Mechanism for the abiotic synthesis of uracil via UV-induced oxidation of pyrimidine in pure H_2O ices under astrophysical conditions

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The UV photoirradiation of pyrimidine in pure H_2O ices has been explored using second-order Møller–Plesset perturbation theory and density functional theory methods, and compared with experimental results. Mechanisms studied include those starting with neutral pyrimidine or cationic pyrimidine radicals, and reacting with OH radical. The *ab initio* calculations reveal that the formation of some key species, including the nucleobase uracil, is energetically favored over others. The presence of one or several water molecules is necessary in order to abstract a proton which leads to the final products. Formation of many of the photoproducts in UV-irradiated H_2O:pyrimidine=20:1 ice mixtures was established in a previous experimental study. Among all the products, uracil is predicted by quantum chemical calculations to be the most favored, and has been identified in experimental samples by two independent chromatography techniques. The results of the present study strongly support the scenario in which prebiotic molecules, such as the nucleobase uracil, can be formed under abiotic processes in astrophysically relevant environments, namely in condensed phase on the surface of icy, cold grains before being delivered to the telluric planets, like Earth. © *2010 American Institute of Physics*. [doi:10.1063/1.3478524]

I. INTRODUCTION

The origin of prebiotic species remains one of the unsolved questions in the study of the origin of life on Earth. Among the hypotheses proposed is the possibility of the delivery of extraterrestrial amino acids, nucleobases, and other molecules of biological significance to the early Earth by comets and meteorites.[1,2] This scenario suggests that many of the ingredients necessary for life were formed in space via abiotic chemical pathways, many of which have yet to be fully understood and identified.

Pyrimidine, purine, and their derived nucleobases, the building blocks of DNA and RNA, have been detected in meteorites,[3–6] pyrimidines being less abundant than purines. However, neither pyrimidine, purine, nor their corresponding nucleobases have yet been observed in the interstellar medium, despite extensive radio-observation campaigns.[7,8] In a recent experimental study it was shown that uracil can form when pyrimidine mixed with pure H_2O ice is exposed to ultraviolet (UV) radiation,[9] although the mechanism(s) for its formation was not explored.

Laboratory simulations have demonstrated in the last 15 years that organic compounds can be formed at low temperature from the UV irradiation of ice mixtures consisting of molecules observed in the interstellar medium and in comets.[10,11] The inventory of organics formed in such experiments covers a large suite of compounds, including molecules of prebiotic/biological interest such as amino acids, the building blocks of proteins in all terrestrial life forms.[12,13] Amino acids and other organics have been detected in carbonaceous chondrites such as Murchison and Murray,[14] supporting an extraterrestrial origin for these compounds of prebiotic interest.

It is well established that polycyclic aromatic hydrocarbons (PAHs) and polycyclic aromatic nitrogen heterocycles (PANHs) are present in interstellar and circumstellar environments in our Galaxy,[15,16] as well as others.[17] The incorporation of nitrogen-bearing species such as HCN during the formation of PAHs may lead to the formation of pyridine and pyrimidine,[18] although other mechanisms of formation of purines and pyrimidines under abiotic conditions have been proposed.[19–21] PAHs and PANHs are believed to condense onto cold grain surfaces in molecular clouds,[22,23] where they may be involved in complex chemistry stimulated by stellar radiation. Laboratory UV photoirradiation and proton bombardment of small PAHs in ices are known to produce oxidized compounds such as quinones, ethers, and other functionalized aromatic species.[12,24–26] More limited studies of PANHs indicate that they undergo similar processes when exposed to radiation in ices.[9,27] Puric and pyrimidic nucleobases are also sensitive to radiation.[28] Ionization, rupture of C–H and/or N–H bonds, and reactions with hydroxyl radical or secondary electrons leading to various oxidized species have also been reported.[29–31]

In the present work, we have carried out *ab initio* quantum chemical computations aimed at understanding the mechanisms for formation of uracil in the previously re-

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ported UV photoirradiated pyrimidine ($C_4H_4N_2$) in pure H_2O ices under astrophysically relevant conditions. By comparing the products detected in such experiments with theoretical calculations of the energies of the reactants, intermediates, and products, the formation mechanisms of oxidized derivatives of pyrimidine, including uracil, via abiotic pathways applicable to interstellar and cometary ice environments can be deduced. First, we examine oxidation of the starting pyrimidine into singly oxidized compounds. Second, we investigate oxidation of singly oxidized pyrimidine products into uracil and other dihydroxypyrimidine isomers.

