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Structural Studies of *S*-Cycloadenosine Derivatives.
II. The Crystal and Molecular Structure of 8,3′-Anhydro-8-mercapto-9-*β*-D-xylofuranosyladenine (8,3′-*S*-Cyclo A)

By Mariko Yoneda, Kaori Tanaka, Takaji Fujiwara and Ken-ichi Tomita

Faculty of Pharmaceutical Sciences, Osaka University, Suita, Osaka 565, *Japan*

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Abstract

8,3′-Anhydro-8-mercapto-9-*β*-D-xylofuranosyladenine monohydrate, $C_{10}H_{11}N_5O_3S.H_2O$, crystallizes in the orthorhombic system, space group $P2_12_12_1$, with $Z = 4$ and cell dimensions: a = 6·846 (4), b = 25·804 (4), c = 6·830 (4) Å. The structure was determined by the heavy-atom method using the intensity data of 912 independent reflections measured by Cu $K\alpha$ radiation and refined to R = 5·9%. The title molecule occurs in a high-*anti* conformation with a glycosidic torsion angle of 75·5 (13)°. The ribose conformation is C(2′)-*exo* and the orientation of the C(5′)—O(5′) bond is *gauche–gauche*. The bases stack along the c axis with an interplanar spacing of 3·4 Å.

Introduction

Cyclonucleotides and -nucleosides have a restricted rotation of the base about the glycosyl bond by a covalent-bond formation between purine and furanose rings through S or O atoms. For this reason, the molecular conformation obtained from single-crystal X-ray diffraction studies may be expected to be preserved even in solution, and to be useful for experimental and theoretical studies of NMR, CD and ORD spectra which are sensitive to the χ value defined by the mutual orientations of base and sugar moieties. Among the previously reported cyclonucleosides, 8,3′-*S*-cyclo A is the only compound in which C(3′) and base are cyclized. A preliminary report of the present study has already been given (Tomita, Tanaka, Yoneda, Fujiwara & Ikehara, 1972). Here we report the structure analysis in more detail.

Experimental

A sample of 8,3′-*S*-cyclo A was kindly supplied by Professor M. Ikehara, Osaka University, and was crystallized as a transparent plate by slow evaporation of aqueous solution at room temperature. Preliminary Weissenberg and precession photographs revealed the crystal to be orthorhombic with space group $P2_12_12_1$ (No. 19). The crystal data are given in Table 1. The intensities of 912 unique reflections within $\sin\theta/\lambda \leq$ 0·65 Å^{-1} were collected with a Rigaku-Denki automatic four-circle diffractometer using Ni-filtered Cu $K\alpha$ radiation (crystal size 0·18 × 0·15 × 0·03 mm). No absorption correction was applied. The density was measured by flotation using a benzene–ethylene bromide mixture.

Structure determination and refinement

The structure was solved by the heavy-atom method. A sharpened Patterson map showed clearly the position of the S atom. All non-hydrogen atoms were located on successive Fourier maps. The structure was refined to an R of 0·079 by a least-squares method using the program's block-diagonal approximation (*UNICS*, 1973) with anisotropic thermal parameters. A difference Fourier synthesis was then calculated which revealed the locations of all H atoms. They were included in the final refinement with anisotropic temperature factors for non-hydrogen atoms and with isotropic ones for H atoms, the final R being 0·059 (0·060, including $F_o = 0$). The final atomic parameters are listed in Tables 2 and 3.* Atomic scattering factors

Table 1. *Crystal data*

Formula	$C_{10}H_{11}N_5O_3S.H_2O$
Molecular weight	299·31
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a (Å)	6·846 (4)
b	25·804 (4)
c	6·830 (4)
V (Å^3)	1206·5
Z	4
D_m (Mg m^{-3})	1·640 (2)
D_x	1·647

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34568 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 2. *Final positional parameters* (×10⁴)

