SYNTHETIC APPROACH TO THE ANTITUMOR ANTIBIOTIC LABENDAMYCIN

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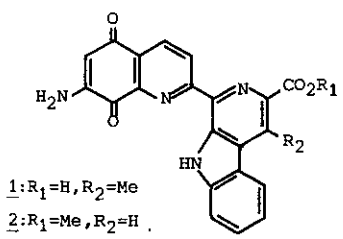
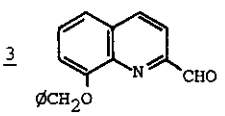
Lavendamycin, a new antitumor antibiotic isolated from Streptomyces lavendulae, strain C22030, was determined by X-ray and ^{13}C-NMR to have structure 1. This structure was similar to that of streptonigrin. We are attempting to develop a total synthesis and syntheses of it's congeners based on the non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



1:R_1=H,R_2=Me
2:R_1=Me,R_2=H



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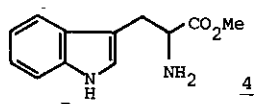

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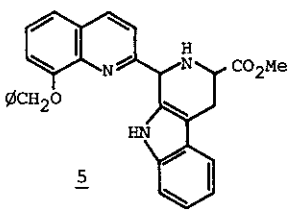

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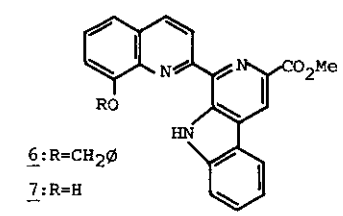
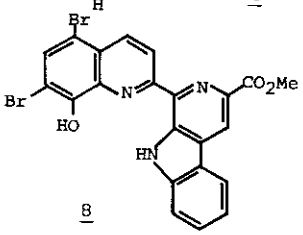


6:R=CH_2Ø
7:R=H



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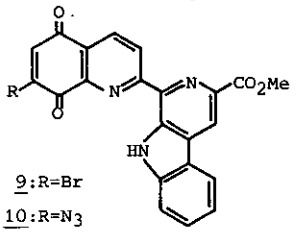

9:R=Br
10:R=N_3