

SYNTHETIC APPROACH TO THE ANTITUMOR ANTIBIOTIC LAVENDAMYCIN

Satoshi Hibino*, Miko Okazaki, Kohichi Sato, Itsuko Morita and Masataka Ichikawa

Faculty of pharmacy & Pharmaceutical Sciences, Fukuyama University

985 Higashimura, Fukuyama, Hiroshima 729-02 Japan

Lavendamyacin, a new antitumor antibiotic isolated from *Streptomyces lavendulae*, strain C22030, was determined by X-ray and ^{13}C -NMR to have structure 1. This structure was similar to that of streptonigrin. We are attempting to develop a total synthesis and syntheses of its congeners based on the non acidic Pictet-Spengler type cyclization of an appropriately substituted quinoline-2-aldehyde 3 with a tryptophane methylester 4 to provide a desmethyllavendamyacin methylester 2 via oxidation of quinoline 8.

Initial study was aimed at the formation of pyridine ring (β -carboline 6), which was successfully prepared by the Pictet-Spengler type reaction of 8-benzyloxyquinoline-2-aldehyde 3 with tryptophane methylester 4 under the none acidic condition, followed by aromatization with 5% Pd-C. Then quinolyl- β -carboline 6 was hydrogenated by 10% Pd-C to give 8-hydroxyquinoline derivatives 7, followed by bromination with 2,4,4,6-tetrabromo-2,5-cyclohexadiene-1-one to have the selective dibromo-compound 8 in excellent yields, respectively. We have found that cerium ammonium nitrate was the best oxidizing agent for the oxidation of quinoline 8 to quinolinequinone 9. Replacement of the bromine of 9 by sodium azide gave azidequinolinequinone 10, and reduction of the azide group of 10 with sodium hydrosulfite afforded the dark red aminoquinolinequinone 2. Work is now in progress on syntheses of 1 and other congeners.

