Aza analogs of nucleic acid bases: infrared and Raman spectra of 5-azauracil and crystal structure of 5-azauracil monohydrate

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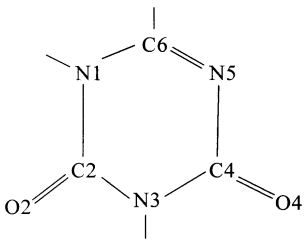
The X-ray crystal structure of 5-azauracil monohydrate ($C_3H_3O_2N_3 \cdot H_2O$, $M_r = 131.10$ Da) has been determined from X-ray diffraction data. In the crystal structure all atoms of the 5-azauracil molecule and the solvated water, including hydrogens, lie exactly in the mirror plane perpendicular to b at $y = 1/4$ in the monoclinic space group $P2_1/m$ and therefore exhibit symmetry m (C_s). The crystal structure comprises solvate-promoted hydrogen-bonded layers in the ac plane, separated by $b/2 = 3.1054$ Å. The X-ray structure of 5-azauracil monohydrate is compared with the previously reported data for uracil, 6-azauracil and a complex of 5-azauracil with its own hydrolysis product. The presence of bands due to C=O stretching vibrations in the infrared and Raman spectra confirms that 5-azauracil exists in its dioxo tautomeric form in both the anhydrous and hydrated crystal forms. The position of a strong Raman band due to the ring breathing vibration is found to be a marker for the state of hydration of 5-azauracil; it appears at 804 cm^{-1} in the solid state Raman spectrum of 5-azauracil and shifts upwards in wavenumber to 816 cm^{-1} in the spectrum of 5-azauracil monohydrate.

The synthesis[1,2] and structure-activity relationships[3] of numerous purine and pyrimidine analogs have been the source of intense investigations over the last five decades. This interest has been, in part, due to their potential uses as anti-neoplastic agents[4,5] and enzyme inhibitors,[6] as well as their bacteriostatic and fungicidal[7,8] properties. Additionally, such compounds are being examined as possible reagents for mutagenicity testing in microbial systems[9] and used in molecular biology protocols.[10] The aza analogs of uracil[11,12] in particular have undergone widespread scientific investigations in relation to the foregoing. Structurally azapyrimidines (*e.g.* 5- and 6-azauracil) differ from the normal bases of nucleic acids in being substituted with a nitrogen atom in place of a CH group at some position in the heterocyclic ring. Such a minor structural modification, when effected at a strategic location in the pyrimidine ring system, causes enormous changes in enzymatic properties of nucleic acids *in vivo*. Consequently, N or NH instead of CH adjacent to the glycosidic bond[13] give rise to subtle geometrical and electronic differences, which are nevertheless of considerable biological significance. 5-Azauracil [allantoxaidin(e); oxaidin; 1*H*-1,3,5-triazine-2,4-dione, $C_3N_3O_2H_3$] is an inhibitor of the enzyme orotate phosphoribosyl transferase, which catalyses the conversion of orotate to orotidine 5′-phosphate in pyrimidine nucleotide synthesis.[8] In addition this compound, in contrast to 6-azauracil, may be a carcinogen.[14] Structural data are available for the azapyrimidines, 6-azathymine and 6-azauracil,[13,15] and for the complex of 5-azauracil with its own hydrolysis product.[16]

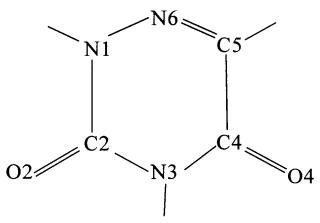
In this study detailed X-ray crystallographic, and FT-IR and Raman spectroscopic data, in the solid state, are reported for 5-azauracil (I) aqueous solvate. Structural and vibrational data are compared with the corresponding data for uracil (III)[17–19] and 6-azauracil (II).[13,15,20] The X-ray crystallographic data for 5-azauracil hydrate are also compared with structural data for the complex of 5-azauracil with its hydrolysis product.[16]

