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3′,5′-Bis(*tert*-butyldimethylsilyl)-5-iodo-2′-deoxycytidine

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Key indicators

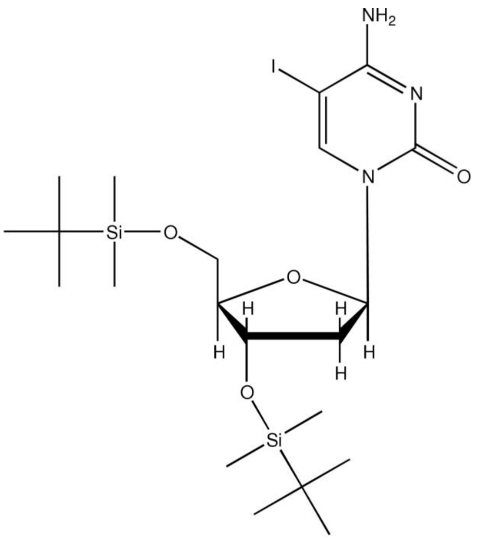
Single-crystal X-ray study
T = 163 K
Mean σ(C–C) = 0.005 Å
Disorder in main residue
R factor = 0.034
wR factor = 0.072
Data-to-parameter ratio = 30.9

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

The title compound, $C_{21}H_{40}IN_3O_4Si_2$, crystallizes with two independent molecules in the asymmetric unit. They are linked by N—H···N hydrogen bonds to form dimers. In each molecule, there is an intramolecular N—H···I hydrogen bond. In the crystal structure, the dimers are connected by an N—H···O hydrogen bond to form helical chains extending along the *b* direction.

Comment

5-Iodo-2′-deoxycytidine is an important building block in medicinal chemistry. It offers the possibility of introducing different substituents at the iodine position *via* transition metal-catalysed cross-coupling reactions. The introduction of nonpolar *tert*-butyldimethylsilyl protecting groups results in improved solubility for the reaction conditions and easy purification of the compounds afterwards (Ogilvie, 1973). Here, we report the crystal structure of the title compound, (I).



(I)

Compound (I) crystallizes with two independent molecules (*A* and *B*) in the asymmetric unit (Fig. 1). The two molecules have very different conformations. The five-membered ring of molecule *A* has a conformation intermediate between a C2′-*endo*,C3′-*exo* twist and a C2′-*endo* envelope. Molecule *B* has an approximate C3′-*exo* envelope conformation. A C3′-*exo*,C4′-*endo* twist conformation has been reported previously for the related compound 5-iodo-2′-deoxycytidine (Ghiassy *et al.*, 1981). The orientations of the silyl side chains are different in the two independent molecules. The orientations about the

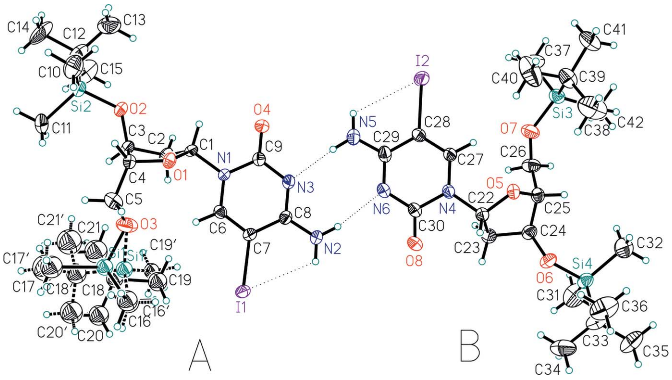


Figure 1

The asymmetric unit of compound (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen bonds are represented by dotted lines. Atoms connected by broken bonds correspond to the disordered *tert*-butyldimethylsilyl group with occupancy factor 0.337.

