Deep-space glycine formation via Strecker-type reactions activated by ice water dust mantles. A computational approach†

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A Strecker-type synthesis of glycine by reacting NH₃, H₂C==O and HCN in presence of ice water (H₂O–ice) as a catalyst has been theoretically studied at B3LYP/6-31+G(d,p) level within a cluster approach in order to mimic reactions occurring in the interstellar and circumstellar medium (ICM). Results indicate that, despite the exothermic character of the considered reactions occurring at the H₂O–ice surface, the kinetics are slow due to relatively high electronic energy barriers (ΔU° = 15–45 kcal mol⁻¹). Reactions occurring within H₂O–ice cavities, in which ice bulk effects have been modeled by assuming a dielectric continuum (ε = 78), show energy barriers low enough to allow NH₂CH₂OH formation but not NH–CH₂ (ΔU° = 2 and 21 kcal mol⁻¹, respectively) thus hindering the NH₂CH₂CN formation, i.e. the precursor of glycine, through Strecker channels. Moreover, hydrolysis of NH₂CH₂CN to give glycine is characterized by high electronic energy barriers (ΔU° = 27–34 kcal mol⁻¹) and cannot readily occur at cryogenic temperatures. Nevertheless, the facts that NH–CH₂ formation can readily be achieved through the radical–radical HCN + 2H → NH–CH₂ reaction [D. E. Woon, Astrophys. J., 2002, 571, L177–L180], and that present results indicate that the Strecker step of NH–CH₂ + HCN → NH₂CH₂CN exhibits a relative low energy barrier (ΔU° = 8–9 kcal mol⁻¹), suggest that a combination of these two mechanisms allows for the formation of NH₂CH₂CN in the ICM. These results strengthen the thesis that NH₂CH₂CN could have been formed and protected by icy dust particles, and then delivered through micro-bombardments onto the early Earth, leading to glycine formation upon contact with the primordial ocean.

Introduction

The general fascination with the existence of interstellar and circumstellar molecules of biological interest is mainly due to the direct connection of this subject with chemical evolution and, ultimately, with the origin of life. By means of several spectroscopic observations there is now convincing evidence of the presence of a wide variety of complex organic molecules in the interstellar and circumstellar clouds of gas and dust which pervade the galaxies.1–6 Space, therefore, might have been an important source of organic molecules for the primordial Earth since some of the terrestrial prebiotic molecules could have firstly been synthesized in the interstellar and circumstellar medium (ICM) and then transported to the early Earth by comets, asteroids and meteories. However, focusing on the exogenous delivery of extraterrestrial molecules relevant for life (namely, amino acids) one gets involved in a controversy. While careful analyses of carbonaceous chondrite meteorites fallen on Earth7,8 and, more recently, of dust cometary grains collected by the Stardust spacecraft9–11 reveal the presence of several amino acids, direct detection of interstellar glycine (the simplest amino acid) is still doubtful.12–17 Despite that, amino acid precursors (molecules that lead to amino acids, usually after hydrolysis) have indeed been detected, as it is the case of aminoacetonitrile (NH₂CH₂CN), the precursor for glycine formation.18 Because of that, the search for glycine in ICM is currently the object of intensive work, which requires the development and application of state-of-the-art astronomical instrumentation for spectroscopic observations.

The plausibility of amino acids’ formation and their survival under the harsh physical conditions of space have been demonstrated by means of several experiments that simulated the conditions of the interstellar medium in the laboratory: (i) the synthesis of amino acids was successfully accomplished by UV-irradiation of interstellar ice analogs;19–22 and (ii) amino acids were observed to be photostable only when they were embedded in dust particle analogs.23 Both experiments highlighted the essential role of the grain particles in the amino acids’ synthesis and their survival. This stresses the fact that amino acids cannot be simply formed by gas-phase reactions alone; instead, their formation may be facilitated by the catalytic role played by dust grain ice particles. Other experiments were focused on the thermal reactivity, i.e., without radiation effects, of laboratory interstellar ice analogs composed of H₂O:NH₃:H₂CO at low temperatures (40–100 K).24,25 Although amino acids formation was not...
detected, it was possible, by means of infrared spectroscopy, to detect the presence of poly-oxyethylene and its derivatives, H₂CO polymers and NH₂CH₂OH as organic residues. Indeed, NH₂CH₂OH is relevant as an intermediate product of the Strecker synthesis, one of the possible routes to synthesize amino acids.

