Supporting Information:

A Plausible Mechanism of Uracil Photohydration Involves an Unusual Intermediate

Woojin Park,[†] Michael Filatov(Gulak),[*,†] Saima Sadiq,[†] Igor Gerasimov,[†] Seunghoon Lee,[‡] Taiha Joo,[*,¶] and Cheol Ho Choi[*,†]

†*Department of Chemistry, Kyungpook National University, Daegu 41566, South Korea*

‡*Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, USA*

¶*Department of Chemistry, Pohang University of Science and Technology (POSTECH), Pohang 37673, South Korea*

E-mail: mike.filatov@gmail.com; thjoo@postech.ac.kr; cchoi@knu.ac.kr

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Remarks about performance of MRSF-TDDFT

The mixed-reference spin-flip (MRSF) TDDFT enables accurate computation of the excitation energies[S9] and the real (and avoided) crossings between the potential energy surfaces of the ground and excited states, the so-called conical intersections,[S10] of organic molecules. Simultaneously, MRSF-TDDFT eliminates the major drawback of the spin-flip TDDFT methods, the spin-contamination of the ground and excited states, without loosing the efficiency and transparency of the formalism.[S11,S12]

MRSF has the ability to accurately reproduce the relative energy (with respect to the Franck-Condon energy) of conical intersections, as shown in comparison between the MRSF and MRCISD+Q energies in Ref. S10 Especially valuable for studying excited state dynamics is the ability of MRSF to correctly describe the adiabatic potential energy surfaces in the vicinity of the Franck-Condon geometry and far from it. S13–S15 In a series of recent studies,[S16,S17] the accuracy of MRSF was benchmarked against the results from three independent types of the equation-of-motion coupled-cluster (EOMCC) methodology abbreviated as δ-CR-EOMCC(2,3), DIP-EOMCC(4h2p)$\{N_o\}$ and DEA-EOMCC(3p1h,4p2h)$\{N_u\}$ as well as multi-state many-body perturbation theory methods, such as XMCQDPT2 or XMS-CASPT2. This study demonstrated that MRSF is capable of reproducing the potential energy surfaces of the ground and excited states of molecules with accuracy approaching the highest levels of wavefunction methodology.

Analysis of the optimized structures

The S_0 equilibrium geometry of uracil obtained with MRSF-TDDFT/BH&HLYP/6-31G* method features planar structure, which is in excellent agreement with the experimental crystallographic geometry and high level theoretical calculation; see Figure S2 and Table. S1. As the consequence of populating the π_1^* orbital, the C_4=C_5 bond is partially broken and this leads to lengthening of the C_4=C_5 bond (See Figure S1 for frontier orbitals of uracil and Figure S2 for optimized structures and atom numbering). The neighboring C_5–C_6 and C_4=O_8 bonds are simultaneously shortened and lengthened as the π_1^* orbital has bonding and anti-bonding characteristic between these atoms respectively. This unique skeletal vibration is denoted as bond length alternation (BLA) and defined as $\mathrm{BLA} = \frac{1}{2}(\Delta R_{\mathrm{C_4=O_8}} + \Delta R_{\mathrm{C_5=C_6}}) - \Delta R_{\mathrm{C_4-C_5}}$, where ΔR's are displacements with respect to the S_0 equilibrium geometry. Along the BLA motion, conical intersection (CI) between the S_2 and S_1 states ($\mathrm{CI}_{21,\,\mathrm{BLA}}$) and excited state S_1 minimum can be found. They have flat ring with a BLA distortion of 0.13 and 0.21 respectively. Therefore, $\mathrm{CI}_{21,\,\mathrm{BLA}}$ is close to Franck-Condon (FC) geometry while S_1 minimum ($S_{1,\,\mathrm{min}}$) is relatively far from FC geometry and exhibits an inversion of double bond(C_4=O_8, C_5=C_6) and single bond(C_4–C_5). It has been recently shown by some of us[S17] that $\mathrm{CI}_{21,\,\mathrm{BLA}}$ is essentially involved in the very early dynamics of thymine.

Figure S1: Frontier orbitals of Uracil (n_{O7}, π_1, π_2, and π_1^*).

Meanwhile, hydrogen out of plane (HOOP) torsion about the C5=C6 bond denoted as ϕ coordinates produces a $CI_{21,\pm}$ with an angle of $\pm 48°$. As both are the mirror images of one another, in the following, only the structures with positive values, *e.g.* $CI_{21,+}$, will be considered. The CI between S_1 and S_0 state ($CI_{10,+}$) and ground state local minimum ($S_{0,\min +}$) are also found with a more HOOP distortion of ϕ = 118.21°and 176.3°respectively.

Recent work by Chakraborty et al.[S1] who recently employed extended multi-state CASPT2 (XMS-CASPT2) in the non-adiabatic molecular dynamics (NAMD) simulation showed that the ethylenic CI_{21} has a very small deviation from planarity, while CI_{10} is considerably non-plnar.

Table S1: Bond lengths (Å) of ground state equilibrium geometry obtained by MRSF-TDDFT/BH&HLYP/6-31G* method in gas phase in comparison with crystallographic data[S7] and theoretical data obtained with high level theoretical calculation CCSD(T)/cc-pwCVTZ.[S8]

Distances	This work	Exp	CCSD(T)/cc-pwCVTZ
N1-C2	1.38	1.37	1.38
C2-N3	1.37	1.37	1.37
N3-C4	1.40	1.37	1.40
C4-C5	1.45	1.43	1.45
C5-C6	1.34	1.34	1.34
C6-N1	1.37	1.36	1.37
C2-O7	1.20	1.22	1.21
C4-O8	1.21	1.24	1.21

Figure S2: Optimized structure of ground state (FC) with atom numbering, $CI_{21,\,BLA}$, $CI_{21,\,+}$, $S_{1,\,min}$, $CI_{10,\,+}$, and $S_{0,\,min\,+}$ (intermediate **4**). The BLA values are given in parenthesis next to respective label while the ϕ values are given in parenthesis next to C_5=C_6 bond. Bond lengths and ϕ values are given in (Å) and (°) respectively. For $CI_{21,\,BLA}$ and $CI_{10,\,+}$, the geometric parameters from the XMS-CASPT2 optimization of Ref. S1 are given in the italicized font.

Figure S3: Mulliken charges on the ground state optimized geometries of FC (**1**) (left panel) and $S_{0,\,\mathrm{min}\,+}$ (intermediate **4**) (right panel). The results obtained by MRSF-TDDFT/BH&HLYP/cc-pVTZ is shown in bold while RKS/BH&HLYP/cc-pVTZ in underlined.

Figure S4: Optimized structures of ground state (FC) with atom numbering, $CI_{21,+}$, $CI_{10,+}$, $S_{0,\,min\,+}$ (intermediate **4**) and *R*-**2** (product), TS_{41}, and TS_{42} with one water molecule included. The ϕ values are given in parenthesis next to C_5=C_6 bond in (°).

Vertical excitation energies

Extensive experimental and theoretical works are collected in Table S2. The three lowest excited states (S_1, S_2, and S_3) are characterized by $n \rightarrow \pi^*$, $\pi_1 \rightarrow \pi_1^*$, and $\pi_2 \rightarrow \pi_1^*$ transitions respectively (See Figure S1 for frontier orbitals of uracil). The failure of CASSCF in the description of uracil photo-dynamics is originated from the overestimation of S_2 state due to the lack of dynamic electron correlation, resulting in S_2-trapping model.[S1] This is because the bright S_2 ($\pi_1 \rightarrow \pi_1^*$) state has a strong ionic character, requiring a proper description of dynamic electron correlation. However, CASSCF is especially deficient for this, which inevitably overestimate the S_2–S_1 energy gap (Δ_{12}). As expected, the CASSCF produce overestimated values of 1.63 $\sim$ 1.64 eV (See Table S2) as compared to the experimental value of 0.70 eV,[S18] while the CASPT2 calculations yield underestimated values 0.18 $\sim$ 0.25 eV. The results obtained by the equation-of-motion coupled cluster (EOMCC) are 0.25 $\sim$ 0.63 eV. The Δ_{12} from MRSF-TDDFT/BH&HLYP/6-31G* is 0.38 eV, making it consistent with the high level quantum methodologies. Although this value is *ca.* 0.32 eV smaller than the experimental 0.7 eV,[S18] it should be remembered that the experimental estimate of the $n \rightarrow \pi^*$ transition corresponds to the origin of the transition band, but the theoretical values correspond to vertical transitions. Therefore, the vertical gap Δ_{12} from the experiment may be somewhat smaller than 0.7 eV; thus, improving the agreement between theory and experiment. Taking into account our previous NAMD study of thymine and its consistency with the high level *ab initio* computations, MRSF-TDDFT in connection with the BH&HLYP density functional was selected for the NAMD simulations in the present work.[S17]

Table S2: Vertical excitation energies of the three lowest singlet ($n_{O7}\pi_1^*$, $\pi_1\pi_1^*$, $\pi_2\pi_1^*$) excited states of uracil obtained with various methods from the literature. All energies are relative to the respective ground state minimum energy and are given in electron volt (eV). See Figure S1 for frontier orbitals of uracil.

