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Hydrogen bonding effects in quantum mechanical force fields of pyrimidine bases: uracil

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Received 19 September 1996; accepted 8 January 1997

Abstract

Using dihydrate uracil as a model of H-bonded compound formed by a uracil and two water molecules in the vicinity of HN1C2O and HN3C4O groups, DFT molecular orbital calculations have been performed in order to evaluate the changes in its simulated IR spectrum. To estimate the effect of intermolecular interactions on the vibrational properties of pyrimidine bases we have used the B3LYP functional and polarised 6-31G basis sets. The normal mode analysis enables us to assign the 30 modes of uracil, the 6 modes of the two water molecules along with the 12 additional modes resulting from their mutual interactions. © 1998 Elsevier Science B.V.

Keywords: Nucleic acid bases; Ab initio calculations; Hydrogen bonding; Molecular interactions; Vibrational spectroscopy

1. Introduction

The analysis of IR, Raman and NIS (neutron inelastic scattering) vibrational spectra for pyrimidine bases through quantum mechanical calculation methods is often impeded by the fact that some experimental data are significantly dependent on the physical state of the studied compound (solid, liquid or gas phases). Most difficulties arise from the hydrogen bonding between the molecules under investigation (solid phase) or between a given molecule and its surrounding water molecules (aqueous phase). To circumvent the difficulties due to hydration effects, theoreticians have

suggested several procedures: (i) empirical scaling of the quantum mechanical force constants of the isolated molecule [1], (ii) use of solvation cavity techniques [2,3], or (iii) modeling of the solvated compound by a molecular complex with water [4]. From a strict ab initio point of view, the last method may be preferred, provided that size of the considered complex is not too large. However, the question whether the supermolecule vibrational modes in excess with respect to those of the constituent fragments should be rejected as a computational artifact [4] or retained [5,6] for the whole vibrational assignments of the calculated modes, still remains crucial.

In this work, we shall give an appraisal of the effects to be theoretically expected from the H-bonding of

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Table 1
Geometrical parameters of hydrogen bonds in uracil dihydrate

Internuclear distances ^a (Å)			Bond angles (degrees)	
N1–H	1.023	(+0.012)		
N1...O _{w1}	2.843	(−0.057)	N1HO _{w1}	144.4
O _{w1} –H'	0.983	(+0.015)		
O2...O _{w1}	2.784	(−0.011)	O2H'O _{w1}	147.1
C2=O2	1.231	(+0.014)		
N3–H	1.025	(+0.011)		
N3...O _{w3}	2.872	(−0.028)	N3HO _{w3}	143.2
O _{w3} –H'	0.983	(+0.015)		
O4...O _{w3}	2.780	(−0.020)	O4H'O _{w3}	148.1
C4=O4	1.234	(+0.014)		

^a In brackets the deviation of H-bonded distances from those calculated for free uracil or water, or from sums of van der Waals atomic radii in the case of non-directly bonded atoms (Ref. [16,17]).

water to uracil by comparing the vibrational wave-numbers issued from the isolated molecule to those obtained from a simple SCRF (self-consistent reaction field) treatment with a spherical cavity and a complete calculation of the model system uracil + 2H₂O depicted in Fig. 1. In fact, experimentally the monohydrate pyrimidine bases have been studied rather than the dihydrates ones [6,7]. Our theoretical model constituted by an uracil and two H₂O molecules in the vicinity of both HNCO groups of uracil can be considered as the onset of the first hydration shell for uracil in solution.

2. Theoretical procedure

For large systems, the density functional theory (DFT) methodology is convenient, because it gives quantum mechanical results including correlation with computational times comparable to SCF calculations. In a previous study of various fragments of nucleic acids [8], it was found that the vibrational

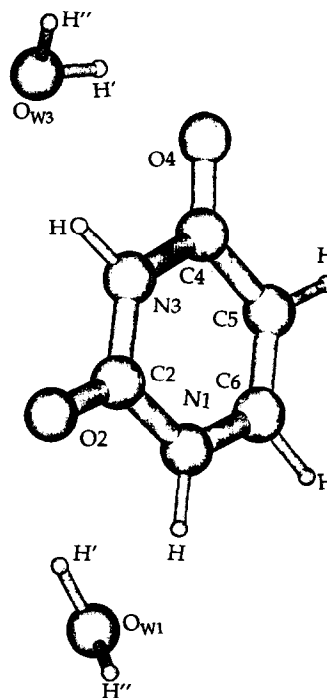


Fig. 1. Atomic numbering of uracil dihydrate.

properties obtained through the B3LYP functional were consistent with those of standard MP2 calculations, using the same sets of atomic orbitals. This is particularly attractive for the time-consuming computations requiring large disk space, as those needed for the vibrational calculations.

