STRUCTURAL INVESTIGATIONS OF AZTHRIMYCIN, ITS DERIVATIVES AND COPPER COMPLEX

Azthrimycin (1) was the first representative of a new class of 15-membered macrocyclic antibiotics with improved pharmacokinetics and greater activity as compared to erythromycin A (Dodick, S. et al., 1988, J. Chem. Res. (S) pp. 152-153). Here we report the structures of one of its derivatives (2), a 1:1 solution of azthrimycin with dimethyl sulfoxide (3), and a 1:2 complex of copper(II) with azthrimycin (4). Both (1) and (2) are dihydrides.

(1) \[ R_1 = R_2 = R_3 = R_4 = H \] \[ R_5 = CH_3 \]

(2) \[ R_1 = R_2 = R_3 = R_4 = H \]

(3) as (1) but a solvate with DMSO

PS-04.01.14 CRYSTAL STRUCTURE OF 30-DECHLORO-30-METHOXY-25-O-METHYL-3-N-METHYLAPTHOMYCIN A


Several attempts to crystallize Naphthomycin A failed, while it was possible to obtain crystals of two derivatives prepared by methylation with CSMe/Ago. By X-ray analysis, one of the two derivatives proved to be 25-O-methylnaphthomycin A isoimethyl ether (W. Keller-Schierlein, M. Moyer, L. Cellai, S. Cecchini, D. Lamba, A. Supple, W. Pedoli, M. Brufani, J. Antibiot. 1984, 37, 1357-1361), while the other is the title compound.

In the crystal structures of both derivatives the molecules display a similar chain-like shape.
Crystal data: S.G. Orthorhombic P2_12_1\_2, \(a=12.925(3), b=14.160(4), c=22.970(6)\) Å, \(C_{43}H_{34}O_2Cl\cdot CH_3Ol\cdot H_2O, \mu_r=79.9, D_r=1.292\) Mg/m\(^3\), Mo-K\(x\) radiation: \(\lambda=0.093\) and \(wR=0.093\) for 3607 F(00)>2.0 (F(00)).

PS-04.01.15 CRYSTAL STRUCTURE OF CALACITIN, A CARDENOLID FROM ASCLEPIAS LINARIA: By T. Hernández-Vizcay*, M. Soriano-García, A. Rodríguez-Romero, C. Valencia, L. Hernández and F. Aguirre. Instituto de Química, Universidad Nacional Autónoma de México, Delegación Coyocacán, México D.F. 04510, México and Area de Productos Naturales, Departamento de Biotecnología, Universidad Autónoma Metropolitana-Unidad Iztapalapa, Delegación Iztapalapa, México D.F. 09340, México.

Cardenolides constitute one of the several groups of plant secondary compounds that are sequestered by phytophagous insects for defense against predation. Most members of the genus Asclepias (Asclepiadaceae) produce the cardiac steroids at varying concentrations. The molecular structure is determined from the X-ray diffraction data and confirms the structure previously assigned on the basis of chemical and spectroscopic evidence. The title compound, \(C_{37}H_{34}O_2\), is crystallized in the orthorhombic space group P2_12_1\_2 with Z=8. The cell parameters are: \(a=29.868(7), b=12.576(4), c_1=14.705(5)\) Å, \(R=0.064\) and \(wR=0.066\). In the two independent molecules, rings A, B, C, and G and F have chair conformations, and D adopts an envelope conformation. The structure is stabilized by a three-dimensional network of hydrogen bonds and a number of C-H−O hydrogen bond interactions.

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PS-04.01.16 UNCOMPLEXED IONOPHORE ANALOGS: CRYSTAL STRUCTURE OF MODIFIED 25-CROWN-7 ETHER: By M. Elizabeth Sobhla and F.K. Chaick. Department of Crystallography and Biophysics, University of Madras, Madras - 600 025, India.

Crown ether macrocycles undergo conformational changes when complexed with various metal salts. The conformation of complexes are often quite different for different salts but in general they all feature the O atoms directed towards the cavity of the macrocycle and the C and H atoms on the periphery. But uncomplexed crown ethers often adopt a more elongated conformation with methylene groups pointing into and filling the cavity. This is usually accomplished by rotation about the bonds to give torsion angles which differ markedly from the expected 150° for C-C bonds. But only a very small number of C-O torsion angles are usually affected to a major extent when the macrocycle geometry is deformed in order to optimize specific ligand - substrate or intramolecular interactions. The 25-Crown-7 ether crystallizes in space group P1 with \(a=10.809(1), b=10.945(l), c=10.256(l)\) Å, \(\alpha=109.85%(1), \beta=104.15(l), \gamma=97.27(l)\) and \(Dc=3.138gcm\(^{-3}\) for Z=2. The structure was solved and refined to an R-value of 0.049. Three torsion angles in the macrocycle take up gauche conformation in contrast to the usual anti conformation. The crystal structure is stabilized by intramolecular van der Waals forces and C-H...O and C-H...N types of interactions. Stacking of the pyridine rings is a noticeable packing feature in the crystal lattice. Other structural details will also be presented.

PS-04.01.17 STRUCTURE AND FUNCTION STUDY ON DITEREPENOID LACTONE IN TRIPETYRIUM WILFORDII: Hook, F., Y. Lu*, Y.Z. Tian, Q.T. Zheng, Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing, 100050, China.

In China there are three kinds of calaetaceae Tripterygium Wilfordii Hook, f., that is Tripterygium Wilfordii Hook. f., Tripterygium hypoglaucum Hutch and Tripterygium Spreng at Takeda, which are distributed in Southwest China, South China and Northeast China.

At the beginning of 30's Chinese scientist Zhao Chenggu first isolated Tripteron from the root to Tripterygium wilfordii Hook f and its structure was determined. Up to now, nearly 20 diterpenoid compounds have been found, which have anti-inflammatory, antitumor, anti-fertility and immuno-suppressive properties. In 1972 Kupchan et al isolated three diterpenoid compounds and found that these compounds have protective activity or antitumor activity. The research group in our country showed that these compounds exhibit various biological activities including anti-inflammatory, antitumor, anti-fertility and immuno-suppression.

The crystal structures of Triptolidol, Triptolide, Triptolide, Triptodonolides, 16,17-dihydroxytriptolide and their derivatives have been determined by X-ray diffraction techniques. The structural and conformational properties with bond lengths, bond angles and torsion angles are analysed systematically. Molecular mechanical calculations have been carried out to optimize conformation and structure in solution. The stereostructure-activity relationship is discussed by molecular graphics method.