



Complexation of carboxylate anions with the arginine gas-phase amino acid: Effects of chain length on the geometry of extended ion binding

Thomas F.M. Luxford, Edward M. Milner, Naruo Yoshikawa, Chad Bullivant, Caroline E.H. Dessent *

Department of Chemistry, University of York, Heslington, York YO10 5DD, UK

ARTICLE INFO

Article history:

Available online 26 May 2013

ABSTRACT

Complexation of deprotonated carboxylic acids with arginine was investigated using collision-induced dissociation to probe the nature of isolated carboxylate–amino acid interactions as a function of anion size. Monocarboxylic $\text{CH}_3(\text{CH}_2)_n\text{COO}^- \cdot \text{Arg}$ ($n = 3-7, 9, 10$) and dicarboxylic acid $\text{COOH}(\text{CH}_2)_n\text{COO}^- \cdot \text{Arg}$ ($n = 3-5, 7-10$) complexes were investigated. For the dicarboxylic acid clusters, chain length has a significant effect on the fragmentation energies with the $n = 9, 10$ systems fragmenting at significantly lower energies than the corresponding shorter chain systems. Molecular mechanics calculations suggest that this fragmentation energy shift is associated with the longer-chain dicarboxylic acid–Arg clusters switching to ring structures.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

The tautomeric stability of isolated amino acids is of key fundamental interest since although the zwitterionic form dominates in aqueous solution over a wide pH range [1], gas-phase amino acids generally exist in their non-charge separated canonical (non-zwitterionic) forms [2]. Whilst isolated neutral zwitterions are unstable in the gas-phase [3], they can be stabilized by complexation with protons, solvent molecules and metal ions [4–7]. Indeed, a great deal of effort has been expended over the last 10 years in establishing the factors that control the stability of metal cation–amino acid complexes through the application of collisional activation techniques, IR multi-photon spectroscopy and computational chemistry.

Given the number of studies that have been conducted into cation–amino acid complexes, it is surprising that anion interactions with isolated amino acids have only very recently been explored experimentally. Infrared multi photon dissociation (IRMPD) and collision-induced dissociation (CID) experiments on halide ion–amino acid complexes [8,9] have found evidence for novel anion-induced zwitterion formation in gas-phase arginine. The IRMPD study investigated the effect of the $\text{X}^- = \text{Cl}^-, \text{Br}^-$ and I^- anions on the zwitterionic stability of glutamic acid, histidine, and arginine (Arg), finding evidence for a spectral band at $\sim 1625 \text{ cm}^{-1}$ associated with a zwitterionic arginine for each of the $\text{X}^- \cdot \text{Arg}$ clusters studied. The authors concluded that the geometric structures of the three anion–zwitterion clusters appear to be similar and attributed this to the relatively large size of the halide anions compared

to metallic cations studied in earlier work [10]. The results of the CID study were consistent with the IRMPD study in confirming that $\text{Br}^- \cdot \text{Arg}$ exists as a zwitterionic cluster. However, the cluster fragmentation patterns observed revealed that the nature of the anion plays a key role in determining the low-energy potential energy fragmentation surfaces for anion–arginine complexes. A small number of purely theoretical studies of anion–amino acid interactions have also recently been conducted [11–13], and it should also be noted that there have been several studies of single electron–amino acid interactions [14–17].

In this Letter, we present the first experimental study to explore the interaction of an extended molecular anion with a gas-phase amino acid, through the investigation of a series of monocarboxylic and dicarboxylic acid–Arg clusters. The interaction of isolated carboxylate anions with amino acids is also important in a broader context since acetates play a key role in the Hofmeister series [18]. Low-energy collision induced dissociation (CID) (or resonance excitation) in a quadrupole ion-trap is used to probe the structures and relative stabilities of the $\text{CH}_3(\text{CH}_2)_n\text{COO}^- \cdot \text{Arg}$ $n = 3-7, 9, 10$ monocarboxylic acid–arginine and $\text{COOH}(\text{CH}_2)_n\text{COO}^- \cdot \text{Arg}$ $n = 3-5, 7-10$ dicarboxylic acid–arginine clusters. The complexation of these monofunctional and bifunctional molecules is compared to investigate whether different binding motifs are observed with the mixed-charged protonated and deprotonated sites of the zwitterionic arginine.

