

## 3,4-Dihydro-6-methyl-3- $\beta$ -D-ribofuranosyl-4,5'-cyclo-9H-imidazo[1,2-a]purin-9-one hydrate<sup>1</sup>

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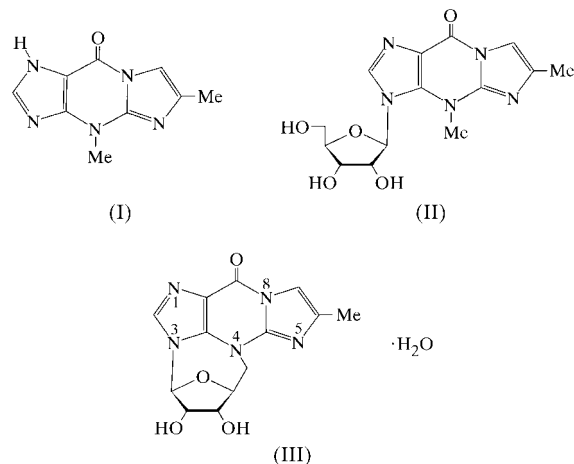
In the title compound, C<sub>13</sub>H<sub>13</sub>N<sub>5</sub>O<sub>4</sub>·H<sub>2</sub>O (4,5'-cyclo-wyosine·H<sub>2</sub>O), the cyclization forces a *syn* arrangement of the aglycon with respect to the sugar moiety. The ribofuranose part of the molecule displays a  $\beta$ -D configuration with an envelope C1'-*endo* pucker. The molecules are arranged in columns along the short *a* axis and are linked to water molecules through O—H···O and O—H···N hydrogen bonds.

### Comment

Intramolecularly cyclized nucleosides and nucleotides have been the focus of much attention as useful models for studies of the stereochemistry of nucleic acids (Mizuno, 1986; Maruyama *et al.*, 1988; Yoshimura *et al.*, 1992, and references therein). Wye (Y or Yt base), (I), is the base of the nucleoside wyosine (Yt), (II). Recently, the structures of wyosine, wybutosine and  $\beta$ -hydroxywybutosine, as a rare nucleoside isolated from yeast tRNA<sup>Phe</sup>, have been unambiguously assigned by chemical means (Itaya & Kanai, 1999). Since the highly fluorescent and structurally unique wye can be selectively excized from the oligonucleotide of its anticodon region (Eisinger *et al.*, 1971), it is a specific example where just one nucleoside can be split off at its *N*-glycosidic bond. The structure of aglycon wye has also been determined crystallographically (Nygiert *et al.*, 1975)

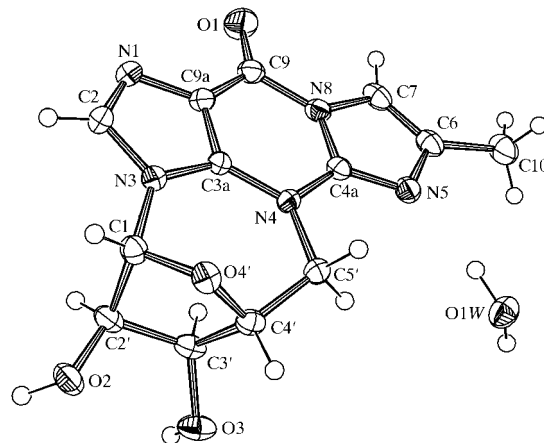
A common feature of wye nucleosides is their unusual susceptibility to acidic hydrolysis (Itaya & Kanai, 1999). However, 4,5'-cyclo-wyosine hydrate, (III), possesses a hydrolytic stability comparable to that of guanosine; the same is true

of 3,5'-cycloguanosine. The large reactivity difference between (II) and (III) may be attributed to the fixation of torsion angles in the sugar moiety and consequently to the anticipated planarity of the imidazo[1,2-*a*]purine ring. In contrast, in the *anti* orientation, the extended form of the molecule is more susceptible to solvation by water molecules (Seela & Bussmann, 1985).