The basis functions used in our work on biological compounds are split-valence sets (i.e. 6-31G) enriched by valence d functions on the first row atoms:

$$\zeta_d^C = 0.75 \quad \zeta_d^N = 0.80 \quad \zeta_d^O = 0.85$$

These sets without hydrogen polarization functions which are not so useful for vibrational purposes will

Table 2
DFT energies (in a.u.) of uracil, water and uracil dihydrate. ZPVE values are indicated in brackets

	Water	Free U	Solvated U ^a	U dihydrate
6-31G(*)	−76.406839 (0.021145)	−414.807983 (0.087296)	−414.812119 (0.087318)	−567.667302 (0.138170)
6-31G(†)				−567.720500 (0.136707)

^a Cavity radius: 3.92 Å, $\epsilon = 78$, solvation energy: 0.005069 a.u.

be hereafter denoted as 6-31G(*). They are able to give vibrational wavenumbers at the MP2 and DFT levels which can most often be used without any scaling. However, by taking into account some inadequacies of such bases in DFT calculations of H-bonded compounds [9], we have added Coulomb polarisation orbitals on the atoms of dihydrate uracil (U, 2H₂O) that are directly involved in hydrogen bonds (the two HNCO sites and the two H₂O molecules): they are semi-diffuse orbitals of s, p, d types for the heavy atoms and s, p types for hydrogens whose exponents:

$$\zeta_s = \zeta_p = 0.05, \quad \zeta_d = 0.30 \text{ and } \zeta_s^H = \zeta_p^H = 0.10$$

are selected in order to correctly reproduce electric polarisabilities [10]. This particular set will be denoted as 6-31G(†); it includes 234 basis functions in (U, 2H₂O) instead of 156 in the case of the 6-31G(*) set. The Gaussian 92/DFT package [11] has been used throughout.

3. Results and discussion

The characteristics of H-bonding in (U, 2H₂O) are given in Tables 1 and 2. The distances separating the oxygen atom of each water molecule O_{w1} (or O_{w3})

Table 3

DFT vibrational wavenumbers (cm⁻¹) and IR intensities (km/mol) for free, solvated and uracil dihydrate

	Main components ^a	Free U ^b	Solvated U ^b	Dihydrated U	
				b	c
1	str. N1H	3637(92)	3623(165)	3318(459)	3413(349)
2	str. N3H	3598(57)	3609(59)	3302(585)	3386(335)
3	str. C5H	3269(0.4)	3270(0.9)	3269(1)	3267(0.8)
4	str. C6H	3229(5)	3237(1)	3227(5)	3228(3)
5	str. C2O2	1846(555)	1833(690)	1809(680)	1784(605)
6	str. C4O4	1809(581)	1784(1012)	1772(577)	1750(565)
7	str. C5C6	1693(68)	1686(137)	1685(24)	1683(313)
8	bend. N1H	1511(94)	1512(139)	1564(34)	1548(43)
9	bend C6H	1428(14)	1428(30)	1460(116)	1452(100)
10	ring str.	1415(111)	1414(141)	1414(44)	1412(45)
11	bend N3H	1389(24)	1385(33)	1491(8)	1473(12)
12	bend C5H	1237(5)	1239(20)	1264(44)	1258(31)
13	ring str.	1203(86)	1203(136)	1250(29)	1244(53)
14	ring str.	1094(7)	1096(10)	1114(0.7)	1111(1)
15	ring trig. def.	992(6)	993(8)	996(14)	999(13)
16	ring str.	969(7)	974(12)	1012(5)	1003(6)
17	wag. C6H	965(0.2)	977(0.4)	978(3)	973(0.2)
18	wag. C5H	815(61)	816(55)	817(33)	819(5)
19	ring str.	773(2)	776(2)	774(148)	786(3)
20	wag. C2O2	759(58)	758(54)	761(218)	762(2)
21	wag. C4O4	730(12)	733(18)	723(2)	718(45)
22	wag. N3H	687(83)	671(110)	960(142)	859(145)
23	ring asym. def.	558(5)	560(7)	584(8)	579(4)
24	wag. N1H	554(48)	583(60)	900(79)	561(16)
26	ring asym. def. ^c	519(19)	518(36)	535(40)	533(42)
27	puck. C=C	393(29)	402(31)	423(19)	417(29)
28	bend C=O	385(21)	381(32)	432(68)	427(37)
29	puck. N1	169(0.6)	178(0.3)	179(11)	171(5)
30	puck. N3	147(0.3)	148(0.5)	172(8)	169(10)

^a Approximate description in terms of internal coordinate with highest coefficient in the PED of free uracil (see also Ref. [8]); str.: stretching; bend.: bending; wag.: wagging; asym.: asymmetric; sym.: symmetric; def.: deformation; puck.: puckering and trig.: trigonal, as defined in Ref. [18].

