(II) are close to those of benzamide (Blake & Small, 1972). A short intramolecular S···O contact was also observed between S(1) and O(2) of the amide group. The S(1)···O(2) distance is 2·717 Å, which is shorter than the corresponding value of (I). In this case, O(2), S(1) and O(1) are also arranged linearly. The dihedral angle between the phenyl group, C(1)–C(6), and the amide plane is 20·0 (1)°.

Molecules are linked by the hydrogen bonds between O(1) of the sulfoxide and the N—H of the amide group at (i) $= \frac{1}{2}-x, y, \frac{1}{2}+z$, forming a zigzag chain along the c axis as shown in Fig. 3. The O(1)···N(1^{i}) distance is 2·851 Å and the O atom of the amide group is not bifurcated.

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Structures of 5-Bromo-6-ethoxy-5,6-dihydrouridine and -thymidine Derivatives, a Class of Potential Antitumoral and Antiviral *N*-Nucleosides

BY G. BERNARDINELLI

Laboratoire de Cristallographie aux rayons X, Université de Genève, 24 quai Ernest Ansermet, CH-1211 Genève 4, Switzerland

AND R. BENHAMZA AND J. M. J. TRONCHET

Institut de Chimie Pharmaceutique de l'Université, Sciences II, CH-1211 Genève 8, Switzerland

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Abstract. (I): (+)-(5*R*,6*R*)-5-Bromo-6-ethoxy-5,6-dihydro-2′,3′-isopropylidene-β-D-ribofuranosyl-uracil, $C_{14}H_{21}BrN_2O_7$, m.p. 408·7–409·6 K, $[\alpha]_D^{23°C}$ = +31·1° (c = 1·2% in MeOH), M_r = 409·2, monoclinic, $P2_1$, a = 9·218 (2), b = 9·6619 (11), c = 10·4938 (14) Å, β = 99·305 (8)°, V = 922·4 (2) Å^3, Z = 2, D_x = 1·47 Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ = 2·24 mm^{-1}, F(000) = 420, room temperature, R (= wR) = 0·046 for 2595 observed reflections [$|F_o| > 4\sigma(F_o)$ and $|F_o| > 8·0$]. (II): (+)-(5*R*,6*R*)-5-Bromo-2′-deoxy-6-ethoxy-5,6-dihydro-β-D-ribofuranosyl-thymine, $C_{12}H_{19}BrN_2O_6$, m.p. 376·1–376·5 K, $[\alpha]_D^{23°C}$ = +58·8° (c = 1·02% in MeOH), M_r = 367·2, monoclinic, $P2_1$, a = 6·0428 (9), b = 8·5270 (15), c = 14·589 (2) Å, β = 96·80 (1)°, V = 746·4 (1) Å^3, Z = 2, D_x = 1·63 Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ = 2·75 mm^{-1}, F(000) = 376, room temperature, R = 0·053 (wR = 0·040) for 1579 observed reflections [$|F_o| > 4\sigma(F_o)$]. Both furanose rings adopt an envelope conformation with C(4′)-*exo* and C(1′)-*exo* for (I) and (II) respectively. The orientation of the dihydropyrimidine base relative to the sugar ring shows an unusual *syn* conformation [χ_{CN} = 62·5 (6)°] for (I) whereas the glycosyl linkage of compound (II) shows an *anti* conformation [χ_{CN} = −134·0 (8)°]. In both compounds the pyrimidine ring displays a half-chair form. The conformation of the hydroxymethyl group at C(4′) is *gauche–gauche* for (I) [φ_{OO} = −68·2 (7)°, φ_{OC} = 50·1 (8)°] and *trans–gauche* for (II) [φ_{OO} = 180 (1)°, φ_{OC} = −61 (1)°]. The absolute configuration of (I) was confirmed by least-squares refinement of x [x = 0·008 (16)] [Bernardinelli & Flack (1985). *Acta Cryst.* A**41**, 500–511] and that of compound (II) deduced from the starting material.