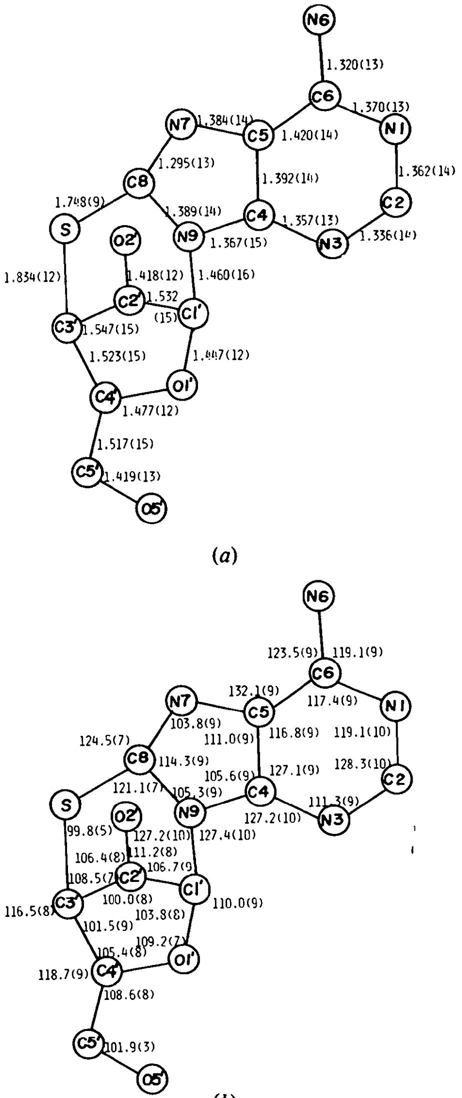
Estimated standard deviations are given in parentheses.

	x	*y*	*z*
N(1)	1816 (12)	−616 (3)	1148 (13)
C(2)	3722 (15)	−465 (3)	1183 (16)
N(3)	4440 (11)	16 (3)	1181 (12)
C(4)	2990 (15)	374 (3)	1137 (14)
C(5)	987 (14)	281 (3)	1111 (14)
C(6)	384 (14)	−245 (4)	1124 (14)
N(6)	−1464 (12)	−392 (3)	1135 (13)
N(7)	−50 (11)	741 (3)	995 (15)
C(8)	1296 (13)	1093 (3)	944 (12)
N(9)	3189 (11)	901 (3)	1025 (17)
C(1′)	5003 (14)	1196 (3)	891 (15)
C(2′)	4642 (14)	1632 (3)	−587 (15)
C(3′)	3368 (14)	1999 (3)	670 (16)
C(4′)	4436 (15)	1983 (3)	2624 (15)
C(5′)	3273 (16)	2067 (4)	4489 (16)
O(1′)	5360 (9)	1467 (2)	2711 (10)
O(2′)	6389 (10)	1906 (2)	−1003 (11)
O(5′)	2103 (10)	1635 (3)	5020 (10)
S	851 (4)	1756 (1)	658 (4)
O(*W*)	8127 (10)	1529 (3)	5655 (11)

Table 3. *Final positional parameters* (×10³) *and isotropic thermal parameters for the hydrogen atoms*

Estimated standard deviations are given in parentheses. The second column shows the non-hydrogen atom to which the hydrogen atom is bonded.

		x	*y*	*z*	*B* (Å²)
H(2)	(C2)	484 (17)	−76 (4)	131 (16)	2 (3)
H(1)	(C1′)	621 (15)	97 (4)	56 (17)	1 (2)
H(2′)	(C2′)	409 (16)	147 (4)	−164 (15)	1 (2)
H(3′)	(C3′)	322 (16)	242 (4)	17 (18)	1 (2)
H(4′)	(C4′)	546 (16)	228 (4)	246 (16)	1 (2)
H(5′)	(C5′)	229 (16)	239 (4)	413 (16)	2 (3)
H(5″)	(C5′)	414 (17)	214 (4)	544 (17)	2 (3)
H(6)	(N6)	−190 (17)	−75 (4)	65 (18)	2 (3)
H(6′)	(N6)	−239 (20)	−16 (4)	138 (18)	3 (3)
H(2″)	(O2′)	700 (17)	176 (4)	−192 (16)	2 (3)
H(5″)	(O5′)	279 (17)	137 (4)	532 (17)	2 (3)
H(*W*)	(O*W*)	764 (17)	143 (4)	449 (18)	2 (3)
H(*W*′)	(O*W*)	914 (17)	158 (4)	537 (17)	2 (3)



(*a*)

(*b*)

Fig. 1. Molecular geometry: (*a*) bond lengths (Å); (*b*) bond angles (°). Standard deviations are given in parentheses.

used for the structure factor calculation were taken from *International Tables for X-ray Crystallography* (1974) and the numerical calculations were carried out on the NEAC 2200-700 computer at the Computing Center of this University.