^b 6-31G(*) set.

^c 6-31G(†) set.

and its adjacent atoms in uracil, i.e. N1 and O2 (or N3 and O4) are almost the same, and are slightly shorter than the sum of the corresponding van der Waals atomic radii. Furthermore, the internuclear distances N–H and C=O in uracil, as well as the bond lengths O_W–H' (Fig. 1) of the nearest hydroxyls of the water molecules are increased. This indicates the existence of a two-fold H-bonding between each water molecule and its adjacent donor or acceptor atoms in uracil. Consequently, closed H-bond structures are created and the concept of « H-bond cooperativity » can be invoked as in cytosine [6].

The energetics of the H-bonding in (U, 2H₂O) can be roughly appreciated by evaluating the energy content of the four H-bonds as the difference between the total electronic energy of the complex and those of its fragments (as given by the same basis set 6-31G(*), Table 2), and correcting the result by taking into account the variation of the zero-point vibration energies (ZPVE). The mean energy of the H-bonds computed in this way for (U, 2H₂O) is:

$$\frac{1}{4}(0.045641 - 0.008584) \text{ a.u.} = 5.81 \text{ kcal.mol}^{-1}$$

In principle, this estimate has to be considered as an upper limit of the binding energy because of the basis

set superposition error (BSSE) included in it; however, studies of typical H-bonded systems indicate that the numerical value of the BSSE corrections does not play a very important role in DFT calculations of intermolecular binding energy [12].

The calculated wavenumbers along with their approximate description are presented in Table 3 and 4 for isolated, solvated and dihydrated uracil. The vibrational mode assignments have been achieved by visualising the vibrational motions computed in cartesian coordinates by means of Vibmol [13] and Molden [14] programs. In the present work, we have not followed the usual way of assigning molecular vibrational motions by the use of the potential distribution (PED) matrix in terms of internal coordinates, given that no fully meaningful system of internal coordinates has been found for (U, 2H₂O) supermolecule. However, it was possible to correlate the vibrational transitions originating, either from the isolated uracil and water moieties, or from the transformation of 12 external translation and rotation motions into internal modes of the complex. From this point of view, the choice of (U, 2H₂O) as a model is free from criticism.

In contrast to the Onsager solvation treatment which does not predict any substantial change in the

Table 4

Same as Table 3 but for water and extra modes of uracil dihydrate

	Main components ^a	Dihydrate U ^a	Free H ₂ O ^b
31	str. (O _{W3} H'')	3812(67)	3848(19) asym. str.
32	str. (O _{W1} H'')	3810(77)	
33	str. (O _{W3} H')	3524(262)	3725(1.4). sym. str.
34	str. (O _{W1} H')	3521(782)	
35	bend. (H'O _{W1} H'')	1688(131)	1709 (99) bend.
36	bend. H'O _{W3} H'')	1678(180)	
37	rot. (O _{W3} H'), rot (O _{W1} H') a''	707(103)	
38	rot. (O _{W1} H'), rot (O _{W3} H') a''	697(325)	
39	rot. (H'O _{W1} H'') a''	408(87)	
40	rot. (H'O _{W3} H'') a''	396(130)	
41	rot. (O _{W1} H''), rot. (O _{W3} H'') a''	225(102)	
42	rot. (O _{W3} H''), rot. (O _{W1} H'') a''	222(108)	
43	inside-inside transl. (H'O _{W1} H'')-(H'O _{W3} H''), rot. U a'	192(11)	
44	inside-outside transl. (H'O _{W1} H'')-H'O _{W3} H''), transl. U a'	186(1)	
45	rot. (H'O _{W1} H'')(H'O _{W3} H''), rot. U a'	147 (12)	
46	rot. (H'O _{W1} H'')(H'O _{W3} H''), transl. U a'	99(12)	
47	rot. (H'O _{W1} H'')(H'O _{W3} H''), rot. U a''	64(4)	
48	rot. (H'O _{W1} H'')(H'O _{W3} H''), rot. U a'	58(2)	

^a U: uracil; str.: stretching; bend.: bending; transl.: translation; rot.: rotation.

