

The Crystal and Molecular Structure of Latumcidin Selenate

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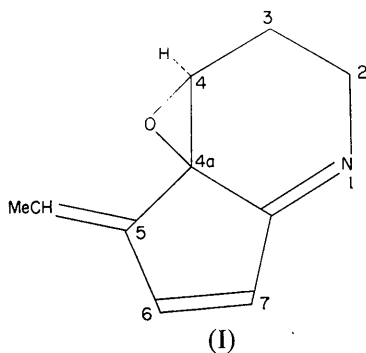
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The crystal structure and absolute configuration of latumcidin selenate ($C_{10}H_{11}NO \cdot H_2SeO_4$), an antiviral antibiotic produced by a *Streptomyces* sp. has been determined by three-dimensional X-ray analysis. Crystals are monoclinic, space group $C2$, with four molecules in the unit cell of dimensions: $a = 26.07$, $b = 4.87$, $c = 9.66$ Å and $\beta = 95.1^\circ$. Refinement was carried out with 1200 observed reflexions by the block-diagonal least-squares method to the final R value of 0.095. The absolute configuration was determined by the use of an anomalous dispersion effect of the selenium atom for Cr $K\alpha$ radiation. The structure of latumcidin conforms to the formula (4*R*,4*aS*)-5-ethylidene-2,3-dihydro-1,5-pyrindine 4,4*a*-oxide.

Introduction

Latumcidin is an antiviral antibiotic isolated from the cultured broth of *Streptomyces reticuli* var. *latumcidicus* by Sakagami, Yamaguchi, Yonehara, Okimoto, Yamanouchi, Takiguchi & Sakai (1958). Latumcidin is identical with abikoviromycin produced by *Streptomyces abikoensis* (Umezawa, Tazaki & Fukuyama, 1951). Structural studies of this antibiotic were carried out by chemical methods by Gurevich, Kolosov, Korobko & Onoprienko (1968). They reported that the substance is (4*S*,4*aR*)-5-ethylidene-2,3-dihydro-1,5-pyrindine 4,4*a*-oxide (I). The structure determination of latumcidin selenate was undertaken to establish the molecular structure as well as the absolute configuration of the antibiotic.



Experimental

Latumcidin selenate was prepared by treating latumcidin with selenic acid in ether-acetone at -10°C . It crystallizes from the solution as colourless needles. The density was measured by the flotation method in ether-carbon tetrachloride mixture. Cell dimensions and the space group were determined from Weissenberg photographs taken with Cu $K\alpha$ radiation (1.5418 Å). Crystal

data are: $C_{10}H_{11}NO \cdot H_2SeO_4$, m.p. 121°C dec., M.W. = 306; Monoclinic, space group $C2$, $a = 26.07 \pm 0.05$, $b = 4.87 \pm 0.02$, $c = 9.66 \pm 0.02$ Å, $\beta = 95.1 \pm 0.2^\circ$, $U = 1221.5$ Å³, $D_m = 1.61$ g.cm⁻³, $Z = 4$, $D_x = 1.67$ g.cm⁻³, $F(000) = 920$, $\mu(\text{Cu } K\alpha) = 47.9$ cm⁻¹. The needle axis is parallel to **b**.

Intensities of 1392 independent reflexions were obtained by visual estimation from equi-inclination Weissenberg photographs, taken around the b axis ($h0l$ to $h4l$) and the c axis ($hk0$) with Cu $K\alpha$ radiation, employing the multiple-film technique. The data were corrected for Lorentz and polarization factors, and then brought to the same arbitrary scale. Since the crystals were fragile and easily destroyed by mechanical force, it was impossible to prepare a crystal with isometric shape for the X-ray work. The data collected from the ($hk0$) photographs were rather inaccurate due to crystal elongation along the b axis; therefore, these data were used only for interlayer scaling at the initial stage. The remaining 1200 reflexions collected around the b axis were used for the structure determination.

