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6-Amino-1,3-dimethyl-5-(4-oxo-2-penten-2-yl)aminouracil

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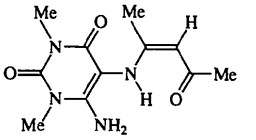
Abstract

The title compound, $C_{11}H_{16}N_4O_3$ [6-amino-1,3-dimethyl-5-(4-oxo-2-penten-2-yl)amino-2,4(1*H*,3*H*)-pyrimidinedione], shows extensive delocalization in the uracil ring. There is an intramolecular hydrogen bond [N···O 2.713 (3) Å] between an amino N—H group and an adjacent carbonyl-O atom. The molecules are linked into sheets that are parallel to the (10$\bar{1}$) plane by intermolecular N—H···O hydrogen bonds [N···O 2.805 (3) and 2.803 (3) Å].

Comment

The bonds and angles of the title compound, (I) (Fig. 1), are very similar to those found for 6-amino-1,3-dimethyluracil (Ferguson *et al.*, 1993) and 6-amino-1,3-dimethyl-5-hydroxyiminomethyluracil (Low, Ferguson, Moreno-Carretero & Hueso-Ureña, 1994). Principal dimensions are in Table 2; the C6—N6 bond [1.336 (3) Å] shows the typical intermediate single–double-bond character as found in the compounds cited above as well as in other 6-aminouracil derivatives. The mean plane of the side chain (N5, C51, C53, C54, O5) attached to C5 is tilted at 75.3 (1)° to that of the pyrimidine base (N1, C2, N3, C4, C5, C6). The deviations for the former mean plane range from −0.024 (2) (for C54) to 0.026 (2) Å (for C53); those for the pyrimidine base are in the range −0.018 (2) (for C4) to 0.023 (2) Å (for N3). The N5—H···O5 intramolecular hydrogen bond (Fig. 1, Table 3) is responsible for the planarity of the atoms of the C5 side chain.



(I)

O—H···N hydrogen bonds link the molecules into infinite chains by operation of the *n*-glide and into infinite spirals along the **b** direction from a 2_1 screw operation (Table 3). The combination of both of these results in sheets of molecules which are parallel to the (10$\bar{1}$) plane (Fig. 2). There are only normal van der Waals interactions between the sheets. Examination of

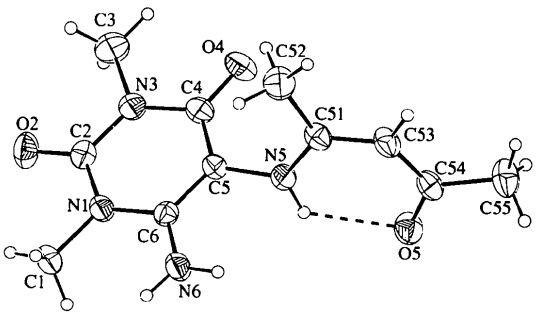


Fig. 1. A view of (I) with our numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

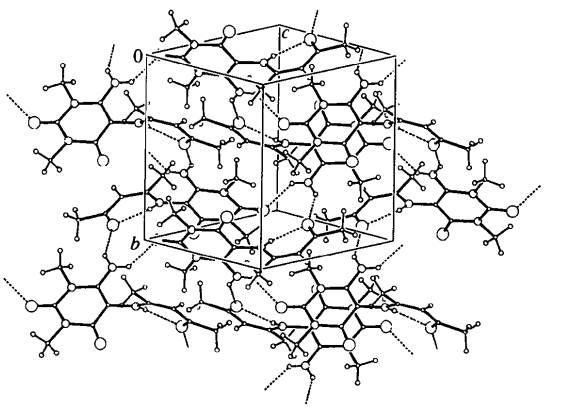


Fig. 2. Packing diagram of the molecule showing the hydrogen bonding.

the structure with *PLATON* (Spek, 1995*a*) showed that there were no solvent-accessible voids in the crystal lattice.

Experimental

A solution of the 5,6-diamino-1,3-dimethyluracil (0.06 mol) and acetylacetone (0.06 mol) in water was refluxed for *ca* 30 min. The solution precipitated a white solid which was washed with ethanol and diethyl ether and air dried (yield: 60%). After a few days a small quantity of pale brown–yellow crystals of the product appeared in the mother liquor. This colour change from powder to crystals is common in 5,6-diaminouracil derivatives.

