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Structures of 3′-Azido-2′,3′-dideoxy-1-β-D-*threo*-pentofuranosyluracil and 3′-Azido-2′,3′-dideoxy-1-β-D-*erythro*-pentofuranosyluracil

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Abstract. 3′-Azido-2′,3′-dideoxy-1-β-D-*threo*-pentofuranosyluracil: $C_9H_{11}N_5O_4$, $M_r = 253{\cdot}2$, orthorhombic, $P2_12_12_1$, $a = 6{\cdot}91\ (1)$, $b = 9{\cdot}16\ (2)$, $c = 17{\cdot}65\ (1)$ Å, $V = 1117$ Å^3, $Z = 4$, $D_x = 1{\cdot}505$ g cm^{-3}, Mo $K\alpha$ radiation, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}010$ cm^{-1}, $F(000) = 528$, $T = 293$ K. $R = 0{\cdot}053$ for 811 unique observed $[I > 3\sigma(I)]$ reflections. The *N*-glycosidic torsion angle χ has a value of $-149\ (1)°$, in the *anti* range. The sugar pucker is $^3T_2$ with $P = 15\ (1)°$ and $\psi = 30\ (1)°$. The C4′–C5′ conformation is *–sc* with $\gamma = -72\ (1)°$. There are two hydrogen bonds in the structure, both involving O4: O4···N3 $(-0{\cdot}5 + x, -1{\cdot}5 - y, -1 - z)$ 2·86 (1) Å and O4···O5′ $(-1{\cdot}5 - x, -1 - y, 0{\cdot}5 + z)$ 2·91 (1) Å. 3′-Azido-2′,3′-dideoxy-1-β-D-*erythro*-pentofuranosyluracil: $C_9H_{11}N_5O_4$, $M_r = 253{\cdot}2$, monoclinic, $P2_1$, $a = 9{\cdot}75\ (1)$, $b = 6{\cdot}77\ (2)$, $c = 8{\cdot}42\ (1)$ Å, $\beta = 87{\cdot}2\ (1)°$, $V = 555$ Å^3, $Z = 2$, $D_x = 1{\cdot}515$ g cm^{-3}, Mo $K\alpha$ radiation, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}012$ cm^{-1}, $F(000) = 264$, $T = 293$ K. $R = 0{\cdot}072$ for 1092 unique observed $[I > 3\sigma(I)]$ reflections. The *N*-glycosidic torsion angle χ has a value of $-160\ (1)°$, in the *anti* range. The sugar pucker is $^2T_3$ with $P = 174\ (1)°$ and $\psi = 35\ (1)°$. The C4′–C5′ conformation is *sc* with $\gamma = 56\ (1)°$. There are two hydrogen bonds in the structure: O4···N3 $(2 - x, 0{\cdot}5 + y, 1 - z)$ 2·84 (1) Å and O2···O5′ $(x, 1 + y, z)$ 2·93 (1) Å. In each case the latter atom is the donor atom.

Introduction. These structures were determined as part of an investigation of potentially anti-viral nucleoside analogues, with particular reference to possible anti-AIDS compounds.

Experimental. The compounds were kindly supplied by Dr J. Rideout of Burroughs Wellcome Co., Research Triangle Park, NC 27709, USA. Crystals were obtained from aqueous solution. Space group and initial cell dimensions were obtained from Weissenberg photographs. Data were collected on a Stoe Stadi 2 diffractometer.

