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STUDIES IN SYNTHETIC PHOTOCHEMISTRY-I
SYNTHESIS OF NAPHTHAPHENANTHRIDINE ALKALOIDS

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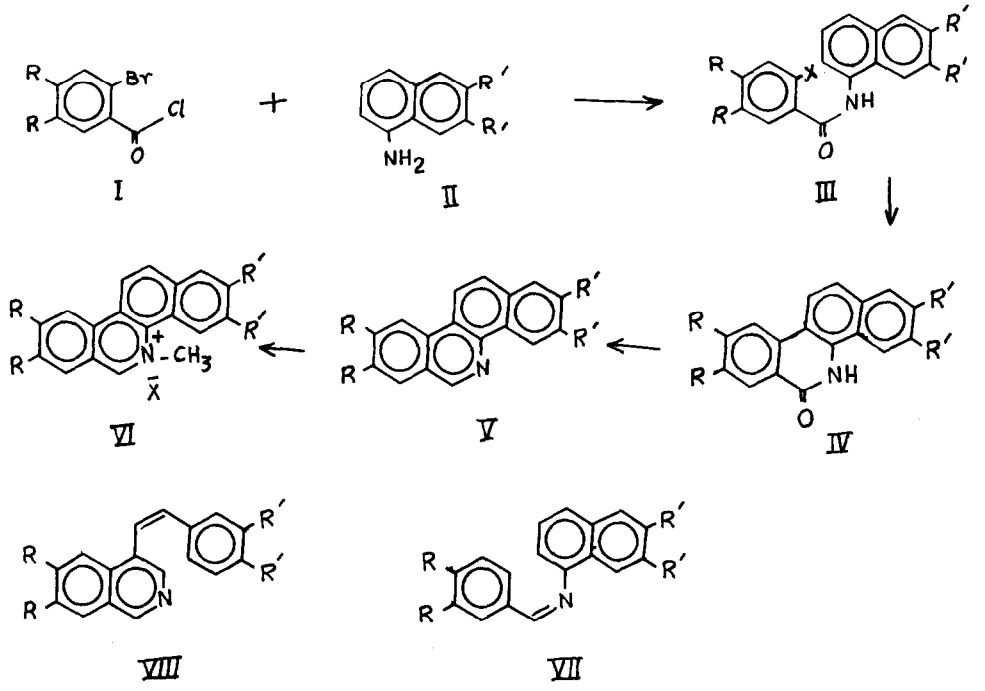
The recent discovery that nitidine and some related compounds exhibit cytotoxic and antileukemic effects has motivated a vigorous search for an efficient route to naphthaphenanthridine alkaloids[1-4]. In this context we report highly effective syntheses of nitidine and avicine through photocyclisation of aromatic amides[5,6].



Irradiation (125 W mercury lamp, 20 hrs, pyrex vessel) of a 0.003M solution of the amide III (R,R = O-CH_2-O, R'= H, X=H, $C_{18}H_{13}NO_3$, m.p. 189-90°)

in benzene : methanol (9:1) containing iodine (0.0005 molar) gave mostly the recovered starting material. However, the bromo-analogue IIIa (R,R = O-CH_2-O, R'=H, X=Br, $C_{18}H_{12}NO_3Br$, m.p. 182-5°) afforded the cyclic amide IVa ($C_{18}H_{11}NO_3$; m.p. above 340°) in 48 % yield on similar irradiation (10 hrs) in absence of iodine. Photocyclisations of the amides IIIb (R=OCH_3, R',R'=O-CH_2-O, $C_{20}H_{16}NO_5Br$ m.p. 246-7°) and IIIc (R,R = R',R' = O-CH_2-O; $C_{19}H_{12}NO_5Br$, m.p. 239-40°), secured from 6,7-methylenedioxy-1-naphthylamine[7] and appropriate bromo-acids, proceeded even more readily (70% yield[8] in 2½ hrs) to give IVb ($C_{20}H_{15}NO_5$; m.p. above 340°) and IVc ($C_{19}H_{11}NO_5$; m.p. above 340°). Reduction of the tetracyclic amides with LAH furnished the benzo(c)phenanthridines Va($C_{18}H_{11}NO_2$; m.p. 225-7°, M^+ at m/e 273), Vb($C_{20}H_{15}NO_4$; m.p. 275-8°) and Vc($C_{19}H_{11}NO_5$, m.p. 325-7°). The latter two bases were found to be identical with the authentic samples[9] and could be converted into nitidine (VIb) and avicine (VIc) salts through the known procedures[10,11,1].

Attempted cyclisation of the Schiff bases of the type VII by irradiation in 98 % sulphuric acid or ethanol was unsatisfactory. Failure to obtain these alkaloids through a stilbene like cyclisation of VIII has been reported earlier[12].

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8. Yields are reported without considering the recovered starting materials and are far superior than those with analogous benzanilides.
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