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Absolute configuration from a redetermination of (+)-5-bromo-1-[(2*R*,4*S*,5*R*)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-pyrimidine-2,4-dione at 118 (2) K

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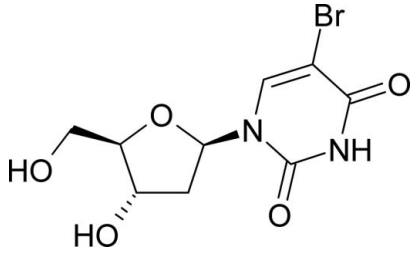
Key indicators: single-crystal X-ray study; T = 118 K; mean σ(C–C) = 0.002 Å; R factor = 0.021; wR factor = 0.055; data-to-parameter ratio = 33.3.

The absolute configuration of the title compound, $C_9H_{11}BrN_2O_5$, has been determined. The crystal structure is stabilized by a network of hydrogen bonds in which atoms from both the uracil and deoxyribose moieties of the molecule participate. The stability of the structure is also affected by several short contacts that are formed by O atoms in the carbonyl groups. The original crystal structure determination [Iball, Morgan & Wilson (1966). *Proc. R. Soc. London Ser. A*, **295**, 320–333] was carried out at room temperature and was refined from data measured by photographic methods. The present crystal structure is of significantly higher precision.

Related literature

For related literature, see: Camerman & Trotter (1965); De Boer *et al.* (2003); Iball *et al.* (1966); Kaufman (1962); Kaufman *et al.* (1962); Tamarit *et al.* (2002); Young & Morris (1973); Zhivkova & Stankova (2000).



Experimental

Crystal data

$C_9H_{11}BrN_2O_5$
M_r = 307.10
Monoclinic, $P2_1$
a = 9.159 (1) Å
b = 5.067 (1) Å
c = 12.041 (1) Å
β = 108.27 (2)°
V = 530.64 (13) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 3.89 mm^{-1}
T = 118 (2) K
0.48 × 0.36 × 0.28 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.20, T_{max} = 0.34
50017 measured reflections
5127 independent reflections
5084 reflections with $I > 2\sigma(I)$
R_{int} = 0.040

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.021
$wR(F^2)$ = 0.055
S = 1.04
5127 reflections
154 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.49 e Å^{-3}
$\Delta\rho_{min}$ = −0.71 e Å^{-3}
Absolute structure: Flack (1983), 2325 Friedel pairs
Flack parameter: 0.003 (4)

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

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3···O3′^{i}	0.86	2.11	2.944 (1)	163
O3′—H3″···O4^{ii}	0.82	2.02	2.745 (1)	148
O5′—H5″···O5′^{iii}	0.82	2.21	2.877 (1)	139

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

Data collection: *HKL-2000* (Otwinowski & Minor, 1997); cell refinement: *HKL-2000*; data reduction: *HKL-2000*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990) and *HKL-3000SM* (Minor *et al.*, 2006); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997) and *HKL-3000SM*; molecular graphics: *HKL-3000SM*, *Mercury* (Macrae *et al.*, 2006), *ORTEPIII* (Burnett & Johnson, 1996) and *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *HKL-3000SM*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH2504).

References

Burnett, M. N. & Johnson, C. K. (1996). *ORTEPIII*. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.
Camerman, N. & Trotter, J. (1965). *Acta Cryst.* **18**, 203–211.
De Boer, R. J., Mohri, H., Ho, D. D. & Perelson, A. S. (2003). *Proc. R. Soc. London*, **270**, 849–858.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Iball, J., Morgan, C. H. & Wilson, H. R. (1966). *Proc. R. Soc. London Ser. A*, **295**, 320–333.
Kaufman, H. E. (1962). *Proc. Soc. Exptl Biol. Med.* p. 251.
Kaufman, H. E., Nesburn, A. B. & Maloney, E. D. (1962). *Arch. Ophthalmol.* **67**, 583.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
Minor, W., Cymborowski, M., Otwinowski, Z. & Chruszcz, M. (2006). *Acta Cryst.* D**62**, 859–866.
Otwinowski, Z., Borek, D., Majewski, W. & Minor, W. (2003). *Acta Cryst.* A**59**, 228–234.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
Tamarit, A., Aberola, J., Galindo, M. J. & Navarro, D. (2002). *J. Virol. Methods*, **105**, 247–251.
Young, D. W. & Morris, E. M. (1973). *Acta Cryst.* B**29**, 1259–1264.
Zhivkova, Z. & Stankova, I. (2000). *Int. J. Pharm.* **200**, 181–185.