2. Experimental section

The experimental method used in this Letter has been described previously [19]. A Bruker Esquire 6000 Quadrupole Ion Trap mass spectrometer was employed for all the experiments performed.

* Corresponding author. Fax: +44 1904 322516.

E-mail address: caroline.dessent@york.ac.uk (C.E.H. Dessent).

The ion signal was optimized using the automatic tuning capabilities of the Esquire, with typical selected settings of nebulising gas pressure of 10.0 psi, drying flow rate of 8 l min⁻¹, capillary temperature of 150 °C, and ion excitation time of 40 ms. The carboxylate anion–arginine complexes were prepared by electrospraying a solution of the carboxylic acid and L-arginine (both 5 × 10⁻⁵ M) in 100% methanol. All chemicals were purchased from Sigma–Aldrich and used without further purification. Fragment ions with *m/z* less than ~50 are not detectable in the instrument since low masses fall outside of the spectral window of the trap. The standard *m/z* resolution for the Esquire 6000 is 0.6 (FWHM) with a maximum resolution of 0.35 (FWHM), for *m/z* 50–3000 [20].

Low-energy collision induced dissociation (CID) (or *resonance excitation*) was performed on isolated ions by applying an excitation AC voltage to the end caps of the trap to induce collisions of the trapped anionic complexes with the He buffer gas. Precursor ion excitation within the quadrupole ion-trap occurs through multiple low-energy collisions with the buffer gas at a frequency of ~10⁴ s⁻¹ [21,22]. The resonance excitation voltage was varied from 0 to 2.5 V zero-to-peak resonant excitation potential. Resonance excitation amplitudes for decomposition of molecular ions within a quadrupole ion-trap have been shown to correlate with the literature critical dissociation energies. However, there is no straightforward conversion from the resonance excitation voltage to absolute dissociation energies: Ref [23] discusses this point. CID energies in this work are therefore quoted as a percentage of the 2.5 V excitation voltage, in line with the standard practice [24,25]. CID graphs were typically recorded over 20–30 min, with each voltage step (CID Energy) given a 1 min time-bin, with these time-bins of data points being averaged to produce individual data points.

3. Experimental results

3.1. Monocarboxylic acid–Arg clusters

Low-energy collision-induced dissociation of the CH₃(CH₂)_{*n*}COO⁻–Arg *n* = 3–7, 9, 10 complexes, resulted in production of deprotonated arginine, [Arg–H]⁻ as the major fragment ion for each cluster. Table 1 lists the fragment ions observed for each of the CH₃(CH₂)_{*n*}COO⁻–Arg *n* = 3–7, 9, 10 complexes. (Note that the *n* = 8 complex was not studied as the precursor ion peak overlaps with the *m/z* of the dimer of the acid.) Since the carboxylic acid will be deprotonated in solution prior to electrospraying, we assume that the precursor ion complexes contain the deprotonated carboxylic acid as the ‘excess’ charge carrier. Considering the case where the Arg exists in its zwitterionic form, it can then form a stable complex

with the deprotonated carboxylic acid (pK_a ~4.5) group interacting with the protonated Arg guanidinium side chain (pK_a 12.5) [26,27]. Collision activated dissociation then results in the excited cluster decaying with deprotonation of Arg as the lowest energy fragmentation pathway. This behaviour mirrors the fragmentation of the F⁻·Arg and Cl⁻·Arg clusters, where the halide ions have a strong propensity to abstract protons and the clusters fragment with deprotonated Arg as the sole ionic product [9]. For the monocarboxylic acid–Arg clusters, the only significant additional fragment ion observed is [Arg–CN₂H₂–H]⁻. This fragment ion has been observed previously in halide ion–Arg clusters, where it has been associated with arginine existing in the zwitterionic state [9].