Crystal data

$C_{11}H_{16}N_4O_3$
$M_r = 252.28$
Monoclinic
$P2_1/n$
$a = 11.916\,(2)$ Å
$b = 9.2894\,(13)$ Å
$c = 12.835\,(2)$ Å
$\beta = 117.607\,(11)°$
$V = 1259.0\,(3)$ Å^3
$Z = 4$
$D_x = 1.331$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.7107$ Å
Cell parameters from 25 reflections
$\theta = 10.15$–$18.10°$
$\mu = 0.099$ mm^{-1}
$T = 294\,(1)$ K
Block
$0.43 \times 0.28 \times 0.22$ mm
Brown–yellow

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
2858 measured reflections
2736 independent reflections
1257 observed reflections $[I > 2\sigma(I)]$

$R_{int} = 0.008$
$\theta_{max} = 27°$
$h = -15 \rightarrow 13$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 16$
3 standard reflections
frequency: 120 min
intensity decay: no decay, variation 1.9%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0477$
$wR(F^2) = 0.1361$
$S = 0.929$
2736 reflections
167 parameters
H atoms riding (*SHELXL* defaults, C—H 0.93 to 0.98, N—H 0.86 Å): see text

$w = 1/[\sigma^2(F_o^2) + (0.0674P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.013$
$\Delta\rho_{max} = 0.149$ e Å^{-3}
$\Delta\rho_{min} = -0.173$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
N1	0.5185 (2)	0.6668 (2)	0.0830 (2)	0.0455 (5)
C1	0.6184 (2)	0.7591 (3)	0.0823 (2)	0.0574 (7)
C2	0.5517 (2)	0.5740 (3)	0.1768 (2)	0.0511 (6)
O2	0.6611 (2)	0.5659 (2)	0.25484 (15)	0.0710 (6)
N3	0.4574 (2)	0.4908 (2)	0.1774 (2)	0.0517 (5)
C3	0.4923 (3)	0.3948 (3)	0.2789 (2)	0.0737 (8)
C4	0.3309 (2)	0.4887 (3)	0.0868 (2)	0.0489 (6)
O4	0.2557 (2)	0.4033 (2)	0.0932 (2)	0.0652 (5)
C5	0.3038 (2)	0.5882 (3)	−0.0052 (2)	0.0459 (6)
N5	0.1811 (2)	0.5870 (2)	−0.1046 (2)	0.0490 (5)
C51	0.0723 (2)	0.6249 (3)	−0.1035 (2)	0.0489 (6)
C52	0.0818 (2)	0.6991 (3)	0.0034 (2)	0.0712 (8)
C53	−0.0444 (2)	0.5954 (3)	−0.1959 (2)	0.0539 (6)
C54	−0.0653 (2)	0.5145 (3)	−0.2951 (2)	0.0510 (6)
C55	−0.2000 (2)	0.4728 (3)	−0.3805 (2)	0.0717 (8)
O5	0.02152 (15)	0.4704 (2)	−0.31572 (15)	0.0622 (5)
C6	0.3957 (2)	0.6767 (2)	−0.0054 (2)	0.0416 (5)
N6	0.3717 (2)	0.7728 (2)	−0.0906 (2)	0.0575 (6)

Table 2. *Selected geometric parameters (Å)*

N1—C1	1.471 (3)	C5—N5	1.427 (3)
N1—C2	1.381 (3)	C5—C6	1.370 (3)
N1—C6	1.378 (3)	N5—C51	1.349 (3)
C2—O2	1.223 (3)	C51—C52	1.493 (3)
C2—N3	1.367 (3)	C51—C53	1.373 (3)
N3—C3	1.471 (3)	C53—C54	1.399 (3)
N3—C4	1.415 (3)	C54—O5	1.250 (2)
C4—O4	1.228 (3)	C54—C55	1.515 (3)
C4—C5	1.414 (3)	C6—N6	1.336 (3)

Table 3. *Hydrogen-bonding geometry (Å, °)*

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5···O5	0.86	2.09	2.713 (3)	129
N6—H6A···O2^i	0.86	2.08	2.805 (3)	142
N6—H6B···O5^{ii}	0.86	2.06	2.803 (3)	144

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

The crystal did not diffract well; only 46% of the data were significant at the $2\sigma(I)$ level. H-atom treatment: methyl groups were allowed to rotate. H atoms attached to N were located in a difference map and the N atoms were planar, consistent with the consequent refinement.

Data collection: *CAD*-4 (Enraf–Nonius, 1992). Cell refinement: *SET*4 and *CELDIM* (Enraf–Nonius, 1992). Data reduction: *DATRD*2 in *NRCVAX*94 (Gabe, Le Page, Charland, Lee & White, 1989). Program(s) used to solve structure: *SOLVER* in *NRCVAX*. Program(s) used to refine structure: *NRCVAX*94 and *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *NRCVAX*94, *PLATON* (Spek, 1995*a*), *PLUTON* (Spek, 1995*b*), *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *NRCVAX*94, *SHELXL*93 and *WordPerfect* macro *PREPCIF*.

