriate precursor for the loss of formic acid. Alternatively, a 1,3-H shift would connect this structure with a very stable tricoordinated complex **T1** between Cu$^+$ and formaldehyde, carbon monoxide, and water. Complex **T1** can dissociate by losing a molecule of CO or a molecule of water. In these processes, the product ions **P1** and **P2**, respectively (see Figure 8), would be formed. As illustrated in Figure 7, both processes are equally exothermic. It is also worth noting that a simultaneous loss of CO + H$_2$O would be also an overall exothermic process. Nevertheless, this mechanism, which resembles closely that proposed for glycine$-$Ni$^+$ reactions,[57] has to be discarded because it involves activation barriers, those associated with **TSI1I4** and **TSI4C2**, much higher than the entrance channel. In other words, if this mechanism would be possible, one should observe Cu$^+$ as a product of the reaction, which is not the case. This means that the fact that the binding energy of Cu$^+$ to glycolic acid is smaller than that of glycine implies that mechanisms that are open for glycine$-$Cu$^+$ reactions cannot play any significant role in glycolic$-$Cu$^+$ reactions, for which the potential energy surface, in particular, those parts of it that are substantially affected by metal$-$ion or intramolecular H-bonding interactions with the NH$_2$ or the OH group, appear shifted up with respect to the entrance channel.

There are however alternative ways of producing the desired complexes **C1**$-$**C5** starting from adduct **4** (see Figure 7). Furthermore, the isomerization barrier between **1** and **4** through the **TS14** transition state is well below the entrance channel, which implies that such a mechanism can also have its origin in structure **1**. Apparently, the easiest way of going from structure **4** to a complex with a carbenic moiety would be a proton transfer through the corresponding intramolecular hydrogen bond; however, structure **4a** is not a stationary point of the PES because it collapses to **4**.



4a

Hence, the only remaining alternative step consists of an

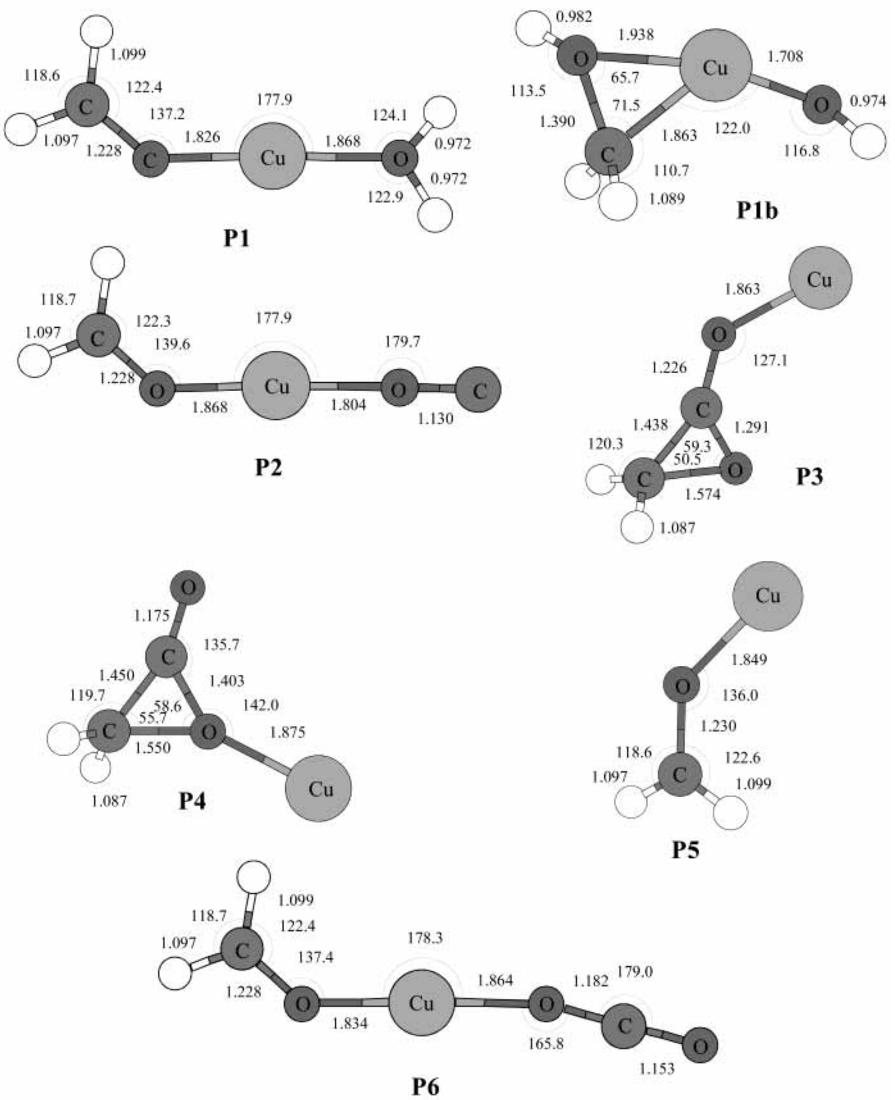


Figure 8. Optimized structures of some relevant product ions of the gas-phase reactions between glycolic acid and Cu^+. Bond lengths are in Å and bond angles in deg.