supplementary materials

Acta Cryst. (2007). E**63**, o4159-o4160 [**doi:10.1107/S1600536807046077**]

Absolute configuration from a redetermination of (+)-5-bromo-1-[(2*R*,4*S*,5*R*)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]pyrimidine-2,4-dione at 118 (2) K

P. Sledz, M. Chruszcz and W. Minor

Comment

5-Bromo-2'-deoxyuridine (BDU, I), together with its iodine analogue, are useful in treating the viral disease herpes simplex (HSV) without causing any damage to the host (Kaufman *et al.*, 1962; Kaufman, 1962). BDU and other thymidine analogues have found application not only in the treatment of HSV, but also other viruses like varicella zoster virus (VZV), cytomegalovirus (CMV) and Epstein-Barr virus (EBV) (Zhivkova & Stankova, 2000). Moreover, BDU is used as a molecular tracer in measuring and indicating the presence of HIV-1 and SIV viruses (Tamarit *et al.*, 2000; De Boer *et al.*, 2003). Therefore determination of the absolute configuration of BDU is important for better understanding of the molecular interactions responsible for the antiviral activity. The structural data may also help in the design of other antiviral compounds.

The room temperature structure has been previously reported (Iball *et al.*, 1966). The structure reported here was determined at 118 K and its absolute configuration was elucidated. The title compound crystallizes in the $P2_1$ space group with one molecule in the asymmetric unit (Fig. 1). The packing in the crystal structure (Fig. 2) is very similar to the one observed in an analogous compound with chlorine substituted for bromine (Young & Morris, 1973). The iodine analogue crystallized in the triclinic system (Camerman & Trotter, 1965). The crystal lattice of the title compound is densely packed and stabilized by several hydrogen bonds (Table 1, Fig. 2), which results in a rigid structure and diffraction to high resolution. Moreover the crystal is stabilized by multiple short contacts, such as between atoms O1 and C2.

Experimental

(+)-5-Bromo-2'-deoxyuridine (97%) was purchased from Aldrich. The crystal of used for X-ray diffraction study, was obtained by slow evaporation of an ethanol solution of the title compound.

Refinement

All hydrogen atoms were placed in ideal positions and were allowed to refine using the riding model with an isotropic displacement parameter 1.2 times that of the adjacent non-hydrogen atom. The distances were set up as *SHELXL* (Sheldrick, 1997) default values.

Figures

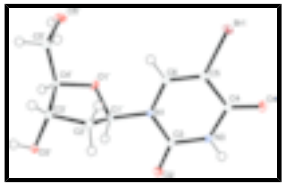

Fig. 1. The molecular structure of the title compound. Displacement ellipsoids are drawn at the 50% probability level and hydrogen atoms are drawn as spheres of an arbitrary radius.

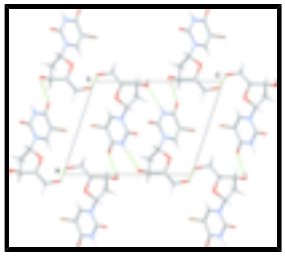

Fig. 2. The molecular packing shown along the [010] axis. Hydrogen bonds are marked in green.

(+)-5-bromo-1-[(2*R*,4S,5*R*)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]- pyrimidine-2,4-dione

Crystal data

$C_9H_{11}BrN_2O_5$	F_{000} = 308
M_r = 307.10	D_x = 1.922 Mg m^{-3}
Monoclinic, $P2_1$	Mo $K\alpha$ radiation λ = 0.71074 Å
Hall symbol: P 2yb	Cell parameters from 50017 reflections
a = 9.159 (1) Å	θ = 3.4–36.3º
b = 5.067 (1) Å	μ = 3.89 mm^{-1}
c = 12.041 (1) Å	T = 118 (2) K
β = 108.27 (2)º	Block, colourless
V = 530.64 (13) Å^3	0.48 × 0.36 × 0.28 mm
Z = 2	

Data collection

Rigaku R-AXIS RAPID diffractometer	5127 independent reflections
Radiation source: fine-focus sealed tube	5084 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.040
Detector resolution: 10 pixels mm^{-1}	θ_{max} = 36.3º
T = 118(2) K	θ_{min} = 3.4º
ω scans with χ offset	h = −15→15
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)	k = −8→8
T_{min} = 0.20, T_{max} = 0.34	l = −20→19
50017 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.021	$w = 1/[\sigma^2(F_o^2) + (0.0319P)^2 + 0.2794P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.055	$(\Delta/\sigma)_{max}$ = 0.001
S = 1.04	$\Delta\rho_{max}$ = 0.49 e Å^{-3}

