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The N^1-(2′-deoxyribofuranoside) of 3-iodo-5-nitroindole: a universal nucleoside forming nitro–iodo interactions

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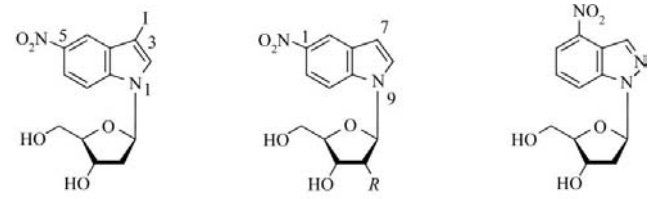
The title compound [systematic name: 1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3-iodo-5-nitro-1*H*-indole], $C_{13}H_{13}IN_2O_5$, exhibits an *anti* glycosylic bond conformation with a χ torsion angle of −114.9 (3)°. The furanose moiety shows a twisted C2′-*endo* sugar pucker (*S*-type), with P = 141.3° and τ_m = 40.3°. The orientation of the exocyclic C4′—C5′ bond is +*ap* (*gauche*, *trans*), with a γ torsion angle of 177.4 (2)°. The extended crystal structure is stabilized by hydrogen bonding and I···O contacts, as well as by stacking interactions. The O atoms of the nitro group act as acceptors, forming bifurcated hydrogen bonds within the *ac* plane. Additionally, the iodo substituent forms an interplanar contact with an O atom of the nitro group, and another contact with the O atom of the 5′-hydroxy group of the sugar moiety within the *ac* plane is observed. These contacts can be considered as the structure-determining factors for the molecular packing in the crystal structure.

Comment

Universal nucleosides pair equally well with the canonical nucleic acid constituents. They are utilized to overcome sequence ambiguities in primer and probe design (Loakes, 2001). The most commonly used universal nucleoside is 2′-deoxyinosine, which forms base pairs with the four common DNA constituents (Topal & Fresco, 1976). The base pairing properties of the closely related 7-deaza-2′-deoxyinosine are similar to those of 2′-deoxyinosine (purine numbering) (Seela & Mittelbach, 1999). Another universal nucleoside strategy makes use of base stacking as the dominant stabilizing effect of duplex DNA. In this context, a series of hydrophobic compounds were synthesized and incorporated into DNA, *e.g.* 5-nitroindole 2′-deoxyribonucleoside, the regioisomeric 4-nitroindazole N^1- and N^2-(2′-deoxyribonucleosides), as well as 3-nitropyrrole and 4-nitrobenzimidazole 2′-deoxyribonucleosides (Loakes & Brown, 1994; Loakes *et al.*, 1995; Seela & Jawalekar, 2002). The introduction of substituents such as halogens or alkyl, alkenyl and alkynyl groups at position C7 of the pyrrole ring of modified nucleobases improves duplex stability relative to the unsubstituted analogue. This effect has been attributed to an increased hydrophobicity and a favourable increase in π-stacking energy (Balow *et al.*, 1998). In this context, the title compound, 3-iodo-5-nitroindole 2′-deoxyribonucleoside, (I), was synthesized and incorporated into duplex DNA (Leonard *et al.*, 2005, 2009). Hybridization studies showed that the iodinated 5-nitroindole 2′-deoxyribonucleoside (I) stabilizes duplex DNA compared with the unsubstituted nucleoside when placed opposite to the four canonical DNA constituents (Leonard *et al.*, 2005, 2009). Furthermore, the iodinated 5-nitroindole 2′-deoxyribonucleoside (I) can be employed as a precursor for Sonogashira cross-coupling reactions, leading to a broad spectrum of alkylated, alkenylated and alkynylated indole nucleosides for various purposes (Leonard *et al.*, 2005, 2009).



As the conformational properties of (I) are unknown, a single-crystal X-ray analysis was performed. The conformation and molecular dimensions of (I) are compared with those of the closely related structures of 5-nitroindole 2′-deoxyribonucleoside, (II*a*) (Loakes *et al.*, 1997), and 5-nitroindole ribonucleoside, (II*b*) (Harki *et al.*, 2007), as well as with those of the similar 4-nitroindazole 2′-deoxyribonucleoside, (III) (Seela *et al.*, 2004).

