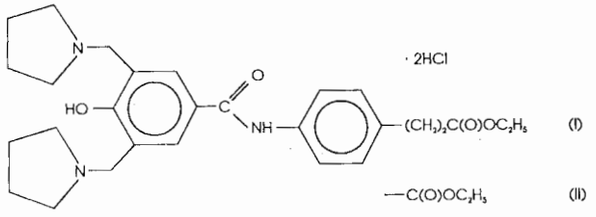
protonated compounds of that type (*J.Med.Chem.* **34**, 2678; *Acta Cryst.* C47, 1038) showed that protonation of the pyrrolidine ring N atom is a key determinant of conformation; hence, we have determined the structures of two diprotonated derivatives to complete the study.

Crystal data: (I) H_2O, 0.5 CH_3OH, C2/c, Z=8, a=20.301, b=11.296, c=24.901Å, β=93.19°, R=0.071. (II) $P2_1/c$, Z=4, a=12.903, b=16.430, c=13.731Å, β=103.64°, R=0.057.

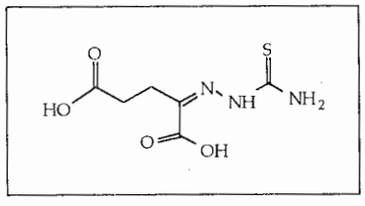


PS-04.01.21 **A STRUCTURAL INVESTIGATION ON THE α-KETOGLUTARIC ACID THIOSEMICARBAZONE IN METAL COMPLEXES** By M. Belicchi Ferrari, G. Gasparri Fava, C. Pelizzi, P. Tarasconi and G. Pelosi, Istituto di Chimica Generale ed Inorganica, Centro di Studio per la Strutturistica Diffrattometrica del CNR, Viale delle Scienze, 43100 Parma, Italy

Thiosemicarbazones present biological and chemical properties which cover a broad spectrum of potentially useful chemotherapeutic properties (antitumoral, antibacterial, as well as antiviral) (S.Padhyè & G.B.Kauffman, Coord.Chem.Rev. ,1985, 63, 127-160).

Our research aims at the understanding of the correlation between the structural features and the biological properties of this class of compounds under different experimental conditions. Many pyruvic acid and pyridoxal thiosemicarbazone complexes have already been synthesised and characterised. Some of them containing copper or cobalt, tested in vitro, have shown an inductive effect on FLC (Friend erythroleukemia cells) erythroid differentiation and a suppressive efficacy on their proliferation (M.Belicchi Ferrari, G.Gasparri Fava, P.Tarasconi, R.Albertini, S.Pinelli & R.Starcich, J.Inorg. Biochem., 1993, accepted for publication).

At present we are studying the behaviour of the α-ketoglutaric acid thiosemicarbazone, a ligand which presents many potential donor



atoms and a variety of potential conformations, in complexes with different co-ordinating ions such as zinc, copper and nickel. All of the cited compounds have been synthesised and characterised spectroscopically and their crystal structures have been determined by X-ray analysis.

PS-04.01.22 **CRYSTAL STRUCTURE OF A QUINOLONE DERIVATIVE WITH ANTIMALARIAL ACTIVITY**. By **Mario V. Capparelli*** (Fac. Ciencias, Univ. Central de Venezuela, Caracas 1050, Venezuela), **Jaime E. Charris** (Fac. Farmacia, Univ. Central de Venezuela, Caracas 1050, Venezuela) and **Duilio Cascio** (Molec. Biology. Inst., UCLA. Los Angeles, CA 90024, USA)

According to the World Health Organization malaria is still the chief cause of human death, aside from natural causes. The antimalarial drugs currently in use, mainly aminoquinolines, pyrimidines, sulfonamides and sulfones, are being rendered increasingly ineffective by the appearance of resistant strains of *Plasmodium*.

A number of new N-methylated quinolones were synthesized as a part of a program to develop more active and less toxic new antimalarial drugs. These compounds were tested *in vitro* for antimalarial activity and seven of them were found to be between 100% and 75% effective in inhibiting the growing of *P. falciparum*.

The crystal structure of one of the active compounds, *viz.* 2,4-diamino-10-methyl-9-methoxypyrimido[4,5-b]5-(10H)-quinolone (activity 89%), was determined. The tricyclic molecule is essentially planar, with both methyl groups out of the plane. Bond lengths and angles are within normal values; the C=O distance, 1.263(2) Å, indicates a weakened double bond. The molecules are stacked along [101], with N-H...O and N-H...N bonds connecting molecules in adjacent piles.

Crystal Data: $C_{13}H_{13}N_5O_2$, M_r = 271.28, monoclinic, $P2_1/n$, a = 10.664(2), b = 10.111(2), c = 11.318(2) Å, β = 99.351(4)°, D_x = 1.50 gcm^{-3}, Z = 4, F(000) = 568, μ(Mo-Kα) = 1.00 cm^{-1}. The structure was solved by direct methods and refined to R = 0.049 for 1941 unique reflections with I > 3 σ(I).

