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# Study of the Reactivity of $\text{CH}_3\text{COOH}^{+\bullet}$ and $\text{COOH}^+$ Ions With $\text{CH}_3\text{NH}_2$ : Evidence of the Formation of New Peptide-like C(O)-N Bonds

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## **Abstract**

Acetamide, a small organic compound containing a peptide bond, was observed in the interstellar medium, but reaction pathways leading to the formation of this prebiotic molecule remain uncertain. We investigated the possible formation of a peptide-like bond from the reaction between acetic acid ( $\text{CH}_3\text{COOH}$ ) and methylamine ( $\text{CH}_3\text{NH}_2$ ), that were identified in the interstellar medium. From an experimental point of view, a Quadrupole / Octopole / Quadrupole mass spectrometer was used in combination with Synchrotron radiation as tunable source of VUV photons for monitoring the reactivity of selected ions. Acetic acid was photoionized, and the reactivity of  $\text{CH}_3\text{COOH}^{+\bullet}$  as well as  $\text{COOH}^+$  (produced either from acetic or formic acid) ions with neutral  $\text{CH}_3\text{NH}_2$  was further studied. With no surprise, charge transfer, proton transfer, and concomitant dissociation processes were found to largely dominate the reactivity. However, a C(O)-N bond formation process between the two reactants was also evidenced, with a weak cross section reaction. From a theoretical point of view, results concerning reactivity and barrier heights were obtained using density functional theory, with the LC- $\omega$ PBE range-separated functional in combination with the 6-311++G(d,p) Pople basis set and are in perfect agreement with the experimental data.

## **I. Introduction**

As telescopes become more sophisticated and space missions for in situ collection or analysis of molecules increase, we are discovering more and more molecules involving complex chemical reactions. So-called complex organic molecules (COM) detected in the interstellar medium, in icy dust grains and in the comae of comets are carbon-bearing molecules with at least six atoms.<sup>1</sup> COM include a wide range of prebiotic molecules such as sugars (glycolaldehyde),<sup>2,3</sup> carboxylic acids and amines.

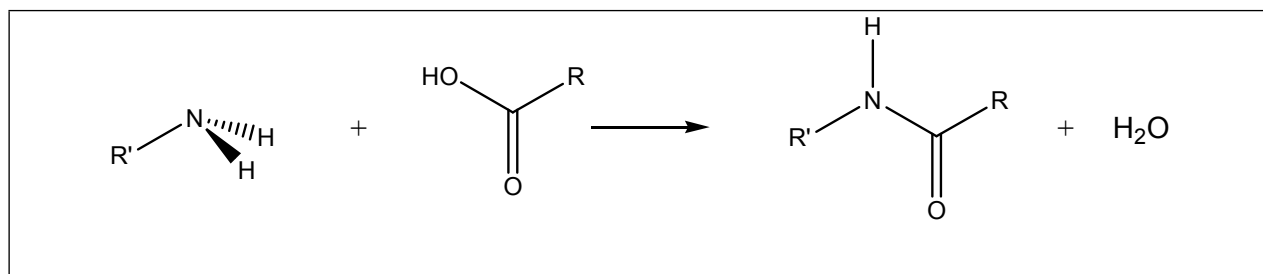
Among primary amines, formamide  $\text{NH}_2\text{CHO}$  was identified as early as 1971 in the SGR B2 cloud,<sup>4</sup> followed three years later by methylamine  $\text{CH}_3\text{NH}_2$  identified in the SGR B2 and Orion A clouds, while hydroxylamine  $\text{NH}_2\text{OH}$  was recently identified (2020) in the quiescent molecular cloud G+0.693-0.027.<sup>5</sup> Methylamine has also been detected in the comet 67P/Churyumov-Gerasimenko by the Rosetta

mission.<sup>6,7,8</sup> This mission also detected glycine and alanine in the same comet 67P/Churyumov-Gerasimenko.<sup>6,7,8</sup> Among carboxylic acids, formic acid HCOOH was the first to be detected in the interstellar medium (1971, SGR B2 cloud<sup>9</sup>), and it was only in 1997 that acetic acid CH<sub>3</sub>COOH was detected in the SGR B2, Orion KL and W51 clouds.<sup>10</sup>

Paradoxically, in spite of increasingly in-depth studies, issues concerning the reaction mechanisms involved in the chemistry of these media are ever-increasing: how are such complex molecules formed? Is the chemistry of the interstellar medium dominated by mechanisms catalyzed in solid phase by dust grains (purely mineral or mixed with water ice) frozen at very low temperature (T<20K)? Are higher temperature gas phase processes also involved? It seems obvious that interstellar dust grain processes play an important role, including in the mechanisms of formation of comet constituents. However, a thorough study of the volatiles and refractory materials that were captured during the Stardust mission also revealed the role of gas-phase reactions at higher temperatures.<sup>6,7,8</sup> Theoretical and laboratory experimental studies under varied and complementary conditions are clearly still required for the elucidation of these processes. Such laboratory studies are fundamental to improve our understanding of chemical reactions in extreme environments. Numerous studies have made it possible to propose mechanisms for some of the chemical species that have been identified in space, but we are still far from having a complete and satisfactory model to explain all the reactions, and systematic laboratory studies seem to be indispensable, both from a theoretical and experimental point of view.<sup>11,12</sup>

From a prebiotic point of view, the detection of carboxylic acids and amines in interstellar medium (ISM) is very interesting because it opens the way to reactions that can lead to the formation of new peptide-like C(O)-N bonds (*Scheme 1*).

In addition, the study of such reaction mechanisms would also allow to better describe the formation of atmospheric aerosols,<sup>13-17</sup> the formation of prebiotic molecules in hot-cores, hot-corinos<sup>18</sup> and in complex environments,<sup>19-24</sup> as well as to contribute to more fundamental studies on reactivity<sup>25</sup>.



**Scheme 1:** Reactions of the peptide bond formation between a carboxylic acid and an amine.

An energy barrier of about 150 kJ/mol (1.55 eV) is often associated with the formation of this bond in the gas phase. In line with this energy barrier, the formation of a C(O)-N bond at the molecular level, from a carboxylic acid and an amine taken in their fundamental state has not yet been demonstrated experimentally, to our knowledge.<sup>26,27,28</sup> This is why it has been proposed, in the context of prebiotic chemistry, that this reaction could be catalyzed by surfaces such as siliceous clays or meteorite rocks. Moreover, G. Bouchoux et al.<sup>29</sup> showed that in the presence of one to four water molecules the energy barrier associated with the reaction of NH<sub>3</sub> or NH<sub>4</sub><sup>+</sup> on formic acid was strongly lowered. An explicit role of water in the reaction process was further demonstrated by the authors.

The aim of this work is to initiate an in-depth research on the binding formation conditions of a peptide-like type bond from reagents of prebiotic interest taken in their fundamental state, or in weakly excited states. We present here a first part of this work as two independent papers. This first article is dedicated to the highlighting of the formation of a C(O)-N bond from CH<sub>3</sub>COOH<sup>+</sup> or COOH<sup>+</sup> with CH<sub>3</sub>NH<sub>2</sub> using a

1 coupled theoretical/experimental approach. The second article<sup>30</sup> is dedicated to the introduction of a  
2 new methodology for the algorithmic investigation of reaction paths for the formation of CH<sub>3</sub>-NH-CO-CH<sub>3</sub>  
3 from neutral CH<sub>3</sub>NH<sub>2</sub> and CH<sub>3</sub>COOH isolated in the gas phase with or without the presence of a few  
4 explicit water molecules.  
5

6 For this first study, synchrotron radiation was used as a tunable source of VUV photons. This makes it  
7 possible to monitor the potential effect of internal energy of prepared cations and radical cations. The  
8 CH<sub>3</sub>COOH<sup>++</sup> and COOH<sup>+</sup> cations formed from CH<sub>3</sub>COOH and/or HCOOH precursors were then selected in  
9 mass using a mass spectrometer. The addition of the neutral CH<sub>3</sub>NH<sub>2</sub> partner in a reaction chamber  
10 before detection of the formed species allows the identification of the reaction products as a function of  
11 the energy of the photons used for the photoionization or the dissociative photoionization step. The  
12 absolute cross sections of the reaction were derived from a multi-step methodological approach,  
13 involving the following steps:  
14  
15

- 16 1. the recording of spectra of ionized species in the absence of reactive gas,
- 17 2. the study of metastable fragmentation, and collision-induced ion fragmentation in the presence  
18 of a chemically (relatively) inert target: argon,
- 19 3. the study of the products obtained in the presence of the reagent as a function of photon energy  
20 and collision energy,
- 21 4. the comparison of spectra obtained in steps 2 and 3 to characterize the reactivity.  
22  
23  
24  
25

26 To help identifying the products formed under experimental conditions, it is essential to carry out a  
27 theoretical study of the reaction pathways. For this study, we have chosen Density Functional Theory  
28 (DFT) calculations. In addition to proton transfer, charge transfer and hydride transfer processes, this  
29 double theoretical and experimental approach has allowed us to highlight for the first time C(O)-N bond  
30 formation reactions between ions formed from carboxylic acids and methylamine.  
31  
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## 33 ***II. Methods***

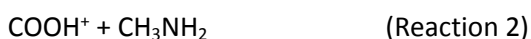
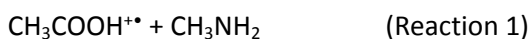
### 34 ***a. Experimental approach***

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36  
37  
38 The experiments have been performed using the CERISES apparatus, an associated experiment to the  
39 SOLEIL synchrotron radiation facility. Since the set-up was described in details previously, only the most  
40 relevant details will be given here.<sup>31,32</sup> CERISES is a guided ion beam tandem mass spectrometer  
41 composed of two octopoles located between two quadrupole mass spectrometers in a Q1-O1-O2-Q2  
42 configuration that permits investigation of bi-molecular reactions of mass-selected ions occurring in a 4cm  
43 long reaction cell located at the end of the first octopole. By measuring the yields of parent- and product-  
44 ions, absolute reaction cross sections and branching ratios as a function of both photon- and collision  
45 energy are derived.  
46  
47  
48

49 CH<sub>3</sub>COOH<sup>++</sup> and HCCO<sup>+</sup> reactant ions were produced by dissociative photoionization of their gaseous  
50 precursor introduced at roughly 10<sup>-6</sup> mbar in the ion source of CERISES connected to the DESIRS beamline  
51 of SOLEIL synchrotron. The undulator-based DESIRS beamline provides tunable radiation in the vacuum  
52 ultraviolet (VUV) range from 5 to 40 eV.<sup>33</sup> Photons at the desired energies are selected and scanned  
53 simultaneously with the undulator peak energy by a normal incidence monochromator equipped with a  
54 low dispersion uncoated SiC grating (200 grooves/mm) optimized to provide photon flux up to 10<sup>13</sup>  
55 photon/s. In the present experiments, the photon energies required to produce and react the ions are in  
56 the range 10–15.5 eV. The monochromator slits were set in the range 300 to 600 μm, corresponding to a  
57 resolution of 20 to 40 meV, compromising for a maximum of signal and avoiding detector saturation. The  
58 monochromator was operated at its first order of diffraction. Higher orders were removed from the  
59  
60

1 incident beam by use of a gas filter installed on the beam line filled with argon at a pressure of 0.2 mbar  
2 as absorber.<sup>34</sup> This removes efficiently any photons above 15.7 eV. The absolute scale of the photon  
3 energies was checked by using sharp absorption lines of atomic Argon around 11.828 and 14.304 eV that  
4 were observed with systematic shifts of about 10-20 meV above their tabulated values.<sup>35,36</sup>

6 The kinetic energy of the parent ion, and hence the collision energy, was set by the difference between  
7 the ion source and the reaction cell potentials. This was determined by the stopping potential method on  
8 the parent ion beam, giving a kinetic energy width of 400 meV FWHM, on average. By changing the  
9 potentials of the reaction cell and all subsequent elements, the kinetic energy of the parent ion was  
10 increased up to 20 eV in the lab, corresponding to a collision energy of 6.5 and 8 eV in the center of mass  
11 frame and a width of 130-160 meV for the reactions 1 and 2, respectively:



19 The resolution of quadrupole mass filters was compromised in order to have good signals as well as  
20 sufficient removal of ions at + or - 1 mass unit from the considered species. Our estimate is a removal of  
21 99.99% of neighbour ions for Q1 and 99.90% of neighbour ions for Q2 at the lowest collision energy with a  
22 loss of performance reaching 98.80% of neighbour ions when operated at the highest collision energy.