The three-dimensional structure of (I) is shown in Fig. 1 and selected geometric parameters are listed in Table 1. For purine nucleosides, the orientation of the nucleobase relative to the sugar moiety is defined by the torsion angle χ (O4′—C1′—N9—C4) (purine numbering; IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). The preferred conformation at the N-glycosylic bond of the common purine nucleosides is usually *anti* (Saenger, 1984). The corresponding torsion angle in (I), namely χ (O4′—C1′—N1—C7*A*), is −115.1 (3)°, reflecting an *anti* conformation. For the parent 5-nitroindole 2′-deoxyribonucleoside, (II*a*), an almost identical torsion angle was observed [χ = −113.3 (2)°; Loakes *et al.*, 1997], indicating that the introduction of the 3-iodo substituent in (I) has no significant influence on the orientation of the indole moiety relative to the sugar residue. In contrast, (II*b*) adopts a *syn* conformation at the glycosylic bond [χ = −83.0 (2)°; Harki *et al.*, 2007]. For (III), the torsion angle is

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shifted towards the high-*anti* range [$\chi = -105.3\ (2)^\circ$; Seela *et al.*, 2004]. The glycosylic bond length (C1′—N1) of (I) is 1.450 (3) Å, which is close to that of (II*a*) [1.444 (2) Å; Loakes *et al.*, 1997], (II*b*) [1.446 (2) Å; Harki *et al.*, 2007] and (III) [1.449 (2) Å; Seela *et al.*, 2004].

The most frequently observed sugar ring conformations of purine nucleosides are C2′-*endo* ('south' or *S*) and C3′-*endo* ('north' or *N*) (Arnott & Hukins, 1972). The 2′-deoxyribose ring of (I) shows an *S*-type sugar pucker with a pseudorotation phase angle *P* of 141.3° and a maximum puckering amplitude τ_m of 40.3°, which corresponds to an unsymmetrical twist of C1′-*exo*—C2′-*endo* ($_1T^2$). This sugar pucker is consistent with the predominant conformation of (I) observed in solution (73% *S*). The conformer ratio was obtained from the vicinal ^3J(H,H) coupling constants of the ^{1}H NMR signals determined in a dimethyl sulfoxide/D_2O mixture, applying the program *PSEUROT* (Van Wijk *et al.*, 1999).

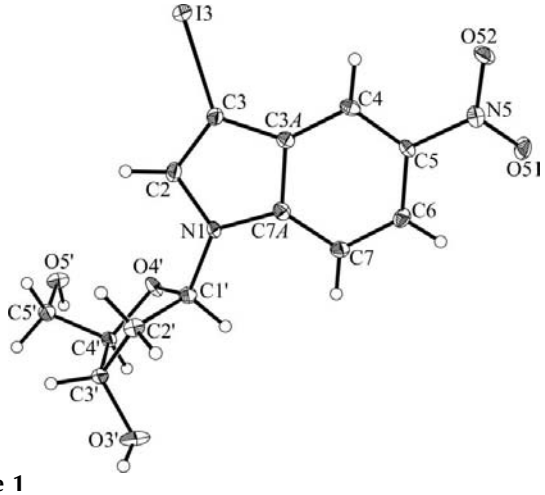

Figure 1
A perspective view of nucleoside (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary size.