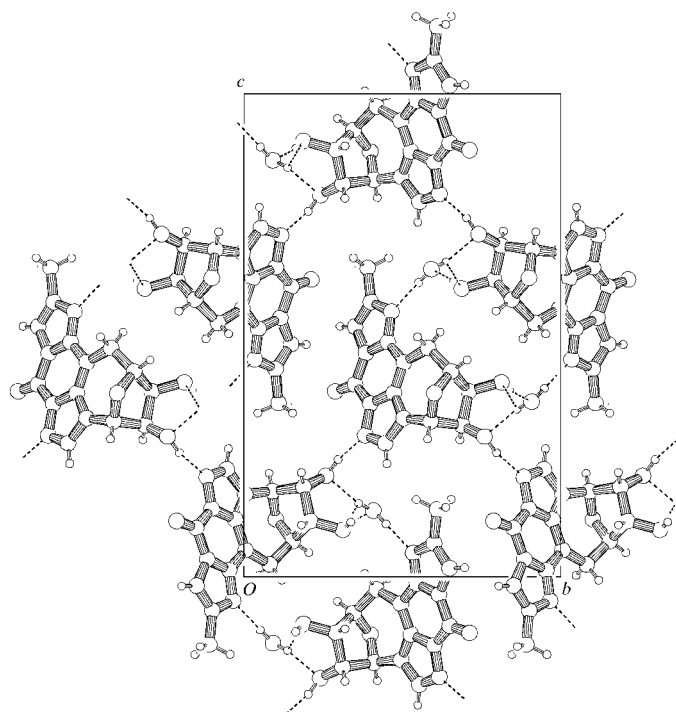
A pre-check using the Cambridge Structural Database (Release 5.2.1, April 2001; Allen & Kennard, 1993) gave no results of structural work on nucleosides with wye (I) as the aglycon moiety. Therefore, to the best of our knowledge, this paper provides the first accurate structural parameters for 4,5'-cyclo-wyosine (3,4-dihydro-6-methyl-3- $\beta$ -D-ribofuranosyl-4,5'-cyclo-9H-imidazo[1,2-*a*]purin-9-one) hydrate, (III), and confirms the prediction by Reese & Whittall (1976) and Seela & Bussmann (1985) based on the chemical evidence. However, the molecule crystallizes with one water molecule in the asymmetric unit (Fig. 1 and Table 1).

The orientation of the heterocyclic base wye relative to the sugar moiety is *syn*, as determined by the torsion angle about the *N*-glycosidic bond (Sundaralingam, 1975; IUPAC-IUB Joint Commission on Biochemical Nomenclature, 1983). The appropriate torsion angles O4'—C1'—N3—C2 and O4'—



**Figure 1**  
ORTEPII (Johnson, 1971) view of the title molecule with the atomic numbering. Displacement ellipsoids are drawn at the 30% probability level.

<sup>1</sup> Systematic name: 2,4-ethano-15,16-dihydroxy-12-methyl-1,2-dihydro-1,3,5-oxadiazepino[3,4,5-*ci*]imidazo[1,2-*a*]purin-9(4H)-one hydrate.



**Figure 2**  
PLUTON (Spek, 1991) view of the packing of the unit cell along the short *a* axis.

$C1'-N3-C3a$  in this study are  $-151.7(2)$  and  $38.0(2)^\circ$ , respectively. The ribofuranose moiety exhibits a  $\beta$ -D configuration with an envelope  $C1'$ -endo pucker. The conformation about the  $C4'-C5'$  bond [torsion angle  $O4'-C4'-C5'-N4 -63.5(2)^\circ$ ] is in the *gauche* range. The Cremer–Pople (Cremer & Pople, 1975) puckering parameters  $q_2$  and  $\varphi_2$  are  $0.380(2) \text{ \AA}$  and  $223.2(3)^\circ$ , respectively (Spek, 1998; Farrugia, 2000). The bond lengths and angles are normal and in agreement with the values reported for related compounds. The bond lengths of the aglycon moiety (wye) [ $C3a-C9a$   $1.380(2) \text{ \AA}$ ,  $C6-C7$   $1.355(2) \text{ \AA}$ ,  $N1-C2$   $1.306(2) \text{ \AA}$  and  $C4a-N5$   $1.312(2) \text{ \AA}$ ] suggest some double-bond character. The dihedral angles between the planes defined by atoms  $N1/C2/N3/C3a/C9a$  (plane *A*),  $C3a/N4/C4a/N8/C9$  (plane *B*) and  $C4a/N5/C6/C7/N8$  (plane *C*) are  $A/B$   $2.1(1)^\circ$  and  $B/C$   $3.9(1)^\circ$ . The overall geometry of the wye entity is very similar to that found in the structure of the Yt base (Nygjerd *et al.*, 1975). The bond distances in both structures were checked by a one-parameter significance test,  $t_0$  (Cruickshank & Robertson, 1953). For bond lengths, the mean value was 0.8, which implies that the distances are not significantly different in both structures. Only the distances  $N1-C2$  and  $C2-N3$  differ, because a wye moiety is linked to the sugar part and there is no H atom attached to  $N1$ .