25 Methylamine (and argon for the CID study) was introduced in the cell at a pressure of up to 200 nbar,  
26 which allows to consider essentially single collision processes over the 4 cm long reaction cell by keeping  
27 secondary reactions at reduced level, but still provides with accurate pressure measurements and large  
28 detection dynamics on reaction cross section between 200 and 0.01 Å<sup>2</sup>. The absolute pressure in the cell  
29 was measured using the MKS 398H differential manometer instrument. All data were collected with  
30 either reaction gas in the cell or in the surrounding chamber, therefore allowing for the removal of any  
31 signal resulting from collisions occurring outside the reaction cell, corresponding at maximum to 5 % of  
32 the total reactivity signal.

36 The absolute cross sections acquisition method, either for photon or collision energy scans, was  
37 performed in so-called multiscan mode, which implies recording signals for all ionic species at a single  
38 point before to move to the next point. This method reduces drastically effects of drifts in source  
39 pressure, reaction cell pressure or photon flux.

42 The CERISES apparatus being a tandem instrument, it is possible to derive information on metastable  
43 processes related to the ion produced in the source, mass-selected with Q1, and let to fly freely through  
44 O1 and O2. Potential metastable products can then be detected with Q2. Such measurements were  
45 performed in the case of acetic acid cation selected at m/z=60, and producing metastable products at  
46 m/z=42. In our experimental conditions, the flight time for those ions to reach the end of Q1 is 161μs.  
47 Three measurements performed at acceleration potentials of 0.25, 2 and 12V correspond to flight times  
48 at the end of O2 of m/z=60 ion of 460, 381 and 261μs, respectively.

52 The chemicals (acetic acid, formic acid, and methylamine) were purchased from Sigma Aldrich at  
53 chromatographic grade (99.8%) and used without further purification.

### 57 ***b. Theoretical approach***

59 All the calculations were performed with the Gaussian09 software (revision D.01).<sup>37</sup> The DFT approach,<sup>38,</sup>  
60<sup>39, 40,</sup> which allows a good compromise between reliability of results and calculation time, has been chosen

here. Since the reaction paths may involve the formation of non-covalent complexes between reagents, the LC- $\omega$ PBE<sup>41,42,43</sup> range separation functional was used with the empirical correction GD3BJ proposed by Becke and Johnson, and formalized by Grimme.<sup>44</sup> These calculations were performed using the triple  $\zeta$  Pople basis 6-311++G(d,p).<sup>45</sup> In addition, the following calculation options were used: scf=(Tight,MaxCycle=500) Int=UltraFine opt=(MaxCycle=500). The reliability of such level of theory was previously benchmarked by Grimme et al. and Dilabio et al.<sup>46,47</sup>

The nature (local minimum or transition state) of the stationary points was determined by performing a frequency calculation at the same calculation level as the optimization. For the C(O)-N bond formation reactions, the potential energy surface was investigated by performing an Intrinsic Reaction Coordinate (IRC) calculation from the transition state. For the reaction paths involving simple breaks, relaxed scans were performed. The ZPE correction was only taken into account for stationary points.

### III. Experimental evidence for bond-forming reactions

#### a. Background

Evidence of the formation of new chemical bonds from isolated species in the gas phase taken in their fundamental state remains relatively rare. The use of mass spectrometry coupled with synchrotron radiation allows the preparation of cation radicals with tunable internal energy. These species can then be selected in mass, and their reactivity can be probed as a function of the energy of the ionizing photons. The dications have thus been shown to be highly reactive, even in their fundamental state.<sup>48,49</sup> Bond formations were found with different neutral unsaturated reagents such as benzene,<sup>49,50</sup> as well as small molecules such as methane,<sup>48</sup> CO<sub>2</sub>, H<sub>2</sub>O, HCl, N<sub>2</sub>, O<sub>2</sub>,<sup>51-52</sup> or rare gases<sup>53</sup> for example. This wide range of reactivity of the dications has led to the introduction of the "super-electrophiles" concept. The formation of new chemical bonds by reaction between a monocation and a neutral species has been the subject of numerous studies. It should be noted, however, that these systems mainly lead to proton, hydride or atomic hydrogen transfers or charge transfers rather than to the formation of new chemical bonds between the two partners. As in the case of dications, it is often unsaturated species that lead to the formation of new chemical bonds. Thus, regarding the reactivity of neutral methylamine with a monocation, some of the reactions that have been studied are presented in *Table 1*.

Reagent	Observed mechanism	Reference
HCN <sup>+</sup>	PT	
HCNH <sup>+</sup>	PT, CT, H-T, adduct	54, 55
HCNH <sub>2</sub> <sup>+</sup>	PT, CT, H-T	55
CH <sub>2</sub> NH <sub>2</sub> <sup>+</sup>	PT, CT, H-T, adduct	54
CH <sub>3</sub> NH <sub>2</sub> <sup>+</sup>	PT, CT, H-T, adduct	54
CH <sub>3</sub> NH <sub>2</sub> D <sup>+</sup>	PT	
(CH <sub>3</sub> ) <sub>2</sub> NH <sub>2</sub> <sup>+</sup>	PT	
(CH <sub>3</sub> CN) <sub>2</sub> H <sup>+</sup>	PT, exchange in an adduct, adduct	
CH <sub>3</sub> OCH <sub>2</sub> <sup>+</sup>	CH <sub>3</sub> NHCH <sub>2</sub> <sup>+</sup> + CH <sub>3</sub> OH (CH <sub>3</sub> ) <sub>2</sub> NH <sub>2</sub> <sup>+</sup> + H <sub>2</sub> CO	56
C <sub>2</sub> H <sub>5</sub> OH <sub>2</sub> <sup>+</sup>	PT	
(C <sub>2</sub> H <sub>5</sub> OH) <sub>2</sub> H <sup>+</sup>	exchange in an adduct	
(C <sub>2</sub> H <sub>5</sub> OH) <sub>3</sub> H <sup>+</sup>	exchange in an adduct	
H <sub>2</sub> CCHCO <sup>+</sup>	PT, adduct	
HCCCHOH <sup>+</sup>	PT, adduct	
c-C <sub>6</sub> H <sub>5</sub> OH <sup>+</sup>	PT	
CH(OH) <sub>2</sub> <sup>+</sup>	PT	
CH <sub>3</sub> C(OH) <sub>2</sub> <sup>+</sup>	PT	

1	$((\text{CH}_3)_2\text{O})_2\text{H}^+$	PT, exchange in an adduct	
2	$((\text{CH}_3)_2\text{CO})_2\text{H}^+$	exchange in an adduct, adduct	
3	$\text{H}(\text{CH}_3\text{COH})_3^+$	exchange in an adduct	
4	$(\text{CHOOH})_2\text{H}^+$	exchange in an adduct	
5	$(\text{CH}_3\text{COOH})_2\text{H}^+$	adduct	
6	$(\text{CH}_3\text{COOCH}_3)_2\text{H}^+$	exchange in an adduct, adduct	
7	$(\text{C}_8\text{H}_{17}\text{O}_4(\text{CH}_3\text{OH}))^+$	Insertion in a crown ether	57
8	$(\text{CHOOH})_3\text{H}^+$	PT, exchange in an adduct	
9	$(\text{CH}_3\text{COOH})_3\text{H}^+$	PT, exchange in an adduct,	
10		adduct	

**Table 1:** Compilation of ion-molecule reactions involving methylamine reported in the Anicich database.<sup>58</sup> PT, CT and HT stand for proton transfer, charge transfer and hydride transfer, respectively.

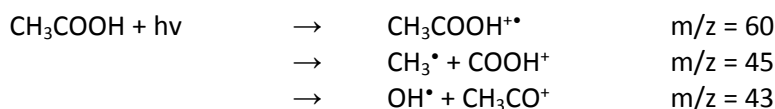
To our knowledge, no reaction has been carried out on a cation (not an adduct) containing a carboxylic acid function and an amine. The first step of our work was to determine whether, in addition to proton, hydride or charge transfer processes, reactions leading to the formation of new chemical bonds between the cation and the amine occurred.

As stated in the introduction, the derivation of the absolute cross-sections of the reaction requires a multi-step process. It seemed essential to present the main results of the different steps under our experimental conditions, although some aspects have been previously studied by other groups (such as the metastability of the parent ion  $\text{CH}_3\text{COOH}^{+\bullet}$ , and its collision induced dissociation in the presence of argon<sup>59</sup>). We were thus first interested in the ionization threshold of acetic acid, then in the metastability of the parent ion  $\text{CH}_3\text{COOH}^{+\bullet}$ , and its dissociation induced by collision with an inert partner, argon.

As a comparison, we were also interested in the formation and reaction of the  $\text{COOH}^+$  ion from formic acid. Therefore the ionization threshold of formic acid, the metastability of the  $\text{COOH}^+$  ion, and its dissociation induced by collision with argon were also studied.

#### Photoionization of acetic acid

In perfect agreement with the previous studies, the main ionic channels observed are the following (*Figure 1*):



To better understand these fragmentations, the ion yields as a function of the photon energy have been measured (*Figure 1*). Our combined experimental and theoretical approach allows us to determine the ionization threshold of acetic acid at 10.6 eV ( $I_{\text{theo}} = 10.64$  eV,  $I_{\text{exp}} = 10.6 \pm 0.05$  eV). These results are fully consistent with those of Leach et al.<sup>59</sup> who had experimentally determined an ionization threshold of  $10.58 \pm 0.02$  eV. The first fragmentation process at  $m/z$  43 associated to products  $\text{CH}_3\text{CO}^+$  and OH appears at  $11.5 \pm 0.1$  eV. For the appearance threshold of the  $\text{COOH}^+$  fragment at  $m/z$  45, an experimental value of  $12.1 \pm 0.02$  eV is obtained. From a theoretical point of view, the formation of this cation with the concomitant loss of the  $\text{CH}_3^{\bullet}$  radical, is calculated with a threshold of appearance of 12.27 eV (the optimized structures are presented in SI), which is a good theoretical/experimental agreement, as well as a good consistency with the already-published data.<sup>60</sup>

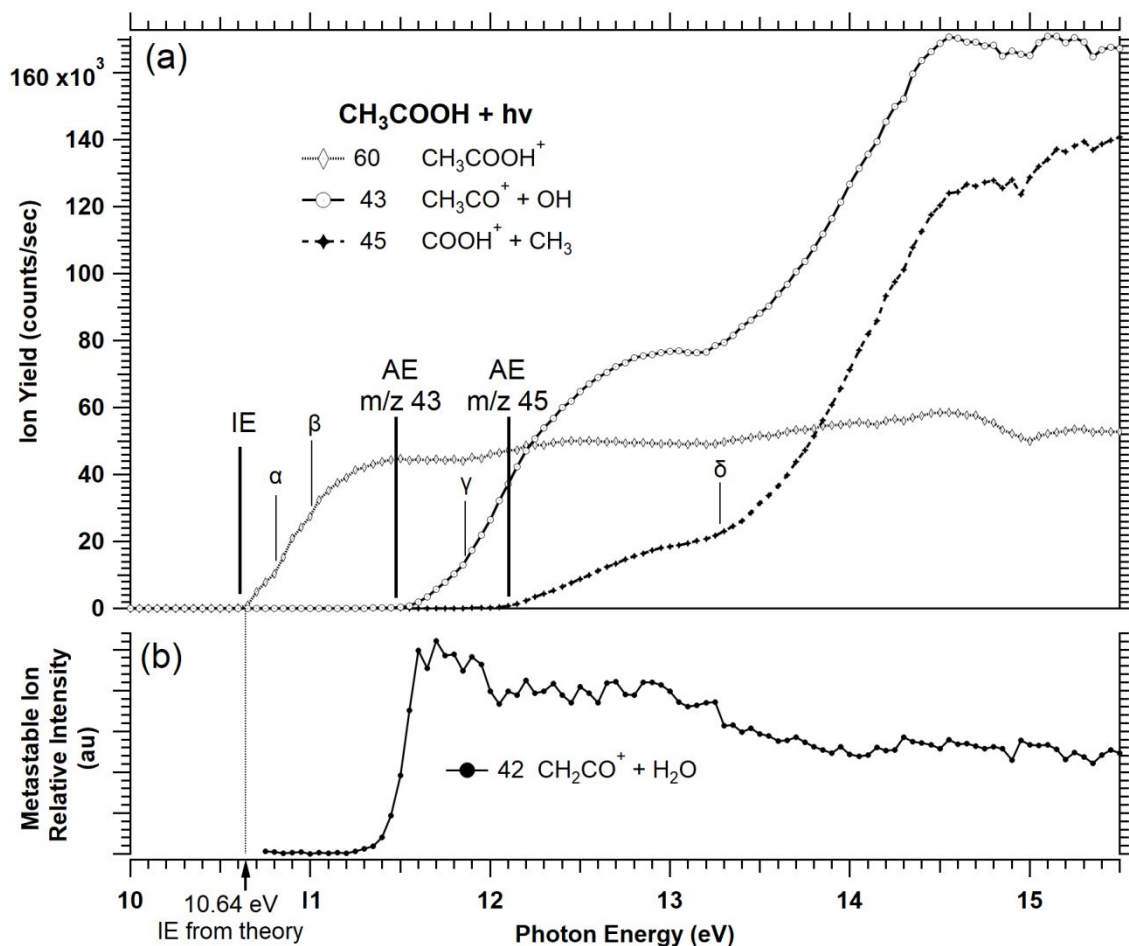


Figure 1: Evolution as a function of the ionizing photon energy for acetic acid of (a) the yields of the three major ionic products, and (b) the metastable process leading to the  $m/z=42$  ion. IE and AE stand for ionization energy and appearance energy, respectively.

