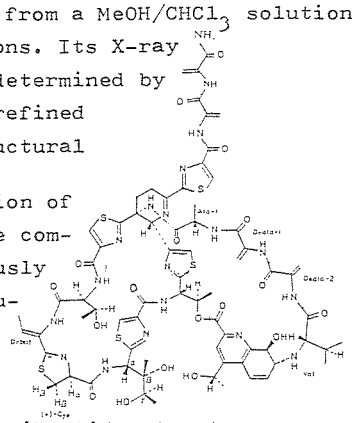
03.3-18 HIGHLY OXIDIZED PEPTIDIC ANTIBIOTIC: CRYSTAL CONFORMATION OF SIOMYCIN-A. By C. Pascard and T. Prangé, Institut de Chimie des Substances Naturelles, CNRS, 91190 Gif sur Yvette, France.

Siomycin-A (mw=1486) is a cysteine-containing polycyclic polypeptide, largely modified by dehydrogenation. It differs from its parent thiostrepton (Anderson et al., Nature (1970), 225, 233) by three peptide units included in a lateral macrocycle. It crystallizes in large tetragonal crystals from a MeOH/$CHCl_3$ solution in precise proportions. Its X-ray structure has been determined by direct methods and refined using 4620 obs. structural factors.



The conformation of the backbone will be compared to the previously reported n.m.r. results in solution (Tori et al., J. Antibiot.(1979),32, 1072), and to the nosiheptide structure (Prangé et al. Nature (1977) 265, 189).

03.3-19 THE CRYSTAL AND MOLECULAR STRUCTURE OF THE TERNARY COMPLEXES WITH IONOPHORIC ANTIBIOTICS, Rb^+ CATION AND UNCOUPLER. By Y. Nishibata, A. Itai and Y. Iitaka, Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Tokyo, Japan, and Y. Nawata, Chugai Pharmaceutical Co. Ltd., Takada, Tokyo, Japan.

Proton uptake and the release of K^+ cations from liposomes containing potassium phosphate were catalyzed by the uncoupler 3,5-di-t-butyl-4-hydroxybenzylidenmalonònitrile (hereafter abbreviated as SFH) in the presence of valinomycin, and the formation of the ternary complex K^+.valinomycin.SF^- (I) in the liposomal membrane was suggested (A. Yamaguchi & Y. Anraku, Biochem. Biophys. Acta, 501, 150, 1978).

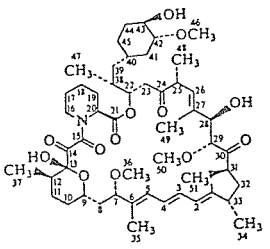
We succeeded in obtaining the crystals of (I) as well as Rb^+.valinomycin.SF^- (II) and Rb^+.tetranactin. SF^- (III). Crystal structures of the latter two were solved by the heavy-atom method. R indices of 0.17 and 0.08 were obtained for (II) and (III), respectively. Structures of the complexed cations in (II) and (III) are very similar to those observed in valinomycin-KI_3 (K. Neupert-Laves & M. Dobler, Helv. Chim. Acta, 58, 432, 1975) and tetranactin-KSCN (T. Sakamaki, et al., Acta Cryst., B32, 768, 1976). In the crystals of (II) and (III), Rb^+-ionophore complexes and SF^- anions are piled up alternatively, forming columns. t-Butyl groups of SF^- approach the cavities of Rb^+-valinomycin complexes, although malononitrile groups of SF^- are near to the surface of Rb^+-tetranactin complexes. In both cases, non-bonded interactions between Rb^+-ionophore and SF^- anions are predominant.

03.3-20 X-RAY CRYSTALLOGRAPHIC AND NMR STUDIES ON BARIUM-VALINOMYCIN COMPLEXES. By S. Devarajan, C.M.K. Nair, K.R.K. Easwaran and M. Vijayan, Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India.

As part of a programme of crystallographic and spectroscopic studies aimed at exploring the conformational possibilities of ionophores, the crystal structures of 1:2 complexes of valinomycin with barium perchlorate and barium thiocyanate have been determined. A preliminary account of the X-ray analysis of the perchlorate complex has already been published (Nature (1980) 286, 640-641). The structure, including 15 solvent atoms, has subsequently been refined to an R of 0.109 for 3504 observed reflections. The valinomycin molecule in the structure has an unusual hitherto unnoticed conformation in which the extended depsipeptide chain, with no internal hydrogen bond, is wound in the form of an ellipse. The barium ions are located approximately at the foci. The crystal structure of the barium thiocyanate complex, analysed later and refined to an R of 0.125 for 2237 observed reflections, is not isomorphous to the corresponding perchlorate complex. The overall molecular conformation and the pattern of metal coordination in the two complexes are, however, similar although significant differences exist in details. The structure analysis of the two complexes thus establishes the possibility of a novel conformation, without internal hydrogen bonds, for valinomycin. Proton NMR studies in solution, especially those using nitroxide free radicals, also indicate the absence of internal hydrogen bonds in the complex.

03.3-21 THE STRUCTURE OF THE ANTIFUNGAL ANTIBIOTIC RAPAMYCIN. Peter S. White and D. C. Neil Swindells, Department of Chemistry, University of New Brunswick, Fredericton, New Brunswick, Canada E3B 6E2.

Rapamycin, $C_{51}H_{79}NO_{13}$, has been shown effective against Candida albicans whilst having no activity against the bacteria which normally supress the emergence of candidiasis. Crystalline rapamycin is orthorhombic, space group $P2_12_12_1$, a = 34.866(9), b = 13.069(5), c = 12.262(7) Å. Data were collected on a Picker FACS-I diffractometer using CuKα radiation (λ = 1.5418 Å) for $2\theta \leq 120°$ resulting in 4638 reflections of which 3737 were considered observed ($I > 3\sigma(I)$). Initial attempts to solve the structure by direct methods (MULTAN) failed. However, the inclusion of some structural information from ^{13}C nmr in the normalisation of the structure factors lead to a number of recognisable fragments (32 atoms) in the E-map. A series of fourier syntheses then yielded the full structure



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