Methods	S_1 ($n_{O7}\pi_1^*$)	S_2 ($\pi_1\pi_1^*$)	S_3 ($\pi_2\pi_1^*$)	Ref
Experiment	4.38[a)]	5.08[b)]	6.63[b)]	S18,S19
3SA-CASSCF(12e, 9o)/ cc-pVDZ[c)]	5.04	6.67	-	S1
MRCIS/ cc-pVDZ[c)]	5.24	6.12	-	S1
XMS-CASPT2/ cc-pVDZ[c)]	4.86	5.04	-	S1
TD-DFT/B3LYP/ 6-31G*[c)]	4.67	5.31	-	S1
SCS-ADC(2)/ aug-cc-pVDZ[d)]	4.56	5.13	6.12	S20
SA4-CASSCF(14e,10o)/ 6-31G*	5.18	6.82	7.29	S21
SA4-CASPT2(14e,10o)/ 6-31G*	4.93	5.18	6.18	S22
SA7-CASPT2(14e,10o)/ 6-31G*[e)]	4.91	5.09	-	S22
EOM-CCSD/ 6-31G*	5.30	5.93	7.05	S23
CR-EOM-CCSD(T)/ 6-31G*	5.19	5.65	6.77	S23
EOM-CCSD/ aug-cc-pVTZ	5.23	5.59	-	S23
CR-EOM-CCSD(T)/ aug-cc-pVTZ	5.00	5.25	-	S23
MRCISD+Q/ TZVP	5.05	5.76	6.65	S24
SC-NEVPT2/ TZVP	5.10	5.39	6.33	S24
PC-NEVPT2/ TZVP	5.04	5.27	6.22	S24
XMCQDPT2/ TZVP	4.43	4.88	5.62	S24
CASPT2(20,14)/ 6-31G* (U-H_2O)[f)]	4.96	5.20	-	S25
MRSF-TDDFT/ BH&HLYP/ 6-31G*	5.72(0.0012)	6.10 (0.6352)	6.80 (0.0002)	This work
MRSF-TDDFT/ BH&HLYP/ cc-pVTZ[g)]	5.70 (0.0007)	5.97 (0.6087)	6.75 (0.0446)	This work
MRSF-TDDFT/ BH&HLYP/ 6-31G* (U-H_2O)[f)]	5.93 (0.0010)	6.01 (0.6024)	6.87 (0.0942)	This work
MRSF-TDDFT/ BH&HLYP/ 6-31G* (at $S_{0,\,\mathrm{min}\,+}$)	4.20 (0.1059)	4.94 (0.0575)	5.41 (0.0258)	This work
MRSF-TDDFT/ BH&HLYP/ 6-31G* (at $S_{0,\,\mathrm{min}\,+}$–H_2O)[f)]	4.16 (0.1077)	5.03 (0.0566)	5.33 (0.0294)	This work

[a)] In a supersonic jet from Ref. S18. [b)] Absorption maximum in vapor from Ref. S19.
[c)] At DFT/B3LYP/6-31G* optimized geometry.
[d)] Spin-component scaling algebraic diagrammatic-construction method. The effect of vibrational averaging and temperature are included. Note that $\pi_2\pi_1^*$ state is S_5 state in Ref. S20.
[e)] It included four singlet states (S_0, S_1, S_2, S_3) and three triplet states (T_1, T_2, T_3).
[f)] -H_2O denotes Uracil with water molecule. [g)] In the MRSF/BH&HLYP/6-31G* optimized geometry.

Table S3: Relative energies of the three lowest singlet (S_2, S_1, S_0) states of uracil obtained by MRSF with different basis set and functional. The relative energies (in eV) are given relative to the respective ground state energy in the BH&HLYP/6-31G* optimized geometries.

	S2	S1	S0
	FC geometry		
BH&HLYP/6-31G*	5.72	6.10	6.80
BH&HLYP/cc-pVTZ	5.70	5.97	6.75
	$CI_{21,\,BLA}$		
BH&HLYP/6-31G*	5.58	5.58	0.34
BH&HLYP/cc-pVTZ	5.57	5.47	0.78
	$S_{1,\,min}$		
BH&HLYP/6-31G*	6.02	4.22	1.20
BH&HLYP/cc-pVTZ	5.98	4.29	1.22
	$CI_{10,\,+}$		
BH&HLYP/6-31G*	7.50	4.35	4.35
BH&HLYP/cc-pVTZ	7.51	4.35	4.32

Minimum energy paths

Figure S5: Minimum energy paths (MEPs) on the S_2 (blue), S_1 (red), and S_0 (black) PESs of uracil obtained using the nudged elastic band (NEB) optimization[S2,S3] in connection with the MRSF-TDDFT/BH&HLYP/6-31G* method.

Results of MRSF-TDDFT gas phase NAMD Simulations

The four-state (S_0, S_1, S_2, and S_3) NAMD simulations were initiated by sampling the Wigner function of a canonical ensemble[S26,S27] at T = 300K around the S_0 equilibrium geometry. The nonadiabatic coupling vectors are computed numerically by using a fast overlap calculation.[S28] The NAMD has been performed based on the fewest-switches surface-hopping algorithm.[S29] Hundred Trajectories in connection with MRSF-TDDFT/BH&HLYP/6-31G* were initiated to the bright $\pi\pi^*$ state and propagated using the NVE ensemble with a time step of 0.5 fs until 5 ps for a propagation of the nuclear degrees of freedom and with a sub time-step size 10^{-5} fs for a propagation of the electronic degrees of freedom.[S30] Among hundred trajectories, 88 trajectories have finished successfully and were used for the entire analysis. 78 out of 88 trajectories have bright S_2 state, while 10 out of 88 trajectories have bright S_1 state at t=0 fs. The MRSF-TDDFT computations were performed with a locally modified version of the GAMESS-US code as described in Refs. S11,S12.

The time evolution of the adiabatic populations from NAMD simulations is shown in Figure S6 in comparison with the result from Ref. S1. While the extended multi-state

(a) (b)

Figure S6: Time evolution of the adiabatic S_0, S_1, S_2, and S_3 populations for 300fs duration obtained in the (a) MRSF-TDDFT/BH&HLYP/6-31G* and in the (b) XMS-CASPT2/cc-pVDZ NAMD simulations from Ref. S1.

CASPT2 (XMS-CASPT2) starts with *c*a. 40 % of S_2 state, the MRSF-TDDFT starts with *c*a. 90 % of S_2 state, which perhaps makes the τ_1 (the $S_2 \rightarrow S_1$ internal conversion process) of the former (12.5 fs) slightly smaller than the latter (37.0 $\pm$1.2 fs) (See Table. S4). In the MRSF-TDDFT NAMD simulations, within the first *ca.* 20 fs, the population of the S_2 state drops to around 40 % (due to the $S_2 \rightarrow S_1$ population transfer) and becomes almost negligible at $t \gtrsim 100$ fs. In both simulations, the S_0 state population starts to appear at *ca.* 40 fs and MRSF-TDDFT remarkably well reproduce the overall dynamics; the rise of S_0, decrease of S_1 and even their population cross between 150 $\sim$ 250 fs of XMS-CASPT2 as shown in Figure S6.

Regarding the ground state population changes, as discussed in the main text, two distinctively different dynamics (fast and slow decay channel) are seen in both simulations although it is limited to 300 fs in the case of XMS-CASPT2. The overall dynamics proceed similarly.