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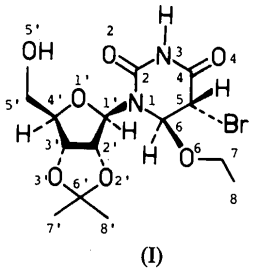
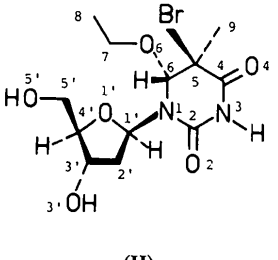
An intramolecular hydrogen bond occurs between the hydroxymethyl and the pyrimidine of (I). In both structures, the molecular packing is fixed by a network of hydrogen bonds.

Introduction. 5-Halogenopyrimidine and 5,6-dihydropyrimidine bases and their corresponding nucleosides represent a class of potential antitumoral and antiviral drugs (Miyashita, Matusmura, Shimadzu & Hashimoto, 1981; Heidelberger, 1970; Danenberg & Heidelberger, 1976). For example, (II) showed a significant (MIC_{50} 1·5 μM) selective antiviral activity against cytomegalovirus, whereas de-*O*-isopropylidenated (I) and its 6-alkoxy homologs were active, either against HIV (6-butoxy, 25% inhibition, 0·55 μ *M*), or herpes virus (6-methoxy, total inhibition at 85 μ *M*; 6-ethoxy and 6-propoxy, partial inhibition at 81 and 157 μ *M* respectively) (Tronchet, Benhamza & Zerial, unpublished results). The 5-halogeno-5,6-dihydropyrimidine derivatives have been used in the structural analysis of radiation-induced damage in nucleic acids (Cadet & Teoule, 1972). They were also considered as being a new class of masked 5-halogenopyrimidines (Miyashita, Kasahara, Matsumura, Shimadzu, Takamoto & Hashimoto, 1982) and so as a potential class of prodrugs.

We describe here the X-ray analysis of two 5-bromo-6-alkoxy-5,6-dihydropyrimidic nucleosides, for which the absolute configuration of the substituents in the pyrimidine ring was unknown.



(I)



(II)

Experimental. Experimental data and structure refinement are summarized in Table 1. Synthesis of (I) and (II) was conducted in ethanol from the corresponding nucleosides (uridine and thymidine) in the presence of Bu_2SnO (one equivalent) (Tronchet, Mekhael, Graf-Poncet, Benhamza & Geoffroy, 1985). Addition of bromine (concentrated or diluted in CH_2Cl_2) until persistence of the yellowish coloration of the bromine excess, evaporation and purification through silica-gel chromatography produced pure samples of compounds (I) and (II). Single crystals were grown at room temperature from EtOAc and EtOH [for compounds (I) and (II) respectively] solutions. Philips PW 1100 diffractometer, graphite-monochromated Mo $K\alpha$; $\omega/2\theta$ scans; two standard reflections, varied by $< 2\sigma(I)$, Lorentz–polarization; no absorption correction; systematic absences $0k0$: $k = 2n + 1$; structure solved by *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). Full-matrix least squares using $|F|$ values. No secondary-extinction correction. Scattering factors from Cromer & Mann (1968), and anomalous-dispersion corrections for Br atoms from *International Tables for X-ray Crystallography* (1974). All coordinates of H atoms were calculated except for the hydroxyl groups of (II) where the H atoms were located from a difference electron density map and refined. The H atom of the hydroxyl group of (I) was not observed. All calculations performed with a local version of *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) for compound (I) and *XTAL* (Hall & Stewart, 1987) for compound (II). Definition of polar origin: (I) $\sum y_i =$ constant applied as a shift-limiting restraint; (II) $y(\mathrm{Br}) = 0$ applied as a hard constraint.

Table 1. *Summary of crystal data, intensity measurement and structure refinement*

	(I)	(II)
Crystal size (mm)	0·15 × 0·25 × 0·27	0·10 × 0·18 × 0·30
Unit-cell determination*		
No. of reflections	20	22
2θ range (°)	22–37	24–38
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0·595	0·617
h, *k*, *l* ranges	−10,10; 0,11; 0,12 and all antirefl.	−7,7; 0,10; 0,18 and all antirefl.
No. of measured refl.	3692	3272
No. of observed refl.	2595	2726
R_{int} for equiv. refl.	0·018	0·028
Criterion for observed refl.	$\lvert F_o\rvert > 4\sigma(F_o)$ and $\lvert F_o\rvert > 8$	$\lvert F_o\rvert > 4\sigma(F_o)$
Refinement (on *F*)	Full matrix	Full matrix
No. of parameters	218	189
Weighting scheme	$w = 1$	$w = 1/\sigma^2(F_o)$
Max. and average Δ/σ	0·034, 0·003	0·052, 0·009
Max. and min. $\Delta\rho$ (e Å^{-3})	0·42, −0·57	0·90, −0·88
S	3·62	2·57
R, *wR* (%)	4·6, 4·6	5·3, 4·0

* Unit cell determined by least-squares fit.