5127 reflections	$\Delta\rho_{min} = -0.71$ e Å^{-3}
154 parameters	Extinction correction: none
1 restraint	Absolute structure: Flack (1983), 2325 Friedel pairs
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.003 (4)
Secondary atom site location: difference Fourier map	

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
Br1	0.473749 (11)	1.16469 (3)	0.095388 (8)	0.01312 (3)
N3	0.66121 (10)	0.6900 (3)	0.37944 (8)	0.01119 (16)
H3	0.7508	0.6643	0.4291	0.013*
N1	0.40144 (11)	0.5755 (2)	0.30904 (9)	0.00981 (14)
O1'	0.17705 (10)	0.3420 (2)	0.21144 (8)	0.01273 (15)
C3'	0.02368 (12)	0.4037 (2)	0.33875 (10)	0.01077 (16)
H3'	−0.0702	0.5045	0.3315	0.013*
O3'	0.04776 (10)	0.2022 (2)	0.42633 (8)	0.01338 (17)
H3"	−0.0255	0.1003	0.4087	0.016*
C1'	0.27203 (12)	0.4251 (2)	0.32355 (9)	0.00976 (16)
H1'	0.3110	0.2701	0.3725	0.012*
C4'	0.02472 (12)	0.2945 (2)	0.21923 (10)	0.00998 (16)
H4'	0.0046	0.1042	0.2159	0.012*
C4	0.65106 (13)	0.8828 (3)	0.29697 (10)	0.01201 (17)
C6	0.38024 (12)	0.7642 (2)	0.22349 (10)	0.01052 (16)
H6	0.2825	0.7900	0.1708	0.013*
C2	0.54369 (12)	0.5328 (2)	0.39153 (10)	0.01011 (16)
O2	0.56615 (11)	0.3696 (2)	0.46919 (9)	0.01548 (16)
C5	0.49829 (13)	0.9133 (2)	0.21428 (9)	0.01099 (16)
O5'	−0.06987 (12)	0.3682 (2)	0.00909 (8)	0.01670 (16)
H5"'	−0.0772	0.2083	−0.0017	0.025*
C2'	0.16485 (13)	0.5801 (2)	0.37371 (10)	0.01131 (16)
H2'	0.2069	0.5978	0.4580	0.014*
H2"	0.1426	0.7538	0.3386	0.014*
O4	0.76514 (12)	1.0107 (2)	0.29704 (10)	0.01909 (19)
C5'	−0.09319 (14)	0.4298 (3)	0.11780 (10)	0.01425 (19)
H5'	−0.1955	0.3745	0.1154	0.017*

H5"	−0.0862	0.6193	0.1297	0.017*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Br1	0.01537 (4)	0.01416 (4)	0.01014 (4)	−0.00113 (5)	0.00447 (3)	0.00256 (4)
N3	0.0069 (3)	0.0154 (5)	0.0102 (3)	−0.0010 (3)	0.0012 (2)	0.0013 (3)
N1	0.0067 (3)	0.0133 (3)	0.0089 (3)	−0.0016 (3)	0.0017 (3)	0.0012 (3)
O1'	0.0078 (3)	0.0210 (4)	0.0096 (3)	−0.0029 (3)	0.0031 (2)	−0.0052 (3)
C3'	0.0083 (4)	0.0142 (4)	0.0097 (4)	−0.0010 (3)	0.0027 (3)	−0.0003 (3)
O3'	0.0108 (3)	0.0184 (5)	0.0097 (3)	−0.0048 (3)	0.0015 (2)	0.0028 (3)
C1'	0.0077 (4)	0.0125 (4)	0.0089 (4)	−0.0020 (3)	0.0023 (3)	−0.0005 (3)
C4'	0.0075 (3)	0.0128 (4)	0.0086 (4)	−0.0021 (3)	0.0010 (3)	−0.0008 (3)
C4	0.0100 (4)	0.0158 (5)	0.0098 (4)	−0.0025 (3)	0.0025 (3)	0.0007 (3)
C6	0.0085 (4)	0.0136 (4)	0.0087 (4)	−0.0004 (3)	0.0017 (3)	0.0011 (3)
C2	0.0074 (4)	0.0131 (4)	0.0096 (4)	−0.0001 (3)	0.0023 (3)	0.0005 (3)
O2	0.0103 (3)	0.0180 (4)	0.0162 (4)	0.0006 (3)	0.0014 (3)	0.0075 (3)
C5	0.0101 (4)	0.0136 (4)	0.0084 (4)	−0.0004 (3)	0.0017 (3)	0.0014 (3)
O5'	0.0193 (4)	0.0206 (4)	0.0089 (3)	−0.0012 (3)	0.0027 (3)	−0.0009 (3)
C2'	0.0105 (4)	0.0129 (4)	0.0111 (4)	−0.0020 (3)	0.0042 (3)	−0.0026 (3)
O4	0.0116 (4)	0.0262 (5)	0.0175 (4)	−0.0077 (3)	0.0016 (3)	0.0059 (4)
C5'	0.0117 (4)	0.0199 (5)	0.0099 (4)	0.0021 (4)	0.0016 (3)	0.0011 (4)

