Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Galleni, M. & Frère, J. M. (1988). *Biochem. J.* **255**, 119–122.
Kohl, M., Sarlet, G., Renotte, R. & Lejeune, R. (1996). Belg. Patent 09600384.
Kohl, M., Thunus, L. & Lejeune, R. (1997). *Bioconj. Chem.* **8**, 772–779.
Mosher, M. D., Natale, N. R. & Vij, A. (1996). *Acta Cryst.* C**52**, 2513–2515.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1997). *SHELXL97. Program for Crystal Structure Refinement.* University of Göttingen, Germany.
Smith, M. P., Mirzaei, Y. R., Natale, N. R., Scott, B. & Willett, R. D. (1991). *Acta Cryst.* C**47**, 1328–1330.
Stoe & Cie (1987*a*). *DIF*4. *Diffractometer Control Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1987*b*). *REDU*4. *Data Reduction Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1987*c*). *EMPIR. Empirical Absorption Correction Program.* Version 1.2. Stoe & Cie, Darmstadt, Germany.

Acta Cryst. (1998). C**54**, 1959–1961

1-(β-D-Ribofuranosyl)-6-propylcytosine

KARIN BJÅMER BIRNBAUM,[a] DAVID SHUGAR[b] AND KRZYSZTOF FELCZAK[b]

[a]*National Research Council of Canada, Ottawa, ON, Canada K1A 0R6, and* [b]*Institute of Biochemistry and Biophysics, Polish Academy of Sciences, 02-106 Warszawa, Poland. E-mail: karin.birnbaum@nrc.ca*

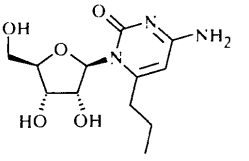
(*Received 11 November 1997; accepted 24 June 1998*)

Abstract

The conformation of the title compound, $C_{12}H_{19}N_3O_5$, in the solid state is *syn*, and the ribose ring is close to the ^4E envelope conformation. The propyl side chain is planar and almost coplanar with the cytosine ring, the deviation between the two being 4.4 (2)°. Hence the overall structure consists essentially of two planes perpendicular [86.2 (2)°] to each other, the plane of the sugar moiety and that of the 6-propylcytosine.

Comment

Most pyrimidine nucleosides exist predominantly in the *anti* conformation about the glycosyl bond, partly due to a stabilizing C6—H···O5′ intramolecular hydrogen bond and partly to repulsive interaction between the C2 carbonyl atom and the furanose ring. However, pyrimidine nucleosides with a bulky C6 substituent are often constrained to the *syn* conformation due to steric hindrance between the sugar ring and the C6 substituent, one early reported example being the naturally occurring orotidine (6-carboxyuridine) (Hruska, 1971). Pyrimidine nucleosides and nucleotides constrained in the *syn* conformation by a C6-substituent are of interest both as (*a*) potential antimetabolites, *e.g.* 6-thiocarboxamide-UMP, a structural analogue of orotidine-5′-phosphate (OMP), is a potent inhibitor of OMP decarboxylase (Cody & Kalman, 1985), and (*b*) model compounds to determine whether the parent non-substituted nucleoside (or nucleotide) is involved in a given enzymatic reaction in the *syn* and/or *anti* conformation, *e.g.* several 6-substituted uridines are reasonable substrates for uridine phosphorylase (Krajewska & Shugar, 1982; Felczak *et al.*, 1996), pointing to involvement of the *syn* conformation of uridine as an intermediate in the reaction. This led to determination of the structures of a variety of 6-substituted uracil nucleoside analogues (Felczak *et al.*, 1996, and references cited), and the solid-state structure of one cytosine nucleoside analogue, 1-(β-D-arabinofuranosyl)-6-methylcytosine (Yamaguchi *et al.*, 1992). We here describe the crystal structure of another such compound, 6-propylcytidine, (I).



(I)

An *ORTEP* (Johnson, 1976) representation of the molecule with atomic labelling scheme is shown in Fig. 1. The conformation about the glycosyl bond is *syn* [C2—N1—C1′—O4′, χ = 73.9 (4)°], which is the one frequently favoured when there is a bulky C6 substituent, despite the resulting repulsion between the C2 carbonyl and the sugar moiety. The closest intramolecular contacts of O2, apart from O2···C1′ [2.695 (3) Å], are O2···C2′ and O2···H2′ [2.777 (3) Å and 2.39 Å] and somewhat longer to C3′, H3′ and O4′ [3.050 (3), 2.50 and 3.002 (3) Å, respectively].

