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3′-Isocyano-2′,3′-dideoxyuridine (NCddUrd): a Nucleoside Analogue

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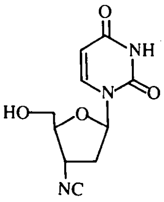
Abstract

The glycosidic torsion angle, χ, of the title compound, $C_{10}H_{11}N_3O_4$, has a value of $-150.5\,(3)^\circ$ in the *anti* range. The sugar pucker is ${}^2T_3$ and the C4′—C5′ conformation is +*sc* with $\gamma = 44.6\,(5)^\circ$. The isocyanide moiety is linear and the pyrimidine ring is planar. The molecular packing is stabilized by a network of hydrogen bonds and van der Waals interactions.

Comment

2′,3′-Dideoxypyrimidine nucleosides are among the most potent and selective *anti*-HIV compounds (Yarchoan & Broder, 1989). NCddUrd, (I), is a nucleoside analogue related to 3′-azido-3′-deoxythymidine (AZT) which has potent activity against HIV-1 in culture. The crystal structure of the title compound has been determined as part of studies aimed at elucidating correlations between the molecular conformations of *anti*-HIV nucleosides.



(I)

The bond distances and angles of the uracil base agree well with the average values quoted by Taylor & Kennard (1982). The C4′—O4′ bond distance is, as expected, longer than the C1′—O4′ bond due to the anomeric effect (Bugg, Thomas, Sundaralingam & Rao, 1971). The C6′—N6′ bond length is 1.135 (6) Å and the C3′—N6′—C6′ bond angle is 178.2 (4)°, which indicate the triple-bond character of the N6′≡C6′ bond and the linear conformation of isocyanide group. The same conformation of the isocyanide group is observed in 3′-isocyanothymidine (Das, Mazumdar & Schwalbe, 1995) and diisocyanoadociane (Baker, Wells, Oberhansly & Hawes, 1976). The geometry of the isocyanide group indicates that the dipolar form —$^+$N≡C$^-$, contributes substantially more to the electronic structure than —N≡C does.

As illustrated in Fig. 1, the orientation of the uracil base relative to the sugar ring is *anti* with a glycosyl torsion angle χ of $-150.5\,(3)^\circ$. The sugar puckering is C2′-*endo*/C3′-*exo* (${}^2T_3$) with $P = 173.2^\circ$ and $\varphi = 33.1^\circ$. The conformation about the C4′—C5′ bond is +*sc* with $\gamma = 44.6\,(5)^\circ$. The +*sc* conformer with an *anti*-oriented base is commonly stabilized by the C6—H···O5′ non-classical hydrogen bond. Similar sugar puckering is observed in other 3-substituted pyrimidine nucleosides, such as 3′AzddEtUrd (van Roey, Salerno, Chu & Schinazi, 1989), 3′AzddClCyd (Das, Mazumdar, Bertolasi & van Aerschot, 1993*a*) and 3′FddClCyd (Das, Mazumdar, Bertolasi & van Aerschot, 1993*b*). The conformation of the title compound is very similar to that of one of the two conformers of AZT (Dyer, Low, Tollin, Wilson & Howie, 1988). The sugar puckering is different from that in the *anti*-AIDS nucleosides such as AZT, where the O4′-*exo*/C3′-*endo* conformation is predominant. It is assumed that this conformation is more favourable for the phosphorylation process than the usual conformation of the native nucleosides (van Roey, Salerno, Chu & Schinazi, 1989).

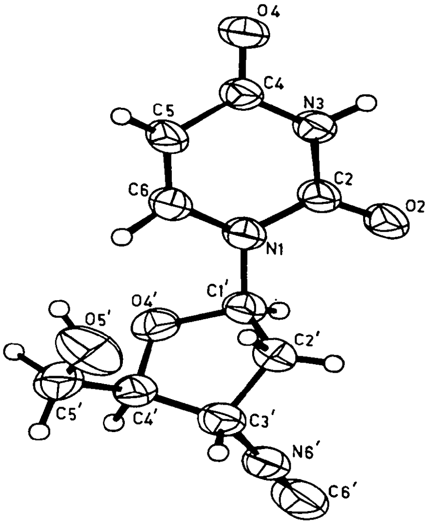


Fig. 1. *ORTEP* (Johnson, 1965) view of the title molecule. Ellipsoids for the non-H atoms are drawn at the 50% probability level.

The molecules in the crystals are linked by hydrogen bonds: N3···O4($-x-1$, $y-\frac{1}{2}$, $-z+2$) [2.845 (5) Å, 173 (3)°] and O5′···O2(x, $y+1$, z) [2.880 (5) Å, 169 (7)°]. The molecular packing (Fig. 2) is also stabilized by segregation of hydrophobic and hydrophilic zones. The hydrophobic zones are formed by bases; each base is linked to its screw-related neighbour by a hydrogen bond between the 4-keto group and N3 of the neighbour.