Geometric parameters (Å, °)

Br1—C5	1.8765 (11)	C1'—H1'	0.9800
N3—C4	1.3752 (17)	C4'—C5'	1.5169 (17)
N3—C2	1.3830 (15)	C4'—H4'	0.9800
N3—H3	0.8600	C4—O4	1.2293 (14)
N1—C6	1.3742 (15)	C4—C5	1.4490 (16)
N1—C2	1.3855 (14)	C6—C5	1.3515 (16)
N1—C1'	1.4647 (14)	C6—H6	0.9300
O1'—C1'	1.4213 (14)	C2—O2	1.2163 (15)
O1'—C4'	1.4476 (14)	O5'—C5'	1.4252 (16)
C3'—O3'	1.4345 (15)	O5'—H5"'	0.8200
C3'—C2'	1.5188 (16)	C2'—H2'	0.9700
C3'—C4'	1.5448 (16)	C2'—H2"	0.9700
C3'—H3'	0.9800	C5'—H5'	0.9700
O3'—H3"	0.8200	C5'—H5"	0.9700
C1'—C2'	1.5221 (16)		
C4—N3—C2	127.34 (9)	O4—C4—N3	120.59 (11)
C4—N3—H3	116.3	O4—C4—C5	125.57 (12)
C2—N3—H3	116.3	N3—C4—C5	113.83 (10)
C6—N1—C2	121.76 (10)	C5—C6—N1	121.45 (10)
C6—N1—C1'	121.46 (9)	C5—C6—H6	119.3
C2—N1—C1'	116.58 (10)	N1—C6—H6	119.3
C1'—O1'—C4'	107.65 (8)	O2—C2—N3	121.51 (10)
O3'—C3'—C2'	107.09 (9)	O2—C2—N1	123.49 (11)

O3'—C3'—C4'	112.66 (10)	N3—C2—N1	115.00 (10)
C2'—C3'—C4'	102.46 (9)	C6—C5—C4	120.61 (10)
O3'—C3'—H3'	111.4	C6—C5—Br1	122.30 (8)
C2'—C3'—H3'	111.4	C4—C5—Br1	117.10 (8)
C4'—C3'—H3'	111.4	C5'—O5'—H5"'	109.5
C3'—O3'—H3"	109.5	C3'—C2'—C1'	100.68 (9)
O1'—C1'—N1	108.55 (9)	C3'—C2'—H2'	111.6
O1'—C1'—C2'	104.53 (9)	C1'—C2'—H2'	111.6
N1—C1'—C2'	115.19 (10)	C3'—C2'—H2"	111.6
O1'—C1'—H1'	109.5	C1'—C2'—H2"	111.6
N1—C1'—H1'	109.5	H2'—C2'—H2"	109.4
C2'—C1'—H1'	109.5	O5'—C5'—C4'	111.51 (10)
O1'—C4'—C5'	109.27 (9)	O5'—C5'—H5'	109.3
O1'—C4'—C3'	106.75 (8)	C4'—C5'—H5'	109.3
C5'—C4'—C3'	112.17 (10)	O5'—C5'—H5"	109.3
O1'—C4'—H4'	109.5	C4'—C5'—H5"	109.3
C5'—C4'—H4'	109.5	H5'—C5'—H5"	108.0
C3'—C4'—H4'	109.5		
C4'—O1'—C1'—N1	−156.77 (9)	C4—N3—C2—N1	1.11 (18)
C4'—O1'—C1'—C2'	−33.36 (12)	C6—N1—C2—O2	179.12 (12)
C6—N1—C1'—O1'	44.95 (14)	C1'—N1—C2—O2	4.17 (18)
C2—N1—C1'—O1'	−140.08 (11)	C6—N1—C2—N3	−1.13 (17)
C6—N1—C1'—C2'	−71.81 (14)	C1'—N1—C2—N3	−176.09 (10)
C2—N1—C1'—C2'	103.16 (12)	N1—C6—C5—C4	−1.67 (18)
C1'—O1'—C4'—C5'	131.84 (10)	N1—C6—C5—Br1	177.99 (9)
C1'—O1'—C4'—C3'	10.32 (12)	O4—C4—C5—C6	−178.98 (13)
O3'—C3'—C4'—O1'	−98.19 (10)	N3—C4—C5—C6	1.47 (17)
C2'—C3'—C4'—O1'	16.54 (12)	O4—C4—C5—Br1	1.34 (18)
O3'—C3'—C4'—C5'	142.16 (10)	N3—C4—C5—Br1	−178.21 (9)
C2'—C3'—C4'—C5'	−103.11 (11)	O3'—C3'—C2'—C1'	83.90 (10)
C2—N3—C4—O4	179.17 (13)	C4'—C3'—C2'—C1'	−34.83 (11)
C2—N3—C4—C5	−1.25 (18)	O1'—C1'—C2'—C3'	42.75 (11)
C2—N1—C6—C5	1.51 (18)	N1—C1'—C2'—C3'	161.76 (9)
C1'—N1—C6—C5	176.22 (11)	O1'—C4'—C5'—O5'	49.61 (13)
C4—N3—C2—O2	−179.14 (13)	C3'—C4'—C5'—O5'	167.79 (10)