The furanose ring is in the unusual C4′-*endo* envelope conformation with C4′ displaced to the same side as C5′ from the plane through the other four atoms by −0.577 (6) Å. However, with the O4′—C1′—C2′—C3′ torsion angle being −3.5 (2)° rather than zero, there is also a slight puckering at C3′, making the conformation strictly speaking $_4T^3$. The puckering of the ring, calculated from the torsion angles (Altona & Sundaralingam, 1972), is P = 50.7°. A trend towards the C3′-*endo* is observed for pyrimidines locked in the *syn* conformation (Saenger, 1984). In C6-substituted uridines in the *syn* conformation, C4′-*exo* and C2′-*endo* have also been observed (Cody & Kalman, 1985). The orientation around the exocyclic C4′—C5′ bond is *ap* (*gauche*, *trans*) with C3′—C4′—C5′—O5′ (γ) = −173.7 (6)° and there is no C5′ hydroxyl intramolecular hydrogen bond.

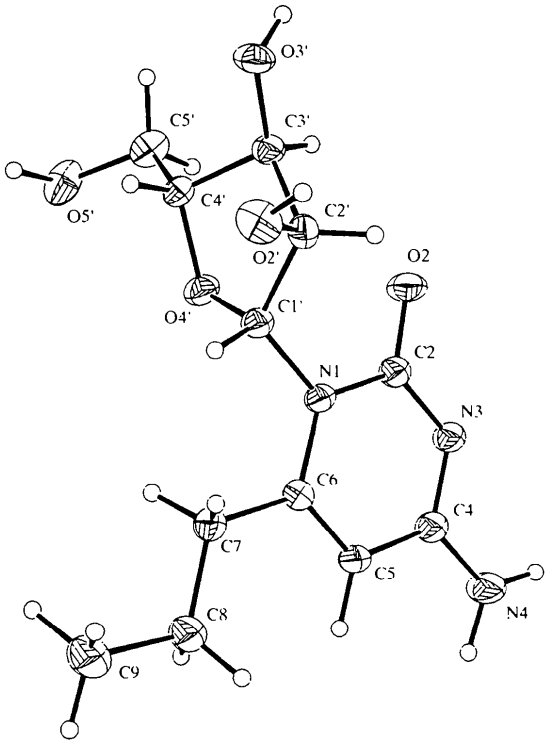


Fig. 1. *ORTEP*II (Johnson, 1976) drawing showing 30% probability displacement ellipsoids and the numbering scheme. H atoms are shown as circles of an arbitrary radius.

The cytosine ring is essentially flat, with only slight deviations of the endocyclic atoms N1 and C2 [−0.021 (4) Å and 0.030 (5) Å] from the ring plane. All of the exocyclic atoms, *viz.* N4, O2, C1′ and C7, are displaced from this plane to some extent, but the largest deviation is only 0.076 (5) Å (for O2). The propyl side chain is planar and almost coplanar with that of cytosine, the angle between the two planes being only 4.4 (2)°. This is in contrast to uridine-6-thiocarboxamide (Cody & Kalman, 1985) where the thiocarboxamide moiety is almost perpendicular to the pyrimidine ring. The C7—C8 bond length [1.512 (4) Å] is significantly shorter than a paraffinic single bond [1.537 (5) Å] (Saenger, 1984) and is equal to that of the C6—C7 bond [1.513 (3) Å].

All of the H atoms of the –OH and $-NH_2$ groups are involved in hydrogen bonds (Table 2) with $D\cdots A$ distances ranging from 2.674 (2) to 3.259 (3) Å, the latter being rather weak. The cytosine rings form base-pairs, linked by N4—H41···N3^{iv} hydrogen bonds. These base pairs are stacked head to tail, with the base planes parallel to the *xz* plane, and the propyl side chain packed between two cytosines separated by the length of the *b* axis. The distances between atoms in the side chain and those of the cytosines are approximately 4 Å, the shortest one being C2···C8^{v} [3.828 (6) Å]. This hydrophobic region alternates with ribose regions, and the O3′—HO3′···O2^{ii} and N4—H42···O5′^{v} hydrogen bonds form cross-links between them. In the sugar regions, the ribose rings are linked *via* O2′—HO2′···O5′^{i} and O5′—HO5′···O3′^{iii} hydrogen bonds.

