THE SYNTHESIS OF DEHYDROPERLOLINE

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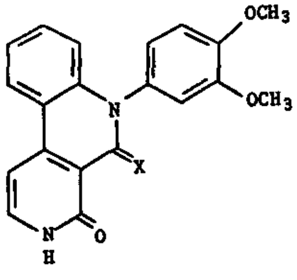
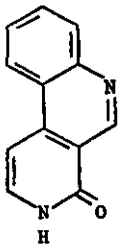
Abstract - Fluorenone and 3-aza-4-oxo-3,4-dihydrofluorenone react with 3,4-dimethoxyphenyllithium to form the corresponding fluorenols, which react with hydrazoic acid to form the phenanthridine. The N-oxides photolyse smoothly to yield dehydroperloline and its analogue as the sole product.

Perloline (1) is the major alkaloid of perennial rye grass (Lolium perenne)[1] and related species and has created some interest because of its implication in "rye grass staggers" in sheep.[2,3] Its structure has been determined by X-ray analysis.[4] Perlolidine (2), a minor alkaloid, has been synthesised by two independent groups,[5,6] but neither perloline, nor its oxidation product, dehydroperloline (3), have been synthesised.



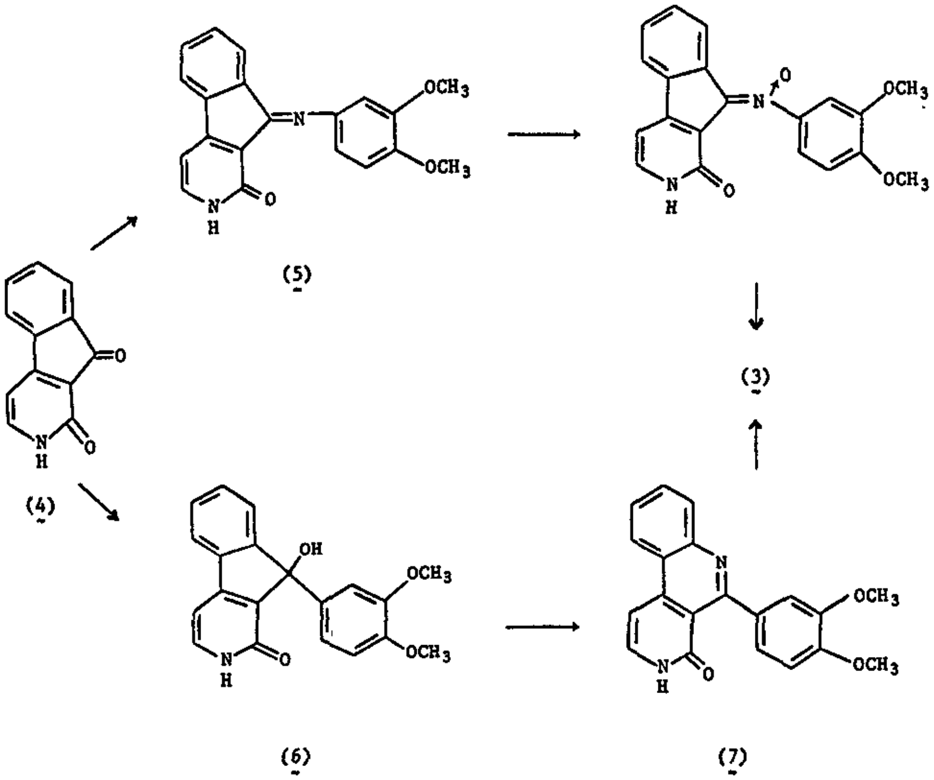
(1, X = H,OH)

(3, X = O)



(2)

Our two independent routes for the synthesis of (3) are shown below.



The two proposed routes were first tested with fluorenone as model. Reaction with 3,4-dimethoxyaniline and zinc chloride (20 min, 150°) gave the anil, m.p. 132-133°, (68%)[7] which was oxidised to the nitrone, m.p. 212° (subl.), with m-chloroperbenzoic acid (72%). The nitrone rearranged to the required lactam, m.p. 204-205°, on photolysis in benzene at 350 nm (92%). Reaction of fluorenone with dimethoxyphenylmagnesium bromide was unpredictable, but the reaction with 3,4-dimethoxyphenyllithium (30 min, -80°) proceeded well (71%). In contrast to 9-phenylfluoren-9-ol, which is reported to give exclusively 6-phenylphenanthridine on reaction with hydrazoic acid in chloroform,[8] the dimethoxyphenyl analogue, m.p. 144-145°, gave mainly the anil under these conditions. Fortunately, hydrazoic acid in polyphosphoric acid gave the required phenanthridine, m.p. 178-179°, (75%), which was converted to the N-oxide and photolysed[9] to give the phenanthridone. The former route was more satisfactory. The fluorenone (4)[10] formed the zinc chloride complex of the anil (5) which could not be satisfactorilly decomposed, and so this pathway was not pursued. The arylfluorenol (6), m.p. 225°, prepared as above (70%) gave the phenanthridine (7), m.p. 281°, with hydrazoic acid in PPA (87%), together with a small amount of the anil (5). The corresponding N-oxide, m.p. 274°, (m-chloroperbenzoic acid, 20°, 15 h) was converted quantitatively to dehydroperloline (3), m.p. 285-7°, on irradiation in ethanol by sunlight for three minutes. In this case, irradiation in chloroform failed to yield (3).[9]

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11. We are grateful to Dr. W.I. Taylor for spectral data that allowed confirmation of the identity of our synthetic material with (3), derived by oxidation of perloline.
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