3′-Azido-2′,3′-dideoxy-1-β-D-*threo*-pentofuranosyluracil: crystals mounted along the *a* and *c* axes were used in the data collection. The crystals had dimensions $0{\cdot}3 \times 0{\cdot}4 \times 0{\cdot}5$ mm and $0{\cdot}4 \times 0{\cdot}3 \times 0{\cdot}4$ mm. Refined cell dimensions were measured using these crystals. Lattice parameters from 32 reflections in 2θ range 10–30°. Range of indices: $0 \le h \le 8$; $-11 \le k \le 11$; $-22 \le l \le 22$. Data measured using ω scans in the range $0 < 2\theta < 55°$. Standard reflections were measured every 100 reflections on each layer. No changes greater than 2σ from the means in the intensities of these reflections were found throughout data collection. Lorentz and polarization factors were applied. No corrections were made for absorption or secondary extinction. Friedel pairs were merged. 1970 independent reflections were measured, giving 811 observed $[I > 3\sigma(I)]$ reflections used in the refinement. $R_{int} = 0{\cdot}036$. The structure was solved using the *SHELX*86 program (Sheldrick, 1986). The *E* map revealed positions of all non-hydrogen atoms. A difference synthesis revealed the position of the hydrogen atom attached to atom O5′. All other hydrogen atoms were included at calculated positions, C—H = 1·08 Å. The hydrogen atoms were given fixed isotropic temperature factors approximately 1·5 times that of the parent atom and allowed to ride on their parent atoms. All other atoms were refined anisotropically. Blocked full-matrix refinement (on *F*) was carried out using the program *SHELX*76 (Sheldrick, 1976). The refinement converged at $R = 0{\cdot}053$, $wR = 0{\cdot}067$, $w = 2{\cdot}1378[\sigma^2(F) + 0{\cdot}001813F^2]^{-1}$. 163 refined parameters; average shift/e.s.d. = 0·001; max. shift/e.s.d. < 0·01; max. diff. peak 0·27 e Å^{-3}; min. diff. peak −0·36 e Å^{-3}.

3′-Azido-2′,3′-dideoxy-1-β-D-*erythro*-pentofuranosyluracil: crystals mounted along the *b* and *c* axes were used in the data collection. Refined cell dimensions were measured using these crystals. The crystals had dimensions $0{\cdot}4 \times 0{\cdot}3 \times 0{\cdot}1$ mm and $0{\cdot}4 \times 0{\cdot}4 \times 0{\cdot}4$ mm. Lattice parameters from 18 reflections in 2θ range 10–30°. Range of indices: $-12 \le h \le 12$; $-8 \le k \le 8$; $-10 \le l \le 10$. Data measured using ω scans in the range $0 < 2\theta < 55°$. Standard reflections were measured every 100 reflections on each layer. No changes greater than 2σ from the means in the

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Table 1. *Coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($\times 10^3$) *for non-hydrogen atoms, with e.s.d.'s in parentheses*