Discussion. Final positional parameters are given in Table 2.* Bond distances are reported in Table 3 and relevant conformational parameters are to be found in Table 4. The absolute configurations of the molecules are shown in Fig. 1.

Pyrimidine moiety. In both compounds the pyrimidine ring exhibits a half-chair conformation with a minimum value of the asymmetry parameter (Nardelli, 1983) associated with C_2 symmetry passing

* Lists of structure factors, atomic positional and anisotropic displacement parameters for all atoms and other information in the printed form of the Standard Crystallographic File Structure of Brown (1985) have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52084 (66 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Fractional coordinates and equivalent isotropic temperature factors for N-nucleosides* (I) *and* (II) *with e.s.d.'s in parentheses*

U_{eq} is the average of the eigenvalues of U.

	x	y	z	U_{eq}(Å^2)
Compound (I)				
C(1′)	0·2435 (6)	0·2508 (6)	0·2102 (6)	0·033 (2)
C(2′)	0·3750 (7)	0·2432 (7)	0·3181 (7)	0·040 (2)
C(3′)	0·3426 (7)	0·1225 (8)	0·4051 (7)	0·044 (2)
C(4′)	0·2092 (7)	0·0497 (6)	0·3299 (6)	0·037 (2)
C(5′)	0·0924 (8)	0·0076 (8)	0·4062 (8)	0·054 (3)
C(6′)	0·5777 (8)	0·1072 (8)	0·3599 (9)	0·063 (3)
C(7′)	0·662 (1)	0·004 (1)	0·294 (1)	0·091 (4)
C(8′)	0·676 (1)	0·192 (1)	0·463 (1)	0·099 (5)
O(1′)	0·1416 (4)	0·1471 (4)	0·2331 (4)	0·033 (1)
O(2′)	0·4957 (5)	0·1953 (5)	0·2641 (5)	0·056 (2)
O(3′)	0·4685 (6)	0·0376 (6)	0·4161 (6)	0·074 (2)
O(5′)	0·0510 (7)	0·1183 (6)	0·4819 (6)	0·069 (2)
Br	−0·15054 (8)	0·3876 (2)	0·01039 (7)	0·0587 (2)
N(1)	0·1641 (5)	0·3841 (8)	0·1975 (4)	0·035 (1)
C(2)	0·1073 (6)	0·4321 (6)	0·2995 (6)	0·033 (2)
O(2)	0·1274 (5)	0·3761 (6)	0·4055 (3)	0·044 (2)
N(3)	0·0222 (6)	0·5514 (5)	0·2810 (5)	0·038 (2)
C(4)	−0·0338 (7)	0·6075 (6)	0·1635 (6)	0·038 (2)
O(4)	−0·1124 (6)	0·7098 (5)	0·1559 (5)	0·059 (2)
C(5)	0·0005 (7)	0·5285 (6)	0·0495 (6)	0·038 (2)
C(6)	0·1494 (7)	0·4613 (6)	0·0769 (5)	0·034 (2)
O(6)	0·2484 (5)	0·5728 (5)	0·0859 (5)	0·045 (2)
C(7)	0·3994 (8)	0·5350 (9)	0·0982 (9)	0·067 (3)
C(8)	0·488 (1)	0·661 (1)	0·095 (1)	0·109 (5)
Compound (II)				
C(1′)	0·301 (2)	0·294 (1)	0·1289 (7)	0·031 (6)
C(2′)	0·050 (2)	0·280 (1)	0·1411 (7)	0·026 (6)
C(3′)	−0·043 (2)	0·436 (1)	0·1052 (7)	0·034 (6)
C(4′)	0·168 (1)	0·545 (1)	0·1116 (6)	0·025 (6)
C(5′)	0·149 (2)	0·687 (1)	0·1721 (7)	0·040 (7)
O(1′)	0·3572 (9)	0·4525 (7)	0·1507 (4)	0·039 (4)
O(3′)	−0·130 (1)	0·4244 (9)	0·0085 (5)	0·054 (5)
O(5′)	−0·036 (1)	0·7805 (9)	0·1357 (6)	0·050 (5)
Br	0·2162 (1)	0·0000	0·34617 (7)	0·0445 (5)
N(1)	0·447 (1)	0·1950 (9)	0·1930 (5)	0·024 (4)
C(2)	0·546 (1)	0·072 (1)	0·1577 (7)	0·030 (6)
O(2)	0·5379 (9)	0·0374 (9)	0·0765 (4)	0·038 (4)
N(3)	0·670 (1)	−0·027 (1)	0·2224 (5)	0·029 (5)
C(4)	0·658 (1)	−0·028 (1)	0·3153 (8)	0·034 (7)
O(4)	0·761 (1)	−0·1240 (9)	0·3666 (5)	0·051 (5)
C(5)	0·514 (1)	0·099 (1)	0·3532 (7)	0·033 (6)
C(6)	0·499 (1)	0·241 (1)	0·2889 (6)	0·027 (5)
O(6)	0·705 (1)	0·3157 (8)	0·3025 (4)	0·032 (4)
C(7)	0·706 (2)	0·474 (2)	0·3382 (7)	0·042 (7)
C(8)	0·933 (1)	0·501 (2)	0·3894 (6)	0·053 (6)
C(9)	0·586 (2)	0·142 (1)	0·4528 (6)	0·040 (6)
H(O3′)	0·748 (14)	0·444 (12)	0·018 (7)	0·051
H(O5′)	0·005 (18)	0·818 (14)	0·092 (7)	0·051

