[Chem. Pharm. Bull. 22(9)1963—1967(1974)]

UDC 547.91.02 : 615.33.011.5 : 543.422.8

Studies on Pentenomycins. III.[1] The X-Ray Crystal Structure Analysis of Monobromopentenomycin Triacetate

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(Received August 3, 1973)

In order to confirm the proposed structure and to elucidate stereochemistry of pentenomycins, an X-ray crystal structure analysis of monobromopentenomycin triacetate ($C_{12}H_{13}O_7Br$) (I) has been carried out. The crystals of (I) are orthorhombic with space group $P2_12_12_1$ and the unit cell dimensions are $a_0=9.588$ (2), $b_0=21.445$ (7) and $c_0=6.983$ (1) Å; $Z=4$. The absolute configuration was determined by the use of the anomalous dispersion effect of the bromine atom for Cu $K\alpha$ radiation. From the analytical data, (I) was confirmed to be 4,5-diacetoxy-5-acetoxymethyl(4: S, 5: S)-2-bromo-cyclopent-2-en-1-one.

Pentenomycin I; $C_6H_8O_4 \cdot 1/2\ H_2O$ and II; $C_8H_{10}O_5 \cdot 1/2\ H_2O$ are new antibiotics produced by *Streptomyces eurythermus* MCRL 0738 and are moderately active against Gram-positive and -negative bacteria.[3] The chemical structures of pentenomycin I and II were elucidated as 4,5-dihydroxy-5-hydroxymethylcyclopent-2-en-1-one and 4-acetoxy-5-hydroxy-5-hydroxymethylcyclopent-2-en-1-one respectively by chemical and spectroscopic methods.[1]

Pentenomycin I and II gave the same triacetyl derivative, from which was derived monobromopentenomycin triacetate (I), a promising derivative for X-ray analysis. The present paper deals with the experimental details of X-ray analysis, from which (I) was confirmed to be 4,5-diacetoxy-5-acetoxymethyl (4: S, 5: S)-2-bromo-cyclopent-2-en-1-one.

Experimental

Monobromopentenomycin triacetate (I) was synthesized as already reported.[1] Recrystallized crystals of (I) (120 mg) was dissolved in hot ether (5 ml) and the solution was kept for 2 days at room temperature. After removal of resulting crystals, the filtrate was seeded with a few crystals selected from the first crop and kept for 2 weeks at room temperature and further 3 weeks in an ice box, to give colorless needles elongated along *C* axis.

The density was measured by the floatation method in an aqueous solution of potassium iodide. Preliminary cell dimensions were obtained from Weissenberg and Precession photographs, which showed the space group to be $P2_12_12_1$. A crystal with the dimensions of 0.3 × 0.3 × 0.4 mm was mounted on a goniometer head along the needle axis and used for data collection on a computer-controlled four-circle diffractometer, AFC (Rigaku Denki). Cu$K\alpha$ radiation from a graphite monochrometor was used. The accurate cell dimensions were determined by the least-squares method using the accurately measured 2θ values of the 20 strong reflections in the range of $40° \leqq 2\theta \leqq 80°$.

Crystal Data——Monobromopentenomycin triacetate (I) ($C_{12}H_{13}O_7Br$), Mol. wt. 349.1, mp 107—108°, $[\alpha]_D^{18}=+59°$ ($c=0.35$, $CHCl_3$). Orthorhombic, $a_0=9.588(2)$, $b_0=21.445(7)$, $c_0=6.983(1)$Å, $V_0=1436$ Å^3, $D_{obs.}=1.62$ g/cm^3, $D_{calc.}=1.617$ g/cm^3, $Z=4$, linear absorption coefficient for Cu$K\alpha$: $\mu=25.2$/cm, $F(000)=704$, absent reflection: $h00$ when h is odd, $0k0$ when k is odd, $00l$ when l is odd.
Space group: $P2_12_12_1$

The three-dimensional intensity data were collected with $\omega/2\theta$ scan technique at a constant scanning rate of 2 deg/min. Three standard reflections were measured after every 50 reflections. The sum of these 3 reflections was used to scale the observed intensity. The maximum deviation of the standard reflections