Results and discussion

The bond lengths and angles are given in Fig. 1. As expected, some of these values are somewhat different from the standard values. In Table 4, selected bond lengths and bond angles are compared with the corresponding ones in orthorhombic 5′-AMP (Neidle, Kühlbrandt & Achari, 1976). For example, C(1′)—N(9)—C(4) is larger by 3·2° and N(9)—C(1′)—C(2′) is smaller by 6·3° than those of 5′-AMP, whereas those of 8,2′-*S*-cyclo 5′-AMP (Tanaka, Fujii, Fujiwara & Tomita, 1979) have differences of 9·9 and 7·8°, respectively. If one considers the difference in the molecular geometry of an *S*-cyclo ring formation by six or five atoms, it is apparent that the strains induced by cyclization in 8,3′-*S*-cyclo A might be smaller than those in 8,2′-*S*-cyclo 5′-AMP. The molecular conformation is shown in Fig. 2 in a stereoscopic presentation. The intramolecular contact between O(5′) and C(8) is 3·168 Å which is equal to the sum of the van

Table 4. *Comparison of some bond lengths* (Å) *and angles* (°) *in* 8,3′-*S*-*cyclo A with those in* 8,2′-*S*-*cyclo AMP*

Deviations from 5′-AMP* are shown in parentheses.

	8,3′-Cyclo A	8,2′-*S*-Cyclo 5′-AMP†
N(9)—C(8)	1·389 (−0·003)	1·349 (−0·043)
N(9)—C(1′)	1·460 (−0·029)	1·465 (−0·024)
C(1′)—N(9)—C(8)	127·2 (−0·2)	119·2 (−8·2)
C(1′)—N(9)—C(4)	127·4 (+3·2)	134·1 (+9·9)
N(9)—C(1′)—C(2′)	106·7 (−6·3)	105·2 (−7·8)

* Neidle, Kühlbrandt & Achari (1976).
† Tanaka, Fujii, Fujiwara & Tomita (1979).

Table 5. *Least-squares planes*

Atoms indicated by an asterisk are those determining the best planes. Deviations from the planes are in Å.

Adenine ring (Plane I)					
N(1)*	0·025 (10)	C(2)*	0·017 (12)	N(3)*	−0·010 (10)
C(4)*	−0·028 (11)	C(5)*	−0·031 (11)	C(6)*	−0·007 (11)
N(7)*	−0·002 (12)	C(8)*	0·024 (10)	N(9)*	0·011 (13)
N(6)	−0·029 (10)	S	0·161 (6)	C(1′)	0·104 (12)
C(3′)	0·169 (12)				
S-Cyclo ring (Plane II)					
S*	0·003 (17)	C(8)*	−0·015 (18)	N(9)*	−0·004 (20)
C(1′)*	0·027 (19)	C(3′)*	−0·045 (20)	C(5′)	−2·658 (20)
O(1′)	−1·277 (18)	C(2′)	0·915 (19)	C(4′)	−1·360 (19)
Sugar ring (Plane III)					
C(1′)*	−0·016 (29)	C(3′)*	0·018 (29)	C(4′)*	−0·025 (29)
O(1′)*	0·010 (28)	C(2′)	−0·671 (29)	C(5′)	1·062 (29)

The equations for the least-squares planes

Plane I $0{\cdot}210x - 0{\cdot}030y - 0{\cdot}999z + 0{\cdot}735 = 0{\cdot}0$
Plane II $0{\cdot}013x - 0{\cdot}100y - 0{\cdot}995z + 0{\cdot}897 = 0{\cdot}0$
Plane III $-0{\cdot}822x - 0{\cdot}398y + 0{\cdot}406z + 3{\cdot}782 = 0{\cdot}0$

Dihedral angles

Planes I and II	4·0 (3)°
Planes I and III	114·3 (4)

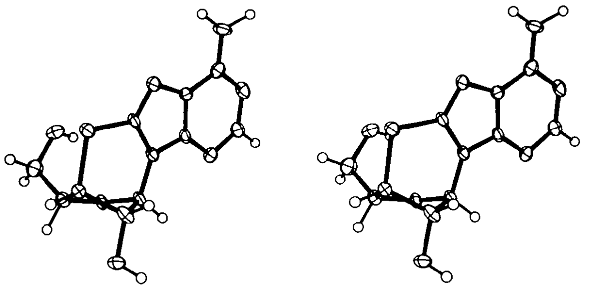


Fig. 2. Stereoscopic view of the molecule; the thermal ellipsoids correspond to 50% probability for the non-hydrogen atoms.

