Theoretical Study of the Interaction between Uracil and Hydrogen Peroxide

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The optimized geometries, energies, harmonic vibrational frequencies and natural charges of the uracil-hydrogen peroxide (U−HP) complexes are computed using density functional theory (B3LYP) combined with the 6-31++G(d,p) basis set. Four stable structures are found on the potential energy surface. In three of these structures labeled A, B, and C, one of the OH bonds of HP accepts the NH acidic proton while donating a proton to the carbonyl oxygen of U, forming a six-membered ring. In structure D, the CH bond of U acts as a proton donor, forming with the two O atoms of HP, a seven-membered ring. For all the structures, complex formation results in an elongation of the NH, CH, and OH bonds, and a red-shift of the corresponding stretching vibrations. For complexes A, B, and C, the binding energies span a range of −28 to −37 kJ mol^{-1}, the most stable complex being formed at the carbonyl site of U characterized by the lowest proton affinity and at the NH bond having the largest acidity. In these complexes, the charge transfer taking place from U to HP is moderate and ranges between 0.013 and 0.019 e. In complex D, the binding energy (−29.7 kJ mol^{-1}) is larger than that expected from the acidity of the CH bond and the charge transfer of 0.030 e is larger than in the three other complexes. These features can be accounted for by a more favorable linear arrangement of the hydrogen bonds in the seven-membered ring. Comparison of the geometrical and vibrational data for the four stable U−H_2O complexes demonstrates that H_2O is a better proton acceptor and HP a better proton donor, in agreement with the experimental gas-phase proton affinities and deprotonation enthapies of both molecules. These conclusions are consistent with the relations between the elongations of the NH and OH bonds and the shifts of the corresponding stretching vibrations.

Introduction

As discussed in a recent work[1], hydrogen peroxide (HP) has proven of considerable interest in several biochemical pathways. HP generates highly reactive radicals, which may damage biomolecules, including DNA. Different modified DNA bases have been identified, and it has been proven that the biological effect of HP is modified by hydrogen bond formation.[2]

The above considerations justify the interest of studying all the nucleobases−HP adducts. Up to now, only the adenine−HP interaction has been the subject of experimental[3] and theoretical investigations.[1] The HP dimer has been investigated theoretically,[4a,4b] but despite their interest, very few studies have been conducted on HP complexed with proton-donor or proton-acceptor molecules. It must be mentioned, however, that recent theoretical calculations have been carried out on HP complexed with water,[4c] hydrogen halides,[4d] and urea.[4e]

Because of the simple structure of uracil (U), which has only two basic and two acidic sites available for hydrogen bond formation, the theoretical analysis of its interaction with one or several water molecules has received a great deal of attention during the past years.[5] In this report, our objective is to systematically analyze the interaction between U and HP. The optimized structures, binding energies, vibrational spectra, and charge redistribution are calculated at the B3LYP/6-31++G(d,p) level. The results are compared with those obtained at the same level for the U−H_2O complexes.[5a,5b] As shown by experimental gas-phase data, H_2O is a better proton acceptor than HP, and HP is a better proton donor than H_2O.[6] It seemed interesting to us to discuss to what extent the basicity/acidity of these two amphoteric molecules influences the geometrical, energetical, and vibrational parameters of their complexes.

Computational Methods

The structure of the U−HP complexes were fully optimized by the density three-parameter hybrid model (DFT/B3LYP)[7] using the 6-31++G(d,p) basis set. It has been shown[5a,8] that DFT and MP2 levels of theory give similar results as far as the geometrical and vibrational features are concerned. It has also been demonstrated that B3LYP/6-31++G(d,p) method is a very reliable method for predicting the acidities of nucleobases.[9] Of several assumed conformations of these complexes, four structures proved to be stationary points (all real frequencies) on the potential energy surface. The harmonic frequencies and infrared intensities were calculated at the same level of theory. The U−HP binding energy was calculated as the difference of the energy of the complex and the sum of the energies of the separated monomers. The counterpoise procedure of Boys and Bernardi[10] was applied to correct for the basis set superposition error (BSSE), similar to our earlier studies.[5a,5b] The zero-point vibrational energy correction (ZPE) has also been included.

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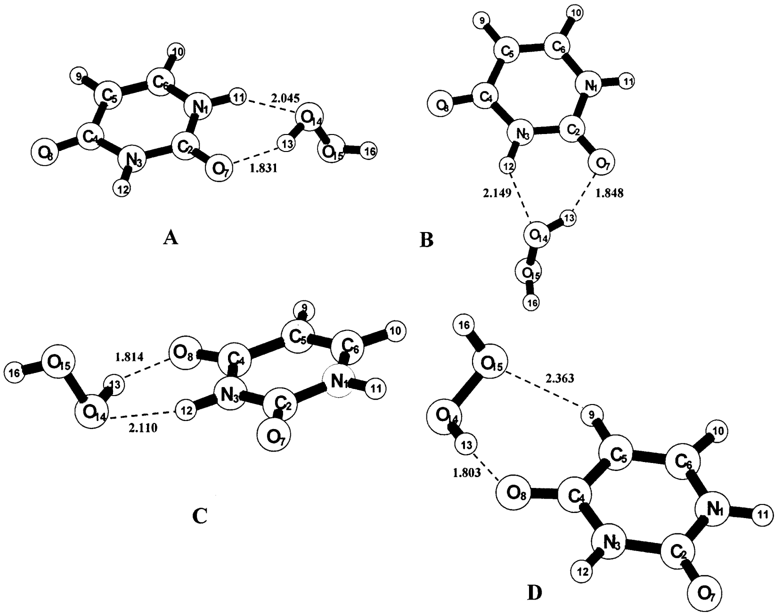

Figure 1. B3LYP/6-31++G(d,p) optimized structures for the **A**, **B**, **C**, and **D** complexes between U and HP (distances in Å).