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[1] Part II: K. Umino, N. Takeda, Y. Ito, and T. Okuda, *Chem. Pharm. Bull.* (Tokyo), 22, 1233 (1974).
[2] Location: *Toda-shi, Saitama.*
[3] Part I: K. Umino, T. Furumai, N. Matsuzawa, Y. Awataguchi, Y. Ito, and T. Okuda, *J. Antibiotics*, 26, 506 (1973).

from their mean value was 1.5%. Those reflections having an intensity exceeding 3 times of the corresponding standard deviations were treated as observed. Thus 1341 reflections out of 1457 measured reflections with $2\theta \leqq 135°$ were retained and corrected for Lorentz and polarization factors but not for absorption and extinction factors.

Discussion

Determination of the Structure

From the three-dimensional Patterson map, the position of the bromine atom could easily be deduced. From a three-dimensional electron density map calculated by the use of the bromine phase angle and a successive three-dimensional electron density map, all the rest 19 non-hydrogen atoms in the asymmetric unit were deduced.

Refinement of the positional parameters of the 20 atoms including bromine atom was carried out by the block-diagonal matrix least-squares method, in which the anisotropic thermal vibration were assumed for bromine atom and the other non-hydrogen atoms were assumed to be carbon atoms. Five cycles of calculations gave an R-value of 0.167. The oxygen atoms were deduced from chemical consideration, from the bond lengths and from the unusually low values of the thermal parameters due to assuming those atoms as carbon. Further refinement carried out by the block-diagonal least-squares method gave an R-value of 0.055. At this stage, Fourier and Difference Fourier syntheses were carried out with the parameters deduced from the above refinement. From these maps, hydrogen atoms were deduced. Five cycles of refinement by the block-diagonal least-squares method gave the final R-value of 0.040 for 1341 non-zero reflections.[4] The computer programs used in these

TABLE I. Final Atomic Parameters and Their Standard Deviations[a] ($\times 10^4$)

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	396(1)	396(0)	763(1)	99(0)	23(0)	285(1)	−10(0)	5(1)	6(0)
C-1	2978(6)	986(2)	−334(8)	103(6)	18(1)	213(13)	0(2)	9(8)	0(3)
C-2	4332(5)	1245(2)	552(8)	86(5)	14(1)	230(11)	0(2)	14(7)	2(3)
C-3	4135(5)	1143(2)	2758(8)	99(6)	19(1)	230(12)	1(2)	−12(7)	0(3)
C-4	2725(6)	850(2)	2962(8)	104(6)	22(1)	209(12)	−1(2)	12(8)	7(3)
C-5	2138(5)	756(2)	1299(8)	85(5)	18(1)	229(12)	−1(2)	12(7)	2(3)
C-6	3515(6)	2291(2)	213(9)	117(7)	19(1)	300(15)	9(2)	8(9)	7(4)
C-7	3972(7)	2954(3)	−36(12)	146(8)	17(1)	457(21)	2(3)	22(12)	6(4)
C-8	5581(6)	891(2)	−243(9)	97(6)	17(1)	318(15)	−14(2)	48(9)	3(3)
C-9	6431(5)	−139(2)	32(8)	93(5)	20(1)	209(11)	5(2)	−3(7)	−11(3)
C-10	6079(6)	−784(2)	679(10)	126(7)	17(1)	289(14)	4(2)	0(10)	0(4)
C-11	5436(7)	1959(3)	4214(10)	150(8)	25(1)	343(17)	6(3)	−107(13)	−16(4)
C-12	5355(12)	2587(4)	5172(15)	264(16)	36(2)	483(25)	7(5)	−114(19)	−62(6)
O-1	2736(5)	960(2)	−2005(6)	151(6)	36(1)	201(9)	−10(2)	−4(7)	8(3)
O-2	4608(4)	1884(1)	65(6)	91(4)	15(1)	314(9)	3(2)	11(6)	6(2)
O-3	2358(4)	2125(2)	525(8)	89(4)	28(1)	450(15)	6(2)	14(8)	16(4)
O-4	5357(4)	256(1)	322(6)	89(4)	16(1)	300(10)	1(2)	22(6)	−4(2)
O-5	7497(4)	22(2)	−703(7)	88(1)	28(1)	363(12)	0(2)	41(7)	−2(3)
O-6	4165(4)	1733(2)	3791(6)	122(5)	23(1)	261(10)	8(2)	−15(6)	−17(3)
O-7	6498(5)	1693(2)	3743(9)	134(5)	28(1)	556(19)	5(2)	−99(10)	−14(4)
H-31	4832	878	3322	3.65[b]					
H-41	2408	779	4032	3.51[b]					
H-81	6446	1015	198	3.19[b]					
H-82	5620	882	−1736	4.29[b]					

