

## Structures of Two Nucleoside Analogues: 1-[(2*R*,6*R*)-6-Hydroxymethyl-1,4-dioxan-2-yl]uracil and 5-Bromo-1-[(2*R*,6*R*)-6-hydroxymethyl-1,4-dioxan-2-yl]uracil\*

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**Abstract.** (I) 1-[(2*R*,6*R*)-6-Hydroxymethyl-1,4-dioxan-2-yl]uracil, C<sub>9</sub>H<sub>12</sub>N<sub>2</sub>O<sub>5</sub>,  $M_r = 228.20$ , trigonal,  $P3_121$ ,  $a = 9.438$  (5),  $c = 19.77$  (2) Å,  $V = 1522$  (2) Å<sup>3</sup>,  $Z = 6$ ,  $D_m = 1.49$ ,  $D_x = 1.494$  Mg m<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71069$  Å,  $\mu = 0.115$  mm<sup>-1</sup>,  $F(000) = 720$ ,  $T = 293$  K, final  $R = 0.036$  for 1541 unique observed [ $F \geq 4\sigma(F)$ ] reflections. (II) 5-Bromo-1-[(2*R*,6*R*)-6-hydroxymethyl-1,4-dioxan-2-yl]uracil, C<sub>9</sub>H<sub>11</sub>BrN<sub>2</sub>O<sub>5</sub>,  $M_r = 307.10$ , triclinic,  $P1$ ,  $a = 4.851$  (4),  $b = 6.409$  (5),  $c = 9.687$  (9) Å,  $\alpha = 70.78$  (7),  $\beta = 83.54$  (7),  $\gamma = 80.01$  (6)°,  $V = 279.5$  (4) Å<sup>3</sup>,  $Z = 1$ ,  $D_m = 1.82$ ,  $D_x = 1.824$  Mg m<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71069$  Å,  $\mu = 3.649$  mm<sup>-1</sup>,  $F(000) = 154$ ,  $T = 293$  K, final  $R = 0.036$  for 959 unique observed reflections [ $F \geq 4\sigma(F)$ ]. Except for N-glycosidic torsion angle, which is 230.9 (2)° for (I) and 210.2 (7)° for (II), the two molecules are conformationally very similar. No intramolecular hydrogen bonds are observed. The crystal packings are stabilized by intermolecular hydrogen bonds and base-stacking forces.

**Experimental.** The synthesis has been described by Van Aerschot, Janssen & Herdewijn (1990). Crystals of compound (I) from acetone/hexane; of compound (II) from ethanol/amyl acetate. Density measured by flotation in (I) *n*-heptane/CCl<sub>4</sub> and in (II) 1,1,2,2-tetrabromoethane/CCl<sub>4</sub>. Space group of (I) determined from systematically absent reflections  $00l$  with  $3n$  odd and from careful inspection of the intensities of five reflections with the intensities of their Laue-related equivalents. Experimental details are set out in Table 1. Stoe Stadi-4 computer-

controlled diffractometer, cell constants by least-squares refinement of the setting angles of 36 (I) or 34 (II) reflections with  $20 \leq 2\theta \leq 30^\circ$ . Intensities of two standard reflections monitored every 2 h showed for (I) a decrease of 8.8% (after 130 h) for which the intensities have been corrected and for (II) only statistical fluctuations. Data reduction with a locally modified version of Stoe & Co (1985) *REDU4* program, Lorentz and polarization corrections. Equivalent reflections of compound (I) were averaged with the program *SDP* (Frenz, 1985). Scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.2B) and for H atoms from Stewart, Davidson & Simpson (1965). Anomalous-dispersion corrections were included for all non-H atoms (Ibers & Hamilton, 1964). No absorption corrections were applied. Structure (I) solved by *MULTAN82* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982), while structure (II) was solved by a Fourier synthesis with phases from Br(5), which was placed at an arbitrary position. Refined on  $F$  by full-matrix least squares, first with isotropic temperature factors and finally anisotropically. In both structures, all H atoms were found in a difference synthesis and in compound (I) their positional parameters were refined with a fixed temperature factor  $B$ , 1.3 times the  $B_{eq}$  of their parent atoms. In compound (II), which contains the heavy-atom Br, all H but H(1) were placed at a riding distance of 0.95 Å with a fixed temperature factor  $B$ , 1.3 times the  $B_{eq}$  of their parent atoms. H(1) was placed at its found position and included in the refinement with a fixed temperature factor  $B$ , 1.3 times the  $B_{eq}$  of O(55'). All calculations were performed on Digital PDP-11/73 and MicroVAX 2000 microcomputers using *SDP* (Frenz, 1985) and *PARST* (Nardelli, 1983).