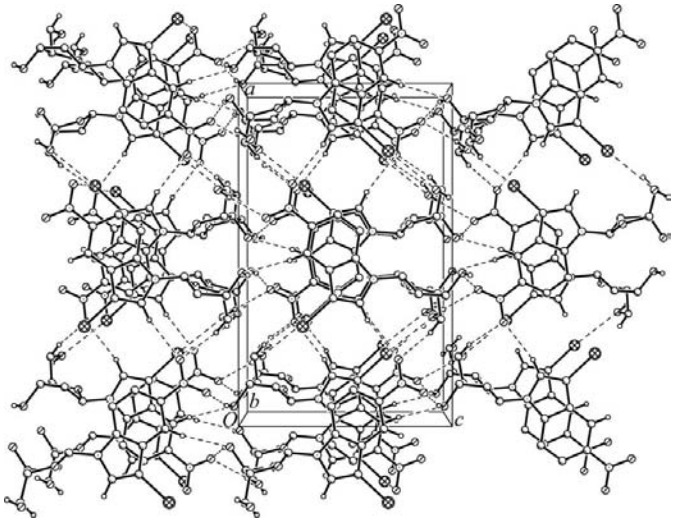

Figure 2
The crystal packing of (I), showing the intermolecular hydrogen-bonding network (in projection parallel to the *b* axis). For the sake of clarity, H atoms not involved in the hydrogen-bonding network have been omitted.

The sugar moieties of (II*a*) and (III) also adopt an *S* conformation, with $P = 176.2\ (2)^\circ$ and $\tau_m = 39.2\ (1)^\circ$ ($^2T_3$; Loakes *et al.*, 1997) and $P = 192.6^\circ$ and $\tau_m = 37.5^\circ$ ($_3T^2$; Seela *et al.*, 2004), respectively, while the 5-nitroindole ribonucleoside (II*b*) displays a C3′-*endo* ($^3T_2$) sugar pucker with $P = 4.8\ (2)^\circ$ and $\tau_m = 35.5\ (1)^\circ$, which corresponds to an *N* sugar conformation (Harki *et al.*, 2007). The γ torsion angle (O5′—C5′—C4′—C3′) characterizes the orientation of the exocyclic 5′-hydroxy group relative to the 2′-deoxyribose ring. In the crystal structure of (I), the C4′—C5′ bond is in an antiperiplanar (+*ap*, *gauche*, *trans*) orientation with $\gamma = 177.4\ (2)^\circ$. For compounds (II*a*) and (III) the torsion angles are −69.8 (2) and −91.5 (2)°, respectively; both correspond to a −*sc* (*trans*, *gauche*) conformation (Loakes *et al.*, 1997; Seela *et al.*, 2004). Conversely, (II*b*) adopts a +*sc* (*gauche*, *gauche*) conformation around the exocyclic C4′—C5′ bond (Harki *et al.*, 2007).

The indole ring of (I) is essentially planar. The deviations of the ring atoms from the N1/C2/C3/C3*A*/C4–C7/C7*A* least-squares plane range from −0.018 (2) (for atom N1) to 0.016 (2) Å (for atom C3), with an r.m.s. deviation of 0.0102 Å. The iodo substituent and atom N5 of the nitro group lie on different sides of the heterocyclic plane [at distances of 0.016 (3) and −0.026 (3) Å, respectively].

Within the crystal structure of (I), the individual molecules stack in columns and form several intermolecular hydrogen bonds (Table 2 and Fig. 2). Atoms O51 and O52 of the nitro group function as the main H-atom acceptor sites, forming bifurcated hydrogen bonds within the *ac* plane (O3′—H3′*B*···O52^{i}, O5′—H5′*A*···O52^{ii}, C5′—H5′*C*···O51^{iii} and C2—H2···O51^{iii}; see Table 2 for symmetry codes and geometry). One more hydrogen bond is formed between the sugar moiety and the heterocycle of neighboring molecules (C4—H4···O3′^{iv}). Moreover, a contact between atoms I3 and O5′($-x+\frac{3}{2}, y-\frac{1}{2}, -z+1$) of the hydroxy group of the sugar moiety within the *ac* plane is observed, with an intermolecular distance of 3.0867 (16) Å.