TABLE 1: Results of B3LYP/6-31++G(d,p) Geometry Optimization (Length in Å, Angles in Deg) for Free U and the U−HP Complexes A, B, C, and D

	free U	complex **A**	complex **B**	complex **C**	complex **D**
N1−C2	1.3935	1.3827	1.3852	1.3964	1.3918
C2−N3	1.3841	1.3756	1.3744	1.3858	1.3874
N3−C4	1.4121	1.4157	1.4146	1.3998	1.4004
C6−N1	1.3767	1.3754	1.3789	1.3726	1.3758
C4−C5	1.4594	1.4572	1.4610	1.4530	1.4530
C5═C6	1.3518	1.3527	1.3503	1.3533	1.3530
C2═O7	1.2201	1.2339	1.2329	1.2181	1.2189
C4═O8	1.2226	1.2200	1.2208	1.2356	1.2334
N1H11	1.0105	1.0205	1.0105	1.0108	1.0108
N3−H12	1.0141	1.0143	1.0225	1.0231	1.0144
C5−H9	1.0811	1.0811	1.0812	1.0808	1.0823

	free HP	complex **A**	complex **B**	complex **C**	complex **D**
O14−O15	1.4568	1.4562	1.4566	1.4565	1.4573
O14−H13	0.9712	0.9895	0.9860	0.9890	0.9871
O15−H16	0.9712	0.9708	0.9705	0.9705	0.9700
∠H13O14O15H16	119.3	−112.2	117.1	115.2	111.7

intermolecular parameters

complex **A**		complex **B**		complex **C**		complex **D**	
O7···H13	1.831	O7···H13	1.848	O8···H13	1.814	O8···H13	1.803
∠O14H13O7	150.3	∠O14H13O7	150.6	∠O14H13O8	152.4	∠O14H13O8	173.6
O14···H11	2.045	O14···H12	2.149	H12···O14	2.110	O15···H9	2.363
∠N1H11O14	141.1	∠N3H12O14	138.4	∠N3H12O14	139.1	∠C5H9O15	144.3
∠O7H13O14 H11	9.3	∠O7H13O14 H12	9.3	∠O8H13O14 H12	9.7	∠O8H13O15 H9	27.6

The charges on individual atoms and orbital occupancies were obtained by using the natural bond population scheme. [11] All calculations were performed with the Gaussian 98 package.[12]

To make an unequivocal comparison of the frequency shifts of the corresponding modes in U and HP monomers and in their complexes, it was necessary to perform a rigorous normal coordinate analysis for the investigated molecules. The nonredudant set of 30 internal coordinates for U and 42 internal coordinates for the U−HP has been derived, as recommended by Fogarasi and Pulay.[13] The potential energy distribution (PED) has been calculated for all the molecules, according to the procedure described in our earlier papers.[14]

Results and Discussion

a. Molecular Structure and Binding Energies. The optimized structures **A**−**D** are cyclic, with two hydrogen bonds being involved in the interaction (Figure 1). All other possible arrangements and other ring structures (of 12 total) are unstable, having one or two imaginary frequencies. Selected optimized geometrical parameters are listed in Table 1. In structures **A,** **B,** and **C**, one O atom of HP and one C═O group of U are acting as proton acceptors and one of the NH bond of U as proton donor, leading to a six-membered ring. In complex **D**, the C5H9 bond is a proton donor. We note that in this structure, both O atoms of HP are involved in the interaction, giving a seven-membered ring.

We begin with analyzing the hydrogen bond parameters. In complexes **A**, **B**, and **C**, the intermolecular (C)═O···H distances ranging from 1.814 to 1.848 Å are markedly shorter than the (N)H···O ones which comprise between 2.045 and 2.149 Å. The OH···O angles ranging from ca. 150 to 152° are larger by ca. 10° than the NH···O ones. As indicated by the values of