Experimental

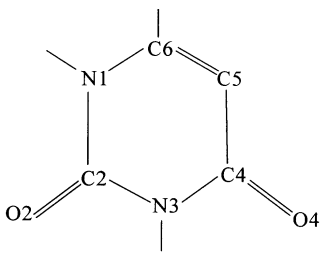
5-Azauracil was obtained from the rare chemicals collection of Sigma Ltd (Poole, Dorset, UK) and used as received, without



(I)
5-Azauracil



(II)
6-Azauracil



(III)
Uracil

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further purification. Its elemental composition and melting point were in agreement with values given in the literature.[21] 5-Azauracil monohydrate was prepared by crystallization of 5-azauracil from double-deionized water. 6-Azauracil and deuterium oxide (99.9 atom%) were also obtained from Sigma Ltd.

FT-IR and Raman spectroscopy

Infrared spectra of polycrystalline samples in KBr pellets were recorded, at room temperature, on a Perkin Elmer Paragon 1000 FTIR spectrophotometer operating at a resolution of 1 cm^{-1}. Raman spectra of samples in the solid phase were recorded at room temperature using a Labram Raman spectrometer equipped with a 1800 g/mm holographic grating blazed at 500 nm, a holographic notch filter, and an Olympus BX40 microscope. The 632.8 nm line of a helium-neon laser was used for excitation and a Peltier-cooled CCD (MPP1 chip) for detection. Raman spectra of aqueous solutions of 5-azauracil were obtained using glass capillaries.

X-Ray crystallography

CAD-4 Express '88 software[22] was used for cell determination and refinement, data collection and data reduction. The crystal showed no significant variations in intensities of three check reflections during the course of data collection. Lorenz and polarization corrections were applied but absorption effects were ignored. Crystal data collection and refinement parameters are given in Table 1.

The structure was solved by direct methods using SHELX-86[23] and refined with SHELXL-93.[24] Non-H atoms were refined anisotropically by full-matrix least-squares techniques on F^2. All H atom positions, including those of the solvated water, were located from difference electron density plots and refined with isotropic displacement parameters. The program SNOOPI[25] was used to prepare the structure drawings.

CCDC reference number 440/079.

Table 1 Crystal data and structure refinement parameters for 5-azauracil monohydrate

Formula	$C_3H_3N_3O_2 \cdot H_2O$
M	131.10
Crystal habit, colour	Prismatic/colourless/ex H_2O
Crystal size/mm	0.30 × 0.30 × 0.20
Crystal system	Monoclinic
Space group	$P2_1/m$
a/Å	6.4316(9)
b/Å	6.2108(9)
c/Å	6.8205(6)
β/°	99.78(1)
U/Å^3	268.54(6)
	Cell parameters from 20 reflections θ = 25–30°
Z	2
Required molecular symmetry	m (C_s)
D_c/g cm^{-3}	1.186
μ/mm^{-1}	1.269
F(000)	1072
T/K	293(2)
Diffractometer	Enraf-Nonius CAD
Radiation	CuKα (λ = 1.541 78 Å)
Scan type	ω/2θ
θ range for data collection/°	6.58–69.41
T_{min}, T_{max}	0.783, 0.952
hkl ranges	−7, −7, −8 to 7,7,7
Reflections collected	1700
Independ. reflect.	538
Obsd reflect. [I > 2σ(I)]	522
	No absorption correction
R_{int}	0.158
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	522/0/71
Goodness-of-fit on F^2	1.083
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0332$, $wR(F^2) = 0.0922$
R indices (all data)	$R1 = 0.0339$, $wR(F^2) = 0.0928$
Extinction coefficient	0.037(4)
$\Delta\rho_{max}$, $\Delta\rho_{min}$/e Å^{-3}	0.152, −0.195
$(\Delta/\sigma)_{max}$	0.133

Results and discussion

IR and Raman spectroscopy

The isolated 5-azauracil molecule exhibits C_s (m) molecular point group and has $\Gamma = 19\ A' + 8\ A''$ vibrations, all of which are infrared and Raman active. However, the bands due to the internal vibrational modes of 5-azauracil in the monohydrate crystal should each split into two: $8\ A_u + 19\ B_u$ are infrared active and $19\ A_g + 8\ B_g$ are Raman active. However, coincidences of some bands can be seen in the infrared and Raman spectra (within the experimental wavenumber accuracy of 1 cm^{-1}), for example, those at 1353 cm^{-1} (infrared and Raman), which are due to δ(C—H), and those at 1616 cm^{-1} (infrared and Raman), which are due to a ring stretching vibration (see Fig. 1 and Table 2). This suggests weak intermolecular vibrational coupling for these modes, as expected in a molecular crystal of this type.