The OH groups of the ribofuranose part, the N atoms of the wye entity and a water molecule are involved in a system of hydrogen bonds (Table 2) of the  $O-H \cdots O$  and  $O-H \cdots N$  types. One water H atom forms a nearly linear hydrogen bond to the  $N5$  atom of the wye unit, whilst the second water H atom is linked to the  $O2$  atom of a neighbouring molecule. The hydroxyl H atoms attached to atoms  $O2$  and  $O3$  are connected

to atom  $N1$  and the water molecule, respectively. There are also three weak  $C-H \cdots O$  interactions. The molecules are stacked in a columnar arrangement parallel to the short *a* axis ( $4.921 \text{ \AA}$ ), as is shown in Fig. 2.

## Experimental

The title compound was synthesized independently in two laboratories at a time when compound (II) was not synthetically available (Reese & Whittall, 1976; Kasai *et al.*, 1976). The procedure of Reese & Whittall (1976) was used in the present case and the compound obtained was recrystallized from acetonitrile.

### Crystal data

$C_{13}H_{13}N_5O_4 \cdot H_2O$   
 $M_r = 321.30$   
 Orthorhombic,  $P2_12_12_1$   
 $a = 4.9211(1) \text{ \AA}$   
 $b = 13.3792(2) \text{ \AA}$   
 $c = 20.5881(4) \text{ \AA}$   
 $V = 1355.53(4) \text{ \AA}^3$   
 $Z = 4$   
 $D_x = 1.574 \text{ Mg m}^{-3}$   
 $D_m = 1.56(5) \text{ Mg m}^{-3}$

Density measured by flotation in bromobenzene/carbon tetrachloride  
 Mo  $K\alpha$  radiation  
 Cell parameters from 2371 reflections  
 $\theta = 3-25^\circ$   
 $\mu = 0.12 \text{ mm}^{-1}$   
 $T = 200(2) \text{ K}$   
 Plate, colourless  
 $0.33 \times 0.28 \times 0.22 \text{ mm}$

### Data collection

Nonius KappaCCD diffractometer  
 $\omega$  scans  
 3821 measured reflections  
 2331 independent reflections  
 2157 reflections with  $I > 2\sigma(I)$

$R_{int} = 0.014$   
 $\theta_{max} = 30.5^\circ$   
 $h = -6 \rightarrow 6$   
 $k = -18 \rightarrow 18$   
 $l = -29 \rightarrow 29$

### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.034$   
 $wR(F^2) = 0.080$   
 $S = 1.04$   
 2331 reflections  
 226 parameters  
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0374P)^2 + 0.3423P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{max} = 0.001$   
 $\Delta\rho_{max} = 0.23 \text{ e \AA}^{-3}$   
 $\Delta\rho_{min} = -0.19 \text{ e \AA}^{-3}$   
 Extinction correction: SHELXL97  
 Extinction coefficient:  $0.019(3)$

**Table 1**

Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ ).

$C1'-O4'$	1.4043 (19)	$N3-C3a$	1.3706 (19)
$C1'-N3$	1.467 (2)	$C3a-N4$	1.3742 (18)
$C1'-C2'$	1.532 (2)	$C3a-C9a$	1.380 (2)
$C2'-O2$	1.4071 (19)	$N4-C4a$	1.3771 (19)
$C2'-C3'$	1.549 (2)	$C4a-N5$	1.3117 (18)
$C3'-O3$	1.4161 (18)	$C4a-N8$	1.377 (2)
$C3'-C4'$	1.539 (2)	$N5-C6$	1.395 (2)
$C4'-O4'$	1.4463 (19)	$C6-C7$	1.355 (2)
$C4'-C5'$	1.508 (2)	$C6-C10$	1.493 (2)
$C5'-N4$	1.4731 (19)	$C7-N8$	1.400 (2)
$N1-C2$	1.306 (2)	$N8-C9$	1.4128 (19)
$N1-C9a$	1.3862 (18)	$C9-O1$	1.217 (2)
$C2-N3$	1.3808 (19)	$C9-C9a$	1.423 (2)
$O4'-C1'-C2'-O2$	77.94 (15)	$O3-C3'-C4'-C5'$	111.86 (15)
$N3-C1'-C2'-O2$	-163.82 (12)	$C2'-C3'-C4'-C5'$	-125.62 (13)
$O4'-C1'-C2'-C3'$	-39.75 (15)	$N3-C1'-O4'-C4'$	-81.63 (14)
$N3-C1'-C2'-C3'$	78.49 (14)	$C2'-C1'-O4'-C4'$	38.91 (15)
$O2-C2'-C3'-O3$	29.3 (2)	$C5'-C4'-O4'-C1'$	103.27 (14)
$C1'-C2'-C3'-O3$	143.13 (14)	$C3'-C4'-O4'-C1'$	-21.60 (15)
$O2-C2'-C3'-C4'$	-88.50 (15)	$O4'-C4'-C5'-N4$	-63.47 (17)
$C1'-C2'-C3'-C4'$	25.31 (15)	$C3'-C4'-C5'-N4$	56.94 (18)
$O3-C3'-C4'-O4'$	-126.53 (13)	$O4'-C1'-N3-C3a$	38.0 (2)
$C2'-C3'-C4'-O4'$	-4.01 (15)	$O4'-C1'-N3-C2$	-151.65 (15)