In spite of the experimental evidence, very little is known about the mechanistic steps through which amino acids form. As quoted previously, the oldest and most known postulated mechanism for amino acids formation is the Strecker-type synthesis. This reaction has been suggested to occur in ICM and also in the primitive Earth atmosphere, as a possible indigenous amino acid synthesis, and is currently the simplest and most economical method for the preparation of \( \alpha \)-amino acids in labs at technical scale. The Strecker reaction overall comprises a condensation of an aldehyde or ketone with an amine, the nucleophilic attack of a cyanide molecule, followed by the subsequent hydrolysis of the resulting \( \alpha \)-amino nitrile. By means of the simplest reactants, namely formaldehyde H₂C=O, ammonia NH₃ and hydrogen cyanide HCN, the final product is glycine NH₂CH₂COOH (see Scheme 1). The fact that such reactants are available in relative abundance in ICM, coupled to the fact that UV-photolysis of a H₂O:CH₂OH:NH₃:HCN interstellar ice analog (CH₂OH decomposes to H₂C=O) resulted in amino acids formation, strengthened the thesis that a Strecker-based reactions may indeed occur in ICM. However, isotopic labeling revealed that the Strecker mechanism accounts only partially for some of the observations, so other mechanisms (e.g. radical–radical) or a mixture of them have also been proposed.

Direct experimental measurements to elucidate reaction mechanisms are difficult to perform, whereas, in contrast, quantum mechanical methods can be readily adopted to study a variety of possible reaction mechanisms by exploring the potential energy surfaces (PES). In this context, ion–molecule reactions and radical–molecule mechanisms occurring in the gas-phase have been studied theoretically. More recently, the role of ice grain water (H₂O–ice) mantles on the thermal formation of the aminoacetonitrile precursor or glycine has been addressed theoretically, showing a strong catalytic effect of H₂O–ice, due to the proton mobility at the ice surface itself. This is similar to that observed for heterogeneous reactions occurring on stratospheric ices, which do not proceed in the gas-phase.

In the present work the Strecker reactions occurring at the surface or within a H₂O–ice mantle of a dust grain under the ultracold and high-vacuum conditions present in the ICM have been simulated by quantum mechanical methods based on density functional theory. For the first time, the whole Strecker mechanism (i.e. the condensation of H₂C=O, NH₃ and HCN to form glycine) on a cluster model mimicking crystalline H₂O–ice has been addressed, with the aim that the present results will contribute to understanding the ease with which the reactive pathways yield glycine precursors.

**Computational details**

All calculations have been performed using the GAUSSIAN03 package. The structure of each stationary point has been fully optimized using the hybrid B3LYP functional with the 6-31+G(d,p) basis set. All structures have been characterized by the analytical calculation of the harmonic frequencies as minima (reactants, intermediates and products) and saddle points (transition states). For more difficult cases, we have carried out intrinsic reaction coordinate (IRC) calculations at the same level of theory to ensure that a given transition structure connects the expected reactants and products. The zero point energy (ZPE)-corrected and Gibbs free energy profiles were obtained by computing the thermochemical corrections to the energy values using the standard harmonic oscillator formulae computed at B3LYP/6-31+G(d,p). In order to account for long-range effects of the H₂O–ice bulk matrix on the energy profiles, single-point energy calculations using the conductor polarized continuum model (CPCM) have been carried out at the optimized gas-phase geometries considering the dielectric constant of ice as equal to that of water (see discussion below). The ZPE-corrected energy profiles including bulk effects were estimated by including the gas-phase ZPE corrections on the CPCM-electronic energies.

**Results and discussion**

**Ice model**

According to a cyclic evolutionary model of interstellar dusts, in molecular clouds, dust grains consist of a core composed of refractory materials such as silicate and amorphous carbon particles, and of a mantle of different frozen molecules covering the core, where ice water is generally the most abundant constituent. At the extremely low pressures and temperatures at which icy grain mantles form, the dominant morphology is probably a high-density amorphous ice. In contrast, when the ice is warmed up, H₂O molecules re-arrange in a crystalline structure, so that both amorphous and crystalline phases are present in ICM. Crystalline ices have indeed been detected in ICM and in cometary comas, and laboratory experiments suggest that their formation may be due to the exposition of dust particles to temperatures of about 150–200 K.