The nomenclature used by Susi and Ard[19] for the in-plane skeletal vibrations of uracil is employed for the assignments that follow. The 5-azauracil molecule, like uracil itself, has eight coplanar heavy atoms giving 13 in-plane vibrations. These are labelled U(I) to U(XIII) in order of decreasing wavenumber.

Infrared spectra

5-Azauracil. Infrared spectral assignments have been aided by comparison of solid state wavenumbers with those obtained from rare gas matrix experiments and *ab initio* Hartree–Foch calculations at the 3-21G and 6-31G** levels.[26] In the high wavenumber region, a strong band at 3213 cm^{-1} in the infrared spectrum and a weaker band at 3208 cm^{-1} in the Raman spectrum are both due to N—H stretching vibrations. These have been calculated to come at 3231 and 3411 cm^{-1}, respectively, using the 3-21G basis set and a scaling factor of 0.9, and at 3499 and 3480 cm^{-1} at the 6-31G** level, also with a scaling factor of 0.9.[26] In addition, weak bands at 3086 cm^{-1} in the infrared spectrum and at 3084 cm^{-1} in the Raman spectrum are assigned to C—H stretching.

The strong bands at 1734 and 1700 cm^{-1} in the infrared spectrum are assigned to the U(I) and U(II) C=O stretching modes, respectively, and the band at 1616 cm^{-1} is assigned to

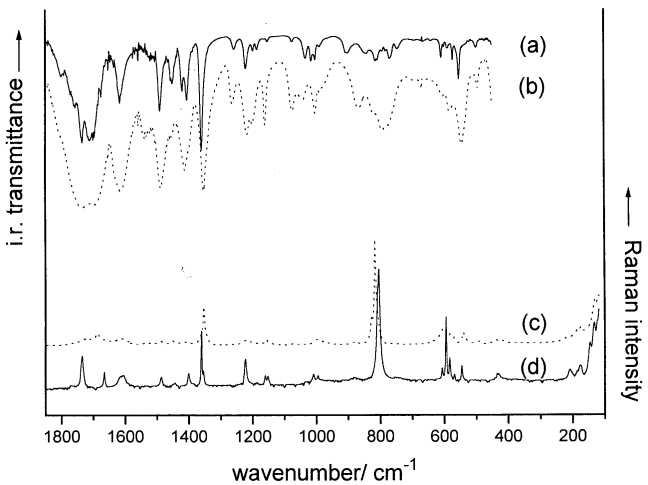

Fig. 1 Infrared spectra of (*a*) 5-azauracil and (*b*) 5-azauracil monohydrate in the solid state. Samples were run as pressed KBr discs. Raman spectra of (*c*) 5-azauracil hydrate and (*d*) 5-azauracil in the solid state. The Raman spectra were obtained by using an excitation wavelength of 632.8 nm; the laser power at the samples was 8 mW.

Table 2 Wavenumbers and tentative assignments of infrared and Raman bands of polycrystalline samples of 5-azauracil and 5-azauracil monohydrate