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···O3'^{i}	0.86	2.11	2.944 (1)	163
O3'—H3"···O4^{ii}	0.82	2.02	2.745 (1)	148
O5'—H5"'···O5'^{iii}	0.82	2.21	2.877 (1)	139

Symmetry codes: (i) −*x*+1, *y*+1/2, −*z*+1; (ii) *x*−1, *y*−1, *z*; (iii) −*x*, *y*−1/2, −*z*.

Fig. 1

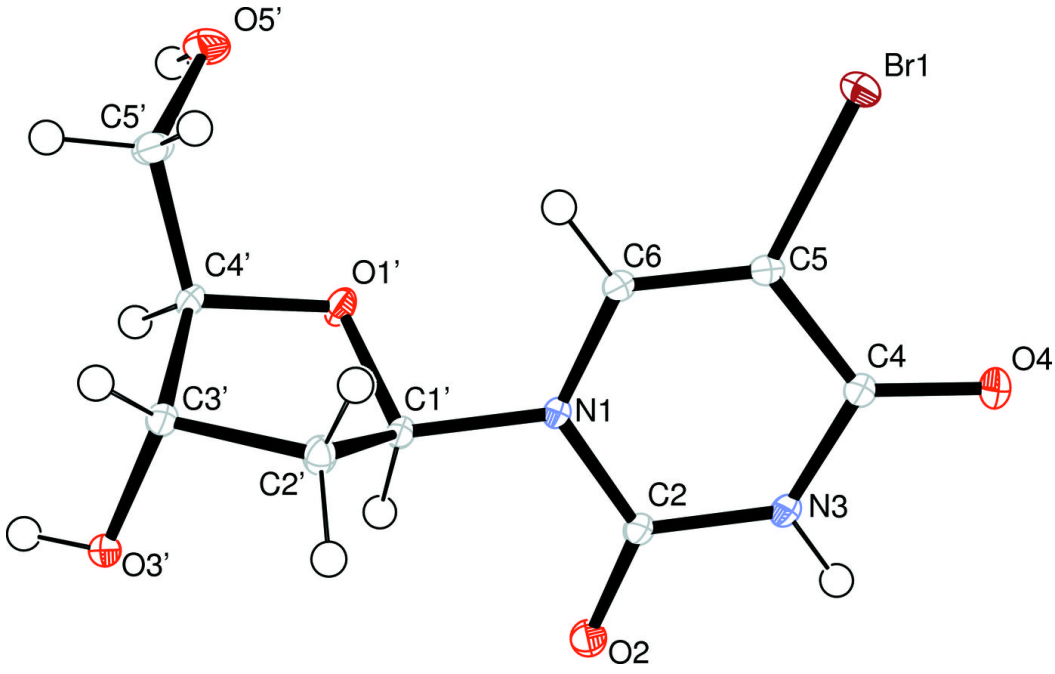

Fig. 2