a) The anisotropic temperature factors are of the form;
$T=\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$.
The estimated standard deviations are given in the parentheses. To represent the correct absolute configuration, the coordinates shoud be referred to the right-handed coordinate system.

b) These values are not $\times 10^4$.

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[4] The atomic scattering factors used in these calculations were taken from "International Tables for X-ray Crystallography," Vol. III, The Kynoch Press, Birmingham, 1968, p. 201.

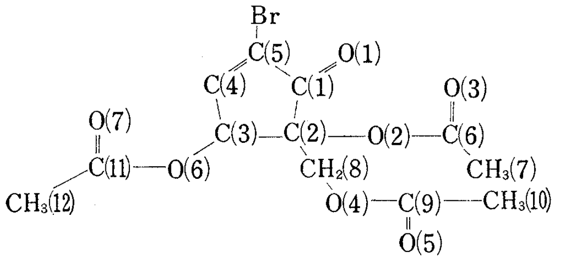

Fig. 1. Nomenclature of Monobromopentenomycin Triacetate (I)

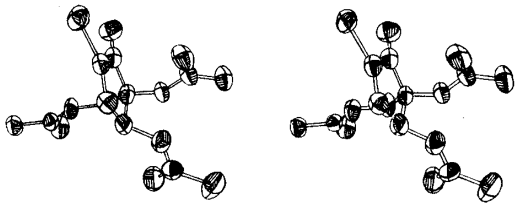

Fig. 2. Stereoscopic View of Monobromopentenomycin Triacetate (I)

calculations were 3DFANDFR[5] and HLSQ.[5]

In this calculation,[4] the anisotropic thermal vibrations were assumed for all non-hydrogen atoms and the isotropic thermal vibrations for hydrogen atoms. The weighting scheme for this calculation were:

$$\sqrt{w}=50/F_o, \quad \text{when } F_o \geqq 50$$
$$\sqrt{w}=1.0, \quad \text{when } 50>F_o \geqq 15$$
$$\sqrt{w}=0.50, \quad \text{when } 15>F_o$$

The final atomic parameter and their standard deviations are shown in Table I. Fig. 2 shows the conformation and thermal vibration of the molecule drawn by the ORTEP.[6] Each ellipsoid covers a 50% probability area of finding the center of the atom in it.

Absolute Configuration

The absolute configuration of the structure was determined by the anomalous dispersion method.[7] $\Delta f'=-0.9$ and $\Delta f''=1.5$ were used as the value of the dispersion corrections for bromine for Cu$K\alpha$ radiation.[8]

Table II. Comparison of the Observed and Calculated Intensity Ratio used to establish the Absolute Configuration

(h,k,l)	$\frac{\lvert F_{calc.}(h,k,l)\rvert^2}{\lvert F_{calc.}(\bar{h},\bar{k},\bar{l})\rvert^2}$	$\frac{\lvert F_{obs.}(h,k,l)\rvert^2}{\lvert F_{obs.}(\bar{h},\bar{k},\bar{l})\rvert^2}$	(h,k,l)	$\frac{\lvert F_{calc.}(h,k,l)\rvert^2}{\lvert F_{calc.}(\bar{h},\bar{k},\bar{l})\rvert^2}$	$\frac{\lvert F_{obs.}(h,k,l)\rvert^2}{\lvert F_{obs.}(\bar{h},\bar{k},\bar{l})\rvert^2}$
1, 1, 1	0.812	0.742	7, 5, 1	0.888	0.901
1, 3, 1	0.846	0.782	8, 3, 1	1.115	1.107
1, 8, 1	1.350	1.229	9, 5, 1	1.134	1.165
2, 1, 1	1.209	1.164	1, 5, 2	0.906	0.861
2, 12, 1	0.764	0.790	2, 4, 2	0.895	0.882
3, 6, 1	0.893	0.876	2, 7, 2	0.759	0.748
4, 4, 1	1.130	1.095	2, 8, 2	0.932	0.895
4, 16, 1	0.930	0.963	3, 2, 2	1.235	1.172
5, 1, 1	0.901	0.947	3, 4, 2	0.789	0.774
5, 4, 1	1.301	1.239	4, 4, 2	1.237	1.152