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

	x	y	z	U_{eq} (Å^2)
3′-Azido-2′,3′-dideoxy-1-β-D-*threo*-pentofuranosyluracil				
N1	−4760 (6)	−6466 (6)	−7217 (2)	26 (1)
C2	−3138 (7)	−6700 (7)	−6768 (3)	26 (1)
O2	−1494 (4)	−6638 (5)	−7019 (2)	36 (1)
N3	−3525 (6)	−6956 (6)	−6014 (2)	26 (1)
C4	−5338 (7)	−7121 (7)	−5698 (3)	27 (1)
O4	−5458 (5)	−7302 (5)	−5001 (2)	39 (1)
C5	−6928 (7)	−7000 (7)	−6209 (3)	31 (1)
C6	−6588 (7)	−6658 (7)	−6926 (3)	31 (1)
C1′	−4413 (8)	−5920 (7)	−7997 (3)	31 (1)
C2′	−4262 (8)	−7118 (8)	−8595 (3)	39 (1)
C3′	−6251 (9)	−7158 (7)	−8952 (3)	35 (1)
N3′*A*	−7453 (8)	−8252 (7)	−8533 (3)	45 (1)
N3′*B*	−8841 (9)	−8729 (6)	−8902 (3)	50 (2)
N3′*C*	−10127 (10)	−9250 (8)	−9202 (4)	83 (3)
C4′	−6973 (8)	−5604 (7)	−8862 (3)	28 (1)
C5′	−9145 (8)	−5353 (7)	−8740 (3)	39 (2)
O5′	−10166 (6)	−5638 (5)	−9430 (2)	56 (1)
O4′	−6016 (5)	−5047 (5)	−8192 (2)	33 (1)
3′-Azido-2′,3′-dideoxy-1-β-D-*erythro*-pentofuranosyluracil				
N1	6348 (4)	1516†	7364 (5)	26 (1)
C2	7011 (4)	3181 (8)	6789 (5)	24 (1)
O2	6534 (4)	4832 (7)	6903 (4)	38 (1)
N3	8299 (4)	2835 (7)	6114 (5)	26 (1)
C4	8913 (4)	1076 (8)	5890 (6)	30 (1)
O4	10071 (4)	962 (7)	5208 (6)	52 (1)
C5	8169 (5)	−644 (9)	6513 (6)	40 (1)
C6	6928 (5)	−331 (8)	7226 (6)	35 (1)
C1′	4931 (4)	1812 (8)	8025 (5)	31 (1)
C2′	3878 (4)	1796 (8)	6737 (5)	28 (1)
C3′	2638 (5)	913 (8)	7649 (6)	36 (1)
N3′*A*	1991 (5)	2614 (8)	8572 (7)	53 (1)
N3′*B*	886 (5)	2311 (9)	9220 (7)	65 (1)
N3′*C*	−170 (7)	2148 (10)	9781 (9)	122 (1)
C4′	3251 (4)	−548 (8)	8749 (5)	32 (1)
C5′	3321 (5)	−2623 (9)	8129 (6)	40 (1)
O5′	4033 (4)	−2816 (7)	6622 (5)	44 (1)
O4′	4608 (3)	160 (7)	9032 (4)	37 (1)

† Fixed parameter.

Table 2. *Interatomic distances* (Å) *and angles* (°)