Experimental

The title compound was synthesized by debenzoylation of the previously reported tribenzoylated 1-(β-D-ribofuranosyl)-4-methylthio-6-propyluracil (Felczak *et al.*, 1996), followed by amination with aqueous ammonia at 363 K. The product, m.p. 474–476 K, was characterized by elemental analysis: calculated for $C_{12}H_{19}N_3O_5$ (C, H, N): C 50.53, H 6.71, N 14.73%; found: C 50.42, H 6.78, N 14.70%. This was further confirmed by mass spectroscopy (LSIMS), *m/z* $(M + H)^+$ for $C_{12}H_{20}N_3O_5$: calculated 286.140289, found 286.140273. Crystals suitable for diffraction were obtained by slow cooling (6 h) to room temperature of an aqueous solution saturated at 373 K.

Crystal data

$C_{12}H_{19}N_3O_5$
M_r = 285.30
Monoclinic
*C*2
a = 16.734 (5) Å
b = 7.830 (4) Å
c = 12.028 (5) Å
β = 119.12 (3)°
V = 1376.8 (10) Å^3
Z = 4
D_x = 1.376 Mg m^{-3}
D_m not measured

Mo *Kα* radiation
λ = 0.71073 Å
Cell parameters from 24 reflections
θ = 20.00–25.00°
μ = 0.11 mm^{-1}
T = 293 K
Platelet
0.38 × 0.30 × 0.22 mm
Colourless

Data collection

Nonius CAD-4 diffractometer
θ/2θ scan
Absorption correction: none
1502 measured reflections
1469 independent reflections
1315 reflections with $I_{net} > 2.5\sigma(I_{net})$

R_{int} = 0.003
θ_{max} = 24.91°
h = −19 → 17
k = 0 → 8
l = 0 → 13
3 standard reflections
every 100 reflections
intensity decay: none

Refinement

Refinement on *F*
R = 0.029
wR = 0.036
S = 1.69
1469 reflections
181 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F) + 0.0002F^2]$
$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max}$ = 0.13 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}
Extinction correction: Larson (1970)
Extinction coefficient: 2.6 (4) × 10^3
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 1. *Selected geometric parameters (Å, °)*

N1—C2	1.408 (3)	C4—C5	1.425 (3)
N1—C6	1.388 (3)	C4—N4	1.323 (3)
N1—C1′	1.460 (3)	C5—C6	1.340 (3)
C2—N3	1.345 (3)	C1′—O4′	1.418 (5)

C2—O2	1.237 (3)	C4′—O4′	1.431 (3)
N3—C4	1.331 (3)		
C6—C7—C8	115.6 (2)	C1′—C2′—C3′	103.1 (3)
N1—C1′—C2′	118.6 (3)	C2′—C3′—C4′	102.3 (2)
N1—C1′—O4′	108.6 (3)	C3′—C4′—O4′	103.4 (2)
C2′—C1′—O4′	107.8 (2)	C1′—O4′—C4′	106.9 (3)
C2—N1—C1′—O4′	73.9 (4)	C1′—C2′—C3′—C4′	25.7 (3)
O4′—C1′—C2′—C3′	−3.5 (2)	C2′—C3′—C4′—O4′	−39.6 (3)
C2′—C1′—O4′—C4′	−22.0 (3)	C3′—C4′—O4′—C1′	38.7 (3)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2′—HO2′···O5′^{i}	0.95	1.78	2.707 (5)	162
O3′—HO3′···O2^{ii}	1.00	1.75	2.674 (2)	152
O5′—HO5′···O3′^{iii}	0.96	1.81	2.737 (3)	160
N4—H41···N3^{iv}	0.95	2.03	2.974 (3)	174
N4—H42···O5′^{v}	0.95	2.32	3.259 (3)	172

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

The structure was solved in the space-group *I*1 on the *NRCVAX* system (Gabe *et al.*, 1989) with the symbolic addition method. After a twofold axis was found, the space group was transformed to *C*2 and refined with full-matrix least-squares methods. A riding model was employed for the H atoms, those of the hydroxyl groups from a difference Fourier map and the remainder in calculated positions.