Each of the three ion yield curves can be split into several features revealing the spectroscopy:

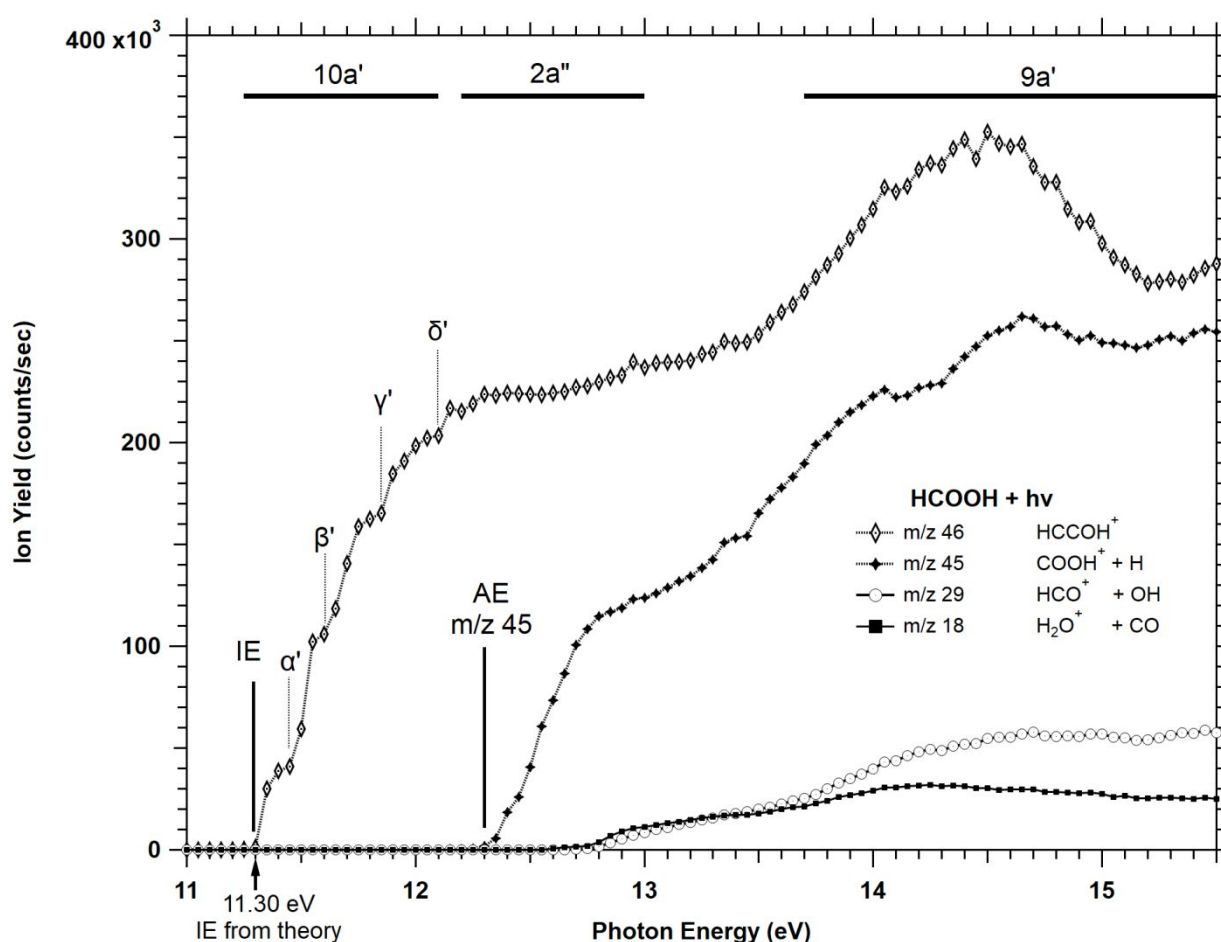
- two (small) slope breaks ( $\alpha$  and  $\beta$  in Figure 1) are observed around 10.8 and 11 eV in the ion yield of the parent ion, which may suggest the populating of vibrationally excited states of the radical cation formed. This is fully consistent with the substructures observed in the  $13a'$  state peak described by Borodin,<sup>61</sup>
- a third (small) slope break ( $\gamma$  in Figure 1) is observed in the ion yield curve of the parent ion, as well as for the ion yield at  $m/z$  43 around 11.85 eV. According to Borodin's work, this corresponds to the population of the electronically excited state  $3a''$ , a state that has an antibonding character on the C=O bond, and probably associated with OH loss,
- a fourth slope break ( $\delta$  in Figure 1) much more pronounced than the three previous ones, is observed around 13.2 eV for the fragments at  $m/z$  43 and 45. To a lesser extent, this slope break is also observed in the ion yield curve of the parent ion. This is well correlated with the second excited electronic state ( $2a''$ ) of the ion which also has an antibonding C=O character. Alternatively, this threshold could correspond to the appearance of isomerization, which would open the way to other channels for its dissociative photoionization. But in such a case, we should have observed the formation of new fragmentation pathways for these photon values, which was not the case. Let us notice, because it will be important here after for our discussion of results, that the increase of intensity for the  $\text{COOH}^+$  fragment beyond this slope break is roughly a factor six to one.

### Dissociative photoionization thresholds of formic acid

The photoionization and dissociative photoionization thresholds shown in [figure 2](#) are consistent with the published data (formic acid ionization threshold around 11.3 eV<sup>62,63,64</sup>). The HCCOH<sup>+</sup> ion appears at 11.3 ± 0.05 eV and the COOH<sup>+</sup> fragment ion appears at 12.3 ± 0.05 eV.

Here as well, several features are visible in the ion yield curves:

- four (small) steps ( $\alpha'$  to  $\delta'$  in Figure 2) observed between 11.3 and 12.2 eV in the ion yield of the parent ion, which are correlated with population of vibrationally excited ( $v=1$  to 4) states of the radical cation formed in its ground state, 10a'. This is fully consistent with the substructures observed at high resolution by Siggel king et al.<sup>64</sup>
- the second state, 2a'', does not exhibit particular structures, but corresponds to the appearance of the COOH<sup>+</sup> fragment, of interest in this study.
- The third state, 9a' appears as a broad structure, is visible in the yield of all product ions, and leads to an increase of intensity by roughly a factor two to one for the COOH<sup>+</sup> fragment.



**Figure 2:** Evolution of the ionic yield as a function of the energy of the ionizing photons, for formic acid, and comparison of the theoretical and experimental values obtained for the ionization threshold and for the threshold of appearance of the ion at  $m/z$  45. IE and AE stand for ionization energy and appearance energy, respectively.

The theoretical and experimental ionization energies of acetic acid and formic acid are compared in the [Table 2](#). The theoretical values obtained at the LC- $\omega$ PBE+ GD3BJ/6-311++G(d,p) computational level are quite consistent with the experimental values, which further supports our choice of this computational level for this study.

	CH <sub>3</sub> COOH	HCOOH
Neutral E <sub>tot</sub> (Hartree)	-228.961593	-189.675281
Cationic E <sub>tot</sub> (Hartree)	-228.570768	-189.259876
Theoretical IE (eV)	10.64	11.30
Experimental IE (eV)	10.60 ± 0.05	11.30 ± 0.05

**Table 2:** Comparison of the experimental and theoretical ionization energies of CH<sub>3</sub>COOH and HCOOH

No metastable or CID processes with Ar in the dissociation of the ion  $m/z$  45 were detected within the limit of our collision energy (20 eV lab). This is why in the subsequent section only the metastability of acetic acid will be discussed.

#### Metastability of CH<sub>3</sub>COOH<sup>+</sup> ion from acetic acid

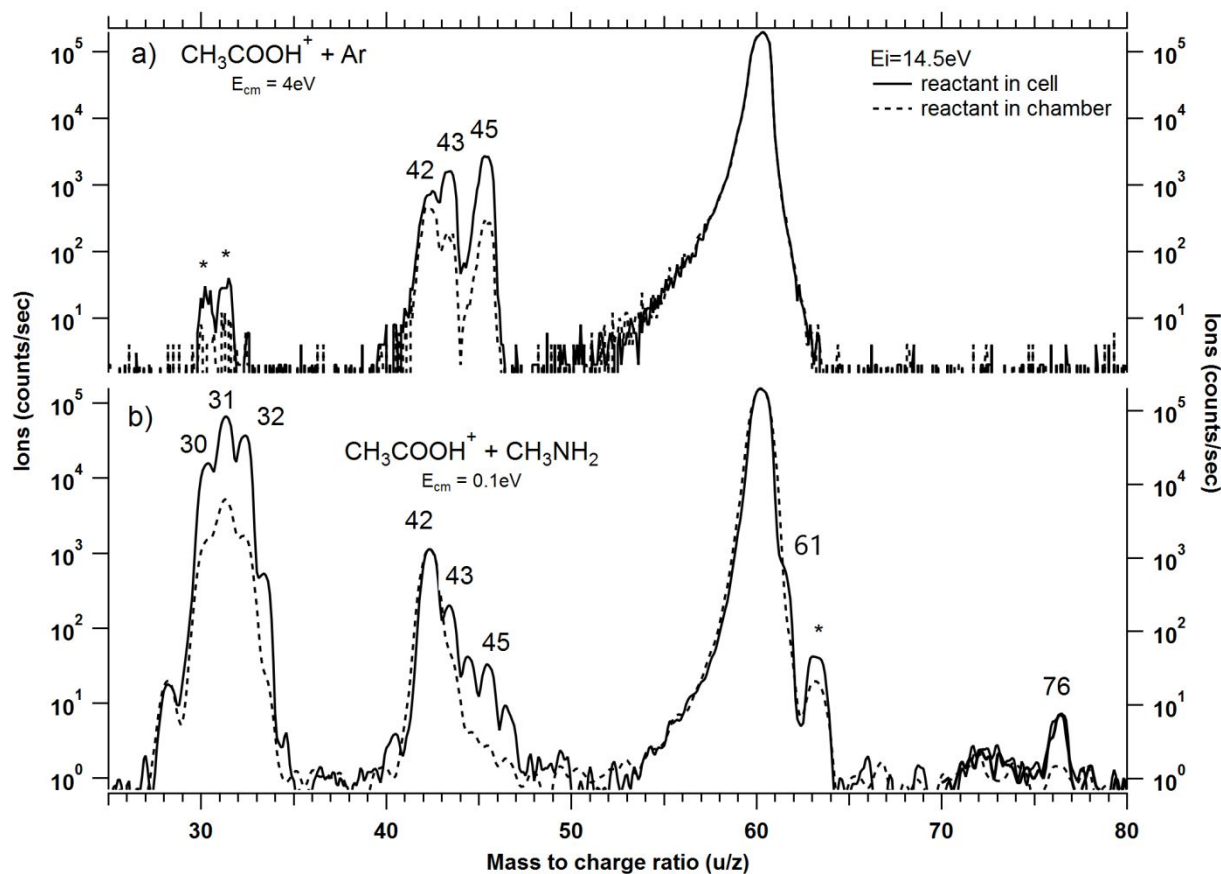
Metastability measurements performed by selecting the  $m/z$  60 ion with first quadrupole and recording the ion present in the beam with the second quadrupole, with no reactive gas in the reaction cell, shows that the  $m/z$  42 fragment is produced. This most likely corresponds to the formation of the CH<sub>2</sub>CO<sup>+</sup> ion, with the concomitant loss of a water molecule from CH<sub>3</sub>COOH<sup>+</sup>, as described in the literature.

In our experimental conditions, fragments at  $m/z$  45 and 43 do not appear as metastable products.

As shown in *figure 1b*, the metastable process has an appearance around 11.45 eV. Its relative intensity to the  $m/z$  60 ion reaches a plateau between 11.6 to 12 eV, followed by two steps down observed around 12 and 13.5 eV. These steps correlate with the population of 3a'' and 2a'' states, and hint at a reduced probability to produce the metastable entity when starting from those states. We have recorded such dependency at three different acceleration voltages (0.25, 2 and 12 V) in the octopoles region. When the applied voltage decreases, the residence time of the ions in the octopoles increases, which increases the metastable signals. The three curves are perfectly proportional in the photon energy range studied (11.5 to 15.5 eV) which indicates that there is no evolution of the metastable lifetime when changing the photon energy. Considering simulated flight times for  $m/z$  60 ions in the octopole region at the 3 acceleration voltages, the evolution of metastable signals let us estimate a metastable lifetime of 300 ± 50 μs.