Figure S7: Panel (a) shows the time evolution of BLA along all the trajectories within the first 100 fs. panel (b) shows the position of BLA vibrations represented as black arrows. Panel (c) shows the time evolution of HOOP torsion angle (ϕ) along all the trajectories within the first 100 fs. Panel (d) represent the position of HOOP torsion angle (ϕ) as an arrows. Panel (e) shows the time evolution of ϕ along all the trajectories within the 1 ps. The red and blue empty dots represent the hopping points of $S_2 \leftrightarrow S_1$ and $S_1 \leftrightarrow S_0$ respectively. The red, blue, and green horizontal lines represent the ϕ value of $CI_{21,\pm}$, $CI_{10,\pm}$, and $S_{0,\,\mathrm{min}\,\pm}$ respectively. The gray vertical dashed lines represent the time at 12 fs.

Figure S8: (a) Time evolution of the adiabatic S_0, S_1, S_2, and S_3 populations for 100fs duration of the NAMD simulations. The margin of error of the exponential decay parameters were determined by bootstrapping.[S4] Time evolution of the fraction of population after decay to the ground state determined by the HC_5C_6H torsion angle until (b) 100fs and (c) 5ps. See Figure S2 for structures.

Figure S9: Snapshots of representatives which returns to planar $S_{0,\,min}$ (a) and stays in intermediate 4 $S_{0,\,min\,+}$ (b) during NAMD simulations. Hydrogen out of plane (HOOP) torsion angles are given next to each figure. (c) Evolution of the HC_5C_6H dihedral angle (φ) during the NAMD simulations. It only shows trajectories which stay in **4**. The trajectory used in (b) is presented in cyan color.

Experimental and theoretical excited state decay constants

Extensive experimental and theoretical works are collected in Table S4. The first pump-probe experiment on uracil reported a mono-exponential decay with a 2.4 ps lifetime.[S31] Subsequent study by time-resolved photoelectron spectroscopy (TRPES) were able to fit three time-constants of $<$ 50fs, 530fs, and 2.4 ps.[S32] A much longer life-time of several nanoseconds has also been found in methylated uracils and was explained by trapping in the dark $n\pi^*$ state[S33,S34] Later Canuel et al. reported decay time constants as 0.13 ps and 1.1 ps.[S35] Strong-field ionization in conjunction with time-of-flight mass spectrometry (TOFMS) (along with 262 nm pump laser) produced two decay time-constants: 70-90 fs and 2.2-3.2 ps.[S36,S37] Recently, TRPES measurement by Yu et al. observed the decay constants of 170 fs, 2.4ps, and $>$ 1 ns whereas, $>$ 1 ns time-constant was attributed to trapping in the triplet state.[S38] Time-resolved photo-ion yield measurements yielded timescales of 65 $\sim$ 80 fs, 200 $\sim$ 455 fs, and 2.0 $\sim$ 3.3 ps.[S39,S40] Generally, the experimental measurements agree on two particular time-constants: one shorter time-constant of $\lesssim$ 200 fs and a longer one between $\sim$2 – 3 ps.

Using complete active space SCF method (CASSCF) method and full multiple spawning (FMS), it was shown that after excitation uracil gets trapped in the S_2 minimum.[S41] One year later, surface hopping trajectories coupled to Car–Parrinello molecular dynamics (CPMD) on potentials calculated with the restricted open Kohn-Sham (ROKS)/BLYP observed a sub-ps (551, 608fs) direct decay from the $\pi\pi^*$ state to the ground state, governed by the so-called ethylenic $\pi\pi^*/S_0$ conical intersection.[S42,S43] Later, two decay constants are found: one is intermediate range (650 $\sim$ 740 fs) characterized by the direct $\pi\pi^* \rightarrow$ ground state, the other is longer range (1.5, 1.8 ps) characterized by the indirect $\pi\pi^* \rightarrow n\pi^* \rightarrow$ ground state decay mechanism.[S44,S45] They have shown the presence of a population trapping on the S_2 state that contributes to the longer time-constant.[S45] However, multi-reference configuration interaction (MRCI) combined with the valence shell model Hamiltonian, orthogonalization

corrected methods (OM2), simulation shows that the ultrafast $S_2 \rightarrow S_1$ de-excitation occurs within 50 fs and internal conversion to the ground state occurs in less than 1 ps.[S46] The CASSCF simulation shows relatively quicker decay time constant of $\pi\pi^*$ state than the other CASSCF based simulations.[S47] Meanwhile, Richter et al. investigated the involvement of intersystem crossing on the dynamics at the CASSCF level and were able to obtain the shorter and the longer timescales similar to most of the experiments once they fitted the total S_0 + T_1 yield of the simulation. Recently, it was demonstrated that trapping on S_2 state is artifact caused by an insufficient account of the dynamic electron correlation by comparing various methodologies on uracil and thymine.[S1,S17]

Table S4: Decay constants of uracil measured by a pump-probe experiments and theoretical simulations using various methods.

Experimentally estimated decay constants					
Pump(nm)	Probe(nm)	τ_1 (fs)	τ_2 (fs)	τ_3 (ps)	Ref
267	n $\times$ 800	-	-	2.4	S31
250	200	< 50	530	2.4	S32
267	2 $\times$ 400	130	-	1.1	S35
267	330	< 100	-	-	S48[a)]
262	n $\times$ 780	$70 \sim 90$	-	$2.2 \sim 3.2$	S36,S37
260	2 $\times$ 295	170	-	2.4	S38
260	n $\times$ IR	$65 \sim 80$	-	$2.5 \sim 3.0$	S39
260	156	–	$325 \sim 455$	$2.0 \sim 3.3$	S39
267	400	–	200	3.0	S40
Theoretically estimated decay constants					
Method		τ_1 (fs)	τ_2 (fs)	τ_3 (ps)	Ref
CPMD/BLYP		-	551, 608	-	S42,S43
OM2/MRCI		21	570	-	S46
3SA-CASSCF(10e,8o)/6-31G*		-	$650 \sim 740$	$> 1.5 \sim 1.8$	S44,S45
4SA-CASSCF(14e,10o)/6-31G*		-	516	-	S47
7SA-CASSCF(14e,10o)/6-31G*		30 ± 1 (8 ± 1)	-	3.2 ± 0.1 (2.6 ± 0.1)	S22[b)]
7SA-CASSCF(14e,10o)/6-31G*		-	-	2.4 ± 0.1 (4.2 ± 0.1)	S22[c)]
7SA-CASSCF(14e,10o)/6-31G*		-	-	2.8 ± 0.1 (5.2 ± 0.1)	S22[d)]
3SA-CASSCF(12e,9o)/cc-pVDZ		-	575.5	-	S1
MRCIS(12e,9o)/cc-pVDZ		66.0	-	-	S1
XMS-CASPT2(12e,9o)/cc-pVDZ		12.5	-	-	S1
TDDFT/B3LYP/6-31G*		129	-	-	S1
SCS-ADC(2)/aug-cc-pVDZ		160 ± 40	-	2.35	S20
SCS-ADC(2)/aug-cc-pVDZ ($U(H_2O)_6$)[e)]		76 ± 18	-	-	S20
MRSF-TDDFT/BH&HLYP/6-31G*		37.0 ± 1.2	107.8 ± 0.4	1.9 ± 0.015	This work

[a)] Fluorescence upconversion in aqueous solution. [b)] Bi-exponential fitting of $\pi\pi^*$ state.
[c)] Mono-exponential fitting of S_0 + T_1 states. [d)] Bi-exponential fitting of S_0 + T_1 states.
[b,c,d)] The results when restricting the excitation energy to a small window are given in parenthesis.
[e)] Dynamics simulation with six water molecules.

Generality of occurrence of 4

Although the formation of an intermediate similar to **4** has not previously been observed in NAMD simulations of other pyrimidine bases, *e.g.*, thymine and cytosine,[S17,S25,S44] its absence among the products obtained theoretically does not necessarily imply the impossibility of its existence. Indeed, typical duration of the NAMD simulations is usually $\lesssim 0.5 - 1$ ps and the number of the propagated trajectories is on the order of 100 or fewer. In the present simulations of the uracil, the probability of formation of **4** is very low, *ca.* 0.08. If for the other pyrimidine nucleobases this probability is even lower, then it may require to propagate a much greater number of trajectories (*e.g.*, several thousand) for a much longer time (*e.g.*, 10 – 50 ps) to observe the formation of a torsionally strained intermediate similar to **4**. Such requirements have not been met in the NAMD simulations performed for the nucleobases so far.

