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Studies on the Ionophorous Antibiotics. II. Silver Salt of Lysocellin

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Abstract. Silver salt of lysocellin, $C_{34}H_{59}O_{10}Ag.\frac{1}{2}H_2O$, M.W. 753·71, m.p. 123°C (decomp.), orthorhombic, $P2_12_12_1$, $a=16{\cdot}283$ (7), $b=26{\cdot}519$ (16), $c=8{\cdot}930$ (5) Å, $D_m=1{\cdot}18$ (by flotation), $D_x=1{\cdot}16$ g cm^{-3}, $Z=4$, $R=0{\cdot}070$ for 1574 observed reflexions. The molecule contains three ether rings and a β-hydroxyl ketone group and is a new member of the polyether antibiotics.

Introduction. A crystal of dimensions 0·32 × 0·29 × 0·15 mm was used to collect the intensity data on the Philips automated four-circle diffractometer. It was coated with colourless nail varnish to prevent deterioration during exposure. Integrated intensities were measured for $2\theta<51°$ by the θ–2θ scan technique with Mo $K\alpha$ radiation ($\lambda=0{\cdot}7107$ Å). Among the 4320 reflexions recorded, 1574 reflexions gave intensities greater than three times their standard deviations and they were used for the structure determination. The structure was solved by the heavy-atom method. The atomic coordinates were refined by a block-diagonal least-squares program with anisotropic temperature factors. The final R became 0·070 for the 1574 observed reflexions. The atomic scattering factors used were those listed in *International Tables for X-ray Crystallography* (1962).* Table 1 lists the final atomic parameters. The absolute configuration was determined with the use of the anomalous scattering of the silver atom ($\Delta f'=-0{\cdot}5$, $\Delta f''=4{\cdot}7$) for Cu $K\alpha$ radiation. Some calculated intensities and observed relations are compared in Table 2. The concordance in Table 2 indicates that the atomic coordinates given in Table 1 correctly represent the absolute configuration of the molecule referred to the right-handed set of axes. A preliminary communication of this work has been published (Ōtake, Koenuma, Kinashi, Sato & Saito, 1975).

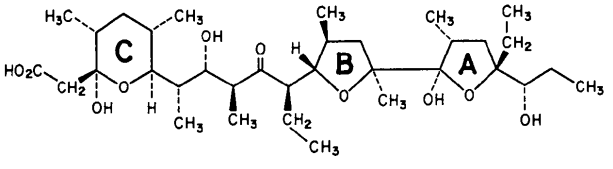

Fig. 1. The absolute structure of lysocellin.

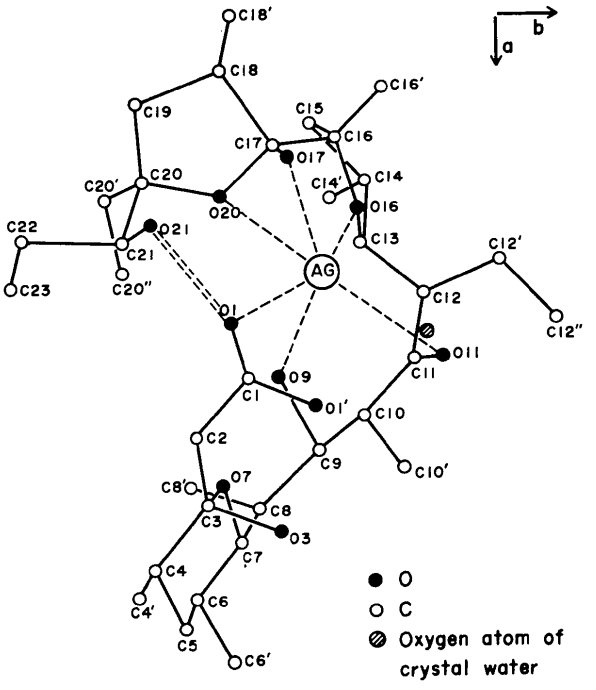

Fig. 2. The molecular structure of the silver salt of lysocellin viewed along the c axis.

