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MIMOCIN, A NEW ISOQUINOLINEQUINONE ANTIBIOTIC

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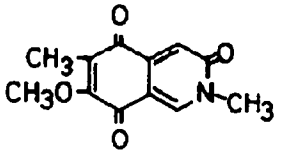
Summary: A new isoquinolinequinone antibiotic, mimocin(2), has been isolated from the strain of *Streptomyces lavendulae*. The structure of mimocin has been deduced from mass and PMR spectral data and confirmed by its synthesis.

We have recently described the structural elucidation of the satellite antibiotics, mimosamycin(1)[1], saframycin A[2], B and C[3], obtained from the fermentation broth of *Streptomyces lavendulae* No. 314. The structure of the minor metabolite, mimosamycin was determined as 2,6-dimethyl-7-methoxy-3,5,8-isoquinolinetrione(1) and the chracteristic feature of the major antibiotics, saframycin A, B, C is a dimeric structure of mimosamycin(1).

Further study of the mimor metabolites has now allowed the isolation of a new antibiotic, mimocin, exhibited strong activity against *B. subtilis* and *C. albicans*. The present work deals with its structure determination and synthesis.

Mimocin(2), yellow prisms, mp 189-191°(decomp)(ether), $C_{15}H_{14}N_2O_5$, gave the following spectral data: MS *m/e*(%): 302(M^+, 1.5), 259(M^+-$COCH_3$, 100), 216(M^+-$COCH_3$-CONH, 55), 186(15); UV λ_{max}^{MeOH} 243, 322 nm; IR $\nu_{max}^{CHCl_3}$ 3380, 1720, 1670 cm^{-1}. The FT-PMR spectrum($CDCl_3$) indicated the



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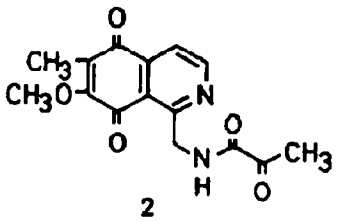
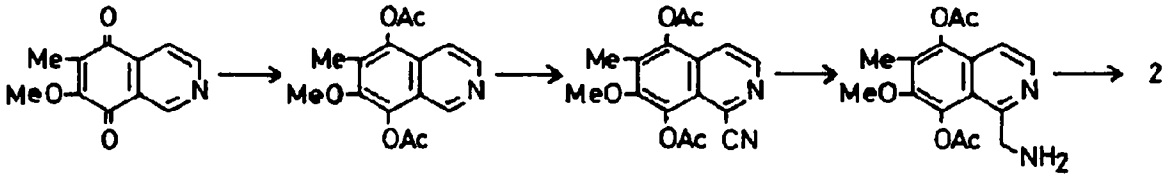


2

three methyl groups[δ 2.09(s, aro CH_3), 2.52(s, $COCH_3$), 4.17(s, aro OCH_3)]; a benzylic methylene group[δ 5.10(d, J=5 Hz)] coupled with a NH proton; C_4 and C_3-isoquinoline protons[δ 7.92(d, J=5 Hz) and 8.94(d, J=5 Hz)]; and a NH proton[δ 8.57(br s)].

These spectral data are consistent with the presence of a 7-methoxy-6-methyl-5,8-isoquinolinedione and of a $-CH_2NHCOCOCH_3$ system, which is common to all saframycin group antibiotics.

Therefore, the structure of mimocin was proposed as 2 and was confirmed by its synthesis starting from 5,8-isoquinolinedione(3), mp 130-131°.



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The hydroquinone diacetate(4), mp 142-145°, was obtained by reductive acetylation of 3 (82 % yield), was converted to 1-cyano-5,8-hydroquinone diacetate(5), mp 152-154°, by the usual manner[4] in 64% yield. Catalytic hydrogenation of 5 over 10% Pd-C in methanol containing hydrogen chloride afforded the sensitive 1-aminomethyl-5,8-hydroquinone diacetate(6), isolated as its dihydrochloride salt. Treatment of dihydrochloride salt of 6 with pyruvic acid in α, α-dichloromethyl methyl ether[5] without solvent (40-50°, 30 min) followed by basic workup afforded directly the desired 2. This compound was identical in all respects (mmp, IR, PMR, MS, TLC) with natural mimocin.

It is interesting to note that an isoquinolinequinone metabolite renierone was recently isolated from a marine sponge.[6]

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