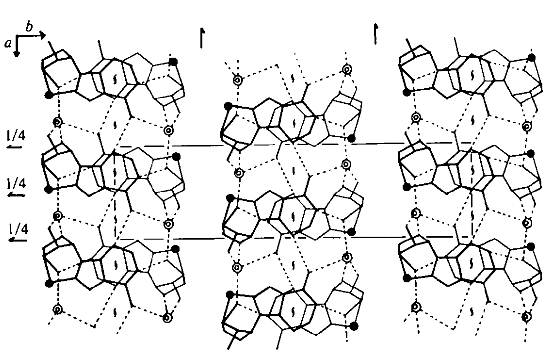


Fig. 3. The crystal structure projected along the *c* axis. The broken lines indicate the hydrogen bonds. The black circles and the double circles indicate S and O(*W*), respectively.

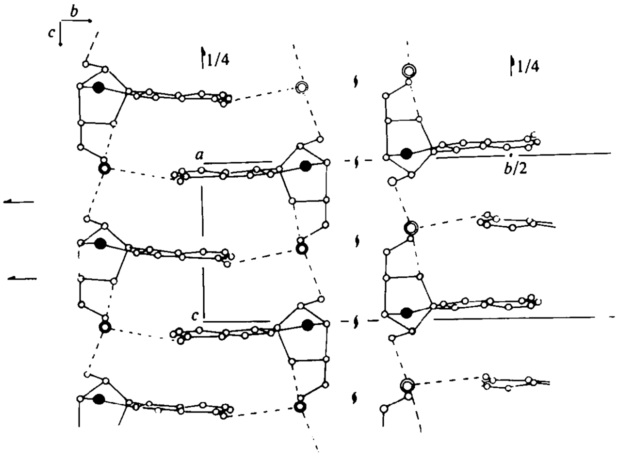


Fig. 4. The crystal structure projected along the *a* axis. The broken lines indicate the hydrogen bonds.

der Waals radii of the atoms involved. The calculated least-squares planes are given in Table 5. The dihedral angles between purine and *S*-cyclo rings and between purine and sugar rings are 4·0 and 114·3°, respectively. The conformation of the sugar ring can be assessed on the basis of endocyclic torsion angles (Table 6). The phase angle of pseudorotation (Altona & Sundaralingam, 1972), $P = 344{\cdot}6°$, corresponds to C(2′)-*exo* (E_2), whereas that of 8,2′-*S*-cyclo 5′-AMP is a C(4′)-*endo* pucker (^4E). The displacement of the C(2′) atom from the least-squares plane through the other four atoms in the sugar ring is 0·677 Å. The glycosidic torsion angle χ [O(1′)—C(1′)—N(9)—C(8)] is 75·5° which is in the high-*anti* region. The orientation of the C(5′)—O(5′) bond is *gauche–gauche*. The molecular packing is shown in Figs. 3 and 4. The base planes stack around the twofold screw axis parallel to the *c* axis with much overlapping and an interplanar spacing of 3·4 Å. The dihedral angle between the stacked purine rings is 4·2 (2)°. Possible intermolecular

Table 6. *Selected torsion angles* (°)

C(1′)–C(2′)–C(3′)–C(4′)	42·7 (10)
C(2′)–C(3′)–C(4′)–O(1′)	−29·3 (10)
C(3′)–C(4′)–O(1′)–C(1′)	3·6 (10)
C(4′)–O(1′)–C(1′)–C(2′)	24·1 (10)
O(1′)–C(1′)–C(2′)–C(3′)	−41·3 (9)
O(1′)–C(1′)–N(9)–C(8)	75·5 (13)
O(1′)–C(1′)–N(9)–C(4)	−108·8 (12)
C(1′)–C(2′)–C(3′)–S	−80·6 (8)
O(2′)–C(2′)–C(3′)–S	163·6 (7)
C(2′)–C(3′)–S–C(8)	42·5 (8)
C(4′)–C(3′)–S–C(8)	71·2 (9)
C(3′)–S–C(8)–N(9)	−2·6 (9)
C(3′)–S–C(8)–N(7)	−178·9 (9)
S–C(3′)–C(4′)–C(5′)	−33·4 (12)
S–C(3′)–C(4′)–O(1′)	88·4 (9)
C(3′)–C(4′)–C(5′)–O(5′)	74·3 (12)
O(1′)–C(4′)–C(5′)–O(5′)	−45·9 (11)