\* Structural Studies on Modified Nucleosides. Part XIII. Part XII: De Winter, Blaton, Peeters, De Ranter, Van Aerschot & Herdewijn (1991).

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Table 1. *Experimental data*

	Compound (I)	Compound (II)
Crystal shape and dimensions (mm)	Irregular 0.6 × 0.6 × 0.3	Needle 0.5 × 0.2 × 0.1
Space group	<i>P</i> 3 <sub>2</sub> 1	<i>P</i> 1
Lattice parameters		
No. of reflections	36	34
2θ range (°)	20 ≤ 2θ ≤ 30	20 ≤ 2θ ≤ 30
Scan technique	ω/2θ	ω/2θ
Maximum 2θ (°)	65	50
<i>hkl</i> range	-14 ≤ <i>h</i> ≤ 14 -14 ≤ <i>k</i> ≤ 0 -30 ≤ <i>l</i> ≤ 0	-5 ≤ <i>h</i> ≤ 0 -7 ≤ <i>k</i> ≤ 7 -11 ≤ <i>l</i> ≤ 11
Standard reflections	120, $\overline{113}$	002, 020
No. of measured reflections	5939	1120
No. of unique reflections	2144	983
No. of unique reflections with $[F \geq 4\sigma(F)]$	1541	959
$R_{int}$ on <i>F</i> for equivalent observed reflections	0.019	—
<i>R</i> , <i>wR</i>	0.036, 0.039	0.036, 0.050
Goodness-of-fit <i>S</i>	2.27	1.95
Weighting scheme	1/(σ <sub>F</sub> <sup>2</sup> + 3 × 10 <sup>-5</sup> F <sub>o</sub> <sup>2</sup> )	1/(σ <sub>F</sub> <sup>2</sup> + 4 × 10 <sup>-4</sup> F <sub>o</sub> <sup>2</sup> )
Max. shift/e.s.d.	0.05	0.01
Min. and max. residual electron density (e Å <sup>-3</sup> )	-0.31, +0.16	-0.65, +0.62 (near Br)
No. of refined parameters	181	154
No. of reflections per refined parameter	8.5	6.2
Absorption coefficient μ (mm <sup>-1</sup> )	0.115	3.649

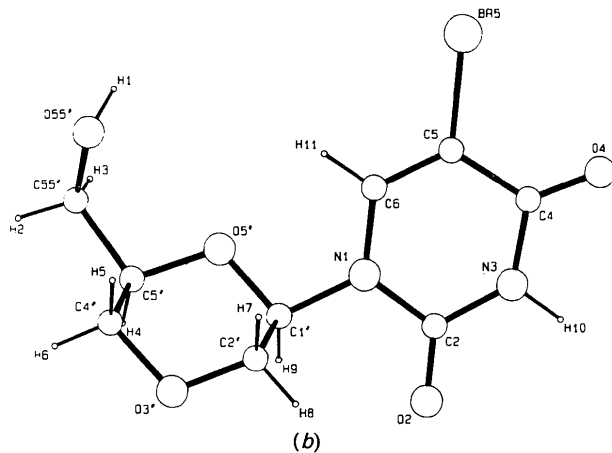
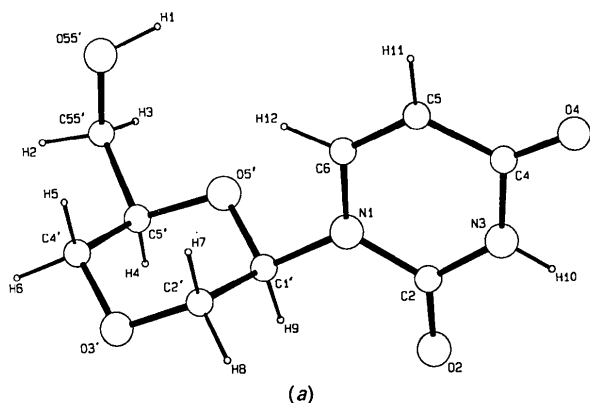