II. Theoretical methods

Geometries of the reactants, intermediates, and products were optimized using density functional theory. Becke's three-parameter exchange functional B3[32] was combined with the correlation functional of Lee, Yang, and Parr.[33] The B3LYP density functional was employed in conjunction with Pople's 6-31G** split valence basis set. Geometrical structures of all the molecules reported in this work were fully optimized and represent true minima, confirmed by a subsequent frequency calculation. The absolute energies and energy differences were obtained at the B3LYP/6-31G** optimized geometry using second-order Møller–Plesset perturbation theory (MP2) for closed shell species and Z-averaged perturbation theory[34,35] for the open shell species in conjunction with Dunning's correlation consistent valence triple zeta basis sets (cc-pVTZ). All the computations were performed using Q-CHEM3.1 suite of *ab initio* quantum mechanical codes.[36] The Cartesian coordinates of the geometries of all the minima are reported in the supplementary information.[37]

III. RESULTS AND DISCUSSION

A. UV photoirradiation of pyrimidine in pure H_2O ices

The UV photoirradiation of pyrimidine in a pure H_2O ice matrix leads to multiple reaction channels for its oxidation. Besides neutral pyrimidine (Py) and H_2O molecules, pyrimidine radical cation ($[Py]^{+\bullet}$), hydroxyl, and pyrimidine radicals, formed by ionization or C–H/O–H bond cleavage, can be present in the ice matrix (radicals are marked by a $^{\bullet}$),

$$Py + h\nu \rightarrow [Py]^{+\bullet} + e^{-},$$

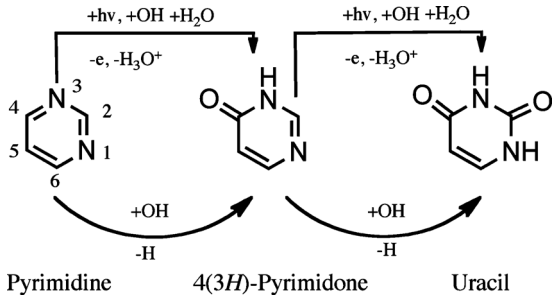
$$Py + h\nu \rightarrow [Py_{/H}]^{\bullet} + H^{\bullet},$$

$$H_2O + h\nu \rightarrow [H_2O]^{+\bullet} + e^{-},$$

$$H_2O + h\nu \rightarrow H^{\bullet} + {}^{\bullet}OH,$$

where $[Py_{/H}]^{\bullet}$ symbolizes a molecule of pyrimidine that has lost an H atom. It is evident that the possible reactions among these species can generate a broad variety of intermediate compounds and products.

The interactions between species formed from the ionization or dissociation of the starting compounds are dominated by ion-molecule, radical-molecule, or radical-radical reactions, which are typically barrierless and fast. Neutral-neutral reactions between H_2O and pyrimidine can also occur but, because of their high activation barriers, they are several orders of magnitude slower than reactions involving radicals or cations, particularly in cold interstellar environments ($T < 100$ K).



SCHEME 1. Schematic diagram of the two-step oxidation of pyrimidine leading first to 4(3*H*)-pyrimidone, followed by its oxidation to uracil.

During simulation experiments, H_2O:pyrimidine=20:1 mixtures were deposited on a cold substrate at 20–30 K under high-vacuum, and simultaneously irradiated with a microwave-powered flowing-H_2 discharge lamp emitting mainly UV photons at 121.6 nm (10.2 eV, Ly α line) and a 20-nm wide molecular transition centered around 160 nm (7.78 eV), in order to simulate conditions of interstellar and/or cometary environments.[9] Due to H_2O possessing a large cross section for photodissociation in this wavelength range,[38] $^{\bullet}OH$ radicals are readily produced in the ice mixture upon irradiation at low temperature. It is therefore reasonable to assume that the chemistry will be dominated by reactions of $^{\bullet}OH$ radicals with other species in the H_2O:pyrimidine mixtures. Since $^{\bullet}OH$ radicals may react with either neutral pyrimidine molecules or cations,[39] the energetics of reactions of $^{\bullet}OH$ radicals with both kinds of species are taken into consideration. Reaction pathways are summarized in Scheme 1. UV irradiation could also produce radical ions of pyrimidine bases via $\pi \rightarrow \sigma^{*}$ type activation of XH linkages in the gas phase, as shown experimentally in adenine,[28] and predicted in uracil and thymine by Hudock *et al.*[40] However, it will be a minor photodissociation process in the presence of (20:1) H_2O matrix in our condense phase experiment.

