

THE STRUCTURE OF
LATUMCIDIN (ABIKOVIROMYCIN)
DETERMINED BY X-RAY
ANALYSIS

Sir:

Latumcidin¹⁾ (abikoviromycin)^{2,3)}, C₁₀H₁₁·NO, is an optically active antiviral antibiotic isolated from the culture broth of *Streptomyces reticuli* var. *latumcidicus*. It is highly unstable and promptly polymerizes during isolation.

In 1968, A. I. GUREVICH *et al.*⁴⁾ reported the structure of abikoviromycin to be (4S, 4aR) 5-ethylidene-2,3-dihydro-1,5-pyridine-4,4a-oxide by chemical method. We have attempted to confirm the structure by nmr and X-ray analysis.

In the nmr spectrum of latumcidin free base in deuteriobenzene there was some uncertainty as to the assignment of the singlet at δ 3.49 as a methine proton adjacent to methylene group, and the multiplet at δ 1.14. An attempt to answer these questions by decoupling study was unsuccessful.

Fortunately, we could crystallize the antibiotic as the selenate. The crystal structure and absolute configuration of the selenate were determined by three-dimensional X-ray analysis as follows.

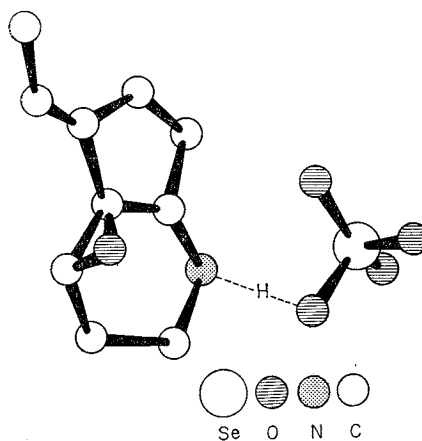
The selenate of latumcidin was prepared by the treatment of latumcidin with ethereal selenic acid in an acetone-ether mixture at -10°C. It was quickly coated with nail polish to prevent the decomposition.

The crystals are colorless needles; C₁₀H₁₁·NO·H₂SeO₄, M.W. 306, m.p. 121°C (dec.).

Table 1. Determination of the absolute configuration

Indexes	Fc(<i>hkl</i>) ²	obs.	Fc(<i>hkl</i>) ²
-11 1 1	2097	>	1678
11 1 1	5117	>	4779
9 1 1	1771	<	2217
-1 1 2	2516	<	3206
-5 1 3	4705	>	4254
9 1 3	1896	<	2110
-3 1 3	486	<	803
3 1 3	3652	<	4842
-5 1 5	4720	>	4320

Fig. 1.

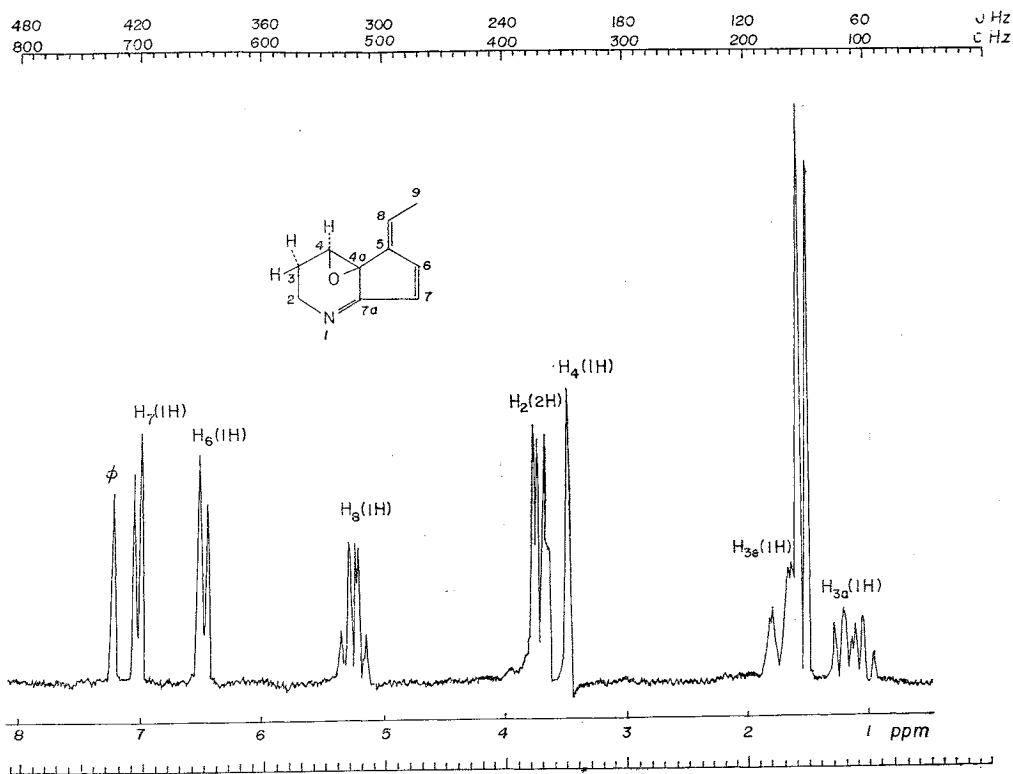


They are monoclinic, space group C2 with four molecules in a unit cell with the dimensions; $a=26.07 \text{ \AA}$, $b=4.87 \text{ \AA}$, $c=9.66 \text{ \AA}$ and $\beta=95.05^\circ$. Intensities of the 1392 independent reflections were measured visually from the equi-inclination WEISSENBERG photographs taken with Cu K α radiation ($\lambda=1.5418 \text{ \AA}$) around the *b*- and *c*-axis. A two-dimensional PATTERSON function was calculated. The location of the selenium atom was easily deduced. The first electron density map, which was synthesized using phase based on the contribution of the selenium atom, revealed the position of three lighter atoms. From successive calculations of three-dimensional FOURIER and difference syntheses, the 14 atoms were found. Parameters thus obtained were refined by the least-squares method. All the atoms were found from the electron density maps synthesized at this stage. Further cycles of least-squares refinement were carried out. The final reliability factor was 9.5 %.

The absolute configuration was determined by use of the anomalous dispersion effect of the selenium atom for Cr K α radiation ($\lambda=2.2909 \text{ \AA}$: $f_{\text{Se}'}=-0.7$, $f_{\text{Se}''}=2.4$, $f_{\text{O}'}=0.1$, $f_{\text{O}''}=0.2$, $f_{\text{N}'}=0.1$, $f_{\text{N}''}=0.1$, $f_{\text{C}'}=0.1$). In Table 1 some of the calculated intensities and observed relations between (*hkl*) and (*hkl*) are compared.

The resulting molecular structure of latumcidin selenate viewed along the *b* axis is illustrated in Fig. 1.

The absolute configuration of the asymmetric carbon atoms are 4(R) and 4a(S)

Fig. 2. NMR spectrum of latumcidin in C_6D_6 (TMS).

respectively. These results are contradictory to the previous report of 4(S) and 4a(R). We speculate that their results are due to an exception to the benzoate rule or to an inversion of the hydroxy group of latumcidin during reduction.

The singlet at δ 3.49 in the nmr spectrum is explained from the fact that the bond angles between the C4 proton and C5 protons are both about 60° . According to the KARPLUS equation the coupling constants should be nearly zero. The multiplet at δ 1.14 is explained from the fact that the hydrogens on the C3 carbon exist separately at δ 1.75 (equatorial) and δ 1.14 (axial) in deuteriobenzene.

The exact details of the X-ray analysis will be presented in *Acta Crystallographica* in the near future.

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