internal rotation of the OH group not involved in the IHB to yield complex **4b**, which evolves through a rather low activation barrier to a carbenic-type complex **C4**. Once complex **C4** is formed, there are two alternative pathways: its direct dissociation to yield $CH_2OCu^+ + HCOOH$ or its isomerization, through the intermediate **C5**, to finally yield complex **C1**. In this way, this second mechanism will be connected with the one discussed previously.

As indicated above, in principle, the combined loss of $H_2 + CO_2$ would be also an exothermic process. This mechanism would involve a **C1**−**C3** isomerization through the **TSC1C3**, which involves an activation barrier of 58 kJ mol^{-1}. Complex **C3** can now either dissociate into $CH_2OCu^+ + HCOOH$ or into **P6** + H_2 (see Figure 8). However, this dissociation takes place through the **TSC3H2** transition state, which lies 87 kJ mol^{-1} above the entrance channel.

In summary, complexes **C1**−**C5** are suitable precursors for the loss of 46 u that can be formed from adducts **1** or **4** or both. On the other hand, the loss of 46 u should correspond dominantly to the loss of formic acid and in a lower proportion to the loss of $CO + H_2O$ but not to a combined loss of $H_2 + CO_2$.

Mechanisms for the Loss of H_2O. According to our previous discussion part of the loss of water may come from the tricoordinated species **T1**. In this case, the product ion **P2** would have enough internal energy to undergo a subsequent dissociation into $CH_2COCu^+ + CO$. On the other hand, the adducts **2** and **6** are also good precursors for the loss of water by means of a proton transfer through the corresponding IHB. In the first case, the product ion would be complex **P3** and in the second one **P4** (see Figure 8). From the values in Table 1, it can be observed, however, that while the first process is slightly exothermic the second one is slightly endothermic. Furthermore, in the second process, the activation barrier for the proton transfer lies above the entrance channel. Therefore, we must conclude that the loss of water can be only produced from adduct **2**. It is also important to mention that the corresponding activation barrier is 70 kJ mol^{-1} lower than that reported by Domingo et al.[58] for the loss of water from neutral glycolic acid. This implies that this unimolecular fragmentation is catalyzed by Cu^+ association, as a direct consequence of the reinforcement of the OH···O intramolecular hydrogen bond, which occurs upon Cu^+ association. Although for the neutral, the subsequent fragmentation of the three-membered ring into $H_2CO + CO$ implies similar activation barriers as those involved in the loss of water,[58] in our case, these barriers would be well above the entrance channel, so a subsequent loss of CO from **P3** cannot be expected.

Mechanisms for the Loss of CO. As we have discussed above, the dissociation of complex **T1** into **P1** + CO is predicted to be as probable as its dissociation into **P2** + H_2O from a thermodynamic point of view. This could be then one of the pathways for the loss of CO, although again the product ion **P1** could eventually dissociate into **P5** + H_2O. An alternative mechanism for the loss of CO might have its origin in complex **I2**, which can be formed from complex **I1** by an internal rotation of the CO_2H moiety through the **TSI1I2** transition state (see Figure 7). The dissociation of the C−OH bond in this latter complex to yield structure **I3** implies an activation barrier of 49 kJ mol^{-1}. Then, complex **I3** would eventually dissociate into CO + **P1b**, which can be viewed as an isomer of the product ion **P1**. However, the **P1b** → **P1** isomerization implies a quite large activation barrier (185 kJ mol^{-1}). It can be observed that this mechanism should be little probable because some of the barriers, as well as the final products, are slightly above the entrance channel.

Complex **I2** can be also formed by insertion of Cu^+ into the C−C bond of adduct **3**. However, the corresponding transition state (**TS3I2**) is estimated to be also 15 kJ mol^{-1} above the entrance channel. Furthermore, the isomerization barrier connecting adduct **3** with the most stable one **1** involves a much lower activation barrier through the **TS13** transition state, which lies 75 kJ mol^{-1} below the entrance channel. Therefore, this should be the dominant process with origin in adduct **3**, leading eventually to the loss of 46 u through the mechanisms already discussed for adduct **1**.

Conclusions

The MIKE spectrum of the gas-phase reactions between glycolic acid and Cu^+ reveals that the adduct ions ($HOCH_2$-$COOH$−Cu^+) decompose spontaneously by losing CH_2O_2, CO, and H_2O. A minor fragmentation corresponding to the loss of H_2 is also observed.