Fig. 1. *PLUTO* (Motherwell & Clegg, 1978) plots of the title compounds with atomic numbering schemes. (a) Compound (I). (b) Compound (II).

Table 2. *Atomic coordinates and equivalent isotropic temperature factors (Å<sup>2</sup> × 10<sup>4</sup>) with e.s.d.'s in parentheses*

$$U_{eq} = (1/3) \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>eq</sub>
Compound (I)				
N1	0.3110 (2)	0.2593 (2)	0.40928 (8)	378 (5)
C2	0.3513 (2)	0.1404 (2)	0.42453 (9)	429 (5)
O2	0.4920 (1)	0.1691 (2)	0.43038 (7)	537 (5)
N3	0.2194 (2)	-0.0145 (2)	0.43155 (8)	448 (5)
C4	0.0540 (2)	-0.0618 (2)	0.42813 (9)	450 (6)
O4	-0.0502 (2)	-0.2045 (2)	0.43771 (8)	560 (6)
C5	0.0246 (2)	0.0701 (2)	0.4132 (1)	428 (6)
C6	0.1503 (2)	0.2221 (2)	0.40453 (9)	427 (6)
C1'	0.4411 (2)	0.4277 (2)	0.3980 (1)	387 (6)
O2'	0.4470 (2)	0.4744 (3)	0.3242 (1)	524 (8)
O3'	0.5647 (2)	0.6430 (2)	0.31540 (8)	533 (6)
C4'	0.5236 (3)	0.7409 (3)	0.3567 (1)	467 (8)
C5'	0.5192 (2)	0.6983 (2)	0.4303 (1)	398 (6)
O5'	0.4043 (2)	0.5265 (1)	0.44000 (6)	389 (4)
C55'	0.4649 (2)	0.7905 (2)	0.4764 (1)	520 (7)
O55'	0.2972 (2)	0.7423 (2)	0.46658 (8)	529 (5)
Compound (II)				
N1	0.511 (2)	0.513 (1)	0.3658 (7)	310 (19)
C2	0.456 (1)	0.488 (1)	0.2358 (7)	282 (25)
O2	0.303 (1)	0.361 (1)	0.2314 (6)	421 (17)
N3	0.591 (2)	0.615 (1)	0.1149 (6)	344 (19)
C4	0.765 (2)	0.765 (1)	0.1070 (8)	323 (23)
O4	0.875 (2)	0.865 (1)	-0.0090 (6)	450 (20)
C5	0.799 (2)	0.786 (1)	0.2474 (9)	333 (24)
Br5*	1.000	1.000	0.250	377 (2)
C6	0.678 (2)	0.663 (1)	0.3688 (8)	315 (24)
C1'	0.368 (2)	0.383 (1)	0.4979 (8)	350 (24)
O2'	0.542 (2)	0.155 (1)	0.5644 (9)	418 (26)
O3'	0.409 (2)	0.039 (1)	0.6956 (7)	488 (23)
C4'	0.380 (2)	0.161 (1)	0.7990 (9)	413 (28)
C5'	0.209 (2)	0.387 (1)	0.7357 (8)	366 (25)
O5'	0.329 (1)	0.5050 (9)	0.5956 (6)	359 (17)
C55'	0.187 (2)	0.535 (1)	0.8307 (9)	442 (27)
O55'	0.459 (1)	0.5879 (9)	0.8430 (6)	416 (19)

\* Parameters kept fixed during refinement.

