Formamide Dehydration and Condensation on Acidic Montmorillonite: Mechanistic Insights from *Ab-Initio* Periodic Simulations

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Abstract. Formamide (NH_2CHO) is a molecule of extraordinary relevance as prebiotic precursor of many biological building blocks. Its dehydration reaction, which could take place during the Archean Era, leads to the production of HCN, the fundamental brick of DNA/RNA nitrogenous bases. Mineral surfaces could have played a crucial role in activating biological processes which in gas phase would have too high activation barriers to occur, thus allowing the event cascade, which finally led to the formation of biological macromolecules. In the present work we studied the dehydration process of formamide ($NH_2CHO \rightarrow HCN + H_2O$) as catalyzed by a surface of acid montmorillonite. In this surface, a silicon atom has been substituted by an aluminium one, thus generating a negative charge that is compensated by an acidic proton on the top of the surface. This proton should, in principle, help the formamide dehydration. However, our results indicate that this particular acidic surface does not exert an efficient catalytic behavior in the decomposition of formamide.

Keywords: Montmorillonite · Formamide · Prebiotic chemistry · DFT

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1 Introduction

The interaction of various materials with biomolecules is a topic of extraordinary relevance due to its broad application in many fields of science [1]: biomedicine [2], nanotechnology [3–5], water-cleaning [6, 7]. Among others, mineral surfaces are also important in the field of prebiotic chemistry. As advocated by Bernal [8], their role in the prebiotic world could have been:

- act as scaffold where small monomers of biomolecules (nitrogenous bases, amino acids, and even their precursors) concentrate because of their favorable interactions with the surfaces;
- protect them from stress-induced processes: organic molecules in general are reactive to thermal heating and UV-photons;
- promote their polymerization, until the formation of small oligomers essential for life generation.

One of the molecules which captured the attention of the scientific community is formamide (NH_2CHO), because it is the precursor of many other molecules of biological interest [9]. In particular, in the present paper, the interest is focused on its dehydration process, which leads to the production of HCN and H_2O. It has been demonstrated by Oró that the polymerization of HCN leads to nitrogenous base of adenine ($C_5H_5N_5$) [10, 11], and, accordingly, it can be a potential reservoir of nitrogenous bases.

Saladino and coworkers studied the decomposition of formamide catalyzed by many mineral surfaces in several environmental conditions [9, 12–21]. As a general trend they showed that high temperatures are needed to obtain at least purine ($C_5H_4N_4$), and that, depending on the nature of the catalyst, the production of the other nitrogenous bases can also be achieved.

Among the several mineral surfaces, montmorillonite plays an important role because it is capable to decompose formamide through the production of DNA/RNA oligomers [17, 22–27].

From a computational point of view many works available in literature have assessed Bernal's hypothesis, investigating mineral surfaces both as scaffold for biomolecules [28–32], and as promoters of chemical reactions among adsorbates [33–36]. In recent studies, the interactions of dry and wet DNA bases with montmorillonite has been analyzed using molecular dynamics simulations [28–30, 37], also proving that nitrogenous bases adsorb with a dimer-like structure, which seems to be prone to form a phosphodiester bond, the first hot spot for a subsequent polymerization. However, a detailed mechanism of the complex process starting from the formamide decomposition to obtain HCN, the subsequent HCN polymerization to form nitrogenous bases, and their reaction with phosphates and sugars to lead to a DNA nucleotide is still missing in the literature.

Therefore, in the present work we study the first step of this process, namely, the dehydration reaction of formamide (in competition with a possible condensation reaction) in the gas phase and once adsorbed on montmorillonite by means of periodic quantum simulations.

