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3-Methyl-5-nitrouracil

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Abstract

The molecules of the title compound, $C_5H_5N_3O_4$, are approximately planar. The nitro group makes a dihedral angle of 1.3 (4)° with the plane of the six-membered ring. This coplanar disposition is a reason for the changes in valence angles in the vicinity of the nitro group. Molecules are connected into dimers by means of N—H···O hydrogen bonds, and these dimers make larger structures with the help of relatively short C—H···O hydrogen bonds.

Keywords

3, methyl, 5, nitrouracil

Disciplines

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3-Methyl-5-nitrouracil

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Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.002 Å
R factor = 0.045
wR factor = 0.128
Data-to-parameter ratio = 10.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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The molecules of the title compound, $C_5H_5N_3O_4$, are approximately planar. The nitro group makes a dihedral angle of 1.3 (4)° with the plane of the six-membered ring. This coplanar disposition is a reason for the changes in valence angles in the vicinity of the nitro group. Molecules are connected into dimers by means of N—H···O hydrogen bonds, and these dimers make larger structures with the help of relatively short C—H···O hydrogen bonds.

Comment

Synthetic analogues of natural biopolymers, such as nucleic acids and peptides, are promising candidates as antisense and antigene drugs, and as diagnostic and biological tools. The improved hybridization properties exhibited by oligonucleotides containing LNAs (locked nucleic acids; Petersen & Wengel, 2003) and PNAs (peptide nucleic acids; Larsen *et al.*, 1999) are particularly interesting for such purposes. The pyrimidine nucleosides and their analogues exhibit extremely diverse physiological activities. For example, 5-fluorouracil is an important anticancer agent widely used in oncology (Longley *et al.*, 2003), 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine (HEPT) is applied as a non-nucleoside reverse transcriptase inhibitor in HIV-infection therapy (Tanaka *et al.*, 1992), and 5-nitro-1-[3-(5-nitro-2-furan-2-yl)acryloyl]uracil exhibits antitumour activity on leukaemia P388 cells (Trusule *et al.*, 1991).

5-Nitrouracil derivatives, besides their biological importance, have also become more interesting for their application in non-linear optics (*e.g.* Puccetti *et al.*, 1993). Knowledge of the factors influencing the crystal packing modes of these compounds is therefore very important and there is a need for more data regarding these modes. For 5-nitrouracil itself, the crystal structures of three polymorphic modifications have been reported, one monoclinic ($P2_1/n$; Kennedy *et al.*, 1998) and two orthorhombic [centrosymmetric *Pbca* reported by Pierce & Wing (1986) and re-examined by Gopalan *et al.* (2000), together with the non-centrosymmetric $P2_12_12_1$ form]. It should be noted, however, that for the orthorhombic structures there are no data in the Cambridge Structural Database (CSD; Version 5.27, January 2006 update; Allen, 2002). There are also two different solvates: a hydrate (Craven, 1967) and a dimethyl sulfoxide solvate (Kennedy *et al.*, 1998). Interestingly, in the CSD there are many more structures of 1-substituted uracils than of 3-substituted: 16 structures of 3-substituted (of which nine are 3-methyl derivatives) and 491 structures of 1-substituted uracils (25 1-methyl); of these, there are 69 1,3-disubstituted (42 1,3-dimethyl) and 89 unsubstituted at positions 1 and 3 (the conditions of search: only organics, no fused rings, coordinates

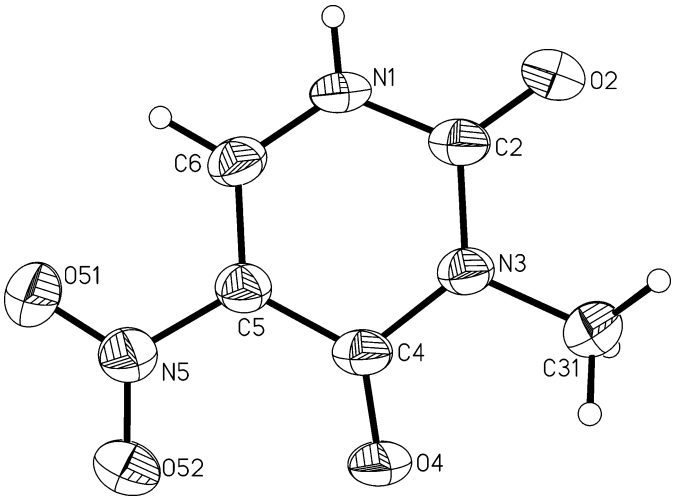


Figure 1
A view of the molecular structure of (I) (Siemens, 1989). Displacement ellipsoids are drawn at the 50% probability level; H atoms are depicted as spheres of arbitrary radii.