Figure S10: Geometries of torsionally distorted structures **4** (**4**-ura) of uracil, **4**-thy of thymine, and **4**-cyt of cytosine. The key bondlength (in Å), the diherdal angle θ (see Figure 1d of the main article for definition), and the relative energy (ΔE in kcal/mol) with respect to the ground state equilibrium structure are given.

Nevertheless, the structures similar to **4** can, in principle, be obtained in the geometry optimizations started with a suitable geometry. If the optimized structure is

a local minimum, such geometry optimization can be a proof of the existence of the intermediate **4** for other pyrimidine nucleobases. To verify this conjecture, a series of geometry optimizations have been performed with the BH&HLYP/cc-pVTZ method for torsionally distorted structures of thymine and cytosine. These optimizations did indeed produce structures similar to **4** for the two other pyrimidine bases. The structures shown in Figure S10 are the local minima on the ground electronic state PES; they were characterized by vibrational analysis, which did not produce imaginary frequencies. The **4**-thy and **4**-cyt structures occur at approximately the same relative energy with respect to the ground state equilibrium geometry as **4**. Hence, these calculations confirm feasibility of existence of the torsionally strained intermediates in other pyrimidine bases.

IR spectra of uracil and intermediate 4

Figure S11 shows the IR spectra of uracil and intermediate **4**. The spectra were built using the experimental matrix isolation IR frequencies and intensities from Ref. S5 and the IR frequencies (cm^{-1}) and intensities (km/mol) computed by the BH&HLYP/cc-pVTZ method in the gas phase. The computed frequencies were scaled by the factor 0.9335.[S6] The spectra were convoluted with the Lorentzian lineshape function with half-width at half maximum 10 cm^{-1}.

Figure S11: IR spectra of uracil. The black line shows the experimental matrix isolation spectrum of **1** from Ref. S5, the blue shows calculated spectrum of **1**, and the red line shows the calculated spectrum of **4**. The vibrational normal modes of **4** contributing to the IR band near 1050 cm^{-1} are shown on the right hand side. The modes were computed by the BH&HLYP/cc-pVTZ method both in gas phase and in water environment modeled by PCM. For both sets of calculation, the vibrational frequencies (cm^{-1}) and the IR intensities (km/mol) are given. The theoretical vibrational frequencies are scaled by the factor 0.9335 recommended in Ref. S6.

Results of MRSF-TDDFT/BH&HLYP/6-31G* calculations

Table S5: Cartesian coordinates at the optimized geometry of **FC** (**1**) in gas phase. Total electronic energy is -414.5842436195 a.u.

Atom	X	Y	Z
N	-0.8507358821	0.1483982487	0.1309638429
N	1.2065759763	1.1506432857	0.3274277750
C	-0.1627300689	1.3190870374	0.3247810122
C	1.8185587237	-0.0598470003	0.1558673228
C	1.1185414026	-1.1861918970	-0.0307273443
C	-0.3301519006	-1.1352576413	-0.0543378164
O	-1.0686630960	-2.0756001362	-0.2142226795
O	-0.6855980352	2.3919625189	0.4785183364
H	-1.8518850184	0.2284706359	0.1222942000
H	1.7369266577	1.9883994559	0.4668204689
H	2.8935665712	-0.0394434137	0.1820457413
H	1.5949835415	-2.1377510911	-0.1651964451

Table S6: Cartesian coordinates at the optimized geometry of $\mathbf{S_{0,min\,+}}$ (**4**) in gas phase. Total electronic energy is -414.5842436195 a.u.

Atom	X	Y	Z
N	-0.9495066127	-0.0442039132	0.0916925779
N	1.1071516065	1.1572973055	-0.0882751850
C	-0.2883767368	1.1976059163	0.1225914552
C	1.5022766026	-0.0982359177	-0.5220222909
C	1.0456678590	-1.0377115754	0.3681674545
C	-0.3769604217	-1.3395691740	0.0161552082
O	-1.0122541673	-2.3137798150	-0.2312537783
O	-0.8855285667	2.2271468475	0.2544415833
H	-1.9515794944	0.0306890442	0.1079496517
H	1.4700350473	2.0218136990	-0.4534049865
H	1.6201259265	-0.2719287664	-1.5836090410
H	1.0696029602	-0.6648677381	1.3853620868

Table S7: Cartesian coordinates at the optimized geometry of $\mathbf{CI_{21,\,BLA}}$ in gas phase. Total electronic energy is -414.3807170548 a.u.

Atom	X	Y	Z
N	-0.0243423944	0.9942084048	0.2148651759
N	0.2083997047	-1.2327654228	-0.4203873193
C	0.7526954158	0.0797938994	-0.3785242107
C	-0.9890970731	-1.6260112457	-0.0095847424
C	-1.8271443100	-0.5451552712	0.5875611945
C	-1.3615757634	0.7740990583	0.6980653678
O	-1.9506698373	1.7372174127	1.1668238255
O	1.8923018150	0.2167678232	-0.7583801401
H	0.3185318112	1.9291243735	0.2657331357
H	0.8515274273	-1.8852901791	-0.8399789002
H	-1.2757752782	-2.6489386334	-0.1299755108
H	-2.8076083824	-0.7656812396	0.9463207200

Table S8: Cartesian coordinates at the optimized geometry of $\mathbf{CI_{21,\,+}}$ in gas phase. Total electronic energy is -414.3904161538 a.u.

Atom	X	Y	Z
N	-1.2435710440	0.1502009501	-0.3632137411
N	0.7778741217	1.0216482638	0.3443773570
C	-0.6124033702	1.2021211935	0.2418852485
C	1.4050035304	-0.0269822643	-0.2219137391
C	0.6277812845	-1.2848847140	-0.1543558330
C	-0.7209634714	-1.1749680713	-0.2601636366
O	-1.5858513997	-2.0898349138	-0.1663986287
O	-1.1328493046	2.2216764738	0.6097325784
H	-2.2448485395	0.2197055609	-0.3837018457
H	1.2628773757	1.8505567978	0.6509290605
H	2.4133158034	0.0859104598	-0.5729264224
H	1.0536350136	-2.1751497362	0.2757496022

Table S9: Cartesian coordinates at the optimized geometry of $\mathbf{S_{1,\,min}}$ in gas phase. Total electronic energy is -414.4289194957 a.u.

Atom	X	Y	Z
N	-0.8593573970	0.1423092184	0.1339940150
N	1.1985677391	1.1611544172	0.3301529782
C	-0.1525699438	1.3178104032	0.3256453526
C	1.8722112526	-0.0546343434	0.1661039252
C	1.0953093558	-1.2157549971	-0.0335405543
C	-0.2442822616	-1.0889868193	-0.0434329347
O	-1.1265818026	-2.0809184729	-0.2148819090
O	-0.7143884410	2.3747573238	0.4727046834
H	-1.8560066546	0.2308955584	0.1143813998
H	1.7090744388	2.0092247862	0.4756799788
H	2.9414823909	-0.0276635092	0.1672852241
H	1.5559301944	-2.1753235625	-0.1698577445

Table S10: Cartesian coordinates at the optimized geometry of $\mathbf{CI_{10,\,+}}$ in gas phase. Total electronic energy is -414.4244502925 a.u.

Atom	X	Y	Z
N	-0.6598119696	-0.1897240473	-0.1841900015
N	0.7138092789	1.6600229185	0.2661379046
C	-0.6007872670	1.1195459648	0.2126404566
C	1.7281750769	0.8875431467	-0.1392536321
C	1.6605996412	-0.4885162491	0.2464258321
C	0.3936441983	-1.1470932295	-0.1009704253
O	0.1230220801	-2.3101956063	-0.1767451016
O	-1.5489234665	1.8257094101	0.4054381864
H	-1.5897210631	-0.5592085007	-0.2779094697
H	0.7235596541	2.6667353422	0.2080197459
H	2.4796266345	1.3385081077	-0.7728599210
H	1.7471622021	-0.5831712569	1.3304174256

Table S11: Cartesian coordinates at the optimized geometry of **FC** (**1**) with one water molecule in the gas phase. Total electronic energy is -490.9678984965 a.u.