Modelling at an *ab initio* level an amorphous material is rather problematic because its disordered nature implies the presence of various surface sites and defects so that, one needs to adopt large unit cells, rendering the calculations very demanding. Nonetheless, for the particular case of ice water, a combined experimental and theoretical work of Allouche et al. intended to analyze the adsorption of CO on different amorphous and nanocrystalline ice samples concluded that, at the molecular scale, the amorphous ice can be partly considered as an ordered material. Based on these results, in the present
Fowler–Pauling (BFP) rules a structural model for Ih because the position of the protons follows the Bernal–hexagonal ice, Ih. Ih is a proton-disordered system, and stable form of ice at low pressures and temperatures is presence of a minute amount of hydroxide anions at 72 K. Ice XI is a proton-ordered low-quantum mechanically. Ice XI is a proton-ordered low-
in agreement with the BFP rules would be very costly to treat

\[ \Delta U^a_{\text{opt}} = \text{ZPE-corrected energy barriers} \]

\[ \text{(kcal mol}^{-1}\text{)} \]

computed at B3LYP/6-31+G(d,p) level are also included.

work, we have resorted to a given crystalline ice phase to model the H2O–ice mantle. On Earth, the naturally occurring stable form of ice at low pressures and temperatures is hexagonal ice, Ih. Ih is a proton-disordered system, and because the position of the protons follows the Bernal–Fowler–Pauling (BFP) rules a structural model for Ih envisaging all the hypothetical proton-ordered substructures in agreement with the BFP rules would be very costly to treat quantum mechanically. Ice XI is a proton-ordered low-temperature analogue of ice Ih, which is formed in the presence of a minute amount of hydroxide anions at 72 K and is the one that has been adopted here as the crystalline model (see Fig. 1a, periodic system). The theoretical study of both bulk and surface structures of ice XI allows to adopt it as a reasonable model for a disordered ice water, because it reflects properly its physico-chemical features in a cost-effective way.70–73

In the present work, we have adopted the cluster model that arises from the (010) ice XI surface, shown in Fig. 1a (cluster model). This H2O–ice model shows two relevant features that need some consideration. First, the cluster becomes dramatically deformed upon full geometry optimization due to the formation of extra hydrogen bonds (H-bonds) at the edge of the cluster, not present in the bulk structure. Thus, in order to overcome such artifact, the atomic positions where the reactions are expected to occur (atoms depicted as balls in Fig. 1a) have been fully optimized, while keeping the atoms at the frontier (atoms depicted as cylinders in Fig. 1a) fixed at their crystal positions. This strategy, while limiting the deformation of the cluster may result in a general increase of the energy barriers for the considered reactions. Second, the ice cluster surface structure allows for an easier proton-transfer between icy protons and the adsorbed molecules by what is called the “proton relay” mechanism. Theoretical works evidenced a strong catalytic effect of this mechanism, including astrochemical reactions occurring at H2O–ice surfaces.41,43

Some calibration of the H2O–ice cluster model was carried out to compute the energy penalty due to the geometrical constraints and to check for the catalytic effect on a possible proton assisted mechanism. The CNH/HCN isomerization in presence of the H2O–ice model was chosen as a model reaction by performing both full and partial geometry relaxation of the cluster. Results are shown in Fig. 1b and reveal that: (i) the ZPE-corrected energy barriers (\( \Delta U^r_0 \)) for the full and the partial relaxation cases are in excellent agreement with each other (7 and 8 kcal mol\(^{-1}\), respectively); and (ii) the H2O–ice cluster does catalyse the reaction compared to gas-phase (\( \Delta U^r_0 = 30 \text{ kcal mol}^{-1}\), see Fig. S1 in the ESI) by helping the H-exchange via surface proton relay scheme. In view of these results, the constrained crystalline-based H2O–ice cluster was adopted as a model catalyst for the formation of glycine via Strecker reactions.

**Strecker reaction on H2O–ice**

As mentioned, the Strecker synthesis consists of several chemical reactions to form \( \alpha \)-amino acids. The proposed mechanism is sketched in Scheme 1, which focuses on glycine formation. The reaction starts by water elimination between ammonia and formaldehyde to give methanimine NH—CH2 as an intermediate. Subsequently, the carbon atom of HCN bonds the carbon atom of NH—CH2 to give aminoacetonitrile NH2CH2CN as the \( \alpha \)-aminonitrilte intermediate. Finally, hydrolysis of NH2CH2CN leads to the formation of glycine as the final \( \alpha \)-amino acid product.

The isolated gas-phase reactions of the Strecker mechanism were computed at the B3LYP/6-31+G(d,p) level of theory, resulting in energy barriers with \( \Delta U^r_0 \) in the 40–55 kcal mol\(^{-1}\) range (ZPE-corrected energy profiles and optimized structures reported in Fig. S2, S3 and S4 of the ESI), so that reactions would barely occur under these conditions.

