

PEPTIDE BOND FORMATION THROUGH GAS-PHASE REACTIONS IN THE INTERSTELLAR MEDIUM: FORMAMIDE AND ACETAMIDE AS PROTOTYPES

PILAR REDONDO, CARMEN BARRIENTOS, AND ANTONIO LARGO
Computational Chemistry Group, Departamento de Química Física, Facultad de Ciencias,
Universidad de Valladolid, E-47011 Valladolid, Spain; predondo@qf.uva.es
Received 2014 June 18; accepted 2014 July 24; published 2014 September 2

ABSTRACT

A theoretical study of the reactions of NH_4^+ with formaldehyde and CH_5^+ with formamide is carried out. The viability of these gas-phase ion–molecule reactions as possible sources of formamide and acetamide under the conditions of interstellar medium is evaluated. We report a theoretical estimation of the reaction enthalpies and an analysis of their potential energy surfaces. Formation of protonated formamide from the reaction between ammonium cation and formaldehyde is an exothermic process, but all the channels located on the potential energy surface leading to this product present net activation energies. For the reaction between methanium and formamide, different products are possible from a thermodynamic point of view. An analysis of its potential energy surface showed that formation of protonated acetamide and amino acetaldehyde takes place through barrier-free paths. Therefore, this reaction could be a feasible source of acetamide and amino acetaldehyde in space.

Key words: astrobiology – astrochemistry – ISM: kinematics and dynamics – ISM: molecules – molecular processes

Online-only material: color figures

1. INTRODUCTION

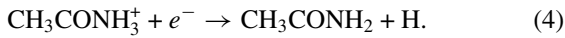
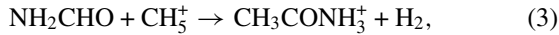
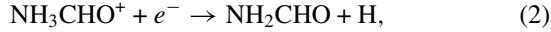
The synthesis of biomolecules under prebiotic conditions is currently one of the most interesting research subjects because it is directly related to the origin of life. In this context, a key step is the formation of peptide bonds between amino acids for obtaining proteins that are essential components of all living systems. In spite of the large number of interstellar molecules detected in space (today more than 170 species), detection of even the simplest amino acid, glycine, still remains to be confirmed (Ceccarelli et al. 2000; Hollis et al. 1980, 2003a, 2003b; Kuan et al. 2003; Snyder et al. 2005). It should be taken into account that even glycine is a relatively complex molecule, and therefore its rotational spectrum has relatively weak lines (Irvine 1998). In this sense, the availability of modern radio telescopes together with interferometry methods could facilitate its detection. In addition, the presence of amino acids in several meteorites suggests the possibility of producing them in extraterrestrial environments.

Among the organic molecules detected in space, there are two molecules with a peptide bond ($\text{NH}-\text{C}=\text{O}$), formamide (Rubin et al. 1971) and acetamide (Hollis et al. 2006). These simple molecules are important as prototypes for understanding peptide bond formation in the interstellar medium. Formamide and acetamide with both amino and carbonyl sites are expected to play a key role in the origin of life. In this way, Saladino et al. (2012) have pointed out that formamide may provide all the components necessary for the formation of nucleic polymers under prebiotic conditions. A theoretical study shows that the decomposition of formamide generates small molecules, which are useful intermediates in the prebiotic synthesis of biomolecules (Nguyen et al. 2011, 2013). The knowledge of the mechanisms involved in the formation of these simple species is essential to understanding more complex molecular evolution. The chemistry in interstellar environments is limited by the low densities and temperatures, making research in theoretical chemistry very useful in the field of astrochemistry.

Different theoretical and experimental works have been devoted to the formamide formation through gas-phase reactions or on the surface of interstellar grains. Formamide has been experimentally obtained from binary ice mixtures of CO and NH_3 irradiated by energetic particles as electrons (Jones et al. 2011). Garrod et al. (2008) proposed a new gas–grain chemical network, in which a wide array of complex species may be formed by reactions involving radicals. Formamide is formed on grain surfaces at low temperatures by successive hydrogenation of accreted OCN. They also considered its gas-phase formation through the radical–neutral reaction between H_2CO and NH_2 , but it presents net activation energy. A theoretical study of the reaction between HCOOH and NH_3 in both gas phase and ices to yield formamide was carried out by Woon (2001), but the most favorable process was found to be the formation of $\text{NH}_2\text{CH}(\text{OH})_2$. Chen & Woon (2011) also performed a theoretical study of the gas-phase reaction between H_2CO and NH_3 . They showed that the energy barrier was lowered if the reaction took place on the surface of glacial ice, using a model system with up to 12 H_2O molecules. In a recent theoretical study, we analyzed different gas-phase reactions that could yield formamide precursors (Redondo et al. 2014). The most favorable reactions from a thermodynamic point of view were the reactions of protonated neutral and ionized hydroxylamine with formaldehyde. However, the analysis of their potential energy surfaces showed that they were not viable processes under interstellar conditions.

Less is known about possible synthetic routes of acetamide in space. Hollis et al. (2006) proposed that the exothermic reaction of formamide with the methylene radical could account for the synthesis of interstellar acetamide, although this reaction involves a spin flip on the CH_2 radical and would not proceed under low temperatures. Quan & Herbst (2007) suggested that formamide and acetamide could be synthesized through radiative association reactions. The reaction of formaldehyde with protonated ammonia has been proposed to obtain formamide. Concerning acetamide, the reactions of either formamide with

CH_3^+ or acetaldehyde with ammonium ion were suggested. The ions formed in these reactions could give formamide and acetamide upon dissociative recombination. However, there are not available results for these reactions, and the estimated rate constants produce abundances lower than those experimentally determined. Recently, Halfen et al. (2011) have carried out extensive observations of acetamide and formamide toward Sgr B2(N). The similarity between the determined abundances and distribution of acetamide and formamide suggests a synthetic connection. They suggested that the following processes might lead to formamide and acetamide:



The validation of this mechanism depends on the viability of these reactions in space. However, with the only exception of the estimated reaction enthalpy for reaction (1) that we have reported in our previous work about synthetic routes of formamide formation (Redondo et al. 2014), there are not available theoretical or experimental results for the ion–molecule reactions proposed.

The objective of this work is to theoretically analyze the viability in the interstellar medium of the gas phase ion–molecule reactions, (1) and (3), which could produce protonated formamide and acetamide, respectively. First, a theoretical estimation of the reaction enthalpies for the proposed processes considering different products is reported. Second, we perform a theoretical study of the potential energy surface in order to determine if they are barrier-free processes.

