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An *Ab initio* MO Study of the Fragmentation Mechanism of the Cycloglycylglycine Ion in Mass Spectrometry

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The unimolecular dissociation of the cycloglycylglycine ion has been investigated using the *ab initio* MO method. The optimized geometries of possible molecular ion conformers, reaction intermediates and fragments have been calculated at the HF/6-31G//3-21G and HF/3-21G//3-21G levels. The potential energy curves for CO and NHCO eliminations from cycloglycylglycine ions have been calculated at low energy. The present study indicates that $[M-CO]^{+\cdot}$ and $[M-NHCO]^{+\cdot}$ are produced *via* proton transfers, which result in stable intermediates with a three-membered ring and a five-membered ring, respectively.

1. Introduction

In mass spectrometry it is very important to elucidate a fragmentation mechanism and to establish a fragmentation rule. We have been doing a systematic quantum chemical investigation of mass spectra by *ab initio* MO calculation. We have already reported the theoretical elucidation of the fragmentation mechanisms of butane and its isoelectronic compounds, propanol and propylamine.^{1)~3)} In the present study, the fragmentation mechanism of a cycloglycylglycine ion, which is the simplest cyclic dimer of the amino acids, has been theoretically investigated using the *ab initio* MO method.

In our previous paper,⁴⁾ we proposed some fragmentation mechanisms of several cyclodipeptides based on the observation of metastable decompositions by the B/E linked scanning technique.

In this paper, two main fragmentation schemes were found for cycloglycylglycine in EI mass spectrometry:

The normal EI mass spectra suggest that Scheme 1 is dominant for the fragmentation of cycloglycylglycine ions because the $m/z\ 71$ peak is much higher than $m/z\ 86$. On the contrary, the B/E linked EI mass spectra suggest that Scheme 2 seems to be more favorable than Scheme 1 because the $m/z\ 86$ peak is higher than $m/z\ 71$. Thus, the normal EI mass spectra provided the opposite results with the B/E linked EI mass spectra.

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In order to elucidate the nature of the fragmentation mechanism of cycloglycylglycine ions we have calculated the potential curves for possible fragmentation schemes by the *ab initio* MO method.

2. Experimental

In order to determine which hydrogen atom participates in the fragmentation, we synthesized the deuterium-labelled compound by the following procedure.

Cycloglycylglycine- d_4 (z) was prepared by the cyclization of methyl ester of glycine (y), which was made from glycine- d_5 (x). An unlabelled cycloglycylglycine was available commercially and was used without further purification.

The normal EI mass spectra were measured at the range of 70 eV–10 eV, and some metastable peaks (m^*) were observed in the spectra. In addition, the metastable decompositions were monitored by a B/E linked scan.

Figure 1 shows the EI mass spectra of (a) cycloglycylglycine and (b) cycloglycylglycine- d_4 at 70 eV and at 15 eV. The m/z 71 peak in Fig. 1(a) represents an NHCO elimination from the molecular ion. The m/z 71 peak in Fig. 1(a) shifts to 75 in Fig. 2(b) by the deuterization. This result shows that the fragment ion at m/z 75 includes all of the deuterium atoms. The m/z 86 peak in Fig. 1(a) represents a CO molecule elimination from the molecular cation.

Figure 2 shows the metastable decomposition from the molecular ion of cycloglycylglycine observed by a B/E linked scan. This spectrum shows that m/z 86 and 71 ions are produced directly from the molecular ion. In the B/E linked EI mass spectra, we found that m/z 42 and 43 ions are produced from the m/z 71 ion by secondary bond cleavages. On the other hand, m/z 59, 58, and 30 ions come from the m/z 86 ion.

3. *Ab initio* MO Calculation

The molecular geometries of radical cations were calculated by the *ab initio* MO method with the 3-21G basis set. The optimized energies of molecular ion conformers, reaction intermediates, and the products were calculated at the HF/6-31G//3-21G and HF/3-21G//3-21G levels using GAUSSIAN 88,⁵⁾ 92,⁶⁾ and HONDO7⁷⁾ programs. In order to obtain the structures of the transition state of an NHCO elimination process, we calculated the potential energy profile by the ROHF and UHF methods. In order to

Fig. 1. EI mass spectra of (a) cycloglycylglycine and (b) cycloglycylglycine- d_4 at 70 eV and 15 eV.