Data collection: *NRCCAD* (Le Page *et al.*, 1986). Cell refinement: *NRCCAD*. Data reduction: *NRCVAX*: *DATRD*2. Program(s) used to solve structure: *NRCVAX*: *SOLVER*. Program(s) used to refine structure: *NRCVAX*: *LSTSQ*. Software used to prepare material for publication: *NRCVAX*: *TABLES* (January 1994 version).

We wish to express our thanks to Dr Eric Gabe and Dr Gary Enright for help with the data collection and the use of the *NRCVAX* computer programs.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1416). Services for accessing these data are described at the back of the journal.

References

Altona, C. & Sundaralingam, M. (1972). *J. Am. Chem. Soc.* **94**, 8205–8212.
Cody, V. & Kalman, T. I. (1985). *Nucleosides Nucleotides*, **4**(5), 587–594.
Felczak, K., Drabikowska, A. K., Vilpo, J. A., Kulikowski, T. & Shugar, D. (1996). *J. Med. Chem.* **39**, 1720–1728.
Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.
Hruska, F. E. (1971). *J. Am. Chem. Soc.* **93**, 1795–1797.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Krajewska, E. & Shugar, D. (1982). *Biochem. Pharmacol.* **31**, 1097–1102.
Larson, A. C. (1970). *Crystallographic Computing*, edited by F. R. Ahmed, S. R. Hall & C. P. Huber, pp. 291–294. Copenhagen: Munksgaard.
Le Page, Y., White, P. S. & Gabe, E. J. (1986). Am. Crystallogr. Assoc. Annu. Meet., June 1986, Abstract PA 23.
Saenger, W. (1984). *Principles of Nucleic Acid Structure*. New York: Springer-Verlag.
Yamaguchi, K., Matsumura, G., Shimizu, M., Tanaka, H. & Miyasaka, T. (1992). *Acta Cryst.* C**48**, 384–385.

Acta Cryst. (1998). C**54**, 1961–1963

1-*tert*-Butyl-9-methoxy-4-methyl-1,2,3,4-tetrahydro-2-azafluoren-3-one, a Novel Fluorenone

SANTIAGO GARCÍA-GRANDA,[a] RAFAEL SANTIAGO-GARCÍA,[a] S. BAMIDELE SANNI,[b] ANGEL SUÁREZ-SOBRINO[c] AND JAVIER SANTAMARÍA[c]

[a]*Departamento de Química Física y Analítica, Facultad de Química, Universidad de Oviedo, Avda. Julián Clavería 8, 33071 Oviedo, Spain,* [b]*Department of Chemistry, University of Benin, Benin City, Nigeria, and* [c]*Instituto Universitario de Química Organometálica Enrique Moles, Unidad Asociada al CSIC, Universidad de Oviedo, Avda. Julián Clavería 8, 33071 Oviedo, Spain. E-mail: sgg@sauron.quimica.uniovi.es*

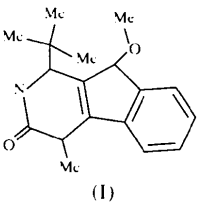
(*Received 26 January 1998; accepted 11 June 1998*)

Abstract

The title compound, $C_{18}H_{23}NO_2$, is the final compound in the reaction between an ethynyl Fischer carbene and a 2-azadiene. The reaction proceeds to the stereoselective formation of a 2-azafluorenone. The structure determination reveals hydrogen bonding linking the carbonyl O atom and the H atom attached to the N atoms of symmetry-related molecules. As a result, the structure packing is composed of dimers connected by two hydrogen bonds. These hydrogen bonds show a similar geometry to those found between pairs of bases in DNA, and the structure itself resembles some synthetic inhibitors of DNA transcription.

Comment

Stabilized Fischer carbene complexes of group 6 metals have been recognized for their important role in the formation of a great variety of carbocyclic rings (Barluenga, Tomás, Ballesteros *et al.*, 1997), and as useful tools in the synthesis of natural products (Santiago-García *et al.*, 1997). In this particular synthesis, a tungsten–(phenylethynyl)carbene complex was used as a dienophile in a Diels–Alder reaction against a 2-azadiene, resulting in the stereoselective formation of a 2-azafluorenone, (I). Knowledge of the structure of this adduct is vital for determining the stereochemical assignment of the other adducts in the referenced work.



(I)