Discussion. Lysocellin, a new antibiotic isolated from the cultured broth of *Streptomyces cacaoi* var. *asoensis*, shows an inhibitorial activity against gram-positive bacteria, mycobacteria and fungi (Ebata, Kasahara, Sekine & Inoue, 1975). This polyether antibiotic forms a metal ion complex effecting the transport of alkaline metal ions across the cell membrane. The chemical structure and the absolute configuration of lysocellin revealed by the present study is shown in Fig. 1. A projection of the structure of the molecule along the c axis is shown in Fig. 2, together with the numbering scheme. It has now been established that lysocellin is a new member of the polyether antibiotics and contains three ether rings, a non-substituted methylene group vicinal to the terminal carboxyl group and a

* A list of structure amplitudes has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31551 (13 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

β-hydroxy ketone group which is identical with those of salinomycin (Kinashi, Ōtake, Yonehara, Sato & Saito, 1975) and lasalocid antibiotics (Westley, Evans, Williams & Stempel, 1970). Among the three ether rings, *A* and *C* have the hemi-ketal groups of five- and six-membered rings, respectively. When the free acid of lysocellin was dissolved in methanol, the isomerization of the five-membered ring *A* into the six-membered ring gradually took place with great ease. It is likely that the new bond formation occurred between O(21) and C(17) instead of O(20) and C(17). At the same time, the decarboxylation and methylation at O(3) also occurred. Accordingly lysocellin might only be stable when it forms a metal complex as shown in Fig. 2. The molecule takes a circular structure like other polyether antibiotics. The hydrophilic groups are oriented toward the interior of the ring and the hydrophobic groups are arranged at the exterior. The terminal hydroxyl O(21) and the carboxyl oxygen atom O(1) are close enough to form a strong hydrogen bond of 2·62 (3) Å. A silver ion is surrounded by six oxygen atoms at dis-

Table 2. *Determination of the absolute configuration*

h k l	F_c (*hkl*)	obs.	F_c ($\bar{h}kl$)
2 1 1	49·1	>	34·6
3 1 1	70·1	>	65·3
4 1 1	46·9	>	43·7
1 2 1	88·2	>	77·4
2 2 1	97·7	>	82·3
4 2 1	76·6	>	62·0
1 3 1	161·4	>	143·9
1 4 1	110·8	>	100·5

Table 1. *Atomic parameters*

Positional and thermal parameters for the non-hydrogen atoms (× 10⁴), with their e.s.d.'s in parentheses. The β_{ij}'s are defined by exp $[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+2hk\beta_{12}+2hl\beta_{13}+2kl\beta_{23})]$.

