The Crystal Structure of Grisorixin Silver Salt

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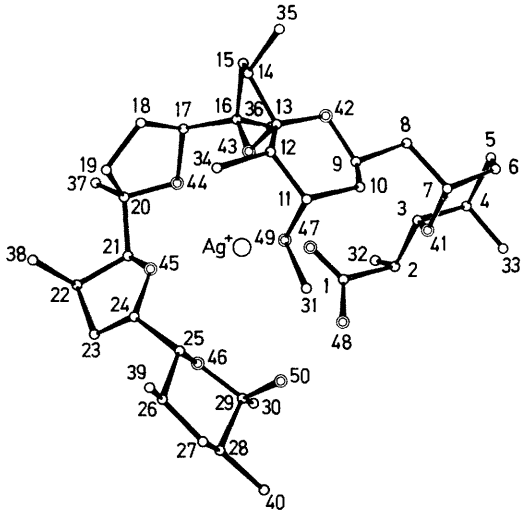
Summary The molecular structure of the antibiotic Grisorixin has been determined from the crystal structure of a silver salt, $C_{40}O_{10}H_{67}Ag$.

THE chemical study of a new biologically active compound, grisorixin, has been described in the preceding communication.[1] Since purely chemical methods failed to provide the full structure an *X*-ray cristallographic analysis was undertaken.

Grisorixin gives a silver salt which can be crystallised easily, from an aqueous acetone solution, by slow evaporation in the dark at room temperature.

Crystal data: Expected molecular weight from mass spectroscopy: 834; D_0 observed density: 1·21; $Z = 4$; space group: $P2_12_12_1$, $a = 20{\cdot}011$; $b = 17{\cdot}266$; $c = 13{\cdot}330$ Å; molecular weight calculated from the final structure: 816; D_c 1·18. 4923 independent reflections were collected with nickel-filtered copper radiation on a Siemens tape-controlled automatic diffractometer. The 2940 non zero reflections for which θ was less than 50°, were used in the calculations.

The silver position was found from a three-dimensional Patterson synthesis. A Fourier synthesis, phased from the co-ordinates of the heavy atom showed the positions of 35 atoms with reasonable interatomic distances. A new Fourier synthesis was computed, assuming that all the light atoms were carbons. 50 light atoms were present in this



FIGURE

new synthesis, and it was even possible, from the electron density of some peaks, to identify some oxygens.

At this stage, a structure factor calculation gave an R value of 0·22. Three cycles of least-squares refinement on positional and isotropic thermal parameters were performed, using the block-diagonal approximation. The R value dropped to 0·12, and it was then possible to state which atoms were oxygens from inspection of the thermal motion parameters. A difference density did not reveal any other light atom, all the peaks in this synthesis being below 1·4 e $Å^{-3}$. After two more cycles using anisotropic thermal parameters, we calculated the structure factors for the two enantiomers including the anomalous dispersion of the silver to determine the absolute configuration of grisorixin. The results ($R = 0·08$ and $R = 0·10$) indicated unambiguously the chirality of the molecule (Figure). The molecular formula of the salt is thus $C_{40}O_{10}H_{67}Ag$.

It seems likely that it will be possible to locate most of the hydrogen atoms from a difference density now being computed.

The crystal structure is very similar to those found for monensin,[2] nigericin,[3,4] and antibiotic X-537 A.[5] The anion is wrapped around the silver. It is held in this conformation by a strong hydrogen bond O(50)–H · · · O(48) (2·64 Å), and by interactions between the silver and the oxygens: in addition to the bond Ag · · · O(47) at 2·20 Å, four silver-oxygen distances lie between 2·4 and 2·7 Å. This conformation of the complex, with almost no oxygen atoms on the outside, explains its extremely low solubility in polar solvents.

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