Determination and refinement of the structure

The two-dimensional Patterson projection along the b axis was calculated. The position of the selenium atom was easily found from the map, which gave only one salient peak in an asymmetric unit besides the origin peak. The y coordinate can be taken to be zero in the present case. The first electron density maps were synthesized with phases based on the contribution of the selenium atom only, utilizing 883 reflexions for which calculated structure factors showed relatively good coincidence with observed ones. Positions of three lighter atoms were revealed from the maps. The R value was 0.37 for the 883 reflexions. With successive three-dimensional Fourier and difference Fourier syntheses, the 14 atoms including the above four were

located. Isotropic least-squares refinement of the parameters of these atoms and of individual-layer scale factors, carried out by five cycles with block-diagonal least-squares program *HBL5 IV* (Ashida, 1967), lowered the *R* value to 0.20. With all 1200 reflexions, five further cycles of least-squares refinement were carried out by assigning anisotropic thermal parameters to the selenium atom. All atoms, except hydrogen atoms, were found in the electron density maps synthesized at this stage. Further refinements of the structure were carried out with anisotropic thermal parameters for all atoms using least-squares program *HBL5 IV*. The final *R* value is 0.095 for all 1200 reflexions. The weighting scheme employed was: $w=1$ when $F_o \geq 5.0$, $w=0.8$ when $F_o < 5.0$. Scattering factors used were taken from *International Tables for X-ray Crystallography* (1962). Final positional parameters together with estimated standard deviations are given in Table 1. Thermal parameters are listed in Table 2. Observed and calculated structure factors are compared in Table 3.

Table 1. Fractional atomic coordinates ($\times 10^4$) with e.s.d.'s in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>
Se	1050 (1)	0 (16)	2210 (2)
O(1)	4025 (5)	5377 (59)	2506 (11)
O(2)	0577 (5)	1300 (44)	1065 (13)
O(3)	1590 (5)	0285 (77)	1626 (14)
O(4)	0828 (7)	-2817 (61)	2744 (19)
O(5)	1028 (8)	2448 (45)	3494 (15)
N(1)	4191 (5)	0267 (78)	0867 (11)
C(1)	4689 (7)	1216 (80)	1639 (19)
C(2)	4619 (7)	1247 (60)	3218 (18)
C(3)	4146 (7)	2999 (71)	3440 (17)
C(4)	3679 (6)	2906 (62)	2435 (15)
C(5)	3116 (7)	3169 (61)	2569 (18)
C(6)	2882 (7)	1275 (57)	1535 (19)
C(7)	3233 (7)	0050 (108)	0732 (17)
C(8)	3761 (6)	1112 (61)	1281 (17)
C(9)	2914 (7)	5032 (115)	3446 (19)
C(10)	2355 (7)	5285 (106)	3561 (24)

The absolute configuration was determined by the use of the anomalous dispersion effect of the selenium atoms for Cr *K* α radiation ($\lambda=2.2909$ Å: $\Delta f''_{Se}=-0.7$, $\Delta f'_{Se}=2.4$, $\Delta f'_{O}=0.1$, $\Delta f'_{C}=0.2$, $\Delta f'_{N}=0$, $\Delta f''_{N}=0.1$, $\Delta f''_{C}=0$, $\Delta f''_{C}=0.1$). Structure factors for the Friedel pairs of reflexions were evaluated by assuming that the coordinates of the atoms were derived from a right-handed set of axes. Some calculated intensities and observed relations are listed in Table 4. Since the crystal has a twofold axis of rotation along the *b* axis intensities of *hkl* reflexions were compared with those of $\bar{h}\bar{k}l$ reflexions on oscillation photographs taken around the *b* axis. From the good accordance in Table

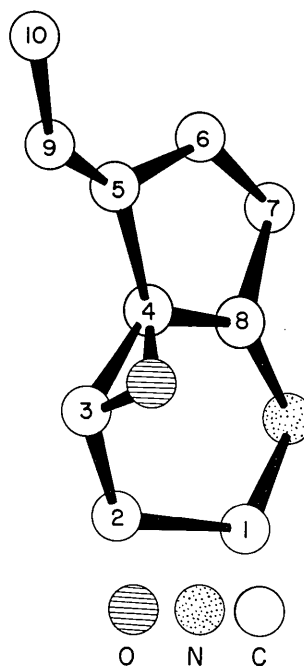


Fig. 1. Molecular structure of latumcidin viewed along the *b* axis.