TABLE 2: B3LYP/6-31++G(d,p) Binding Energies (kJ mol^{-1}), Including BSSE (E^{BSSE}) and ZPE ($E^{\mathrm{BSSE,ZPE}}$) Corrections for the Four Structures of the U−HP Complexes

	complex **A**	complex **B**	complex **C**	complex **D**
E^{BSSE}	−43.9	−34.2	−37.3	−36.2
$E^{\mathrm{BSSE,ZPE}}$	−37.0	−28.1	−31.0	−29.7

the O7(8)H13O14H11(12) dihedral angles, which are equal to ca. 9°, the OH13 bond of HP is sligthly out-of-plane of the U molecule. Complex **D** shows a contrasting behavior. The value of the dihedral angle O8H13O15H9, which takes the value of 27.6°, shows that the departure from the planar arrangment is markedly larger for this complex. The (C═)O···H distance, equal to 1.803 Å, is slightly shorter than in the other structures and in contrast with them, the OH···O bond is nearly linear, as the OH···O angle is 173.6°. The (C)H···O distance of 2.363 Å is the longest one among all the intermolecular hydrogen bonds, evidenced by the present calculations. This reflects the weaker strength of the CH···O hydrogen bonds as compared with the NH···O and OH···O ones. It is is worth mentioning that larger (C)H···O distances have also been predicted in several open complexes.[15] Owing to the intrinsic differences in the OH···O and CH···O distances, the seven-membered ring is preferred over the six-membered one. In this structure, the accessibility of the O15 atom of HP is larger than that in a six-membered ring.

Complex formation results in an elongation of the NH··· bonds by 0.008−0.010 Å (**A**, **B**, and **C**) and a smaller elongation of the CH bond by ca. 0.001Å (**D**). In all the complexes, the C═O··· bond is elongated by 0.011−0.014 Å, the free C═O bond being sligthly contracted by 1−2 mÅ. The variations of the distances in the U ring are small, the largest perturbations being observed for the C−N bonds involved in the formation of the six-membered ring. Complex formation also induces an elongation of the O14H13 bond of HP, between 0.015 and 0.018 Å, and a decrease of the H13O14O15H16 dihedral angle.

Table 2 reports the binding energies (E_{HB}) of the U−HP complexes including the BSSE and ZPE corrections. We must notice that the BSSE corrections are small and comprise between 0.6 (complex **A**) and 1.5 (complex **D**) kJ mol^{-1}. The results indicate that the binding energies are relatively large, ranging from −28.1 to −37.0 kJ mol^{-1}. We have shown in previous works that the binding energies in the complexes formed between U,[5a] uracil derivatives,[16] thymine[5b] and water depend more on the acidity of the proton donor than on the basicity of the proton acceptor. The highest binding energies are predicted when water interacts with the O atom of the C═O group characterized by the smallest proton affinity (PA) and at the NH site characterized by the lowest deprotonation energy (DPE). The same qualitative trend is found for the present complexes. The most stable complex **A** is formed at the NH bond having the highest acidity (DPE = 1391 kJ mol^{-1}) and at the O atom characterized by the lowest PA (PA at the N1 side = 815 kJ mol^{-1}). Structures **B** and **C** involve the less acidic NH bond (DPE = 1447 kJ mol^{-1}). The different binding energies in these two complexes can be accounted for by the smaller PA of the O atoms (PA(O7) at the N1 side = 820 kJ mol^{-1}, PA(O8) at the N3 side = 849 kJ mol^{-1}).

Our calculations demonstrate that the binding energy in complex **D** (−29.7 kJ mol^{-1}) is slightly larger than in complex **B** (−28.1 kJ mol^{-1}). This result was rather unexpected in view of the smaller acidity of the C5H bond. No experimental or theoretical data for the DPE of the C5H bond of U are available. The DPE of this bond can nevertheless be estimated from the correlation between DPE and the electrostatic potential created at the hydrogen atom by the rest of the U molecule.[17] The DPE value calculated in this way is ca. 1580 kJ mol^{-1}, thus larger than the DPE of the NH bonds of U by ca. 130−190 kJ mol^{-1}. The large binding energy calculated for **D** probably results from a more linear arrangement of the OH···O and CH···O hydrogen bonds in the seven-ring structure. This conclusion is in good agreement with earlier data on complexes of uracil derivatives showing that the correlations between hydrogen bond strength and acidity/basicity of the interacting groups depend on intermolecular and dihedral angles.[16] The comparison with U−H$_2$O complexes that will be discussed in the last section of this paper is in good agreement with this interpretation.

b. Vibrational Spectra. The vibrational spectrum of U has been the subject of numerous papers.[18] The frequencies and intensities of isolated U have been recently calculated at the MP2/6-31G(d) or MP2/D95V level[18c,18d] or by B3LYP calculations.[5f,5g,18e] The vibrational spectrum of free U and the comparison with the experimental spectra is not the main scope of the present work. It is, however, worth mentioning that the frequencies calculated at the B3LYP/6-311++G (d,p) level[5f] differ by 10−20 cm^{-1} from the ones calculated in the present work (no PED was reported in ref 5f). It must be also noticed that the frequencies calculated by the B3LYP/6-31G(d) method differ by ca. 40 cm^{-1} for the ν(C═O) vibrations and that other assignments are presented for the γ(NH) vibrations.[5g] Comparison with experimental data on free U reveals that the scaling factors of the frequencies are between 0.952 and 0.978 for the in-plane modes and 0.980 for the out-of-plane modes.[5b] No experimental data are available for the vibrational spectra of the complexes. As can be anticipated from the U−H$_2$O complexes,[5b] the scaling factors will probably be lower for the U−HP complexes owing to the increase of anharmonicity resulting from complex formation.

