Unusual hydroxyl migration in the fragmentation of β-alanine dication in the gas phase†

Dariusz Grzegorz Piekarski,*a Rudy Delaunay,b,c Sylvain Maclot,b,c Lamri Adoui,b,c Fernando Martin,ad Manuel Alcamidi, Bernd A. Huber,b Patrick Rousseau,b,c Alicia Domaracka,a and Sergio Díaz-Tendero*a

We present a combined experimental and theoretical study of the fragmentation of doubly positively charged β-alanine molecules in the gas phase. The dissociation of the produced dicationic molecules, induced by low-energy ion collisions, is analysed by coincidence mass spectrometric techniques; the coupling with ab initio molecular dynamics simulations allows rationalisation of the experimental observations. The present strategy gives deeper insights into the chemical mechanisms of multiply charged amino acids in the gas phase. In the case of the β-alanine dication, in addition to the expected Coulomb explosion and hydrogen migration processes, we have found evidence of hydroxyl-group migration, which leads to unusual fragmentation products, such as hydroxymethyl cation, and is necessary to explain some of the observed dominant channels.

In particular, the fragmentation of positively charged β-alanine has been the object of extensive investigations.14–17 In single ionisation of β-alanine, and other small amino acids, it was found that the loss of the carboxylic group is one of the dominant processes.14–16 In the z-alanine case, photoionisation experiments showed that the principal cationic fragment produced corresponds to NH2CH3CH+, formed by the loss of the COOH radical in a simple Ccarboxylic–C–b bond cleavage.18 C–C and C–C–b bond breaking are the dominant channels for β-amino acids19 and γ-amino acids,20 respectively. For more complex amino acids side chain bond breaking appears in competition.15,16 For double ionisation, simple Coulomb explosion is expected to dominate along the same bond cleavage mentioned above.20,23

In this work, we join theoretical and experimental efforts. Ab initio molecular dynamics and exploration of the potential energy surface (PES) together with multiple-coincidence mass spectrometry techniques allow us to identify all possible exit channels and fragmentation mechanisms following the ionisation processes for excited doubly charged β-alanine in the gas phase. We have found unusual fragmentation mechanism implying hydroxyl group (OH) migration. They appear in competition with other processes such as hydrogen transfer21 or Coulomb explosion. These findings are of high relevance for a better understanding of radiation damage processes, since hydroxyl radicals have been identified as one of the main factors responsible for such damage.22–25 Indeed, it has been shown that in biological tissues the damages produced in the biomolecules are not only caused directly by the particle–matter collision but also by radicals and secondary particles created after the fragmentation of different chemical species along the ionisation path.26,27

1 Introduction

Dicaticonic species, extensively studied due to their unusual stability and reactivity,1,2 are involved in the creation of new biomolecules in planets atmospheres3 and in the interstellar medium.4 Numerous amino acids were detected in Carbonaceous Ivuna chondrites, a type of meteorite, with the simplest β-amino acid, β-alanine (NH2CH2CH2COOH) as the most abundant one.5 This finding can be considered as the manifestation of spontaneous gas phase synthesis of amino acids in the interstellar space.

Moreover, previous theoretical and experimental works showed the important role played by organic radical cations in various chemical reactions,6–13 where the first step is the ionisation of the molecule. For instance an important electrophilic modification of amino acids which takes place after ionisation or nitrosation of alanine10–12 produces lactic acid.11 Therefore, there is a need to understand the chemical behavior of charged amino acids.

† Electronic supplementary information [ESI] available: Details of the experimental procedure and of the theoretical simulations together with some complementary results. See DOI: 10.1039/c5cp01628b

a Departamento de Química, Módulo 13, Universidad Autónoma de Madrid, 28049 Madrid, Spain. E-mail: dariusz.piekarski@uam.es, sergio.diaztendero@uam.es
b CIMP (UMR 6252) - CEA, CNRS, ENSCAEN, Unicaen, Blvd. Henri Becquerel, BP 5133, 14070 Caen Cedex 5, France
c Université de Caen Basse-Normandie, Esplanade de la Paix, CS 14032, 14032 Caen Cedex 5, France
d Instituto Madrileño de Estudios Avanzados en Nanociencias (IMDEA-Nanociencia), Cantoblanco 28049, Madrid, Spain

† Electronic supplementary information [ESI] available: Details of the experimental procedure and of the theoretical simulations together with some complementary results. See DOI: 10.1039/c5cp01628b

PAPERS


Received 20th March 2015,
Accepted 19th May 2015,
DOI: 10.1039/c5cp01628b
www.rsc.org/pccp