2 Computational Details

2.1 Methods

Periodic DFT calculations, as implemented in the Vienna Ab-initio Simulation Package, VASP [38–41], were carried out to compute equilibrium structures and energies. All calculations were performed with the Perdew-Burke-Ernzerhof (PBE) functional [42], with the Grimme's D3 empirical correction for dispersion [43]. The projector-augmented wave (PAW) pseudopotentials [44] describing the ionic cores and a plane wave basis set for the valence electrons were adopted. The energy cutoff was set to 500 eV. The self-consistent field (SCF) iterative procedure was converged to a tolerance in total energy of $\Delta E = 10^{-5}$ eV. The tolerance on gradients for geometry optimization was set to 0.01 eV/Å for each atom in each direction. For transition state optimization, the DIMER method [45–48] was used, and in some difficult cases the climbing image–nudged elastic band (CI-NEB) method [49–53] was used. The k-points mesh was set to (1,1,1) both for molecular and periodic calculations: *i.e.* the unit cell of montmorillonite was large enough that the calculation in the Γ point returned energies already converged.

Visualization and manipulation of computed structures were done with the MOLDRAW package [54]. Figures were rendered with the POVRAY program [55] using MOLDRAW to build up the input file.

2.2 Surface Model

The surface model used in this work was created from a single layer of pristine montmorillonite ($(Na,Ca)_{0.33}(Al,Mg)_2(Si_4O_{10})(OH)_2 \cdot nH_2O$), consisting of two layers of tetrahedral silica interplayed by a layer of octahedral alumina (see Supplementary Material, SM, Figure S1). The cell parameters used are a = 15.48 Å, b = 17.93 Å, c = 25.00 Å, α = 91.18°, β = 100.46°, γ = 89.64°. Such a large supercell ensures that no interaction among adsorbate of neighboring cells occurs, while the non-periodic cell parameter (c) warrants that there is enough vacuum space among fictitious replicas of the surface. A substitution of Si^{4+} with Al^{3+} was done to generate a negative charge which is saturated by a proton (see Fig. 1) [30].

3 Results

As a first step, some calculations have been done both on the formamide in the gas phase (in its protonated state) and adsorbed on the surface, in order to evaluate a good starting structure to study reactivity. In the gas phase this is straightforward as only two possible isomers exist: the H atom protonating the carbonyl O can be in CIS or TRANS

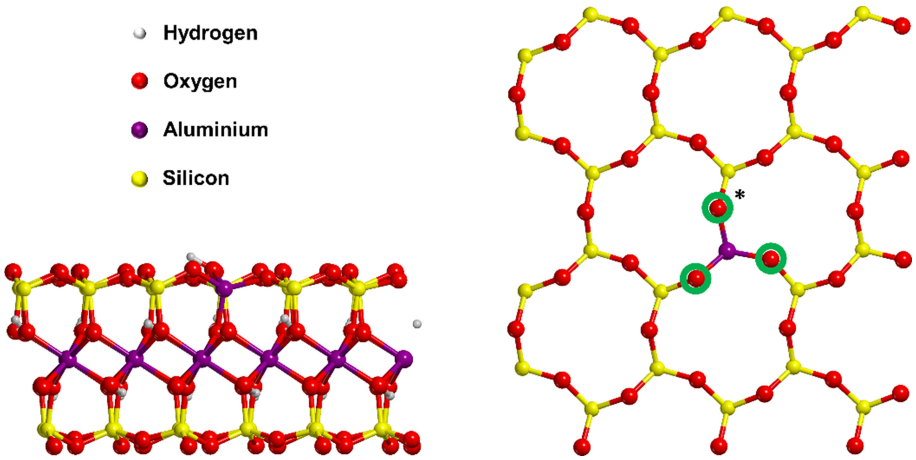

Fig. 1. PBE-D3 optimized geometries of the acidic montmorillonite. Lateral (left) and top (right) views. Green circles correspond to the possible sites to be saturated with a proton. The one marked with the asterisk is the most stable one. (Color figure online)

with respect to the H bound to the C atom (see Figure S2). Calculations show that the CIS isomer (RD_G of Fig. 2) is the most stable one (ΔE = 3 kJ mol^{-1}). Moreover, it is also ready to receive the H from the amino group, the first step for dehydration (TS1_G in Fig. 2).