5-Azauracil		5-Azauracil monohydrate		Tentative assignment
Infrared	Raman	Infrared	Raman	
		3460 m, br		ν(O—H)
3238 sh		3240 s, br		ν(N—H)
3213 s, br	3208 w	3191 s, br		ν(N—H)
3086 w	3084 w	3080 w	3067 w	ν(C—H)
2969 mw		2969 vw		?
2821 w		2823 w		?
2780 mw, br		2796 w		?
1792 sh				overtone or combination
1757 sh				overtone or combination
1734 vs (1662)	1735 m	1734 vs	1721 mw	U(I), ν(C=O)
1700 vs, br (1648)	1665 mw	1695 vs	1687 m	U(II), ν(C=O)
1616 s (1611)	1608 mw, br	1616 s	1616 mw	U(III), ring str.
1490 s	1486 mw	1489 s	1490 w	δ(N—H)
1452 m (1462)	1444 w	1457 w	1453 w	U(IV), ring str.
1420 m, 1406 m	1401 mw	1413 ms	1415 vw	δ(N—H)
1359 vs	1360 ms	1353 s	1353 s	δ(C—H)
1258 mw		1264 mw		?
1221 m (1236)	1223 m	1217 m	1218 mw	U(V), ring str.
1198 mw		1200 w		?
1186 mw				?
1153 w (1104)	1152 mw, 1161 mw	1161 m	1158 mw	U(VI), ring str.
		1075 m, br	1074 vw	ω(C—H)
		1042 w, br		?
1016 m				ω(C—H)
1003 m (1010)	1009 mw	1003 m		U(VI), ring str.
(988)	995 mw	989 w, sh	998 mw, 985 mw	U(VIII), ring str./bend.
901 m, br		867 m	877 w	ω(N—H)
842 w		821 w, sh	828 w, sh	ω(N—O)
814 m, 808 m		794 m		ω(C=O)
(792)	804 vs		816 vs	U(IX), ring breath.
769 mw, 745 w		777 w, sh		ω(C=O)
607 mw, 589 w (579)	606 mw, 594 ms, 583 mw	602 w, 582 mw	605 m, 580 w	U(X), ring bend.
572 mw, 552 m (558)	545 mw	546 s	541 m	U(XI), δ(C=O)
500 mw (540)		494 mw	492 w	U(XII), ring bend.
	435 mw		439 w	ring torsion
(398)				U(XIII), δ(C=O)
	209 mw		218 w	ring torsion or lattice mode
	176 mw		185 w, 177 w	ring torsion or lattice mode

The positions of infrared bands reported for the 13 planar, skeletal modes of uracil are given in parentheses.[19a]

the U(III) ring stretching mode, coming as they do in the characteristic regions for these vibrations. In the infrared spectra of uracil and 6-azauracil, C=O stretching bands have been reported at lower wavenumbers: 1675 and 1716 cm^{-1} for the former,[19a] and 1670 and 1710 cm^{-1} for the latter.[20] It is noteworthy that the U(III) ring stretching vibration of 5-azauracil gives rise to an infrared band at 1616 cm^{-1}, whereas the corresponding band of 6-azauracil has been observed by us at 1597 cm^{-1} and by Rai[20] at 1600 cm^{-1}. This is probably due to a different coupling with other in-plane vibrations.

The bands in the 1550–1050 cm^{-1} region can be assigned to ring stretching and in-plane N—H and C—H bending modes (as seen in Table 2) by analogy with literature assignments of uracil infrared bands.[19a] Indeed, the doublet at 1406 and 1420 cm^{-1} and the band at 1490 cm^{-1}, due to N—H bending, are very close to uracil bands reported at 1417 and 1508 cm^{-1}, and the U(IV) band at 1452 cm^{-1} is very close to its uracil counterpart, which was reported at 1453 cm^{-1}.[19a] Bands due to the U(V) and U(VI) ring stretching modes also come close to their counterparts of uracil, as do the bands due to the U(VII)–U(XII) modes (see Table 2).