This article is licensed under a
Creative Commons Attribution-NonCommercial 3.0 Unported Licence.
This article is © the Owner Societies 2015 Phys. Chem. Chem. Phys., 2015, 17, 16767–16778 | 16767

View Journal

View Issue

View Article Online

Open Access Article. Published on 27 May 2015. Downloaded on 16/10/2017 01:42:54.
Radiation damage of biological tissues at the molecular level has been widely studied by employing experimental techniques involving interaction of biomolecules with ionising particles (X-rays, electrons, ions) in the gas phase\textsuperscript{28-31} in combination with theoretical simulations.\textsuperscript{20,21,30,32,33} The proposed processes in these former studies differ from the mechanisms presented in this work, mainly because in doubly-charged β-alanine, the charge drives the first steps in the fragmentation and thus, the OH migration can be considered as a consequence of the bond breaking due to Coulomb explosion. The importance of OH migration is highlighted here because it leads to ionic products detected with high intensity in the experiments (NH$_2$CH$_2$\textsuperscript{+} in coincidence with CH$_2$OH\textsuperscript{+}), i.e. they come from a dominant channel.

2 Methods

Computational details

Quantum chemistry calculations were carried out using the density functional theory (DFT). In particular, geometry optimisations were performed using the B3LYP functional, which combines the Becke’s three parameter non-local hybrid exchange potential\textsuperscript{19} with the non-local correlation functional of Lee, Yang and Parr.\textsuperscript{40} This functional has been used in combination with the 6-31++G(d,p) basis set. This method has shown to provide an accurate description of the PES of cationic amino acids.\textsuperscript{7,15,20,21,41} Harmonic vibrational frequencies have been also evaluated at the same level to characterise minima and transition states in the PES and to compute the zero point energy (ZPE) correction. For the obtained transition states, intrinsic reaction coordinate (IRC) calculations have been carried out to verify the minima they connect.\textsuperscript{42}

\textit{Ab initio} molecular dynamics (AIMD) were performed using the atom-centered Density Matrix Propagation method (ADMP),\textsuperscript{43-46} employing the B3LYP functional together with the 6-31++G(d,p) basis set. The simulations were carried out using a time step of $\Delta t = 0.1$ fs, a fictitious mass of $\mu = 0.1$ amu and a maximum simulation time of $t_{\text{max}} = 300$ fs. To mimic the experimental conditions we have performed the AIMD simulations in the gas phase by introducing a certain amount of excitation energy, $E_{\text{exc}} \approx 0.03$--4.08 eV, and extracting the two electrons from the excited occupied molecular orbital (HOMO) in a Franck-Condon type transition. This energy range covers the estimated excitation energy in collisions of highly-charged ions with amino acids in the gas phase.\textsuperscript{20,21,47} In the collisions of other type of biomolecules, such as adenine with singly charged ions, a higher excitation energy has been measured (~8 eV) due to the different conditions.\textsuperscript{48} The internal energy was randomly distributed over all the vibrational degrees of freedom in each trajectory. In this way, we reproduce the sudden ionisation and excitation process produced in gas phase collisions of ions with neutral β-alanine molecules. The AIMD simulations were carried out considering the 12 most stable conformers of neutral β-alanine in the gas phase.\textsuperscript{49} For each isomer and each value of the excitation energy we run 20 trajectories. Statistics were then performed over these trajectories. All the calculations were performed using the Gaussian09 program.\textsuperscript{50}

Experimental details

Products of the interaction between O\textsuperscript{6+} ions and isolated β-alanine molecules in the gas phase were studied by means of coincidence time-of-flight (TOF) mass spectrometry. The experiments were performed at the low-energy ion beam facility ARIBE of GANIL in Caen, France. The experimental setup has been described in detail elsewhere,\textsuperscript{51} only a brief description is given here. The O\textsuperscript{6+} ions beam was extracted from the electron cyclotron resonance ion source, mass selected, pulsed, collimated and transported in the interaction zone where the beam crossed a molecular effusive jet of neutral β-alanine molecules produced by the evaporation of a powder from a heated oven device at 400 K. Cationic products of the interaction were extracted into Wiley–McLaren linear time-of-flight mass spectrometer.\textsuperscript{52} At the end of the free-flight region of the spectrometer (TOF tube of 1 m length) these products were accelerated and impacted a gold-coated plate producing secondary electrons which are detected by a microchannel plate detector after deflection by a weak magnetic field produced by Helmholtz coils. This Daly-type detector allowed efficient and uniform detection of the interaction products. The arrival times were measured in an event-by-event mode over a wide mass-over charge ($m/z$) ratio range. Each event was characterised by the number of detected fragments and their associated time-of-flight. This allowed to construct the correlation between the charged fragments proceeding from a single ion-molecule interaction (for details see ref. 20).