Atom	X	Y	Z
N	-0.7638463700	0.4225018261	0.0509076132
N	1.0469059916	1.3215348164	1.1405890629
C	-0.3140553297	1.3760798236	0.9331562234
C	1.8677818214	0.4128831982	0.5324591957
C	1.4007121666	-0.5050873157	-0.3247646715
C	-0.0150733994	-0.5387685227	-0.6152471383
O	-0.5687261152	-1.3146493770	-1.3696693430
O	-1.0277371315	2.1795704725	1.4728779488
H	-1.7526601313	0.4256760175	-0.1265625016
H	1.4066194993	2.0034911117	1.7798870311
H	2.9089432364	0.4884443614	0.7910079436
H	2.0303237631	-1.2266443550	-0.8117656160
O	1.5494502450	-2.9518549668	-2.3353574102
H	1.6330864559	-2.7354045106	-3.2634441147
H	0.6932262248	-2.5857237525	-2.0799303665

Table S12: Cartesian coordinates at the optimized geometry of $\mathbf{S_{0,\,min\,+}}$ (**4**) with one water molecule in the gas phase. Total electronic energy is -490.8317441974 a.u.

Atom	X	Y	Z
N	-0.5677564783	-0.1311876589	0.2363480876
N	0.6609409261	1.8515603740	-0.2847370776
C	-0.4662468040	1.2751028223	0.3323375508
C	1.3187953577	0.9143657272	-1.0679409342
C	1.6161999495	-0.1775732409	-0.2906297591
C	0.4013773581	-1.0417635300	-0.2218836890
O	0.1671289798	-2.2008096383	-0.3997312388
O	-1.3252964292	1.9274147574	0.8496126335
H	-1.4353573860	-0.4980708795	0.5876383206
H	0.5151351538	2.8117904026	-0.5479913125
H	1.0841778610	0.8623852036	-2.1232299243
H	1.8904198438	0.0957023177	0.7206094981
O	2.7433445513	-2.9698749376	0.6978113588
H	3.3816005549	-2.8971477513	-0.0109005097
H	1.8978733479	-3.0527885182	0.2487233228

Table S13: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{41}}$ with one water molecule in the gas phase. Total electronic energy is -490.8186429882 a.u.

Atom	X	Y	Z
N	-1.6947739546	0.2751595437	-0.6580420238
N	-0.0568687724	1.5408932416	0.4550820169
C	-1.3812896335	1.4792905378	-0.1090973865
C	0.6898864385	0.4628305139	0.4683050570
C	0.0617461481	-0.8136254371	0.5728213020
C	-0.9486762802	-0.9445062095	-0.5257271360
O	-1.2729624335	-1.8762944057	-1.1904107566
O	-2.0345635628	2.4781310758	-0.1667970543
H	-2.5007720664	0.2737729478	-1.2593435219
H	0.3084343303	2.4801925397	0.5107265824
H	1.7613839737	0.5964058846	0.3826638099
H	-0.6437882166	-0.6606575675	1.4021366893
O	2.8320856047	-1.5161795752	0.1981393981
H	1.9001008897	-1.6593769802	0.4514048762
H	2.9800572371	-2.1160361086	-0.5318618528

Table S14: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{42}}$ with one water molecule in the gas phase. Total electronic energy is -490.8125341902 a.u.

Atom	X	Y	Z
N	-1.5775224103	0.4447548654	-0.5248736481
N	0.3354463611	0.9623844951	0.7511681456
C	-0.9741779275	1.3013911782	0.3658538558
C	0.9452714531	0.0490248716	-0.1537435404
C	0.1779865258	-1.1899291508	-0.4136585361
C	-1.1764906723	-0.8774963190	-0.8712221622
O	-1.9885308683	-1.5926911594	-1.3874803941
O	-1.4938592331	2.3099011235	0.7606545435
H	-2.5270190274	0.6873758494	-0.7477171966
H	0.8314053314	1.8125932387	0.9706687783
H	1.3379429624	0.5314601090	-1.0436055310
H	0.0104950648	-1.6723793198	0.5521132523
O	2.1762364868	-0.5532773061	0.4488673674
H	1.9317926887	-1.4889697562	-0.0878064344
H	1.9910236647	-0.7241426194	1.3807806010

Table S15: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{12}}$ with one water molecule in the gas phase. Total electronic energy is -490.8653370039 a.u.

Atom	X	Y	Z
N	3.325249255	3.788285442	-4.587956124
N	2.880231215	2.701720155	-2.599545703
C	3.785387929	3.444705714	-3.351857672
C	1.707214636	2.197603015	-3.066094468
C	1.247010553	2.606861712	-4.362164989
C	2.041503130	3.556673158	-5.112920500
O	1.721796302	4.103191936	-6.138471316
O	4.861698598	3.748218983	-2.908775061
H	3.915188119	4.403475088	-5.118661645
H	3.211272068	2.461572220	-1.684025463
H	0.184413830	2.667473016	-4.520497407
H	1.003203815	1.929768195	-2.300718650
O	1.946990672	0.509978209	-3.626901919
H	1.630496323	1.232979374	-4.563031769
H	2.874413556	0.243283782	-3.645747314

Table S16: Cartesian coordinates at the optimized geometry of **R-2** in the gas phase. Total electronic energy is -490.9671196653 a.u.

Atom	X	Y	Z
N	-0.8580235814	0.3593200907	-0.0035538827
N	1.1719964039	1.1474329525	0.7832985903
C	-0.1663004733	1.3835263199	0.6199777126
C	1.8785735269	0.1945845992	-0.0300580430
C	1.0859823445	-1.0935302015	-0.0766246009
C	-0.3692442905	-0.8597577266	-0.4292241104
O	-1.0564242113	-1.6571117113	-0.9769655959
O	-0.7218583550	2.3798799922	1.0048486113
H	-1.8335880859	0.5339032000	-0.1662062774
H	1.6658989569	1.9407117519	1.1470913073
H	2.8452697580	0.0271547700	0.4398808064
H	1.1118429195	-1.5728568403	0.9003447601
O	2.0419132770	0.6070662035	-1.3607621525
H	1.5022536215	-1.7741638461	-0.8074964782
H	2.5070813730	1.4445443780	-1.3810912691

Table S17: Cartesian coordinates at the optimized geometry of **S-2** in the gas phase. Total electronic energy is -490.9659999357 a.u.

Atom	X	Y	Z
N	-0.9245084501	0.3983743169	-0.1256326893
N	0.9942622612	1.2176507963	0.8914491162
C	-0.3167142503	1.4346108959	0.5714502458
C	1.8124683181	0.2379608996	0.2057168809
C	1.0121476233	-1.0446586604	0.0687543055
C	-0.3904373643	-0.8282480919	-0.4607253649
O	-1.0016481903	-1.6399695646	-1.0740968222
O	-0.9261702701	2.4300552661	0.8651057165
H	-1.8810480177	0.5602572733	-0.3859903942
H	1.4664060798	2.0547584534	1.1837472658
H	2.1176487851	0.5968291535	-0.7755448407
H	0.9104745262	-1.4997977130	1.0554918460
O	3.0006724766	0.0566877604	0.9008085063
H	1.5163589643	-1.7535616250	-0.5757309791
H	2.7898663953	-0.2578484495	1.7834516894

Table S18: Cartesian coordinates at the optimized geometry of **S-5** in the gas phase. Total electronic energy is -490.9631789791 a.u.

Atom	X	Y	Z
N	-0.8686522429	0.2809659057	0.0374660078
N	1.1712891087	1.1988245513	0.6394584037
C	-0.1774282529	1.3535693519	0.6088089399
C	1.8608305739	0.2232094591	-0.1780207785
C	1.1339283533	-1.1003546146	-0.0529612835
C	-0.3488568409	-0.9134134341	-0.3810645350
O	-0.9772186540	-1.7615799057	-0.9283070913
O	-0.7707126360	2.3086047352	1.0382682338
H	-1.8588929380	0.4145036639	-0.0677410978
H	1.6597934414	2.0181783557	0.9449379352
H	2.8786155531	0.1163777074	0.1790700678
H	1.1693263160	-1.4242341285	0.9926628039
O	1.6862357410	-2.0404728314	-0.9028436385
H	1.8989601054	0.5110018449	-1.2288808173
H	0.9601545329	-2.5911682229	-1.2156378572

Table S19: Cartesian coordinates at the optimized geometry of **R-5** in the gas phase. Total electronic energy is -490.9609346302 a.u.