There are eight out-of-plane vibrational modes of the isolated, planar 5-azauracil molecule, namely one C—H, two N—H and two C=O wagging vibrations and three ring torsional modes. Of these, the C—H wagging vibration is tentatively assigned to an infrared band appearing at 1016 cm^{-1}, and the N—H wagging vibrations are assigned to broad bands at 842 and 901 cm^{-1} (see Fig. 1), because they come reasonably close to bands at 807 and 850 cm^{-1} assigned to these modes in the solid state, room temperature spectrum of uracil.[18] These bands come at higher wavenumbers in the solid state infrared spectrum than the bands at 587, 659 and 662 cm^{-1} and at 626, 684 and 689 cm^{-1}, which were reported for 5-azauracil isolated in argon and nitrogen matrices, respectively,[26] because of hydrogen bonding involving the N—H groups in the solid state. The C=O wagging vibrations can be assigned to two doublets with components at 745 and 769 cm^{-1} and at 808 and 814 cm^{-1}, as they appear in the same region as bands assigned to C=O wagging, at 750 and 760 cm^{-1}, in the low temperature (15 K) solid state infrared spectrum of uracil.[18] Furthermore, these C=O wagging bands come close to those observed for 5-azauracil at 762 and 791 cm^{-1} in solid nitrogen and at 757 and 786 cm^{-1} in solid argon.[26]

5-Azauracil monohydrate. The infrared spectra reported here are obtained from solid state samples in which the 5-azauracil molecule is shown by X-ray diffraction to be hydrogen bonded to aqueous solvate molecules. Thus, these intermolecular interactions are expected to perturb some of the vibrational modes. The N—H stretching vibrations give rise to strong, broad bands at 3191 and 3240 cm^{-1}, which are shifted by approximately 235 cm^{-1} from their counterparts at 3437 and 3464 cm^{-1} in the infrared spectrum of 5-azauracil isolated in solid argon.[26] This wavenumber shift ($\Delta\nu_s$) is presumably due to hydrogen bonding of the N—H groups in the

solid state and it can provide the means for estimating the N···O distances (R) from the relationship:[28] $\Delta\nu_s = 0.548 \times 10^3(3.21 - R)$. This gives an estimate of 2.78 Å for the N···O distances, which is in quite good agreement with the values of 2.732(1) and 2.747(1) Å obtained from the X-ray structure (see below). Weak bands in the 2700–2900 cm^{-1} region are likely to be due to overtones and combinations.

As expected, the N—H wagging modes are particularly sensitive to differences in the intermolecular interactions between the anhydrous and hydrated crystal forms. Thus, the broad bands at 842 and 901 cm^{-1} in the infrared spectrum of 5-azauracil shift to 821 and 867 cm^{-1} in the infrared spectrum of 5-azauracil hydrate. Smaller shifts are observed for bands due to bending and stretching vibrations involving the C=O groups as can be seen from Table 2. Also, it is clear that formation of the hydrate perturbs the C—H group, since the very strong infrared band at 1359 cm^{-1} due to the in-plane bending vibration of 5-azauracil shifts down to 1353 cm^{-1} in the spectrum of the hydrate. Furthermore, the band at 1016 cm^{-1}, which is tentatively assigned to the C—H wagging vibration of 5-azauracil, also shifts in the spectrum of the hydrate. This perturbation could well be due to the close approach of the water molecule forming a hydrogen bond to N(5) in the hydrate.

Raman spectra

5-Azauracil. The Raman spectrum of 5-azauracil is shown in Fig. 1, and band locations have been listed in Table 2 together with tentative band assignments. The strongest Raman bands are due to in-plane vibrational modes; bands due to out-of-plane vibrational modes are weak, when they are present.

The band at 1735 cm^{-1}, due to the U(I) C=O stretching mode, and the band at 1360 cm^{-1}, due to C—H bending, come at the same wavenumber locations as their infrared counterparts, to within 1 cm^{-1}. The medium intensity band at 1223 cm^{-1} can be assigned to the U(V) ring stretching mode and the intense band at 804 cm^{-1} is assigned to the U(IX) ring breathing mode, by analogy with the assignment of very strong bands at 1236 and 791 cm^{-1}, which have been reported in the Raman spectrum of uracil.[18]

5-Azauracil monohydrate. It is striking that the intense 804 cm^{-1} band in the solid state Raman spectrum of 5-azauracil, which is due to the U(IX) ring breathing mode, shifts upwards to 816 cm^{-1} in the spectrum of 5-azauracil monohydrate. In aqueous solution the ring breathing mode gives rise to a band at 813 cm^{-1}, which is closer to its position in the solid state spectrum of 5-azauracil hydrate. Both the band at 816 cm^{-1} in the solid state spectrum and the band at 813 cm^{-1} in the solution spectrum shift downwards by 5 cm^{-1} on *N* deuteriation (see Table 3). This suggests that the vibration contains a small amount of in-plane N—H bending character. Bands attributed to N—H in-plane bending appear at 1415 and 1490 cm^{-1} and shift to lower wavenumber on *N* deuteriation (see Table 3). The in-plane N—D bending modes almost certainly mix with ring vibrational modes, so a number of bands in the 800–1300 cm^{-1} region are probably due to vibrations that have some N—D in-plane bending character.