PS-04.01.23 X-RAY CRYSTAL STRUCTURAL ANALYSIS OF TWO NEW POTENTIAL ACTIVE ANTIMALARIAL DRUGS. D. Gómez de Andérez[1], R. Avila[1], J. Domínguez[2], and S. Khan[3]. [1]Universidad de Los Andes, Facultad de Ciencias, Mérida-Venezuela, [2]Universidad Central de Venezuela, Facultad de Farmacia, Caracas-Venezuela, [3]University of California, Chemistry Dept., Los Angeles, CA-USA.

Malaria is distributed widely throughout populated areas where the average temperature is 60°F or higher and some extends to more temperate climates. Because of the acute toxicity of some antimalarial drugs, there is interest in testing new compounds against this disease. Methylthio-4-ciano-5-pyrazolone ($C_5H_5N_3OS$) and 3-amino-5-(2-methoxyanilino)-4-metoxy-carbonylpyrazol ($C_{12}H_{14}N_4O_3$) are compounds with potential antimalarial activity.
X-Ray single crystal analysis shows: (a) C_5H_5OS is monoclinic, $P2_1/c$, a=4.514(1), b=13.536(1), c=11.455(1)A and B=92.82(1), Mo K=O, 7107A. F(000)=320, 2349 unique reflections measured, 1167 with I>3σ(I). The structure was solved by direct methods, the final anisotropic refinement using full matrix least-square gave R=0.047, Rw=, GOF=1.77. (b) $C_{12}H_{14}N_4O_5$ is monoclinic $P2_1/n$, a=13.108(3), b=7.739(2), c=13.224(3)A, B=110.65(1) MoKα=0.7107, F(000)=552. 4053 unique reflections measured, 1890 with I>3σ(I). The final anisotropic refinement gave R=0.049, Rw=0.060, GOF=1.683.

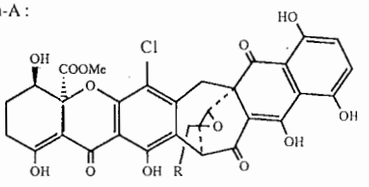
PS-04.01.24 **BETICOLINS, A NEW CLASS OF TOXINS PRODUCED BY CERCOSPORA BETICOLA, A PARASITIC STRAIN OF SUGAR BEETS.** By A. Neuman[1], T. Prangé[1], M.L. Millat[3], J. Einhorn[2], J.P. Blein[3]. . [1]Chimie Biomoléculaire (URA 1430 CNRS) UFR-Biomédicale, 93012-BOBIGNY CEDEX, France ; [2] Laboratoire de Phytopharmacie, I.N.R.A., F-78026 VERSAILLES CEDEX, France ; [3] Laboratoire de Phytopharmacie, I.N.R.A., BV 1540, 21034-DIJON CEDEX, France

Cercospora Beticola is a parasitic fungus responsible for leaf spot disease on sugar beet. The pathogen agent produces, in addition to the red cercosporin, several yellow toxic metabolites with a new

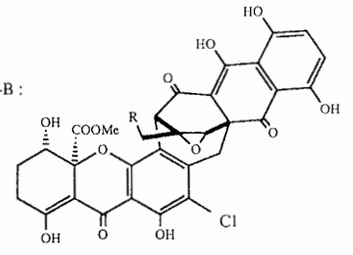
chlorinated Xanthone/Anthraquinone skeleton. Most of these toxins belong to the two families of Beticolin A and B (figure). Both types of toxins differ mainly by the way the two anthraquinone and xanthone moieties are attached together. Beticolin 1 (R=H) and Beticolin 3 (R=OH), part of the beticolin A familly, were crystallized from $CHCl_3$/methanol mixture as $CHCl_3$ solvates (the structures are isomorphous) while Beticolin 2 (B type, R=H) and Beticolin 4 (B type, R=OH) were identified by NMR (Millat et al., 1993) to share the cebetin A structure (Jalal et al, 1992).
The structure of Beticolin 1 was easily solved by direct methods. In the case of Beticolin 3, the crystals so far obtained were too small (max. size : 0.15mm) to produce enough data for direct methods. The structure was solved by Molecular Replacement technique.