**Discussion.** The dioxane ring atoms have been labeled using primes and starting with the C atom to which the pyrimidine base is attached as is usual for pyranosyl sugars. A *PLUTO* view (Motherwell & Clegg, 1978) of the title compounds with the atomic numbering scheme is shown in Fig. 1. The final atomic coordinates and equivalent isotropic thermal parameters are given in Table 2.\* Bond lengths, bond angles and selected torsion angles are given in Table 3.

All bond lengths and bond angles are within the normal range (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987). Except for the O(5')—C(1')—N(1)—C(2) torsion angle  $\chi$ , which is 230.9 (2)° in (I) and 210.2 (7)° in (II) (both *anti*), the two molecules are essentially similar in conformation. Even the orientation of O(55') above the dioxane rings is comparable since both O(55')—C(55')—C(5')—C(4') torsional angles differ by only

\* Lists of structure factors, anisotropic thermal parameters, bond lengths and angles involving H atoms, least-squares planes and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54287 (30 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. Bond lengths (Å), bond angles (°) and selected torsion angles (°) with e.s.d.'s in parentheses

	Compound (I)	Compound (II)
N1—C2	1.385 (3)	1.38 (1)
N1—C6	1.379 (3)	1.37 (1)
N1—C1'	1.460 (2)	1.453 (9)
C2—O2	1.221 (2)	1.21 (1)
C2—N3	1.373 (2)	1.358 (9)
N3—C4	1.394 (3)	1.36 (1)
C4—O4	1.221 (2)	1.213 (9)
C4—C5	1.436 (3)	1.44 (1)
C5—Br5		1.822 (9)
C5—C6	1.339 (2)	1.32 (1)
C1'—C2'	1.513 (3)	1.53 (1)
C1'—O5'	1.415 (3)	1.39 (1)
C2'—O3'	1.424 (2)	1.39 (1)
O3'—C4'	1.424 (3)	1.45 (1)
C4'—C5'	1.501 (3)	1.51 (1)
C5'—O5'	1.444 (2)	1.432 (9)
C5'—C55'	1.514 (3)	1.51 (1)
C55'—O55'	1.425 (3)	1.44 (1)
C2—N1—C6	121.4 (2)	121.5 (6)
C2—N1—C1'	119.5 (2)	116.6 (7)
C6—N1—C1'	119.1 (2)	121.8 (7)
N1—C2—O2	123.3 (2)	122.2 (6)
N1—C2—N3	114.5 (2)	114.7 (7)
O2—C2—N3	122.2 (2)	123.2 (8)
C2—N3—C4	127.6 (2)	128.1 (7)
N3—C4—O4	120.0 (2)	121.3 (8)
N3—C4—C5	113.8 (2)	113.0 (6)
O4—C4—C5	126.2 (2)	125.7 (9)
C4—C5—Br5		117.4 (5)
C4—C5—C6	120.2 (2)	121.3 (8)
Br5—C5—C6		121.2 (7)
N1—C6—C5	122.5 (2)	121.3 (8)
N1—C1'—C2'	110.6 (2)	111.1 (7)
N1—C1'—O5'	106.2 (2)	106.9 (7)
C2'—C1'—O5'	110.9 (2)	110.5 (7)
C1'—C2'—O3'	109.7 (2)	109.9 (7)
C2'—O3'—C4'	110.0 (2)	110.3 (7)
O3'—C4'—C5'	111.1 (2)	109.4 (7)
C4'—C5'—O5'	109.5 (2)	110.8 (7)
C4'—C5'—C55'	113.5 (2)	113.4 (7)
O5'—C5'—C55'	106.6 (2)	106.9 (7)
C1'—O5'—C5'	111.6 (2)	112.7 (6)
C5'—C55'—O55'	112.1 (2)	110.9 (7)
C2—N1—C1'—C2'	110.5 (2)	89.6 (9)
C2—N1—C1'—O5'	-129.1 (2)	-149.8 (7)
C6—N1—C1'—C2'	-69.4 (3)	-94.0 (9)
C6—N1—C1'—O5'	51.0 (3)	27. (1)
N1—C1'—C2'—O3'	174.9 (2)	176.3 (7)
O5'—C1'—C2'—O3'	57.4 (2)	58. (1)
N1—C1'—O5'—C5'	-176.4 (2)	-175.5 (7)
C2'—C1'—O5'—C5'	-56.2 (2)	-54.5 (9)
C1'—C2'—O3'—C4'	-58.8 (2)	-60. (1)
C2'—O3'—C4'—C5'	59.8 (3)	60. (1)
O3'—C4'—C5'—O5'	-57.1 (2)	-55. (1)
O3'—C4'—C5'—C55'	-176.1 (2)	-175.2 (8)
C4'—C5'—O5'—C1'	55.5 (2)	54.2 (9)
C55'—C5'—O5'—C1'	178.7 (2)	178.2 (7)
C4'—C5'—C55'—O55'	68.0 (2)	64. (1)
O5'—C5'—C55'—O55'	-52.6 (2)	-58.4 (9)