In the following, each step of the Strecker mechanism is studied in the presence of the H2O–ice cluster model to assess its catalytic role. For all calculations we have assumed that the reactants are in close proximity to each other when contacted with the ice water. Rigorously, diffusion of the species on the surfaces or in the ice bulk is completely negligible, except for H atoms, if no energy inputs exist. Nevertheless, the harsh physical conditions of space ensure the action of several energy inputs such as UV radiation, cosmic rays, and shock waves onto the ice mixtures, so that, at least in principle, diffusion of the reactants to come closer is expected to easily occur. Despite that, however, it is worth mentioning that UV effects, assumed to be essential in laboratory experiments, have not been taken into account in the present work; that is, only neutral closed-shell species have been considered in the reactions. There are two reasons for that: (i) dealing with open-shell systems would dramatically increase the complexity of the problem and the computational burden; and (ii) the scope of the work is to determine the intrinsic role (namely, without external agents) of the H2O–ice mantles in the interstellar and circumstellar processes as well as to estimate the most
favorable reactive channels of the Strecker synthesis at cryogenic temperatures. The role of UV radiation and cosmic rays will be addressed in future work.

**Methanimine NH==CH₂ formation.** Ammonia adds to formaldehyde by a concerted nucleophilic attack of the N atom towards the carbonyl C atom and a proton transfer from NH₃ to the carbonyl O to give the NH₂CH₂OH intermediate, which is then converted to NH==CH₂ by water elimination. The catalytic role played by the H₂O–ice cluster is seen in the computed ZPE-corrected energy profile shown as Step I of Fig. 2. Starting from the pre-reactant complex R1, the condensation between NH₃ and H₂C==O occurs through a transition state TS₁₁ with the development of a direct N–C bond and the proton transfer from NH₃ to H₂C==O as favoured by the proton relay mechanism within the H₂O–ice cluster. For this process the computed ΔUᵢ is 9.6 kcal mol⁻¹, with the intermediate NH₃CH₂OH (I₁) being 7.1 kcal mol⁻¹ lower in energy than R1. I₁ is a H-bond complex between NH₃CH₂OH and H₂O–ice cluster, whose configuration is not suitable for the successive water elimination. Nevertheless, rotation by 180° of NH₃CH₂OH as a whole (costing around the interaction energy, i.e. 9 kcal mol⁻¹), gives I₁₁ (0.3 kcal mol⁻¹ above I₁) from which the release of water through TS₁₂ (14.5 kcal mol⁻¹ with respect to R1) leads to NH==CH₂ with a final ZPE-reaction energy (ΔU₀) of −6.2 kcal mol⁻¹. The ΔUᵢ values for the analogue reactions in gas-phase are 32 kcal mol⁻¹ and 44 kcal mol⁻¹ for the first and second process, respectively, while the final ΔU₀ is −1 kcal mol⁻¹ (see the ESI for gas-phase reactions†). These data show that the H₂O–ice mantle does indeed lower the considered reactions compared to those occurring in gas-phase.

The reaction of H₂ with HCN also leads to the formation of NH==CH₂. This reaction has also been studied due to the abundance of H₂, although it is not involved in the Strecker mechanism. The computed gas-phase calculations gives ΔUᵢ = 85 kcal mol⁻¹ and Δ₀U₀ = −10 kcal mol⁻¹, which become 49 kcal mol⁻¹ and −13 kcal mol⁻¹, respectively, when it occurs at the surface of the crystalline H₂O–ice (data available in Fig. S5 of the ESI†).

**Aminoacetonitrile NH₂CH₂CN formation.** The gas-phase reaction between HCN and NH==CH₂ does not yield NH₂CH₂CN, but its isomer NH₂CH₂NC (17 kcal mol⁻¹ less stable). This has been computed already by Koch et al. and is confirmed by the present calculations (see the ESI† for details). Thus, in the gas-phase, two steps are needed to form aminoacetonitrile: (i) promotion of HCN into its isomer CNH; and (ii) reaction of CNH with NH==CH₂. This process is energetically costly since ΔUᵢ values for the isomerization and for the aminoacetonitrile formation are 44 and 40 kcal mol⁻¹, respectively (see Fig. S3 of the ESI† for details). Fortunately, the HCN/CNH isomerization is catalyzed by the presence of the H₂O–ice mantle (see Fig. 1b). Indeed, calculations in the presence of crystalline H₂O–ice model (Fig. 3a, Step 2-i) shows that the isomerization of HCN from R₂-i to TS₂₁-i results in a ΔUᵢ of 18.0 kcal mol⁻¹ (TS₂₁-i), and the resulting H-bonded intermediate (I₂-i) is 10.3 kcal mol⁻¹ higher in energy than R₂-i. As shown by Fig. 3a, the above process occurs in presence of NH==CH₂, which remains physisorbed to H₂O–ice as an inert species. H-bond rearrangement in I₂-i leads to the nearly degenerate I₂-r-i intermediate, which can evolve to aminoacetonitrile P₂-i through a ΔUᵢ of 29.9 kcal mol⁻¹ (TS₂-r-i with respect to the R₂-r-i reference state). These data show that the final product P₂-i is thermodynamically very favorable (−15.2 kcal mol⁻¹) and that the H₂O–ice exerts a noticeable catalytic effect. The same reaction was computed by Koch et al., obtaining an energy barrier of 22 kcal mol⁻¹. The energy differences can be rationalized by considering that Koch et al. used three completely free water molecules to simulate the amorphous icy particle, resulting in more degrees of freedom to stabilize the activated complex. Nevertheless, for both