Our DFT calculations on the stationary points of the corresponding PES indicate that the attachment of Cu^+ to glycolic acid gives rise preferentially to two energetically degenerate structures: a chelated form in which Cu^+ interacts with the carbonyl oxygen and the α-hydroxyl oxygen atom and another one in which the attachment of Cu^+ takes place exclusively at the carbonyl oxygen atom. The estimated glycolic acid−Cu^+ binding energy is 222 kJ/mol.

Different mechanisms for the spontaneous fragmentations observed experimentally are proposed. The main conclusion is that the loss of 46 u should correspond dominantly to the loss of formic acid and, in a lower proportion, to the loss of CO + H_2O, but a combined loss of H_2 + CO_2 should not be observed.

The loss of water can be produced from adduct **2**, which preserves the OH···O IHB of the neutral. A similar process with origin in adduct **6** should be discarded for being endothermic.

The loss of carbon monoxide is little probable, in agreement with the experimental findings, because the possible mechanisms either compete with more favorable processes or imply activation barriers slightly above the entrance channel.

Acknowledgment. This work has been partially supported by the DGI Project No. BQU2000-0245 and by the Acción Integrada Picasso HF-1999-0015. A generous allocation of computational time at the CCC of the Universidad Autónoma de Madrid is also gratefully acknowledged.

Supporting Information Available: Optimized geometries of the transition states associated with the reactions between Cu^+ and glycolic acid. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Eller, K.; Schwarz, H. *Chem. Rev.* **1991**, *91*, 1121.

(2) Fontijn, A., Ed. *Gas-Phase Metal Reactions*; North-Holland: Amsterdam, 1992.

(3) Teesch, L. M.; Adams, J. *Org. Mass Spectrom.* **1992**, *27*, 931.

(4) Freiser, B. S., Ed. *Organometallic Ion Chemistry*; Kluwer Academic Publishers: Dordrecht, Netherlands, 1995.

(5) Eller, K. *Coord. Chem. Rev.* **1993**, *126*, 93.

(6) Niu, S.; Hall, M. B. *Chem. Rev.* **2000**, *100*, 353.

(7) Siegbahn, P. E. M.; Blomberg, R. A. *Chem. Rev.* **2000**, *100*, 421.

(8) Stirk, K. M.; Kiminkinen, L. K. M.; Kenttamaa, H. I. *Chem. Rev.* **1992**, *92*, 1649.

(9) Torrent, M.; Solà, M.; Frenking, G. *Chem. Rev.* **2000**, *100*, 439.

(10) Morizur, J.-P.; Desmazieres, B.; Chamot-Rooke, J.; Haldys, V.; Fordham, P.; Tortajada, J. *J. Am. Soc. Mass Spectrom.* **1998**, *9*, 731.

(11) Fordham, P.; Deschasse, M.; Haldys, V.; Tortajada, J.; Morizur, J.-P. *Eur. J. Mass Spectrom.* **2001**, *7*, 213.

(12) Gaucher, S. P.; Leary, J. A. *Anal. Chem.* **1998**, *70*, 3009.

(13) Dongré, A. R.; Wysocki, V. H. *Org. Mass Spectrom.* **1994**, 700.

(14) Sible, E. M.; Brimmer, S. P.; Leary, J. A. *J. Am. Soc. Mass Spectrom.* **1997**, 32.

(15) Eichhorn, G. L. *Adv. Inorg. Biochem.* **1981**, 1.

(16) Sigel, A., Sigel, H., Eds. *Metal ions in biological systems*; Marcel Dekker: New York, 1996; Vols. 32 and 33.

(17) Karlin, D. K., Zubieta, J., Eds. *Biological and Inorganic Copper Chemistry*; Adenine Guiderland: New York, 1986; Vols. I and II.

(18) Whitfield, D. M.; Stojkovski, S.; Sarkar, B. *Coord. Chem. Rev.* **1993**, *122*, 171.

(19) Luna, A.; Alcamí, M.; Mó, O.; Yáñez, M. *Int. J. Mass Spectrom.* **2000**, *201*, 215.

(20) Luna, A.; Amekraz, B.; Tortajada, J.; Morizur, J. P.; Alcamí, M.; Mó, O.; Yáñez, M. *J. Am. Chem. Soc.* **1998**, *120*, 5411.

(21) Cerda, B. A.; Wesdemiotis, C. *J. Am. Chem. Soc.* **1995**, *117*, 9734.

(22) Hoyau, S.; Ohanessian, G. *J. Am. Chem. Soc.* **1997**, *119*, 2016.

(23) Luna, A.; Amekraz, B.; Morizur, J. P.; Tortajada, J.; Mó, O.; Yáñez, M. *J. Phys. Chem. A* **1997**, *101*, 5931.