Table 3 reports the frequencies, intensities, and PED of selected vibrational modes in isolated U and in the four U−HP complexes. The νC6H, νC═C, U ring modes, δC6H and γC6H vibrations undergo small perturbations upon complex formation and are not discussed hereafter. The same remark also holds for the γC2═O and γC4═O vibrations, which are strongly mixed with other modes. Inspection of the results of Table 3 shows that complex formation results in a marked change of the nature of the vibrational modes.

We start with discussing the modes involving the NH groups. The νNH vibrations in free U are purely localized modes but, in contrast, they are coupled with the ν(O14H13) vibration in complexes **A**, **B**, and **C**. The νN1H vibration is red-shifted by 160 cm^{-1} in complex **A** and the νN3H vibration by 146 and 135 cm^{-1} in complexes **B** and **C**, respectively. Shifts of the same order of magnitude, ranging from 115 to 183 cm^{-1} have been computed for the adenine-HP complexes.[1] The intensity changes resulting from complex formation of the ν(NH) vibrations are worth discussing. Table 3 indicates that the infrared intensity of the νN1H vibration markedly increases from 109 km mol^{-1} in the free U molecule to 932 km mol^{-1} in complex **A** and that the infrared intensity of the νN3H vibration increases from 69 to 880 km mol^{-1} in complex **C**. In both cases, the NH and OH bonds are involved in out-of-phase stretching ν(NH...)−ν(O14H13) mode. This large increase of the infrared intensity parallels a large decrease of the Raman intensity. The scattering activity of the νN1H vibration decreases indeed from 98 to 58 Å^4 amu^{-1} in complex **A,** and that of the νN3H vibration from 73 to 8 Å^4 amu^{-1} in complex **C**. In contrast with these results, the infrared intensity in complex **B** is almost unchanged (53 km mol^{-1}) when compared to that in free U. In this case,

TABLE 3: Vibrational Frequencies (cm^{-1}), Infrared Intensities ($km\ mol^{-1}$, First Value in Square Brackets), Raman Scattering Activities ($Å^4\ Amu^{-1}$, Second Value in Square Brackets) and Potential Energy Distribution (PED, %) for Isolated U and HP and for the Complexes A, B, C, and D

free U	complex **A**	complex **B**	complex **C**	complex **D**	assignment[a,b]
3648 [109, 98]	3488 [932, 58]	3648 [112, 95]	3646 [111, 106]	3645 [112, 103]	$(78\ \nu N_1H - 21\ \nu O_{14}H)^A$, $(100\ \nu N_1H)^X$
3607 [69, 73]	3605 [69, 73]	3461 [53, 208]	3472 [880, 8]	3604 [74, 69]	$(63\ \nu N_3H - 37\ \nu O_{14}H)^C$ $(83\ \nu N_3H + 17\ \nu O_{14}H)^B$, $(100\ \nu N_3H)^X$
3263 [1, 106]	3263 [1, 115]	3263 [1, 117]	3266 [1, 106]	3252 [29, 118]	$95\ \nu C_5H$
1808 [640, 29]	1765 [1246, 8]	1767 [1068, 5]	1813 [710, 26]	1812 [738, 26]	$(47\ \nu C_2{=}O - 14\ \nu C_4{=}O)^A$, $(55\ \nu C_2{=}O + 12\ \delta N_3H)^B$, $(72\ \nu C_2{=}O)^X$
1775 [790, 63]	1783 [316, 79]	1784 [392, 79]	1739 [820, 68]	1740 [926, 67]	$(66\ \nu C_4{=}O + 15\ \nu C_2{=}O)^{A,B}$, $(68\ \nu C_4{=}O)^X$
1502 [97, 12]	1521 [44, 31]	1498 [65, 13]	1513 [102, 13]	1508 [109, 15]	$35\ \delta N_1H + 25\ \nu C_6N_1$
1385 [38, 15]	1393 [12, 17]	1439 [25, 10]	1442 [9, 13]	1387 [32, 12]	$(60\ \delta N_3H + 13\ \nu C_4{=}O)^{B,C}$ $(40\ \delta N_3H + 12\ \nu C_2N_3 + 12\ \delta C6H + 10\ \delta C5H)^X$
811 [56, 0]	815 [47, 0]	815 [93, 0]	807 [45, 2]	836 [72, 0]	$46\ \gamma C_5H + 37\ \gamma C_4{=}O + 12\ \gamma C_6H$
677 [86, 1]	671 [30, 1]	800 [70, 1]	819 [169, 2]	682 [82, 1]	$(60\ \gamma N_3H + 37\ \gamma C_4{=}O + 18\ \gamma C_5H)^C$, $(86\ \gamma N_3H)^X$
562 [46, 0]	765 [132, 2]	569 [62, 0]	582 [62, 0]	579 [49, 0]	$(66\ \gamma N_1H + 17\ \gamma C_2{=}O)^A$, $(90\ \gamma N_1H)^X$
free hp					
3769 [11, 102]	3771 [43, 119]	3775 [38, 109]	3778 [38, 113]	3775 [31, 109]	$100\ \nu O_{15}H$
3768 [60, 33]	3428 [146, 254]	3511 [745, 29]	3425 [97, 248]	3474 [887, 211]	$(79\ \nu O_{14}H + 21\ \nu N_1H)^A$, $(83\nu O_{14}H - 17\nu N_3H)^B$ $(63\ \nu O_{14}H + 37\ \nu N_3H)^C$, $(100\ \nu O_{14}H)^X$
1445 [0, 8]	1485 [45, 8]	1487 [42, 9]	1492 [53, 11]	1526 [28, 3]	$96\ \delta$ HP
1301 [96, 2]	1346 [84, 6]	1338 [96, 4]	1341 [89, 5]	1337 [61, 6]	$97\ \delta$ HP
945 [1, 18]	951 [10, 17]	950 [5, 18]	950 [7, 18]	943 [3, 13]	$98\ \nu O_{14}O_{15}$
374 [222, 1]	251 [133, 1]	224 [117, 1]	232 [120, 1]	250 [154, 1]	$90\ \tau$ HP
intermolecular modes					
	202 [6, 1]	196 [2, 1]	205 [3, 1]	198 [4, 1]	$(52\ \nu O\cdots H_{13} + 35\ \tau$ HB ring): $(O_7)^{A,B}$; $(O_8)^C$ $(56\ \nu O_8\cdots H_{13} + 15\ \delta C5H)^D$
	131 [17, 1]	112 [6, 1]	117 [7, 0]	79 [4, 0]	$(54\ \nu O_{14}\cdots H + 32\ \tau$ HB ring): $(H_{11})^A$; $(H_{12})^{B,C}$ $(84\ \nu O_{15}\cdots H_9)^D$