The structure factors for the Bijvoet pairs of the reflections were calculated and compared with the observed values by assuming a right-handed set of axes. The results are shown in Table II.

A comparison between the observed and calculated intensities indicated that the assumed configuration was correct. Thus the absolute configuration of monobromo-

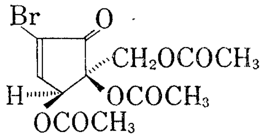

Fig. 3. Absolute Configuration of Monobromopentenomycin Triacetate (I)

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5) Y. Iitaka, 3DFANDFR and HLSQ, Tokyo University, Tokyo.

6) C.K. Johnson (1965), ORTEP. ORNL-3794, Oak Ridge National Laboratory. Oak Ridge, Tennessee.

7) J.M. Bijvoet, A.F. Peerdeman and A.J. van Bommel, *Nature*, **168**, 271 (1951).

8) C.H. Dauben and D.H. Templeton, *Acta Cryst.*, **8**, 841 (1955).

Table III. Bond Lengths and Their Standard[a] Deviations (Å)

Br-C5	1.879(0.005)	C6-C7	1.497(0.008)
C1-C2	1.542(0.007)	C6-O3	1.186(0.007)
C1-C5	1.481(0.008)	C8-O4	1.434(0.006)
C1-O1	1.191(0.007)	O4-C9	1.349(0.006)
C2-C3	1.567(0.008)	C9-C10	1.494(0.007)
C2-C8	1.524(0.007)	C9-O5	1.195(0.007)
C2-O2	1.436(0.005)	O6-C11	1.345(0.008)
C3-C4	1.499(0.007)	C11-C12	1.506(0.011)
C3-O6	1.456(0.006)	C11-O7	1.213(0.008)
C4-C5	1.306(0.008)	O2-O6	1.368(0.007)
C3-H31	0.96	C8-H81	0.92
C4-H41	0.82	C8-H82	1.04

[a] The estimated standard deviations are given in parentheses.

Table IV. Bond Angles and Their Standard Deviations

C2-C1-C5	105.6°(0.4°)	Br-C5-C4	129.6°(0.4°)
C2-C1-O1	125.1 (0.5)	C1-C5-C4	113.6 (0.5)
C5-C1-O1	129.3 (0.5)	C2-O2-C6	116.7 (0.4)
C1-C2-C3	104.1 (0.4)	O2-C6-C7	111.9 (0.5)
C1-C2-C8	109.6 (0.4)	O2-C6-C7	122.5 (0.4)
C1-C2-O2	113.8 (0.4)	O3-C6-C7	125.5 (0.5)
C3-C2-C8	112.5 (0.4)	C2-C8-O4	104.8 (0.4)
C3-C2-O2	112.9 (0.4)	C8-O4-C9	116.2 (0.4)
C8-C2-O2	104.2 (0.4)	O4-C9-O5	122.4 (0.5)
C2-C3-C4	105.1 (0.4)	O5-C9-C10	126.2 (0.5)
C2-C3-O6	111.3 (0.4)	C3-O6-C11	116.1 (0.4)
C4-C3-O6	109.6 (0.4)	O6-C11-O7	122.1 (0.6)
C5-C4-C3	111.6 (0.5)	O6-C11-C12	112.0 (0.7)
Br-C5-C1	117.9 (0.4)	O7-C11-C12	125.8 (0.7)

Table V. Bond Lengths arranged in Groups of Similar Bonds (Å)