Atom	X	Y	Z
N	-0.8288628394	0.3163969094	-0.0002421770
N	1.1619984299	1.3474478663	0.5454633540
C	-0.1882640737	1.4417801064	0.5227856476
C	1.9088264859	0.3242253674	-0.1438395611
C	1.2189422433	-1.0166272483	-0.0260394657
C	-0.2812891154	-0.9119468126	-0.2445999080
O	-0.9448911284	-1.8730607122	-0.5440508584
O	-0.8129553191	2.3895769970	0.9133411477
H	-1.8316960280	0.3782821666	-0.0156794719
H	1.6256042458	2.1709841282	0.8760560850
H	2.8959844960	0.2465197104	0.2971673509
H	1.6094246694	-1.6926085737	-0.7846169496
O	1.4418882144	-1.5187417164	1.2680780847
H	2.0259559257	0.5729939773	-1.2005880040
H	0.9801773825	-2.3564084090	1.3458725317

Table S20: Cartesian coordinates at the optimized geometry of $\mathbf{CI_{21,+}}$ with one water molecule in the gas phase. Total electronic energy is -490.7669920038 a.u.

Atom	X	Y	Z
N	1.097962909	1.207555467	-0.660159828
N	0.426560217	0.598097518	1.466464417
C	1.292707811	1.373392854	0.690240596
C	-0.402239019	-0.320983976	0.919343396
C	-0.977921316	0.104883335	-0.379315575
C	-0.181873586	0.865053181	-1.170690471
O	-0.482990463	1.398063259	-2.282133070
O	2.143215904	2.062762255	1.187243308
H	1.654627532	1.811562447	-1.237192723
H	0.652002531	0.610203590	2.448126783
H	-0.650983466	-1.219438836	1.448906585
H	-2.044554836	0.129459699	-0.532050743
O	-1.097586309	-2.986519122	-0.359316961
H	-1.111612364	-2.180097139	-0.882233847
H	-0.317315546	-3.453994535	-0.657231867

Table S21: Cartesian coordinates at the optimized geometry of uracil $\mathbf{CI_{10,+}}$ with one water molecule in the gas phase. Total electronic energy is -490.8050982429 a.u.

Atom	X	Y	Z
N	-0.7527456571	-0.3027398947	-0.2040986454
N	0.9575521986	1.2703531683	0.1114103055
C	-0.4075711615	1.0312087117	-0.1161041482
C	1.8125024943	0.2219611823	0.1344093046
C	1.2868245126	-0.9440498203	0.7986330692
C	-0.0075619709	-1.4084945914	0.2475882488
O	-0.4891540454	-2.5042725701	0.2499323817
O	-1.1791420616	1.9309952737	-0.2969093333
H	-1.7103315907	-0.4740832350	-0.4566604504
H	1.2422185043	2.2045897927	-0.1339158931
H	2.7397171020	0.2665961247	-0.4136430043
H	1.1701398043	-0.8169995337	1.8751216881
O	3.7988086587	-1.9645193021	-0.5978902165
H	3.1048975970	-2.0619460255	0.0639412340
H	3.5874180675	-2.6174814106	-1.2648994554

Results of the R-BH&HLYP/cc-pVTZ computations

Table S22: Cartesian coordinates at the optimized geometry of **1** in the gas phase. Total electronic energy is -414.7449870639 a.u. (PCM: -414.7649304103 a.u.)

Atom	X	Y	Z
N	-0.8503855526	0.1473165159	0.1290023636
N	1.2021710872	1.1478965402	0.3268200834
C	-0.1621332474	1.3127594045	0.3237961024
C	1.8109196654	-0.0595996340	0.1554213671
C	1.1191363677	-1.1809073510	-0.0293838643
C	-0.3303343250	-1.1304284625	-0.0536165634
O	-1.0624135804	-2.0665688267	-0.2121171571
O	-0.6848875042	2.3792669575	0.4775306299
H	-1.8480215245	0.2266907636	0.1212453892
H	1.7327040306	1.9809076861	0.4631720125
H	2.8833930924	-0.0424652002	0.1808734053
H	1.5965551767	-2.1281061791	-0.1637441970

Table S23: Cartesian coordinates at the optimized geometry of **4** in the gas phase. Total electronic energy is -414.6111551638 a.u. (PCM: -414.6276625748 a.u.)

Atom	X	Y	Z
N	-0.9495263756	-0.0461286653	0.1161974129
N	1.1102206291	1.1523951311	-0.0975336242
C	-0.2834470372	1.1896005234	0.1407656275
C	1.4810688007	-0.1100101252	-0.5127214678
C	1.0458050526	-1.0248755706	0.3806283235
C	-0.3687042367	-1.3353978479	0.0072413249
O	-0.9853507890	-2.2983697267	-0.2884888160
O	-0.8699409834	2.2164480866	0.2785804842
H	-1.9476594996	0.0312007704	0.1220726542
H	1.4587528981	2.0038947237	-0.4950795941
H	1.6229213854	-0.2937723897	-1.5666729155
H	1.0365141580	-0.6207289971	1.3828053264

Table S24: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{41}}$ for ring planarization in the gas phase. Total electronic energy is -414.5981860544 a.u. (PCM: -414.6249692871 a.u.)

Atom	X	Y	Z
N	-1.2331673333	-0.0714395293	0.1462636845
N	0.7961158539	1.0452493916	-0.2216153599
C	-0.5907085180	1.1203781616	0.1401494370
C	1.3186751711	-0.1301416171	-0.4767911574
C	0.8531204208	-1.2701438690	0.2349904135
C	-0.6290402973	-1.3711915210	0.1233707611
O	-1.3453274127	-2.3137224860	0.1389261544
O	-1.0922429686	2.1904765981	0.2818055442
H	-2.2318383945	-0.0225523175	0.2065544786
H	1.1578042251	1.9125042939	-0.5795160357
H	2.0777967532	-0.1520610489	-1.2495557772
H	0.8650424232	-0.8872706286	1.2687377515

Table S25: Cartesian coordinates at the optimized geometry of the $\mathbf{T}_1$ uracil in the gas phase. Total electronic energy is -414.6284475895 a.u. (PCM: -414.6451212950 a.u.)

Atom	X	Y	Z
N	-0.9804882859	-0.0124625019	-0.1009089205
N	1.0296091039	1.1473045438	0.0127771898
C	-0.3425464937	1.1989811070	0.0684569953
C	1.7420813618	0.0198993894	-0.3464111932
C	1.0488279166	-1.2326855802	-0.0063288938
C	-0.3961250807	-1.2675945333	-0.0119450407
O	-1.0651238048	-2.2589867236	0.1024424030
O	-0.9434876060	2.2211759195	0.2287787101
H	-1.9774168657	0.0204378648	-0.0250645586
H	1.4613302990	2.0483405137	-0.0065755219
H	2.4089864021	0.0894367493	-1.1894287988
H	1.5623280190	-2.0779937964	0.4079182820

Table S26: Cartesian coordinates at the optimized geometry of uracil **1** with one water molecule in the gas phase. Total electronic energy is -491.1746122164 a.u. (PCM: -491.1982692499 a.u.)

Atom	X	Y	Z
N	-0.6117617092	-0.0642647779	0.3152574975
N	0.4467458685	1.8109588409	-0.4669629296
C	-0.7152370983	1.2702395022	0.0242779418
C	1.5916885419	1.0930874625	-0.6433855883
C	1.6711695144	-0.2028304757	-0.3469517571
C	0.5037048847	-0.8712685393	0.1850125675
O	0.4403898219	-2.0327114707	0.5092530706
O	-1.7158690110	1.9079657836	0.1810827814
H	-1.4377313053	-0.4950582528	0.6817604293
H	0.4054791921	2.7831754854	-0.6854551117
H	2.4238786693	1.6450747209	-1.0355299785
H	2.5659709436	-0.7758119453	-0.4776198963
O	3.0199696659	-3.1349053298	0.1254361722
H	2.9437885132	-3.8297317390	-0.5169047986
H	2.1177319382	-2.9225413048	0.3734590997

Table S27: Cartesian coordinates at the optimized geometry of **4** with one water molecule in the gas phase. Total electronic energy is -491.0386375761 a.u. (PCM: -491.0595570110 a.u.)