[a] Only the vibrations contributing to at least 10% to the PED are included. When PED elements of the corresponding mode are similar for several molecules, the average percent contribution is shown. Different PEDs are explicitly indicated in parentheses for each complex or the isolated molecule. X = the remaining molecules (complexes **A**, **B**, **C**, or **D** or isolated U or HP). [b] ν = stretching, δ = in-plane deformation, γ = out-of-plane deformation, τ = torsional, τ(HB ring) = torsional vibration of the hydrogen bond ring. The minus sign denotes the out-of-phase stretching vibration.

the mode at 3461 cm^{-1}, whose Raman intensity increases from 73 to 208 $Å^4\ amu^{-1}$ corresponds to the in-phase stretching mode ν(N3H...) (83) + ν(O14H13) (17). In the same complex, the mode at 3511 cm^{-1} involving the mixing of ν(O14H13) (83) and ν(N3H) (−17) is characterized by an extremely high infrared intensity (745 km mol^{-1}), indicating that some intensity is borrowed from the νN3H to the νO14H13 stretching vibrations. A similar effect is found for the γ(NH...) vibration, which is usually very sensitive to the molecular interactions. In complex **B**, this vibration is shifted to higher frequencies by more than 100 cm^{-1}. Its intensity, however, is slightly smaller than that in free U.

In isolated U, the main components of the δN1H and δN3H vibrations are predicted at 1502 and 1385 cm^{-1}, respectively. Both components, which are also strongly mixed in the complexes, are blue-shifted.

In isolated U, the νC5H vibration is predicted with a very weak infrared intensity (1 km mol^{-1}) at 3263 cm^{-1}. In complex **D**, where the C5H bond is involved in complex formation, the νC5H vibration is red-shifted by 11 cm^{-1}. Its infrared intensity increases up to 29 km mol^{-1}. This shift parallels a small elongation of the C5H bond. This clearly indicates that the C5H···O hydrogen bond involving an sp^2 hybridized C atom can be categorized as a conventional hydrogen bond in contrast with the "blue-shifting" $C(sp^3)H\cdots O$ hydrogen bonds where the intensity of the νCH vibration decreases upon complex formation.[15] The main component of the γC5H vibration is calculated at 811 cm^{-1} in free U. In complex **D**, the corresponding mode is shifted to 836 cm^{-1}.

The νC2═O and νC4═O vibrations in free U may be coupled creating in-phase and out-of-phase vibrations.[19] Recent theoretical calculations[18] have, however, shown that the high-frequency mode at 1808 cm^{-1} has a predominant νC2═O character, and that the low-frequency one at 1775 cm^{-1} predominantly involves the νC4═O vibration. In agreement with these data, our calculations do not indicate any coupling between the two C═O stretches. The ν(C2═O) vibration is sligthly mixed (less than 10%) with the νC2N3 and δN1H vibrations and the νC4═O vibration is coupled with the νC4C5 and δN3H ones. Interestingly, complex formation in **A** and **B** results in a mixing of the two νC═O stretches. This is consistent with the fact that in both complexes, the ν(C2═O) vibration is shifted to lower frequencies by ca. 40 cm^{-1}, while the frequency of the ν(C4═O) vibration increases by ca. 10 cm^{-1}. We must also