3 Results and discussion

The total mass spectrum of positively charged products from collisions of O\textsuperscript{6+} at 48 keV ions with neutral β-alanine molecules in the gas phase is shown in Fig. 1. A strong peak associated with the intact molecule ($m/z = 89$ amu) is observed and represents 3% of the total intensity. However, the mass spectrum is dominated by fragmentation products. The dominant exit channels for heavier fragments ($m/z \geq 24$ amu) come from C$_{\text{carboxyl}}$–C$_{\alpha}$ and C$_{\alpha}$–C$_{\beta}$ bond cleavages and subsequent fragmentations. The peak at $m/z = 30$ amu dominates the spectrum and corresponds to the iminium cation (NH$_2$CH$_2$\textsuperscript{+}). Fragment ion assignments to the most intense peaks have already been made in previous works.\textsuperscript{14,18} Interestingly, in the inclusive mass spectrum we can also observe the presence of molecular dications like in the case of the simplest amino acid glycine.\textsuperscript{21} The different chemical mechanisms leading to cationic fragments are inferred with the quantum chemistry simulations. We first present the theoretical results obtained in the \textit{ab initio} molecular dynamics simulations. In the 4080 trajectories performed for the doubly charged β-alanine, we have characterised seventeen different
mechanisms that can be classified into three groups: (i) Coulomb explosion, (ii) isomerisation and (iii) combined processes. Ten snapshots of these processes are shown in Fig. 2, 3 and 4, respectively. Trajectories 1, 2, 3, 4, 5, 9 and 10 are observed with larger probability and represent the main fragmentation mechanisms. Detailed information of all mechanisms is given in the ESL.

The Coulomb explosion dominates (see Fig. 5a). Four different Coulomb explosion processes can be distinguished (see Fig. 2): C\textsubscript{carboxylic}-C\textsubscript{a} bond cleavage leading to (1) NH\textsubscript{2}CHCH\textsubscript{3}\textsuperscript{+} + COOH\textsuperscript{+}, (2) NH\textsubscript{3}CHCH\textsubscript{2}+ + COOH\textsuperscript{+} and (3) NH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}+ + COOH\textsuperscript{+}; and C\textsubscript{a}-C\textsubscript{b} bond cleavage leading to (4) NH\textsubscript{2}CH\textsubscript{2}+ + CH\textsubscript{2}COOH\textsuperscript{+}. Among them, channels (1) and (4) strongly dominate with \approx 40\% and 30\%, respectively (see Fig. 5b). In the processes (1) and (2) we observe H migration to the terminal C and N atoms, stabilising the produced iminium and ammonium cation, respectively. On the other hand, the mechanism (3) is an example of geometry reorganisation, leading to a stable cyclic isomer of the NH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}+ cation. The carboxyl ion (COOH\textsuperscript{+}) produced in (1), (2) and (3) is very stable. However, fragmentation of this ion was evaluated for other organic systems leading to strongly observed signals at 28\textsuperscript{+} and 29\textsuperscript{+}, associated with CO\textsuperscript{-} and COH\textsuperscript{+}, respectively.\textsuperscript{53} Mechanism (4) leads to the very stable NH\textsubscript{2}CH\textsubscript{2}+ cation, which dominates the mass spectrum.

Fig. 3 shows the time evolution of different isomerisation processes of \textbeta-alanine leading to the diol\textsuperscript{2\textsuperscript{+}} (5), 5-membered ring\textsuperscript{2\textsuperscript{+}} (6), linear NH\textsubscript{2}CH\textsubscript{2}CHCOOH\textsuperscript{2\textsuperscript{+}} (7) and 4-membered ring\textsuperscript{2\textsuperscript{+}} (8) structures. Only one of them does not show H transfer and leads to the stable cyclic form of \textbeta-alanine\textsuperscript{2\textsuperscript{+}} (mechanism (6) in Fig. 3). This structure has not been previously reported, but a similar 5-membered ring intermediate (ozalone) was proposed by Harrison,\textsuperscript{54} after fragmentation of a peptide followed by further elimination of water. 5-Membered ring structures were previously observed after hydrogen migration and water emission in the homologous series of carboxylic acids HOOC(CH\textsubscript{2})\textsubscript{n}COOH.\textsuperscript{53} In competition with cyclisation the formation of linear NH\textsubscript{2}CH\textsubscript{2}CHCOOH\textsuperscript{2\textsuperscript{+}} is also observed, which requires H transfer and appears sporadically in the simulations. H transfer in amino
acids is commonly observed in solution\textsuperscript{12,55} and has been recently reported in the gas phase after the interaction with highly charged ions.\textsuperscript{21}