	Beticolin 1	Beticolin 3
Xtal size (mm) :	0.25x0.25x0.5	0.05x0.05x0.15
nb. of Fobs observed :	2480	1027
R factor (%) :	6.0	9.4

Beticolin-A :



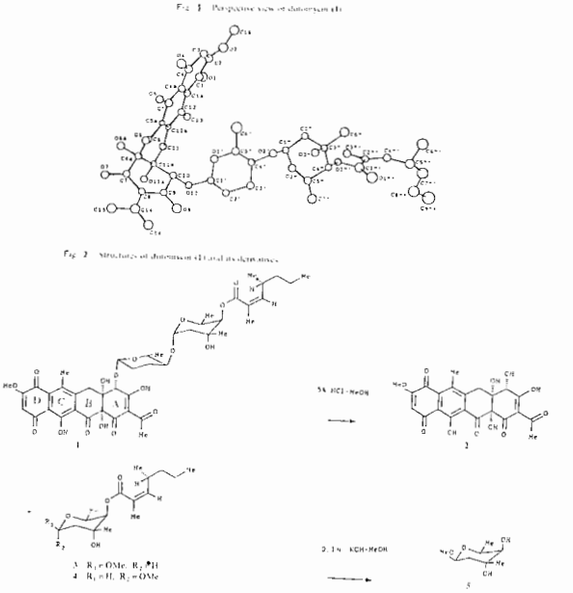
Beticolin-B :



References :
-M.A.F. Jalal, M.B. Bilayet Hossain, D.J. Robeson, D. van der Helm (1992) J. Amer. Chem. Soc, 114, 5967-5971.
-M.L. Millat, J.P. Blein, J. Einhorn, J.C. Tabet, P.H. Ducrot, J.Y. Lallemand (1993) Tetrahedron Lett., submitted.

PS-04.01.25 THE STRUCTURE OF DUTOMYCIN. Ming-Qin Chen* and Jie Liu, Research Center of analysis & Measurement, Fudan University, Shanghai, P.R.China, 200433. Li-Jiang Xuan, Sao-Hua Xu, Hai-Lin Zhang and Ya-Ming Xu, Shanghai Institute of Materia Medica, Academia Sinica, P.R.China.

Dutomycin, a new antitumor antibiotic, has been found in the culture of Streptomyces SP1725 (Ya-Ming Xu and Ming-Qin Chen, et al.(1992) J.Antibiotics, 45, 715). The antibiotic was active against leukemia P388 and 100% inhibition was acheived as a concentration of 1 μg/ml. We report herewith its molecular structure and absolute configuration.
The empirical formula was established as $C_{44}H_{71}O_{17}\cdot 2C_1H_1$ on the basis of X-ray diffraction analysis and reconfirmed by elemental analysis, NMR spectral analysis and chemical degradation. The compound crystallized in the orthorhombic space group $P2_12_12_1$ with a=18.045(3), b=18.963(3), c=15.611(3)Å, V=5341.8Å^3, Z=4. Based on 5223 unique and 1612 observed reflections ($I>3\sigma(I)$), the structure was solved by direct methods and refined by full matrix least squares to the final R value of 0.0773. The molecule has a naphthacene carbon skeleton which is structurally related to the tetracycline and Anthracycline antibiotics, such as SF2575 (Masahiro Hatsu, et al.(1992) J. Antibiotics, 45, 325), and is unique by bearing glycosides and 2,4-dimethylheptene-2 acid moieties and containing many carbonyl groups which may relate to its biological activity as shown in Fig. 1.
In the aglycone moiety intramolecular hydrogen bonding between the exocyclic oxygen atoms on neither rings B and C nor C and D has been observed. However, the intramolecular hydrogen bonding $O_{13}\cdots H_{11}\cdots O_{12}$ may exist. This differs from that observed in most anthracycline antibiotics. The rings B, C, D are nearly coplanar (except C_{11} atom) because of the configuration among these atoms. It resembles the shape observed in all the anthracycline antibiotics.
The absolute configuration of Dutomycin was elucidated by subsequent chemical degradation (See Fig. 2). Methanolysis of 1 with methanolic hydrochloric acid gave the aglycone 2 and a pair of anomeric isomers 3 and 4. 3 was further methanolized in alkaline methanol and L-axenose methyl glycosides 5 was obtained (Arcamone,F. et al. (1973) J.Am.Chem.Soc., 95,2008). Since the configuration of 5 was known and consistent with that found in Dutomycin, the determined structure was thus implied absolute meaning due to the retention of the configuration during degradations. The chiral carbon atoms C_{11}, C_{12}, C_{13}, $C_{1'}$, $C_{3'}$, $C_{5'}$ and $C_{5''}$ thus have the configuration of (S,S,R,R,R,S,R).



PS-04.01.26 THE PROTOTYPES OF THE ENNIATIN B CHANNELS IN THE CRYSTAL STRUCTURE OF THIS MEMBRANE-ACTIVE ANTIBIOTIC

By G.N.Tishchenko*, N.E.Zhukhlistova, V.I.Andrianov, Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia and P.Main, Department of Physics, University of York, York, England.

The crystal structure of the title compound has been determined by a single-crystal three-dimensional X-ray diffraction study. The compound crystallised from heptane in the space group $P2_1$ with four $C_{33}H_{57}N_3O_9$ molecules in one asymmetric unit. The unit cell dimensions are a=29.178(15), b=28.294(15), c=10.840(5)A, g=121.12(5)°. The structure was solved by direct