2. COMPUTATIONAL METHODS

Potential energy surfaces for the ion–molecule reactions proposed in this study are analyzed. Stationary points on each surface, namely, reactants, intermediates, transition states, or products, are located at the Møller–Plesset level (MP2; Møller & Plesset 1934) in conjunction with Dunning’s aug-cc-pVTZ (correlation-consistent polarized valence triple-zeta including diffuse functions) basis set (Dunning 1989; Woon & Dunning 1993). Energy of the stationary points are refined by single point calculations at coupled-cluster level with singles and doubles and a perturbative inclusion of triple excitations (CCSD(T); Raghavachari et al. 1989) employing the aug-cc-pVTZ, and aug-cc-pVQZ (correlation-consistent polarized valence quadruple-zeta including diffuse functions) bases (Dunning 1989; Woon & Dunning 1993).

Minima and transition states are characterized by the analysis of the computed harmonic vibrational frequencies carried out at the MP2/aug-cc-pVTZ level. Zero negative eigenvalues of the analytical Hessian corresponds to a local minimum and one negative eigenvalue to a first-order saddle point. The calculated harmonic vibrational frequencies also allow us to estimate the zero-point vibrational energy (ZPVE) correction for each structure. To confirm that transition states connect the desired minima, an intrinsic reaction coordinate (IRC; Fukui 1981) has been calculated for each one.

All results reported in this work were obtained by using the *Gaussian-09* program package (Frisch et al. 2009).

Table 1
Reaction Enthalpies for the Gas-phase Reaction
 $\text{NH}_4^+(^1A') + \text{H}_2\text{CO}(^1A_1)$ Calculated at 0 K

Products	ΔH^a (kcal mol ⁻¹)	ΔH^b (kcal mol ⁻¹)	ΔH^c (kcal mol ⁻¹)
$\text{NH}_2\text{CHOH}^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-3.17	-3.12	-3.68
$\text{NH}_3\text{CHO}^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	12.52	12.91	12.89
$\text{NH}_2\text{OCH}_2^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	80.42	76.18	76.80
$\text{OH}_2\text{NCH}_2^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	77.38	72.62	73.12
$\text{OHNHCH}_2^+(^1A) + \text{H}_2(^1\Sigma_g^+)$	56.00	52.75	52.59
$\text{OHNCH}_3^+(^1A) + \text{H}_2(^1\Sigma_g^+)$	94.19	88.64	89.05
$\text{NH}_2\text{CH}_2\text{OH}^+(^2A) + \text{H}(^2S)$	95.64	93.27	93.83
$\text{NH}_3\text{CH}_2\text{O}^+(^2A'') + \text{H}(^2S)$	97.10	92.56	93.58
$\text{NH}_2\text{OCH}_3^+(^2A'') + \text{H}(^2S)$	121.13	119.46	120.26
$\text{OH}_2\text{NCH}_3^+(^2A) + \text{H}(^2S)$	149.02	144.49	145.71
$\text{OHNHCH}_3^+(^2A) + \text{H}(^2S)$	115.13	112.36	112.85

Notes.

^a Calculated at the MP2/aug-cc-pVTZ level (ZPVE included).

^b Calculated at the CCSD(T)/aug-cc-pVTZ//MP2/aug-cc-pVTZ level (ZPVE included).

^c Calculated at the CCSD(T)/aug-cc-pVQZ//MP2/aug-cc-pVTZ level (ZPVE included).

3. RESULTS AND DISCUSSION

3.1. $\text{H}_2\text{CO} + \text{NH}_4^+$ Reaction

The ion–molecule reaction between formaldehyde and ammonium cation has been proposed as a possible source of formamide in space (Halfen et al. 2011; Quan & Herbst 2007). Both reactants are present in the interstellar medium (Synder et al. 1969; Cernicharo et al. 2013). This reaction is viable in space from a thermodynamic point of view according to the reaction enthalpy calculated in our previous work (Redondo et al. 2014). We found that the formation of protonated formamide is an exothermic process by -3.06 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVQZ//B3LYP/aug-cc-pVTZ level. However, to determine the possible role of this reaction in the formation of formamide, an exhaustive study of the potential energy surface is necessary. Before analyzing the potential energy surface, we have computed the reactions enthalpies for the formation of various products. These results are collected in Table 1.

A possible product that we can obtain from the reaction of NH_4^+ and formaldehyde is protonated formamide. Protonation of formamide can take place at the oxygen atom or the nitrogen one, giving two different isomers: O-protonated formamide, $\text{NH}_2\text{CHOH}^+(^1A')$, and N-protonated formamide, $\text{NH}_3\text{CHO}^+(^1A')$, respectively. From the results shown in Table 1, we can see that only the process giving O-protonated formamide, $\text{NH}_2\text{CHOH}^+(^1A')$, is exothermic ($\Delta H = -3.68$ kcal mol⁻¹ at the CCSD(T)/aug-cc-pVQZ level). Other possible products considered are ionized aminometanol, $\text{NH}_2\text{CH}_2\text{OH}^+(^2A)$, and its isomer $\text{NH}_3\text{CH}_2\text{O}^+(^2A'')$; both processes are endothermic by more than 90 kcal mol⁻¹. Formation processes of isomers with N–O–C connectivity, namely, $\text{NH}_2\text{OCH}_2^+(^1A')$ and $\text{NH}_2\text{OCH}_3^+(^2A'')$, are clearly endothermic ($\Delta H = 76.80$ and 120.26 kcal mol⁻¹, respectively, at the CCSD(T)/aug-cc-pVQZ level). We have also considered different compounds which have O–N–C connectivity, but formation of these species from the reaction of NH_4^+ with formaldehyde is clearly endothermic (see Table 1). Therefore, only the formation of O-protonated