^b 6-31G(*) set.

^c 6-31G(†) set.

vibrational spectrum of uracil, the dihydrate model indicates that the formation of H-bonds with water induces very significant upfield and downfield shifts. For instance, the stretching NH modes (no. 1 and 2) are lowered by almost the same amount (224 and 212 cm^{-1} , respectively, for the 6-31G(†) set), whereas the bending and the wagging modes (no. 8, 11 and 22,

24) are increased; the change is particularly striking for the latter two, with a rise from 687 to 859 cm^{-1} for N3H and from 554 to 797 cm^{-1} for N1H. Clearly, the downfield shift of the NH bond stretch modes is a direct consequence of the H-bonding; this is also remarked in the C=O stretch wavenumbers (60 cm^{-1} shifts in the modes no. 5 and 6) as well as in those of

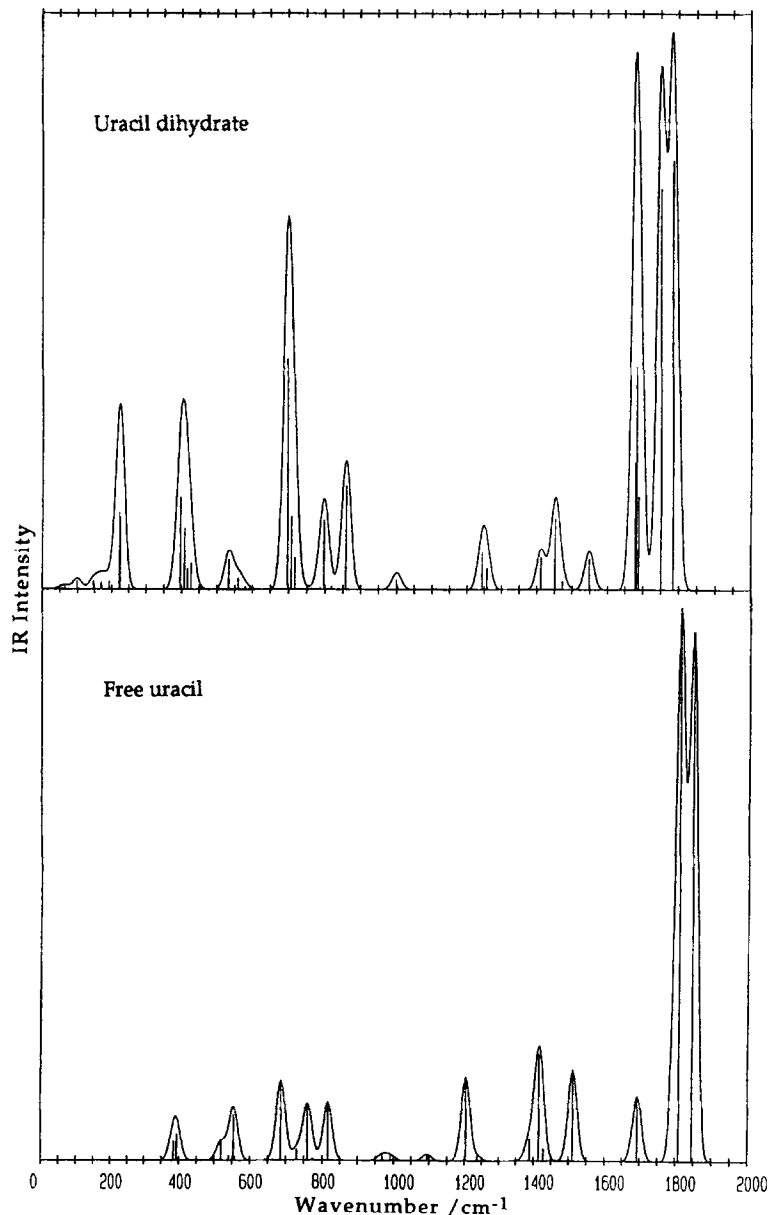


Fig. 2. Theoretical IR spectra of uracil (bottom) and uracil dihydrate (top) in the region below 2000 cm^{-1} .

the water OH' stretching (about 200 cm^{-1} shifts in the modes no. 33 and 34). In the case of bending and wagging motions, the consequence of H-bonding may be seen as a kind of friction effect.