Atom	X	Y	Z
N	-0.2761422610	-0.2326425745	-0.0876463754
N	0.3203844733	2.0675090277	0.1853178728
C	-0.7006801939	1.0937352575	0.1001237723
C	1.5456474300	1.5163112189	-0.1169372675
C	1.7395194335	0.4108017252	0.6441474722
C	1.0585032535	-0.6855196741	-0.1024363202
O	1.3950329510	-1.6947526701	-0.6317150433
O	-1.8536804096	1.3890266687	0.1035105505
H	-1.0080261805	-0.8562143625	-0.3667469442
H	0.0167017222	2.9729174672	-0.1202781389
H	1.9922407612	1.6776589216	-1.0845117391
H	1.2475690691	0.5057635205	1.6017599426
O	3.2822958274	-0.1008293150	-2.2422013916
H	3.3965442545	-0.3634908263	-3.1473573188
H	2.9953790690	-0.8860574646	-1.7809400513

Table S28: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{41}}$ with one water molecule in the gas phase. Total electronic energy is -491.0321957534 a.u. (PCM: -491.0575243395 a.u.)

Atom	X	Y	Z
N	-1.6446007082	0.2472045434	-0.6623106197
N	-0.0744754324	1.5562297553	0.5043476445
C	-1.3640218984	1.4624664935	-0.1171568085
C	0.6803636330	0.4830634652	0.5468719811
C	0.0301746996	-0.7756243184	0.6900108805
C	-0.8904446113	-0.9502780193	-0.4794013747
O	-1.1269624613	-1.8894517062	-1.1588224590
O	-2.0265689503	2.4432136901	-0.2305592062
H	-2.4053428630	0.2370967056	-1.3141876402
H	0.2833915942	2.4948032335	0.5355918327
H	1.7475897108	0.6051940649	0.4249928523
H	-0.7333891210	-0.5577025348	1.4467430110
O	2.7558971284	-1.5115738335	0.0469991600
H	1.8761060942	-1.6896432422	0.4041935413
H	2.8922828857	-2.1549982968	-0.6373127951

Table S29: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{42}}$ for water insertion to **4**. Total electronic energy is -491.0165892139 a.u. (PCM: -491.0470614097 a.u.)

Atom	X	Y	Z
N	-1.5730805204	0.4353732970	-0.5198955448
N	0.3395389252	0.9861745846	0.7355949439
C	-0.9776441298	1.2972081752	0.3656744965
C	0.9491782372	0.0679888376	-0.1471683699
C	0.1866792934	-1.1754471989	-0.3961765940
C	-1.1649284316	-0.8768592246	-0.8702270062
O	-1.9551051969	-1.5936282860	-1.4065059556
O	-1.5132902052	2.2872227430	0.7704877447
H	-2.5194556099	0.6729413369	-0.7451986116
H	0.8263807908	1.8358524118	0.9569447266
H	1.3618324198	0.5287999312	-1.0356160166
H	0.0137165903	-1.6578014401	0.5684681331
O	2.1857006269	-0.5962975857	0.4408558609
H	1.8024417428	-1.4657232554	-0.0964278304
H	2.0380358675	-0.7458042265	1.3791891236

Table S30: Cartesian coordinates at the optimized geometry of $\mathbf{TS_{12}}$ for direct water insertion to **1**. Total electronic energy is -491.0744112433 a.u. (PCM: -491.0990184682 a.u.)

Atom	X	Y	Z
N	3.3179402551	3.7977613385	-4.5839117640
N	2.8787309957	2.7137167220	-2.5938684981
C	3.7745941064	3.4533035793	-3.3514915945
C	1.7125945360	2.2061339654	-3.0561876830
C	1.2476159470	2.6067118306	-4.3661315059
C	2.0457557921	3.5513442107	-5.1165113160
O	1.7332928038	4.0847146125	-6.1431050839
O	4.8454255470	3.7590747040	-2.9150593673
H	3.9127464954	4.4002966358	-5.1170733627
H	3.2185693821	2.4629936497	-1.6890152054
H	0.1874071679	2.6744794319	-4.5129822502
H	1.0110921672	1.9184485702	-2.2999078792
O	1.9568010587	0.5007000264	-3.6469070170
H	1.6377211746	1.2905799080	-4.5534045682
H	2.8557825718	0.1755308141	-3.6418129046

Table S31: Cartesian coordinates at the optimized geometry of **R-2** in the gas phase. Total electronic energy is -491.1739912918 a.u. (PCM: -491.1964115661 a.u.)

Atom	X	Y	Z
N	-0.8629218738	0.3642441844	-0.0141917260
N	1.1643253448	1.1533510097	0.7630436773
C	-0.1715076589	1.3794136172	0.6161864854
C	1.8764591226	0.1937341323	-0.0305325723
C	1.0798735573	-1.0873258649	-0.0957020419
C	-0.3693391126	-0.8497329102	-0.4208255084
O	-1.0669922561	-1.6605364163	-0.9527470739
O	-0.7263624748	2.3634330021	1.0153371501
H	-1.8384664219	0.5324355890	-0.1591469465
H	1.6572381127	1.9310418709	1.1487420645
H	2.8290073586	0.0187625430	0.4558291115
H	1.1171942187	-1.5854744488	0.8667271866
O	2.0774413785	0.6104909432	-1.3552355133
H	1.4876733301	-1.7523692679	-0.8404617706
H	2.5571466284	1.4311354357	-1.3705272344

Table S32: Cartesian coordinates at the optimized geometry of **S-2** in the gas phase. Total electronic energy is -491.1725566742 a.u. (PCM: -491.1926335341 a.u.)

Atom	X	Y	Z
N	-1.5890105099	0.3530777834	-0.4051049088
N	0.3442816486	1.0502494228	0.6616794631
C	-0.9503314409	1.3256208053	0.3470133494
C	1.1340410303	0.0693900173	-0.0483799789
C	0.2908979381	-1.1663020815	-0.2682315159
C	-1.0895630327	-0.8658247720	-0.7825473337
O	-1.7302964244	-1.6320209088	-1.4388583380
O	-1.5242952355	2.3209783112	0.6858153911
H	-2.5338046096	0.5623183998	-0.6599740240
H	0.8416837639	1.8412709097	1.0176666210
H	1.4755663858	0.4630418266	-1.0010437742
H	0.1622108990	-1.6796442626	0.6817319816
O	2.3000598791	-0.1902681368	0.6580060516
H	0.7703989417	-1.8507032008	-0.9510277027
H	2.0798899628	-0.5590044744	1.5089407960

Table S33: Cartesian coordinates at the optimized geometry of **S-5** in the gas phase. Total electronic energy is -491.1685130109 a.u. (PCM: -491.1862794812 a.u.)

Atom	X	Y	Z
N	-0.8997541788	0.3426129081	-0.0318275853
N	1.2011366478	1.1575424511	0.4787305436
C	-0.1355003882	1.3292768426	0.5895753318
C	1.8000591334	0.2524712630	-0.4751724984
C	1.0431139458	-1.0556151533	-0.4325186815
C	-0.4359696774	-0.7966843090	-0.6129981325
O	-1.1377180829	-1.5622703600	-1.2121669104
O	-0.6619635413	2.2348428109	1.1707235107
H	-1.8874923716	0.5033141504	-0.0348967142
H	1.7373840264	1.9173205282	0.8382988950
H	2.8328317442	0.0864148346	-0.2059535737
H	1.1551981871	-1.4877107337	0.5638040315
O	1.5044740704	-1.9223541280	-1.4084961480
H	1.7745397504	0.6438370573	-1.4887886754
H	0.7461610855	-2.3880126383	-1.7595260641

Table S34: Cartesian coordinates at the optimized geometry of **R-5** in the gas phase. Total electronic energy is -491.1622058011 a.u. (PCM: -491.1830064494 a.u.)

Atom	X	Y	Z
N	-0.8500010079	0.3188692133	-0.1015847694
N	1.2417489816	1.1157136806	0.4496415007
C	-0.0894451908	1.2492109776	0.6039449529
C	1.8437281798	0.2870933916	-0.5638319378
C	1.1027098278	-1.0190164866	-0.6910481077
C	-0.4019142667	-0.8157181887	-0.7096242795
O	-1.1434655996	-1.6317456798	-1.1788635799
O	-0.6202148443	2.0799026845	1.2870779691
H	-1.8403462888	0.4226778910	0.0016241102
H	1.7855803680	1.8067512874	0.9182509580
H	2.8661934720	0.0761936802	-0.2857327325
H	1.3687705093	-1.5024365999	-1.6250219603
O	1.4280811730	-1.8294372145	0.4091162267
H	1.8489767874	0.7838313133	-1.5313416975
H	0.9489051991	-2.6493213068	0.3416271991

Cytosine and Thymine

Table S35: Cartesian coordinates at the equilibrium geometry of Cytosine in the gas phase. Total electronic energy is -394.8533291586 a.u.