**Table 2**  
Hydrogen-bonding geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
O1W—H1W...N5	0.91 (3)	1.98 (3)	2.890 (2)	179 (2)
O1W—H2W...O2 <sup>i</sup>	0.91 (3)	1.95 (3)	2.808 (2)	158 (2)
O1W—H2W...O3 <sup>i</sup>	0.91 (3)	2.44 (3)	3.051 (2)	125 (2)
O2—H2O...N1 <sup>ii</sup>	0.94 (3)	1.85 (3)	2.770 (2)	166 (2)
O3—H3O...O1W <sup>i</sup>	0.84 (3)	1.91 (3)	2.743 (2)	170 (2)
C2—H2A...O1W <sup>iii</sup>	0.95	2.27	3.187 (2)	161
C3'—H3...O4 <sup>iv</sup>	1.00	2.37	3.350 (2)	164
C10—H10C...O1 <sup>v</sup>	0.98	2.44	3.162 (3)	130

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

All H atoms were found in a difference electron-density map and were placed at calculated positions (C—H = 0.95–1.00 Å), with isotropic displacement parameters taken from the adjacent atom multiplied by 1.2 (1.5 for methyl), except for the hydroxyl and water H atoms, which were freely refined. In the absence of suitable anomalous scatterers of Mo  $K\alpha$  radiation, the determination of the absolute configuration was not possible from the X-ray data. The absolute configuration was assigned to agree with the known chirality of the ribofuranose moiety and the Friedel diffraction data were merged accordingly.

Data collection: *KappaCCD Reference Manual* (Nonius, 1998); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1971), *PLATON* (Spek, 1998) and *ORTEP-3* (Farrugia, 1999); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1488). Services for accessing these data are described at the back of the journal.

## References

- Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 1, 31–37.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- Cruickshank, D. W. J. & Robertson, A. P. (1953). *Acta Cryst.* **6**, 698–705.
- Eisinger, J., Feuer, B. & Yamane, T. (1971). *Nature New Biol.* **231**, 126–128.
- Farrugia, L. J. (1999). *ORTEP-3 for Windows*. Version 1.05. University of Glasgow, Scotland.
- Farrugia, L. J. (2000). *PLATON for 32-bit Windows*. University of Glasgow, Scotland.
- Itaya, T. & Kanai, T. (1999). *Tetrahedron Lett.* **40**, 8003–8006.
- IUPAC-IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.
- Johnson, C. K. (1971). *ORTEPII*. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee, USA.
- Kasai, H., Goto, M., Ikeda, K., Zama, M., Mizuno, Y., Takemura, S., Matsuura, S., Sugimoto, T. & Goto, T. (1976). *Biochemistry*, **15**, 898–904.
- Maruyama, T., Adachi, Y. & Honjo, M. (1988). *J. Org. Chem.* **53**, 4552–4555.
- Mizuno, Y. (1986). *The Organic Chemistry of Nucleic Acids*, pp. 113–133. Amsterdam: Elsevier.
- Nonius (1998). *KappaCCD Reference Manual*. Nonius BV, Delft, The Netherlands.
- Nygjerd, G., McAlister, J., Sundaralingam, M. & Matsuura, S. (1975). *Acta Cryst.* **B31**, 413–417.
- Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter & R. M. Sweet, pp. 307–326. London: Academic Press.
- Reese, C. B. & Whittall, N. (1976). *Nucleic Acids Res.* **4**, 3439–3445.
- Seela, F. & Bussmann, W. (1985). *Tetrahedron*, **41**, 935–940.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Spek, A. L. (1991). *PLUTON*. University of Utrecht, The Netherlands.
- Spek, A. L. (1998). *PLATON*. University of Utrecht, The Netherlands.
- Sundaralingam, M. (1975). *Ann. New York Acad. Sci.* **255**, 3–42.
- Yoshimura, Y., Otter, B. A., Ueda, T. & Matsuda, A. (1992). *Chem. Pharm. Bull.* **40**, 1761–1769.