	x	*y*	*z*	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Ag	4455 (1)	6833 (1)	5503 (2)	50 (1)	35 (0)	151 (2)	−7 (0)	−2 (1)	−1 (0)
C(1)	5677 (5)	6247 (2)	7934 (17)	37 (10)	34 (6)	82 (10)	−10 (10)	−9 (25)	7 (7)
C(2)	6322 (4)	5811 (3)	8120 (10)	46 (10)	22 (5)	168 (1)	−10 (5)	6 (2)	8 (10)
C(3)	7124 (16)	5959 (12)	7299 (15)	71 (13)	17 (3)	134 (9)	−12 (3)	−39 (1)	−1 (1)
C(4)	7810 (1)	5557 (1)	7338 (50)	85 (2)	24 (4)	195 (17)	17 (1)	−37 (4)	16 (17)
C(4′)	8105 (4)	5446 (13)	8945 (11)	96 (4)	28 (4)	143 (12)	8 (1)	−69 (4)	11 (5)
C(5)	8531 (15)	5756 (3)	6349 (8)	55 (14)	30 (6)	221 (55)	19 (10)	8 (36)	−5 (0)
C(6)	8212 (4)	5848 (2)	4754 (5)	76 (20)	27 (1)	152 (32)	30 (1)	−13 (2)	−23 (9)
C(6′)	8940 (4)	6109 (1)	3861 (4)	61 (30)	50 (11)	300 (87)	24 (8)	59 (17)	42 (5)
C(7)	7515 (13)	6264 (0)	4855 (12)	35 (3)	24 (4)	131 (12)	7 (4)	7 (8)	11 (1)
C(8)	7119 (11)	6362 (16)	3330 (6)	58 (5)	13 (14)	168 (17)	8 (1)	−48 (3)	−2 (12)
C(8′)	6843 (8)	5915 (4)	2455 (29)	80 (14)	25 (2)	181 (21)	17 (2)	−18 (26)	−8 (8)
C(9)	6385 (16)	6757 (3)	3649 (22)	41 (1)	14 (7)	172 (48)	0 (2)	−7 (5)	−3 (13)
C(10)	6082 (2)	6991 (5)	2180 (4)	30 (1)	24 (12)	153 (23)	12 (7)	−14 (1)	7 (9)
C(10′)	6737 (6)	7314 (0)	1426 (3)	37 (4)	16 (1)	213 (34)	−5 (1)	33 (14)	52 (1)
C(11)	5382 (3)	7350 (11)	2644 (14)	47 (24)	15 (2)	177 (27)	−15 (2)	−23 (12)	27 (20)
C(12)	4703 (7)	7457 (8)	1492 (3)	19 (15)	11 (2)	223 (1)	−1 (5)	−8 (4)	30 (22)
C(12′)	4323 (8)	7985 (2)	1604 (1)	80 (5)	9 (1)	263 (2)	2 (6)	7 (8)	32 (12)
C(12″)	4960 (3)	8357 (1)	1053 (17)	124 (12)	15 (4)	338 (74)	−3 (4)	62 (21)	26 (7)
C(13)	4064 (2)	7010 (2)	1701 (14)	40 (6)	18 (4)	93 (20)	4 (4)	24 (1)	18 (11)
C(14)	3324 (3)	7026 (2)	671 (0)	25 (1)	26 (9)	112 (8)	10 (5)	32 (8)	34 (11)
C(14′)	3558 (1)	6815 (11)	−873 (4)	52 (1)	59 (7)	101 (8)	14 (10)	−30 (13)	−24 (5)
C(15)	2719 (1)	6705 (13)	1505 (7)	50 (4)	23 (8)	76 (20)	−4 (5)	−28 (2)	13 (10)
C(16)	2852 (1)	6829 (8)	3171 (14)	32 (2)	20 (2)	199 (32)	2 (6)	−10 (10)	11 (8)
C(16′)	2264 (0)	7214 (3)	3866 (9)	38 (6)	18 (1)	162 (8)	7 (1)	44 (4)	−2 (0)
C(17)	2883 (0)	6352 (5)	4194 (27)	14 (1)	13 (9)	253 (10)	4 (0)	21 (2)	−55 (9)
C(18)	2152 (0)	5989 (4)	4015 (9)	38 (11)	14 (3)	252 (2)	−4 (3)	−4 (10)	14 (18)
C(18′)	1456 (6)	6103 (13)	5180 (15)	31 (0)	22 (4)	320 (15)	2 (3)	53 (2)	−10 (8)
C(19)	2529 (2)	5475 (5)	4249 (13)	25 (3)	21 (2)	281 (34)	−8 (2)	28 (9)	5 (7)
C(20)	3436 (4)	5513 (7)	3834 (13)	52 (1)	15 (12)	128 (1)	10 (4)	0 (1)	−28 (6)
C(20′)	3594 (8)	5265 (6)	2201 (20)	71 (20)	23 (5)	157 (7)	6 (1)	−23 (7)	−4 (8)
C(20″)	4470 (2)	5353 (2)	1573 (29)	49 (1)	30 (5)	253 (7)	9 (3)	−5 (9)	−34 (2)
C(21)	4040 (3)	5319 (7)	4984 (4)	44 (6)	35 (6)	153 (32)	18 (1)	−25 (17)	−16 (5)
C(22)	4003 (15)	4726 (3)	5207 (14)	120 (2)	8 (3)	303 (13)	17 (7)	−103 (2)	19 (7)
C(23)	4585 (14)	4600 (13)	6503 (3)	88 (5)	27 (2)	303 (33)	9 (2)	−19 (3)	4 (14)
O(1)	5047 (9)	6141 (1)	7173 (13)	49 (4)	40 (1)	177 (5)	−6 (2)	−9 (19)	3 (2)
O(1′)	5880 (9)	6672 (5)	8458 (21)	46 (1)	31 (4)	233 (15)	−9 (3)	−14 (13)	−32 (7)
O(3)	7422 (3)	6416 (7)	7960 (14)	42 (5)	28 (7)	194 (2)	−7 (1)	−1 (6)	−16 (1)
O(7)	6886 (4)	6040 (2)	5814 (5)	41 (1)	18 (3)	140 (18)	3 (0)	−24 (2)	−5 (6)
O(9)	5683 (4)	6445 (0)	4156 (11)	38 (4)	18 (4)	156 (5)	−1 (1)	−8 (3)	8 (0)
O(11)	5416 (3)	7606 (0)	3798 (13)	50 (4)	15 (2)	198 (3)	−8 (3)	17 (10)	−1 (0)
O(16)	3680 (7)	7050 (2)	3225 (3)	36 (2)	11 (9)	121 (5)	4 (1)	−7 (3)	6 (1)
O(17)	3078 (3)	6467 (2)	5639 (12)	52 (4)	28 (5)	67 (11)	−5 (1)	8 (7)	−15 (2)
O(20)	3560 (5)	6054 (4)	3590 (6)	46 (0)	10 (1)	159 (16)	−2 (1)	−4 (12)	9 (7)
O(21)	3822 (4)	5558 (14)	6370 (3)	56 (10)	22 (2)	189 (2)	0 (4)	21 (5)	8 (3)
O(H_2O)	5127 (5)	7432 (10)	7072 (20)	49 (25)	36 (12)	290 (3)	−13 (29)	38 (12)	−52 (0)