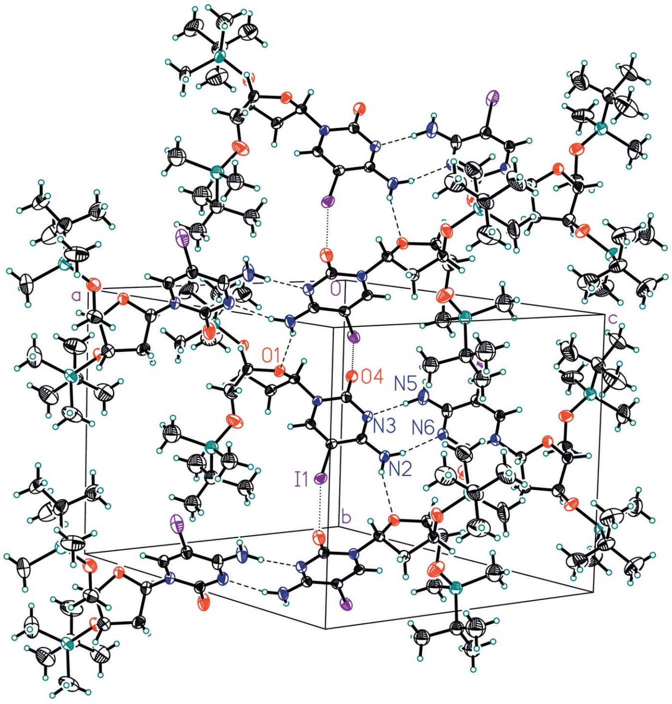


Figure 2

The crystal packing of compound (I); the view direction is near [101]. Disordered atoms with occupancy of 0.337 have been omitted for clarity. Hydrogen bonds are represented by dashed lines and I$\cdots$O contacts as dotted lines.

C4′—C5′ bond are *gauche–gauche* for molecule *A* and *gauche–trans* for molecule *B*. The base has an *anti* orientation about the glycosyl bond, with O4′—C1′—N1—C2 torsion angles of −131.0 (2) and −168.4 (2)° for molecules *A* and *B*, respectively. The cytosine rings are essentially planar. The largest torsion angle in the six-membered ring is −2.4 (4)° for molecule *A* and 0.9 (4)° for molecule *B*. The I atom deviates by 0.099 (4) Å from the plane of the six-membered ring for molecule *A* and by 0.066 (4) Å for molecule *B*.

The crystal packing of compound (I) is shown in Fig. 2 and details of the hydrogen bonding are given in Table 1. The molecules from dimers *via* two intermolecular N—H$\cdots$N hydrogen bonds. The second H atom of each NH_2 group is involved in an intramolecular N—H$\cdots$I hydrogen bond. The N2—H2*D* bond is also involved in a rather weak intermolecular N—H$\cdots$O hydrogen bond, which connects the dimers to form helical chains extending along the *b* direction.

The crystal packing also shows two weak intermolecular C(furanosyl)—H$\cdots$O(keto) and two weak intermolecular C(methyl)—H$\cdots\pi$(cytosine) interactions. Atom I1 shows a contact distance of 3.289 (2) Å with keto atom O4 of a symmetry-related molecule (Fig. 2). This distance is about 0.2 Å shorter than the sum of the van der Waals radii of I and O (Bondi, 1964). It could be a forced contact. However, even shorter intermolecular I$\cdots$O(keto) contacts (3.062 and 3.163 Å) occur in the crystal structure of 5-iodocytosine (Okabe *et al.*, 1995), where they play an important role in the crystal packing. A very short intermolecular I$\cdots$O(keto) distance of 2.96 Å has been reported in the crystal structure of 5-iodo-2′-deoxyuridine (Camerman & Trotter, 1965).

Experimental

2′-Deoxycytidine hydrochloride (6 g, 22.8 mmol) was dissolved in dimethylformamide (45 ml). *tert*-Butyldimethylsilyl chloride (100 ml as a 1 *M* tetrahydrofuran solution) and imidazole (13.63 g, 200 mmol) were added at room temperature under an Ar atmosphere and the mixture was stirred overnight. Methanol was added, then all solvents were removed. The resulting 3′,5′-di(*tert*-butyldimethylsilyl)-2′-deoxycytidine was dissolved in CH_2Cl_2 and extracted with saturated aqueous $NaHCO_3$ and NaCl solutions and H_2O, then dried over Na_2SO_4, filtered and dried overnight *in vacuo* (Ogilvie, 1973). The resulting product (7.58 g, 17 mmol) was dissolved in acetic acid (43.5 ml, 760 mmol) and CCl_4 (43.5 ml). It was iodinated at 313 K by adding iodine (2.59 g, 10.2 mmol) and iodic acid (2.69 g, 15.3 mmol). The solution was stirred overnight and then all solvents were removed. The yellow–reddish solid obtained was dissolved in CH_2Cl_2, and any remaining iodic acid was filtered off. The filtrate was washed with a saturated aqueous sodium thiosulfate solution, then extracted with saturated aqueous $NaHCO_3$ and NaCl solutions and H_2O. The organic layer was dried over $MgSO_4$ (Chang & Welch, 1961; Bobek *et al.*, 1987) to give compound (I) (yield: 70%, 6.93 g, 11.9 mmol). Single crystals of (I) were obtained by recrystallization from ethyl acetate.