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**Fig. 2.** ZPE-corrected B3LYP/6-31+G(d,p) potential energy profile for the reaction NH₃ + H₂C==O → NH==CH₂ + H₂O (Step I) in presence of H₂O–ice model following the Strecker mechanism. Relative energy values refer to the R1 structure. Energies in kcal mol⁻¹; bond distances in Å. Only the optimized part of the H₂O–ice model is shown for the sake of clarity.
cases, the computed energy barriers are rather high for the ICM conditions, so that alternative reaction paths may be feasible.

One of the main features of water, irrespective of its state, is its capacity to stabilize charged species. In the ICM this is not an exception and, indeed, it is widely accepted that both anions and cations exist in space, probably confined within ice water, as theoretical results pointed out. Following this idea, Koch et al. reported a new mechanism for the aminoacetonitrile formation arising from the reaction between CN and NH$_2$CH$_2$+, in which both ionic species are stabilized by water molecules. In the gas-phase this process cannot proceed because of the extremely high energy barrier due to charge separation cost. However, icy particles may screen charged species, so that this mechanism is analyzed in presence of the crystalline H$_2$O–ice model. Results are shown in Fig. 3b (Step 2-ii). The first barrier refers to the formation of the CN$^-$ and NH$_2$–CH$_2$$^+$ ions, in which the proton of HCN is transferred to the nitrogen atom of NH$\equiv$CH$_2$ via a proton relay mechanism involving two H$_2$O molecules of the six-membered ring of H$_2$O-ice. The $\Delta U_0^a$ for this transfer is 17.5 kcal mol$^{-1}$ (TS$_2$-ii) and the resulting intermediate I$_2$-ii, which carries the (CN$^-$)/(NH$_2$–CH$_2$$^+$) ion pair, remains 15.5 kcal mol$^{-1}$ above R$_2$-ii. From I$_2$-ii, the C–C bond formation leads to NH$_2$CH$_2$CN with a $\Delta U_0^a = 16.2$ kcal mol$^{-1}$ (TS$_2$-ii) with respect to R$_2$-ii and a negative $\Delta U_0$ of $-14$ kcal mol$^{-1}$ (P$_2$-ii). It is worth to note that, if I$_2$-ii is taken as the reference state for the (CN$^-$)/(NH$_2$–CH$_2$$^+$) reaction, the process for the aminoacetonitrile formation is practically barrierless. This observation highlights the role of polar ices as plausible drivers to induce astrochemical ion pair reactions at low energy cost. It is worth mentioning that if a C–N bond formation from I$_2$-ii ...
occurs, the final product would be the NH$_2$CH$_2$NC isomer. Although the energy barrier is similar to the other path, the $\Delta_U^0$ is positive so its formation is thermodynamically unfavoured (see Fig. S6 of the ESI† for details).

**Hydrolysis of NH$_2$CH$_2$CN.** The final steps leading to glycine formation envisage the nucleophilic attack of one H$_2$O molecule towards the nitrile group of NH$_2$CH$_2$CN to give NH$_2$CH$_2$(=O)NH$_2$ (Fig. 4a, Step 3), followed by the nucleophilic attack of a second H$_2$O molecule to the carbonyl C atom to give ammonia and glycine NH$_2$CH$_2$(=O)OH as final products (Fig. 4b, Step 4). In liquid water, the hydrolysis of NH$_2$CH$_2$CN towards glycine is immediate; clearly this will not be the case on icy particles in which water mobility is reduced by the crystalline field and by the very low temperatures. Here, the H$_2$O molecules responsible of steps 3 and 4 are assumed to derive from evaporation processes occurring at the icy surface particles so that in the calculation they have been added to the reaction as they were coming from gas-phase.