TABLE 4: Natural Atomic Charges (e) Calculated at the B3LYP/6-31++G(d,p) Level for Free U and HP and the Four U−HP Complexes

atom	free U	free HP	A	B	C	D
N1	−0.643		−0.641	−0.635	−0.638	−0.638
C2	0.811		0.821	0.821	0.812	0.811
N3	−0.680		−0.670	−0.678	−0.678	−0.669
C4	0.644		0.644	0.645	0.654	0.657
C5	−0.388		−0.386	−0.378	−0.387	−0.391
C6	0.040		0.047	0.036	0.051	0.049
O7	−0.625		−0.665	−0.665	−0.613	−0.618
O8	−0.595		−0.591	−0.584	−0.635	−0.636
H9	0.270		0.271	0.271	0.271	0.291
H10	0.248		0.251	0.249	0.250	0.251
H11	0.456		0.469	0.458	0.457	0.458
H12	0.461		0.463	0.475	0.475	0.464
H13		0.493	0.518	0.515	0.514	0.511
O14		−0.493	−0.534	−0.526	−0.529	−0.515
O15		−0.493	−0.492	−0.495	−0.496	−0.522
H16		0.493	0.495	0.492	0.492	0.496
charge transfer[a]			0.013	0.014	0.019	0.030

[a] Charge transfer taking place from U to HP.

TABLE 5: Selected Data (Lengths and Elongations in Å, Angles in Deg, Energies in kJ mol^{-1}, Frequency Shifts in cm^{-1}) for the U−H$_2$O Complexes A, B, C, and D

parameter[a]	**A**[b]	**B**[b]	**C**[b]	D
ΔrNH...	0.0128	0.0115	0.0121	
ΔrC=O...	0.0121	0.0114	0.0116	
ΔrO$_w$H$_w$	0.0134	0.0108	0.0130	
O7(8)···H$_w$	1.941	1.975	1.921	1.923[c]
(N)(C)H···O$_w$	1.927	1.988	1.968	2.383[c]
$\angle$O7(8)H$_w$O$_w$	142.6	141.6	144.0	157[c]
$\angle$ N(C)H$_w$O$_w$	144.3	142.6	143.0	131[c]
E$_{HB}$	−32.8	−24.5	−26.7	−17.5[c]
$\Delta\nu$NH...	−222	−192	−207	
$\Delta\nu$C=O...	−24	−27	−28	−25[d]
$\Delta\nu$O$_w$H$_w$...	−193	−150	−192	
$\Delta\nu$NH...	−222	−192	−207	
$\Delta\nu$C=O...	−24	−27	−28	−25[d]
$\Delta\nu$O$_w$H$_w$...	−193	−150	−192	

[a] O$_w$H$_w$ and O$_w$ refer to OH or H involved in hydrogen bond formation. [b] From ref 5b. [c] From ref 5g (B3LYP/6-311++G(d) calculations). The E_{HB} value calculated at the MP2/DZP$_i$ level is very similar and equal to −17.9 kJ mol^{-1}.[5e] [d] From ref 5f.

notice that in **A**, the infrared intensity of the mode at 1765 cm^{-1} (1246 km mol^{-1}) which involves an out-of-phase vibration is larger than the one at 1783 cm^{-1} (316 km mol^{-1}), which is predominantly an in-phase vibration. The reverse holds for the scattering activities of these two modes, which are equal to 79 and 8 Å^4 amu^{-1}, respectively. Complexes **C** and **D** show a contrasting behavior; the preferred interaction site is the C=O4 bond and the corresponding stretching vibration decreases by ca. 35 cm^{-1}, the ν(C=O2) vibration being blue-shifted by ca. 5 cm^{-1}.

Marked perturbations are also noticed for the vibrational modes of HP. The νO14H13 vibrations are red-shifted by 257−340 cm^{-1}, and in complexes **B** and **D**, they are characterized by a strong infrared intensity enhancement. This in good agreement with the above discussion. The δH$_2$O$_2$ vibration undergoes upward shifts from 35 to 80 cm^{-1}. The strong decrease (123−150 cm^{-1}) of the frequencies of the torsional mode of HP is also worth mentioning.

The six intermolecular modes are strongly mixed with the torsional vibrations of the hydrogen bond ring. The most significant ones are the intermolecular stretches. The modes with predominant νO7···H13 and νO8···H13 contributions are predicted between 196 and 205 cm^{-1} for the four complexes. The intermolecular νO14···H11 and νO14···H12 vibrations are calculated between 112 and 131 cm^{-1} for complexes **A**, **B**, and **C**. The νO15···H9 vibration is predicted at 79 cm^{-1} in complex **D**. Our results indicate that larger intermolecular frequencies are roughly associated with shorter intermolecular distances, the shortest ones being the O7(8)···H13 ones and the longest distance being the O15···H9 one.