On the surface a more careful conformational exploration was required as formamide can adsorb in several stable adsorption modes. Five different starting positions were explored (see Figure S3) and, finally, we started with the reactivity pathway from the most stable structure (see R_MNT of Fig. 3).

3.1 Dehydration

For the sake of comparison between the dehydration reaction in the gas-phase and on the acidic montmorillonite surface, the gas phase reaction has been performed accounting for a protonated formamide.

Figures 2 shows the reaction profile of the dehydration process of formamide in the gas phase. Its decomposition is analogous as for a neutral formamide molecule which has been already discussed in details in a previous paper of some of us [56]. In this case, just one proton transfer is needed to obtain a water molecule. However, there is still a high barrier to be overcome which can be lowered by a proper catalyst. The acidic montmorillonite surface is capable to both accept and donate protons and, accordingly, is a good candidate to help the dehydration reaction of formamide.

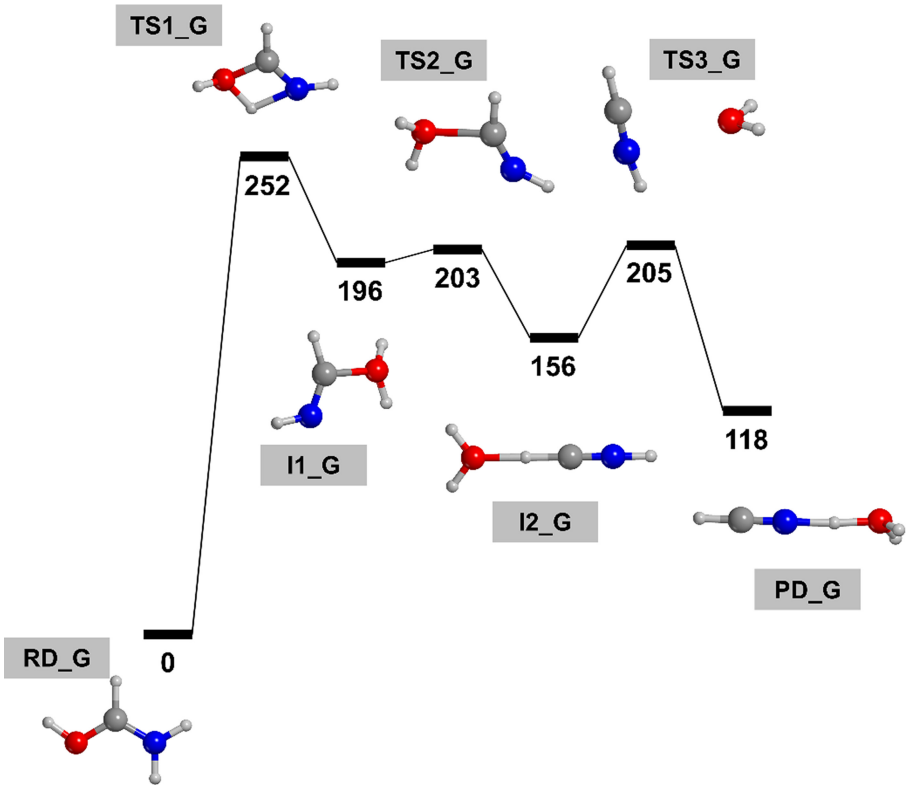

Fig. 2. PBE-D3 potential energy surface of the dehydration reaction of protonated formamide. Hydrogen in white, carbon in grey, nitrogen in blue, oxygen in red. Energy units are in kJ mol^{-1}. (Color figure online)

Figure 3 shows the reaction profile of the dehydration process of formamide catalysed by acidic montmorillonite. As one can see, montmorillonite does not exert an efficient catalytic role in this process, the highest barrier in the gas phase (252 kJ mol^{-1}, see Fig. 2 TS1_G) modestly decreases on the surface (204 kJ mol^{-1}, see Fig. 3 TS1_MNT), probably due to some stabilizing effects of the H-bond between the four-member ring in the transition state and the acidic surface proton. In both cases the activation barrier is very high, due to the presence of a strained four-member ring in the transition state. Moreover, the reaction on montmorillonite presents another important barrier, the isomerization of HNC to give HCN (see Fig. 3, TS4_MNT). From a thermodynamic point of view, both the processes are endothermic. These results are in line with the experimental results showing that formamide starts its decomposition only at high temperatures (160 °C) [16, 17].