Crystal data

$C_{21}H_{40}IN_3O_4Si_2$
$M_r = 581.64$
Monoclinic, $P2_1$
$a = 13.9645\ (11)$ Å
$b = 12.1448\ (13)$ Å
$c = 16.906\ (3)$ Å
$\beta = 97.134\ (9)^\circ$
$V = 2845.0\ (6)$ Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 1.24$ mm^{-1}
$T = 163\ (2)$ K
0.56 × 0.44 × 0.10 mm

Data collection

Siemens SMART 1K CCD area-detector diffractometer
Absorption correction: numerical (*SHELXTL*; Sheldrick, 1996)
$T_{\min} = 0.519$, $T_{\max} = 0.882$
49199 measured reflections
17038 independent reflections
14411 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.036$

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Refinement

$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.072$
$S = 1.03$
17038 reflections
552 parameters
3 restraints
H-atom parameters constrained
$\Delta\rho_{\max} = 1.23$ e Å^{-3}
$\Delta\rho_{\min} = -1.13$ e Å^{-3}
Absolute structure: Flack (1983), with 7779 Friedel pairs
Flack parameter: −0.019 (8)

Table 1
Hydrogen-bond geometry (Å, °).

CgA and *CgB* are the centroids of the cytosine rings of molecules *A* and *B*, respectively.

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2C···N6	0.88	2.15	3.017 (3)	168
N2—H2D···I1	0.88	2.85	3.328 (2)	115
N2—H2D···O1$^{\rm i}$	0.88	2.39	3.211 (3)	155
N5—H5C···N3	0.88	2.07	2.930 (4)	166
N5—H5D···I2	0.88	2.83	3.305 (3)	115
C1—H1A···O4	1.00	2.34	2.763 (3)	104
C4—H4A···O8$^{\rm ii}$	1.00	2.40	3.138 (3)	130
C6—H6A···O3	0.95	2.50	3.392 (4)	156
C20—H20C···$CgB^{\rm i}$	0.98	2.76	3.386	131
C24—H24A···O4$^{\rm iii}$	1.00	2.57	3.515 (3)	158
C27—H27A···O5	0.95	2.35	2.693 (3)	100
C27—H27A···O7	0.95	2.37	3.245 (3)	154
C41—H41B···$CgA^{\rm iv}$	0.98	2.87	3.757	150

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

The *tert*-butyldimethylsilyl group attached to O3 was found to be disordered over two orientations. Atoms of this group were refined with isotropic split atoms. The occupancy factor refined to 0.663 (3) for atoms Si1 and C16–C21 and to 0.337 (3) for atoms Si1′ and C16′–C21′. Atoms C16 and C16′ are too close to be resolved and were constrained: the same isotropic displacement parameter was used for both atoms and the Si1—C16 and Si1′—C16′ distances were restrained to be 1.86 (1) Å. The H atoms were positioned geometrically and treated as riding atoms, with N—H = 0.88 Å with $U_{\rm iso}$(H) = 1.2$U_{\rm eq}$(N), and C—H = 0.95–1.00 Å with $U_{\rm iso}$(H) = 1.2 or 1.5$U_{\rm eq}$(C). The maximum and minimum electron-density peaks in the final difference map are both located about 0.7 Å from atom I2.

Data collection: *SMART* (Siemens, 1995); cell refinement: *SMART*; data reduction: *SAINT* (Siemens, 1995); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Sheldrick, 1996); software used to prepare material for publication: *SHELXL97*.

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