X-Ray Crystallographic Proof of a Cyclol Structure in a Tripeptide

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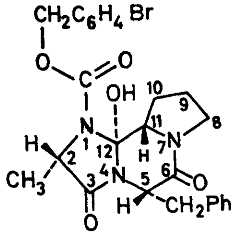
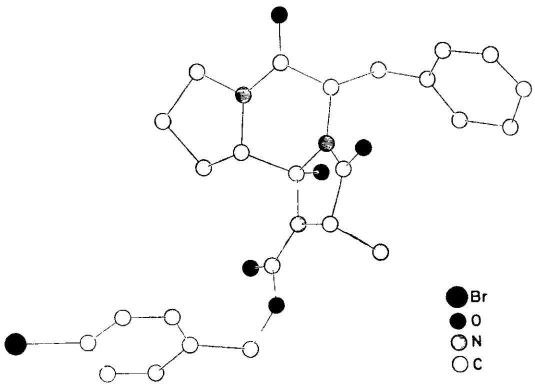
Summary The cyclol structure assigned to the product obtained by mild alkaline treatment of the *p*-nitrophenyl ester of *N*-benzyloxycarbonyl-L-alanyl-L-phenylalanyl-L-proline has been confirmed by *X*-ray analysis.

IN order to establish the molecular structure of the products which were obtained by cyclization of the tripeptide *p*-nitrophenyl esters (1) and (2) (see preceding communication), a three-dimensional *X*-ray analysis of the reaction product (4) was undertaken in our laboratory. Suitable single crystals were grown from ethyl acetate by slow cooling. Crystal data: $C_{25}H_{26}N_3O_5Br$, $M = 528{\cdot}4$; orthorhombic, space group $P2_12_12$ (D_2^3, No. 18), from systematic absences; $a = 23{\cdot}819 \pm 0{\cdot}015$, $b = 15{\cdot}826 \pm 0{\cdot}010$, $c = 6{\cdot}351 \pm 0{\cdot}007$ Å; $U = 2394{\cdot}1$ Å^3, $Z = 4$, $D_c = 1{\cdot}46$ g cm^{-3}. Zr-filtered Mo-K_α radiation, λ taken as 0·7107 Å, $\mu = 18{\cdot}5$ cm^{-1}. The intensity data were collected on a Siemens AED automatic four-circle diffractometer at room temperature. 1330 independent non-zero reflections were recorded in the ω-scan mode up to a maximum $\sin\theta/\lambda$ value of 0·53, corresponding to a spacing limit of about 0·95 Å. The crystals appeared to suffer from *X*-ray decay and this was taken account of by periodically checking some standard reflections. Absorption corrections were not applied, nor were extinction corrections. The structure was solved by the heavy-atom method. The atomic positions were refined by block-diagonal least-squares calculations: the atomic species were finally assigned on the basis of chemical evidence and by the behaviour of the individual isotropic temperature factors. Isotropic thermal motion was assumed for all atoms apart from the bromine atom which was refined anisotropically in the later stages. The current *R* value is 0·11.



The formula in this communication shows the relative configuration of the asymmetric carbon atoms as established from the *X*-ray analysis. This representation corresponds to the absolute configuration, based on the known configuration of the starting materials (no anomalous



FIGURE

dispersion measurements were performed). The absolute configuration of C(12) which becomes an asymmetric centre as a consequence of the cyclization reaction, is thus also determined.

The Figure shows all the conformational and configurational features found in the present structure.

Several factors such as the *X*-ray decay and the limited amount of data, prevented an accurate refinement: so far large e.s.d.'s as well as unusual discrepancies from the expected values are found for some bond distances and angles. The short intramolecular distance of about 3·0 Å, between the hydroxylic oxygen attached to C(12) and the oxygen atom of the carbonyl group attached to N(1) may be due to a hydrogen-bond-type interaction which would tend to stabilize the structure.

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