B. Oxidation of pyrimidine

The possible reactions between a pyrimidine cation or molecule with an OH radical lead to the formation of two types of intermediates,

$$[Py]^{+\bullet} + {}^{\bullet}OH \rightarrow [Py\text{–}OH]^{+},$$

$$Py + {}^{\bullet}OH \rightarrow [Py\text{–}OH]^{\bullet}.$$

Reactions involving a pyrimidine cation and an OH radical (first step in Scheme 1) are presented in Fig. 1. Since the OH radical is very reactive, it can attack any of the six positions on the pyrimidine ring. The OH radical adduct closed-shell cationic intermediates (see Figs. 1 and 2) span a wide energy range at the MP2/cc-pVTZ level of theory relative to the starting pyrimidine cation and OH radical. OH addition at position 2 leads to an intermediate at −88.3 kcal mol^{-1} relative to reactants. Rearrangement of a proton to the nitrogen makes the most stable cationic intermediate at

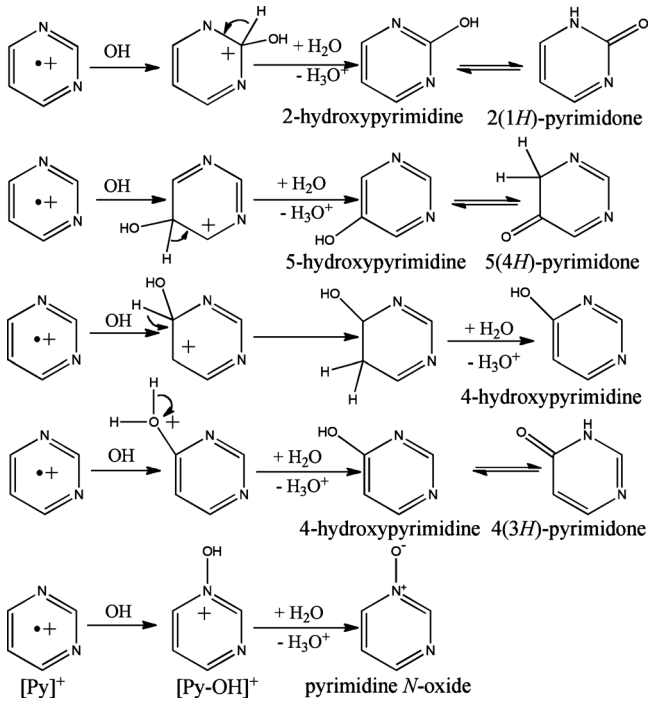


FIG. 1. Schematic reactions of OH radical with pyrimidine cation; the first step is the addition of OH to the ring and the second step is a proton abstraction leading to product formation.

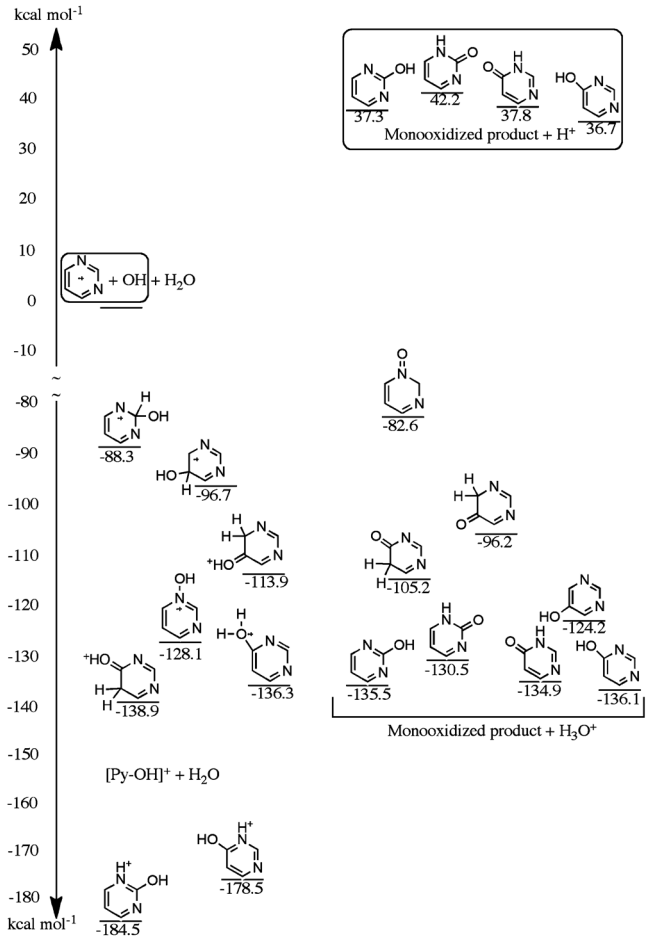


FIG. 2. Diagram indicating the energies (kcal mol^{-1}) of reactants, intermediates (plus H_2O), and products (plus H_3O^+) of the reaction between the pyrimidine cation and an OH radical. The boxes indicate relative energies without considering H_2O and H_3O^+.