hydogen bonds found in the crystal are summarized in Table 7. The contact between S(x,y,z) and O(2′)($-1+x, y, z$) is 3·28 Å which is equal to the sum of the van der Waals radii of the atoms involved. As a whole, the 8,3′-*S*-cyclo A molecules form a piled-layer structure parallel to (010) by base-stacking and a hydrogen-bond network involving water molecules, with the layers separated by van der Waals contacts in the **b** direction.

Table 7. *Distances* (Å) *and angles* (°) *involved in hydrogen bonds*

Standard deviations are in parentheses.

The superscripts refer to the equivalent positions:

(i)	x,y,z	(iv)	$x, y, -1+z$
(ii)	$-1+x, y, z$	(v)	$\frac{1}{2}-x, -y, -\frac{1}{2}+z$
(iii)	$1+x, y, z$	(vi)	$\frac{1}{2}-x, -y, \frac{1}{2}+z$.

D^{i}–H···A	D···A	H···A	∠D–H···A	∠H–D···A
N(6)–H(6′)···N(3^{ii})	2·995 (12)	2·22 (14)	146 (12)	25 (9)
N(6)–H(6)···O(W^{v})	3·166 (11)	2·18 (13)	161 (10)	13 (7)
O(2′)–H(2′)···O(W^{iv})	2·752 (10)	1·92 (12)	168 (11)	8 (8)
O(5′)–H(5″)···N(1^{vi})	2·838 (11)	2·04 (12)	154 (11)	18 (8)
O(W)–H(W')···O($5'^{iii}$)	2·770 (10)	2·04 (12)	169 (12)	8 (9)
O(W)–H(W)···O($1'^{i}$)	2·767 (10)	1·99 (12)	145 (11)	24 (8)

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Structure Cristalline d'un Métabolite Fongique Original du Groupe des Epidithio-3,6 Dioxo-2,5 Pipérazines: l'Epicorazine B ($C_{18}H_{16}N_2O_6S_2.\frac{1}{2}C_2H_5OH$)

Par Gérard Deffieux, Michel Gadret, Jean Michel Leger et Alain Carpy

Laboratoire de Chimie Analytique, Faculté de Pharmacie, ERA n° 626, *CNRS, Université de Bordeaux* II,
91 *rue Leyteire,* 33000 *Bordeaux, France*

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Abstract

Crystals of the title compound, $C_{18}H_{16}N_2O_6$-$S_2.\frac{1}{2}C_2H_5OH$, M_r = 443·49, m.p. = 465 K, are monoclinic, space group $P2_1$, with Z = 4 (2 independent molecules of epicorazine B) in a cell of dimensions a = 15·716 (2), b = 8·074 (1), c = 16·221 (3) Å, β = 109·41 (1)°, d_m = 1·43, d_x = 1·50 Mg m^{-3}. The structure was determined by heavy-atom Patterson techniques and refined by diagonal-matrix least squares to a conventional residual of 0·067 for 2561 structure amplitudes. The results are discussed by comparison with the structure of epicorazine A previously described by the same authors.

Introduction

L'épicorazine A, métabolite fongique original extrait d'*Epicoccum nigrum* (groupe des Adélomycètes) par Baute, Deffieux, Baute, Filleau & Neveu (1976) a fait l'objet d'un précédent article dans cette revue (Deffieux, Gadret, Leger & Carpy, 1977).

Ce travail est relatif à l'étude radiocristallographique d'un second métabolite original extrait du même champignon par Deffieux, Baute & Filleau (1978). Ces auteurs en ont proposé une formule développée à partir des résultats obtenus par spectroscopie de masse, IR et RMN (Fig. 1) ainsi que le nom d'épicorazine B. Les nomenclatures choisies pour ces

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