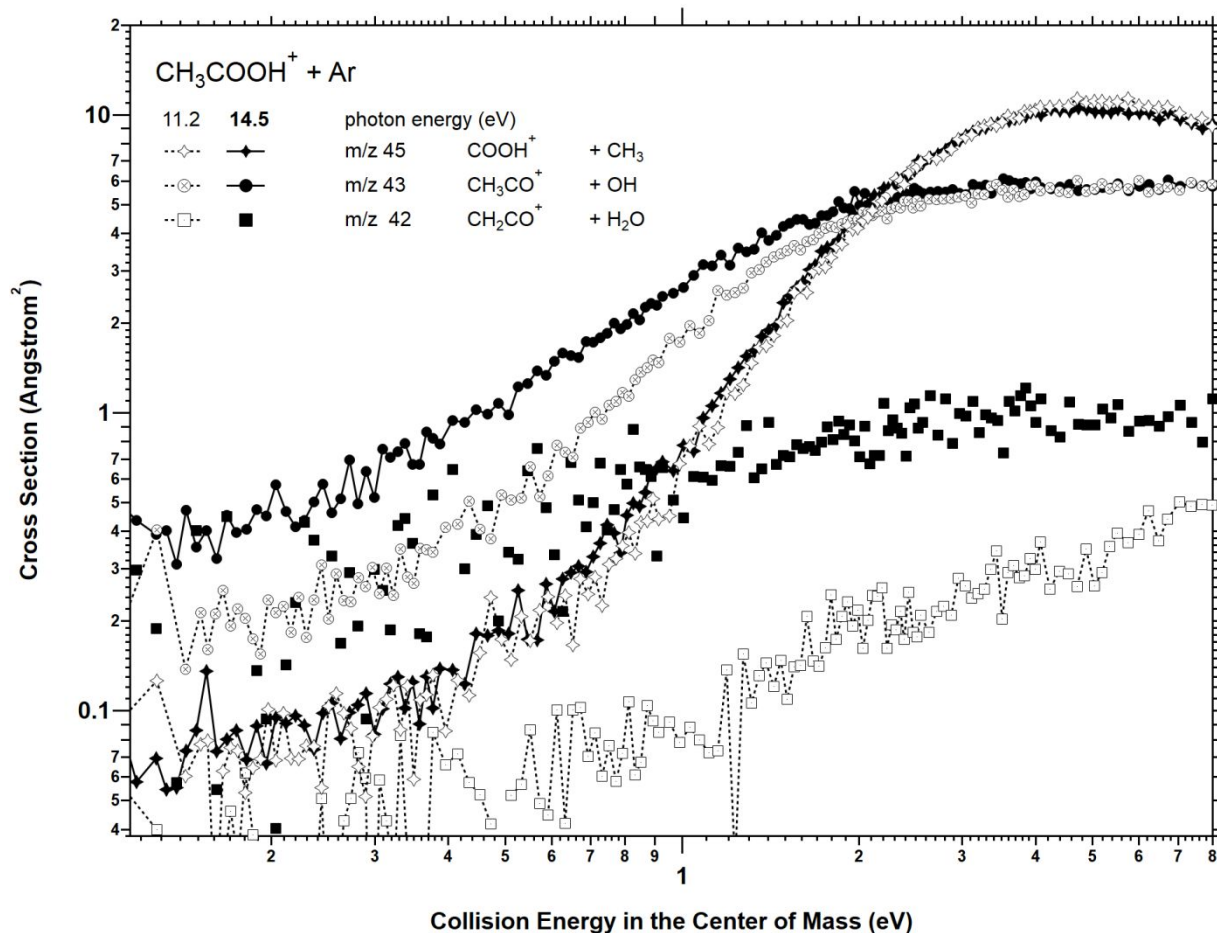
#### CID of acetic acid with argon

In order to decipher reactions and collision induced process in our system, non-reactive argon was introduced in the reaction cell to characterize collision-induced dissociations. The mass spectra obtained with photons having an energy of 14.5 eV are shown in *figure 3* and reveal product ions at  $m/z$ , 42 (C<sub>2</sub>H<sub>2</sub>O<sup>+</sup> + H<sub>2</sub>O), 43 (C<sub>2</sub>H<sub>3</sub>O<sup>+</sup> + OH) and 45 (CO<sub>2</sub>H<sup>+</sup> + CH<sub>3</sub>), the latter two being a clear effect of the collision, while the first one is essentially the metastable signature described before.



**Figure 3:** Mass spectra recorded at 14.5 eV photon energy, obtained when selecting parent ion at  $m/z$  60 ( $\text{CH}_3\text{COOH}^{**}$ ) and colliding in the reaction cell with either argon (a), or methylamine (b). In each case, two spectra are shown with either the reactant gas introduced in the cell (continuous line, left scale) or in the chamber surrounding the cell (dashed line, right scale). The mass region between  $m/z$  70 and 80 in b) has been collected with an increased accumulation time (x10) and is represented with a bold line. Mass peaks indicated with a (\*) correspond to ions that cannot be described as result of the considered ion molecule reactions, and most probably result from reactions with remnants of neutral samples previously introduced in the reaction cell.

Absolute reaction cross sections were determined for the three product ions as a function of collision energy in the center of mass (Figure 4). They all three exhibit a threshold behaviour, associated to an increase of yield when increasing the collision energy. It is noticeable that the measurements performed with the ionic target produced close to its ionization energy, i.e. with small internal energy, request for higher collision energy to exhibit the two channels leading to  $\text{CH}_2\text{CO}^+$  and  $\text{CH}_3\text{CO}^+$ . The  $\text{COOH}^+$  channel ( $m/z$  45) is not affected at all by the photon energy, indicating that the energy requested to induce this dissociation is hardly provided into the selected  $m/z$  60 ion produced by the photoionization process. The three channels show similar asymptotic behaviour.



**Figure 4:** Absolute fragmentation cross sections of  $\text{CH}_3\text{COOH}^{+\bullet}$  colliding with argon as a function of the center of mass collision energy. Results obtained when performing photoionization of acetic acid with 11.2 eV photons are presented with empty symbols, while results at 14.5 eV are presented with filled symbols

#### $\text{CH}_3\text{COOH}^{+\bullet} + \text{CH}_3\text{NH}_2$

The reactivity of the  $\text{CH}_3\text{COOH}^{+\bullet}$  ion with  $\text{CH}_3\text{NH}_2$  is illustrated by the mass spectrum shown in [figure 3b](#). The comparison of the spectra with the reactive gas in the cell and in the chamber suggests that the following reaction would take place:

- the hydride transfer reaction:
 
$$\text{CH}_3\text{COOH}^{+\bullet} + \text{CH}_3\text{NH}_2 \rightarrow \text{CH}_2\text{NH}_2^+ + \text{CH}_3\text{C}(\text{OH})_2^\bullet \quad (\text{H-T, } m/z = 30, \text{ Reaction 1a})$$
- a dissociative charge transfer:
 
$$\rightarrow \text{CH}_2\text{NH}_2^+ + \text{H}^\bullet + \text{CH}_3\text{COOH} \quad (\text{DCT, } m/z = 30, \text{ Reaction 1b})$$
- the charge transfer reaction:
 
$$\rightarrow \text{CH}_3\text{NH}_2^{+\bullet} + \text{CH}_3\text{COOH} \quad (\text{CT, } m/z = 31, \text{ Reaction 1c})$$
- the proton transfer reaction:
 
$$\rightarrow \text{CH}_3\text{NH}_3^+ + \text{CH}_3\text{COO}^\bullet \quad (\text{PT, } m/z = 32, \text{ Reaction 1d})$$
- another very minor ion, key to this study, which can be associated to a peptide-like bond formation corresponds to the loss of methyl from an (unobserved) adduct:
 
$$\rightarrow \text{CH}_3\text{NH}_2\text{COOH}^+ + \text{CH}_3^\bullet \quad (m/z = 76, \text{ Reaction 1e})$$
- a small amount of m/z 61 ion is also observed suggestion that the hydrogen transfer reaction also take place:
 
$$\rightarrow \text{CH}_2\text{NH}_2^\bullet + \text{CH}_3\text{C}(\text{OH})_2^+ \quad (\text{HT, } m/z = 61, \text{ Reaction 1f})$$

- 1 ➤ the ion at  $m/z$  42, 43 and 45 were observed in our initial study and are associated to metastability and  
2 CID fragmentation processes. Alternatively, the ion at  $m/z$  43 may be due to a further dehydration  
3 of the  $\text{CH}_3\text{C}(\text{OH})_2^+$  ion:  $\text{CH}_3\text{C}(\text{OH})_2^+ \rightarrow \text{H}_2\text{O} + \text{CH}_3\text{CO}$  ( $m/z = 43$ , Reaction 1g)  
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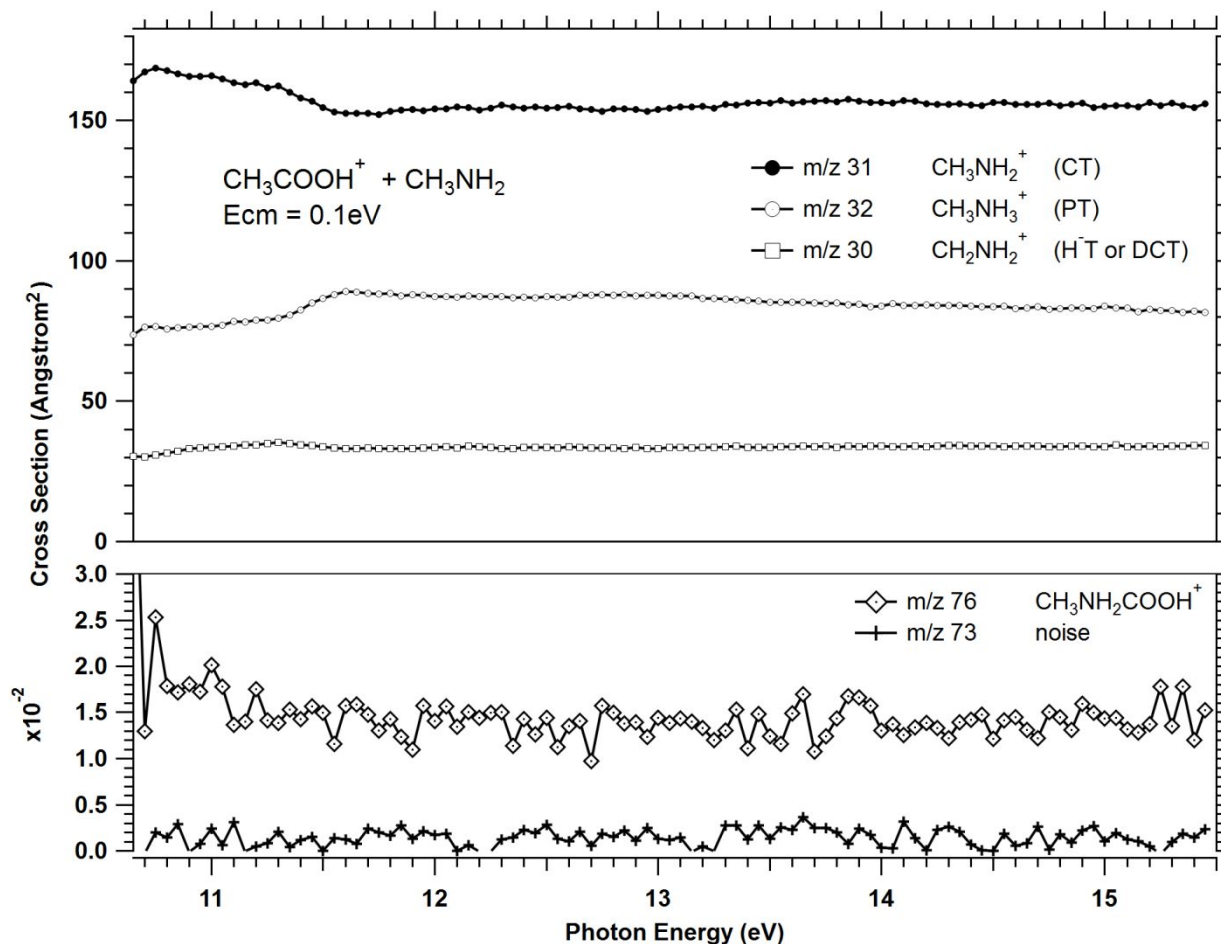
5 Other minor signals are visible at  $m/z$  40, 46 and 63 but they could not be ascribed to a direct reaction of  
6 the two reactants considered. The signals are very minor and could result from impurities present in the  
7 methylamine sample, or even to samples studied previously in the instruments which might be released  
8 from the metallic surfaces of the gas lines. The species were not further studied.  
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11 The absolute reaction cross sections for the four products at  $m/z$  30,31,32 and 76 were measured, as well  
12 as their evolution when changing either photon or collision energy.  
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15 We show in *figure 5* the absolute cross section of the four ionic channels as a function of the photon  
16 energy. Measurements were performed at very small collision energy (0.1 eV, center of mass) in order to  
17 maximize the yield of the peptide-like bond product at  $m/z$  76. A fake channel at  $m/z$  73 was collected in  
18 the same conditions in order to evaluate the sensitivity of our measurements to the detector noise.  
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21 One can notice that noticeable modulation of all channels is visible in the photon energy between  
22 ionization energy (10.6 eV) and roughly 12 eV. Hence, one observes a decrease of the major CT, and  
23 concomitant increase of PT. A step is noticeable in both curves at 11.55 eV, a photon energy  
24 corresponding to the appearance of the first dissociative photoionization channel ( $m/z$  43) as well as the  
25 maximum yield of the metastable channel at  $m/z$  42. This indicates a modulation of the internal energy of  
26 the reactive ion that reflects into its reactivity.  
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30 The peptide-like bond formation channel is extremely faint (1/10 000 of the major channel) but it is  
31 clearly larger than the noise level, and it also exhibits some sensitivity with the photon energy. Hence, the  
32 highest cross section is recorded at the lowest photon energy, with a constant decrease reaching a  
33 plateau from 12eV and beyond. This behavior can be associated to the need for the intermediate adduct  
34 to survive for a sufficient period of time to proceed through the rearrangement leading to the product.  
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**Figure 5:** Absolute reaction cross sections of the products resulting from the reaction of  $\text{CH}_3\text{COOH}^{+\bullet}$  with methylamine as a function of the photon energy used to produce the parent ion. Two scales are used in order to highlight the very minor channels. A fake channel at  $m/z$  73 is shown to illustrate the conservative noise level associated to the measurements