X-Ray crystallography

Bond distances and angles of 5-azauracil monohydrate are listed in Table 4. A view of the hydrated molecule is shown in Fig. 2. It is of interest to compare the molecular geometry of 5-azauracil (I), determined here, with related structures: (*a*) hydrated complex of 5-azauracil and its hydrolysis product;[16] (*b*) 6-azauracil[13,15] (II) and (*c*) uracil[17] (III). Of these structures, the present determination is the most precise (mean bond length esd of 0.0009 Å, mean bond angle esd of 0.06° (degree) for non-H atoms, compared to values of around 0.002 Å and 0.2° (degree) for the related structures listed above). A comparison of bond lengths in these structures is given in Table 5. Apart from the exceptions noted below, the geometries of the two 5-azauracil structures are in good agreement. Of the ring bond lengths in hydrated 5-azauracil, N1—C2 is slightly longer than in the other structures, while N1—C6 is noticeably shorter. This may be attributed to the long-range effect of the substitution of N for CH in position 5 compared to uracil and 6-azauracil, and is slightly more marked in 5-azauracil hydrate. As a point of interest the stretching of the N1—C2 bond in 5-azauracil hydrate to 1.3847(9) Å agrees well with the value of 1.384 Å assigned from a theoretical CNDO2 study.[29] The O2=C2 carbonyl bond length in 5-

Table 3 Wavenumbers and tentative assignments of Raman bands of polycrystalline samples of 5-azauracil monohydrate and its *N*-deuteriated isotopomer

5-Azauracil monohydrate	*N*-deuteriated 5-azauracil monohydrate	Tentative assignment
	2375 w	ν(N—H)
3067 w	3067 w	ν(C—H)
1721 mw (1739)	1711 m (1728)	U(I), ν(C=O)
1687 m (1697)	1687 w (1695)	U(II), ν(C=O)
1660 w	1660 w	?
1616 mw	1613 mw (1617)	U(III), ring str.
1490 w, 1415 w	861 w, 949 w, 1126 mw (1122), 1264 mw (1258)	δ(N—H)
1453 w	1461 w	U(IV), ring str.
1353 ms (1368)	1352 ms (1342, 1373)	δ(C—H)
1218 mw (1231)		U(V), ring str.
1158 mw	1157 w	U(VI), ring str.
1074 w		ω(C—H)
998 mw, 985 mw	992 mw	U(VIII), ring str./bend.
877 w	609 mw, br	ω(N—H)
828 w, sh		?
816 vs (813)	811 s (808)	U(IX), ring breath.
605 m (604), 580 w (584)	571 m (575)	U(X), ring bend.
541 m (540)	542 w (526)	U(XI), δ(C=O)
492 w		U(XII), ring bend.
439 w	430 mw	ring torsion
218 w	217 mw	ring torsion or lattice mode
185 w, 177 mw	182 mw	ring torsion or lattice mode

The positions of bands in Raman spectra of solutions of 5-azauracil in H_2O and D_2O are given in parentheses.

