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THE STRUCTURE OF TETRONOLIDE, THE AGLYCONE OF ANTITUMOR ANTIBIOTIC TETROCARCIN

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Summary: X-ray analysis has determined the structure of tetronolide, which has a unique spiro γ-lactone group.

Tetrocarcins are novel antitumor antibiotics produced by *Micromonospora chalcea* KY11091. Mild hydrolysis of tetrocarcin A ($C_{67}H_{96}N_2O_{24}$), a major component of tetrocarcins, gave the component 1 and two moles each of L-amicetose and L-digitoxose.[1] Further hydrolysis of the component 1 gave the novel nitrosugar and the aglycone, tetronolide. The molecular formula was determined as $C_{32}H_{40}O_8$ [found:m/e 552.2697,required:m/e 552.2723] by a high resolution mass measurement. We report here an X-ray analysis of tetronolide.

Recrystallization of tetronolide from ethyl acetate containing trace amount of methanol gave well formed crystals; orthorhombic with space group $P2_12_12_1$, a=20.146(5), b=22.679(4), c=7.845(2) Å, V=3584 Å^3, D_x=1.19g.cm^{-3}, Z=4. The intensity data were collected on a Rigaku four-circle automated diffractometer with graphite monochromated Mo Kα radiation. 3577 independent reflexions ($|Fo|>3.0\sigma(|Fo|)$) with $2\theta\leq50°$ were obtained and corrected for Lorentz and polarization effects but not for absorption and extinction. The structure was solved by MULTAN 78.[2] The resulting E map revealed the locations of all non-hydrogen atoms. All hydrogen atoms and the disordered solvent molecules were located by the difference syntheses. Block-diagonal least-squares refinement of positional and thermal parameters reduced R to 0.083. Although the absolute configuration has not been determined, a perspective view of one of its enantiomers is shown in Fig.1 and the corresponding chemical structure is shown in Fig.2. Tetronolide exhibits several unique structural features: first, it has a thirteen-membered macrocyclic ring; second, the macrocyclic ring can be also recognized as a fourteen-membered macrolide which contains a spiro γ-lactone structure; third, it has a β-diketone part and can form metal complexes. There is an intramolecular hydrogen bond between a carbonyl group and a hydroxyl group as shown by dotted lines in the figures. Two cyclohexene rings take half-chair

conformation and the cyclohexane ring does chair conformation. The crystal structure and the nature of the metal complexes of tetronolide will be discus: in detail elsewhere.

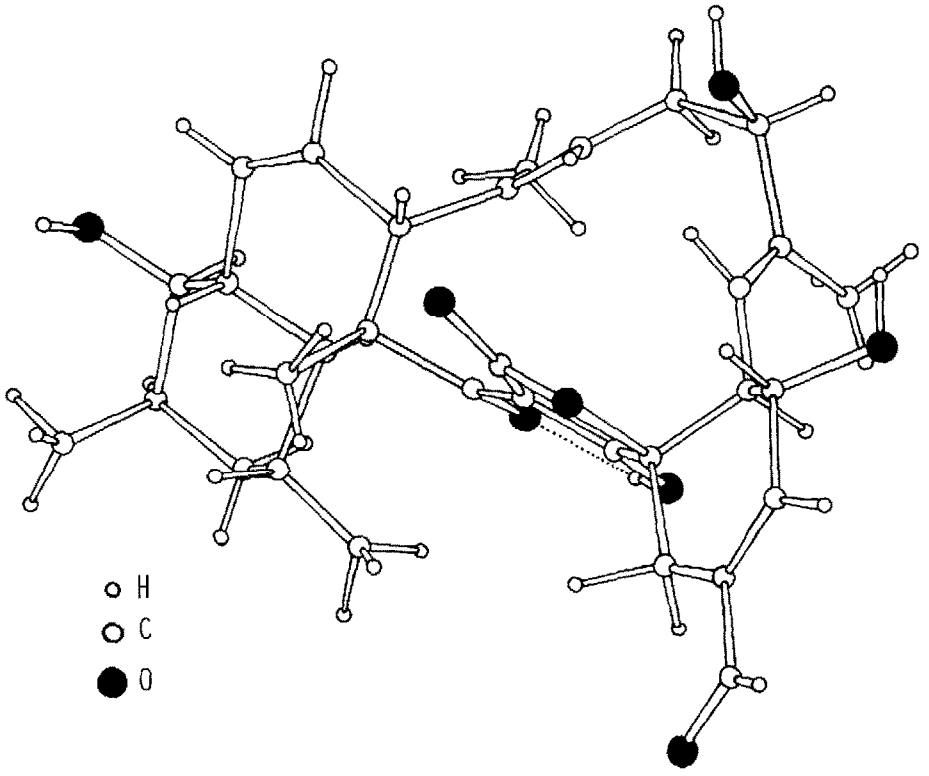

Fig.1

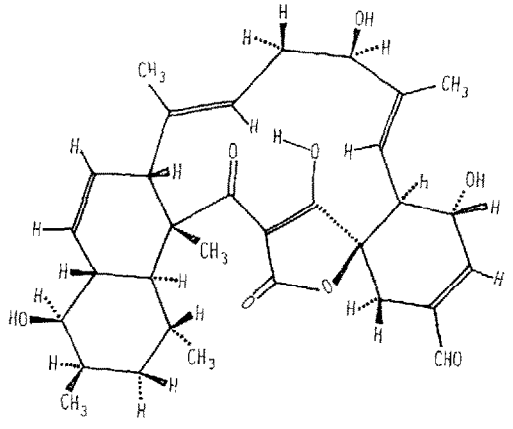

Fig.2

References

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2) P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq and M. M. Woolfson, *MULTAN 78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data, Univs. of York, England, and Louvain, Belgium (1978)*

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