−184.5 kcal mol^{-1}. The large energy difference between 2(2*H*)-hydroxypyrimidine and 2(3*H*)-hydroxypyrimidine cations is mainly due to the increased aromaticity. The two lowest energy products, namely, 4-hydroxypyrimidine and 2-hydroxypyrimidine, both have large proton affinities. The intermediates lose a proton to the H_2O matrix to form the final products shown in Fig. 1. According to Fig. 2, in all cases the $[Py-OH]^+$ species (energy of intermediate and one H_2O) are lower in energy, sometimes by several kcal mol^{-1}, than the monooxidized product+H_3O^+ species (energy of product and H_3O^+), but this does not account for the fact that several water molecules are present in the ice matrix. The proton solvation enthalpy for H_2O is known very accurately to be 274.9 ± 0.2 kcal mol^{-1}.[41] We computed the proton affinity of H_2O to be 172.0 kcal mol^{-1}. *Ab initio* calculations, including ours, have shown that solvation enthalpy is approached rapidly with increasing size of water clusters, providing ample thermodynamic driving force.[42] More than 80% of the total proton solvation energy, calculated at the MP2/cc-pVTZ level, is recovered with only four H_2O molecules. A graph is included in the supporting information. Moreover, studies have shown that H_2O can significantly lower (even remove) intrinsic reaction barriers by stabilizing the transition state for proton abstraction.[43,44] Cyclic complexes involving the intermediate, hydroxyl radicals, and H_2O will accelerate the proton abstraction reaction in the condensed phase. This enhancement of the reaction rate can occur even with the help of a single H_2O molecule. Examples of H_2O mediated proton transfer and abstraction reactions are abundant.[45,46] Hence, in the presence of several H_2O molecules, the proton abstraction is thermodynamically favorable. This would be only possible in the presence of the ice matrix, without which oxidation of pyrimidine would not be energetically favored.

The two lowest energy intermediates are protonated 2(1*H*)-pyrimidone and 4(3*H*)-pyrimidone cations (and H_2O) at −184.5 and −178.5 kcal mol^{-1}, below the free reactants Py^+, OH, and H_2O, respectively. 4(3*H*)-Pyrimidone cation, an isomer of 4-hydroxypyrimidine cation, and the *N*-hydroxy cation are at −138.9, −136.3, and −128.1 kcal mol^{-1} with respect to reactants, respectively (Fig. 2). 5-Hydroxy- and 2-hydroxypyrimidine cation intermediates are the least stable at −96.7 and −88.3 kcal mol^{-1}, respectively, and prone to rearrangement. The lowest-energy oxidized product of pyrimidine is 4-hydroxypyrimidine, and the computed energy of 4-hydroxypyrimidine and H_3O^+ is −136.1 kcal mol^{-1} relative to the reactants (Fig. 2). It is followed by 2-hydroxypyrimidine, 4(3*H*)-pyrimidone, and 2(1*H*)-pyrimidone at −135.5, −134.9, and −130.5 kcal mol^{-1} below reactants, respectively. Other products such as 5-hydroxypyrimidine and pyrimidine *N*-oxide (also named 1- or *N*-hydroxypyrimidine) are also fairly stable compared to the reactants, as seen in Fig. 2. Therefore, although all these products are expected to form, 4-hydroxypyrimidine and 2-hydroxypyrimidine and their tautomers are the most favored mono-oxidized products.

Oxidation of pyrimidine can also occur via another barrierless pathway, where an OH radical attacks a neutral pyrimidine molecule, which leads to open-shell radical intermediates, followed by the loss of an H atom to the H_2O ice matrix. This reaction is found to be energetically favorable, although less favorable than the pathways illustrated in Figs. 1 and 2. Indeed, the so-formed 2-, 4-, and 5-hydroxypyrimidine radicals were found to be energetically lower than the reactants by −23.4, −22.1, and −19.8 kcal mol^{-1}, respectively. The pyrimidine *N*-oxide radical, however, appears to have a slightly higher energy than the reactants.

These calculations indicate a clear regioselectivity for the oxidation of pyrimidine, leading to the formation of 4-hydroxypyrimidine (or 4(3*H*)-pyrimidone) and 2-hydroxypyrimidine (or 2(1*H*)-pyrimidone), whose formations are energetically favored over those of 5-hydroxypyrimidine and pyrimidine *N*-oxide.