Table 3. *Interatomic distances and hydrogen bonds* (Å) *with e.s.d.'s in parentheses*

	(I)	(II)		(I)	(II)
C(1′)—O(1′)	1·420 (7)	1·418 (12)	N(1)—C(2)	1·348 (8)	1·339 (13)
C(1′)—N(1)	1·477 (9)	1·475 (12)	N(1)—C(6)	1·456 (8)	1·451 (11)
C(1′)—C(2′)	1·521 (8)	1·556 (14)	C(2)—O(2)	1·224 (7)	1·217 (12)
C(2′)—O(2′)	1·406 (9)	—	C(2)—N(3)	1·390 (8)	1·412 (12)
C(2′)—C(3′)	1·540 (10)	1·514 (15)	N(3)—C(4)	1·369 (8)	1·366 (14)
C(3′)—O(3′)	1·411 (9)	1·449 (12)	C(4)—O(4)	1·221 (8)	1·229 (13)
C(3′)—C(4′)	1·522 (9)	1·571 (13)	C(4)—C(5)	1·496 (9)	1·531 (15)
C(4′)—O(1′)	1·450 (7)	1·452 (10)	C(5)—Br	1·943 (6)	1·978 (9)
C(4′)—C(5′)	1·499 (11)	1·506 (14)	C(5)—C(6)	1·503 (9)	1·529 (14)
C(5′)—O(5′)	1·421 (10)	1·425 (13)	C(5)—C(9)	—	1·512 (13)
C(6′)—O(2′)	1·436 (9)	—	C(6)—O(6)	1·406 (7)	1·396 (11)
C(6′)—O(3′)	1·416 (10)	—	O(6)—C(7)	1·425 (9)	1·448 (15)
C(6′)—C(7′)	1·498 (14)	—	C(7)—C(8)	1·469 (13)	1·501 (13)
C(6′)—C(8′)	1·532 (13)	—			

	Equivalent position for second atom	
Compound (I)		
O(5′)···O(2)	x, y, z	2·743 (8)
N(3)···O(5′)	$-x, \frac{1}{2}+y, 1-z$	2·759 (8)
Compound (II)		
O(5′)···O(3′)	$-x, \frac{1}{2}+y, -z$	2·727 (11)
N(3)···O(5′)	$1+x, y-1, z$	2·826 (12)
O(3′)···O(2)	$-x, \frac{1}{2}+y, -z$	2·797 (8)

through the C(5)—C(6) bond. The bond lengths and bond angles are similar to those reported for 5,6-dihydrouridine (Suck, Saenger & Zechmeister, 1972; Sundaralingam, Rao & Abola, 1971), 5,6-dihydrothymidine (Grand & Cadet, 1978) or 5,6-dihydrothymine (Furberg & Jensen 1968) derivatives. The diketo form is clearly observed owing to the C=O bond lengths [mean value of 1·223 (5) Å]. In both compounds, the 5*R*,6*R* configuration was confirmed. The ethoxy group and the Br atom are *trans* and assume axial positions whereas the methyl group of (II) is in a quasi-equatorial position.

