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X-RAY ANALYSIS OF CHAETOGLOBOSIN A, AN INDOL-3-YL-[13]CYTOCHALASAN FROM *Chaetomium globosum*

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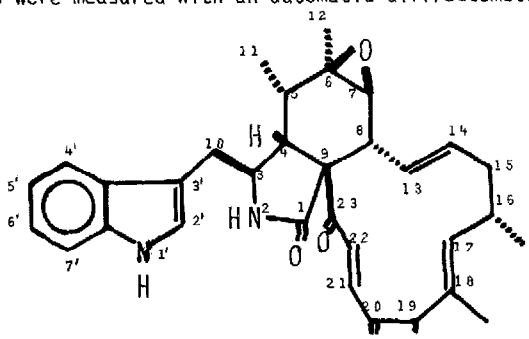
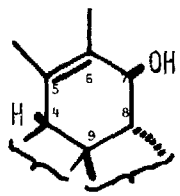
CHAETOGLOBOSINS A - F are cytotoxic metabolites of *Chaetomium globosum* causing polynucleation and multipolar division of HeLa cells and acute toxicity in mice.[1] From chemical and spectroscopic studies, especially precise ^{1}H-NMR examinations, structures were proposed for chaetoglobosins A and B as novel [13]cytochalasans containing indol-3-yl groups.[2] The Structures have now been verified and the relative stereochemistry has been established for chaetoglobosin A by X-ray analysis as shown in the formula (I) (adopting the absolute stereochemistry assigned to phomin,[3] cytochalasin D,[4] and cytochalasin E[5]).

The crystals of chaetoglobosin A used for the analysis were recrystallized from acetone as pale yellow prisms of mp 188° (the solvent and mp are different from those reported in the previous paper[2]). Crystals are orthorhombic, space group $P2_12_12_1$, with 4 molecules in the unit cell. The cell dimensions are a = 10.036 (1), b = 16.888 (1), c = 17.092 (2) Å. 3207 independent reflections were measured with an automatic diffractometer. The structure was solved by direct



(I)



(II)

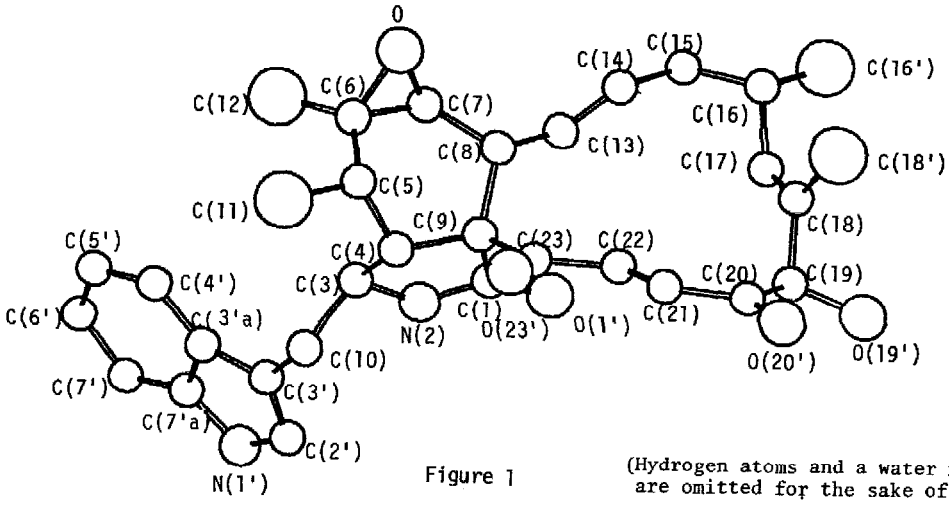


Figure 1 (Hydrogen atoms and a water molecule are omitted for the sake of simplicity)

methods making use of new techniques involving quartet invariants[6] and has been refined to an R-factor of 0.033 with all hydrogen atoms located. A computer generated drawing[7] is shown in Figure 1.

The X-ray analysis indicated that the asymmetric unit also contains one water molecule which is involved in considerable hydrogen bonding. The five-membered ring in the isoindole unit is cis-fused to the six-membered ring, while the thirteen membered ring is trans-fused to the six-membered ring. As was expected from the presence of an epoxide ring the six-membered ring adopts a slightly twisted boat conformation.

Chaetoglobosin B is an isomer of chaetoglobosin A and the formation of B from A by the cleavage of the epoxide ring was shown in the previous paper.[2] Since the coupling constant (10 Hz) of the C_7-carbinyl proton to the C_8-proton suggests the trans relation, the relative configuration of chaetoglobosin B was established as II.

REFERENCES

1. M. Umeda, K. Ohtsubo, M. Saito, S. Sekita, K. Yoshihira, S. Natori, S. Udagawa, F. Sakabe, and H. Kurata, *Experientia*, 31, 435 (1975).
2. S. Sekita, K. Yoshihira, S. Natori, and H. Kuwano, *Tetrahedron Letters*, 1973, 2109.
3. G. M. McLaughlin, G. A. Sim, J. R. Kiechel, and Ch. Tamm, *Chem. Comm.*, 1970, 1398.
4. Y. Tsukuda and H. Koyama, *J. Chem. Soc., Perkin II*, 1972, 739.
5. G. Büchi, Y. Kitaura, S.-S. Yuan, H. E. Wright, J. Clardy, A. L. Demain, T. Glinsukin, N. Hunt, and G. N. Wogan, *J. Am. Chem. Soc.*, 95, 5423 (1973).
6. G. T. DeTitta, J. W. Edwards, D. A. Langs, H. A. Hauptman, *Acta Cryst.*, A31, 472 (1975).
7. R. J. Feldman, C. R. T. Bacon, and J. S. Cohen, *Nature*, 244, 113 (1973).