From an experimental point of view, High Performance Liquid Chromatography (HPLC) and gas chromatrography mass spectroscopy (GC-MS) studies of residues formed from the UV irradiation of pyrimidine in pure H_2O ices led to the identification of a few oxidized pyrimidine derivatives as well as bipyrimidine isomers. 4(3*H*)-Pyrimidone, predicted by theory to be the lowest-energy singly oxidized photoproduct, or its tautomer 4-hydroxypyrimidine, was detected with both chromatography techniques, and appeared to be the most abundant photoproduct formed in these experiments, whereas 2-hydroxypyrimidine was not detected by chromatography.[9] This nondetection is surprising even though the 2-hydroxypyrimidine cation intermediate is predicted to be energetically lower than the 4-hydroxypyrimidine cation (Fig. 2). The forward reaction leading to 2-hydroxypyrimidine and its tautomer (after proton abstraction by H_2O) is favorable and comparable to that of 4(3*H*)-pyrimidone (or 4-hydroxypyrimidine). 2-Hydroxypyrimidine may be formed in the ice matrix and/or during the warm-up to room temperature, but at the same time converted or destroyed via some other process(es), resulting in a very low, nondetectable abundance in the final residues. The presence of 5-hydroxypyrimidine in these residues could not be verified because its standard is not commercially available.[9] However, GC-MS chromatograms clearly indicate the presence of other compounds having the same mass as singly oxidized pyrimidines in the residues, so one of these unidentified compounds might be 5-hydroxypyrimidine. Therefore, our theoretical predictions for the relative energies of intermediates and products, favoring the formation of 4(3*H*)-pyrimidone (or 4-hydroxypyrimidine) over that of other singly oxidized compounds, are confirmed by the experimental results.

As a last remark, the presence of pyrimidine *N*-oxide in such residues was recently confirmed by HPLC analysis and will be published elsewhere. However, such a compound is not seen in GC-MS chromatograms, probably because it is not derivatized similarly to other singly oxidized pyrimidines, indicating that pyrimidine *N*-oxide is only stable in its keto form. According to Fig. 2, the formation of pyrimidine *N*-oxide is favorable via the cationic pathway. Therefore, the presence of this compound in residues with a measurable abundance tends to favor the cation pathway over other possibilities for the oxidation of pyrimidine. This is supported by the fact that at the MP2/cc-pVTZ level, the neutral route to form the pyrimidine *N*-oxide radical intermediate is unfavorable by several kcal mol^{-1}.

C. Formation of uracil and its isomers

Considering that the products of oxidation of pyrimidine can be themselves further oxidized by OH radicals, we have explored both the cationic and neutral mechanisms for the oxidation of hydroxypyrimidines, leading to the formation of doubly oxidized intermediates and products,

$$[\text{Py–OH}]^{+\bullet} + {}^{\bullet}\text{OH} \rightarrow [\text{Py}(-\text{OH})_2]^{+},$$

$$\text{Py–OH} + {}^{\bullet}\text{OH} \rightarrow [\text{Py}(-\text{OH})_2]^{\bullet}.$$

The detailed stepwise reaction schemes for the radical cations of 4-hydroxypyrimidine and its tautomer 4(3*H*)-pyrimidone are included in the supporting information. The attack of an OH radical on 4-hydroxypyrimidine and 4(3*H*)-pyrimidone cations produces various intermediates, which all lead to stable products after subsequent proton abstraction by H_2O or clusters of H_2O molecules, as discussed above. The water matrix can act as a catalyst in the final step and lower the barrier by stabilizing the cationic charge of the transition state between the intermediate and the product. The large proton solvation enthalpy of −274.9 kcal mol^{-1} will drive the proton abstraction reaction forward, as discussed for the first step in this reaction mechanism. Figure 3 illustrates the energetic order of these intermediates and products, and shows that all cationic intermediates of the OH radical addition to 4-hydroxypyrimidine radical cation are energetically lower than the reactants at the MP2/cc-pVTZ level of theory. The lowest energy intermediate is the compound where the OH radical has been added to position 2 of 4-hydroxypyrimidine (at −147.1 kcal mol^{-1}, H_2O included). The overall reaction is favorable by −106.7 kcal mol^{-1} (see Fig. 3) for the formation of 2,4-dihydroxypyrimidine (tautomer of uracil) from 4-hydroxypyrimidine (cation), OH, and H_2O. The 4(3*H*)-pyrimidone cation accepts an OH radical at position 2 to form the 2-hydroxy-4(3*H*)-pyrimidone cation, which subsequently produces the lowest energy product, namely, uracil in its diketo form. This diketo form is 10.5 kcal mol^{-1} lower in energy than the corresponding dienol form, whereas the hybrid isomer (one keto and one enol) is 10.0 kcal mol^{-1} above uracil. The energies of formation of 4,6-dihydroxy- and 4,5-dihydroxypyrimidines are favorable by 94.5 and 80.2 kcal mol^{-1}, respectively. Thus, it appears that the formation of uracil, with a reaction energy of −104.3 kcal mol^{-1}, is favored over that of other dioxidized products.