Table 2. Thermal parameters ($\times 10^4$) in the form $\exp [-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl)]$

Standard deviations ($\times 10^4$) are in parentheses.

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Se	13 (0)	588 (10)	68 (1)	56 (4)	0 (1)	41 (12)
O(1)	20 (2)	656 (138)	81 (12)	-89 (34)	16 (8)	-103 (79)
O(2)	26 (3)	1102 (159)	73 (14)	84 (36)	-43 (11)	184 (76)
O(3)	19 (2)	1486 (201)	141 (18)	-190 (53)	-23 (11)	293 (154)
O(4)	25 (3)	1340 (195)	185 (26)	-71 (47)	-4 (15)	356 (128)
O(5)	46 (5)	738 (127)	112 (19)	-47 (45)	43 (16)	-414 (89)
N(1)	15 (2)	799 (138)	53 (119)	-62 (45)	0 (8)	-6 (110)
C(1)	13 (3)	1623 (352)	77 (20)	31 (50)	-2 (12)	-170 (129)
C(2)	15 (3)	954 (195)	71 (19)	26 (40)	-24 (12)	-166 (99)
C(3)	15 (3)	1225 (222)	50 (17)	-62 (46)	-6 (11)	14 (109)
C(4)	12 (3)	1064 (186)	39 (15)	-123 (39)	-2 (10)	-11 (91)
C(5)	14 (3)	859 (173)	76 (19)	-6 (39)	-1 (12)	13 (103)
C(6)	14 (3)	750 (153)	87 (20)	-12 (36)	-17 (12)	34 (94)
C(7)	15 (3)	859 (154)	109 (20)	-108 (62)	-8 (12)	-115 (184)
C(8)	10 (2)	1097 (235)	73 (18)	-10 (36)	-11 (11)	156 (99)
C(9)	14 (3)	1047 (179)	128 (23)	91 (74)	23 (13)	159 (223)
C(10)	13 (3)	765 (192)	209 (32)	28 (58)	35 (15)	85 (204)

accordance with the value (1.47 Å) reported for the group in 1,2-epoxycyclopentane (Erlandsson, 1955).

The shape of the SeO_4 group is fairly different from shapes observed in ordinary orthoselenates. In the present substance, there are two kinds of Se–O distances, while the SeO_4^{2-} anion is an almost regular tetrahedron (e.g., in K_2SeO_4 ; Kálmán, Stephens & Cruickshank, 1970). The two longer distances are in good agreement with the length between Se and bridging O atoms in selenium trioxide (Mijlhoff, 1965), indicating that these are of Se–OH. The remaining Se–O distances, as well as all the bond angles, are also in excellent agreement with corresponding distances and angles in SeO_3 .

Table 5. Least-squares plane and distances (Å) of atoms from the plane

Equations of plane: $lX+mY+nZ+P=0$ with $X=ax+cz\cos\beta$, $Y=by$, $Z=cz\sin\beta$.

Plane	l	m	n	P		
	-0.033	0.761	-0.648	0.720		
Distances						
C(1)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)
-0.25	-0.03	0.03	-0.01	0.00	0.01	0.19
C(10)	N(1)					
0.27	-0.08					

The five-membered ring is planar. The equation of the least-squares plane and deviations of atoms from the plane are given in Table 5. Atoms C(1), C(9), C(10) and N are also nearly coplanar with the five-membered ring. The six-membered ring has a half-chair conformation with C(1) displaced largely from the least-squares plane defined by the other five constituent atoms.