Results for the first and second H$_2$O additions are reported in Fig. 4. Step 3 and Step 4, respectively. The first H$_2$O nucleophilic attack (Fig. 4a) involves the C$_{\text{nitrile}}$-O$_{\text{water}}$ bond formation along with a proton transfer (assisted by the H$_2$O-ice) from water to the N$_{\text{nitrile}}$ atom. This process exhibits a large $\Delta U^0$ of 37.9 kcal mol$^{-1}$ (TS$_{31}$) and the resulting NH$_2$CH$_2$(=OH)NH intermediate I$_3$ corresponds to the enol tautomeric form of 2-aminoacetamide. The keto-enol tautomerization given through a proton relay ring transition state (TS$_{32}$) of low activation energy ($\Delta U^0 = 4.8$ kcal mol$^{-1}$ with respect to R$_3$) leads to the more stable keto NH$_2$CH$_2$(=O)NH$_2$ form (P$_3$). The second H$_2$O nucleophilic attack proceeds similarly to the first one (Fig. 4b); i.e., C$_{\text{amide}}$-O$_{\text{water}}$ bond is formed simultaneously to a proton transfer from water to the N$_{\text{amide}}$ atom, followed by ammonia elimination. However, at variance with the previous steps, this one proceeds without a direct proton assistance from the H$_2$O-ice cluster (see TS$_4$) with a $\Delta U^0$ value of 39.0 kcal mol$^{-1}$. The same process directly assisted by the H$_2$O-ice cluster has

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**Fig. 4** ZPE-corrected B3LYP/6-31 + G(d,p) potential energy profile for reaction (a) NH$_2$CH$_2$CN + H$_2$O $\rightarrow$ NH$_2$CH$_2$(=O)NH$_2$ (Step 3) and (b) NH$_2$CH$_2$(=O)NH$_2$ + H$_2$O $\rightarrow$ NH$_2$CH$_2$(=O)OH + NH$_3$ (Step 4) in presence of H$_2$O-ice model following the Strecker mechanism. Relative energy values refer to R$_3$ and R$_4$ structures for Step 3 and Step 4, respectively. Energies in kcal mol$^{-1}$; bond distances in Å. Only the optimized part of the H$_2$O-ice model is shown for the sake of clarity.
also been studied (see Fig. S7 of the ESI† for details); the computed $\Delta U^r_0 = 50.8$ kcal mol$^{-1}$ is, however, much higher than the case in which the water molecule remained far from the icy particle. The reason for the higher barrier of the latter process can be explained by considering that the highest energy TS4 (see Fig. S7, the ESI†) envisages the icy particle as proton donor towards the NH$_2$ group and as proton acceptor from the water involved in the nucleophilic attack. This implies a large and costly proton rearrangement within the icy surface ring, which is absent for the TS4 of Step 4 (Fig. 4), in which the icy particle more naturally acts as proton acceptor from the NH$_3^+$ group and as proton donor to the OH$^-$ moiety.

Environmental factors affecting reaction profiles

Most of the considered energy profiles exhibit rather high energy barriers for these reactions to easily occur within the ICM physico-chemical conditions. However, the computed profiles are based on ZPE-corrected values, that is, $T = 0$ K and the cluster is considered isolated from its surroundings. In order to have a deeper insight onto the possible role of different environmental factors, the effect of temperatures higher than 0 K and the co-presence of H$_2$O–ice bulk surrounding the active surface have been investigated on Step 1, Step 2–ii, Step 3 and Step 4, respectively.

**Temperature effects.** Deep-space is usually at ultra-cold temperatures, namely between 10–20 K. However, particular regions can have higher temperatures, as is the case of hot molecular cores, whose temperature may range between 100–200 K. Due to that, the thermochemistry of the stationary points involved in the different reactions paths has been computed at $T = 10$, 100 and 200 K. The new relative free energy values computed at these temperatures ($\Delta G_T$) are reported in Table 1. It is worth noting that at $T = 200$ K in the ICM is totally desorbed, so that $\Delta G_{200}$ values have been provided just to emphasize the trend with increasing $T$. In most of the stationary points the relative ZPE-corrected and free energy values at $T = 10$ K are practically identical; however, higher temperatures slow down and disfavor the reactions as the energy barriers and the reaction energies increase slightly, by about 2 kcal mol$^{-1}$ at the most. This is due to entropic effects since the computed relative enthalpy values differ only by 0.1–0.3 kcal mol$^{-1}$ with respect to the ZPE-corrected ones. This is consistent with the facts that: (i) molecules in the TS need to be properly oriented in order to adopt a proton relay mechanism, so that the entropy decreases in the TS compared to the reactants; (ii) P2–ii (Fig. 3b) and P3 (Fig. 4a) (products with one adsorbed molecule only) arise from the collision of two reactant molecules, so that their entropy is disfavored with respect to R2–ii and R3. Indeed, for cases in which the number of adsorbed species is the same in reactants and products (P1, Fig. 1 and P4, Fig. 4b) free energies almost coincide with ZPE-corrected profiles. Overall, these results indicate that an increase of temperature disfavors all the considered reactions due to unfavourable entropic contributions.