The chemical pathway involving the reaction of OH radical with neutral 4-hydroxypyrimidine leads to three energetically bound intermediates, namely, 4,5-, 2,4-, and 4,6-dihydroxypyrimidine radicals, whose energies are favorable by −20.1, −19.4, and −16.1 kcal mol^{-1}, respectively. The

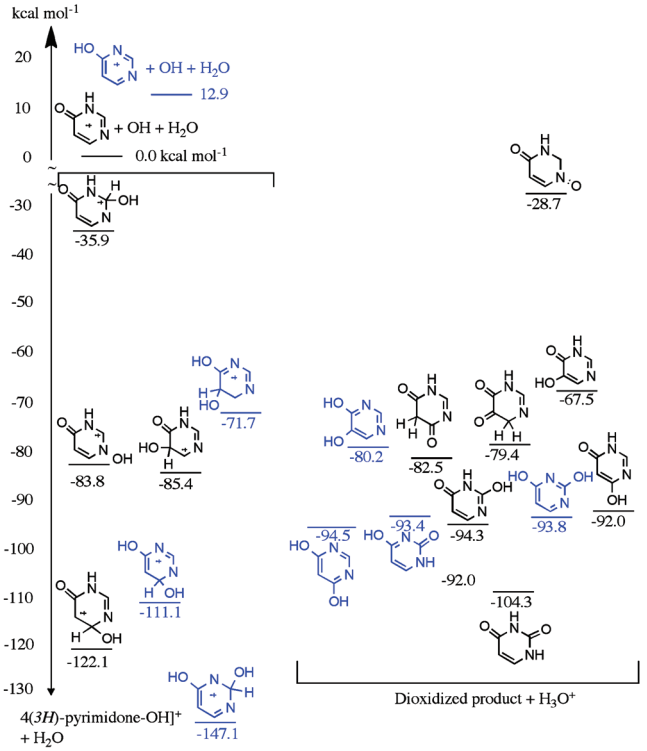


FIG. 3. Diagram indicating the energies (in kcal mol^{-1}), intermediates (plus H_2O), and products (plus H_3O^+) of the reactions between (1) 4-hydroxypyrimidine and an OH radical (in blue) and (2) between 4(3*H*)-pyrimidone and an OH radical (in black).

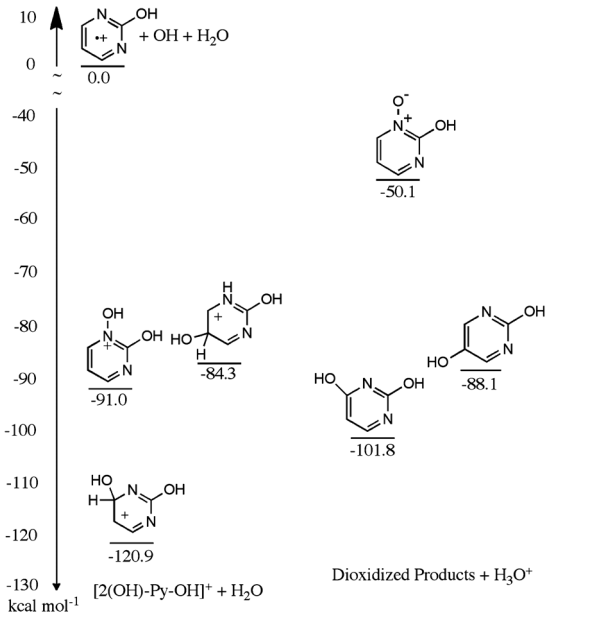


FIG. 4. Diagram indicating the energies (in kcal mol^{-1}) of the intermediates (plus H_2O) and products (plus H_3O^+) of the reactions between the 2-hydroxypyrimidine cation and an OH radical.

pyrimidine *N*-oxide intermediate is higher in energy than the reactants, although the subsequent loss of a hydrogen atom to the ice matrix leads to stable products. Therefore, the radical intermediate pathway is also a viable route for the formation of uracil and other dioxidized pyrimidine derivatives.