Figure 1 displays %fragmentation curves for the CH₃(CH₂)_{*n*}COO⁻·Arg *n* = 3, 10 monocarboxylic acid–Arg clusters, to illustrate the decay profiles of the precursor ion and appearance profiles of the fragment ions across the collisional activation range. The precursor cluster ions of both complexes are stable across the low-energy CID excitation range, illustrating that these clusters represent stable molecular systems and are not metastable prior to resonance excitation [28]. The fragmentation profile of the [Arg–CN₂H₂–H]⁻ product ion can be seen as a very minor channel for CH₃(CH₂)₁₀COO⁻·Arg. Comparing the onset and decay curves for the two complexes, the *n* = 3 complex begins to fragment at ~4.5% CID, with the *n* = 10 complex beginning to fragment at a slightly higher value of ~5%. Similarly, the *E*_{1/2} values for the *n* = 3 and *n* = 10 systems are 7% and 8%, respectively, *i.e.* a modest shift to higher %fragmentation energy with increasing size.

The %fragmentation decay curves for the entire CH₃(CH₂)_{*n*}COO⁻·Arg *n* = 3–7, 9, 10 series are overlaid in Figure 2, illustrating that there is a smooth increase in fragmentation energy with increasing chain length. The *E*_{1/2} values (the collision energy necessary to induce 50% fragmentation of parent into fragment) are listed in Table 1. CID fragmentation energies are influenced by a number of factors, with one being the mass of the ion studied since the maximum collision energy converted into internal energy is inversely proportional to the parent ion mass [29]. The small increase in fragmentation energy observed for the monocarboxylic acid–Arg clusters in Figure 2, can therefore at least partially be attributed to the higher excitation energy that is necessary to fragment the heavier ions. This indicates that any structural changes influencing the fragmentation barrier heights are modest.

3.2. Dicarboxylic acid–Arg clusters

Collision-induced dissociation mass spectra were also acquired for the COOH(CH₂)_{*n*}COO⁻·Arg *n* = 3–5, 7–10 dicarboxylic acid–Arg

Table 1
*E*_{1/2} fragmentation energies and fragment ions for the RCOO⁻·Arg (R = (CH₂)_{*n*}CH₃ *n* = 3–7, 9, 10) monocarboxylic acid–Arg complexes and the R'COO⁻·Arg (R' = (CH₂)_{*n*}COOH *n* = 3–5, 7–10) dicarboxylic acid–Arg complexes.^a

	<i>E</i> _{1/2}	Product ions
<i>R</i> = CH ₃ (CH ₂) _{<i>n</i>}		
<i>n</i> = 3	7.0	[Arg–H] ⁻
<i>n</i> = 4	6.8	[Arg–H] ⁻
<i>n</i> = 5	6.9	[Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , RCOO ⁻
<i>n</i> = 6	7.0	[Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , RCOO ⁻
<i>n</i> = 7	7.4	[Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , RCOO ⁻
<i>n</i> = 9	7.7	[Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , RCOO ⁻
<i>n</i> = 10	7.9	[Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , RCOO ⁻
<i>R'</i> = COOH(CH ₂) _{<i>n</i>}		
<i>n</i> = 3	8.8	R'COO ⁻ , [Arg–H] ⁻ , [R'COO–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻
<i>n</i> = 4	9.1	R'COO ⁻ , [Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , [R'COO–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻
<i>n</i> = 5	9.6	[Arg–H] ⁻ , R'COO ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , [R'COO–H ₂ O–CO ₂] ⁻ , [R'COO–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻
<i>n</i> = 7	10.4	R'COO ⁻ , [Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , [R'COO–H ₂ O–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻
<i>n</i> = 8	11.6	R'COO ⁻ , [Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , [R'COO–H ₂ O–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻
<i>n</i> = 9	6.5	R'COO ⁻ , [Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , [R'COO–H ₂ O–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻
<i>n</i> = 10	6.8	R'COO ⁻ , [Arg–H] ⁻ , [Arg–CN ₂ H ₂ –H] ⁻ , [Arg–NH ₃ –H] ⁻ , [R'COO–H ₂ O–CO ₂] ⁻ , [R'COO–H ₂ O] ⁻

^a Product ions are listed in order of decreasing fragment ion intensity.

Download English Version:

<https://daneshyari.com/en/article/5381810>

Download Persian Version:

<https://daneshyari.com/article/5381810>

[Daneshyari.com](https://daneshyari.com)