C-Br		$C(sp^2)$-$C(sp^2)$	
C5-Br	1.879	C4-C5	1.306
C=O		$C(sp^2)$-$C(sp^3)$	
C1-O1	1.191	C1-C5	1.481
C6-O3	1.186	C3-C4	1.499
O9-O5	1.195	average	1.490
C11-O7	1.213		
average	1.196	$C(sp^3)$-$C(sp^3)$	
		C1-C2	1.542
O-C(=O)		C2-C3	1.567
C6-O2	1.368	C2-C8	1.524
C9-O4	1.349	average	1.544
C11-O6	1.345		
average	1.354	$C(sp^3)$-$C(\equiv H)_3$	
		C6-C7	1.497
C-O(-C)		C9-C10	1.494
C2-O2	1.436	C11-C12	1.506
C3-O6	1.456	average	1.499
C8-O4	1.434		
average	1.442		

Table VI. Deviations of the Atoms from the Least-Squares Plane (Å)[a]

Atom	Deviation
C2	0.000
C3	−0.007
C4	0.013
C5	−0.013
C1	0.007
Br	0.026
O1	0.030

[a] equation of the least-squares plane: $0.42580\,x-0.90193\,y-0.07230\,z+0.66804=0$

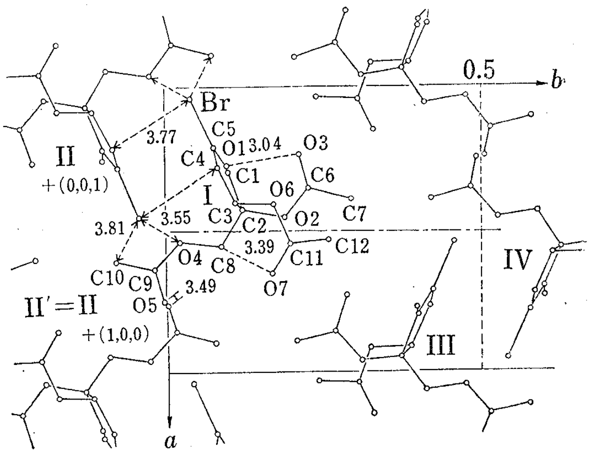

Fig. 4. Projection of the Crystal Structure along c Axis

pentenomycin triacetate (I) is established as Fig. 2 or Fig. 3 which show the configuration around 4C and 5C to be *S* and *S* respectively.

Discussion of the Structure

The molecular structure of monobromopentenomycin tiacetate (I) determined by the present analysis is shown in Fig. 1. As was expected from chemical and spectroscopic studies, the two acetyl groups bond to 4 and 5 carbon atoms take *cis* conformation.

The bond lengths and angles of molecule, calculated from the coordinates given in Table I. are shown in Table III and IV, respectively. The mean bond lengths averaged over groups of similar type are listed in Table V. These mean bond lengths are in agreement with the normally accepted values. The planarity of the ring and the perpendicular distances of atoms from the least-squares plane are shown in Table VI. The projection of the crystal structure along *C* axis is shown in Fig. 4. In this figure, the shortest intermolecular distances from molecular I to the surrounding molecules are shown by broken lines with distance values in Å.

The molecules are designated by the molecular number specifying the equivalent positions in the unit cell and also by the subscript in the parentheses denoting the translations along the three edges of the cell. The equivalent positions are: I at (x,y,z), II at $(\frac{1}{2}-x, -y, -\frac{1}{2}+z)$, III at $(\frac{1}{2}+x, \frac{1}{2}-y, -z)$ and at $(-x, \frac{1}{2}+y, \frac{1}{2}+z)$ where x,y,z are the coordinates given in Table I. The molecules seem to be packed together mainly through van der Waals forces between oxygen atoms of acetoxymethyl groups of the molecule (I) and of the molecule (II′), which is obtained by the translation of the molecule (II) along *a* axis.

Acknowledgement We wish to express our thanks to Prof. Y. Iitaka of Tokyo University for his appropriate advice, and also to Mr. M. Asao and Mr. H. Yoshikawa of our computer center for their supports and cooperations. We are indebted to Dr. T. Okuda, manager of our laboratory for his interest in this work.