SYNTHESIS OF ISOQUINOLINEQUINONE ANTIBIOTICS

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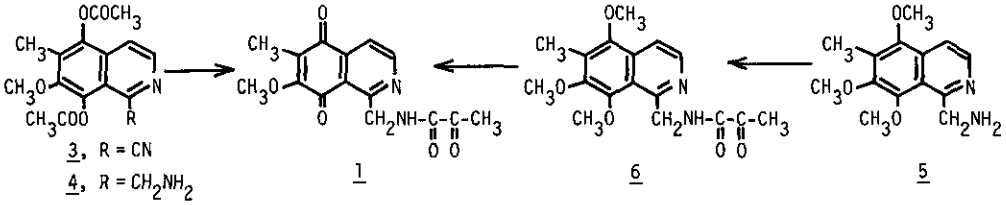
We have recently elucidated the structure of the satellite antibiotics, saframycins, mimosamycin, and mimocin(1), possessing unusual isoquinolinequinone nucleus. Furthermore, an isoquinolinequinone metabolite, renierone(2), was isolated from a marine sponge.

Mimocin(1), 1-pyruvoylaminomethyl-6-methyl-7-methoxyisoquinoline-5,8-dione, was synthesized. Catalytic hydrogenation of 3 over 10% Pd-C in methanol containing hydrogen chloride afforded the sensitive 4. Treatment of dihydrochloride salt of 4 with pyruvic acid in α,α-dichloromethyl methyl ether afforded the desired 1. The compound 1 was also obtained by oxidation of 1-pyruvoylaminomethyl-6-methyl-5,7,8-trimethoxyisoquinoline(6) with ceric ammonium nitrate (CAN).

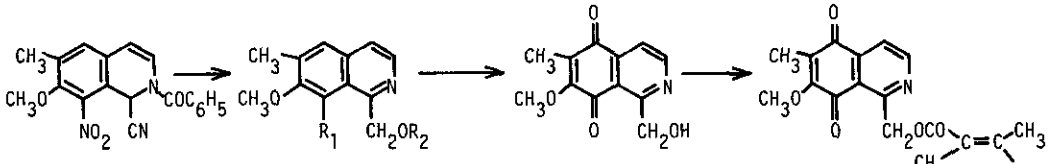


3, R = CN

4, R = CH_2NH_2

1 6 5

Renierone(2), 1-(7-methoxy-6-methyl-5,8-dioxoisoquinolyl)carbinyl angelate was synthesized from 7-methoxy-6-methyl-8-nitroisoquinoline(7), which was converted to the Reissert compound (8). The lithium salt of 8 was treated with gaseous formaldehyde to yield 9. The Fremy's salt oxidation of 10 obtained by hydrolysis and catalytic reduction of 9 provided 11. The compound 11 was treated with phenyllithium in dioxane-ether at -20° followed by addition of angeloyl chloride to afford 2.



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9, $R_1 = NO_2$, $R_2 = COC_6H_5$

10, $R_1 = NH_2$, $R_2 = H$

11 2