Concerning the extra modes of (U, $2\text{H}_2\text{O}$), they can be classified in two distinct types, named a' and a'' in Table 4, in spite of the planarity defects of the supermolecule and they always appear in pairs. Modes 37–38 and 41–42 are especially noticeable, as describing rotation of bonded water; the first pair (around 700 cm^{-1}) correspond to the hindered rotation of a linked hydroxyl $\text{O}_\text{w}\text{H}'$ around the other $\text{O}_\text{w}\text{H}''$, and the second pair (around 225 cm^{-1}) to less hindered rotation of a quasi-free hydroxyl $\text{O}_\text{w}\text{H}''$ around $\text{O}_\text{w}\text{H}'$.

In the discussion above, many details due to the coupling between the uracil and water motions have been omitted. For instance, for certain fundamentals, large changes in IR intensities often arise from apparently small contributions included in the overall vibration. However, the uracil and water patterns are still recognisable in the synthetic IR spectra presented in Fig. 2. In fact, in solution spectra, one generally removes the bands located around 1650 and 750 cm^{-1} , assigned to the H_2O bending and intermolecular torsions, when comparing the observed spectra with those obtained by calculations.

4. Conclusion: relevance of the model

At first sight, simulating the environment of uracil in condensed phase by only two solvent molecules may appear too limitative, and more realistic models using more computational resources should be certainly developed in future. However, the primitive dihydrate model has its own merits. Two water molecules are sufficient to generate H-bonds with the four functional groups of uracil and this enables us to correlate the properties of the (U, $2\text{H}_2\text{O}$) complex with some observables. We will only mention the rather good agreement of the $\text{O}_\text{w}\cdots\text{O}$ distances with the value observed in crystalline monohydrate [7]. For the comparison between the experimental data concerning the NH and CO vibrational motions of uracil in condensed phase and the calculated ones obtained from the uracil dihydrate model, the reader is referred

to one of our recent papers [15]. Briefly, the calculated N–H wagging wavenumbers in the supermolecule are quite close to those observed in solid phase.

Acknowledgements

The authors are indebted to Mrs M.H. Baron and L. Grajcar (CNRS, Thiais) for helpful experimental information. The CNRS computing center (IDRIS, Orsay) and the computing facilities of University of Modena (CICAIA) are gratefully acknowledged. The work was supported in part by CNR funds. A. A. is partly supported by a fellowship from the government of Morocco.

References

- [1] R.W. Williams, A.H. Lowrey, *J. Comput. Chem.* 12 (1991) 861.
- [2] L. Paglieri, G. Corongiu, D.A. Estrin, *Int. Quan. Chem.* 50 (1995) 615.
- [3] J. Tomasi, M. Persico, *Chem. Rev.* 94 (1994) 2027.
- [4] R.W. Williams, J.L. Cheh, A.H. Lowrey, A.F. Weir, *J. Phys. Chem.* 99 (1995) 5299.
- [5] W.B. Person, J.E. DelBene, W. Szajda, K. Szczepaniak, M. Szczepaniak, *J. Phys. Chem.* 95 (1991) 2770.
- [6] J. Smets, L. Adamowicz, G. Maes, *J. Phys. Chem.* 100 (1996) 6434.
- [7] R. Gerdil, *Acta Cryst.* 14 (1961) 333.
- [8] G. Berthier, B. Cadioli, E. Gallinella, A. Aamouche, M. Ghomi, *J. Mol. Struct. (Theochem)* 390 (1997) 11.
- [9] J.E. DelBene, W.B. Person, K. Szczepaniak, *J. Chem. Phys.* 99 (1995) 10705.
- [10] R.S. Mulliken, *J. Chem. Phys.* 36 (1962) 3428.
- [11] M.J. Frisch et al., *Gaussian 92/DFT, Revision F.2*, Gaussian, Inc., Pittsburgh, 1994.
- [12] Z. Latajka, Y. Bouteiller, *J. Chem. Phys.* 101 (1994) 9793.
- [13] R. Zanasi, *Vibmol. QCPE* 13 (1993) 5.
- [14] G. Schaftenaar, Molden, CAOS/CAMM Center, Nijmegen, 1991.
- [15] A. Aamouche, M. Ghomi, B. Cadioli, G. Berthier, L. Grajcar, M.H. Baron, *J. Mol. Struct. (Theochem)* 410–411 (1997) 323.
- [16] L. Pauling, *The Nature of the Chemical Bond and the Structure of Molecules and Crystals*, 2nd ed., Cornell Univ. Press, Ithaca, New York, 1940.
- [17] G.C. Pimentel, A.L. McClellan, *The Hydrogen Bond*, W.H. Freeman, San Francisco, 1962.
- [18] P. Pulay, G. Fogarasi, F. Pang, J.E. Boggs, *J. Amer. Chem. Soc.* 101 (1979) 2550.