c. **NBO Analysis.** Full NBO analysis, which is more reliable than the Mulliken one,[20] has revealed interesting details on the electron density transfer in these systems. The charge transfer can be defined as the sum of atomic charges on complexed U. Table 4 contains the natural atomic charges for free U, free HP, and the four U−HP complexes. Our results demonstrate that most of the atoms of U loose electronic charge, resulting in a moderate charge transfer from U to HP ranging from 0.013 to 0.030 e. As in numerous hydrogen bonds, complex formation results in an increase of the polarity of the C=O... group, the C atom loosing 0.010−0.013 e and the O atom gaining 0.040 e. In contrast, the O atom of the nonbonded C=O group loses 0.004−0.012e, indicating decreasing electronic delocalization in these groups. This is as expected from the small decrease of the C=O distances and the increase of the infrared frequencies of the C=O stretches which have been discussed in sections **a** and **b**. It must be further noticed that the occupancy of the π*C=O antibonding orbital increases by 0.038−0.041 e in the bonded C=O groups but decreases slightly, from 0.004 to 0.009 e in the nonbonded C=O groups.[21] From these data, an anticooperative effect of the nonbonded C=O group can be anticipated. Our calculations show further that the hydrogen atom of the NH proton donor group loses 0.013−0.014 e, with the charge on the N atom remaining almost unchanged. This may be due to electronic delocalization in the HNC=O... group. In contrast, in complex **D**, the polarity of the C5H9 group increases, the C atom gaining 0.003 e and the H5 atom loosing 0.021 e. These data demonstrate that the variations of the charges on both atoms of the proton donor group are larger in the weaker C5H9···O hydrogen bond. This can be accounted for by the fact that the C5 atom is singly bonded to the C4 and C6 carbon atoms, restricting the delocalization in this part of the U molecule. It is also worth mentioning that in complex **D**, complex formation results in a small increase of 0.006 e of the occupation of the σ*C5H9 antibonding orbital. The increase in occupancy of the σ*NH orbital is much larger, 0.018−0.022 e, which is directly correlated to the larger bond weakening.

In the HP molecule, complex formation results in marked increase of the polarity of the O14H13 bond, with the O14 atom gaining 0.033−0.041 e and the H13 atom loosing 0.018−0.025e. The marked increase of the occupancy of the σ*O14H13 orbital, which ranges between 0.042 and 0.035 e, parallels the large red-shift and infrared intensity increase of the νO14H13 vibration.

We may also notice that the amount of charge transfer is not correlated to the binding energies. The largest charge-transfer value of 0.030 e is predicted in complex **D**. This can be accounted for by the fact that the charge transfer is spread over both O14 and O15 atoms, which gain 0.021 and 0.029 e, respectively. This conclusion is in good agreement with the fact that the occupancy of the valence lone pairs orbitals of the O15 atom is the same in free U and in complexes **A**, **B**, and **C**; in contrast, in complex **D**, this occupancy decreases by 0.006 e.

d. Comparison With the U−H$_2$O Complexes. Table 5 contains selected geometrical, energetical, and vibrational parameters that are useful for the comparison between the U−HP and U−H$_2$O interactions. The four stable U−H$_2$O complexes are the ones in which water accepts the acidic NH

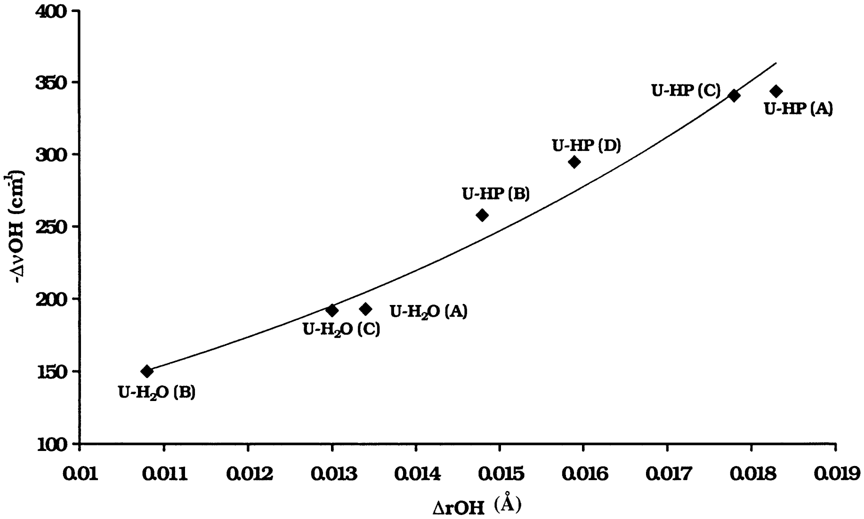

Figure 2. $\Delta\nu$OH (cm^{-1}) as a function of ΔrOH (Å) for the U$-$HP and U$-H_2O$ complexes.

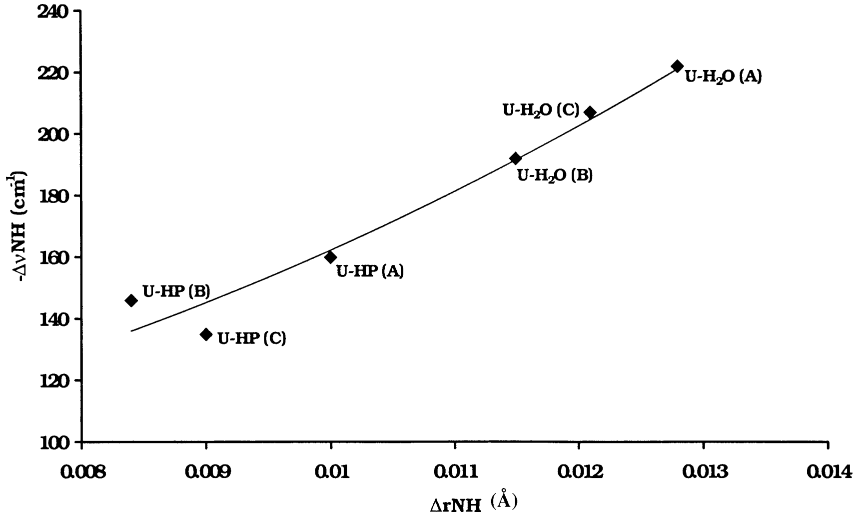

Figure 3. $\Delta\nu$NH (cm^{-1}) as a function of ΔrOH (Å) for the U$-$HP and U$-H_2O$ complexes.