3.2 Condensation

Figure 4 shows the condensation between two formamide molecules both in gas phase (left) and on the acidic montmorillonite (right). Also in this case the reactions involve high-energy transition states, and hence that the surface does not seem to help the process at all. In this case the reaction involves only one step with the nucleophilic attack of the nitrogen of neutral formamide to the carbon of protonated formamide, and, in a concerted fashion, the proton transfer of the amidic hydrogen of neutral formamide to the protonated oxygen to form water. Both in gas phase and on the surface the transition state involves a strained four-member ring (see TS_G and TS_MNT in Fig. 4) which strongly destabilizes the structure.

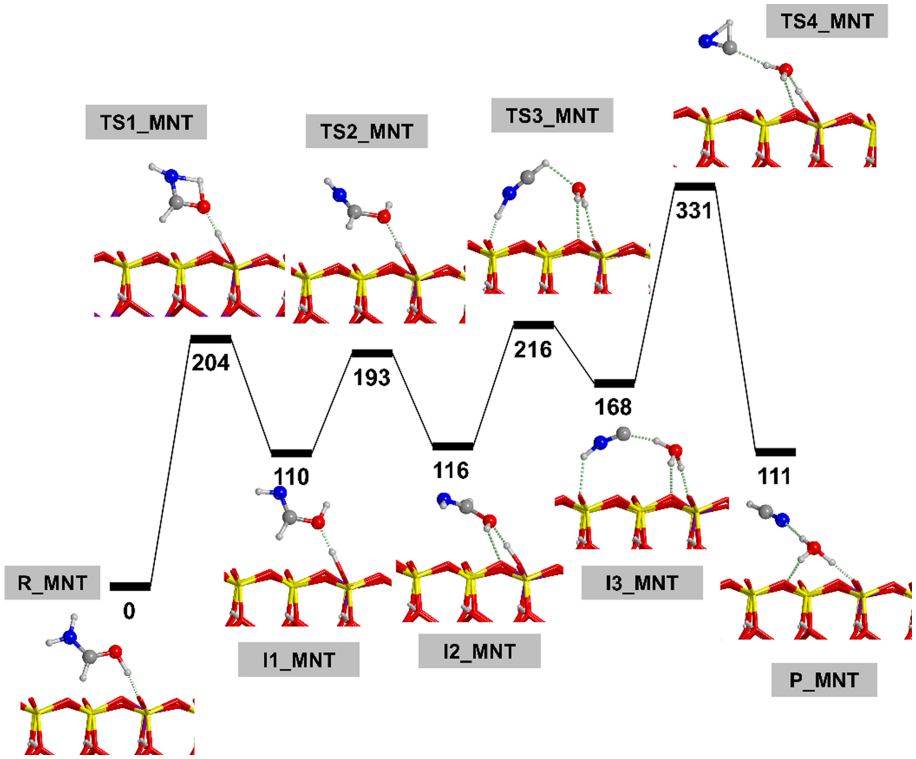

Fig. 3. PBE-D3 potential energy surface of the dehydration reaction of formamide on the acidic montmorillonite surface. Hydrogen in white, carbon in grey, nitrogen in blue, oxygen in red, silicon in yellow. Energy units are in kJ mol^{-1}. (Color figure online)

Therefore, from a kinetic standpoint, if in gas phase the two processes (i.e., dehydration vs condensation) are competitive (252 *vs* 249 kJ mol^{-1}), on the surface dehydration is less energetic than condensation (204 *vs* 242 kJ mol^{-1}).