**H$_2$O–ice bulk effects.** The reactions shown above are meant to occur at the surface of H$_2$O–ice in which molecules from the gas-phase are adsorbed at the surface of icy grain particles. The considered model can, however, be confined within cavities of the icy mantles so that the reactive processes can suffer the effect of the dielectric response due to bulky ice. In quantum chemistry different strategies have been proposed to account for bulk effects, for instance when one needs to simulate solvent effects. In this respect, the continuum solvent field method is often employed due to its good balance between accuracy and simplicity. 77 This method, which has been also applied for biomolecular simulations, 78 represents the bulk as a continuous medium which is characterized by a dielectric constant, $\varepsilon$. Eyring and coworkers, in a seminal paper, reported the dielectric constant of various forms of ice, the value of ice Ih at 216.3 K being $\varepsilon = 114.79$ Nonetheless, the actual value of the dielectric constant of the interstellar ices at cryogenic temperatures is vaguely known, so that in the present work the H$_2$O–ice cluster model including the adsorbates has been embedded in a continuum model with dielectric constant $\varepsilon = 78$, equal to that of liquid water.

Table 2 summarises the computed relative ZPE-corrected energies under the effect of bulk ice. Results indicate that bulk effects lower considerably some energy barriers, and especially those involving charged species. This is the case for Step 1 and Step 2–ii: in the former, the first energy barrier TS1 decreases to 2 kcal mol$^{-1}$ and the second TS1 to 10 kcal mol$^{-1}$; in the latter, the overall energy profile lowers in energy due to the stabilization of the (CN$^-$/NH$_2$H$^-$/CH$_3^-$) ion pair, energy barriers being around 8–9 kcal mol$^{-1}$. Nonetheless, for the steps concerning the aminoacetonitrile hydrolysis (Step 3 and Step 4), although the barriers are lowered by some amount (specifically TS4, involving the zwitterion-like structure), they are still high (27–43 kcal mol$^{-1}$) to proceed at cryogenic temperatures.

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Table 2  B3LYP/6-31 +G(d,p) relative ZPE-corrected energy values of the stationary points involved in the most favorable paths of the glycine formation for the isolated H2O–ice cluster and when embedded in a water dielectric medium (ε = 78), [H2O–ice]w, simulating the bulk ice. Data in kcal mol⁻¹

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<th>I1</th>
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<td>[H2O–ice]w</td>
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Discussion and concluding remarks

Reactions between NH3, H2C=O and HCN confined on or within interstellar and circumstellar H2O-ice mantles have been investigated quantum mechanically at the B3LYP/6-31+G(d,p) level with the purpose of simulating the Strecker glycine synthesis in ICM. As a first step, the reaction mechanisms and the intrinsic role of water ice as catalyst have been studied. A water cluster (H2O–ice model) extracted from the proton ordered water cluster (H2O–ice model) extracted from the proton ordered and the intrinsic role of water ice as catalyst have been studied. A 6-31+G(d,p) level with the purpose of simulating the Strecker mechanism referred as "proton relay", in which water molecules belonging to rings of the icy surface behave simultaneously as proton acceptor/donor. The proton relay significantly lowers the energy barriers compared to gas-phase mechanisms, up to 30 kcal mol⁻¹ as a maximum. Additionally, also some of the reaction energies are somehow more favorable in presence of H2O-ice due to H-bonds with the ice surface. An important outcome of the present calculations has been to show that H2O-ice surfaces strongly stabilize charged species, so that mechanisms involving ion pairs may become favoured. This is indeed the case for the reaction between HCN and NH—CH2, in which the H2O-ice surface stabilizes the (CN⁻)(H2N—CH2⁺) ion pair to be subsequently converted into aminoacetonitrile via almost barrierless direct C–C bond formation.