3′-Azido-2′,3′-dideoxy-1-β-D-*threo*-pentofuranosyluracil			
C2···N1	1·389 (6)	C6···N1	1·375 (6)
C1′···N1	1·484 (6)	O2···C2	1·222 (5)
N3···C2	1·377 (7)	C4···N3	1·379 (6)
O4···C4	1·244 (6)	C5···C4	1·425 (7)
C6···C5	1·325 (7)	C2′···C1′	1·526 (9)
O4′···C1′	1·409 (7)	C3′···C2′	1·513 (9)
N3′*A*···C3′	1·496 (8)	C4′···C3′	1·517 (9)
N3′*B*···N3′*A*	1·239 (8)	N3′*C*···N3′*B*	1·139 (8)
C5′···C4′	1·534 (8)	O4′···C4′	1·448 (6)
O5′···C5′	1·432 (7)		
C6–N1–C2	120·6 (4)	C1′–N1–C2	116·8 (4)
C1′–N1–C6	122·5 (4)	O2–C2–N1	122·5 (4)
N3–C2–N1	114·9 (4)	N3–C2–O2	122·7 (5)
C4–N3–C2	125·8 (4)	O4–C4–N3	118·3 (4)
C5–C4–N3	116·0 (4)	C5–C4–O4	125·7 (5)
C6–C5–C4	119·0 (5)	C5–C6–N1	123·3 (5)
C2′–C1′–N1	114·2 (5)	O4′–C1′–N1	106·9 (4)
O4′–C1′–C2′	107·1 (4)	C3′–C2′–C1′	104·0 (5)
N3′*A*–C3′–C2′	108·4 (5)	C4′–C3′–C2′	103·4 (5)
C4′–C3′–N3′*A*	113·2 (5)	N3′*B*–N3′*A*–C3′	114·0 (5)
N3′*C*–N3′*B*–N3′*A*	174·9 (8)	C5′–C4′–C3′	118·5 (5)
O4′–C4′–C3′	105·4 (4)	O4′–C4′–C5′	106·3 (5)
O5′–C5′–C4′	109·7 (5)	C4′–O4′–C1′	111·0 (4)
3′-Azido-2′,3′-dideoxy-1-β-D-*erythro*-pentofuranosyluracil			
C2···N1	1·375 (5)	C6···N1	1·375 (6)
C1′···N1	1·477 (5)	O2···C2	1·212 (6)
N3···C2	1·373 (5)	C4···N3	1·342 (7)
O4···C4	1·244 (6)	C5···C4	1·456 (8)
C6···C5	1·341 (6)	C2′···C1′	1·530 (6)
O4′···C1′	1·429 (6)	C3′···C2′	1·523 (6)
N3′*A*···C3′	1·509 (7)	C4′···C3′	1·499 (7)
N3′*B*···N3′*A*	1·202 (7)	N3′*C*···N3′*B*	1·117 (8)
C5′···C4′	1·498 (8)	O4′···C4′	1·439 (6)
O5′···C5′	1·422 (6)		
C6–N1–C2	122·0 (4)	C1′–N1–C2	115·9 (3)
C1′–N1–C6	121·9 (3)	O2–C2–N1	123·7 (4)
N3–C2–N1	114·3 (4)	N3–C2–O2	122·0 (4)
C4–N3–C2	127·0 (4)	O4–C4–N3	120·6 (5)
C5–C4–N3	116·6 (4)	C5–C4–O4	122·8 (5)
C6–C5–C4	117·2 (5)	C5–C6–N1	122·7 (5)
C2′–C1′–N1	112·3 (4)	O4′–C1′–N1	107·0 (4)
O4′–C1′–C2′	106·2 (4)	C3′–C2′–C1′	100·9 (3)
N3′*A*–C3′–C2′	105·2 (4)	C4′–C3′–C2′	103·8 (4)
C4′–C3′–N3′*A*	110·8 (4)	N3′*B*–N3′*A*–C3′	116·5 (5)
N3′*C*–N3′*B*–N3′*A*	175·3 (7)	C5′–C4′–C3′	114·6 (4)
O4′–C4′–C3′	106·3 (4)	O4′–C4′–C5′	110·1 (4)
O5′–C5′–C4′	114·1 (4)	C4′–O4′–C1′	109·9 (4)

intensities of these reflections were found throughout data collection. Lorentz and polarization factors were applied. No corrections were made for absorption or secondary extinction. Friedel pairs were merged. 3675 independent reflections were measured, giving 1092 observed [$I > 3\sigma(I)$] reflections used in the refinement. The 110 and 102 reflections were not used in the refinement on the grounds of extinction. $R_{int} = 0{\cdot}026$. The structure was solved using the *SHELXS*86 program (Sheldrick, 1986). The E map revealed positions of all non-hydrogen atoms. The position of the hydrogen atom attached to O5′ was obtained from a difference synthesis. All other hydrogen atoms were included at calculated positions, C–H = 1·08 Å. The hydrogen atoms were given fixed isotropic temperature factors approximately 1·5 times that of the parent atom and allowed to ride on their parent atoms. All other atoms were refined anisotropically. Blocked full-matrix refinement (on F) was carried out using the program *SHELX*76 (Sheldrick, 1976). The refinement converged at $R = 0{\cdot}072$, $wR = 0{\cdot}116$, $w = 2{\cdot}7536[\sigma^2(F) + 0{\cdot}001240F^2]^{-1}$. 162 refined parameters; average shift/e.s.d. = 0·010; max. shift/e.s.d. <0·01; max. diff. peak 0·58 e Å^{-3}; min. diff. peak −0·33 e Å^{-3}. The largest difference peaks are in the vicinity of atoms C2′ and C3′. This and the fact that C2′ is non-positive definite suggests a certain amount of disorder in the positions of these atoms but not sufficient for discrete disordered sites to be located on an appropriate difference map. This disorder would also explain why the refinement stops at an R of 0·072.

