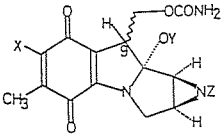
03. 3–1 REVISED ABSOLUTE CONFIGURATIONS OF MITOMYCINS. N.Hirayama and K.Shirahata,Tokyo Research Laboratories,Kyowa Hakko Kogyo Co.Ltd.,3-6-6 Asahimachi, Machida,Tokyo 194,Japan

Mitomycins are very important group of antitumor compounds,and mitomycin C,a prominent member of them,is clinically used extensively and successfully today. Tulinsky et al.(J.Am.Chem.Soc.(1967),89,2905) and Yahashi et al.(J.Antibiot.(1976),29,104;ibid.(1978),31, (6),correction) disclosed the absolute configurations of mitomycins A and B,respectively,by X-ray analysis. The results,however,are inconsistent with those predicted from the biosynthetic studies on the antibiotics. In addition,it seems that the both analyses are not necessarily decisive from the crystallographic points of view. Therefore,we have reinvestigated the absolute configurations of mitomycins A,B,and C by X-ray analysis. Their crystallographic data are as follows:(A)1-N-(p-bromobenzoyl)mitomycin A;$P2_12_12$,a=20.277,b=27.320,c=8.348A,Z=8. (B)7-demethoxy-7-p-bromoanilinomitomycin B;$P2_12_12_1$,a= 29.183,b=9.251,c=7.932A,Z=4.(C)1-N-(p-bromobenzoyl)mitomycin C;$P6_5$,a=13.534,c=21.146A,Z=6. X-Ray intensities were measured by automated diffractometry. All structures were solved by direct methods and refined by full-matrix least-squares techniques. Final R factors are as follows (A)0.047,(B)0.057,and (C)0.036. The absolute configurations were determined by the Bijvoet difference method. The results indicate that previously employed absolute configurations of mitomycins were incorrect and should be revised as shown in the figure. Some problems related to the absolute configuration determination will also be discussed.

	X	Y	Z	9
(A)	OCH_3	CH_3	H	β
(B)	OCH_3	H	CH_3	α
(C)	NH_2	CH_3	H	β



03. 3–2 STRUCTURE OF A SULFONAMIDE AND A SYMPATHOMIMETIC AMINE. By J. K. Dattagupta, C ε M. B. Division, Saha Institute of Nuclear Physics, Sector-I, Block-'AF', Bidhan Nagar, Calcutta-700 064, India.

Sulfisomidine is a rapidly absorbed and rapidly excreted sulfonamide and is a close structural isomer of sulfamethazine. This sulfonamide has been used extensively for the treatment of urinary tract infections. The crystal structure of sulfisomidine dihydrochloride dinydrate has been solved by direct methods using diffractometric data. Structural features in the compound will be reported and compared with those of other 'sulfa' drugs.

Xylometazoline is a sympathomimetic amine and is used chiefly as a nasal vasoconstrictor. The crystal structure of Xylometazoline hydrochloride has been solved using diffractometric data and direct methods. The chemical structure of xylometazoline differs from that of the usual sympathomimetic amines. The conformation of these drug molecules is commonly expressed by torsion angles τ_1 and τ_2 which are found to be 76° and -142° respectively in xylometazoline. The ethylamine side chain, which is a part of the heterocyclic ring in xylometazoline, can be said to be extended and is approximately normal to the phenyl ring. This is similar to the conformation mostly preferred by this class of drugs and which is thought to be responsible for their action at the receptor sites. The conformational aspects will be discussed and compared with other chemically and pharmacologically similar compounds.

03. 3–3 CRYSTAL AND MOLECULAR STRUCTURE OF TWO CHLORAMPHENICOL ANALOGUES. By A.De,Department of Physics(X-ray Lab.),University College of Science;92,A.P.C.Road;Calcutta-700009,INDIA

The crystal structures of (I) p-nitro-ω,ω-dichloroacetanilide and (II) 3-chloro,4-amino-ω,ω-dichloroacetophenone have been studied as structural analogues of chloramphenicol, D(-)-threo,-2,2-dichloro-N-[β-hydroxy-α-(hydroxymethyl)-p-nitrophenethyl]acetamide. Crystal and experimental data: (I)$C_8H_6O_3N_2Cl_2$,M_r=249.07,monoclinic,$P2_1/c$, a=7.966(2),b=13.985(10),c=9.301(2)Å, β=92.55(2)°,V=1035(1)Å^3,D_m=1.62,D_x=1.60Mg m^{-3}, Z=4, (MoK_α)=0.7107Å,μ=0.61mm^{-1},F(000)=504, T=297°K,R=0.047 with 1527"observed" reflections.(II)$C_8H_6ONCl_3$,M_r=238.515,monoclinic, $P2_1/a$,a=7.425(4),b=9.089(5),c=14.202(4)Å, β=97.27(3)°,V=950.779Å^3,Z=4,D_m=1.69,D_x=1.67 Mg m^{-3}, (CuK_α)=1.5418Å,μ=8.35mm^{-1},F(000)=480, T=297°K,R=0.065 with 1279 "observed" reflections.Both the structure were solved by the Patterson heavy - atom methods.Structure(I) was refined by full-matrix least-squares and structure(II) by block-diagonal least-squares. The parameters of the hydrogen atoms were also refined for (I).The expected distorsion in the benzene nucleus consequent to the substitution of electron releasing and withdrawing groups (Domenicano,Vaciago & Coulson,Acta Cryst. (1975),B31,221)have been observed.Both the structures are stabilised by intermolecular N-H...O hydrogen bonds.

03. 3–4 ON THE POLYMORPHISM OF DRUGS. By E. Laine, V. Tuominen, H. Jalonen, J. Haapaniemi and P. Ilvessalo, Dept. of Phys. Sci., University of Turku, SF-20500 Turku 50, Finland.

When a substance can exist in more than one crystalline state it is said to exhibit polymorphism. While the subject of polymorphism is extensively covered in the scientific literature, there are relatively fewer reports regarding its importance in the area of pharmaceutics. The polymorphs may differ substantially with respect to certain physicochemical properties; for example, crystal shape, colour density, melting point, hardness, dissolution rate.

The methods for studying polymorphism were x-ray diffraction, infrared spectroscopy, differential scanning calorimetry, thermogravimetry, electron microscopy and the hot stage polarizing microscopy.

The results of investigation on polymorphism and pseudopolymorphism (formation of hydrates) of different drug substances are presented. Tienilic acid (ticrynafen) was found to have three crystalline forms and an amorphous one. Detomidine hydrochloride and cyclophosphamide had pseudopolymorphism. Both were observed to have a hydrate and an anhydrous form. The transition from one form to another in both cases was reversible. The transition from carbamatzepine anhydrate to dihydrate was very fast in the humid conditions. The rapid growth (about 1 μms^{-1}) of dihydrate crystals refers to whisker mechanism. It was conduded that a very important phase of preformulation work is determining the crystal forms and polymorph stability of drug substances.