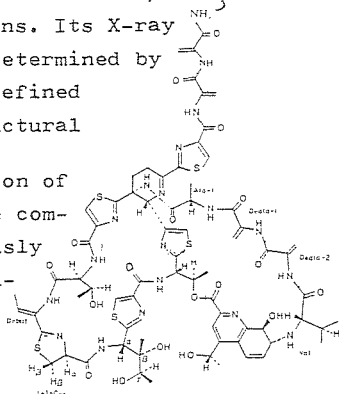


03.3-18 HIGHLY OXIDIZED PEPTIDIC ANTIBIOTIC: CRYSTAL CONFORMATION OF SIOMYCIN-A. By C. Pascard and T. Prangé, Institut de Chimie des Substances Naturelles, CNRS, 91190 Gif sur Yvette, France.

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<sub>3</sub> 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 IONOPHORE ANTIBIOTICS, Rb<sup>+</sup> 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<sup>+</sup> cations from liposomes containing potassium phosphate were catalyzed by the uncoupler 3,5-di-t-butyl-4-hydroxybenzylidene malonitrile (hereafter abbreviated as SFH) in the presence of valinomycin, and the formation of the ternary complex K<sup>+</sup>.valinomycin.SF<sup>-</sup> (I) in the liposomal membrane was suggested (A. Yamaguchi & Y. Anraku, Biochem. Biophys. Acta, 501, 150, 1978).

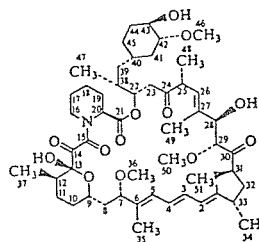
We succeeded in obtaining the crystals of (I) as well as Rb<sup>+</sup>.valinomycin.SF<sup>-</sup> (II) and Rb<sup>+</sup>.tetranactin.SF<sup>-</sup> (III). Crystal structures of the latter two were solved by the heavy-atom method. R indices of 0.17 and 0.08 were obtained for (II) and (III), respectively. Structures of the complexed cations in (II) and (III) are very similar to those observed in valinomycin-KI<sub>3</sub> (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<sup>+</sup>-ionophore complexes and SF<sup>-</sup> anions are piled up alternatively, forming columns. t-Butyl groups of SF<sup>-</sup> approach the cavities of Rb<sup>+</sup>-valinomycin complexes, although malonitrile groups of SF<sup>-</sup> are near to the surface of Rb<sup>+</sup>-tetranactin complexes. In both cases, non-bonded interactions between Rb<sup>+</sup>-ionophore and SF<sup>-</sup> 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 depsi-peptide 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<sub>51</sub>H<sub>79</sub>N<sub>13</sub>, has been shown effective against *Candida albicans* whilst having no activity against the bacteria which normally suppress the emergence of candidiasis. Crystalline rapamycin is orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, 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 2θ ≤ 120° resulting in 4638 reflections of which 3737 were considered observed (I > 3σ(I)). Initial attempts to solve the structure by direct methods (MULTAN) failed. However, the inclusion of some structural information from <sup>13</sup>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



and after several cycles of least squares refinement the locations of the hydrogens were established by a difference synthesis. The final R value was 0.068 for the observed reflections.

The structure consists of a 31-membered macrolide ring with an oxygen bridge between C(9) and C(13). The absolute configuration as shown in the figure was ascertained (J. A. Findlay and L. Radics, *Can. J. Chem.* **58**, 579-590, 1980) by isolating L(-)-pipecolic acid from hydrolysis products.

**03.4-02** <sup>1</sup>-CHOLESTERYL ESTERS : CRYSTAL AND LIQUID CRYSTALLINE STRUCTURES. Patricia Sawzik and B. M. Craven, Department of Crystallography, University of Pittsburgh, Pittsburgh, PA 15260 USA.