Fig. 2. The B/E linked EI mass spectrum of cycloglycylglycine.

Fig. 3. The numbering of the atoms in cycloglycylglycine.

Fig. 4. Optimized geometries and the spin density distributions of cycloglycylglycine ions, $[\text{cyclo}(\text{gly-gly})]^{\cdot+}$.

determine whether the structures obtained by geometry optimization are located at an equilibrium state or a transition state, we carried out vibrational analysis by using an analytical second derivative method.

4. Results and Discussion

4.1 Molecular ions

Since the fragmentation in mass spectrometry starts from the molecular cation radical, first of all we calculated the molecular cation radical by the *ab initio* MO method with the 3-21G basis set. Figure 3 shows the numbering of the atoms in cycloglycylglycine. The two optimized geometries in Fig. 4 were calculated for the molecular cation radicals. Figure 4 shows that in structure (a) the spin is distributed in the molecular plane and localized on the oxygen atom. In structure (a), the C₅-O₈ bond distance increases to 1.319 Å, while the C₂-O₇ bond distance is 1.201 Å. The N₄-C₅ bond is stronger than the N₁-C₂ bond. That is, the stronger N₄-C₅ bond seems to be a double

Table 1. Calculated Total Energies of the Cycloglycylglycine Ions (M^{•+})^{a, b)}

Structures	UHF/6-31G//UHF/3-21G	UHF/3-21G//UHF/3-21G	ROHF/3-21G//ROHF/3-21G
(a)	-413.122879	-411.010224	-411.008061
(b)	-413.117190	-411.003415	-410.981216

^{a)} Total energies are given in hartrees.

^{b)} The notation B//A means that the molecular energy is computed at level B using the optimized geometry at level A.

Fig. 5. The calculated molecular ions, reaction intermediates and fragment ions.

Fig. 6. The calculated energy diagram for molecular ions, reaction intermediates and fragment species.

bond, and the C_3-N_4 bond is weakened greatly. This result suggests that the structure (a) is expected to precede the NHCO elimination. On the other hand, the spin in the structure (b) is localized on the nitrogen atom.

Table 1 shows the calculated total energies of two different structures of molecular cations at UHF/6-31G//UHF/3-21G, UHF/3-21G//UHF/3-21G, and ROHF/3-21G//ROHF/3-21G levels. Structure (a) is slightly stabler than structure (b).

4.2 Energy profile of the fragmentation species

As we pointed out in the previous paper,³⁾ the fragmentation at the low energy electron bombardment should proceed to the stablest reaction products, if there are no energy barriers or only a small energy barrier in the reaction course. In order to elucidate the fragmentation mechanism of the cycloglycylglycine ion, we have calculated the optimized geometries and the electronic states for all possible fragment ions using the 3-21G basis set. The calculated species were shown in Fig. 5.

Figure 6 shows the calculated energy diagram for the molecular ions and all possible fragment species at the UHF/6-31G//UHF/3-21G level. The right half of Fig. 6 shows the small fragments produced by further decompositions. Figure 6 shows the four isomers calculated for the m/z 86 ions and the six isomers for the m/z 71 ions. For the m/z 86 ions, the five-membered ring structure (d) is the stablest. In this structure (Fig. 5, m/z 86 (d)), the proton is transferred to the nitrogen atom. On the other hand, the open structures in the m/z 71 ions are stabler than the four-membered ring structure (c). The reason is due to the strain energy in the four-membered ring structure.

From the energy diagram in Fig. 6, it may be expected that the intensity of the m/z 86 ion is stronger than that of m/z 71. This is the case in the B/E linked scanning experiment (see Fig. 2). But in the normal EI mass spectra of cycloglycylglycine (Fig. 1

Fig. 7. The optimized structure and the normal mode of the transition state for an NHCO elimination.