4 (1)°. A fit on the dioxane and base ring atoms using *BMFIT* (Nyburg, 1974) showed very close geometric similarity between the two dioxane and pyrimidine rings (r.m.s. deviations are 0.017 and 0.021 Å respectively).

In furanosyl nucleosides, the *anti* orientation around  $\chi$  is often stabilized by an intramolecular hydrogen bond between O(5') and H—C(6) (Saenger, 1988). However, in the title compounds the five-membered furanosyl sugar ring is replaced by a six-membered dioxane ring on which the pyrimidine base is equatorially placed and thus oriented away from O(5'). Consequently, the distance between

Table 4. Geometry of intermolecular hydrogen bonds (Å, °) with e.s.d.'s in parentheses

X—H...Y	<i>d</i> (H...Y)	<i>d</i> (X...Y)	X—H...Y
Compound (I)			
O55'—H1...O2	(1) 1.98 (2)	2.884 (3)	157 (2)
N3—H10...H10	(2) 1.94 (3)	2.823 (3)	168 (2)
Equivalent positions: (1) <i>y</i> , <i>x</i> , 1 - <i>z</i> ; (2) <i>x</i> , <i>y</i> - 1, <i>z</i> .			
Compound (II)			
O55'—H1...O3'	(1) 1.83	2.750 (8)	178
N3'—H10...O55'	(2) 1.90	2.846 (10)	174
Equivalent positions: (1) <i>x</i> , <i>y</i> + 1, <i>z</i> ; (2) <i>x</i> , <i>y</i> , <i>z</i> - 1.			

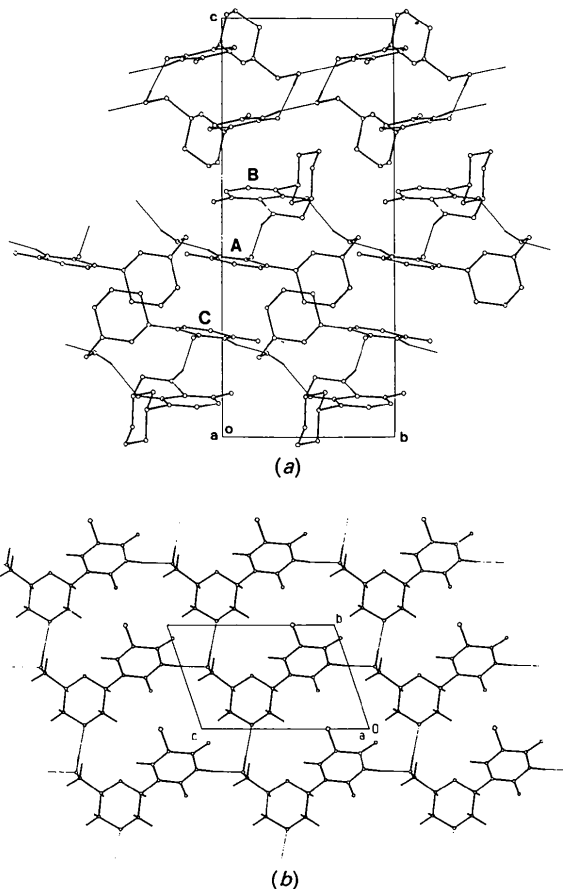


Fig. 2. *PLUTO* (Motherwell & Clegg, 1978) plots of the crystal packings. Thin lines indicate hydrogen bonds. (a) Compound (I). All hydrogens except H(1) and H(10) were omitted for reasons of clarity. (b) Compound (II).