(or CH) proton while donating a proton to the carbonyl O of uracil. In the four optimized structures, the hydrogen bonds form a six-membered ring.[5]

The differences between the geometrical and vibrational properties of the U$-$HP and U$-H_2O$ complexes can be discussed as a function of the proton donor and acceptor abilities of HP and H_2O. The experimental PAs of H_2O and H_2O_2 in the gas phase are equal to 697 and 678 kJ mol^{-1}, and the PAs of the OH^- and HO_2^- anions are equal to 1635 and 1573 kJ mol^{-1}, respectively,[6] showing that H_2O is a better proton acceptor and H_2O_2 a better proton donor. Therefore, the (C)=O···HO hydrogen bonds are expected to be stronger in the U$-$HP complexes than in the U$-H_2O$ complexes and the reverse holds for the NH···O hydrogen bonds. Our results are in conformity with these expectations. The comparison of the data of Tables 1 and 5 reveals that, in the **A**, **B**, and **C** complexes, the intermolecular O···HO distances are markedly shorter, by 0.13$-$0.30 Å in the U$-$HP complexes. The reverse holds for the NH···O distances, which are shorter by 0.12$-$0.16 Å in the U$-H_2O$ complexes. The difference in the intermolecular hydrogen bond strength is also reflected in the elongations of the NH bond, which span a range of 0.008$-$0.012 Å in the HP$-$U complexes and of 0.012$-$0.013 Å in the U$-H_2O$ complexes. Further, the higher acidity of the OH bond of HP is also demonstrated by the larger elongations of the bonded OH groups which comprise between 0.015 and 0.018 Å in the U$-$HP complexes and between 0.011 and 0.013 Å in the U$-H_2O$ complexes. Marked differences are also observed for the intermolecular angles which are approximately equal in the **A**, **B**, and **C** complexes of U$-H_2O$. In the U$-$HP complexes, the OH···O angles are larger by at least 10° than the NH···O ones. The differences are still larger in the **D** complexes, with the OH···O bond being approximately linear in the U$-$HP complex and the deviation from the linearity being more than 20° in the U$-H_2O$ complex.

Theoretical results on the HP$-H_2O$ dimer are useful for the comparison. Calculations carried out at the MP2/6-31+G(d,p) level have shown that the cyclic dimer is characterized by a strongly asymmetrical five-membered two-hydrogen-bonded structure.[4c] The O_w···H(HP) and H_w···O(HP) are equal to 1.910 and 2.294 Å, respectively. The O_w···HO(HP) and O_wH_w···O(HP) angles are equal to 148 and 115°, respectively. This also illustrates the larger acidity of HP as compared with that of H_2O.

Marked differences are also observed for the binding energies. The binding energies are larger by 3.6$-$4.4 kJ mol^{-1} in the U$-$HP complexes **A**, **B**, and **C**. Again, the **D** complexes show a contrasting behavior, with the U$-$HP complex being more stable than the U$-H_2O$ complex by 12.2 kJ mol^{-1}. This can be accounted for by a more linear arrangement in the seven-membered ring. A comparison of the data of refs 5b and 1 also indicates that the adenine−HP complexes are more stable than the adenine-H_2O ones.

The data reported in Tables 3 and 5 clearly indicate that the frequency shifts of the νOH vibrations are larger for the U−HP complexes and that the reverse holds for the νNH vibrations. We have shown in earlier works[5b,22] that the frequency shifts of the νOH and νNH vibrations in the complexes involving nucleobases and H_2O are correlated to the elongations of the corresponding bonds. These correlations can be extended to the HP complexes and are illustrated in Figures 2 and 3. A least-mean square treatment yields the following equations ($\Delta\nu$ in cm^{-1}, Δr in Å)

$$-\Delta\nu^{s}\mathrm{OH} = 42.4e^{117.4\Delta r\mathrm{OH}}\ (r = 0.9856) \qquad (1)$$

$$-\Delta\nu\mathrm{NH} = 53.8e^{110.4\Delta r\mathrm{NH}}\ (r = 0.9728) \qquad (2)$$

It is worth noticing that the U−HP complex **B** is characterized by a larger $\Delta\nu$NH value than that predicted by eq 2. This results from the mixing of the νOH and νNH vibrations, which are calculated at 3511 and 3461 cm^{-1}. This coupling is strongly attenuated in the U−H_2O complex **B**, owing to the larger differences of the frequencies which are equal to 3654 and 3415 cm^{-1}, respectively.[5b]

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