Table 2. The Calculated Vibrational Frequencies of the Transition State (TS) for an NHCO Elimination

Calculated vibrational frequencies/cm ⁻¹							
798 <i>i</i>	99	155	253	371	440	456	545
566	625	650	756	936	951	1002	1034
1110	1162	1244	1280	1317	1383	1412	1488
1613	1631	1650	1731	1979	2231	3590	3591
3707	3747	3953	4015				

(a)), the intensity of the m/z 71 peak is higher than that of the m/z 86 peak. This is an interesting problem with the fragmentation of a cycloglycylglycine ion. However, the reason for this is not yet elucidated.

Referring to these results, we can confirm that there are two kinds of reaction schemes, Scheme 1 and Scheme 2 mentioned above. Scheme 1 is an NHCO elimination and Scheme 2 is a CO elimination of molecule ion.

4.3 Transition state in Scheme 1

It is interesting to calculate the optimized structure and vibrational modes in the transition state for the elucidation of the fragmentation mechanism. Figure 7(a) shows the optimized structure of the transition state in an NHCO elimination from a cycloglycylglycine ion. The three-membered ring is formed among the N₁, C₂, and C₃ atoms, and the bond between C₃ and N₄ is weakened. This appears to be the transition state appropriate for the NHCO elimination. The calculated vibrational frequencies of the transition state are shown in Table 2. There is one normal mode with an imaginary frequency. This mode represents the reaction coordinate. The normal mode of this imaginary frequency is shown in Fig. 7(b). This figure shows the large amplitudes for the C₃-N₄ bond-stretching and the N₁-C₃ bond-stretching. The former displacement mode brings the C₃-N₄ bond cleavage, and the latter displacement mode makes the N₁-C₃ bond. These bond cleavage and bond formation processes may occur concertedly. Therefore, the three-membered ring formation occurs with the C₃-N₄ bond break.

Fig. 8. The optimized geometries in an NHCO elimination to produce the m/z 71 ion, which corresponds to Scheme 1.

Fig. 9. The optimized geometries of (a) **intermediate 1** and (b) **intermediate 2**.

Fig. 10. The calculated energy profile of an NHCO elimination to produce the m/z 71 ion.

4.4 Proton transfers

When we lengthen the C_3-N_4 bond slightly, the reaction system proceeds automatically to **intermediate 1** (see Fig. 8). The optimized geometry of **intermediate 1** is shown in Fig. 9(a). We expect this intermediate proceeds to the m/z 71 ion. Figure 10 shows the calculated energy profile of an NHCO elimination to produce the m/z 71 ion. The molecular ion travels to **intermediate 1** via the transition state TS. In this process, a

Fig. 11. The calculated energy profile of a CO elimination to produce the m/z 86 ion.

proton transfer occurs from the N_1 atom to the N_4 atom. **Intermediate 1** proceeds to the m/z 71 fragment ion accompanying a proton transfer. There are two different possibilities of proton transfers: (i) the proton moving from N_4 to N_1 to produce $[\text{COCH}_2\text{NH}=\text{CH}_2]^+$ (m/z 71), or (ii) the proton moving from N_4 to C_6 to produce $[\text{COCH}_2\text{N}-\text{CH}_3]^+$ (m/z 71).

In the course of looking for the reaction path from the molecular ion to the m/z 86 ion, we accidentally found the stable **intermediate 2** (see Figs. 9(b) and 11). Figure 11 shows the calculated energy profile of a CO elimination to produce the m/z 86 ion. A proton transfer occurs from the C atom to the N atom in this process. The calculation of the transition state for a CO elimination is in progress. The fragmentation from **intermediate 2** to the m/z 86 ion occurs very easily, because the energy barrier is found to be only 0.2 eV.

Fragmentation reactions for cycloglycylglycine ions occur *via* rather complicated proton transfers, which result in stable intermediates. Thus, the reaction process involves two steps rather than a single step. The present study indicates that $[\text{M}-\text{CO}]^{+}$ and $[\text{M}-\text{NHCO}]^{+}$ are produced *via* proton transfers, which result in stable intermediates with a three-membered ring and a five-membered ring, respectively.

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Keywords

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