Combined processes are defined as those trajectories that show Coulomb explosion and molecular rearrangement simultaneously. They are also associated with the emission of neutral moieties. The most important and dominant complex molecular rearrangement of those observed (see Fig. 4) is the migration of the hydroxyl group, leading to the emission of neutral carbon monoxide: $\text{NH}_2\text{CH}_2\text{OH}^+ + \text{CO} \rightarrow \text{NH}_2\text{CH}_2\text{CO}^+$. This mechanism appears in competition with Coulomb explosion showing $\approx 15\%$ of probability. Another observed channel is $\text{NH}_2\text{CCH}_2^+ + \text{H}_2 + \text{COO}^-$ (10). Mechanisms leading to emission of neutral $\text{CO}_2$, $\text{NH}_3$ and $\text{CH}_2$ also appear (see ESI\textsuperscript{†}) but they are very rare processes (with less than 2\% of probability).

It is important to notice that the fragmentation pattern strongly depends on the geometry of the conformers (see details in the ESI). This can be explained by the fact that the structure of the dication formed at the initial stage of the fragmentation (in the ionisation) determines the reaction path and, thus,
the fragmentation products. However, since the temperature in the oven is 400 K, only the most stable neutral conformers will be populated before the collision and thus, not all the conformers included in the calculations will contribute to the fragmentation pattern because they are too high in energy to be present in the beam. Statistical details about all mechanisms are presented in the ESL.

Molecular dynamics simulations were performed up to 300 fs. To evaluate the energetics and the mechanisms of the subsequent processes we have thoroughly explored the potential energy surface (PES). The exploration of the PES has been performed starting from the most probable and relevant processes as observed in the statistics of the molecular dynamics simulations: i.e. mechanisms (1), (2), (3), (4), (5), (9) and (10). Firstly, we calculated all of the possible pathways corresponding to the mechanisms obtained in the molecular dynamics simulations. Later, we associated the lowest energy channels with the peaks observed in the experimental measurements. Using this approach we obtained a complete picture of the fragmentation dynamics and further energetic information of each channel which becomes comparable with the experimental measurements, done at the µs timescale. We present these results separately considering the following order: (a) C\text{carboxyl}–C\text{a} bond cleavage, (b) C\text{a}–C\text{b} bond cleavage, (c) H migration and (d) unexpected OH migration.

(a) C\text{carboxyl}–C\text{a} bond breaking

Fig. 6 shows zooms in the most interesting regions of the correlation map, which displays the time-of-flights (in ns) of the heavier fragments (TOF 2) as a function of the time-of-flights of the lighter ones (TOF 1). It shows the islands with the highest intensities with special emphasis on the ion pairs (42+/45+), (30+/42+), (30+/31+) and (28+/30+). Direct bond cleavage of \(\beta\)-alanine does not explain most of these islands. The assignments of such species and the understanding of their production require some complementary studies. Quantum chemistry calculations allow us to propose the mechanisms underlying the formation of the different molecular cations observed after C\text{carboxyl}–C\text{a}. Starting from the NH\text{2}CHCH\text{3}⁺ + COOH⁺ exit channel we can easily explain the peaks observed in the zoom on the coincidence map (Fig. 6a). Fig. 7 presents the part of potential energy surface corresponding to these pathways. The most intense islands related to C\text{carboxyl}–C\text{a} are those corresponding to COOH⁺ (\(m/z = 45\) amu) in correlation with other species: \(m/z = 44, 43, 42\) and 41 amu. Processes corresponding to further fragmentation of the COOH⁺ appear at much higher energy and thus, the corresponding islands contribute in much lower percentage in the correlation map: slight signals coming from COOH⁺ fragmentation due to O or OH emissions are observed, similarly to those previously reported in the literature. The coincidence measurement at (44+/45⁺) presents low intensity. This is in agreement with the simulations assuming that NH\text{2}CHCH\text{3}⁺ (\(m/z = 44\) amu) possesses enough internal energy to undergo further fragmentation since this channel is almost 9 eV below the entrance channel (1st + 2nd vertical ionisation potential, VIP). The observation of the islands at (43'/45⁺) and (42'/45⁺) corresponds to the emission of H and H\text{2} from this fragment. The strong intensity of these islands in the correlation map (Fig. 6a) confirm the proposed mechanisms. The peak at \(m/z = 43\) amu is assigned to NH\text{2}CHCH\text{3}⁺ and NH\text{2}CHCH\text{3}⁺⁺ (see Fig. 7); they are cationic forms of acetaldimine and vinylamine, respectively.
After emission of one hydrogen atom, dehydrogenated acetaldehyde (NHCH₂⁻) and vinylamine (NH₂CCH₂⁻) cations (m/z = 42 amu) become more stable than their original forms. The intramolecular hydrogen transfer between them is an exact analogue to the previously studied imine/enamine tautomerisation processes.57