Furanose ring. Both furanose rings adopt an unusual envelope conformation with a minimum value of the asymmetry parameter corresponding to C_s symmetry but the out-of-plane atom differs from one to the other. Compound (I) exhibits a $_4E$ (Sundaralingam, 1971) [C(4′)-*exo*] conformation whereas (II) shows a $_1E$ [C(1′)-*exo*] conformation. The dioxolane ring fused to the furanose of compound (I) exists in a twisted *T* conformation with maximum puckering amplitudes for O(2′) and C(6′). In compound (I) the C(4′)—C(5′) bond adopts the preferred *gauche–gauche* conformation [$\varphi_{OO} = -68{\cdot}2$ (7)°, $\varphi_{OC} = 50{\cdot}1$ (8)°] allowing the pyrimidine base to form an intramolecular hydrogen bond [O(5′)···O(2) = 2·743 (8) Å]. This was not observed in compound (II) where C(4′)—C(5′) exhibits the less favourable *trans–gauche* conformation [$\varphi_{OO} = 180$ (1)°, $\varphi_{OC} = -61$ (1)°]. This situation has been reported in other dihydrouridine derivatives (Sundaralingam, Rao & Abola, 1971) and appears to be advantageous for nucleosides in the loop region of tRNA. It should be noted that for an *anti* conformation of the base relative to the sugar moiety, the steric hindrance induced by the ethoxy substituent at C(6) can inhibit the C(4′)—C(5′) bond from adopting the more stable *gauche–gauche* conformation.

In solution (CD_3OD), the conformational analysis based on NMR coupling constants ($J_{1'-2'}$, $J_{2'-3'}$ and $J_{3'-4'}$) and related pseudorotational parameters (Altona & Sundaralingam, 1972, 1973) has confirmed the $_1E$ preferred conformation of (II) whereas for compound (I) the data were uninterpretable. A study made on a homologous compound of (I) [(5*R*, 6*R*)-bromo-5,6-dihydro-6-propyloxy-2′,3′-isopropylidene-β-D-ribofuranosyluracil] has shown an unusual ^O_4T conformation. This conformation is close to the observed solid state $_4E$ conformation for the compound (II) ($\Delta\varphi_2 = 18°$).

Glycosidic linkage. The orientation of the base ring relative to the sugar moiety may be described by the glycosidic torsion angle χ_{CN} [O(1′)—C(1′)—N(1)—C(2)] (Sundaralingam, 1969). The compound

Table 4. *Selected torsional angles* (°), *ring-puckering parameters and minimum values of asymmetry parameters*

Ring-puckering parameters (Q_2, Q_T, φ_2, θ_2)* according to Cremer & Pople (1975); asymmetry parameters (ΔC_s, ΔC_2) according to Nardelli (1983) and conformational nomenclature (E, T, χ_{CN}, φ_{OO}, φ_{CO}) according to Sundaralingam (1971).