GF thanks NSERC (Canada) for Research Grants.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: JZ1155). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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A Cyclic Side-Chain-Linked Biphenyl Ether Tripeptide: H_3N^+-*cyclo*-[$Phe^{(4-O)}$-Phe-$Phe^{(3-O)}$]-OMe.Cl^-

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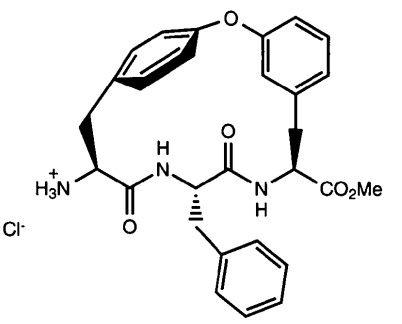
Abstract

The crystal structure of the chloride salt of H_3N^+-*cyclo*-($Phe^{(4-O)}$-Phe-$Phe^{(3-O)}$)-OMe, *cyclo*-phenylalanyl-phenylalanyl-phenylalaninium chloride methyl esther, $C_{28}H_{30}N_3O_3^+.Cl^-$, is described. It is oxidatively linked through a biaryl ether linkage formed from the hydroxyl of 4-hydroxyphenylalanine and the *meta* position of the distal phenylalanine residue. This is the first reported crystal-structure determination of a cyclic 17-membered biphenyl ether tripeptide, a class which includes the natural products K-13 and OF4949 I–IV. An unusual C—H···O hydrogen bond is formed between the methine H atom of the N-terminal Cα and a carbonyl-O atom of a neighboring molecule [C···O = 2.995 (4) Å].

Comment

We are interested in the synthesis and conformation of cyclic biphenyl ether peptides related to natural products K-13 (Yasuzawa, Shirahata & Sano, 1987) and OF4949 I–IV (Sano *et al.*, 1986). During our synthesis of cyclic biphenyl ethers *via* S_NAr macrocyclizations of peptidyl ruthenium π-arene complexes (Janetka & Rich, 1995), we became interested in elucidating their crystal structures. The only other structures available are from NMR (Hobbs & Still, 1989; Yasuzawa, Shirahata & Sano, 1987; Sano *et al.*, 1986). We were unable to crystallize N-protected cyclic biaryl ether tripeptides but were able to crystallize the hydrochloride salt of the free amino cyclic biphenyl ether tripeptide H_3N^+-*cyclo*-[$Phe^{(4-O)}$-Phe-$Phe^{(3-O)}$]-OMe, (I), from ethanol.



(I)

The two rings of the cyclic biaryl ether are in different orientations (Fig. 1). The *para*-substituted ring is rotated out of the plane of the *meta*-substituted ring by 83.3°. As a consequence of this twisting, the *ortho*-H atom [H(C25)] of the *meta*-substituted ring is located near the shielding region of the *para*-substituted ring which is consistent with the upfield shifted resonance in the NMR spectrum for this aromatic proton.

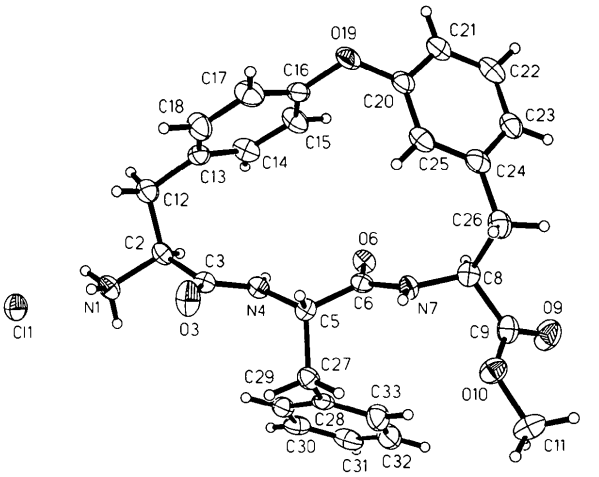


Fig. 1. Plot of the title compound with the atomic numbering scheme. Displacement ellipsoids are plotted at the 50% probability level.

The tripeptide backbone φ and ψ torsion angles (Table 2) are similar to the torsion angles of a β-sheet motif (φ −120°, ψ 120°). Thus, the cyclic 17-membered biphenyl ether tripeptide ring system is a conformational mimic of a β-sheet. As seen in the crystal structures of enzyme-inhibitor complexes, many protease inhibitors bind in an extended β-sheet conformation (Rich, 1990; Swain *et al.*, 1990). This compound can be expected to be a good mimic of protease inhibitors.

Two molecules stack one on top of the other along the *a* axis (Fig. 2) with the peptide of a lower molecule forming one β-sheet hydrogen bond to an upper