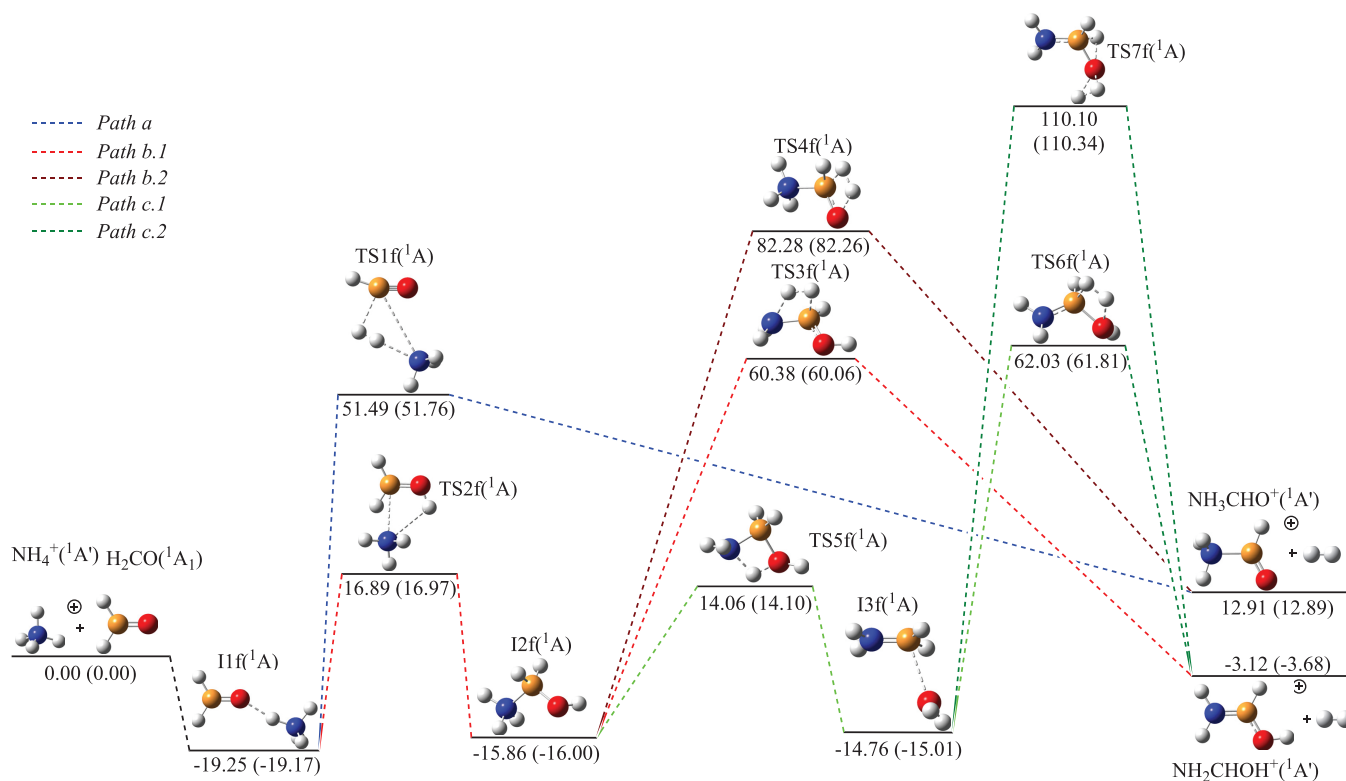


Figure 1. Energy profile, in kcal mol⁻¹, for the reaction of NH₄⁺ with H₂CO at the CCSD(T)/aug-cc-pVTZ//MP2/aug-cc-pVTZ and CCSD(T)/aug-cc-pVQZ//MP2/aug-cc-pVTZ (in parentheses) levels. Zero-point vibrational energy differences are included.

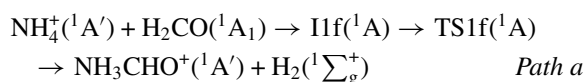
(A color version of this figure is available in the online journal.)

formamide is an exothermic process. This product could give formamide upon a recombination dissociative reaction.

Finally, we can see in Table 1 that the results obtained at the MP2 level are relatively close to those computed at the CCSD(T) level. The differences found between energies calculated at the CCSD(T) level with the aug-cc-pVTZ and the aug-cc-pVQZ bases are less than 1 kcal mol⁻¹.

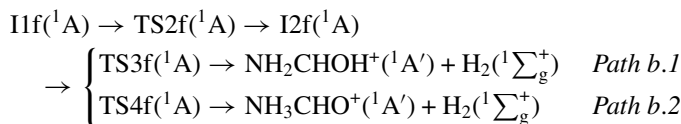
Now, we will focus on the study of the potential energy surface in order to analyze if the formation of the exothermic product, NH₂CHOH⁺(¹A'), is a barrier-free process and therefore viable in the interstellar medium. The relevant intermediate species and products, as well as the transition states of the reaction between formaldehyde and ammonium cation, are shown in Figure 1. This reaction takes place on the singlet potential surface, given the multiplicity of reactants (H₂CO(¹A₁) and NH₄⁺(¹A')). We denote intermediates and transition states for this reactions with *I**n**f* and *TS**n**f* (*n* = 1, 2, ...), respectively. As we can see in Figure 1, a similar energy profile is obtained at the CCSD(T) level with the aug-cc-pVTZ and aug-cc-pVQZ bases. The differences between the relative energies obtained with both bases are less than 0.5 kcal mol⁻¹.

The reaction of ammonium cation with formaldehyde starts with the interaction between one of the hydrogen atoms of NH₄⁺ with the carbonyl oxygen of formaldehyde resulting in the formation of an ion-molecule complex I1f(¹A'). From this complex, five different evolution channels are possible. If I1f(¹A') evolves through transition state TS1f(¹A'), we reach the less stable isomer of protonated formamide. This process corresponds to *Path a* in Figure 1 and can be summarized as



In TS1f(¹A'), formation of the C–N bond and H₂ elimination take place simultaneously. This transition state is located at 51.76 kcal mol⁻¹ above the reactants at the CCSD(T)/aug-cc-pVQZ level. Therefore, the global process, endothermic and with a net activation energy, is not feasible under interstellar conditions.

Intermediate I1f(¹A') can also isomerize to N-protonated aminomethanol, NH₃CH₂OH⁺(I2f(¹A')). Transition state TS2f(¹A') connects both intermediates. Once intermediate I2f(¹A') is reached, elimination of molecular hydrogen through transition states TS3f(¹A') and TS4f(¹A') yields both isomers of protonated formamide, NH₂CHOH⁺(¹A') and NH₃CHO⁺(¹A'), respectively (*Paths b.1* and *b.2*, Figure 1):



Path b.1 leads to the formation of the most stable isomer of protonated formamide. This process, as we have previously commented, is exothermic, but the two transition states involved, TS2f(¹A') and TS3f(¹A'), are located above the reactants (16.97 and 60.06 kcal mol⁻¹ at the CCSD(T)aug-cc-pVQZ level, respectively), and therefore this channel is not viable under interstellar conditions. N-protonated aminomethanol, I2f(¹A'), could isomerize to O-protonated aminomethanol (NH₂CH₂OH₂⁺(¹A'), I3f(¹A')) through transition state TS5f(¹A'). Both isomers of protonated formamide, NH₂CHOH⁺(¹A') and NH₃CHO⁺(¹A'), can be also reached from O-protonated aminomethanol, I3f(¹A'), by molecular hydrogen abstraction. These processes (*Paths c.1* and

Table 2
Reaction Enthalpies for the Gas-phase Reaction
 $\text{CH}_3^+ (^1A') + \text{NH}_2\text{CHO} (^1A')$ Calculated at 0 K

