X-Ray Crystal Structure and Absolute Configuration of p-Bromophenacylseptamycin Monohydrate, a Polyether Antibiotic

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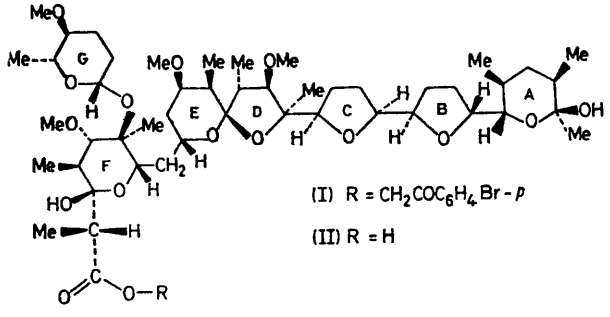
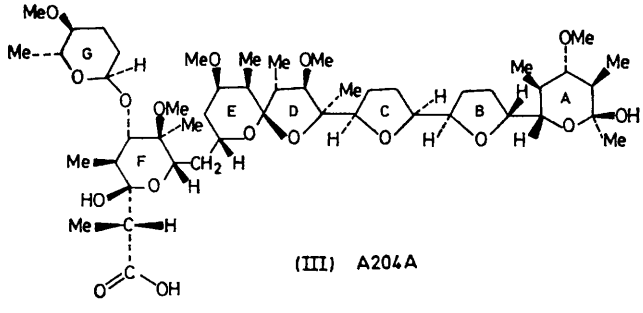
Summary The constitution and absolute configuration of the polyether antibiotic $C_{48}H_{81}O_{16}^-Na^+$ has been established by *X*-ray crystal structure analysis of the *p*-bromophenacyl derivative.

SEPTAMYCIN may be isolated[1] as a crystalline sodium salt $C_{48}H_{81}O_{16}^-Na^+$ from *Streptomyces hygroscopicus*. Such material, however, is not ideally suited for a crystal structure analysis, so we have studied the *p*-bromophenacyl derivative in order to determine the chemical constitution and the relative and absolute configurations.





Crystal data: *p*-Bromophenacyl septamycin monohydrate, $C_{56}H_{87}BrO_{17},H_2O$, $M = 1130{\cdot}2$, orthorhombic, $a = 12{\cdot}728(3)$, $b = 9{\cdot}909(2)$, $c = 48{\cdot}708(7)$ Å, $U = 6143(3)$ Å^3, $Z = 4$, $D_c = 1{\cdot}22$, space group $P2_12_12_1$ (D^4_2, No. 19).

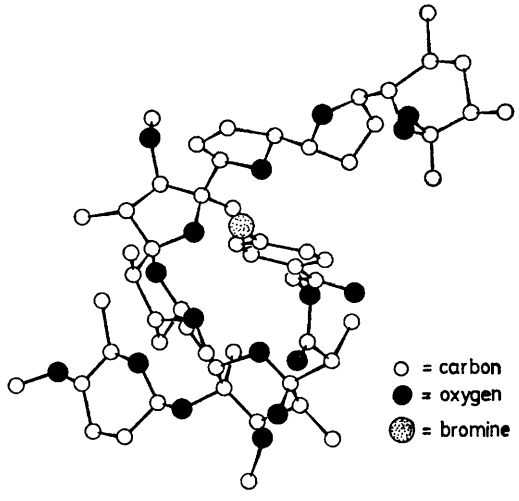


FIGURE. Projection of *p*-bromophenacylseptamycin down the crystallographic *a*-axis.

Intensity data were collected on a four-circle diffractometer employing graphite-monochromatised Cu-K_α radiation for $\theta \leqslant 55°$. A total of 4698 measurements yielded 3190 symmetry-independent significant $[I \geqslant 3\sigma(I)]$ reflections. The heavy atom was located from a Patterson synthesis and the structure was solved by repeated cycles of structure-factor calculation and Fourier synthesis. The one molecule of water of crystallisation, which is hydrogen-bonded between the hydroxy-group of ring A and the ether oxygen atom of ring B, was located in a difference Fourier synthesis towards the end of this process. Refinement was

carried out by block-diagonal least squares using anisotropic temperature factors. Hydrogen atoms were introduced in calculated positions at a late stage and kept fixed. The present value of R is 0·13. Profile analysis[2] of the original data at the termination of refinement suggests the presence of instrumental instability during data collection. Further refinement with these data is not contemplated. An R-factor ratio test[3] significant at the 0·005 level established the absolute configuration as that shown in (I) which also gives the structural formula of the phenacyl derivative. The formula of native septamycin is hence (II).

Septamycin is a polyether which in part closely resembles nigericin,[4] but has seven rings in contrast to the six of nigericin; the polyether which it most closely resembles is antibiotic A204A,[5] the largest yet characterised (III). Septamycin differs from this in the lack of a methoxy-group on ring A and in the different configuration and point of attachment of ring G. The conformation of the *p*-bromophenacyl derivative of septamycin, with hydrogen atoms omitted for clarity, is shown in the Figure, projected down the crystallographic *a*-axis. Examination of a CPK-space-filling model indicates that rings A–F may fold about a central metal cation in exactly the same way as do nigericin and A204A. The resulting molecule is roughly globular in shape with a 'tail' composed of ring G. It may be regarded as a collar around the metal atom, buttoned by the formation of a hydrogen bond between the hydroxy-group on ring A and the carboxylic acid group on ring F.

We thank Z. Kis and C. Keller for providing the material.

(*Received, 28th June* 1974; *Com.* 768.)

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