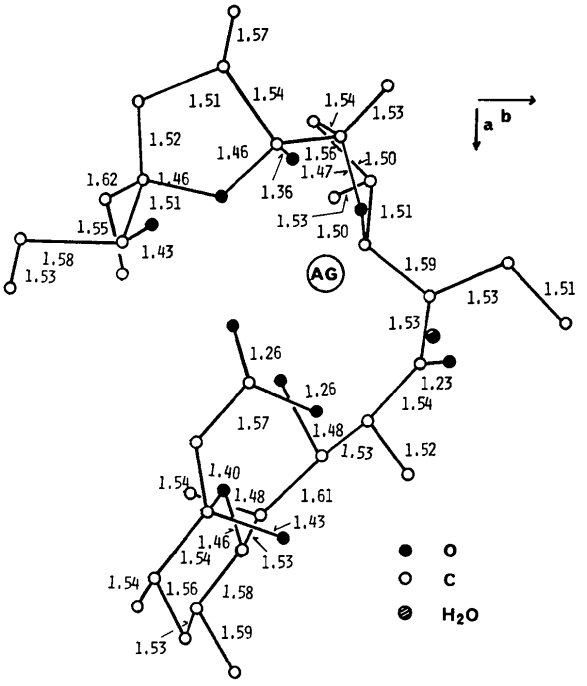

Fig. 3. Bond lengths (Å). The mean standard deviation is 0·03 Å.

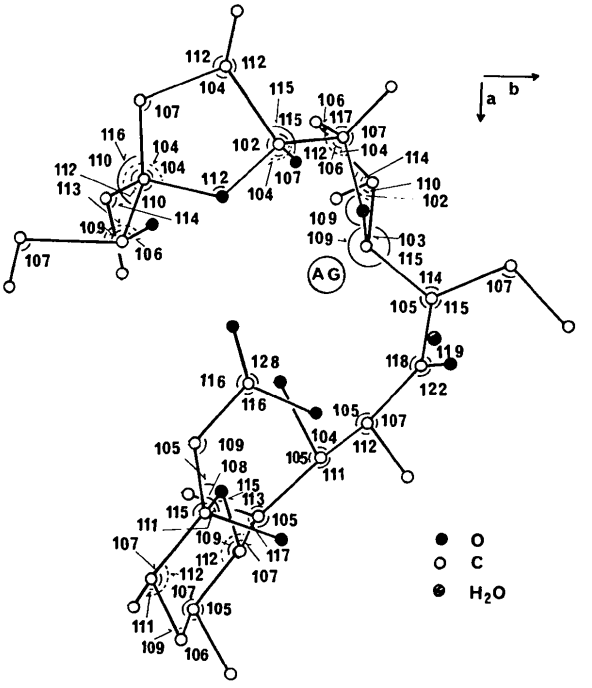

Fig. 4. Bond angles (°). The mean standard deviation is 2°.

tances ranging from 2·39 (2) to 2·99 (2) Å. The five-membered rings, *A* and *B*, take an envelope conformation and the six-membered ring *C* adopts a chair conformation. For ring *C*, the methyl groups of C(4′) and C(6′) along with the two substituents of C(2) and C(8) at the α-position of the tetrahydropyran function are equatorial, while the hydroxyl group of O(3) is axial. Bond lengths and angles are shown in Figs. 3 and 4, respectively. They do not differ significantly from the normal values.

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Two Acid Rearrangement Products from Substituted Pentacyclododeca-5,12-diones: $C_{18}H_{24}O_2$ and $C_{16}H_{20}O_4$

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Abstract. (II) $C_{18}H_{24}O_2$, $P2_1/c$, $a=6{\cdot}818$ (4), $b=12{\cdot}586$ (6), $c=17{\cdot}966$ (9) Å, $\beta=106{\cdot}8$ (1)°, $Z=4$, $d_{calc}=1{\cdot}22$ g cm^{-3}, $\sim(0{\cdot}8\times0{\cdot}6\times0{\cdot}2)$ mm. This molecule has a bisnordiadamantane ring skeleton. (III) $C_{16}H_{20}O_4$, $P2_1/n$, $a=12{\cdot}247$ (7), $b=9{\cdot}972$ (6), $c=12{\cdot}242$ (7) Å, $\beta=102{\cdot}9$ (1)°, $Z=4$, $d_{calc}=1{\cdot}26$ g cm^{-3}, $\sim(0{\cdot}5\times0{\cdot}5\times0{\cdot}8)$ mm.