In contrast, from a thermodynamic standpoint, condensation is more favorable than dehydration, both in the gas phase and on the surface. It is important to notice that the

condensation process leads to products where some favorable interaction of the newly formed molecules is missing (see PC_G and PC_MNT in Fig. 4). Therefore, we rearranged the products in order to maximize those interactions (in these case H-bonds and dispersive forces) which stabilize the structure.

4 Discussion and Conclusion

In this work, the formamide decomposition *vs* condensation reactions are discussed both in the gas phase and on an acidic model of montmorillonite. As formamide is a very stable molecule, its decomposition in the prebiotic era is thought to be due to stressing environmental conditions: thermal [57–59] and light shocks [59–61], or surface-catalyzed processes [17, 19]. In the present paper we study the formamide dehydration *vs* its condensation on an acidic model of montmorillonite [30].

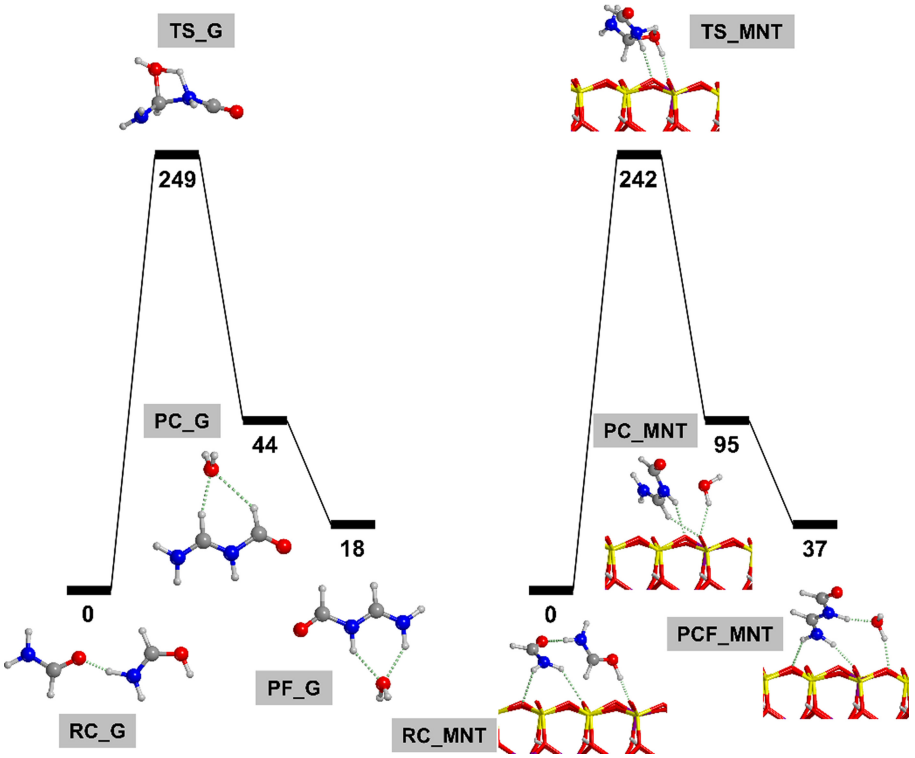

Fig. 4. PBE-D3 potential energy surfaces of the condensation reaction between two formamide molecules in the gas phase (left) and on the acidic montmorillonite surface (right). Hydrogen in white, carbon in grey, nitrogen in blue, oxygen in red, silicon in yellow. Energy units are in kJ mol^{-1}. (Color figure online)

Results show that the basal plane of acidic montmorillonite apparently does not exert a remarkable catalytic effect for any of these two processes. A slight decrease of the activation barrier for the dehydration channel (compared to the gas-phase process) is observed, while regarding the condensation, the surface does not play any catalytic role.

According to the results, we can conclude that the basal plane of acidic montmorillonite is not a suitable mineral surface that allows us to explain the catalytic activity of minerals in formamide decomposition. A plausible possibility could be that adsorption and reactivity take place at clay edges, where the chemistry (and so the reactivity) should be completely different, as silanol groups and Mg/Fe coordinated water molecules are present in the outermost layer of the surface [37].

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