(24) Alcamí, M.; Mó, O.; Yáñez, M.; Luna, A.; Morizur, J. P.; Tortajada, J. *J. Phys. Chem. A* **1998**, *102*, 10120.

(25) Luna, A.; Amekraz, B.; Morizur, J. P.; Tortajada, J.; Mó, O.; Yáñez, M. *J. Phys. Chem. A* **2000**, *104*, 3132.

(26) Luna, A.; Morizur, J. P.; Tortajada, J.; Alcamí, M.; Mó, O.; Yáñez, M. *J. Phys. Chem. A* **1998**, *102*, 4652.

(27) Hoyau, S.; Ohanessian, G. *Chem.*−*Eur. J.* **1998**, *4*, 1561.

(28) Dean, I. K. L.; Bush, K. L. *Org. Mass Spectrom.* **1988**, *24*, 733.

(29) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372.

(30) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B: Condens. Matter* **1988**, *37*, 785.

(31) Wachters, A. J. H. *J. Chem. Phys.* **1970**, *52*, 1033.

(32) Hay, P. J. *J. Chem. Phys.* **1977**, *66*, 4377.

(33) Halgren, T. A.; Lipscomb, W. N. *Chem. Phys. Lett.* **1977**, *49*, 225.

(34) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.3; Gaussian, Inc.: Pittsburgh, PA, 1998.

(35) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

(36) Bader, R. F. W. *Atoms in Molecules. A Quantum Theory*; Clarendon Press: Oxford, 1990.

(37) Godfrey, P. D.; Rodgers, F. M.; Brown, R. D. *J. Am. Chem. Soc.* **1997**, *119*, 2232.

(38) Blom, C. E.; Bauder, A. *J. Am. Chem. Soc.* **1982**, *104*, 2993.

(39) Hasegawa, H.; Ohashi, O.; Yamaguchi, I. *J. Mol. Struct.* **1982**, *82*, 205.

(40) Jensen, J. H.; Gordon, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 8159.

(41) Abboud, J. L. M.; Yáñez, M.; Elguero, J.; Liotard, D.; Essefar, M.; El Mouhtadi, M.; Taft, R. W. *New J. Chem.* **1992**, *16*, 739.

(42) Alcamí, M.; Mó, O.; Yáñez, M. *J. Phys. Chem.* **1989**, *93*, 3929.

(43) Tortajada, J.; Leon, E.; Luna, A.; Mó, O.; Yáñez, M. *J. Phys. Chem.* **1994**, *98*, 12919.

(44) Bertrán, J.; Rodríguez-Santiago, L.; Sodupe, M. *J. Phys. Chem. B* **1999**, *103*, 2310.

(45) Marino, T.; Russo, N.; Toscano, M. *J. Inorg. Biochem.* **2000**, *79*, 179.

(46) Bouchonnet, S.; Hoppilliard, Y.; Ohanessian, G. *J. Mass. Spectrom.* **1995**, *30*, 170.

(47) Lavanant, H.; Hoppilliard, Y. *J. Mass Spectrom.* **1997**, *32*, 1037.

(48) Wen, D.; Yalcin, T.; Harrison, A. G. *Rapid Commun. Mass Spectrom.* **1995**, *9*, 1155.

(49) Yalcin, T.; Wang, J.; Wen, D.; Harrison, A. G. *J. Am. Soc. Mass Spectrom.* **1995**, *30*, 172.

(50) Lei, Q. P.; Amster, I. J. *J. Am. Soc. Mass Spectrom.* **1996**, *7*, 722.

(51) Polce, M. J.; Beranova, S.; Nold, M. J., Wesdemiotis, C. *J. Mass Spectrom.* **1996**, *31*, 1073.

(52) Goddard, J. D.; Yamaguchi, Y.; Schaefer, H. F., III *J. Chem. Phys.* **1992**, *96*, 1158.

(53) Francisco, J. S. *J. Chem. Phys.* **1992**, *96*, 1167.

(54) Reddigton, R. L.; Bock, C. W.; Aboad, B. *J. Mol. Struct.* **1990**, *224*, 89.

(55) Wiedmann, F. A.; Cai, J.; Wesdemiotis, C. *Rapid Commun. Spectrom.* **1994**, *8*, 804.

(56) Burgers, P. C.; McGibbon, G. A.; Terlouw, J. K. *Chem. Phys. Lett.* **1994**, *224*, 539.

(57) Rodriguez-Santiago, L.; Sodupe, M.; Tortajada, J. *J. Phys. Chem. A* **2001**, *105*, 5340.

(58) Domingo, L. R.; Andres, J.; Moliner, V.; Safont, V. S. *J. Am. Chem. Soc.* **1997**, *119*, 6415.