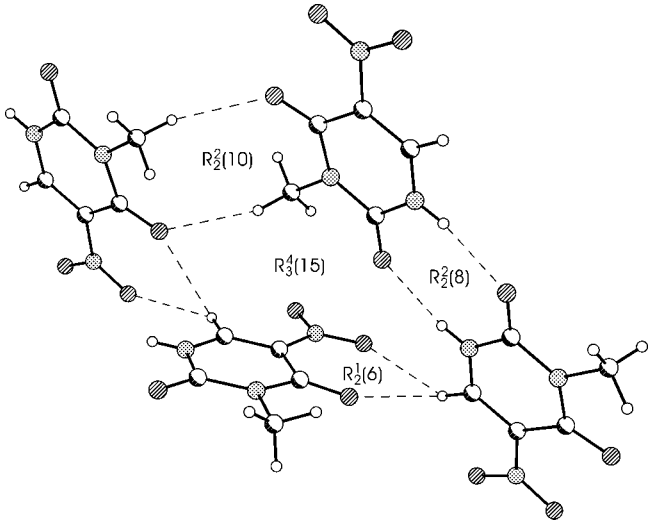
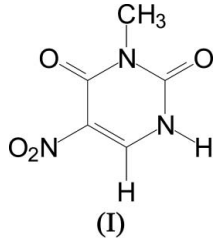


Figure 2
A fragment of the hydrogen-bond pattern (Siemens, 1989); the ring graph symbols are shown. Hydrogen bonds are depicted as dashed lines.

available, error-free). Therefore, new data on simple 3-methyluracils might be of interest. We report here the crystal structure of 3-methyl-5-nitrouracil, (I).



(I)

The pyrimidine ring is almost planar (Fig. 1), the largest deviation from the least-squares plane being 0.024 (1) Å. Carbonyl atom O2 lies in this plane [insignificant deviation of 0.007 (3) Å], while the other three substituents deviate more significantly, although slightly, from the ring plane. Owing to the steric stress, the directions of deviations are opposite for neighbouring atoms: −0.019 (3) Å for C31, 0.092 (2) Å for O4 and −0.042 (3) Å for N5. Overall, the whole molecule is almost planar; the dihedral angle between the ring plane and the nitro group is as small as 1.3 (4)°. Bond lengths and angles are typical and similar to those of related compounds. There is an asymmetry in C—N—O angles caused by steric factors; the angle on the side of the C4/O4 group, C5—N5—O52, of 120.6 (2)°, is significantly larger than the angle on the other side, C5—N5—O51 [117.8 (2)°]. The same asymmetry is observed for C—C—N angles; the C4—C5—N5 angle of 121.6 (2)° is more than 3° larger than C6—C5—N5, of 117.3 (2)°. This proves that, in order to gain the advantage of being coplanar with the π-electron system and in the absence of the steric hindrance, the nitro group has to accommodate the more flexible geometrical parameters, valence angles.

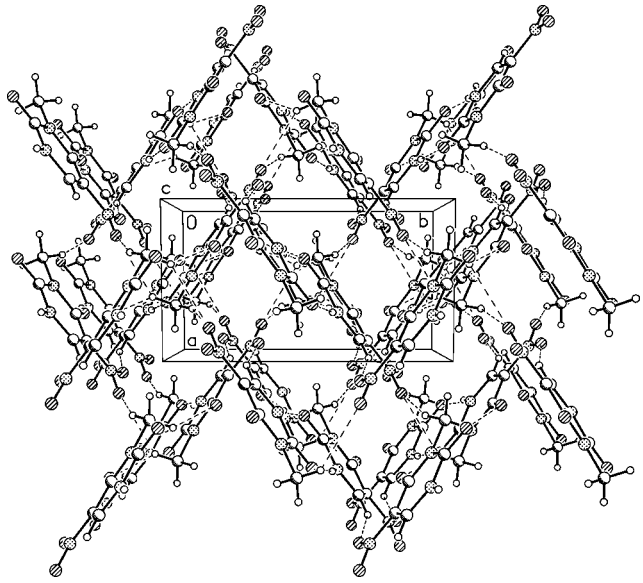


Figure 3
The packing of the molecules, as seen along the *c* axis (Siemens, 1989). Hydrogen bonds are depicted as dashed lines.