Table 4 Bond lengths (Å) and angles (°) in 5-azauracil monohydrate

N1—C2	1.3847(9)	N3—C4	1.3670(8)
N1—H1	0.905(9)	N3—H3	0.92(1)
N1—C6	1.3394(9)	O4—C4	1.2168(8)
C6—H6	0.96(1)	N5—C4	1.3839(9)
N3—C2	1.3628(9)	N5—C6	1.2871(8)
O2—C2	1.2099(9)		
Water			
O4A—H41	0.91(1)	O4A—H42	0.92(1)
C6—N1—C2	121.61(6)	O2—C2—N1	123.12(6)
C6—N1—H1	117.6(6)	N3—C2—N1	112.83(6)
C2—N1—H1	120.8(6)	O4—C4—N3	121.14(6)
C2—N3—C4	125.26(6)	O4—C4—N5	120.88(6)
C2—N3—H3	121.6(6)	N3—C4—N5	117.97(6)
C4—N3—H3	113.1(6)	N5—C6—N1	124.93(7)
C6—N5—C4	117.39(6)	N5—C6—H6	117.2(5)
O2—C2—N3	124.05(7)	N1—C6—H6	117.9(5)
Water			
H41—O4A—H42	119(1)		

azauracil is noticeably shorter than O4=C4, a reversal of the situation in the 5-azauracil complex structure. The O4=C4 bond, in uracil, is significantly longer than in any of the other structures. For uracil this effect has been attributed to differences in H-bond participation.[30] The present work confirms that in all of the other structures, both O2 and O4 participate in one H bond, whereas in uracil there are two H bonds to O4 and none to O2. All of the ring bond angles follow the suggested rule of Singh,[31] with a marked increase at protonated sites.

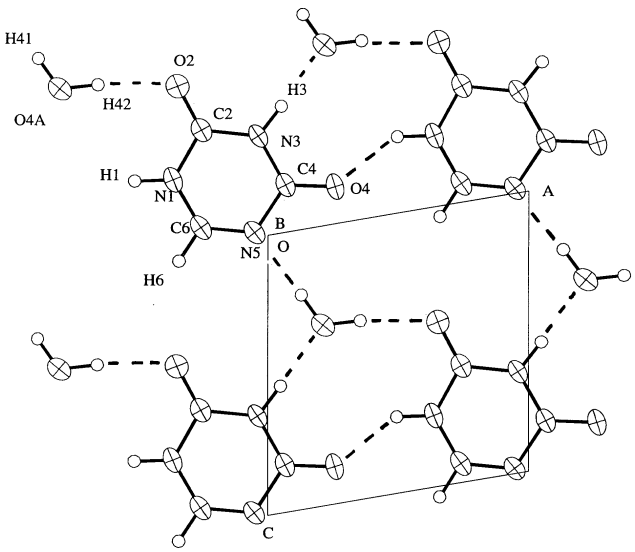

Fig. 2 Hydrogen bonding in the crystal structure of 5-azauracil monohydrate viewed along *b*, showing 50% probability thermal ellipsoids.

Table 6 Hydrogen bonds and other short contacts (in Å) in 5-azauracil monohydrate

D—H	D···A	H···A	D—H···A
Hydrogen bonds:			
N1—H1	N1···O4$^{(1)}$	H1···O8$^{(1)}$	N1—H1···O8$^{(1)}$
0.904(7)	2.732(1)	1.957(7)	142.9(7)
N3—H3	N3···O4A$^{(2)}$	H3···O4A$^{(2)}$	N3—H3···O4A$^{(2)}$
0.924(8)	2.747(1)	1.824(8)	177(2)
O4A—H42	O4A···O2	H42···O7	O4A—H42···O7
0.956(9)	2.803(1)	1.893(8)	158.1(9)
O4A—H41	O4A···N5$^{(3)}$	H41···N5$^{(3)}$	O4A—H41···N5$^{(3)}$
0.915(8)	2.807(1)	1.912(7)	165(1)
Additional short contacts:			
N15—H1	N1···O4A	H1···O4A	N1—H1···O4A
0.904(7)	3.492(1)	2.874(7)	126.9(6)
O4A—H42	O4A···N1	H42···N1	O4A—H42···N1
0.956(9)	3.492(1)	2.925(8)	119.2(6)
O4A—H41	O4A···O4$^{(3)}$	H41···O4$^{(3)}$	O4A—H41···O4$^{(3)}$
0.915(8)	3.376(1)	2.750(8)	126.6(6)
C6—H6	C6···O4$^{(1)}$	H6···O8$^{(1)}$	C6—H6···O8$^{(1)}$
0.966(7)	3.094(1)	2.681(7)	106.3(6)
C6—H6	C6···O2$^{(4)}$	H6···O2$^{(4)}$	C6—H6···O2$^{(4)}$
0.966(7)	3.422(1)	2.569(7)	147.3(7)

Symmetry code: (1) $+x-1$, $+y$, $+z$; (2) $+x+1$, $+y$, $+z$; (3) $+x-1$, $+y$, $+z-1$; (4) $+x$, $+y$, $+z+1$.