Products	ΔH^a (kcal mol ⁻¹)	ΔH^b (kcal Mol ⁻¹)	ΔH^c (kcal mol ⁻¹)
$\text{CH}_3\text{CONH}_3^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-55.30	-56.35	-55.80
<i>c</i> - $\text{CH}_3\text{COHNH}_2^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-66.91	-68.64	-68.63
<i>t</i> - $\text{CH}_3\text{COHNH}_2^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-69.63	-71.32	-71.33
$\text{CH}_3\text{NH}_2\text{CHO}^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-41.32	-43.26	
$\text{CH}_3\text{NHCHOH}^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-56.96	-58.99	
$\text{CH}_3\text{CNHOH}_2^+(^1A) + \text{H}_2(^1\Sigma_g^+)$	-26.00	-27.68	
$\text{NH}_3\text{CH}_2\text{COH}^+(^1A') + \text{H}_2(^1\Sigma_g^+)$	-49.59	-51.33	
<i>c</i> - $\text{NH}_2\text{CH}_2\text{CHOH}^+(^1A) + \text{H}_2(^1\Sigma_g^+)$	-21.28	-24.25	
<i>t</i> - $\text{NH}_2\text{CH}_2\text{CHOH}^+(^1A) + \text{H}_2(^1\Sigma_g^+)$	-34.54	-35.62	
$\text{NH}_2\text{CHCH}_2\text{OH}^+(^1A) + \text{H}_2(^1\Sigma_g^+)$	-41.10	-44.35	
$\text{CH}_3\text{COHNH}_3^+(^2A) + \text{H}(^2S)$	25.49	24.50	
$\text{NH}_3\text{CH}_2\text{CHOH}^+(^2A) + \text{H}(^2S)$	24.86	23.59	
$\text{CH}_3\text{CHNH}_2\text{OH}^+(^2A) + \text{H}(^2S)$	41.40	37.18	
$\text{NH}_2\text{CH}_2\text{CH}_2\text{OH}^+(^2A) + \text{H}(^2S)$	41.44	37.48	

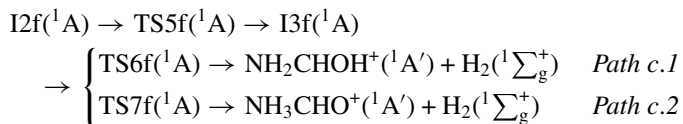
Notes.

^a Calculated at the MP2/aug-cc-pVTZ level (ZPVE included).

^b Calculated at the CCSD(T)/aug-cc-pVTZ//MP2/aug-cc-pVTZ level (ZPVE included).

^c Calculated at the CCSD(T)/aug-cc-pVQZ//MP2/aug-cc-pVTZ level (ZPVE included).

c.2 in Figure 1) can be summarized as



We can see in Figure 1 that these processes have net activation barriers since transition states involved in these paths, TS5f(¹A), TS6f(¹A), and TS7f(¹A), are clearly located above the reactants (14.10, 61.81, and 110.34 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVQZ level, respectively).

Summarizing, the analysis of the potential energy surface of the reaction between ammonium cation and formaldehyde shows that formation of O-protonated formamide (NH₂CHOH⁺(¹A')), in spite of being an exothermic process, is not viable under interstellar conditions because the different paths leading to this isomer present net activation energies. Therefore, this reaction cannot be considered as a possible source of formamide in space. If we take into account our previous results for the gas-phase reactions of ionized, protonated, and neutral hydroxylamine with formaldehyde (Redondo et al. 2014) where formation of formamide precursors is not viable from these reactions, we can conclude that other alternative routes, such as reactions on ice surfaces, should be investigated.

3.2 $\text{CH}_3^+ + \text{NH}_2\text{COH}$ Reaction

In this section, we will discuss the feasibility of acetamide formation under interstellar conditions from the reaction of methanium with formamide. It should be pointed out that CH₃⁺ has not been detected in space, but it is considered as reactant in different interstellar models. First, we analyze the reaction enthalpies for different products that can be obtained from these reactants. Reaction enthalpies are shown in Table 2. Taking into account that reaction enthalpies calculated in the

previous section at the CCSD(T)/aug-cc-pVTZ level are close to those computed at the CCSD(T)/aug-cc-pVQZ one for these systems, energy calculations are only carried out at the CCSD(T)/aug-cc-pVTZ level. As possible products, we have taken into account systems resulting from hydrogen molecule abstraction; [C₂H₆NO]⁺ + H₂. [C₂H₆NO]⁺ isomers are obtained from protonation of neutral [C₂H₅NO] systems. In a theoretical study, Lattelais et al. (2010) show that the two [C₂H₅NO] isomers of lower energy contain a peptide bond. The most stable one is acetamide CH₃CONH₂, and the next one is N-methyl formamide, CH₃NHCHO. The enolic form of acetamide, CH₃COHNH, is the third in stability. We will focus on the protonated form of these isomers which present a N–C–O connectivity and could be precursors of molecules with a peptide bond. In addition, due to its prebiotic interest, we have also considered the protonation products of amino acetaldehyde, NH₂CH₂COH, a possible precursor of glycine.

The first product that we have considered is protonated acetamide. Protonation of acetamide can take place on the nitrogen atom or on the oxygen one giving two isomers, N-protonated acetamide (CH₃CONH₃⁺(¹A')) and O-protonated acetamide (CH₃COHNH₂⁺(¹A')), respectively. Formation of N-protonated acetamide (CH₃CONH₃⁺(¹A')) is an exothermic process ($\Delta H = -56.35$ kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level). When protonation takes place on the oxygen atom, two different conformers are localized depending on the relative orientation of the proton with respect to the NH₂ unit, namely, *cis*-O-protonated acetamide (*c*-CH₃COHNH₂⁺(¹A')) and *trans*-O-protonated acetamide (*t*-CH₃COHNH₂⁺(¹A')). The formation processes of these conformers of O-protonated acetamide are exothermic ($\Delta H = -68.64$ and -71.32 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level, respectively). In order to check our energetic predictions, we have computed the reaction enthalpies for protonated acetamide at the CCSD(T)/aug-cc-pVQZ level, and as we can see in Table 2, the results are, as in the reaction between protonated ammonia and formaldehyde, close to those obtained with the aug-cc-pVTZ basis set.

Both N-protonated (CH₃NH₂CHO⁺(¹A')) and O-protonated (CH₃NHCHOH⁺(¹A')) N-methyl formamide are exothermic products ($\Delta H = -43.26$ and -58.99 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level, respectively). As in the case of acetamide, protonation on the oxygen atom is more favorable than protonation on the nitrogen one. Formation of the CH₃CNHOH₂⁺(¹A) isomer is also an exothermic process. This isomer can be considered as resulting from the oxygen atom protonation of the enolic form of acetamide. When the protonation of CH₃COHNH takes place on the nitrogen atom, we obtain O-protonated acetamide, CH₃COHNH₂⁺(¹A'). Protonation of amino acetaldehyde, on either an oxygen atom or a nitrogen one, are clearly exothermic processes. It should be noted that two different conformers are considered for the product protonated on the oxygen atom that corresponds to different orientations of the OH group with respect to the NH₂ one. Finally, we have also included the isomer corresponding to the enolic form of protonated amino acetaldehyde, NH₂CHCH₂OH⁺(¹A), which is clearly an exothermic product ($\Delta H = -44.35$ kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level). All the [C₂H₆NO]⁺ isomers considered will be reached from the reaction of CH₃⁺ with formamide.

