03.3-5 METAL-DRUG INTERACTIONS: STRUCTURE, CONFORMATION AND PROPERTIES OF COBALT COMPLEX OF A PEPTIDE—RESEMBLING PORTION OF ANTITUMOR ANTIBIOTIC BLEOMYCIN. By S.K. Arora, Drug Dynamics Institute, University of Texas, Austin, Texas 78712 and P.K. Mascharak, Department of Chemistry, University of California, Santa Cruz, CA 95064.

A metal ion as cofactor is now believed to be a requirement for the antitumor activity of glycopeptide antibiotic bleomycin. This realization has initiated active research in the area of metal-bleomycin complexes. A cobalt complex of a peptide-resembling portion of bleomycin has been prepared and its structure and properties studied. The complex $Co(pep)_2ClO_4.H_2O$ crystallizes in trigonal space group $P3_121$ with cell dimensions of a=13.434, b=13.434, c=11.543Å and Z=3. The structure was solved by the combination of Patterson, direct and Fourier synthesis methods. The structure has been refined with isotropic thermal parameters to an R of 0.093. Further refinement is in progress. The coordination around cobalt is octahedral. Details of structure, spectroscopic results and models for metal-bleomycin complex will be presented.

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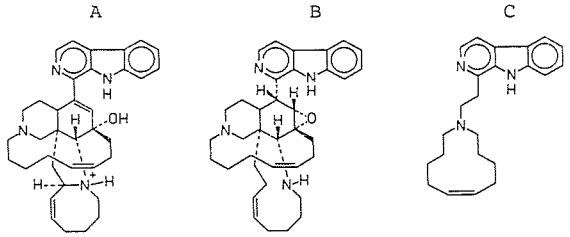
03.3-6 MOLECULAR STRUCTURES OF MANZAMINE A, B, AND C, THREE NEW ALKALOIDS FROM HALICONA SP.

by G. Bernardinelli and C. W. Jefford, Laboratoire de Cristallographie and Département de Chimie Organique, University of Geneva, 1211 Genève 4, Switzerland, and R. Sakai and T. Higa, Harbor Branch Foundation-SeaPharm Research Laboratories, Fort Pierce, Florida 33450 and Department of Marine Sciences, University of the Ryukyus, Senbaru 1, Nishihara, Okinawa 903-01, Japan.

Three previously unknown alkaloids, containing the β-carboline group, have been isolated from a sponge (halicona sp) collected near Manzamo in Okinawa. The first constituent, manzamine A (R. Sakai, T. Higa, C. W. Jefford & G. Bernardinelli, J. Amer. Chem. Soc. 1986, 108, 6404-6405) exhibits significant antitumor activity and possesses a structure which defied conventional spectroscopic analysis. The absolute configuration of its hydrochloride was successfully determined by refinement of the x parameter (G.Bernardinelli & H.D.Flack 1985, Acta Cryst. A41, 500-511). The molecule consists of an unusual arrangement of 5-, 6-, 8- and 13-membered rings, an allylic alcohol grouping and a pyrrolidinium ring as the locus of the positive charge. The second constituent, manzamine B, is a free base closely related in structure to manzamine A from which its absolute configuration was deduced. The essential difference resides in the presence of an epoxide function in place of the allylic alcohol and the cleavage of the pyrrolidine ring so forming an 11-membered olefinic ring enclosing a secondary amino group. The third constituent, manzamine C, is a much less complicated racemic alkaloid retaining the 11-membered ring of manzamine B and joined through the nitrogen atom via an ethane fragment to the β-carboline entity. Unlike odd-membered macrocycles in general, those found in manzamine A, B and C are all observed to be rigid, showing no disorder. Apart from the β-carboline substituent, the attached rings in manzamine A and B are unprecedented in nature and are difficult to rationalize in ordinary biosynthetic terms. Compounds B and C display significant biological activities.

Manzamines



03.3-7 ANTIFUNGAL COMPOUNDS ISOLATED FROM NEW ZEALAND PLANTS. By H. E. Harvey, J. M. Waring and G. J. Gainsford, Chemistry Division, Department of Scientific and Industrial Research, Private Bag, Petone, New Zealand.

Extracts from the NZ flax *Phormium cookianum* have been isolated using column chromatography as part of a programme to investigate NZ plants reported to have medicinal properties (H. E. Harvey and J. M. Waring, Journal of Natural Products, submitted 1986). Purification difficulties and sample sizes precluded chemical identification by normal methods. Fortunately, two of the extracts with antifungal properties yielded crystals:

[5] Pale brown needles, Monoclinic, $P2_1/c$, a = 7.0431(17), b = 18.142(7), c = 7.2375(17) Å, β = 96.44(2)°, V = 918.9(4) $Å^3$, Z = 4 at 133 K. The structure has been solved by direct methods (see Figure below) and refined by full matrix least squares of 1415 observed reflections to a conventional R of 0.040. The independent molecules, common name methyl β-orsellinate, ($C_{10}H_{12}O_4$) are approximately planar with an angle of 7.5° between the benzene and carboxyl planes, and are hydrogen-bonded via the carboxyl oxygen, O(1) and hydroxyl proton H(O4). An intramolecular hydrogen-bond exists between the same O(1) and H(O3) (1.66Å apart).

[17] A few thin transparent, slightly fractured needles, typically 0.5 x 0.15 x 0.04 mm have been isolated. Only one crystal is adequate: it is triclinic with a = 6.985(4), b = 16.056(22), c = 16.566(17) Å, α = 81.92(10), β = 85.05(7) and γ = 79.34(8)°, V = 1804(3) $Å^3$ at 133 K. Formula weight based on calculated density of [5], 1.42 g cm^{-3}, in space group $P\bar{1}$ is 770 atomic units, which should prove an excellent test for some of the current direct methods