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SYNTHESIS OF (±)-DYSAZECINE

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Dysazecine (1), a novel dibenzazecine alkaloid from Dysoxylum lenticellare Gillespie, was synthesized by utilizing a photochemical reaction of the bromophenolic compound (5).

KEYWORDS——dysazecine; Dysoxylum lenticellare Gillespie; Meliaceae; dibenzazecine alkaloid; homoerythrina alkaloid; photocyclization reaction

Dysazecine (1) was recently isolated[1)] from the leaves of Dysoxylum lenticellare Gillespie (family Meliaceae) along with the known homoerythrina alkaloids 3-epischelhammericine and 2,7-dihydrohomoerysotrine. This compound (1) is the first naturally occurring alkaloid found with a dibenzazecine skeleton and it strongly supports the idea that 3,12-dihydro-2,13-dimethoxy-5,6,7,8,9,10-hexahydrodibenz[d,f]azecine may proceed to homoerythrina alkaloids by phenol oxidation reaction in the biosynthesis[2)] of homoerythrina alkaloids.

We wish to report here the first synthesis of a dibenzazecine skeleton by utilizing photochemical reaction of the bromophenolic compound (5), and subsequently a synthesis of (±)-dysazecine. The synthesis scheme is shown in Chart 1.

The starting material (4) (mp 135 - 136°C)[3)] was prepared in 70% yield by refluxing 3-(6-bromo-3,4-methylenedioxyphenyl)propionic acid (2)[4)] with 3-benzyloxy-4-methoxyphenethylamine (3) in decalin. Debenzylation[5)] of 4 with boron trifluoride-etherate and ethyl mercaptan in dichloromethane for 4 h under reflux afforded the bromophenolic compound (5) (mp 124 - 125°C; 73% yield). Irradiation[6] of 5 in methanol in the presence of sodium hydroxide with a 100 W high pressure mercury lamp at room temperature for 3 h led to the formation of three products (6, 7, and 8 in 17%, 13%, and 26%, respectively). The compound (8) was reduced with diborane in dry tetrahydrofuran to provide the corresponding amine (9). The ^{1}H-NMR spectrum of 9 showed characteristic four proton singlets attributable to aromatic protons at δ 6.47, 6.54, 6.72 and 6.83, indicating that a photochemical reaction had occurred at the *para*-position to the hydroxyl group in 5.

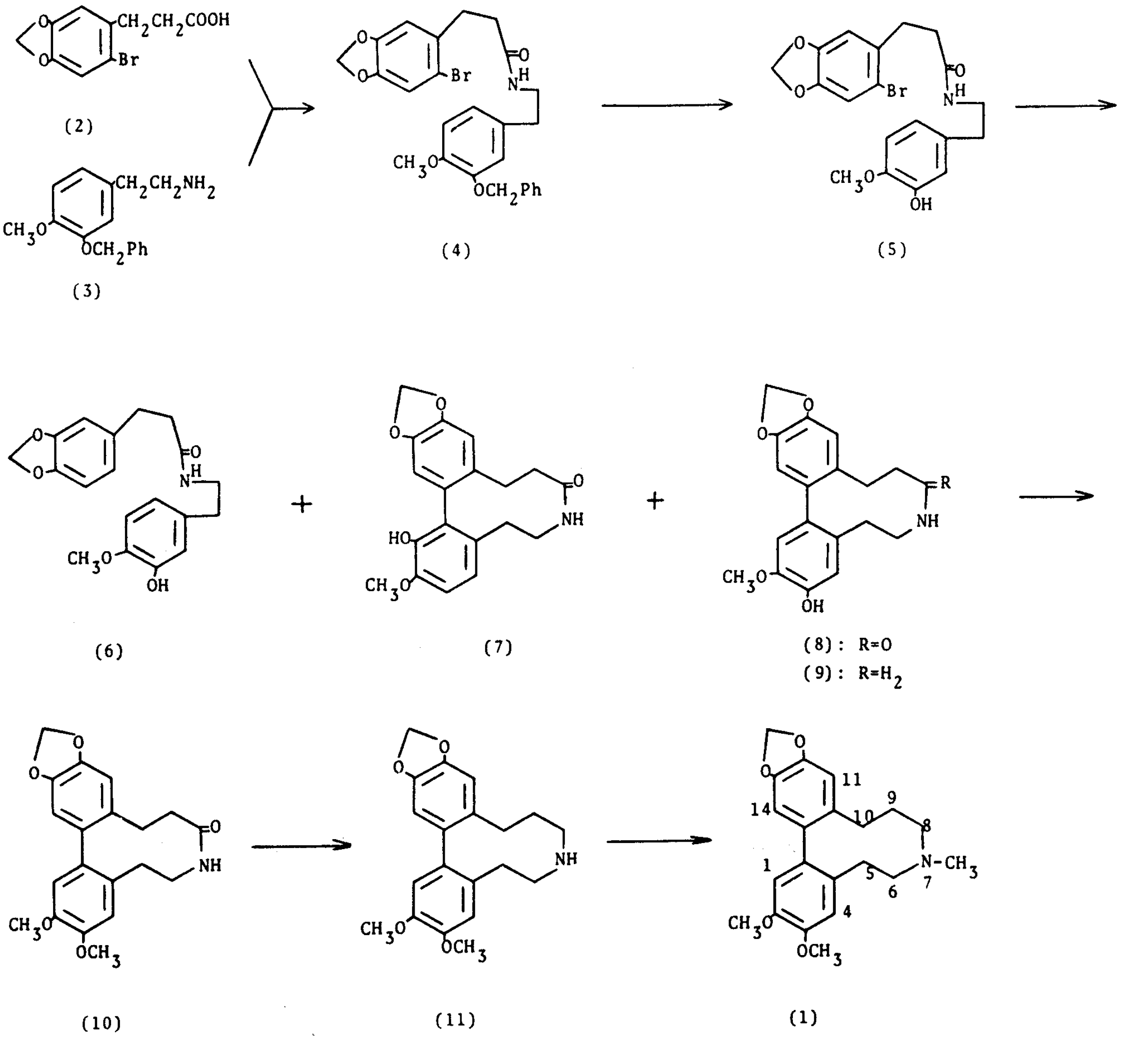

Chart 1

The conversion of 8 to dysazecine (1) was achieved in the usual manner. Namely, 8 was allowed to react with methyl iodide and potassium carbonate in EtOH at 60°C for 5 h to give the O-methyl derivative (10) (mp 182-183°C; 94% yield). Reduction of 10 with sodium borohydride and boron trifluoride-etherate at room temperature in dry tetrahydrofuran afforded the expected amine (11) (colorless oil; 96% yield). N-Methylation of 10 with formaldehyde and sodium borohydride gave (±)-dysazecine (1), which was shown to be completely identical with natural dysazecine (TLC, ^{1}H-NMR, ^{13}C-NMR, and IR).

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