	(I)	(II)
Sugar ring		
Conformation	${}_4E$	${}_1E$
C(4′)—O(1′)—C(1′)—C(2′)	−13·7 (4)	−39·2 (9)
O(1′)—C(1′)—C(2′)—C(3′)	1·4 (7)	37·6 (9)
C(1′)—C(2′)—C(3′)—C(4′)	10·5 (7)	−20·8 (9)
C(2′)—C(3′)—C(4′)—O(1′)	−18·5 (7)	−1·3 (9)
C(3′)—C(4′)—O(1′)—C(1′)	20·5 (6)	25·5 (9)
Q_2	0·187	0·371
φ_2	−33·5	35·0
ΔC_s	C(4′) = 0·009	C(1′) = 0·009
Pyrimidine ring		
Conformation	Half-chair	Half-chair
C(6)—N(1)—C(2)—N(3)	6·0 (8)	−76·2 (10)
N(1)—C(2)—N(3)—C(4)	14·3 (9)	15·0 (13)
C(2)—N(3)—C(4)—C(5)	1·2 (9)	−6·0 (13)
N(3)—C(4)—C(5)—C(6)	−33·9 (7)	−25·4 (11)
C(4)—C(5)—C(6)—N(1)	50·2 (7)	47·2 (9)
C(5)—C(6)—N(1)—C(2)	−37·8 (7)	−43·2 (11)
Q_T	0·432	0·428
φ_2	92·3	103·2
θ_2	117·4	115·8
ΔC_2 [C(2)—N(3)]	0·011	0·055
Dioxolane ring		
Conformation	${}^{C(4')}_{O(2')}T$	
O(2′)—C(2′)—C(3′)—O(3′)	14·5 (6)	
C(2′)—C(3′)—O(3′)—C(6′)	8·3 (7)	
C(3′)—O(3′)—C(6′)—O(2′)	−27·7 (8)	
O(3′)—C(6′)—O(2′)—C(2′)	37·5 (7)	
C(6′)—O(2′)—C(2′)—C(3′)	−31·6 (6)	
Q_2	0·331	
φ_2	132·5	
ΔC_2	C(3) = 0·021	
Miscellaneous		
φ_{CO} [C(3′)—C(4′)—C(5′)—O(5′)]	50·1 (8)	−61·0 (11)
φ_{OO} [O(1′)—C(4′)—C(5′)—O(5′)]	−68·2 (7)	−179·9 (12)
χ_{CN} [O(1′)—C(1′)—N(1)—C(2)]	62·5 (6)	−134·0 (8)
O(1′)—C(1′)—N(1)—C(6)	−117·9 (5)	39·4 (10)
N(1)—C(6)—O(6)—C(7)	67·8 (7)	121·3 (8)
C(6)—O(6)—C(7)—C(8)	175·1 (8)	152·9 (8)

* The starting position and direction for ring puckering calculations are: O(1′) to C(4′) for furanose, N(1) to C(6) for pyrimidine and C(2′) to O(2′) for dioxolane.

(I) adopts an unusual *syn* conformation with a χ_{CN} value of 62·5 (6)° whereas for pyrimidine nucleosides the *anti* conformation greatly dominates (Saenger, 1984). It should be noted that the torsion angle about C(1′)—N(1) is correlated to the sugar conformation. Thus, the *syn* conformation of the nucleosides shows a preference for C(2′)-*endo* puckered sugar whereas the compound (I) is C(4′)-*exo*. It seems that this situation results from the constraint provided by the fused dioxolane to the furanose ring. For a ${}_4E$ conformation of the sugar, the hydroxymethyl group is in a quasi-equatorial position, *i.e.* sufficiently distant from the pyrimidine to allow the latter to rotate and favor the bonding interaction with O(2) of the base. Moreover the substitution at C(6) by an ethoxy group could contribute to the destabilization of the *anti* conformation.

To our knowledge only a few pyrimidine nucleosides present a *syn* conformation in the crystalline state. The 4-thiouridine (Saenger & Scheit, 1970) exhibits a *syn* conformation for which the inclusion of water of hydration seems to play an important role. In this latter compound, the O(5′)···O(2) distance is too long (> 3·5 Å) to form an intramolecular hydrogen bond as is the case in compound (I). The 6-methyluridine (Suck, Saenger & Zechmeister, 1972) exhibits a *syn* conformation with a usual C(2′)-*endo* puckering of the sugar and shows an intramolecular hydrogen bond. This conformation of the glycosidic linkage is attributed to the influence of the bulky methyl group in the 6 position of the base rather than the stabilization due to the intramolecular hydrogen bond between O(5′) and O(2) (2·817 Å).

In the 5,6-dihydrothymidine derivative (II), the orientation of the pyrimidine base is *anti* with O(2) pointing away from the furanose ring. Although the sugar ring of (II) exhibits an unusual ${}_1E$ [C(1′)-*exo*] conformation, the glycosidic bond [χ_{CN} = −134·0 (8)°] may be regarded as in good agreement with the maximum and minimum value ($-180 < \chi_{CN} < -115°$) observed for such nucleosides (Saenger, 1984).