The latumcidin molecule has two asymmetric carbon atoms. Absolute configurations of these atoms are:

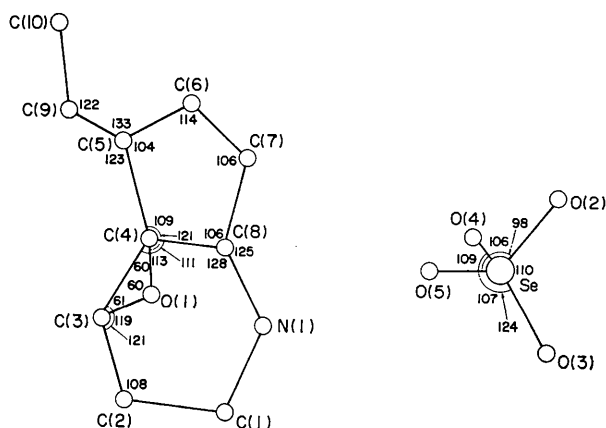


Fig. 3. Bond angles ($^\circ$) in latumcidin selenate.

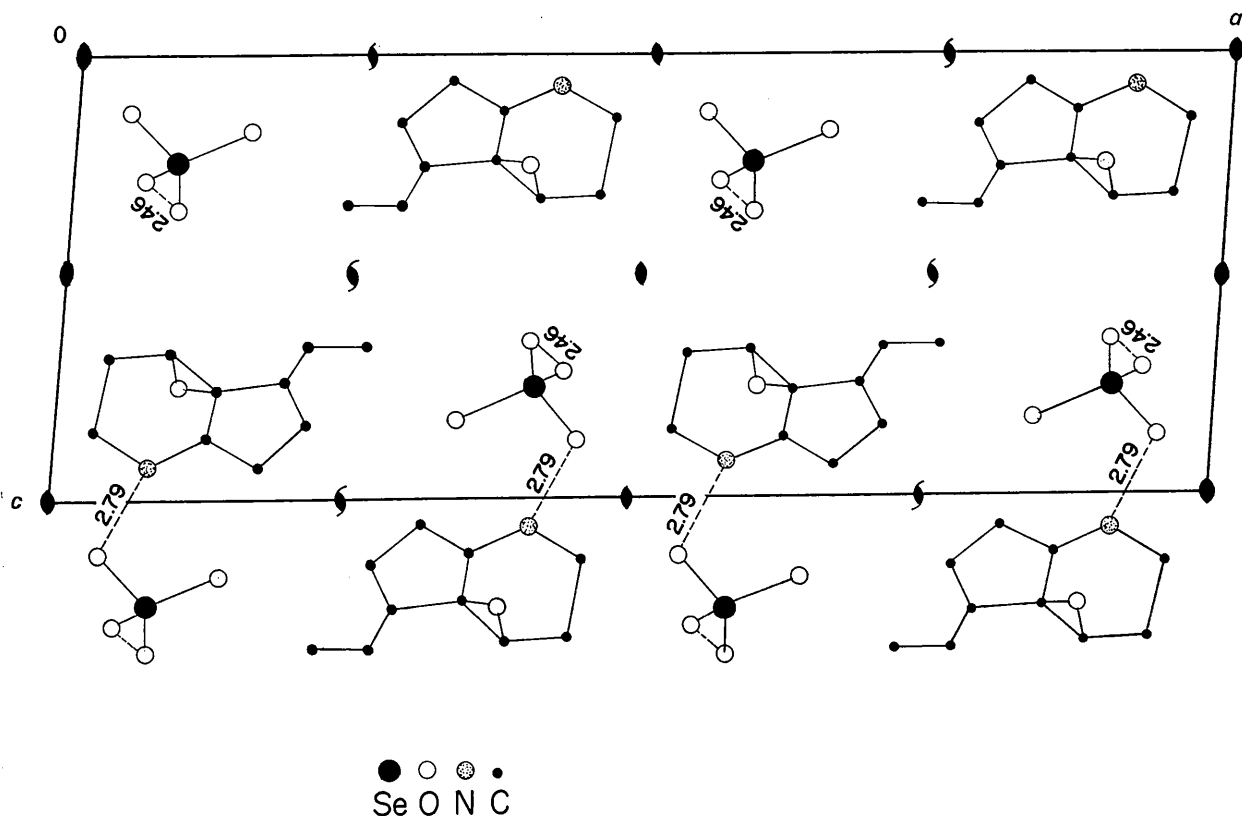


Fig. 4. Projection of the crystal structure of latumcidin selenate along the b axis. The short contact between molecules is shown by broken lines (Å).