The analysis of the slopes in the detected islands provide information of the fragmentation mechanisms58 (see ESI† for details): the pair (43+/45+) corresponds to the charged fragments NH₂CHCH₃⁺ + COOH⁻, which shows very similar relative intensities (see Table S1 in ESI†). The latter explains the correlation 18+/45+ (barrier on the PES at 20.74 eV). Both coincidence measurements (18+/45+ and 27+/45+) show very similar relative intensities (see Table S1 in ESI†). Accordingly, both channels require similar fragmentation energies.

Further fragmentation of NH₃CHCH₂⁺, proposed in Fig. 8, provides the mechanisms to explain the peaks related to the theoretical slopes of the three pairs (27+/45+) and (30+/45+). The theoretical slopes of the three pairs (27+/45+) and (30+/45+) are respectively 1.63, 1.57 and 1.47, which is also in agreement with the experimentally measured slopes (see Table S1 in ESI†). They correspond to Coulomb explosion with Cα-carbocyclic-Cβ bond breaking followed by emission of neutral moieties.

Further fragmentation of NH₃CHCH₂⁺, proposed in Fig. 8, provides the mechanisms to explain the peaks related to 18+/45+. The latter explains the correlation 18+/45+ (barrier on the PES at 20.74 eV). Both coincidence measurements (18+/45+ and 27+/45+) show very similar relative intensities (see Table S1 in ESI†). Accordingly, both channels require similar fragmentation energies.

Further fragmentation of NH₃CHCH₂⁺, proposed in Fig. 8, provides the mechanisms to explain the peaks related to 18+/45+. The latter explains the correlation 18+/45+ (barrier on the PES at 20.74 eV). Both coincidence measurements (18+/45+ and 27+/45+) show very similar relative intensities (see Table S1 in ESI†). Accordingly, both channels require similar fragmentation energies.

Further fragmentation of NH₃CHCH₂⁺, proposed in Fig. 8, provides the mechanisms to explain the peaks related to 18+/45+. The latter explains the correlation 18+/45+ (barrier on the PES at 20.74 eV). Both coincidence measurements (18+/45+ and 27+/45+) show very similar relative intensities (see Table S1 in ESI†). Accordingly, both channels require similar fragmentation energies.
observe the signal at m/z = 59 amu (see Fig. 1). This cation can easily break by losing CH₃ or OH without barriers. Indeed, the relatively low energies calculated for the fragments produced in the corresponding pathways, HOCH₂CO⁺ or CH₂COOH⁺, and the absence of a peak at m/z = 59 amu in the experiments, allow us to conclude that the fragment at m/z = 59 amu undergoes further fragmentation, in these kinetically favourable processes, leading to signals at (30+/42+) and (30+/45+) (see Fig. 9 for the corresponding mechanisms). The observation of the signal at (30+/42+) also indicates that the molecule has enough internal energy to break leading to NH₂CH₂⁺ + CH₂CO⁺ + OH. These species can be obtained in two different pathways. (i) OH emission followed by Coulomb repulsion \[\beta\text{-alanine}^{2+} \rightarrow \text{NH₃CH₂CH₂CO}^{2+} + \text{OH} \rightarrow \text{NH₃CH₂}⁺ + \text{CH₂CO}⁺ + \text{OH} \], (ii) first Coulomb explosion \[\beta\text{-alanine}^{2+} \rightarrow \text{NH₃CH₂}⁺ + \text{CH₂COOH}⁻\] and then emission of neutral OH \[\text{NH₃CH₂}⁺ + \text{CH₂CO}⁺ + \text{OH}\]. The associated computed slopes are −1 and −0.71, respectively. The experimentally measured slope suggests first emission of neutral OH leading to NH₂CH₂CH₂CO⁺ followed by Coulomb repulsion producing NH₂CH₂⁺ + CH₂CO⁺ (see pathway in Fig. 9).

The right part of Fig. 9 shows that the evaporation of CH₂ from CH₃COOH⁺ leads to the coincidence (30+/45⁺). Further fragmentation of NH₃CH₂⁺ by emission of H₂ leads to NHCH⁺ in coincidence with COOH⁺, island (28+/45⁺).