Previously, the intermolecular iodo–nitro interactions of aromatic compounds containing an I atom together with a nitro group were reported to be a determining factor for crystal structure and have been employed in crystal engineering (Allen *et al.*, 1994; Kelly *et al.*, 2002; Ranganathan & Pedireddi, 1998; McWilliam *et al.*, 2001; Garden *et al.*, 2002). Owing to $\delta+$ polarizability, I atoms can form bifurcated symmetrical as well as unsymmetrical contacts with oxygen as electron acceptor (Allen *et al.*, 1994; Messina *et al.*, 2001). A similar phenomenon is found for the crystal structure of (I). An interplanar interaction between atom I3 and atom O51($-x+1, -y+2, z$) of the nitro group exists, with a distance of 3.5364 (16) Å, which is within the range of iodo–nitro contacts described in the literature (Ranganathan & Pedireddi, 1998; Kelly *et al.*, 2002). The iodo–nitro contact of (I) constrains the molecules within each column into an alternating arrangement with a reverse orientation of the molecules. This is controlled by the interaction of atoms I3 and O51. In the crystal structure of the parent compound (II*a*), which lacks the iodo substituent, the nitro groups are stacked within a column (Loakes *et al.*, 1997).

Experimental

Compound (I) was synthesized as reported previously (Leonard *et al.*, 2005, 2009). Slow crystallization from methanol afforded (I) as yellow plates (decays above 413 K). For the diffraction experiment, a single crystal was mounted on a MiTeGen MicroMounts fibre in a thin smear of oil.

Crystal data

$C_{13}H_{13}IN_2O_5$
M_r = 404.15
Orthorhombic, $P2_12_12$
a = 17.549 (3) Å
b = 7.0981 (10) Å
c = 10.9242 (19) Å
V = 1360.8 (4) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 2.38 mm^{-1}
T = 100 K
0.10 × 0.10 × 0.03 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2008)
T_{min} = 0.797, T_{max} = 0.932
37202 measured reflections
2791 independent reflections
2678 reflections with $I > 2\sigma(I)$
R_{int} = 0.044

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.017
$wR(F^2)$ = 0.034
S = 1.04
2791 reflections
192 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.56 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}
Absolute structure: Flack (1983), 1163 Friedel pairs
Flack parameter: −0.013 (15)

Table 1
Selected geometric parameters (Å, °).

N1—C1′	1.450 (3)	N5—O51	1.225 (2)
C3—I3	2.072 (2)	N5—O52	1.248 (2)
C5—N5	1.451 (3)		
C2—C3—I3	126.56 (17)	O51—N5—C5	119.52 (19)
C3*A*—C3—I3	125.80 (15)	O52—N5—C5	118.24 (18)
N1—C2—C3—I3	−178.92 (19)	C6—C5—N5—O52	−169.0 (2)
I3—C3—C3*A*—C4	−0.6 (4)	C7*A*—N1—C1′—O4′	−115.1 (3)
C4—C5—N5—O51	−168.4 (2)	C2—N1—C1′—O4′	62.8 (3)
C6—C5—N5—O51	11.3 (3)	C3′—C4′—C5′—O5′	177.43 (18)
C4—C5—N5—O52	11.3 (3)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3′—H3′*B*···O52^{i}	0.82	2.17	2.970 (3)	164
O5′—H5′*A*···O52^{ii}	0.82	2.14	2.909 (2)	156
C2—H2···O51^{iii}	0.93	2.52	3.422 (3)	165
C4—H4···O3′^{iv}	0.93	2.47	3.387 (3)	169
C5′—H5′*C*···O51^{iii}	0.97	2.57	3.519 (3)	166

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

All H atoms were found in a difference Fourier synthesis. In order to maximize the data/parameter ratio, H atoms bound to C atoms were placed in geometrically idealized positions (C—H = 0.93–0.98 Å; AFIX 43) and constrained to ride on their parent atoms, with U_{iso}(H) values of 1.2U_{eq}(C). The OH groups were refined as rigid groups allowed to rotate but not tip (AFIX 147), with O—H distances of 0.82 Å and U_{iso}(H) values of 1.5U_{eq}(O).

Data collection: *APEX2* (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2009).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: TR3054). Services for accessing these data are described at the back of the journal.

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