

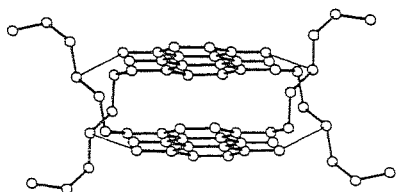
09.2-16 CRYSTAL AND MOLECULAR STRUCTURE OF MITOXANTRONE $C_{22}H_{24}N_4O_8 \cdot 2HCl \cdot 7H_2O$

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Mitoxantrone is a recently discovered anticancer drug which has been found effective against breast cancer and leukemia. We report here its crystal and molecular structure. The anticancer drugs are believed to act with nucleic acids as target molecules. The present structure suggests a possible mode of interaction of mitoxantrone with the DNA double helix.

Crystals were grown by diffusing acetone into an aqueous solution containing mitoxantrone dihydrochloride and sodium chloride. They are triclinic with space group P1 and $a = 7.225$, $b = 14.079$, $c = 16.108$ Å, $\alpha = 111.06^\circ$, $\beta = 94.57^\circ$, $\gamma = 104.00^\circ$. Three dimensional intensity data are collected up to $\theta = 60^\circ$ on a CAD-4 diffractometer using $Cu K\alpha$ radiation. 1680 reflections are considered to be observed ($F_o \geq 2\sigma(I_o)$) out of 3200 collected. Lorentz and polarization corrections are made but without any absorption correction. During data collection it was found that hkl reflections with $h = 2n+1$ were generally weak, as if 'a' value was 3.615 Å suggesting a pseudo translational symmetry along the 'a' axis.

Structure is solved by direct methods using MULTAN 11/82 and refined to R value of 0.154. The analysis shows the OH groups in the side-chains of the drug and four of the seven solvent water molecules are positionally disordered. All the bond lengths and angles are normal.



The anthraquinone chromophore is planar with the side-chains on the same side of the aromatic ring. The molecules related by the centre of symmetry from a dimer, with the basic NH_2^+ groups of the side-chains hydrogen bonded to the hydroxyl oxygen atoms of chromophore (3.06, 3.03 Å) as shown in figure. In the dimer, the chromophores are positioned on top of each other at 3.6 Å parallel to the 'bc' plane, which explains the pseudo translational symmetry found in the crystal along the a-axis. The rest of the structure and the solvent atoms do not have this symmetry.

The nature of hydrogen bonding found in the crystal structure suggests a possible mode of drug binding with A.T base pairs of DNA double helix. Modelling study clearly shows that one of the drugs in the dimer can be replaced by an A.T base pair with the H-bonding interactions from the side-chain NH_2^+ groups however still retained but with N3 and O2 atoms of the adenine and thymine bases respectively.

09.2-17 CRYSTAL AND MOLECULAR STRUCTURE OF 5 α -CHOLESTANE-3,6-DIONE. By D.K. Sen and B.S. Basak, X-ray Laboratory, Presidency College, Calcutta, India.

The above compound $C_{27}H_{44}O_2$ a ketone derivative, space group P2₁, with two formula units in the unit cell of dimensions $a=8.218(1)$, $b=7.638(6)$, $c=19.694(7)$ Å and $\beta=92.92(2)^\circ$ with $D_c=1.086$ gm.cm⁻³, $D_m=1.080$ gm.cm⁻³. Out of 2500 reflections only 480 significant reflections could be obtained on a CAD-4 diffractometer. With this small number of reflections only the ring portion of the structure could be obtained by successive use of MULTAN and EXFFT search programmes. The chain was constructed from chemical considerations and fitted to the main ring portion by trial and error methods. For the refinement of the structure 820 significant reflections obtained by photographic methods gave the R value of 11.4 percent. The molecular model is rather complicated. All bond lengths except one which is a little too long are within the acceptable limits. From the good general agreement between the observed and calculated values of F, it seems that there is no gross source of error in the structure determination.

09.2-18 CRYSTAL AND MOLECULAR STRUCTURE OF 10-METHOXY-8, 8-DIMETHYL 2H, 8H-BENZO (1,2-b:5,4-b) - DIPYRON-2-ONE By A.K.Pal, R.Bandopadhyay and B.S.Basak, X-Ray Laboratory, Presidency College, Calcutta-700 073; D. Heijdenrijk and K. Goubitz, J.H.Van't Hoff Instituut, Amsterdam.

Crystal and molecular structure of the above mentioned compound has been determined from the three dimensional x-ray diffraction data for 2132 unique reflections taken on a CAD-4 diffractometer using graphite-monochromated $CuK\alpha$ - radiation. The crystal data are: Molecular formula = $C_{15}H_{14}O_4$, triclinic, $a = 8.3911(9)$, $b = 11.6166(15)$, $c = 7.4611(10)$ Å, $\alpha = 99.014^\circ$ (sig cos $\alpha = 0.0002$), $\beta = 116.476^\circ$ (sig cos $\beta = 0.0002$), $\gamma = 75.886^\circ$ (sig cos $\gamma = 0.0002$), $Z = 2$, $D_m = 1.32$ g.cm⁻³ (floatation), $D_c = 1.36$ g.cm⁻³, $\mu(CuK\alpha) = 8.27$ cm⁻¹. The structure was solved by direct method of Karle & Hauptman and refined by full-matrix least squares calculations. The final R-value was 0.052 for 835 measured reflections. The final refinement cycle gave R=0.132 for all the 2132 reflections. The bond lengths and angles and intermolecular contact distances have all regular and acceptable values.