The most intense island observed in the experiment is m/z = 30 amu (NH₃CH₂⁺) in correlation with m/z = 42 amu (CH₂CO⁺) coming from C₂–C₈ bond breaking. For the first fragment we observe similar many body fragmentation processes as the one described above, i.e. loss of one or two hydrogen atoms from NH₂CH₂⁺ leading to the pairs (29+/42⁺) and (28+/42⁺), respectively. In Fig. 6b, we can see that the three pairs have an experimental slope very close to −1. This is an indication that the molecular dication \(\beta\text{-alanine}^{2+}\) first loses a neutral OH fragment and then splits into two singly charged cations. Another group of islands involving the most prominent cation NH₂CH₂⁺ is observed in correlation with the COOH⁺ fragment.

Interesting molecular structures are observed for the spectra associated with the peaks at m/z = 44, 43, 42 and 41 amu (see Fig. 10). These cations present resonant structures with \(\pi\) delocalised electrons or strong N=–C, N\equiv C bonds. The associated exit...
channels appear a few eV below the entrance channel due to the high stability of such species (see Fig. 7). However, this trend is not observed for the row at m/z = 30, 29 and 28 amu (see Fig. 6b). The lack of the peak at m/z = 29 amu in the experiment is caused by the fact that this molecule is a radical and its relative stability is much lower than the corresponding closed shell molecules (m/z = 30, 28 amu) (see Fig. 9).

(c) H migration

We now focus on the exit channels produced after the most important isomerisation mechanism observed in the dynamics simulations: formation of the doubly charged geminal diol NH\(_2\)CHCH\(_2\)CO\(_2\)+ (43+/18+). In particular, we analyse two mechanisms: (i) Coulomb explosion after H transfer (see Fig. 11) and (ii) emission of neutral fragments leading to stable dicaticonic species (see Fig. 12). Both mechanisms are in competition with the rest of the processes but occur with lower probability, similar to our previous observations for glycine.\(^{21}\)

Fragmentation of dio\(_2\)+ due to the Coulomb explosion implies three exit channels: NH\(_2\)CHCH\(_2\)CO\(^+\) + H\(_2\)O\(^+\) (71+/18+), NH\(_2\)CHCHCO\(^+\) + H\(_2\)O\(^+\) (70+/19+). A subsequent fragmentation pathway of NH\(_2\)CHCH\(_2\)CO\(^+\) has also been calculated leading to a neutral carbon monoxide molecule. Fig. 11 shows the corresponding pathways in the PES. All of them are below the entrance channel but they can be produced only if one considers atomic rearrangement (even double H transfer) before fragmentation. The corresponding correlation islands present low relative intensity in the experiment and, accordingly, in the AIMD simulations the probability to occur is very small.

Hydrogen migration can be also followed by emission of neutral fragments. Indeed, the stable small dicaticonic molecules detected in the experiment are produced after emission of neutral species: H\(_2\)O, H, H\(_2\), CH\(_2\), CO, CO\(_2\) or CH\(_2\)CO from doubly charged diol. The study of this part of the PES is presented in Fig. 12 and it explains the different chemical mechanisms leading to molecular dications experimentally detected at signals: m/z = 35.5, 35, 34.5, 34, 21.5, 21, 20.5, 20 and 14.5 amu (see zooms-in in Fig. 1). The pathways explaining these peaks come from the key structure NH\(_2\)CHCH\(_2\)CO\(^2+\) produced after neutral H\(_2\)O loss from the doubly charged diol, through the formation of the intermediate, weakly bonded complex NH\(_2\)CHCH\(_2\)COH\(_2\)+. NH\(_2\)CHCH\(_2\)CO\(^+\) is a very stable acyl ion showing a resonant structure. The dehydration mechanism does not involve the amine group\(^61\) and energetically is more preferable than splitting the charge into two fragments. This is the reason why in the experiment we almost do not observe the pair (71+/18+) in the coincidence map (even if this channel appears at lower energy than the entrance one). Starting from the key structure NH\(_2\)CHCH\(_2\)CO\(^+\) the loss of H, H\(_2\), CO and CH\(_2\)CO explain the peaks at 35, 34.5, 21.5 and 14.5 amu: NH\(_2\)CHCH\(_2\)+, NH\(_2\)CH\(_2\)CO\(^+\), NH\(_2\)CHCH\(_2\)+ and NH\(_2\)CH\(_2\)+, respectively. A subsequent emission of H and H\(_2\) from these dications explain the rest of peaks corresponding to doubly charged molecules: (m/z = 34, 21, 20.5 and 20 amu). Moreover, H migration after H transfer (see Fig. 11) and (ii) emission of neutral fragments leading to stable dicaticonic species (see Fig. 12). Both mechanisms are in competition with the rest of the processes but occur with lower probability, similar to our previous observations for glycine.\(^{21}\)

