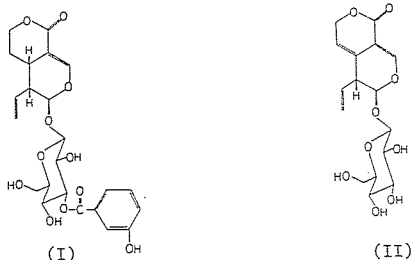


03.3-18 STRUCTURES OF TWO SECOIRIDOID GLUCOSIDES:

DECENTAPICRIN A, $C_{23}H_{25}O_{11}$ AND GENTIOPICROSIDE HEMIHYDRATE, $C_{16}H_{20}O_9 \cdot H_2O$, B.Kojić-Prodić and A.L. Spek, Vakgroep Algemene Chemie, afdeling Kristal- en Structuurchemie, University of Utrecht, 3508 TB Utrecht, The Netherlands.

The crystal and molecular structures of secoiridoid glucosides decentapicrin A(I) and gentiopicroside(II) with fungitoxic properties, isolated from plant *Centaureum litorale* [W.G. van der Sluis & R.P. Labadie, *Planta medica* (1981) 41,150-160] will be described.



The crystals of both compounds are orthorhombic with space group $P2_12_12_1$. Unit cells: (I), $a=5.8234(6)$, $b=12.512(2)$, $c=31.693(5)\text{\AA}$, $Z=4$; $D_x=1.373\text{gcm}^{-3}$; (II), $a=8.175(2)$, $b=12.810(2)$, $c=31.99(1)\text{\AA}$, $Z=8$; $D_x=1.449\text{gcm}^{-3}$. The final $R=0.053$ for 1088 reflexions [$I>1.5\sigma(I)$] (I) and $R=0.043$ for 1789 reflexions (II) [$I>2.5\sigma(I)$].

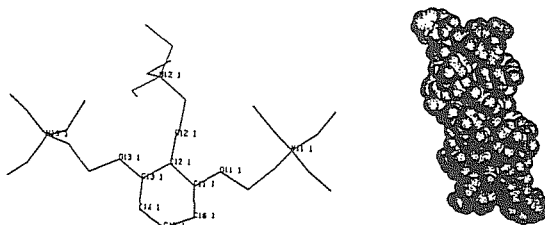
The structure of decentapicrin A reveals a non-planar secoiridoid moiety; the δ -lactone and pyran rings exhibit puckered conformation which can be approximated to an envelope type with C(6) and C(9) as the flaps. The β -D-glucose moiety is in the chair, 4C_1 , conformation. The molecular packing is realized through intermolecular hydrogen bonds forming spiral chains in the a and b directions. These perpendicular spirals are connected by hydrogen bonds enclosing hydrophobic and hydrophilic areas. In the crystal of gentiopicroside hemihydrate there are two conformers which have different conformations of the δ -lactone ring: nearly planar [mean value of torsion angle $=5(1)^\circ$] and half-chair. Both conformers show a skew-boat conformation of pyran ring. The β -D-glucose moiety appears in the chair, 4C_1 , conformation. Molecular packing is dominated by hydrogen bonds between the water molecule and both sugar residues, sugar-sugar, and the sugar-secoiridoid moieties (involving only conformer with non-planar δ -lactone ring). The molecules connected by hydrogen bonds form wavy layers [in the (ab) plane] which are separated by ethenyl residues.

03.3-19

X-RAY STRUCTURE AND CONFORMATIONAL FLEXIBILITY OF GALLAMINE OF BROMIDE: A POTENT NEUROMUSCULAR BLOCKER

By Jasmine Husain and Rex A. Palmer, Department of Crystallography, Birkbeck College, Malet Street, London WC1E 7HX.

The structure of the classical neuromuscular blocking agent gallamine has been determined by direct methods and difference Fourier synthesis. The crystals are triclinic space group P1, $a = 14.216(1)$, $b = 14.081(1)$, $c = 20.895(2)\text{\AA}$, $\alpha = 104.9^\circ$, $\beta = 92.6^\circ$, $\gamma = 94.5^\circ$ with 4 independent gallamine molecules per unit cell. Extensive disorder is observed amongst the bromide counterions which are distributed in 17 sites and both water and ethanol solvent molecules have been located. The gallamine molecules were refined by constrained least squares and occupancy factors were refined for the disordered bromide structure.



Gallamine Molecule

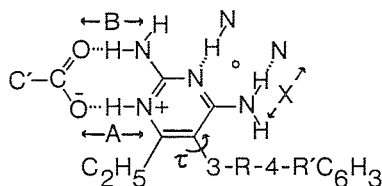
Stacking of 4 Gallamine Molecules

03.3-20

GEOMETRY OF ANTIFOLATE DRUGS: EFFECT OF COUNTER IONS AND SUBSTITUENTS ON PYRIMETHAMINE SALTS.

By P.K. Bryant, J. Colby, R.G. Jenks, P.R. Lowe, and C.H. Schwalbe, Department of Pharmacy, University of Aston in Birmingham, Gosta Green, Birmingham B4 7ET, UK.

The action of several important anti-infective and anti-cancer drugs is inhibition of the enzyme dihydrofolate reductase (DHFR). Now that the crystal structure of DHFR from eukaryotic as well as prokaryotic sources is available, it should be possible to design a selective inhibitor that is a perfect fit to DHFR of an invading organism, but a poor fit to host DHFR. However, such rational design is hampered by the relatively low precision of the protein crystallographic data. The present study supplies precise data on one type of drug: pyrimethamine and its analogues. With pyrimethamine hydrochloride (1) as a reference, structural data are reported for pyrimethamine acetate hydrate (2), pyrimethamine salicylate (3), and pyrimethamine salicylate isopropanol solvate (4), thus modeling the ionic and hydrogen bonding link between the drug and a side chain carboxylate ion of DHFR, which is believed to be of major importance for drug binding.



(1)-(4) $R=H, R'=Cl$

(5) $R=NO_2, R'=C_5H_{10}N; Cl^-$ salt