Oxidation of the 2-hydroxypyrimidine radical cation and its tautomer 2(1*H*)-pyrimidone was also explored theoretically. The reaction schemes are included in the supporting information. The results (Fig. 4) indicate that the reaction of the cations of these compounds with an OH radical, followed by an H_2O assisted proton abstraction, leads to three different products and their tautomers. The cationic intermediates and products (H_2O included in each case) are all significantly lower in energy compared to the reactants. As shown in Fig. 4, 2,4-dihydroxypyrimidine is the lowest-energy product (-101.8 kcal mol^{-1}), followed by 2,5-dihydroxypyrimidine and 2,*N*-dihydroxypyrimidine products (-88.1 and -50.1 kcal mol^{-1}, respectively). Figure 4 also shows that for this pathway, 2,4-dihydroxypyrimidine, the dienol tautomer of uracil, is again the most stable doubly oxidized product after subsequent proton abstraction by H_2O.

Experimentally, several peaks that could be assigned to doubly oxidized pyrimidines were found in GC-MS chromatograms of residues.[9] Among those compounds, only uracil was clearly identified, its abundance appearing to be higher than any other doubly oxidized isomer. 4,6-Dihydroxypyrimidine was searched for in the residues but not found. Other dihydroxypyrimidines such as 2,5- and 4,5-dihydroxypyrimidines may also be present, although this could not be verified because of the lack of corresponding standards. Finally, the presence of *N*-dihydroxypyrimidines is less plausible since those compounds are energetically higher or very close to the reactants with reaction barriers, as shown by our MP2/cc-pVTZ calculations (Fig. 4). The presence of these compounds in the residues could not be investigated experimentally because their standards are not available either.

D. Formation of higher-degree oxidized pyrimidines

There is *a priori* no reason why the oxidation of pyrimidine should stop after the formation of dioxidized compounds. The addition of one or more OH radical(s) or H_2O molecule(s) to the remaining available peripheral atom(s) of the pyrimidic ring is theoretically possible. However, experiments have shown that such molecules probably do not form under the same experimental conditions as described above, since barbituric and isobarbituric acids (tautomers of 2,4,6- and 2,4,5-trihydroxypyrimidines, respectively) have not been detected via HPLC and GC-MS in residues.[9] Steric hindrance, formation of unstable intermediates and products, and low concentration of starting materials could be the reasons why the addition of a third OH radical or H_2O molecule to pyrimidine is not efficient. Ring rupture is also possible.

E. Formation of other photoproducts: Bipyrimidines and their derivatives

UV photoirradiation can also break C–H bonds homolytically, leading to the loss of an H atom and the production of pyrimidine radicals, $[Py_{/H}]^{\bullet}$. The recombination of a $[Py_{/H}]^{\bullet}$ radical with a pyrimidine molecule, a pyrimidine cation, or another $[Py_{/H}]^{\bullet}$ radical in the matrix can lead to the formation of several bipyrimidine isomers. The structure of the final bipyrimidine will then depend on which C–H bond has been broken before recombination,

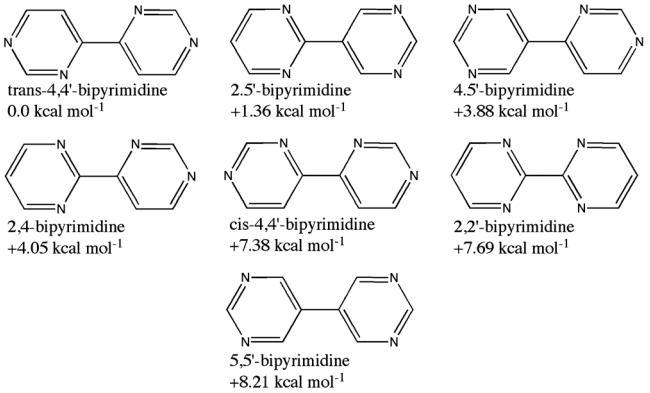


FIG. 5. Relative energies (kcal mol^{-1}) of all seven bipyrimidine isomers with respect to the lowest energy isomer, namely, trans-4,4′-bipyrimidine.

$$[Py_{/H}]^{\bullet} + [Py_{/H}]^{\bullet} \rightarrow [\,Py_{/H}\,]\text{–}[\,Py_{/H}\,] \quad \text{(bipyrimidines)},$$

$$[Py_{/H}]^{\bullet} + Py \rightarrow [\,Py_{/H}\,]\text{–}[\,Py_{/H}\,] + H^{\bullet}.$$

