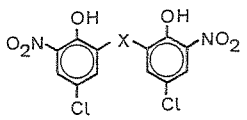
03.1-17 STRUCTURAL STUDIES ON CARCINOGENIC POLYCYCLIC AROMATIC HYDROCARBONS AND THEIR ACTIVE METABOLITES; SOME INSIGHTS INTO MODES OF ACTION. By S. Neidle, A. Subbiah, S. Islam and S.D. Cutbush. Cancer Research Campaign Group, King's College, London WC2B 5RL, UK.

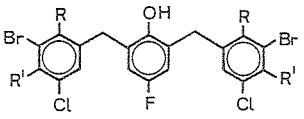
Structural studies have been performed on a series of hydroxylated derivatives of the carcinogens benzo*[a]*pyrene and benzo*[a]*anthracene. These compounds represent stages in the metabolic pathways leading to ultimate carcinogenic species that may react with cellular DNA. The molecular structures have revealed the systematic conformational changes produced in the aromatic systems as they become progressively de-aromatised and more reactive in succeeding stages of metabolism.

The determination of the molecular structures of several derivatives of the hepatic carcinogen acetylaminofluorene, have shown the existence of a preferred conformation for the active moiety. This has been confirmed by both semi-empirical and *ab initio* calculations, and has led us to suggestions for the structure of possible carcinogen-nucleic acid adducts.

03.1-18 CONFORMATIONAL STUDIES OF HALOGENATED BISPHENOLS IN RELATION TO FLUKICIDAL ACTIVITY. By D.G. Hay, M.F. Mackay and A.C. Sindt-Josem, Department of Physical Chemistry, La Trobe University, Bundoora, Victoria, Australia 3083.

X-ray crystallographic analyses of compounds, (I) to (IV), (VII) and (VIII), have been carried out as part of a programme in which a possible correlation between structure and activity against *Fasciola Hepatica* (liver-fluke) infection in sheep is being investigated (*Aust. J. Chem.*, 34, 81, 1981 ; *Aust. J. Chem.*, 1981, in press). More recently, further two bisphenols, (V) and (VI), have been studied. The compounds, together with a number of other halogenated bisphenols, have been synthesized by ICI Australia Ltd.





I : X = $C(CH_3)_2$ II : X = $CHCH_3$
III : X = $CHCCl_3$ IV : X = $C{=}CCl_2$
V : X = $CHOC_6H_5$ VI : X = $CHOCH_2C_6H_5$
VII : R = OH, R' = H VIII : R = H, R' = OH

In molecule (V), the diphenyl moiety adopts a twist conformation with one hydroxyl group in the *proximal* orientation; in molecule (VI) the conformation is butterfly. As the activity in the series of compounds (I) to (VI) increases there is less steric interaction between the *ortho* hydroxyl substituents and the π-electrons of the adjacent ring.

03.2-01 CRYSTAL STRUCTURE AND CONFORMATION OF 8-BROMO-9-β-D-XYLOFURANOSYLADENINE HYDRATE. By G.I. Birnbaum and M. Cygler, Division of Biological Sciences, National Research Council, Ottawa, Canada K1A 0R6; and I. Ekiel and D. Shugar, Department of Biophysics, Institute of Experimental Physics, University of Warsaw, 02-089 Warsaw, Poland.

9-β-D-Xylofuranosyladenine (xyloA) possesses both antitumour and antiviral activities, while its 5'-triphosphate inhibits *de novo* purine biosynthesis. The title compound is a model of xyloA in *syn* conformation, as it occurs, to some extent, in solution. 8-Bromo-xyloA hydrate crystallizes in the triclinic space group $P\bar{1}$, with a = 8.964(2), b = 16.510(4), c = 7.140(1) Å, α = 90.76(2), β = 89.10(3), γ = 103.72(1)°, Z = 3. The structure was solved by the heavy-atom method and the refinement, which included most hydrogen atoms, converged at R = 0.037 for 4191 observed reflections. As expected, all three independent molecules are in the *syn* conformation, but the conformations of their sugar rings are not identical. In two molecules the xylose ring adopts the unusual C(4') exo pucker, stabilized by intramolecular O(3')-H···N(3) hydrogen bonds, while in the third molecule the ring is in the commonly observed C(2') endo conformation, with an O(5')-H···N(3) intramolecular hydrogen bond. The conformations of the $-CH_2OH$ side chains are different in each molecule: eclipsing H(4') in one, trans in the second, and gauche$^+$ in the third. These results have been used to improve the conformational analysis of xylonucleosides by NMR spectroscopy.

03.2-02 STRUCTURE AND CONFORMATION OF A THYMIDINE ANALOG: 4-(2-DEOXY-β-D-erythro-PENTOFURANOSYL)-6-METHYL-3-OXO-1,2,4-TRIAZINE 1-OXIDE*. By M.L. Główka+, R. Parthasarathy and M. Bobek, Center for Crystallographic Research and Grace Cancer Drug Center, Roswell Park Memorial Institute, Buffalo, New York 14263, USA

Some aza analogs of thymidine have antibacterial activity and other analogs have activity against leukemia L1210 cells in vitro and in vivo. The title compound was synthesized as a part of search for modified nucleosides that might have chemotherapeutic action. The crystals of the compound, $C_9H_{13}N_3O_5$ were recrystallized from methanol. The unit cell parameters are: a = 6.832(1), b = 15.550(1), c = 5.109(1)Å, β = 105.29(1)°. Space group is $P2_1$ with Z = 2. The structure was solved by direct methods and refined to R = 0.026(R_w = 0.046) for 1271 reflections collected with copper radiation on a CAD4 diffractometer.

The bond lengths and angles are in good agreement with those found in similar structures. The molecule has the anti conformation with a very low X value (X_{CN} = 2.6°) and short H(6)···O(1'), H(6)···O(5') and H(2')···O(3) contacts of 2.25, 2.54 and 2.51Å, respectively. The ribose ring has the twist conformation: C(3')-endo C(2')-exo, with O(5') in g^+ orientation. The pseudorotation parameters are τ_m = 36.1 and P = 3·9°. There are two intermolecular hydrogen bonds: O3'···O1(2.84Å) and O5'···O3(2.74Å).

*Supported by NIH-GM 24864.
+Temporary leave of absence from Institute of General Chemistry, Technical University of Łódz, Poland.