Formation of products obtained when one hydrogen atom abstraction takes place, [C₂H₇NO]⁺ + H, is also considered. Different isomers of the [C₂H₇NO]⁺ system are taken into account, namely, CH₃COHNH₃⁺(²A), NH₃CH₂CHOH⁺(²A),

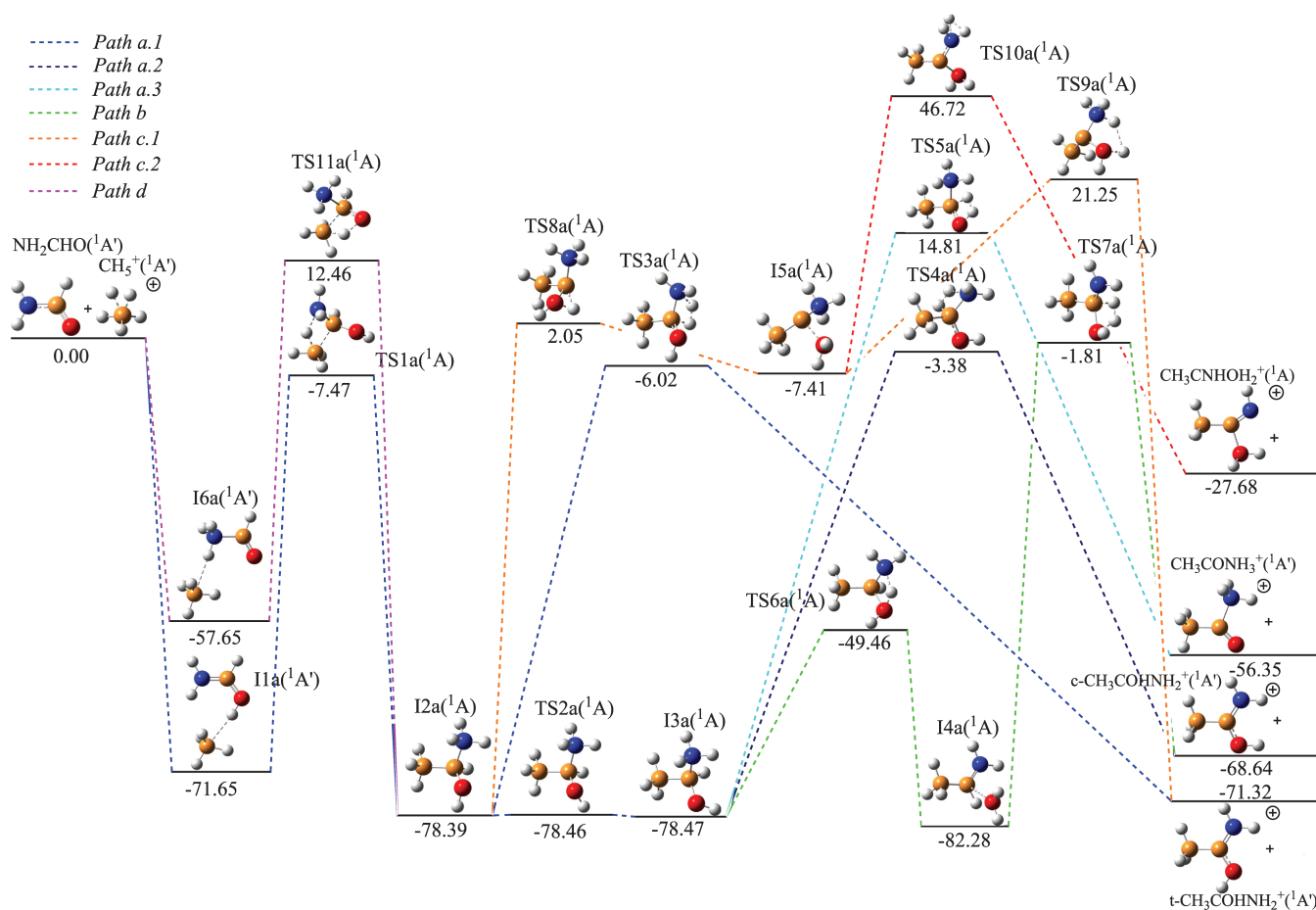


Figure 2. Energy profile (part I), in kcal mol⁻¹, for the reaction of CH₅⁺ with NH₂CHO at the CCSD(T)/aug-cc-pVTZ//MP2/aug-cc-pVTZ level. Zero-point vibrational energy differences are included.

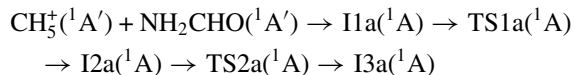
(A color version of this figure is available in the online journal.)

CH₃CHNH₂OH⁺(²A), and NH₂CH₂CH₂OH⁺(²A), but as we can see in Table 2, all the processes are clearly endothermic, and therefore they are not viable in the interstellar medium.

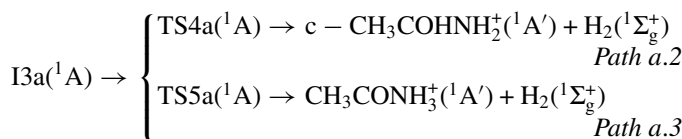
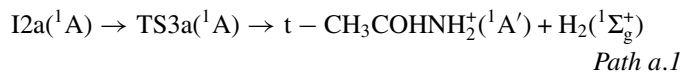
We have localized different intermediates and transition states on the singlet [C₂H₃NO]⁺ surface in order to find reliable routes leading to the formation of exothermic products. To simplify the results, the global profile for this reaction is split into two figures (Figures 2 and 3). Paths leading to the two conformers of O-protonated acetamide and N-protonated acetamide and to the formation of the oxygen atom protonated of the enolic form of acetamide are collected in Figure 2. In addition, Figure 3 shows channels leading to the formation of protonated N-methyl formamide and amino acetaldehyde on both oxygen and nitrogen atoms. Considering that the relative energies calculated with the aug-cc-pVTZ basis set and the aug-cc-pVQZ one at the CCSD(T) level are found close for the previous reaction and given the size of this system, we have just calculated relative energies at the CCSD(T)/aug-cc-pVTZ level. Intermediates and transition states for this reaction are denoted by I_na and TS_na (*n* = 1, 2, ...), respectively.

Figure 2 shows that the reaction of CH₅⁺ with formamide starts with the proton transfer from CH₅⁺ to the carbonyl oxygen of formamide, giving the intermediate I1a(¹A). Then formation of a C–C bond and the simultaneous hydrogen atom transfer from carbon to nitrogen take place through transition state TS1a(¹A) producing a second intermediate, I2a(¹A). This species can isomerize into I3a(¹A), which only differs from I2a(¹A) in the relative orientation of the O–H bond. The transition state

involved in this isomerization TS2a(¹A) is located at the MP2 level, but it is found to disappear when correlation energy is included at the CCSD(T) level; therefore, isomerization of I2a(¹A) into I3a(¹A) seems to be a spontaneous process.