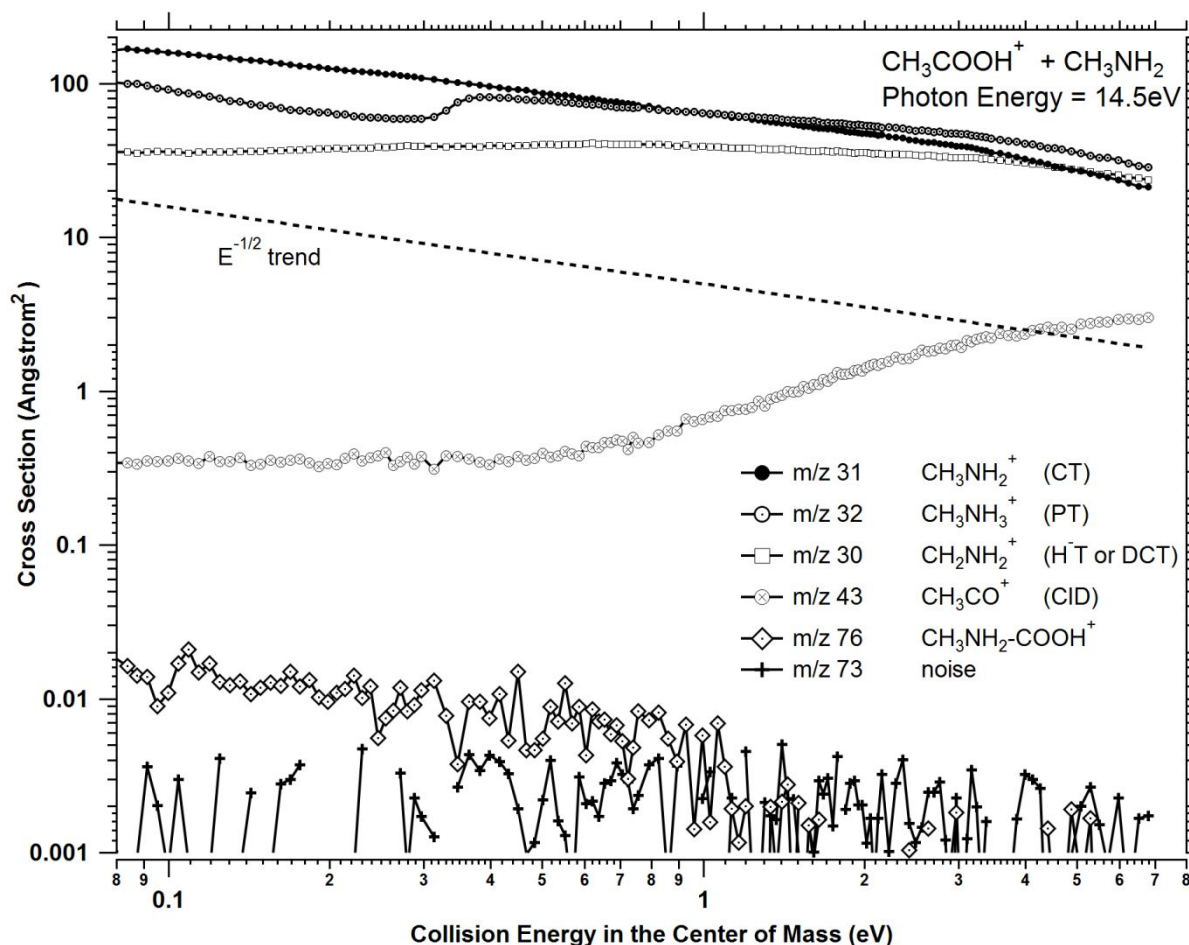
We show in [figure 6](#) the absolute cross section of the same ionic channels as a function of the collision energy. The measurements shown were performed at 14.5 eV, photon energy but the same acquisitions were performed at 11.2 and 12 eV and show similar trends.

An additional ionic channel corresponding to a CID process ( $\text{CH}_3\text{CO}^{+\bullet}$  at  $m/z$  43) was also recorded and exhibits an increase with collision energy, similar to the results obtained in the measurements with argon.

The cross section related to the  $m/z$  30 ion ( $\text{CH}_2\text{NH}_2^+$ ) is almost flat, and all other channels exhibit a decrease. It is worth mentioning that the cross section related to the  $m/z$  31 ion, associated to the charge transfer shows a significant decrease with the collision energy (with a slope close to the  $E^{-1/2}$  trend, drawn in [figure 6](#) as a guide). This is surprising, as the usual behavior of charge transfer, due to its long range interaction, is relatively insensitive to the collision energy as has been previously observed in our apparatus.<sup>65,66,67</sup> In order to reconcile these observations, our hypothesis is that the  $m/z$  31 ion is a poorly stable product of charge transfer, which dissociates to form the  $m/z$  30 ion. Indeed, the dissociative charge transfer of  $\text{CH}_3\text{NH}_2^{+\bullet}$  is known to occur for an internal energy of 1.5 eV.<sup>68</sup> The quantum chemical calculations presented in the following will confirm that, under our experimental conditions, the radical cation  $\text{CH}_3\text{NH}_2^{+\bullet}$  formed by charge transfer dissociates to form  $\text{CH}_2\text{NH}_2^+$  and  $\text{H}^{\bullet}$ . The transfer of some part of the kinetic energy imparted in the collision might be transferred in this process, leading to a comparatively increased signal at  $m/z$  30 and a decreased signal at  $m/z$  31.

One can observe a step between 0.3 and 0.4 eV in the cross section of the product at  $m/z$  32 ( $\text{CH}_3\text{NH}_3^+$ ) corresponding to proton transfer. This behaviour is well known from previous results obtained in the CERISES

instrument<sup>65</sup> and is the signature of secondary reactions leading to proton transfer between slowly moving ionic products and the neutral species in the cell. It is usually associated to processes occurring at large distance (such as  $e^-$ ,  $H^+$ ,  $H$  or  $H^-$  transfers) as those do not request an intermediate complex and do not transfer impulsion into the ionic products. Those products are therefore moving at the initial speed of the neutral species, i.e. roughly 20 meV in the center of mass. The step behaviour corresponds to the potential (0.9V) at which the ions moving backward in the instrument are repelled by a lens potential towards the detector (while they are attracted by the lens and lost at lower potentials). The amplitude of the step is informative of secondary reactions, associated to processes that do not involve an intermediate complex formation.



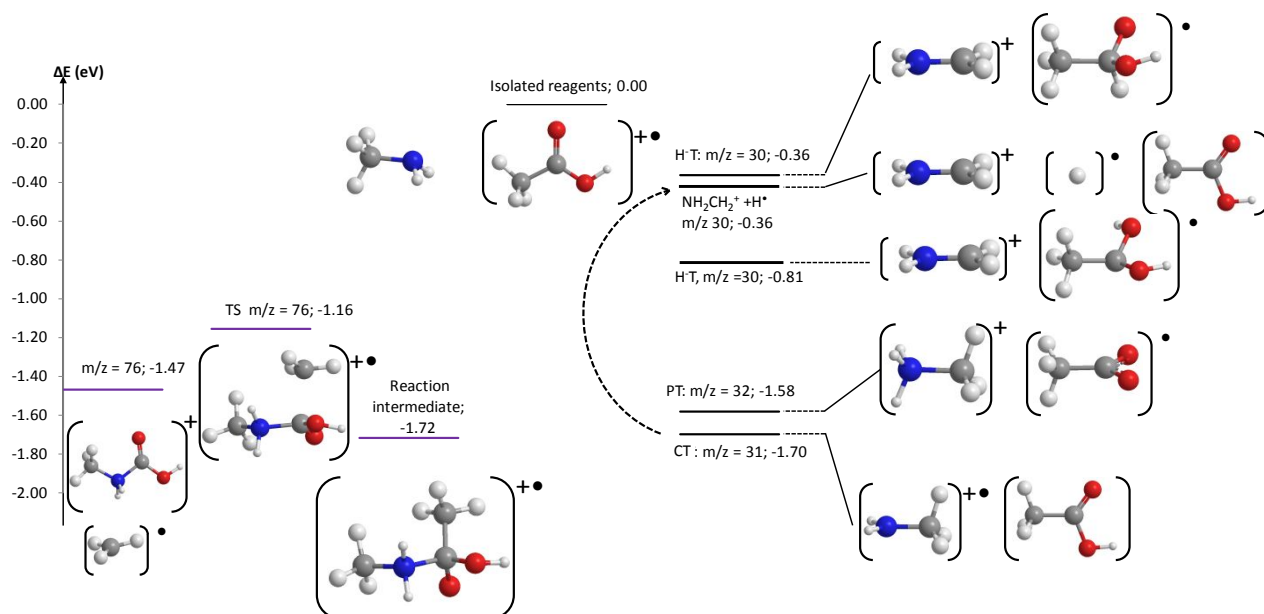
**Figure 6:** Absolute reaction cross sections of the products resulting from the reaction of CH<sub>3</sub>COOH<sup>+</sup> with methylamine as a function of the collision energy. A fake channel at m/z 73 is shown to illustrate the conservative noise level associated to the measurements.

The analysis of absolute cross sections shows that:

- the CT, DCT and PT mechanisms are clearly prevalent (between 150 and 30 Å<sup>2</sup>). This is typical when the proton affinity and/or electron affinity of the neutral partner is higher than that of the cation radical reagent,
- the effective ion-forming cross sections at m/z 76 is very small, but these ions are clearly evidenced above the background and do therefore correspond to reaction products.