For reactions considered to occur on the surface of the ice water mantles theoretical calculations show that the first (NH3 + H2C=O → NH=CH2 + H2O) and the second (NH—CH2 + HCN → NH2CH2CN) steps exhibit the lowest energy barriers, although still considerably high (between 10–18 kcal mol⁻¹) to occur at cryogenic temperatures. Hydrolysis of NH2CH2CN that finally yields glycine (here modeled by nucleophilic attack of two H2O molecules) results in very high energy barriers. The computed reaction energies ΔU0 associated with different steps of the Strecker mechanism bringing reactants to glycine are in the −3 and −19 kcal mol⁻¹ range, showing favorable thermodynamics.

Reactions considered to occur within ice cavities, where the long-range electrostatic effects exerted by the H2O-ice bulk (here simulated by the inclusion of a dielectric continuum with ε = 78) are present, exhibit significantly lower energy barriers than those occurring at the H2O-ice surface (see Table 2). For Step 1, such a lowering is indeed important in its first part i.e., the NH2CH2OH formation, ΔU0 being reduced to 2 kcal mol⁻¹, but not enough as to reach the final NH—CH2 product, as the computed ΔU0 from I1 is 21 kcal mol⁻¹, too high for reactions at cryogenic temperatures. Accordingly, whereas the first part is expected to proceed the second one is hampered by kinetic reasons. These results are in full agreement with the experimental work of Bossa et al., 25 in which the reaction between NH3 and H2CO to give NH2CH2OH was observed to occur in laboratory in the presence of interstellar ice analogs and by thermal activation, whereas the de-hydration step leading to NH—CH2 was not observed. The kinetic barriers of Step 2 decrease to 8–9 kcal mol⁻¹, thus partly allowing the aminoacetonitrile formation in ICM conditions through charged intermediates. Calculations, however, show that glycine formation via aminoacetonitrile hydrolysis is hindered by too high kinetic barriers of the Step 3 and Step 4, namely ΔU0 = 34 and 30 kcal mol⁻¹, respectively.

In summary, despite the dramatic energy barrier lowering caused by the action of H2O-ice, some of the computed values are still exceedingly high, too high to allow the reactions to occur at cryogenic temperatures, and accordingly, suggest that glycine formation cannot proceed via Strecker-type mechanisms in its closed-shell formulation and via thermal promotion. Because of that, in addition to temperature, other substantial energy inputs available in space such as UV radiation or cosmic rays are required for the Strecker synthesis to be a reaction channel for glycine formation in ICM. Clearly, alternative mechanisms yielding glycine are also possible. For instance, the radical–radical mechanism studied by Woon36 by means of highly accurate quantum-mechanical calculations, suggested glycine formation from a direct recombination of the COOH and NH2CH2 radicals which, in turn, were generated through several radical–radical complex reactions characterized by low energy barriers. A different proposal comes from the experimental work of Bossa et al., 11 in which the formation of glycine in protostellar environments was simulated by studying the reaction of CO2 and CH3NH2 in a water-dominated interstellar ice analog. In this work it was found that these two species thermally reacted to form the [CH3NH3⁺][CH2NHCOO⁻] salt, and, upon vacuum ultraviolet photolysis, this was converted to a glycine salt precursor [CH2NH3⁺][NH2CH2COO⁻], whose presence is in line with the glycine and methylvamine detection in the samples returned from the Stardust mission.

As quoted before, the barriers of aminoacetonitrile formation through Step 2 of the Strecker mechanism occurring within ice water cavities are of the order of 8–9 kcal mol⁻¹. These values, although slightly too high for cryogenic temperatures and in absence of UV, cannot exclude Step 2 as a possible channel towards aminoacetonitrile. The major concern to this channel, however, is the lack of NH—CH2 reservoirs, due to the high energy barrier for its formation in the previous step.
Nonetheless NH—CH$_2$ can readily be achieved through other paths, as it is for instance the successive H addition to HCN (HCN + 2H → NH—CH$_2$) predicted theoretically by Woon. Accordingly, the present work predicts a possible channel for the aminoacetonitrile formation in the ICM, which arises from a combination of a radical-radical mechanism for NH—CH$_2$ formation and the Streeker-type NH—CH$_2$ + HCN reaction leading to NH$_2$CH$_2$CN. In that respect, the variance with that found for aminoacetonitrile. Since nitriles are able to simulate the IR spectra of the species involved and to estimate the isotopic shifts to aid the detection of interstellar molecules and the elucidation of reaction paths.

Acknowledgements

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