Once I2a(¹A) or I3a(¹A) are reached, hydrogen molecule elimination leads to O-protonated acetamide, involving transition states TS3a(¹A) or TS4a(¹A), or N-protonated acetamide, where transition state TS5a(¹A) is implicated. These processes (Paths *a.1*, *a.2*, and *a.3* in Figure 2) can be summarized as



Path *a.1* leads to the formation of *trans*-O-protonated acetamide, an exothermic ($\Delta H = -71.32$ kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level) and barrier-free process. The transition states found along this path, TS1a(¹A), and TS3a(¹A), are located below the reactants ($\Delta E = -7.47$ and

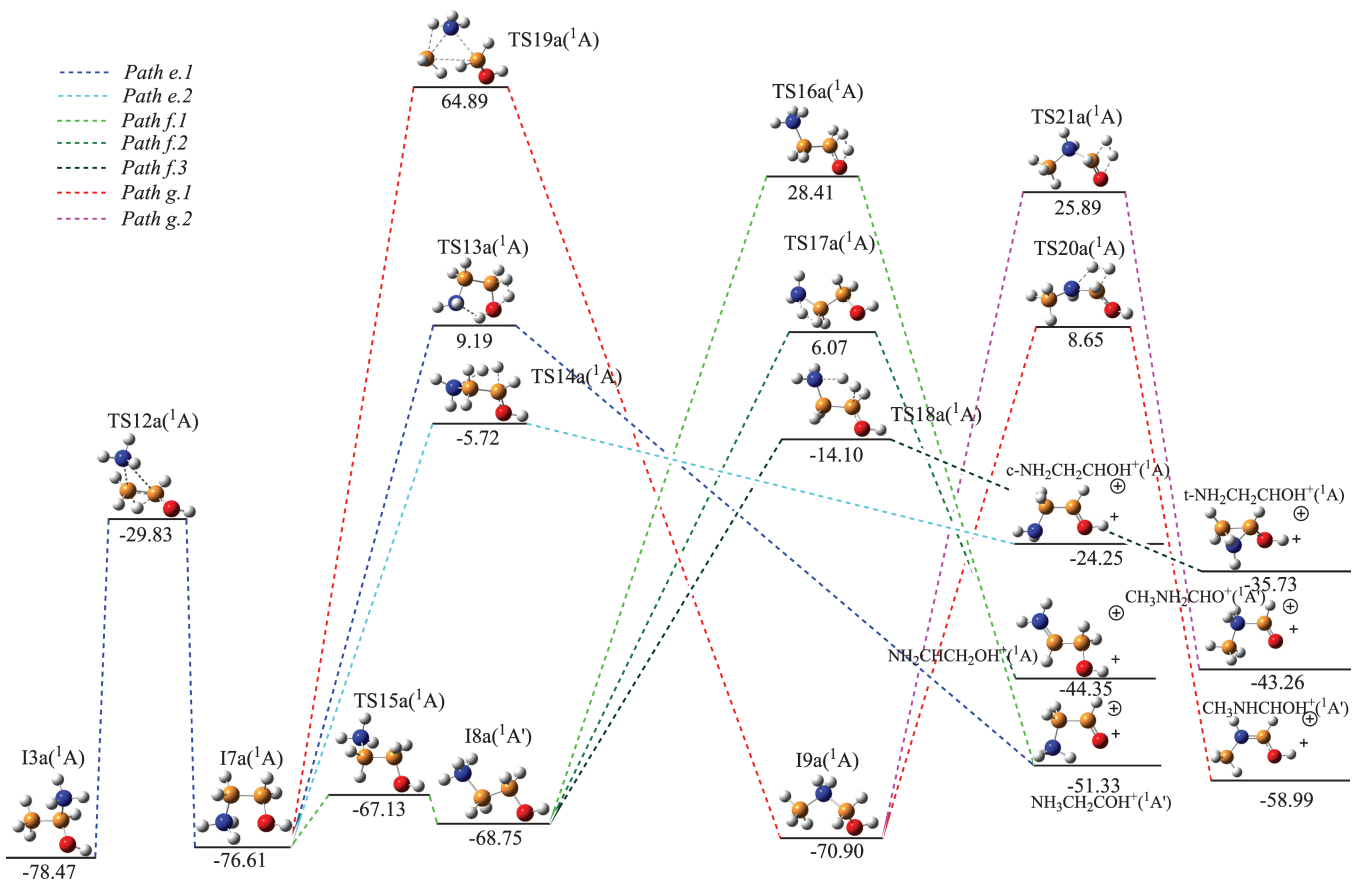
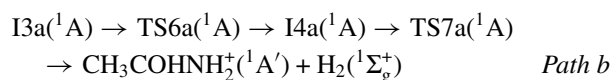


Figure 3. Energy profile (part II), in kcal mol⁻¹, for the reaction of CH₅⁺ with NH₂CHO at the CCSD(T)/aug-cc-pVTZ//MP2/aug-cc-pVTZ level. Zero-point vibrational energy differences are included.

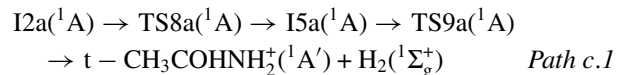
(A color version of this figure is available in the online journal.)

−6.02 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level, respectively). From I3a(1A), one can reach *cis*-O-protonated acetamide through transition state TS4a(1A) (*Path a.2*). The global process is also exothermic ($\Delta H = -68.64$ kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level) and barrier free (TS4a(1A) is located 3.38 kcal mol⁻¹ below the reactants at the CCSD(T)/aug-cc-pVTZ level). Therefore, the reaction between CH₅⁺ and formamide can yield both conformers of O-protonated acetamide under interstellar conditions. It should be pointed out that both conformers could coexist in space because the interconversion process presents a net activation barrier of 7.91 kcal mol⁻¹ evaluated at the CCSD(T)/aug-cc-pVTZ level. However, formation of the N-protonated acetamide through *Path a.3* is not viable under interstellar conditions because involves transition state TS5a(1A) which is clearly located above the reactants (14.81 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level).