In the crystal structure the molecules are linked into centrosymmetric pairs by means of relatively strong and linear N1—H1···O2 hydrogen bonds. Using graph-set notation (Etter *et al.*, 1990; Bernstein *et al.*, 1995) the appropriate symbol is $R_2^2(8)$. The tendency towards creating hydrogen-bonded pairs in uracil derivatives is so strong that, even in the case of 1,3-dimethyluracil, the C(methyl)—H···O hydrogen bonds can take the pattern-determining role (Banerjee *et al.*, 1977). Only in the case of the non-centrosymmetric structure of 5-nitrouracil (Gopalan *et al.*, 2000) and, what is even more surprising, in the centrosymmetric structure of 3-methyluracil (Portalone *et al.*, 2002), are no dimers formed. Weaker C—H···O bonds are also involved in the determination of crystal packing (*cf.* Table 2 and Fig. 2). These bonds connect molecules into *C*(5) chains which are interconnected by ring

structures of $R_2^2(10)$; all these patterns make larger rings, $R_3^4(15)$. These interactions, together with other weak hydrogen bonds (*cf.* Table 2) and van der Waals interactions, create a grid-like structure of molecules (Fig. 3).

Experimental

Direct alkylation by methyl iodide of 5-nitrouracil in dimethylformamide in the presence of Bu_4NOH gave 3-methyl-5-nitrouracil in moderate yield (Blank & Fox, 1970). Crystals for X-ray data collection were grown from a methanol solution.

Crystal data

$C_5H_5N_3O_4$
M_r = 171.12
Monoclinic, $P2_1/c$
a = 5.7510 (12) Å
b = 10.176 (2) Å
c = 11.775 (2) Å
β = 100.69 (3)°
V = 677.1 (2) Å^3
Z = 4
D_x = 1.679 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 50 reflections
θ = 4–32°
μ = 0.15 mm^{-1}
T = 295 (1) K
Block, colourless
0.4 × 0.2 × 0.1 mm

Data collection

Kuma KM-4 diffractometer
ω–2θ scans
Absorption correction: none
1256 measured reflections
1196 independent reflections
926 reflections with $I > 2\sigma(I)$
R_{int} = 0.066
θ_{max} = 25.1°
$h = -6 \rightarrow 6$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 14$
2 standard reflections
every 100 reflections
intensity decay: 0.3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.128
S = 1.04
1196 reflections
119 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0911P)^2 + 0.05P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.067 (11)

Table 1
Selected geometric parameters (Å, °).

N1—C6	1.329 (2)	C4—O4	1.209 (2)
N1—C2	1.376 (2)	C4—C5	1.449 (3)
C2—O2	1.220 (2)	C5—C6	1.356 (2)
C2—N3	1.371 (2)	C5—N5	1.440 (2)
N3—C4	1.404 (2)	N5—O52	1.212 (2)
N3—C31	1.470 (2)	N5—O51	1.216 (2)
C6—N1—C2	123.3 (2)	N5—C5—C4	121.6 (2)
N3—C2—N1	115.9 (2)	O52—N5—O51	121.7 (2)
C2—N3—C4	125.4 (2)	O52—N5—C5	120.6 (2)
N3—C4—C5	113.3 (1)	O51—N5—C5	117.8 (2)
C6—C5—N5	117.3 (2)	N1—C6—C5	120.9 (2)
C6—C5—C4	121.1 (2)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O2^{i}	0.82 (2)	2.05 (2)	2.859 (2)	169 (2)
C31—H31A···O51^{ii}	0.95	2.55	3.260 (3)	132
C31—H31A···O4^{iii}	0.95	2.57	3.330 (2)	138
C31—H31B···O51^{iv}	0.97	2.58	3.474 (3)	155
C6—H6···O52^{v}	0.96 (2)	2.48 (2)	3.281 (3)	141 (2)
C6—H6···O4^{v}	0.96 (2)	2.59 (2)	2.958 (2)	103 (1)

Symmetry codes: (i) $-x+1, -y, -z+1$; (ii) $-x, y-\frac{1}{2}, -z+\frac{3}{2}$; (iii) $-x+1, -y, -z+2$; (iv) $x+1, -y+\frac{1}{2}, z+\frac{1}{2}$; (v) $x, -y+\frac{1}{2}, z-\frac{1}{2}$.

The H atoms of the methyl group were found in a difference Fourier map and then refined as a rigid body (AFIX 3); their U_{iso}(H) values were refined as a common FVAR.

Data collection: *KM-4 Software* (Kuma Diffraction, 1991); cell refinement: *KM-4 Software*; data reduction: *KM-4 Software*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *Stereochemical Workstation Operation Manual* (Siemens, 1989); software used to prepare material for publication: *SHELXL97*.

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