In both compounds, the glycosidic bond length [C(1′)—N(1) = 1·476 Å] clearly shows a significant decrease from the mean value of 1·52 Å observed for compounds where χ_{CN} is near 180° (Saenger, 1984).

Molecular packing. In both compounds the packing is stabilized by hydrogen bonds involving all potential donors. Each hydroxyl group takes part in a bifurcated hydrogen bond. In compound (I) this situation arises for O(5′) *via* an intra- and intermolecular interaction. All hydrogen-bond distances

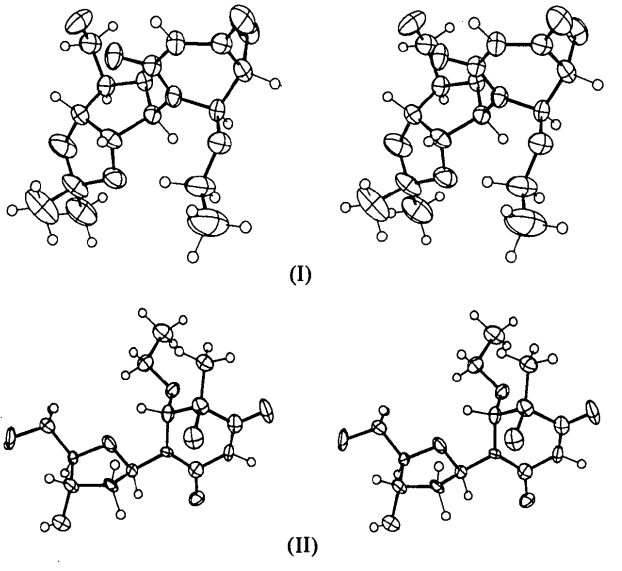


Fig. 1. Stereopairs of *N*-nucleosides (I) and (II).

are reported in Table 3. Moreover, in both compounds, the Br atom has a short contact distance with an O atom of the substituted base [(I): Br···O(6) ($-x$, $y-\frac{1}{2}$, $-z$) = 3·285 (5) Å; (II): Br···O(4) ($x-1$, y, z) = 2·993 (7) Å]. The pyrimidine moiety being non-planar due to the substitutions, no base stacking was observed in either compound.

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Structure of 5-Methoxy-2-{[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl}-1*H*-benzimidazole (Omeprazole)

BY HIROFUMI OHISHI, YASUKO IN, TOSHIMASA ISHIDA* AND MASATOSHI INOUE

Osaka University of Pharmaceutical Sciences, 2-10-65 *Kawai, Matsubara, Osaka* 580, *Japan*

AND FUMIO SATO, MITSUHITO OKITSU AND TOMOCHIKA OHNO

Suntory Institute for Biomedical Research, 1-11 *Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka* 618, *Japan*

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Abstract. $C_{17}H_{19}N_3O_3S$, M_r = 345·42, triclinic, $P\bar{1}$, a = 10·686 (5), b = 10·608 (7), c = 9·666 (6) Å, α = 119·75 (5), β = 112·02 (5), γ = 68·33 (4)°, V = 859 (1) Å^3, Z = 2, D_m = 1·332 (2), D_x = 1·335 g cm^{-3}, Cu $K\alpha$, λ = 1·5418 Å, μ = 18·04 cm^{-1}, $F(000)$ = 364, T = 293 K, R = 0·057 for 1962 observed reflections. The methylsulfinyl group, which adopts a *trans* conformation, links the pyridine and benzimidazole rings in an almost coplanar orientation. Thus the molecule, as a whole, adopts a nearly extended form. Two centrosymmetrically related molecules form a cyclic dimer by intermolecular N—H···O hydrogen bonding, and the dimers are held together by van der Waals contacts between the neighboring aromatic rings in the crystal structure.

Introduction. Recently, H^+,K^+-ATPase has been recognized as the acid pump involved in the terminal steps of the gastric acid secretory process, and H^+,K^+-ATPase inhibitors have attracted much attention for peptic ulcer therapy (Sachs, Carlsson, Lindberg & Wallmark, 1988). Omeprazole (1), a potent inhibitor for this enzyme, is presently under extensive clinical evaluation (Clissold & Campoli-

* To whom correspondence should be addressed.

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