(d) OH migration

In the ion-induced fragmentation of glycine, hydrogen migration was observed in competition with direct Coulomb explosion and
was essential to understand the fragmentation dynamics.\textsuperscript{21} For β-alanine our molecular dynamics simulations have shown a quite probable fragmentation pathway in competition with H migration and Coulomb explosion: hydroxyl group migration accompanied with emission of neutral CO and leading to two singly charged fragments (NH\textsubscript{2}CH\textsubscript{2}+ and CH\textsubscript{2}OH\textsuperscript{+}). This channel appears at very low energy in the PES (see Fig. 13) and is assigned to the correlation (30\textsuperscript{+}/31\textsuperscript{+}) measured with a very strong relative intensity (see Fig. 6c and Table S1 in ESI\textsuperscript{†}). Moreover, from the entropic point of view it is more favourable than other channels. The computed mechanism reveals that the metastable HOCH\textsubscript{2}CO\textsuperscript{+} structure is involved before the loss of a neutral carbon monoxide and finally producing the detected ions: NH\textsubscript{2}CH\textsubscript{2}+ and HOCH\textsubscript{2}+. The metastable structure observed in the molecular dynamics (HOCH\textsubscript{2}CO\textsuperscript{+}) is an isomer of a CO protonated α-lactone.\textsuperscript{62} These species were previously observed in the gas phase reactions of amino acids with the nitrosonium ion (NO\textsuperscript{+}).\textsuperscript{63} Moreover, previous studies have demonstrated that the open carbo-cation CH\textsubscript{2}COOH\textsuperscript{+} is not a saddle point on the PES.\textsuperscript{64,65} AIMD simulations show that CH\textsubscript{2}COOH\textsuperscript{+} easily collapses to a CO protonated α-lactone (a transient species previously described in mass spectrometry experiments\textsuperscript{66}), and the ring opens to form a more stable cation (OCCH\textsubscript{2}OH\textsuperscript{+}). Further fragmentation of this cation leads to hydroxymethyl (CH\textsubscript{2}OH\textsuperscript{+}) or to formaldehyde (CH\textsubscript{2}O\textsuperscript{+}) cations. The latter one was also previously detected.\textsuperscript{67} Interestingly, both species have been identified from spectral lines in the interstellar medium\textsuperscript{68} and reactions between them can produce glycol aldehyde, acetic acid and methyl formate.\textsuperscript{69} On the other hand, the hydroxymethyl cation (m/z = 31 amu) was previously observed only in the single ionisation process after direct side chain bond breaking of serine.\textsuperscript{16}

The fragmentation mechanism presented here is the only possibility to explain the coincidence island at (30\textsuperscript{+}/31\textsuperscript{+}). For the double ionisation process the driving force for this mechanism is the high stability of the products NH\textsubscript{2}CH\textsubscript{2}+ + HOCH\textsubscript{2}+ + CO (18.25 eV) with a relative energy 8 eV lower than the entrance channel and much lower than other channels with different charge distributions (e.g. NH\textsubscript{2}CH\textsubscript{2}+ + HOCH\textsubscript{2} + CO\textsuperscript{+} appears at 24.72 eV). The iminium cation (NH\textsubscript{2}CH\textsubscript{2}+) possesses a strong hydride ion affinity.\textsuperscript{70} Thus, in the first fs of the fragmentation the amino methyl cation can attract the hydride group from the other fragment CH\textsubscript{2}COOH\textsuperscript{+}, causing the reorganisation of the geometry and allowing the movement of the OH group. This is indeed, the third most probable channel and leads to NH\textsubscript{2}CH\textsubscript{2}+ + CO + CH\textsubscript{2}OH\textsuperscript{+} (see Fig. 5b). Further fragmentation in this channel corresponds to the emission of neutral hydrogen molecule from NH\textsubscript{2}CH\textsubscript{2}+ and leads to the coincidence measurement with 28\textsuperscript{+}/31\textsuperscript{+} [NHCH\textsubscript{3}\textsuperscript{+}/HOCH\textsubscript{2}+]. The presence of the pairs...
(30′/31′) and (28′/31′) (see Fig. 6c.) can not be explained by
the direct bond fragmentation of the molecular dication
β-alanine\(^+\) and must involve a rearrangement after Coulomb
explosion. This OH migration is about three times slower than
ultrafast H transfer and appears at around 120 fs of the
simulations (see Fig. 4). Moreover, this mechanism can be
considered as one of the dominant at longer timescales due
to the subsequent fragmentation of the products of mechanism
(4). The exit channel after process (9) is energetically more
favourable than the exit channel after process (4). Thus, at
longer simulation time, products from (4) can easily evolve to
products from (9) (see Fig. 13). Indeed the second most intense
coincidence island corresponds to the products of mechanism
(9): \( \text{NH}_2\text{CH}_2^+ + \text{CH}_2\text{OH}^+ \) (30′/31′).