A series of X-ray crystal structure determinations of cholesteryl n-alkanoate (n=2, 6, 8-12, 14) and n-alkenoate (n=16:1<sup>Δ9</sup>, 18:1<sup>Δ9</sup>) esters has been undertaken, one aim being to seek features which may be relevant to molecular association in the less ordered liquid crystalline phases. The saturated cholesteryl esters with chain length C<sub>6</sub>-C<sub>18</sub> and the unsaturated palmitoleate and oleate have one of three crystal structure types as the most stable form at room temperature. These crystal structure types are designated as monolayers II (ester chain length C<sub>6</sub>-C<sub>9</sub>, C<sub>18:1</sub><sup>Δ7</sup>), monolayers I (C<sub>9</sub>-C<sub>12</sub>, C<sub>16:1</sub><sup>Δ9</sup>) and bilayers (C<sub>13</sub>-C<sub>18</sub>) with cholesteryl-cholesteryl, cholesteryl-alkyl, and alkyl-alkyl interactions becoming successively dominant. The X-ray diffraction patterns for the smectic phase of the cholesteryl esters suggest a relationship with the monolayer type I crystal structures. Diffracted orders from the crystal monolayers (l = 2 through 5) are very weak. The strong first order has a d-spacing similar to that of the single sharp intense inner diffraction ring of the smectic phase. X-ray diffraction patterns for the cholesteric and smectic phases are similar but in the cholesteric the inner ring is more diffuse. This may be due to a short range ordering of antiparallel pairs of molecules as found in the bilayer crystal structures.

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**03.4-01** PHASE TRANSITION AND 37°C CRYSTAL STRUCTURE OF CHOLESTEROL. Leh-Yeh Hsu and C. E. Nordman, Department of Chemistry, University of Michigan, Ann Arbor, MI 48109, U.S.A.

The unit cell of cholesterol (C<sub>27</sub>H<sub>46</sub>O) above the 31.6°C phase transition (Petropavlov & Kostin, *Kristallografiya* (1976) **21**, 168) is triclinic, space group P1, with  $\bar{a} = 27.565$ ,  $\bar{b} = 35.776$ ,  $\bar{c} = 10.748$ ,  $\alpha = 94.45^\circ$ ,  $\beta = 90.90^\circ$ ,  $\gamma = 73.87^\circ$ , at 37°C. There are 16 independent molecules, compared to 8 in the room temperature (RT) cell (Shieh et al., *Nature* (1977) **267**, 287; *Acta Cryst.*, in press). A restrained-group Gauss-Seidel (FGLS) refinement procedure (Hoard & Nordman, *Acta Cryst.* (1979) **A35**, 1010) was used to deduce a refinable structure from the RT starting model. A combination of FGLS and anisotropic block-diagonal refinement presently gives R = 0.09 for 18,047 reflections. The bilayer structure of hydrogen-bonded chains of molecules bears an overall resemblance to the RT phase, differing from the latter in that several molecules have turned about their long axes by varying amounts, up to 160°. Side chain conformations also differ in the two phases. Two of the 16 molecules have side chains forming an 80° angle with the steroid long axis, a feature not previously encountered in cholesterol structures. Strong thermal motion is present in all side chains. A remarkable rotational pseudosymmetry relates eight of the sixteen independent molecules to the other eight, giving a pseudo-asymmetric unit of 8 molecules as contrasted with 4 in the RT phase.

**03.4-03** CRYSTAL STRUCTURE OF THE 2:1 COMPLEX BETWEEN DEOXYCHOLIC ACID AND d-CAMPHOR. By J.G. Jones, S. Schwarzbaum, and L. Lessinger, Chemistry Dept., Barnard College, New York, USA

Bile is the source of several hydroxylated derivatives of the steroid 5 $\beta$ -cholan-24-oic acid which play important physiological roles in the digestion of fats and in excretion. One bile acid, deoxycholic acid (DCA), forms stoichiometric crystalline complexes with a wide variety of organic compounds. The complex 2:1 DCA:camphor crystallizes in space group P2<sub>1</sub>2<sub>1</sub>2 with a=27.353, b=13.814, c=7.233 Å, D<sub>m</sub>=1.137, D<sub>x</sub>=1.139 g/cm<sup>3</sup> for Z=4 of C<sub>24</sub>H<sub>40</sub>O<sub>4</sub> ·  $\frac{1}{2}$ (C<sub>10</sub>H<sub>16</sub>O).

The structure was solved by direct methods and refined to R=0.07. It consists of bilayers of DCA molecules, held together by hydrogen bonds between the two halves of the bilayer, and stacked with their hydrophobic surfaces in contact. The shape of the DCA steroid is such that between adjacent bilayers are formed channels, in which the camphor molecules stack. The channels are centered on crystallographic two-fold rotation axes; the roughly spherical camphor molecules are two-fold disordered.

The structure is compared to the several other known crystal structures of DCA with hydrophobic guest molecules. While DCA forms very similar bilayers in all these structures, there are some major and some subtle differences among them. The differences which allow for the formation of DCA complexes with molecules of such widely varying sizes and shapes as camphor, phenanthrene, cyclohexanone, acetic acid, and palmitic acid will be illustrated.