The reaction paths corresponding to these different processes were investigated using DFT-D calculations. From a theoretical point of view, we have identified the different stationary points corresponding to these

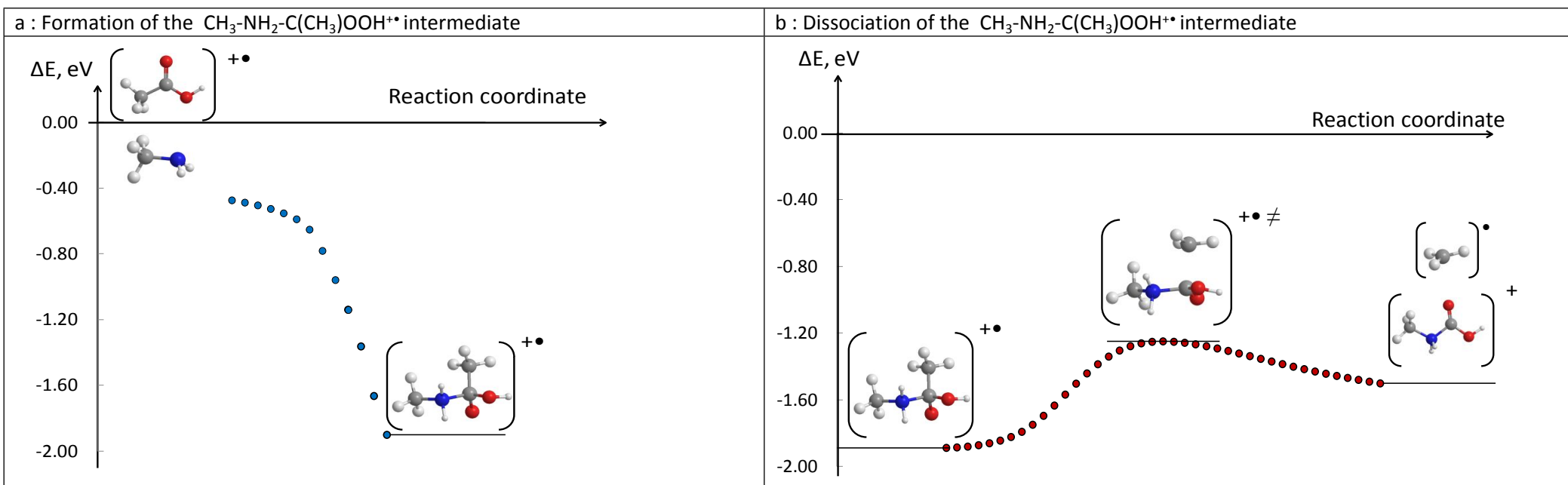
processes. Two possible structures were found for the  $C_2H_5O_2^{\bullet}$  radical formed from the hydride transfer (See Figure 7 and Supplementary Data). The values presented in *figure 7* takes into account the ZPE correction, and the frequency calculations allowed us to verify the nature (minimum or transition state) of the stationary points. (The minor 1f and 1g reaction pathways are presented in Supplementary Data).



**Figure 7:** Identification of stationary states on the potential energy surface for the reaction between  $CH_3COOH^{+\bullet}$  and  $CH_3NH_2$ . (The minor 1f and 1g reaction pathways are presented in Supplementary Data)

The mechanisms of proton transfer, charge transfer and hydride transfer are calculated to be exothermic.

As pointed out in the analysis of the cross-sections presented in *figure 6*, we have also considered the subsequent charge transfer dissociation of  $CH_3NH_2^{+\bullet}$  ( $m/z$  31) into  $CH_2NH_2^+$  ( $m/z$  30) and  $H^{\bullet}$ . As the internal energy that can be stored in the  $CH_3NH_2^{+\bullet}$  CT product is higher than the energy needed to fragment it with a H loss, the DCT channel is indeed energetically feasible. This fragmentation allows to explain the behaviour observed in *figure 6*.



23 **Figure 8:** Identification of a two-step mechanism to explain the formation of the C(O)-N bond and production of the  $\text{CH}_3\text{-NH}_2\text{-COOH}^+$  cation with concomitant loss of the methyl radical from the reaction of the  $\text{CH}_3\text{COOH}^{**}$  radical cation and methylamine.

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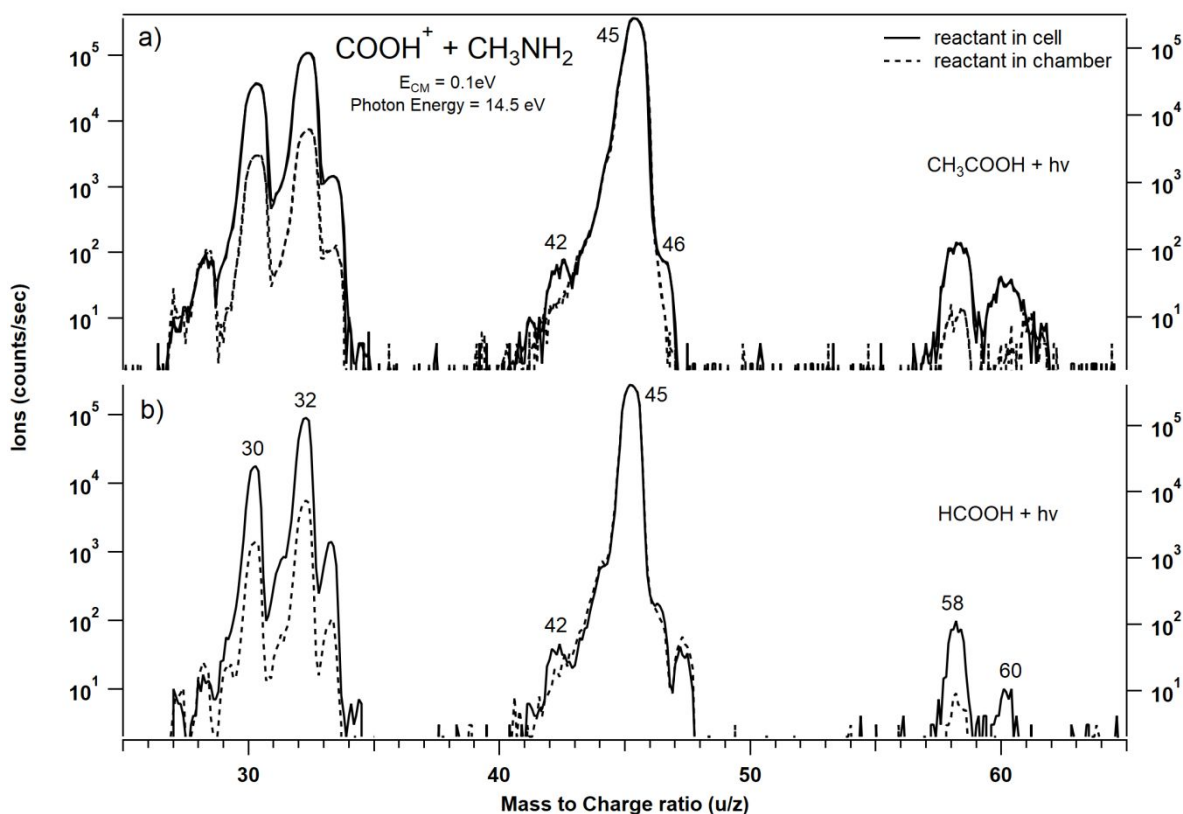
1 For the reaction leading to the formation of the ion at  $m/z$  76, a two-step mechanism can be  
2 proposed, with a simple association mechanism of the two species (*figure 8*). From this reaction  
3 intermediate, a transition state leads to the formation of the product  $\text{CH}_3\text{-NH}_2\text{-COOH}^+$  with the  
4 concomitant loss of the  $\text{CH}_3$  radical. This mechanism was confirmed by partially relaxed scan  
5 calculations (for the formation of the reaction intermediate from the reagents, *figure 8,a*) and IRC,  
6 for the part of the mechanism leading to the reaction products from the reaction intermediate,  
7 *figure 8,b*). Note that these potential energy surfaces do not take into account the ZPE correction,  
8 hence the slight discrepancy between the values in *figure 7* and in *figure 8*.

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10 Thus, from the parent ion  $\text{CH}_3\text{COOH}^{**}$  taken in its fundamental state, a "C(O)-N bond-forming  
11 reaction" is observed. The effective cross section of this reaction is about 10,000 times smaller than  
12 that of the PT, CT and H-T processes, but quantum chemistry calculations confirm that the parent ion  
13  $\text{CH}_3\text{COOH}^{**}$  taken in its ground state can react with  $\text{CH}_3\text{NH}_2$  to form  $\text{CH}_3\text{-NH}_2\text{-COOH}^+$  with the  
14 concomitant loss of the  $\text{CH}_3^*$  radical. This is not formally a peptide-bond, but rather the formation of  
15 a carbamate cation.

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17 We aimed at finding out if another "C(O)-N bond-forming reaction" could take place with the  
18 concomitant loss of a water molecule, to get closer to the typical peptide C(O)-N bond-forming  
19 processes. This is why we focused on the reactivity of the fragment ion at  $m/z=45$   $\text{COOH}^+$ , the only  
20 one that may lead to this type of process among the most abundant ions formed in the dissociative  
21 photoionization of  $\text{CH}_3\text{COOH}$ .

#### 22 $\text{COOH}^+ + \text{CH}_3\text{NH}_2$

23  
24 The dissociative photoionization of acetic acid leads to the formation of the  $\text{COOH}^+$  cation ( $m/z$  45).  
25 From the parent ion  $\text{CH}_3\text{COOH}^{**}$ , the  $\text{COOH}^+$  fragment ion was selected in mass with the quadrupole I  
26 in order to introduce it into the reaction cell and study its reactivity with  $\text{CH}_3\text{NH}_2$ . The mass spectrum  
27 obtained at a photon energy of 14.5 eV is presented in *figure 9, a*. The formation of ions at  $m/z$  30,  
28 32, 46, 58 and 60 is observed. Compared to what was observed in the case of the reaction of  
29  $\text{CH}_3\text{COOH}^{**}$  with  $\text{CH}_3\text{NH}_2$ , one can notice the absence of the ion at  $m/z$  31. Hence the faint signal  
30 located between  $m/z$  30 and 32 can be ascribed to the  $^{13}\text{C}$  isotope abundance present in  
31 methylamine.  
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**Figure 9:** Mass spectra of ions produced in the reaction of  $\text{COOH}^+$  and methylamine, with the  $m/z$  45 parent ion prepared through dissociative photoionization at 14.5 eV photon energy of (a) acetic acid or (b) formic acid. In each case, two spectra are shown with either the methylamine reactant gas introduced in the cell (continuous line, left scale) or in the chamber surrounding the cell (dashed line, right scale).

The comparison of the spectra with the reactive gas in the cell and in the chamber suggests that the following reaction would take place:

- the hydride transfer reaction:  
 $\text{CH}_3\text{NH}_2 + \text{COOH}^+ \rightarrow \text{CH}_2\text{NH}_2^+ + \text{HCOOH}$  (H-T,  $m/z = 30$ , Reaction 2a)
- the proton transfer reaction:  
 $\rightarrow \text{CH}_3\text{NH}_3^+ + \text{CO}_2$  (PT,  $m/z = 32$ , Reaction 2b)
- the dissociative proton transfer:  
 $\rightarrow \text{CH}_2\text{NH}_2^+ + \text{H}_2 + \text{CO}_2$  (DPT,  $m/z = 30$ , Reaction 2c)
- the C(O)-N bond formation reaction:  
 $\rightarrow \text{CH}_3\text{NHCO}^+ + \text{H}_2\text{O}$  (CN,  $m/z = 58$ , Reaction 2d)
- other minor product ions are observed at  $m/z$  46 and 60.

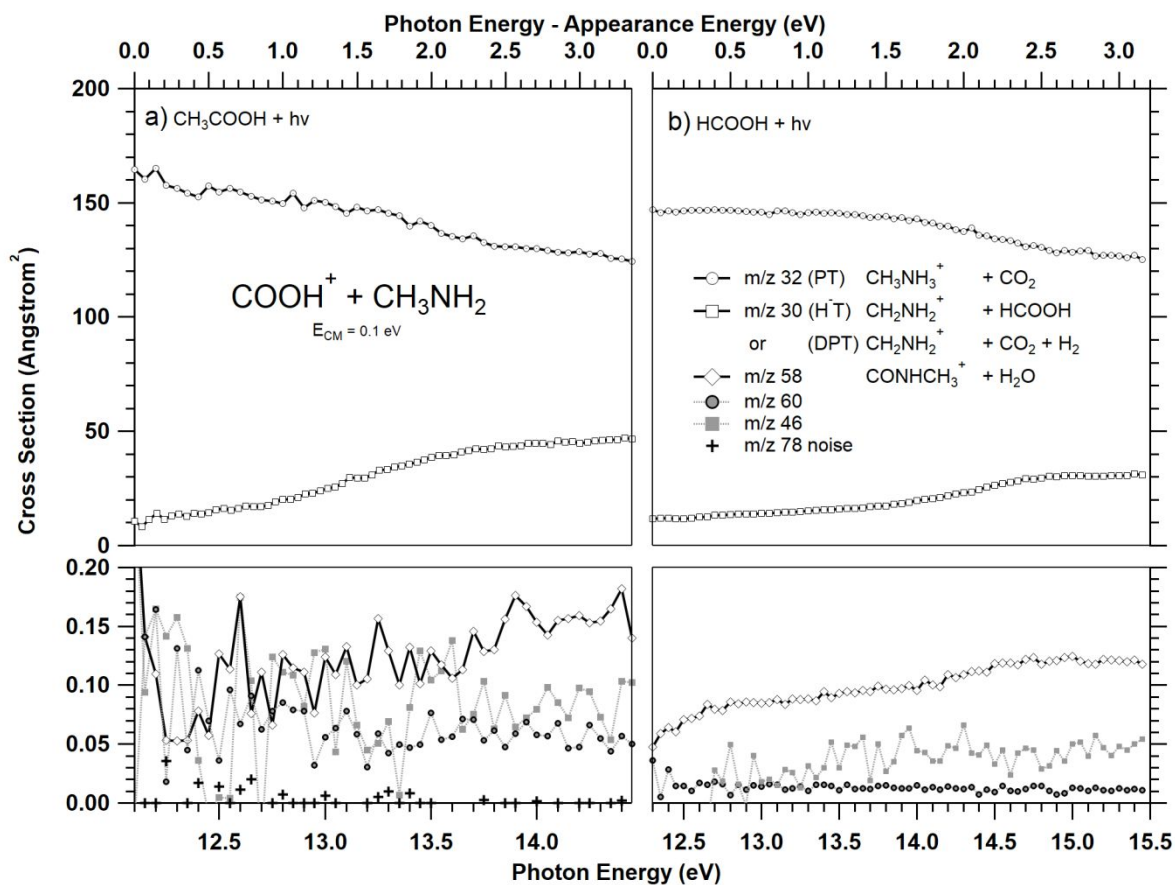
As a comparison, we also investigated the reaction of  $\text{CH}_3\text{NH}_2$  with  $\text{COOH}^+$  ions formed by dissociative photoionization of another precursor, the formic acid,  $\text{HCOOH}$ . *Figure 9, b* shows very similar ionic products obtained when using formic acid as precursor of the  $\text{COOH}^+$  ion.

