

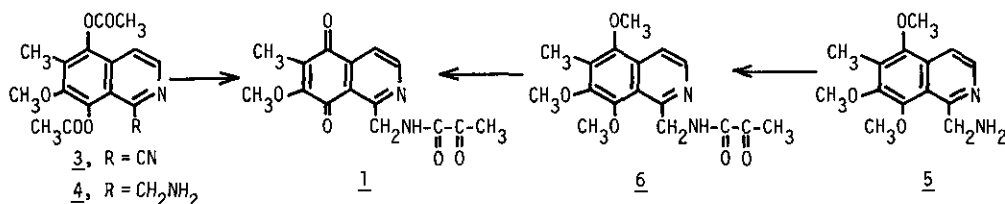
SYNTHESIS OF ISOQUINOLINEQUINONE ANTIBIOTICS

Akinori Kubo, Yoshiyasu Kitahara, Shinsuke Nakahara, Naoki Saito, and
Ryoichi Iwata

Meiji College of Pharmacy, 1-35-23 Nozawa, Setagaya-ku, Tokyo, 154, Japan

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).



Renierone(2), 1-(7-methoxy-6-methyl-5,8-dioxoisoquinolyl)carbonyl 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.