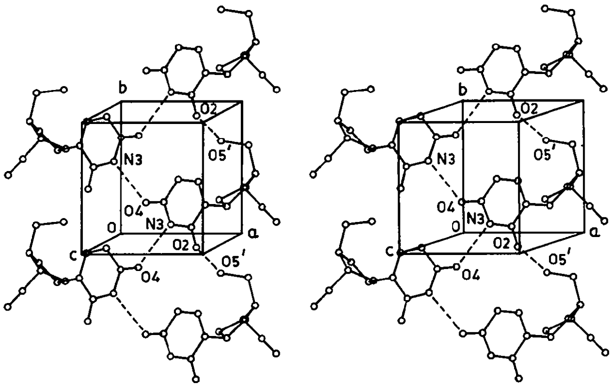


Fig. 2. Stereoview of the molecular packing in the unit cell. Hydrogen bonds are shown as dashed lines.

Experimental

Details of the synthesis of the title compound have been published elsewhere (Hiebl, Zbiral, Balzarini & Declercq, 1990). Crystals suitable for X-ray analysis were grown by slow evaporation of chloroform/methanol solution of the compound.

Crystal data

$C_{10}H_{11}N_3O_4$
$M_r = 237.22$
Monoclinic
$P2_1$
$a = 6.169\ (2)$ Å
$b = 6.894\ (2)$ Å
$c = 12.797\ (2)$ Å
$\beta = 101.98\ (3)°$
$V = 532.4\ (3)$ Å^3
$Z = 2$
$D_x = 1.480$ Mg m^{-3}

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 28 reflections
$\theta = 12–39.5°$
$\mu = 0.946$ mm^{-1}
$T = 293$ K
Prismatic
0.54 × 0.33 × 0.21 mm
Transparent, colourless

Data collection

Siemens AED diffractometer
$\omega/2\theta$ scans
Absorption correction: none
1155 measured reflections
1109 independent reflections
1045 observed reflections $[F > 4\sigma(F)]$

$R_{\rm int} = 0.011$
$\theta_{\rm max} = 70°$
$h = -7 \rightarrow 7$
$k = 0 \rightarrow 8$
$l = 0 \rightarrow 15$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F
$R = 0.037$
$wR = 0.040$
$S = 1.161$
1045 reflections
197 parameters
All H-atom parameters refined

$w = 1/[\sigma^2(F) + 0.001|F|^2]$
$(\Delta/\sigma)_{\rm max} = 0.08$
$\Delta\rho_{\rm max} = 0.227$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.198$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *SHELX*76 (Sheldrick, 1976)

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

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

	x	y	z	$U_{\rm eq}$
N1	−0.0367 (4)	0.3480	0.8295 (2)	0.045 (1)
C2	−0.1425 (5)	0.1846 (5)	0.8547 (2)	0.045 (1)
N3	−0.2879 (4)	0.2161 (5)	0.9216 (2)	0.045 (1)
C4	−0.3344 (5)	0.3917 (5)	0.9637 (2)	0.044 (1)
C5	−0.2248 (5)	0.5565 (6)	0.9296 (3)	0.049 (1)
C6	−0.0819 (5)	0.5300 (5)	0.8651 (2)	0.048 (1)
O2	−0.1106 (4)	0.0230 (5)	0.8217 (2)	0.061 (1)
O4	−0.4607 (4)	0.3970 (5)	1.0272 (2)	0.056 (1)
C1′	0.1237 (5)	0.3262 (6)	0.7587 (2)	0.047 (1)
C2′	0.0202 (6)	0.3549 (7)	0.6412 (3)	0.056 (1)
C3′	0.2094 (5)	0.4423 (6)	0.5982 (3)	0.051 (1)
C4′	0.3338 (5)	0.5608 (6)	0.6912 (2)	0.049 (1)
O4′	0.2853 (3)	0.4723 (5)	0.7858 (2)	0.050 (1)
N6′	0.3531 (5)	0.2907 (6)	0.5726 (2)	0.061 (1)
C6′	0.4662 (8)	0.1749 (7)	0.5504 (4)	0.089 (2)
C5′	0.2766 (9)	0.7744 (6)	0.6883 (4)	0.076 (2)
O5′	0.0418 (7)	0.8026 (6)	0.6598 (3)	0.095 (1)

Table 2. *Selected geometric parameters* (Å, °)