*Figure 10, a* shows the absolute cross sections of the reaction of the  $\text{COOH}^+$  fragment ion from acetic acid with methylamine as a function of the energy of the photons used for ionization. As in the previous case, the H-T and PT mechanisms are highly dominant. Moreover, these results show that:

- the appearance energy of the  $\text{COOH}^+$  fragment ion is  $EA_{exp}^{45} \approx 12.1 \text{ eV}$  (see Fig. 1)

- the two major products appear at the first energies probed, as do the minor  $m/z = 58$  product within uncertainties of its low signal.

This allows one to consider that the reactions take place already from the reagents taken in their fundamental state.



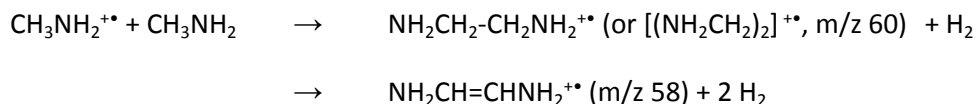
**Figure 10:** Absolute reaction cross sections for the various product channels in the reaction of  $\text{COOH}^+$  with methylamine as a function of the photon energy used to produce the parent ion. Two horizontal scales are used to differentiate  $\text{COOH}^+$  reactant ion produced from a) acetic or b) formic acid. Two vertical scales are used in order to highlight the minor channels. A fake channel at  $m/z = 78$  is shown to illustrate the conservative noise level associated to the measurements

**Figure 10 b** shows the absolute cross sections of the reaction of the  $\text{COOH}^+$  fragment ion from formic acid with methylamine as a function of the energy of the photons used for ionization. These results show that:

- the appearance energy of the  $\text{COOH}^+$  fragment ion is  $EA_{exp}^{45} = 12.3 \pm 0.05 \text{ eV}$  (see Fig. 2)
- the appearance energies of all the  $m/z = 30, 32$  and  $58$  products of the reaction are close to this value.

Thus, the  $\text{COOH}^+$  ion taken in its fundamental electronic state can react with neutral  $\text{CH}_3\text{NH}_2$  to form the  $\text{CH}_2\text{NH}_2^+$ ,  $\text{CH}_3\text{NH}_3^+$  and  $\text{CH}_3\text{NHCO}^+$  products.

It is worth mentioning that secondary reactions involving methylamine radical cation could also lead to the formation of ions  $\text{NH}_2\text{CH}_2\text{-CH}_2\text{NH}_2^{+\bullet}$  and  $\text{NH}_2\text{CH=CHNH}_2^{+\bullet}$  with  $m/z$  ratios of 60 and 58, respectively:



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However, we showed that the  $\text{CH}_3\text{NH}_2^{+\bullet}$  species could not be formed in the case of the reaction of  $\text{COOH}^+$  with  $\text{CH}_3\text{NH}_2$ , so these processes can be eliminated. Moreover, the ions at  $m/z$  58 and either 30, 31 or 32 do not have a similar behavior, which makes it possible to eliminate this secondary reaction process (the theoretical data are nonetheless provided in SI).

Furthermore, *figure 10* allows comparison of the reactivity with  $\text{CH}_3\text{NH}_2$  of  $\text{COOH}^+$  ions coming either from  $\text{CH}_3\text{COOH}$  or from  $\text{HCOOH}$ . Notable differences in the cross section of the ions at  $m/z$  30 and 32 can be observed, depending on the photon energy and nature of the ionized precursor:

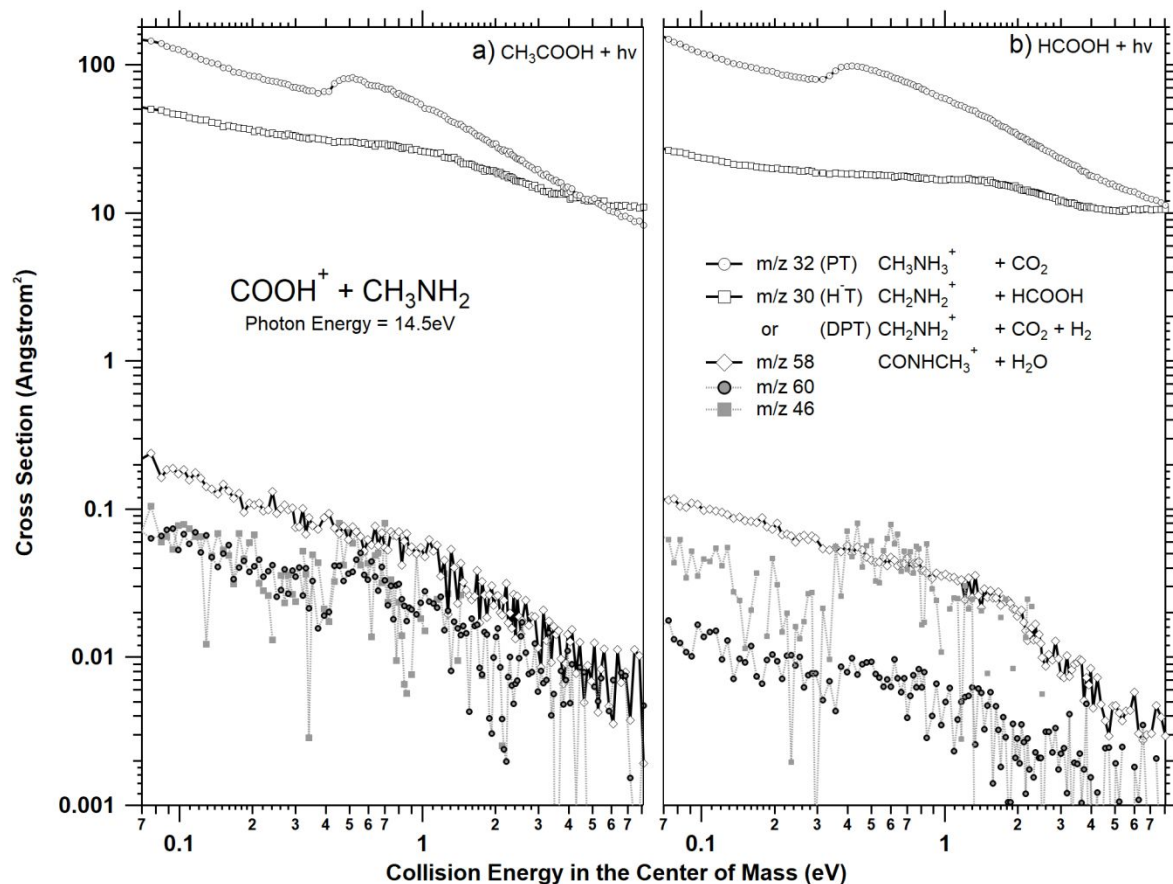
- the cross section for the formation of the  $\text{CH}_3\text{NH}_3^+$  ion ( $m/z$  32) at threshold is lower in the reaction of the  $\text{COOH}^+$  ion produced from formic acid than from acetic acid,
- conversely, the cross section for the formation of the  $\text{CH}_2\text{NH}_2^+$  ion ( $m/z$  30) at threshold is higher in the reaction of the  $\text{COOH}^+$  ion produced from formic acid than from acetic acid.
- In both cases, there is an important (times five) increase of the cross section of the  $\text{CH}_2\text{NH}_2^+$  product and a concomitant decrease in the cross section of the  $\text{CH}_3\text{NH}_3^+$  product with photon energy.
- furthermore, the amplitude of the variations for both cross sections with photon energy is larger in the case of the reaction of the  $\text{COOH}^+$  ion formed from  $\text{CH}_3\text{COOH}$ .

These results are in favor of our description of the channel products at  $m/z$  32 and 30 as being the result of proton transfer and dissociative proton transfer process. One can therefore assume that some excess of energy will lead to a transfer of cross section from one channel to the other, as is observed here. These results further underline a strong sensitivity of the reactive channels to the internal energy of the  $\text{COOH}^+$  ions, and the ability to alter significantly the  $\text{COOH}^+$  internal energy when changing the photon energy, though there is here no control of the amount of energy released in the photoelectron nor in the neutral partner (either  $\text{CH}_3^*$  or  $\text{H}^*$ ). The amplitude of the variation can be correlated to the presence of the second excited state, described in figures 1 and 2 (states 2a" and 9a' for acetic and formic acid, respectively). Hence, as was noted, the yield of  $\text{COOH}^+$  ions exhibit a stronger increase (6 to 1) for acetic acid than for formic acid (1 to 1) when this state is produced. One can therefore assume that the larger amount of excited precursor will induce a larger amount of excited  $\text{COOH}^+$  reactant, and therefore produce more contrasted results, as in observed in figure 10. The most intriguing result is the different behaviour at threshold, which suggests that the  $\text{COOH}^+$  ions are formed in different internal energy states, depending on the neutral partner that is released in the dissociative photoionization process. One can note here that in the case of acetic acid, the neutral partner is  $\text{CH}_3^*$ , while it is  $\text{H}^*$  in formic acid. This corresponds to the breakage of a C-C bond in one case and a C-H bond in the other case. The latter being a stronger bond, one can expect the need to produce a population of precursor with comparatively larger internal energy to produce the  $\text{COOH}^+$  fragment in the case of formic acid, that would induce the observed phenomenon.

The cross section for the production of  $m/z$  58 product related to the peptide-like bond formation exhibit also some sensitivity to the photon energy. Hence, for both precursors, there is a slight increase above threshold and a second increase correlated to the abovementioned excited state production. An excess of internal energy in the reactants is not mandatory, but beneficial to its formation.

Finally, the cross sections presented in *figure 10* confirm that the ions at  $m/z$  46 and 60 are due to reactions with residual compounds as their evolution with the photon energy exhibit a large variability in their intensity between the two experimental sets, most probably related to their

transient behavior, with a lower relative intensity when performing measurements at a later stage of the experimental session.



**Figure 11:** Absolute reaction cross sections of the various product channels in the reaction of  $\text{COOH}^+$  with methylamine as a function of the collision energy. Two horizontal scales are used to differentiate  $\text{COOH}^+$  reactant ion produced from a) acetic or b) formic acid.

Figure 11 shows the absolute cross sections of the reaction of the  $\text{COOH}^+$  fragment ion from acetic and formic acid with methylamine as a function of the collision energy. Similarly to results obtained with the  $\text{CH}_3\text{COOH}^{*+}$  precursor (shown in figure 6), a step function is observed in the PT channel, signature of some amount of secondary reactions. As discussed earlier, the products at  $m/z$  30 and 32 exhibit a coupled behaviour, with comparatively increased cross section for the  $m/z$  30 ion when collision energy is increased. Furthermore, the hypothesis that  $\text{COOH}^+$  ion brings more energy in the reaction when using acetic acid as precursor is clearly confirmed, as the two partners have closer cross sections at threshold and  $m/z$  30 even surpass  $m/z$  32 at 8 eV collision energy.

