

SYNTHESIS OF MIMOSAMYCIN (2,6-DIMETHYL-7-METHOXY-3,5,8-ISOQUINOLINETRIONE)

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Streptomyces lavendulae No. 314 produces mimosamycin, which is responsible for the antibiotic activity on mycobacteria including streptomycin-resistant strains of human tubercle bacilli, in addition to chlorocarcins A, B, and C.

The structure of mimosamycin was determined to be 2,6-dimethyl-7-methoxy-3,5,8-isoquinolinetriene by X-ray crystallographic study. The characteristic feature of the structure is a heterocyclic quinone consisted of 3,5,8-isoquinolinetriene, which has been never found in the literature.

A starting material, 6-methyl-7-isoquinolinol, was prepared in 80% over-all yield in five steps from *m*-methoxytolualdehyde by the application of the method of Jackson et al. Oxidation of 6-methyl-7-isoquinolinol with oxygen in the presence of cupric acetate and morpholine gave 3,5-dimorpholino-6-methyl-7,8-isoquinolinedione. Upon treatment with sulfuric acid-methanol followed by diazomethane, the *o*-quinone was converted to 7-methoxy-6-methyl-3-morpholino-5,8-isoquinolinedione. Reductive acetylation with zinc-acetic acid and acetic anhydride gave 5,8-diacetoxy-7-methoxy-6-methyl-3-morpholinoisoquinoline, which was quaternized at isoquinoline nitrogen with methyl iodide. In this *N*-methylation reaction, no concurrent *N*-methylation of morpholine nitrogen was observed. Treatment of the iodomethylate with silver oxide gave rise to in one-step 2,6-dimethyl-7-methoxy-3,5,8-isoquinolinetriene, which was identified with a specimen of natural mimosamycin by mixed mp and the comparison of IR, UV, NMR, and MS spectra and *R_f* value of TLC.