O(55') and H—C(6) [3.85 (2) in (I) and 3.655 (7) Å in (II)] is considerably larger than in comparable furanosyl nucleosides, and prevents hydrogen-bond formation. Rigid rotation around the C(55')—C(5') and the C(1')—N(1) bonds of compound (I) reveals that when O(55')—C(55')—C(5')—C(4') = 115° and O(5')—C(1')—N(1)—C(2) = 180°, the distance between O(55') and H(12) becomes the smallest

achievable but remains larger than 3.0 Å, still far too large to form a stable hydrogen bond.

Using the method of Cremer & Pople (1975), we calculated almost equal phase angles  $\varphi_2 = -61$  (7) (I) or  $-70$  (13)° (II) and  $\theta_2 = 177.7$  (2) (I) or  $175.5$  (9)° (II), with total puckering amplitudes  $Q = 0.563$  (2) (I) or  $0.56$  (1) Å (II) for the sequences C(1')—C(2')—O(3')—C(4')—C(5')—O(5').

The packing in both crystals is partly determined by hydrogen bonds involving atoms of the dioxane and base rings (Table 4 summarizes all the intermolecular hydrogen bonds) and partly by parallel base-stacking forces. *PLUTO* plots of the crystal packings are shown in Fig. 2. In structure (I), two different stacking patterns are observable: (1) the closest stacking [ $d_{\text{mean}} = 3.4$  (2) Å] is found between pairs of bases related to each other by the twofold axis along *i* [bases *A* and *B* in Fig. 2(a); dihedral angle between the two bases =  $10.80$  (1)°]; (2) the other pattern [ $d_{\text{mean}} = 3.6$  (2) Å] is found between bases which are related by the twofold axis lying along *a* or *b* [bases *A* and *C* in Fig. 2(a); dihedral angle =  $12.86$  (1)°]. The stacking patterns for both observations are similar: the rings are only partially overlapped and the carbonyl groups and the ring N atoms often form close contacts with adjacent bases while the C atoms are less involved. In structure (II) only Br(5) is positioned in close contact with the adjacent base and is located above the center of the ring [ $d_{\text{mean}} = 3.31$  (1) Å].

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## Structure of the *cis* Isomer of a Six-Membered Phosphorus Phenylhydrazine Ring

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**Abstract.** 3,6-Bis(methylthio)-1,4-diphenyl-3,6-dithio-oxo-1,2,4,5-tetraaza-3 $\lambda^5$ ,6 $\lambda^5$ -diphosphorinane crystallizes with two solvent molecules of acetonitrile, C<sub>14</sub>H<sub>18</sub>N<sub>4</sub>P<sub>2</sub>S<sub>4</sub>·2CH<sub>3</sub>CN,  $M_r = 514.64$ , monoclinic,  $C2/c$ ,  $a = 12.118$  (8),  $b = 13.452$  (10),  $c = 15.608$  (4) Å,  $\beta = 98.22$  (4)°,  $V = 2518$  Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.353$  Mg m<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71069$  Å,  $\mu = 4.64$  mm<sup>-1</sup>,  $F(000) = 1072$ ,  $T = 293$  K,  $R = 0.038$  for 2513 unique observed reflections with  $I \geq 2\sigma(I)$ . The

molecules of the title compound have point symmetry 2. In accordance with the *cis* stereochemistry of the methylthio substituents the six-membered ring adopts a twist conformation; torsion angles PNNP + 67.87 (3), NNPN – 45.81 (3) and NPNN – 19.73 (1)°.

**Introduction.** To extend our knowledge of the preparative potential of py.PS<sub>2</sub>Cl (1) (py = pyridine), the