Scattering factors were taken from *International Tables for X-ray Crystallography* (1974). The program packages *XANADU* (Roberts & Sheldrick, 1975) and *PLUTO* (Motherwell & Clegg, 1978) were also used. All calculations were carried out on the Dundee University PRIME computer. The compounds were supplied with known chirality. The conformational parameters are in acordance with the IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983) guidelines.

Discussion. The atomic numbering is shown in Fig. 1. Tables 1 and 2 give the atomic parameters, bond

lengths and angles.* Fig. 2 shows the hydrogen bonding. The differences in conformation between the two title molecules can be accounted for in terms of the different positions of the azido group. The *erythro* compound is the uracil analogue of the potent anti-AIDS drug 3′-azido-3′-deoxythymidine, AZT. This latter compound has two separate molecules in its asymmetric unit with χ of -126 and $-172°$ and sugar ring puckers $P = 171$ and 213°, respectively (Dyer, Low, Tollin, Wilson & Howie, 1988). The *erythro* compound ($\chi = -160°$ and pucker $P = 174°$) has a glycosidic torsion angle similar to one AZT molecule and a pucker similar to the other.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51581 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

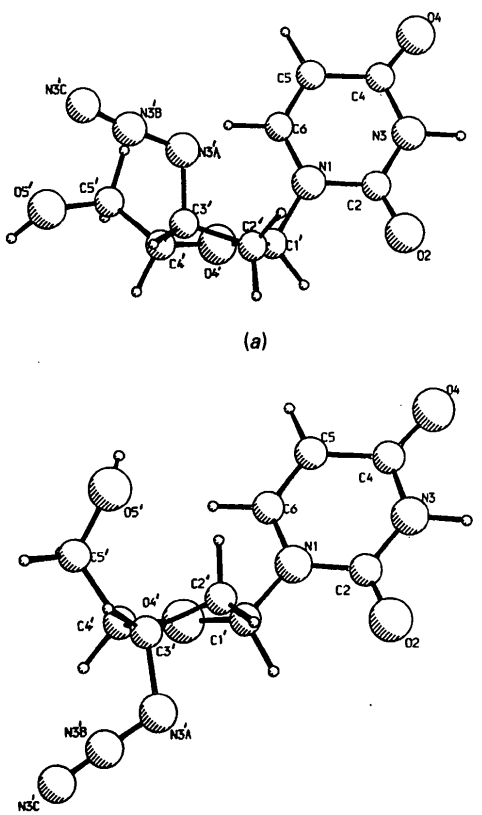

Fig. 1. View of (*a*) the *threo* molecule and (*b*) the *erythro* molecule, giving atomic numbering.

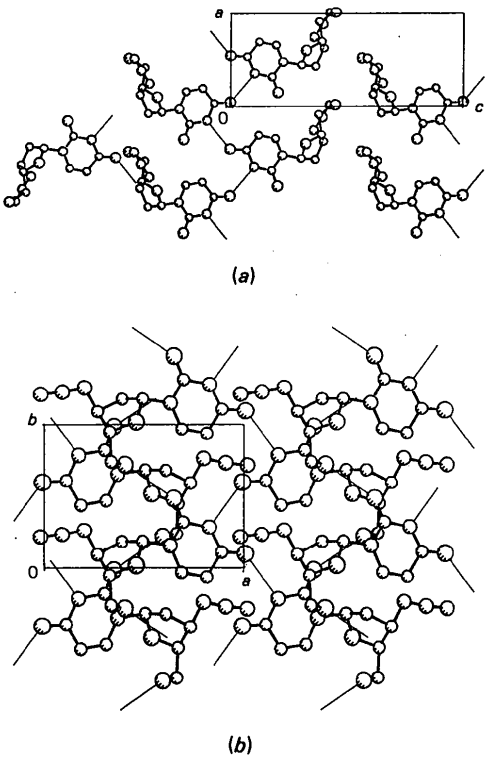

Fig. 2. Packing of (*a*) the *threo* compound viewed down **b** and (*b*) the *erythro* compound viewed down **c**.

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