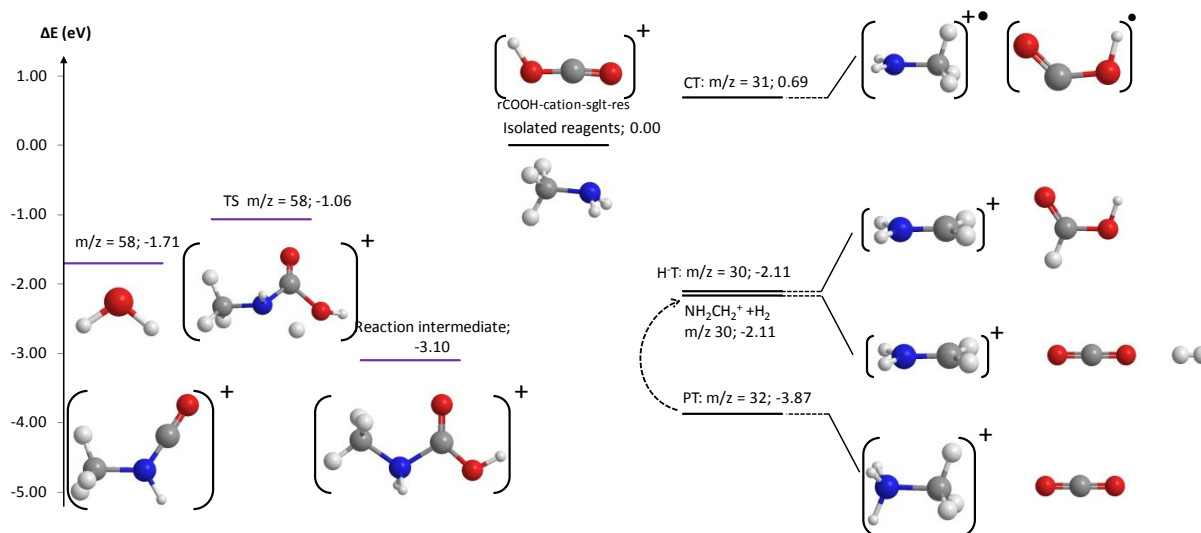
The absolute cross section trend for the formation of a peptide-like bond exhibit a  $E^{-1/2}$  trend, signature of a complex formation, and maximum reactivity at very low collision energy. However, this reaction is 100 to 1,000 times less efficient than the proton and dissociative proton transfer processes.

Finally, the reaction pathways deduced from experimental observations (Reactions 2a - 2d) were investigated using DFT-D calculations. It is worth mentioning that the formation of the ion at  $m/z$  31,  $\text{CH}_3\text{NH}_2^{*+}$ , has not been observed. An attempt has been made to understand why, considering it as one of the possible processes.

Several structures were investigated for the ions at  $m/z$  60 and 46, as well as for the corresponding neutral fragments, but no exothermic pathway could be identified. Since these fragments are very minor, they may be products formed after reaction with residual gases present in the reaction chamber.

The stationary points that could be identified on the potential energy surface for the reaction between  $\text{CH}_3\text{NH}_2$  and  $\text{COOH}^+$  are shown in *figure 12*. All energies given in this figure take into account the ZPE correction and have been calculated at LC- $\omega$ PBE/6-311++G(d,p) + GD3BJ. The nature (TS or local minimum) of the stationary points has been verified by frequency calculations.

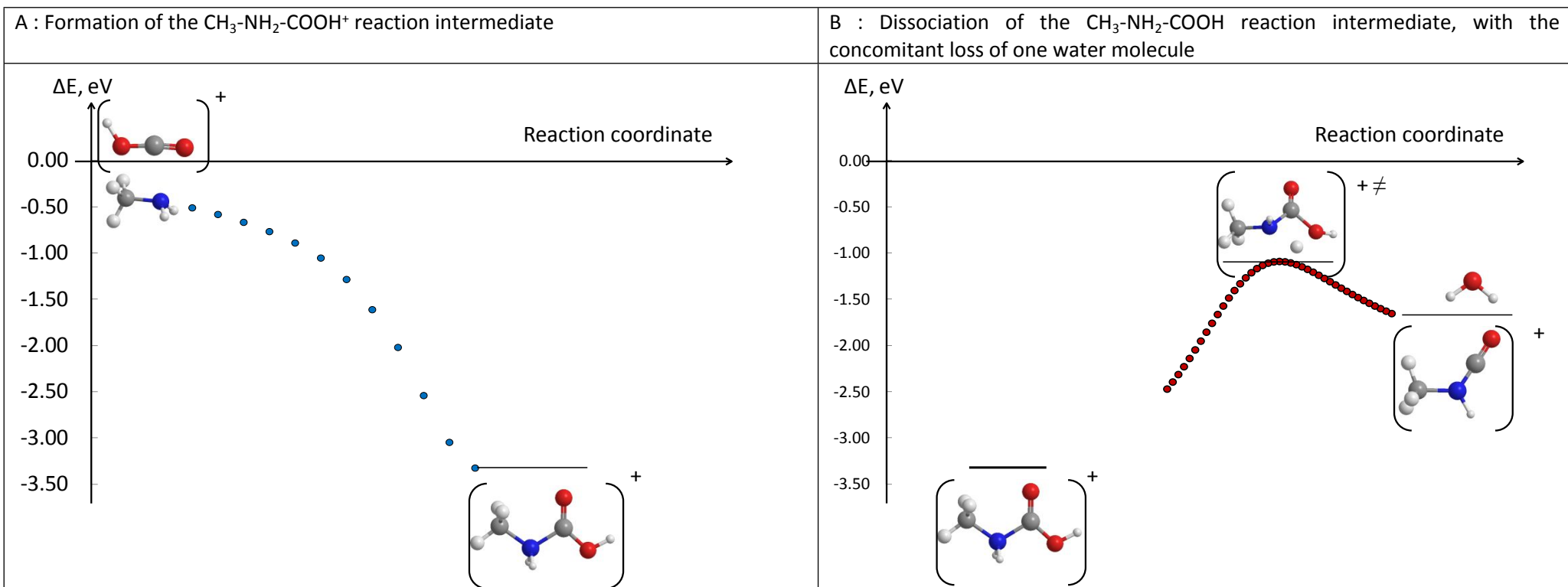
It is worth mentioning that the calculations suggest that the  $\text{COOH}^+$  fragment ion formed by dissociative photoionization of acetic acid and formic acid have the same structure. They may however differ in their internal energies, which could directly affect their reactivity.



**Figure 12:** Identification of stationary states on the potential energy surface for the reaction between the  $\text{COOH}^+$  ion and  $\text{CH}_3\text{NH}_2$ .

A basic energy analysis provides an understanding of the absence of ion formation at  $m/z$  31: the charge transfer, which would lead to the formation of a radical and a cation radical from a cation and a neutral species, is calculated as being endothermic.

As in the case of the formation of the ion at  $m/z$  76 from the  $\text{CH}_3\text{COOH}^{++}$  and  $\text{CH}_3\text{NH}_2$  species, a two-step mechanism could be identified for the formation of the ion at  $m/z$  58 from the  $\text{COOH}^+$  and  $\text{CH}_3\text{NH}_2$  reagents taken in their fundamental state (*figure 13*).



27 **Figure 13:** Identification of a two-step mechanism to explain the formation of the C(O)-N bond and the production of the  $\text{CH}_3\text{-NH-CO}^+$  cation with concomitant loss of a water molecule from the  $\text{COOH}^+$  cation and  
28 methylamine.

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- the formation of the  $\text{CH}_3\text{-NH}_2\text{-COOH}^+$  intermediate, following an inverse process of the expected simple cleavage of the C(O)-N bond in the  $\text{CH}_3\text{-NH}_2\text{-COOH}^+$ : no energy barrier is associated with this process. The formation of this intermediate is accompanied by a strong stabilization of the system ( $\Delta E = 3.10$  eV, *figure 13 a*),
  - a rearrangement, including the migration of a hydrogen atom from the nitrogen atom to the oxygen atom, leading to the loss of water. The energy barrier associated with this process is  $\Delta E = 2.04$  eV (*figure 13 b*), thus below the entrance channel energy.

#### 10 11 12 13 ***IV. Discussion***

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In this work, we have identified two reactions leading to the formation of a peptide C(O)-N bond between methylamine and a cation or a radical cation taken in their fundamental state:

- the  $\text{CH}_3\text{NHCOOH}^+$  ( $m/z$  76) formation with the concomitant loss of the  $\text{CH}_3^{\bullet}$  radical from the reaction of the  $\text{CH}_3\text{COOH}^{+\bullet}$  radical cation produced by photoionization of acetic acid,
- the  $\text{CH}_3\text{NHCO}^+$  formation with the concomitant loss of one water molecule from the reaction of the  $\text{HCOO}^+$  cation produced by dissociative photoionization of acetic and formic acid.

In both cases, theoretical studies have revealed a two-step reaction mechanism: i) the formation of a reaction intermediate without an energy barrier, following a process that is the reverse of that of the simple cleavage of a chemical bond, and ii) a rearrangement within this reaction intermediate, leading to the loss of a radical or molecular species. No energy excess seems necessary for these processes, which are of major interest for prebiotic chemistry, to occur.

This result is very different from what is calculated in the case of the reaction between neutral  $\text{CH}_3\text{COOH}$  and  $\text{CH}_3\text{NH}_2$ :<sup>30</sup> the photoionization of the acid partner greatly favors the reaction, from a thermodynamic point of view. This is somewhat similar to the results recently reported by Darla and Sitha on the theoretical study of the reaction between  $\text{NH}_3$  and  $\text{CO}$ ,  $\text{NH}_3^+$  and  $\text{CO}$  and  $\text{NH}_3$  and  $\text{CO}^+$ :<sup>69</sup> the mechanism of formation of the C(O)-N bond is clearly favored from a thermodynamic point of view in the case of  $\text{NH}_3$  and  $\text{CO}^+$  compared to the other two cases. It is also worth underlying that another possible C(O)-N bond forming reaction that could occur in the interstellar medium was recently evidenced from acrylonitrile and ammonia.<sup>70</sup>

Furthermore, it should be noted that ions at  $m/z$  76 were also observed from the reaction between  $\text{NH}_3\text{OH}^+$  and  $\text{CH}_3\text{COOH}$ ,<sup>71</sup> as well as in infrared assisted synthesis of prebiotic glycine.<sup>72</sup> Further studies on the formation of such prebiotic ions would be of great interest.

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#### ***V. Conclusion***

Effects of photon and collision energy on the various reaction channels have been recorded and constitute a coherent set of information, showing important internal energy effects, related to the presence of excited states in the considered energy range. The particular case of producing  $\text{COOH}^+$  from two different precursors allowed to identify specific behaviour, related to the probable larger internal energy content for the ion produced by dissociative photoionization from acetic acid than from formic acid.

1 The C(O)-N bond-forming processes herein evidenced proved to be possible, but much less efficient  
2 than the non-specific mechanisms of proton, hydride and charge transfer and associated dissociative  
3 processes between methylamine and the mass-selected ion. Thus, it seems essential to further study  
4 this kind of reactions in order to determine whether, in some cases, peptide-like C(O)-N bond  
5 formation reactions between simple precursors present in the interstellar medium could be more  
6 efficient and lead to the formation of prebiotic species. In particular, the presence of a few water  
7 molecules could greatly promote these processes, as has been demonstrated experimentally by G.  
8 van der Rest et al.<sup>73,74</sup> and theoretically by G. Bouchoux et al.,<sup>29</sup> for example. This is why we plan to  
9 couple the CERISES set-up with a supersonic jet on the DESIRS beamline of the SOLEIL synchrotron, to  
10 study the reaction of the  $\{\text{CH}_3\text{COOH}^+, (\text{H}_2\text{O})_n\}$  and  $\{\text{COOH}^+, (\text{H}_2\text{O})_n\}$  complexes with methylamine,  
11 with  $1 \leq n \leq 4$ .  
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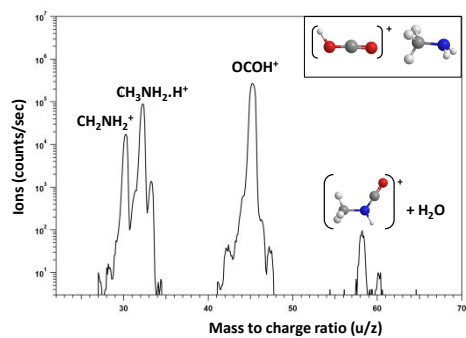
### 13 **Acknowledgments**

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16 We thank the DESIRS beamline team, for assistance during the synchrotron measurements. We are  
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18 the project n°20190680.  
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### 20 **Supporting Information.**

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23 Determination of the experimental lifetime for the metastable process leading to m/z 42 ion in the  
24 dissociative photoionization of acetic acid.  
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27 Optimized geometries of the species at the LC-wPBE/6-311++G(d,p) level of theory with their  
28 energies (including ZPE corrections).  
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**For Table of Contents Only**

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