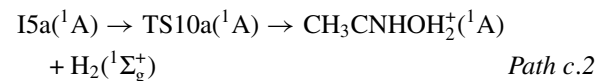
An alternative channel to obtain O-protonated acetamide is *Path b* (Figure 2), where a hydrogen transfer from the NH₃ group to the oxygen atom in I3a(1A) leads to I4a(1A). Once this intermediate is formed, H₂ elimination leads to O-protonated acetamide. In this process, TS6a(1A) and TS7a(1A) are implicated, both transition states are located below the reactants (−49.46 and −1.81 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level, respectively). Therefore, *Path b* is an alternative viable channel to obtain the *cis* conformer of O-protonated acetamide in space:



From I2a(1A), we can also reach the *trans* conformer of O-protonated acetamide following *Path c.1*:



Intermediate I5a(1A) is obtained from I2a(1A) through transition state TS8a(1A), where a hydrogen atom migration takes place from the central carbon atom to the oxygen one. Then hydrogen molecule abstraction gives a *trans* conformer of O-protonated acetamide. Transition states involved in this process, TS8a(1A) and TS9a(1A), are located above the reactants (2.05 and 21.25 kcal mol⁻¹ at the CCSD(T)/aug-cc-pVTZ level, respectively). Thus, *path c.1* is not viable under interstellar conditions because it presents a net activation barrier. Isomer CH₃CNHOH₂⁺(1A) can also be reached from I5a(1A) when molecular hydrogen is eliminated from the NH₃ group in TS10a(1A) (located 46.72 kcal mol⁻¹ above the reactants at the CCSD(T)/aug-cc-pVTZ level). Therefore, formation of the oxygen atom protonated of the enolic form of acetamide seems not viable under interstellar conditions:

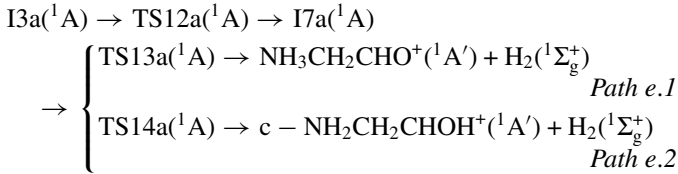


Intermediate I6a(1A) can be reached directly from reactants when proton transfer takes place from CH₅⁺ to the nitrogen atom of formamide. This intermediate evolves through transition state TS11a(1A) to intermediate I2a(1A) (*Path d*, Figure 2).

TS11a(¹A) involves the formation of a C–C bond and the hydrogen atom transfer from CH₄ group to oxygen atom. However, in this case, TS11a(¹A) is located 12.46 kcal mol^{−1} above the reactants at the CCSD(T)/aug-cc-pVTZ level, making the evolution of intermediate I6a(¹A) not viable under interstellar conditions. It should be pointed out that the initial formation of intermediate I1a(¹A) is more favorable than I6a(¹A) by 14 kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level.

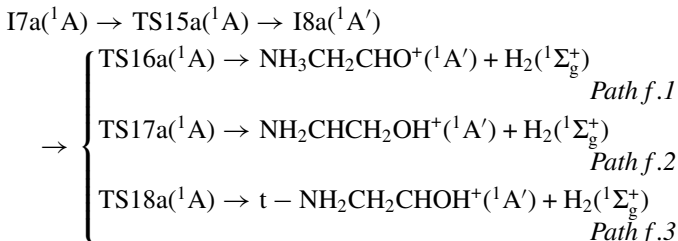
Different channels leading to the formation of protonated N-methyl formamide and amino acetaldehyde on both oxygen and nitrogen atoms (exothermic processes) are also located and collected in Figure 3. All paths start from intermediate I3a(¹A), which, as we have previously mentioned, can be reached from the reaction of CH₅⁺ with formamide under interstellar conditions (see Figure 2).

As one can see in Figure 3, the evolution of intermediate I3a(¹A) starts by its isomerization into I7a(¹A). This step involves transition state TS12a(¹A), where the NH₃ group migration from central carbon to the terminal one and simultaneous H migration in the opposite direction take place. Transition state TS12a(¹A) is clearly located below the reactants (−29.83 kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level), and therefore formation of intermediate I7a(¹A) is a feasible process in space. Then, molecular hydrogen elimination can take place through transition state TS13a(¹A) or TS14a(¹A) giving N- or O-protonated amino acetaldehyde (*cis* conformer), respectively:



Formation of N-protonated amino acetaldehyde is exothermic, $\Delta H = -51.33$ kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level, but presents a net activation barrier (TS13a(¹A) is located 9.19 kcal mol^{−1} above the reactants at the CCSD(T)/aug-cc-pVTZ level), and therefore it is not feasible under interstellar conditions. Nevertheless, formation of the *cis* conformer of O-protonated amino acetaldehyde is possible under interstellar conditions; *Path e.2* is exothermic ($\Delta H = -24.25$ kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level) and barrier free (transition state related to molecular hydrogen elimination, TS14a(¹A), is located 5.72 kcal mol^{−1} below the reactants at the CCSD(T)/aug-cc-pVTZ level).

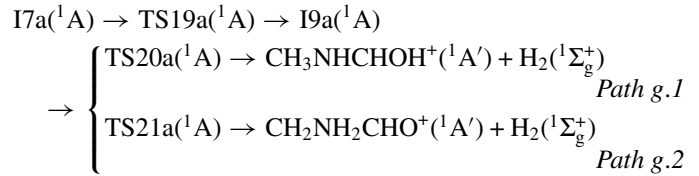
Intermediate I7a(¹A) can isomerize into its conformational isomer I8a(¹A') through transition state TS15a(¹A), clearly located below the reactants (−67.13 kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level). Then, from intermediate I8a(¹A'), we can obtain the three isomers of protonated amino acetaldehyde following the paths



We can see in Figure 3 that transition states TS16a(¹A) and TS17a(¹A), corresponding to molecular hydrogen abstraction from I8a(¹A), are located above the reactants (28.41 and

6.07 kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level, respectively). Therefore, both *paths f.1* and *f.2*, are not viable under interstellar conditions. However, formation of O-protonated amino acetaldehyde in its *trans* conformation (*Path f.3*) is an exothermic ($\Delta H = -35.73$ kcal mol^{−1} at the CCSD(T)/aug-cc-pVTZ level) and barrier free process (TS18a(¹A) involved in the molecular hydrogen elimination is located −14.10 kcal mol^{−1} below the reactants at the CCSD(T)/aug-cc-pVTZ level), therefore feasible in space.

Finally, intermediate I7a(¹A) can also isomerize to I9a(¹A) through transition state TS19a(¹A'), where the insertion of the NH₂ group into the C–C bond takes place. From this isomer, we can reach protonated isomers of N-methyl formamide. These processes can be summarized as



It is readily seen in Figure 3 that even though formation O- and N-protonated N-methyl formamide are clearly exothermic processes (−58.99 and −43.23 kcal mol^{−1} at CCSD(T)/aug-cc-pVTZ level, respectively), formation of I9a(¹A) presents a high activation barrier (TS19a(¹A) is located 64.89 kcal mol^{−1} above the reactants at the CCSD(T)/aug-cc-pVTZ level), and consequently, the reaction between CH₅⁺ and formamide cannot be a source of protonated N-methyl formamide in the interstellar medium.

The detailed analysis of the singlet potential energy surface, [C₂H₈NO]⁺, shows that protonated acetamide can be formed under interstellar conditions from the reaction of CH₅⁺ with formamide. *Paths a.1*, *a.2*, and *b* giving the two conformers of O-protonated acetamide isomer are exothermic and barrier-free processes (see Figure 2). In addition, the two conformations of protonated amino acetaldehyde can also be reached from this reaction through *Paths e.2* and *f.3* (see Figure 3). It should be pointed out that both isomers, as in the case of O-protonated acetamide, could be found in space because isomerization involves an energy barrier of 4.26 kcal mol^{−1}, estimated at the CCSD(T)/aug-cc-pVTZ level. On the other hand, our results show that precursors of N-methyl formamide are not formed in agreement with the fact that the higher-lying isomer of acetamide, N-methyl formamide, has not been detected in space in spite of being searched for in the same sources where acetamide was observed (Halfen et al. 2011).