C(3)*R* and C(4)*S* respectively. They are opposite to the previously reported configurations C(3)*S* and C(4)*R*, which were assigned on the basis of the benzoate rule (Gurevich *et al.*, 1968). The contradiction may be due to the limitation of the benzoate rule or to the inversion of the hydroxy group of latumcidin during reduction.

Table 6. Intermolecular contacts less than 3.50 Å

i	$\frac{1}{2} - x$	$\frac{1}{2} + y$	$-z$
ii	$\frac{1}{2} + x$	$\frac{1}{2} + y$	z
iii	$\frac{1}{2} + x$	$-\frac{1}{2} + y$	z
iv	x	$1 + y$	z
v	$\frac{1}{2} - x$	$-\frac{1}{2} + y$	$-z$

O(2)–N(1 ⁱ)	2.790 Å	O(3)–C(7 ⁱ)	3.309 Å
C(7)–O(3 ⁱ)	3.473	C(2)–O(4 ⁱⁱ)	3.257
C(1)–O(4 ⁱⁱⁱ)	3.104	C(1)–O(2 ⁱⁱⁱ)	3.410
O(5)–O(4 ^{iv})	2.459	O(2)–O(4 ^{iv})	3.329
O(1)–C(2 ^{iv})	3.295	O(1)–C(7 ^{iv})	3.428
O(1)–C(8 ^{iv})	3.087	O(1)–N(1 ^{iv})	2.912
O(3)–C(7 ^v)	3.473	C(7)–O(3 ^v)	3.309
N(1)–O(2 ^v)	2.790		

A projection of the crystal structure viewed along the *b* axis, with designations of short intermolecular atomic distances, is shown in Fig. 4. Also, molecular contacts less than 3.50 Å are given in Table 6. Strong hydrogen bonds (2.46 Å) are observed between atoms O(5) and O(4'); chains of selenic acid molecules are formed parallel to the *b* axis. Here, the prime means that the atom belongs to the adjacent molecule displaced by a unit translation along the *b* axis. Hydrogen bonds are also observed between O(2) and N(1) atoms (2.79 Å). Distances O(1)···N(1') (2.91 Å) and O(1)···C(8') (3.09 Å) are fairly short. These distances may indicate some

interaction between O(1) and N(1'), and/or between O(1) and C(8'). The former interaction may be due to charge-transfer from O(1) to N(1'). Thus, the structure is made up of chains of selenic acid and columns of latumcidin molecules parallel to the *b* axis. Each chain of selenic acid is connected to a column of latumcidin with the hydrogen bonds. These structural units are laterally combined by the van der Waals force. Thus, the needle-like form of the crystal is well explained by the existence of the rather strong intermolecular forces along the *b* axis.

Calculations were carried out on the HITAC 5020E computer at the computer centre of this university. The authors acknowledge Dr Yasuaki Ogawa for his kind collaboration on this work.

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Sur Quelques Fluométallates Alcalino-Terreux. I. Structure Cristalline de BaFeF₅ et SrAlF₅

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The crystal structure of the tetragonal A^{II}B^{III}F₅ phases has been determined by single-crystal analysis of BaFeF₅ and SrAlF₅. In the BaFeF₅ lattice iron and fluorine atoms are grouped in two different kinds of chains, both having the formula (FeF₃)₂ⁿ⁻: the first is linear, the second ramified. To a first approximation the space group is *I4*, but a small distortion along the *c* axis in fact doubles the *c* parameter, the space group becoming *P4*.

Lors de l'étude des systèmes AF₂–FeF₂–FeF₃ dans lesquels A était un élément alcalino-terreux, Ravez, Viollet, de Pape & Hagenmuller (1967) ont mis en évidence

un grand nombre de composés inédits parmi lesquels la phase quadratique BaFeF₅ semblait jouer le rôle de pivot (Ravez & Hagenmuller, 1967; Ravez *et al.*, 1967; Ravez, 1968). D'après ces auteurs cette phase donne des solutions solides avec un autre fluoferrite Sr₃(FeF₆)₂ et avec une phase Sr₂Fe₂F₉ dans laquelle le fer se trouve simultanément aux degrés d'oxydation

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