N1—C1′	1.482 (4)	C3′—N6′	1.451 (5)
C2—O2	1.222 (5)	C4′—O4′	1.441 (4)
C4—O4	1.238 (4)	N6′—C6′	1.135 (6)
C1′—O4′	1.409 (5)	C5′—O5′	1.432 (7)
C2′—C3′—N6′	110.4 (3)	C3′—N6′—C6′	178.2 (4)
C1′—O4′—C4′	110.8 (2)		
C2—N1—C1′—O4′	−150.5 (3)	C3′—C4′—C5′—O5′	44.6 (5)
O4′—C4′—C5′—O5′	−75.0 (4)	C1′—C2′—C3′—N6′	84.0 (4)

The space groups $P2_1$ or $P2_1/m$ were determined from systematic absences ($0k0$, k = odd); the former was chosen on the basis of statistical analysis of the intensity distribution and the chirality of the molecule, and confirmed by successful refinement. Lorentz–polarization corrections were applied. The crystal structure was solved by the direct-methods program *SHELX*86 (Sheldrick, 1985) and refined by the full-matrix least-squares method using *SHELX*76 (Sheldrick, 1976). All H atoms were located from difference Fourier maps and refined isotropically. There were no significant features in the final difference Fourier map. All geometrical calculations were performed using *PARST* (Nardelli, 1983) and ellipsoids were drawn with *ORTEP* (Johnson, 1965). The handedness was chosen according to the known chirality.

We wish to thank Drs J. Heibl and E. Zbiral for provision of the sample.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: VJ1016). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Benzo-1,3,2-dithiazolium Iodide

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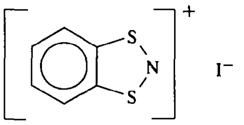
Abstract

The molecular structure of the iodide salt of the benzo-1,3,2-dithiazole cation, $C_6H_4NS_2^+.I^-$, has been determined. The cation was found to be planar to within 0.04 Å. The C_2S_2N ring is slightly asymmetrical, with S—N bonds of 1.584 (5) and 1.617 (6) Å. There is also significant localization of bonds within the benzene moiety. The ions are found to stack approximately parallel to the x axis. Alternating stacks are related by a 2_1 screw axis.

Comment

This study builds on our interest in the structures and transport properties of the charge-transfer salts of neutral heterocyclic thiazyl radicals (Bryan, Cordes, Haddon, Hicks, Kennepohl *et al.*, 1994; Bryan, Cordes, Haddon, Hicks, Oakley *et al.*, 1994; Bryan *et al.*, 1993). The title compound, (I), was prepared by oxidation of the neutral benzo-1,3,2-dithiazolyl radical (Awere *et al.*, 1990) with iodine in acetonitrile. Crystals of the salt suitable for X-ray study were grown by slow evaporation of the solvent.



(I)

The structure of the benzo-1,3,2-dithiazolium cation is shown in Fig. 1. The mean values for the chemically equivalent molecular parameters are similar to those found in the related chloride salt (Awere *et al.*, 1990), but the structure is less symmetrical. The two S—N distances are 1.584 (5) and 1.617 (6) Å. The C—C bond distances indicate significant localization of the bonding within the ring, as observed in the chloride salt. The closest I···S contact, 3.275 (1) Å, is between I and $S(1)(x-\frac{1}{2}, \frac{3}{2}-y, 1-z)$. The internal bond lengths of the heterocyclic ring, which are shorter than those found in the radical dimer (Awere *et al.*, 1990), coupled with the observation of discrete well separated iodide ions $[I\cdots I(\frac{1}{2}+x, \frac{3}{2}-y, 2-z)$ 4.959 (2) Å], indicates a fully oxidized cation. This is in contrast to the structure of 4-phenyl-1,2,3,5-dithiadiazolium iodide, $PhCN_2S_2I$, which exists in the solid state as an intermediate oxidation state system $[PhCN_2S_2]_3[I_3]$ (Bryan *et al.*, 1993).

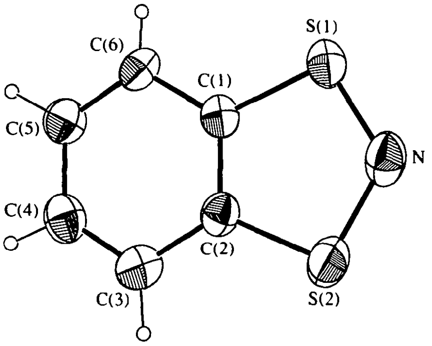


Fig. 1. *ORTEP*II plot (Johnson, 1976) of the title cation. Displacement ellipsoids are drawn at the 50% probability level.

In contrast to the chloride salt, the crystal structure of the iodide salt consists of slipped stacks of $H_4C_6S_2N$ rings and chains of iodide ions running parallel to the x axis (Fig. 2). Alternating stacks are related by a 2_1 screw axis. The perpendicular mean plane to mean plane separation of the herringbone-like arrays along the molecular stacks is 3.43 (2) Å.