All possible bipyrimidine isomers in which the two pyrimidic rings are linked by a C–C bond are predicted to be energetically bound within a range of 9 kcal mol^{-1} from the lowest energy isomer. Figure 5 shows the seven isomers of bipyrimidines along with their computed relative energies in kcal mol^{-1}, and suggests that the energetic order of the bipyrimidine isomers correlates perfectly with the number of favorable N···H interactions. Trans-4,4′-bipyrimidine was found to be the isomer with the lowest energy, since it possesses two favorable N···H interactions between the rings. Similarly, 2,5′-bipyrimidine, the second-lowest energy isomer, also contains two N···H interactions, although its geometry differs slightly from Trans-4,4′-Bipyrimidine. 4,5′-bipyrimidine is 3.88 kcal mol^{-1} above the global minimum, and possesses one N···H interaction, while two H atoms are hindered on the other side. Similarly, 2,4′-bipyrimidine has two N lone pairs that repel and one favorable interaction (+4.08 kcal mol^{-1}). The *cis*-4,4′-bipyrimidine isomer (7.38 kcal mol^{-1} above the *trans*-isomer) has two repulsive interactions. Finally, 2,2′-bipyrimidine (+7.69 kcal mol^{-1}) has four N lone pairs leading to two repulsive interactions, while 5,5′-bipyrimidine, the highest (relative) energy isomer (+8.21 kcal mol^{-1}), has two H-atom pair repulsions. As a last remark, it should be noted that bipyrimidines formed from two pyrimidic rings bound together via C–N or N–N bonds may also be possible, however they were not studied here.

The 2,2′-bipyrimidine isomer has been positively identified by HPLC and GC-MS analysis. Other isomers could not be rigorously identified because their standards are not available. However, GC-MS data clearly indicate that at least two other isomers of bipyrimidines are formed in the residues.[9] Moreover, the intensities of GC-MS peaks indicate that 2,2′-bipyrimidine, sixth lowest energy isomer estimated theoretically, is not the most abundant isomer formed in these residues, although it is impossible to verify which other isomer is the most abundant without standards. This result suggests that not all bipyrimidines are formed under these experimental conditions, and that the pathways leading to the formation of these compounds are selective and probably correlated with the stability of the $[Py_{/H}]$ radical, which depends on the localization of the unpaired electron. It is important to note that the individual GC-MS peaks may also be representative of two or more isomers that were not separated in the column by the particular chromatographic separation method used in Ref. 9, although again this cannot be verified without a comparison with standards.

Finally, it is likely that bipyrimidines themselves may be oxidized in the presence of H_2O molecules and OH radicals. In fact, some GC-MS data indicate that compounds with masses of 231 and 361 amu, that correspond to the most intense peaks for mono- and dihydroxybipyrimidine tBDMS derivatives, respectively, may also be formed in the residues. However, their standards are not available, so the presence of such compounds cannot be verified. For this reason, they were not studied theoretically in this work.

IV. CONCLUSIONS

The experimental UV photoirradiation of pyrimidine in pure H_2O ices leads to the formation of various oxidation products, including the nucleobase uracil.[9] In the work reported here, plausible mechanisms for their formation were explored with *ab initio* MP2 and density functional quantum chemical methods, along with correlation-consistent basis sets. These calculations predicted uracil to be the energetically most favorable doubly-oxidized product, consistent with the experimental observations.

During the first oxidation step, both 4-hydroxypyrimidine and its tautomer 4(3*H*)-pyrimidone, and 2-hydroxypyrimidine and its tautomer 2(1*H*)-pyrimidone, are predicted to be the most favorable products. 4(3*H*)-Pyrimidone was found to be the major product in laboratory residues.[9] In the second step, at the same level of theory, we found that uracil is the most energetically favored doubly oxidized product when 4-hydroxypyrimidine, 2-hydroxypyrimidine, or their tautomers are oxidized. This prediction is consistent with experimental observation where uracil was found to be the most abundant doubly oxidized product.

Ab initio quantum chemical computations also indicate that reactions of $[Py]^{+\bullet}$ or neutral Py with OH radical are energetically favorable only in the presence of the H_2O matrix. Therefore, a pure gas-phase oxidation mechanism appears energetically unfavorable. This very important result indicates that the formation of uracil, as well as other pyrimidine derivatives, including nucleobases, via oxidation of pyrimidine under astrophysical conditions is viable only in the condensed phase of icy mantles, in the presence of ionizing radiation.

Other oxidation products predicted by *ab initio* quantum chemical methods, such as bipyrimidines, have been identified in experiments.[9] The comparison between theoretical predictions and experimental observations supports a mechanistic pathway for the formation of oxidized pyrimidines and other pyrimidine derivatives involving a cationic intermediate. Theoretical and experimental results both support the

scenario in which biomolecules such as nucleobases can be formed abiotically in the condensed phase under interstellar and cometary conditions, before they are delivered to surfaces of planets by cometary dust and meteorites.

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