Atom	X	Y	Z
N	-1.1169319234	-0.5873129088	0.3160344323
N	0.0106469334	1.2513954429	-0.6059957311
C	-1.1750212159	0.7077545300	-0.0849839994
C	1.1518846624	0.5562851965	-0.7144396194
C	1.2044948555	-0.7223827883	-0.3174493303
C	-0.0113005610	-1.2636024056	0.2117082638
O	-2.1469298851	1.4117183838	-0.0285298737
H	-0.0494528607	2.2040786645	-0.8962791350
H	1.9971746845	1.0731749040	-1.1276281809
H	2.1030847209	-1.2982914936	-0.3942175307
N	-0.0229798461	-2.5404653853	0.6260116107
H	-0.8709180928	-2.9112094970	0.9930537866
H	0.7857570885	-3.1134279896	0.5736442453

Table S36: Cartesian coordinates at the optimized geometry of Cyt-**4** in the gas phase. Total electronic energy is -394.7184033386 a.u.

Atom	X	Y	Z
N	-1.0377241661	-0.1095016954	0.0517555562
N	1.0886004104	1.0855602387	-0.1852208027
C	-0.3629599595	1.0926277702	0.1274040232
C	1.5171017652	-0.1439179294	-0.4982056654
C	1.0658642343	-1.0705652671	0.4268297741
C	-0.3670302747	-1.2171867822	0.0359971597
O	-0.8641778960	2.1529090124	0.3023014846
H	1.3621777764	1.9046688942	-0.6971018848
H	1.8605992135	-0.3594065681	-1.5001434935
H	1.0240575524	-0.5723821659	1.3888382165
N	-0.9354111800	-2.3702232074	-0.2774599679
H	-1.9060305550	-2.3987299467	-0.5072313972
H	-0.4201335773	-3.2130924306	-0.1667507770

Table S37: Cartesian coordinates at the equilibrium geometry of Thymine in the gas phase. Total electronic energy is -454.0511460610 a.u.

Atom	X	Y	Z
N	-1.2215160791	0.3701945687	0.0376575982
N	0.6650437104	1.6473547478	-0.1273797097
C	-0.6812557140	1.5636689506	-0.3582082634
C	1.3998816574	0.6382617881	0.4336837680
C	0.8662141339	-0.5214532555	0.8127276682
C	-0.5675743060	-0.7063401188	0.6172843866
O	-1.1765200406	-1.6962130903	0.9197094861
O	-1.3171145527	2.4487791909	-0.8578032990
H	-2.2062785971	0.2680348533	-0.1077759988
H	1.0942963624	2.5032792948	-0.4044362000
H	2.4461102020	0.8487861635	0.5499479829
C	1.6379597902	-1.6395317272	1.4223708669
H	1.2678378920	-1.8694350933	2.4140857120
H	1.5316112337	-2.5428155438	0.8340891624
H	2.6893901160	-1.3929618194	1.4914549509

Table S38: Cartesian coordinates at the optimized geometry of Thy-**4** in the gas phase. Total electronic energy is -453.9117862599 a.u.

Atom	X	Y	Z
N	-0.9611307977	-0.0172902741	0.0387042317
N	1.0827010757	1.2090127485	-0.0985081355
C	-0.3109933863	1.2386649288	0.0590587066
C	1.4467886956	-0.0839971539	-0.4908480807
C	1.0242631064	-0.9604223432	0.4419604213
C	-0.3759924186	-1.3070396166	0.0291205929
O	-0.9814474792	-2.2948581133	-0.2081350213
O	-0.9328605819	2.2505719427	0.1590634600
H	-1.9599870794	0.0490539554	0.0550340722
H	1.4576873121	2.0541955409	-0.4827513068
H	1.3696206741	-0.3109397614	-1.5444793239
C	1.2178527435	-0.7379284039	1.9079664736
H	0.3096632802	-0.4371997133	2.4196660750
H	1.5320097275	-1.6765096162	2.3539760644
H	1.9867309630	-0.0007690269	2.0899733218

Results of the CCSD/CCSD(T) computations for uracil

Table S39: Cartesian coordinates at the CCSD/cc-pVTZ optimized geometry of uracil **1** in the gas phase. Total electronic energy at the CCSD/cc-pVTZ level is -414.1317358 a.u. (CCSD(T)/aug-cc-pVTZ -414.2075025 a.u.)

Atom	X	Y	Z
N	-0.856188	0.146632	0.130432
N	1.206718	1.156978	0.328421
C	-0.164544	1.323552	0.324828
C	1.821488	-0.061220	0.155460
C	1.123353	-1.191284	-0.031827
C	-0.337589	-1.139817	-0.054878
O	-1.075891	-2.084167	-0.214618
O	-0.696764	2.396947	0.477409
H	-1.859945	0.230074	0.121959
H	1.741206	1.994273	0.467560
H	2.900298	-0.041428	0.181306
H	1.604563	-2.143777	-0.167052

Table S40: Cartesian coordinates at the CCSD/cc-pVTZ optimized geometry of intermediate **4** in the gas phase. Total electronic energy at the CCSD/cc-pVTZ level is -414.0099053 a.u. (CCSD(T)/aug-cc-pVTZ -414.0911412 a.u.)

Atom	X	Y	Z
N	-0.945024	-0.047643	0.090710
N	1.128356	1.166681	-0.061044
C	-0.279884	1.201801	0.127619
C	1.492783	-0.104279	-0.518136
C	1.050608	-1.033376	0.381528
C	-0.372008	-1.349526	0.010245
O	-0.998343	-2.328919	-0.259192
O	-0.884978	2.232310	0.251870
H	-1.949205	0.032911	0.103832
H	1.475025	2.020509	-0.470959
H	1.569604	-0.278756	-1.586644
H	1.063723	-0.647458	1.397965

Table S41: Cartesian coordinates at the CCSD/cc-pVTZ optimized geometry of $\mathbf{TS_{41}}$ in the gas phase. Total electronic energy at the CCSD/cc-pVTZ level is -413.9904706 a.u. (CCSD(T)/aug-cc-pVTZ -414.0687992 a.u.)

Atom	X	Y	Z
N	0.122446	-0.980460	-0.063727
N	-1.216038	0.955797	-0.083110
C	-1.139268	-0.484036	0.045831
C	-0.108527	1.656583	-0.209255
C	1.111992	1.195272	0.405809
C	1.357277	-0.226192	-0.003092
O	2.378091	-0.825953	-0.169269
O	-2.159722	-1.114184	0.108597
H	0.184200	-1.977937	-0.196416
H	-2.130162	1.284081	-0.368142
H	-0.201625	2.579907	-0.779377
H	0.726937	0.957929	1.421425

Table S42: Cartesian coordinates at the CCSD/cc-pVTZ optimized geometry of $\mathbf{TS_{42}}$ in the gas phase. Total electronic energy at the CCSD/cc-pVTZ level is -490.3262753 a.u. (CCSD(T)/aug-cc-pVTZ -490.4141903 a.u.)

Atom	X	Y	Z
N	-1.369014	0.063670	0.187847
N	0.574040	-1.254634	-0.141373
C	-0.839828	-1.188971	-0.050329
C	1.186522	-0.099145	0.421505
C	0.728758	1.201721	-0.135411
C	-0.731928	1.333039	0.019503
O	-1.424603	2.315712	-0.054560
O	-1.511802	-2.187390	-0.127604
H	-2.376750	0.081566	0.207423
H	0.862514	-2.156645	0.215027
H	1.279149	-0.131476	1.506147
H	0.857665	1.138364	-1.226568
O	2.655877	0.015063	-0.013472
H	2.440327	1.065573	-0.058036
H	2.684994	-0.287586	-0.935829

Table S43: Cartesian coordinates at the CCSD/cc-pVTZ optimized geometry of water molecule in the gas phase. Total electronic energy at the CCSD/cc-pVTZ level is -76.3336555 a.u. (CCSD(T)/aug-cc-pVTZ -76.3422829 a.u.)

Atom	X	Y	Z
O	0.000000	0.000000	0.117993
H	0.000000	0.753668	-0.471974
H	0.000000	-0.753668	-0.471974

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