The crystal structure comprises exactly parallel hydrogen-bonded layers perpendicular to *b*, the layers being held together entirely through van der Waals' forces. The layer separation is $b/2 = 3.1054(5)$ Å, the distance between the two *m* planes. Fig. 2 shows one hydrogen-bonded layer in which all atoms, including those of the solvent, lie in the *m* plane, an exceptional situation for this type of structure. Full use is made of all H bond donors and acceptors. Details of the H bond geometry and other close contacts are shown in Table 6.

Conclusions

The presence of bands due to C=O stretching vibrations in the infrared and Raman spectra confirms that 5-azauracil exists in its dioxo tautomeric form in both the anhydrous and monohydrate crystals. Infrared bands due to the N—H stretching vibrations of 5-azauracil hydrate come approximately 235 cm^{-1} to lower wavenumber than infrared bands reported for these modes when 5-azauracil is isolated in argon matrices.[26] This is undoubtedly due to the participation of the N—H groups in hydrogen bonding with water molecules in the hydrate. An estimate of 2.78 Å for the N···O distances is in reasonably good agreement with the values of 2.732(1) and 2.747(1) Å from the X-ray structure.

The intense band at 804 cm^{-1}, which is observed in the solid state Raman spectrum of 5-azauracil and is due to the ring breathing mode, is observed to shift upwards in wavenumber to 816 cm^{-1} in the Raman spectrum of 5-azauracil

Table 5 Comparison of selected bond lengths (Å) for 5-azauracil monohydrate (this work) and related molecules

	5-Azauracil monohydrate	5-Azauracil complex[15]		6-Azauracil[13,14]	Uracil[21]
		molecule 1	molecule 2		
N1—C2	1.3847(9)	1.373(3)	1.372(3)	1.366(2)	1.371(3)
N1—C6	1.3394(9)	1.343(3)	1.347(3)		1.358(3)
N3—C2	1.3628(9)	1.355(3)	1.354(3)	1.378(2)	1.376(3)
O2—C2	1.2099(9)	1.214(3)	1.216(3)	1.224(2)	1.215(3)
N3—C4	1.3670(8)	1.369(3)	1.362(3)	1.359(2)	1.371(3)
O4—C4	1.2168(8)	1.209(3)	1.211(3)	1.224(2)	1.245(3)
N5—C4	1.3839(9)	1.387(3)	1.384(3)		1.430(3)
N5—C6	1.2871(8)	1.281(3)	1.279(3)		1.340(3)
N6—C5				1.291(2)	

monohydrate. Indeed, this intense band can be used as a marker of the hydration of 5-azauracil.

Coincidences of infrared and Raman bands occur in the spectra of 5-azauracil hydrate, in spite of the centrosymmetric structure, due to weak intermolecular vibrational coupling of some modes in the molecular crystal.

The crystal structure of 5-azauracil hydrate is exceptional; all atoms in the asymmetric unit, including hydrogen, being located on the crystallographic m plane of space group $P2_1/m$. Refinement of the structure in the non-centrosymmetric space group $P2_1$ with 878 reflections and 103 parameters converges to $R = 0.0303$, compared to $R = 0.0332$ for $P2_1/m$ for 522 reflections and 71 parameters. Although Hamilton's significance test[32] is in favour of space group $P2_1$, test calculations show that a variety of structures in $P2_1$ will refine to the same R factor whilst exhibiting different distributions in distance above and below the least-squares plane at approximately $y = 0.25$, all with RMS deviations of around 0.005 Å from the plane. It is therefore concluded that the refinement of the structure as presented here in space group $P2_1/m$ is the more appropriate.

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