Recently, Halfen et al. (2011) have pointed out that the similarity between the abundances and distribution of CH₃CONH₂ and NH₂CHO suggests a synthetic connection. Our results show that such a connection exists because acetamide can be obtained in space from formamide. In addition, protonated amino acetaldehyde, a glycine precursor, also can be formed. Therefore, biological molecules could be formed from formamide. In the same way, given the relatively large abundance of acetamide, this molecule could also be a source of more complex molecules.

4. CONCLUSIONS

In the present work, we theoretically analyze the viability in the interstellar medium of two gas-phase ion–molecule reactions, namely, NH₄⁺ + H₂CO and CH₅⁺ + NH₂CHO, which

could produce formamide and acetamide precursors in space, respectively. A theoretical estimation of the reaction enthalpies for the two reactions considering several products is reported. In order to determine if exothermic processes are barrier free, we perform an analysis of the corresponding potential energy surfaces.

The calculated reaction enthalpies for the reaction between ammonium cation and formaldehyde show that only formation of O-protonated formamide ($\text{NH}_2\text{CHOH}^+(^1A')$) is an exothermic process. However, the analysis of the potential energy surface shows that this process is not viable under interstellar conditions because all the paths leading to that product present net activation energies. Therefore, this reaction cannot be considered as a possible source of formamide in space. Considering our previous results for the gas-phase reactions of ionized, protonated, and neutral hydroxylamine with formaldehyde (Redondo et al. 2014), we can conclude that other alternative routes, such as reactions on the surface of interstellar grains, should be considered.

For the second reaction, $\text{CH}_5^+ + \text{NH}_2\text{CHO}$, formation of both conformers of O-protonated acetamide and N-protonated acetamide are clearly exothermic processes ($\Delta H = -71.33$, -68.63 , and $-55.80 \text{ kcal mol}^{-1}$ at the CCSD(T)/aug-cc-pVQZ level, respectively). In addition, processes giving O- or N-protonated N-methyl formamide, the oxygen protonated of the enolic form of acetamide, and O- or N-protonated amino acetaldehyde are also exothermic. The detailed analysis of the singlet potential energy surface shows that formation of O-protonated acetamide ($\text{CH}_3\text{COHNH}_2^+(^1A')$) is viable under interstellar conditions (exothermic and barrier-free process). Both conformers of O-protonated acetamide could be obtained. In addition, the two conformations of protonated amino acetaldehyde (a possible precursor of glycine) can also be reached through this reaction. Our results also show that precursors of N-methyl formamide (a high-lying isomer of acetamide) are not formed in the reaction of CH_5^+ with formamide. We can conclude that acetamide could be synthesized from formamide in the interstellar space. This synthetic connection could explain the similarity found between their abundances and distribution, as was suggested previously by Halfen et al. (2011).

Finally, taking into account the results of the present study, as well as previous works on formamide production (Redondo

et al. 2014) and glycyglycine formation (Redondo et al. 2013), it seems that formation of a peptide bond through gas-phase ion–molecule reactions is rather difficult in space. However, once a peptide bond exists, more complex molecules could be obtained through gas-phase reactions.

Financial support from the Spanish “Ministerio de Educación y Ciencia” (grant QCT2010-16864) and the “Junta de Castilla y León” (grant VA077U13) is gratefully acknowledged.

REFERENCES

- Ceccarelli, C., Loinard, L., Castets, A., Faure, A., & Lefloch, B. 2000, *A&A*, 362, 1122
- Cernicharo, J., Tercero, B., Fuente, A., et al. 2013, *ApJL*, 771, L10
- Chen, L., & Woon, D. E. 2011, *JPCA*, 115, 5166
- Dunning, T. H. 1989, *JChPh*, 90, 1007
- Frisch, M. J., Trucks, G. W., Schlegel, H. B., et al. 2009, *Gaussian 09* (Wallingford CT: Gaussian, Inc.)
- Fukui, K. 1981, *Acc. Chem. Res.*, 14, 363
- Garrod, R. T., Widicus Weaver, S. L., & Herbst, E. 2008, *ApJ*, 682, 283
- Halfen, D. T., Ilyushin, V., & Ziurys, L. M. 2011, *ApJ*, 743, 60
- Hollis, J. M., Snyder, L. E., Suenram, R. D., & Lovas, F. J. 1980, *ApJ*, 241, 1001
- Hollis, J. M., Pedelty, J. A., Boboltz, D. A., et al. 2003a, *ApJL*, 596, L235
- Hollis, J. M., Pedelty, J. A., Snyder, L. E., et al. 2003b, *ApJ*, 588, 353
- Hollis, J. M., Lovas, F. J., Remijan, A. J., et al. 2006, *ApJL*, 643, L25
- Irvine, W. 1998, *OLEB*, 28, 365
- Jones, B. M., Bennett, C. J., & Kaise, R. I. 2011, *ApJ*, 734, 78
- Kuan, J.-Y., Charnley, S. B., Huang, H.-C., Tseng, W.-L., & Kisiel, Z. 2003, *ApJ*, 593, 848
- Lattelais, M., Pauzat, F., Ellinger, Y., & Ceccarelli, C. 2010, *A&A*, 519, A30
- Møller, C., & Plesset, M. 1934, *PhRv*, 46, 618
- Nguyen, V. S., Abbott, H. L., Dawley, M. M., et al. 2011, *JPCA*, 115, 841
- Nguyen, V. S., Orlando, T. M., Leszczynski, J., & Nguyen, M. T. 2013, *JPCA*, 117, 2543
- Quan, D., & Herbst, E. 2007, *A&A*, 474, 521
- Raghavachari, K., Trucks, G. W., Pople, J. A., & Head-Gordon, M. 1989, *CPL*, 157, 479
- Redondo, P., Barrientos, C., & Largo, A. 2014, *ApJ*, 780, 181
- Redondo, P., Martinez, H., Cimas, A., Barrientos, C., & Largo, A. 2013, *PCCP*, 15, 13005
- Rubin, R. H., Swenson, G. W., Benson, R. C., et al. 1971, *ApJL*, 169, L39
- Saladino, R., Crestini, C., Pino, S., Costanzo, G., & Di Mauro, E. 2012, *Phys. Live Rev.*, 9, 84
- Snyder, L. E., Buhl, D., Zuckerman, B., & Palmer, P. 1969, *PhRvL*, 22, 679
- Snyder, L. E., Lovas, F. J., Hollis, J. M., et al. 2005, *ApJ*, 619, 914
- Woon, D. E. 2001, *IJQC*, 88, 226
- Woon, D. E., & Dunning, T. H. 1993, *JChPh*, 98, 1358