4 Conclusions

We have studied the fragmentation dynamics and different
de-excitation pathways characterising the decay of excited doubly-
charged β-alanine molecules in the gas phase. Experimentally,
excited molecular dications were produced in collisions with \( \text{O}^+ \) ions and the fragments were identified by coincidence time-of-
flight mass spectrometry allowing to determine the fragmentation
dynamics and highlighting the presence of new ionic
species. Theoretically, we have found in \textit{ab initio} molecular
dynamics simulations that three types of processes occur in
competition: (i) Coulomb explosion leads to the detection in
competition of two singly charged fragments; (ii) the formation
of small stable dications produced by evaporation of neutral
fragments following ultrafast intramolecular hydrogen migration
(\(~ 40 \text{ fs}\) ); (iii) Coulomb explosion followed by hydroxy group
migration. The third process has not been previously reported
and is expected to occur in other biomolecules. The good agreement
between our simulation in the electronic ground state with
the experimental measurements also sheds light on the charge
state and excitation energy of the molecule after ionisation with
highly charged ions and allows us to confirm that the excitation
energy is quickly distributed over the vibrational degrees of
freedom of the molecule.

Acknowledgements

The experimental studies have been performed at the
low-energy ion beam facility ARIBE at GANIL (Caen, France). We
thank the support given by the CMAP team. We acknowledge
the generous allocation of computer time at the Centro de
Computación Científica at the Universidad Autónoma de Madrid
(CCC-UAM). Financial support received from the CNRS PICS-
05356 program, the ANR Programme Blanc PIBALE/ANR-09-
BLAN-013001 and the Conseil Régional de Basse-Normandie is
gratefully acknowledged. Research was conducted in the scope of the International Associated Laboratory (LIA) “Fragmentation
DYNAMics of complex MOlecular systems – DYNAMO” and in
the COST actions XLIC (CM1204) and Nano-IBCT (MP1002).
Work was partially supported by the projects FIS2013-42002-R
and CTQ2013-43698-P (MINECO), and NANOFRONTMAG (CAM).

D.G.P. acknowledges the support of the Erasmus Mundus
program of the European Union (FPA 2010-0147) and the
FPI doctorate grant of the Universidad Autónoma de Madrid.
S. D.-T. gratefully acknowledges the “Ramón y Cajal” program
of the Spanish Ministerio de Educación y Ciencia.

References

3 C. L. Ricketts, D. Schröder, C. Alcaraz and J. Roithová,
4208–4209.
5 P. Ehrenfreund, D. P. Glavin, O. Botta, G. Cooper and
2138–2141.
6 J. H. Kang, K. S. Kim, S. Y. Choi, H. Y. Kwon, M. H. Won and
89–96.
7 A. Gil, S. Simon, L. Rodríguez-Santiago, J. Bertrán and
9 S. Naumov, I. Janovsky, W. Knolle and R. Mehnert,
1–18.
11 J. Casado, A. Castro, J. R. Leis, M. Mosquera and M. E. Pena,
\textit{26}, 1167–1178.
14 S. Bari, P. Sobociński, J. Postma, F. Alvarado, R. Hoekstra,
V. Bernigaud, B. Manil, J. Rangama, B. Huber and
15 S. Bari, F. Alvarado, J. Postma, P. Sobociński,
81–87.
16 S. Simon, A. Gil, M. Sodupe and J. Bertrán, \textit{THEOCHEM},
17 P. Sobociński, S. Bari, J. Postma, F. Alvarado, R. Hoekstra,
B. Manil, J. Rangama, V. Bernigaud, B. Huber and
18 H.-W. Jochims, M. Schwell, J.-L. Chotin, M. Clemen,
F. Dulieu, H. Baumgaertel and S. Leach, \textit{Chem. Phys.}, 2004,
\textit{298}, 279–297.
19 S. Bari, F. Alvarado, J. Postma, P. Sobociński, R. Hoekstra
20 M. Capron, S. Díaz-Tendero, S. Maclot, A. Domaracka,
E. Lattouf, A. Ławicki, R. Maisonny, J.-Y. Chesnel, A. Méry,
J.-C. Pouilly, J. Rangama, L. Adoui, F. Martin, M. Alcamí,