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THE MOLECULAR STRUCTURE AND ABSOLUTE CONFIGURATION OF PICROTOXININ

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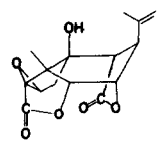
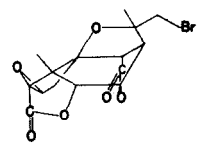
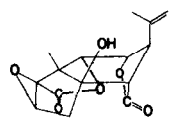
THE structure (Ia) proposed for picrotoxinin ($C_{15}H_{16}O_6$) by Conroy[1,2] and supported by his conformational analysis has now been confirmed by the crystal structure analysis of a bromo derivative ($C_{15}H_{15}O_6Br$) using the methods of X-ray diffraction. Crystals of α-bromopicrotoxinin, for which



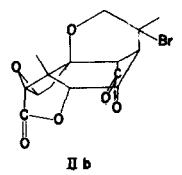
Ia



IIa



Ib



IIb

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[1] H. Conroy, J. Amer. Chem. Soc. 73, 1889 (1951).

[2] H. Conroy, J. Amer. Chem. Soc. 89, 5550 (1957).

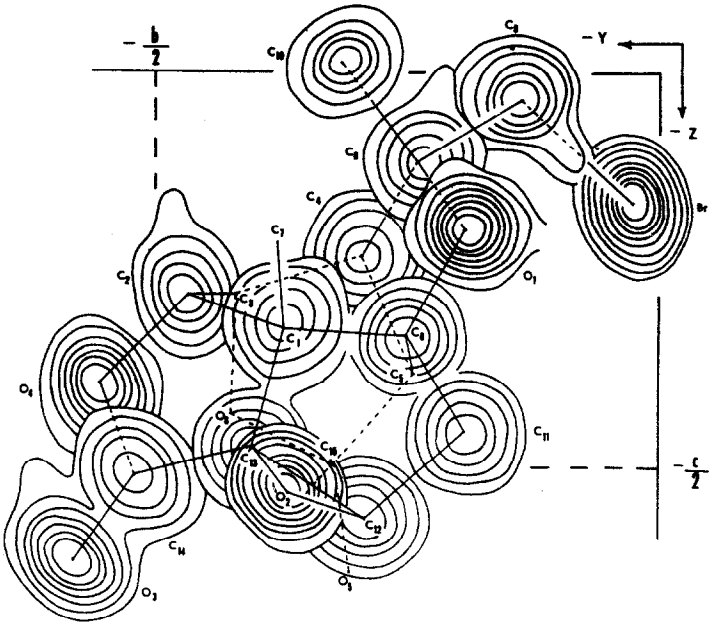

FIG. 1(a).

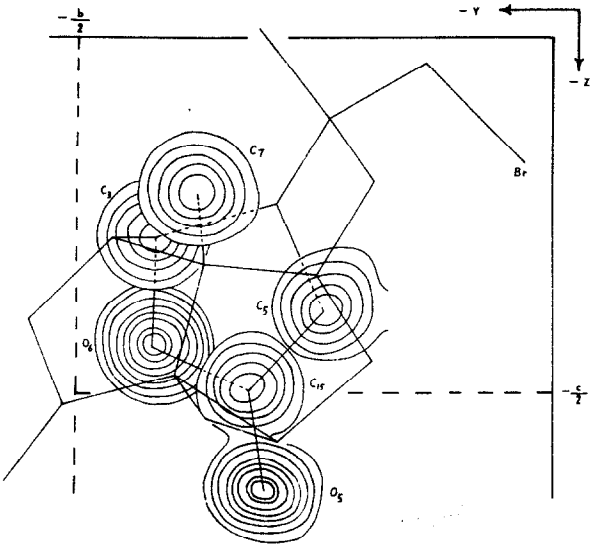

FIG. 1(b).

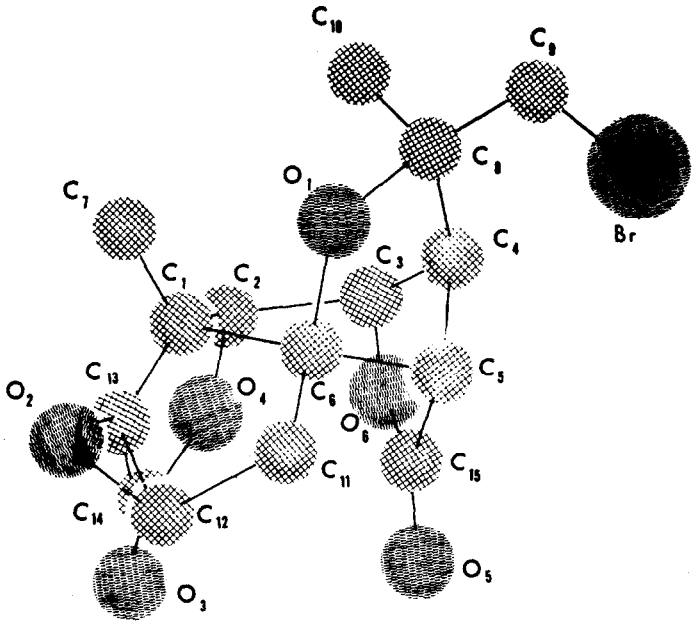

FIG. 2.

the structures (IIa) or (IIb) were proposed by Conroy have been shown to be a mixture of two crystalline modifications,[3] here called α_1 and α_2. The relationship between these is still unknown. The final electron density distribution calculated in the three-dimensional crystal structure analysis of α_1 - bromopicrotoxinin is represented in Fig. 1(a) and (b) in which the atomic labeling is that of Conroy. The corresponding molecular structure which is shown in Fig. 2 is the mirror image of the structure (IIa) as it appears in Conroy's papers. No chemical evidence has yet been advanced as to which of the two enantiomorphs represented in II(a) and Fig. 2, is the true configuration. The evidence of anomalous X-ray scattering has been

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[3] B. M. Craven, Acta Cryst. 12, 254 (1958).

examined according to the methods of Bijvoet et al.[4] and this shows the true molecular configuration to be that of Fig. 2.

It follows that the true configuration of picrotoxinin itself is (Ib), which is also the mirror image of the structure as it appears in Conroy's papers.

It is an important feature of Conroy's conformational analysis of picrotoxinin that there should be steric hindrance to a rearward nucleophilic attack at the epoxide ring ($C_{12}O_2C_{13}$). From the crystal structure studies, the two lactone bridges C_5 to C_3 and C_{13} to C_2 indeed are found to form a protective "cage" behind the epoxide ring, some of the cage dimensions being, - $C_{12} - O_5$, 3.29 Å; $C_{12} - C_{15}$, 3.18 Å; $C_{13} - C_{15}$, 3.11 Å; $C_{14} - C_{15}$, 3.34 Å.

The detailed results of the X-ray analysis are being prepared for publication.

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[4] J. M. Bijvoet, A. F. Peerdemann and A. J. van Bommel, Nature, Lond. 168, 271 (1951).