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A NEW APORPHINE SYNTHESIS. PHOTOCYCLIZATION OF A BROMOPHENOXIDE

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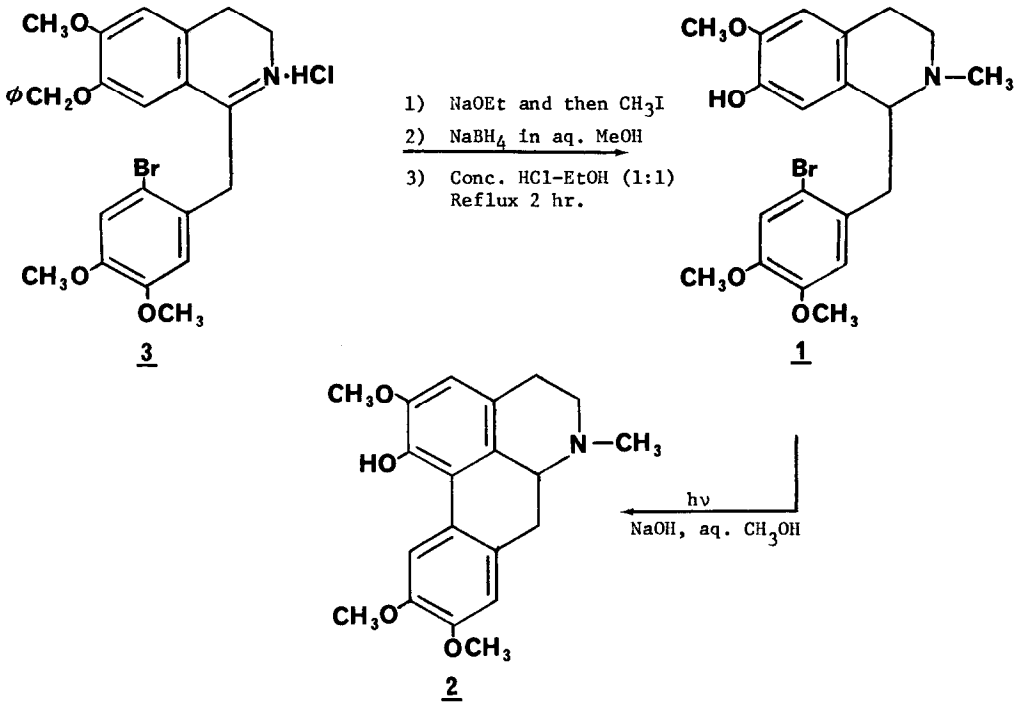
The photolysis of halophenoxides in aqueous alkali solution has been shown to produce dihydroxybiphenyls as major products via an intermolecular coupling process.[1] Intramolecular photocyclization of bromophenoxides has been recently demonstrated[2] and the reaction has been utilized in the synthesis of naturally occuring spiroenones.[3,4] We wish to report that the intramolecular photocyclization of appropriate bromophenoxides provides a convenient synthesis of aporphine alkaloids from readily accessible 1-benzyltetrahydroisoquinoline precursors.



Thus a solution of (±)-bromophenol 1 (178 mg) and NaOH (200 mg) in 90% aqueous methanol (10 ml) was irradiated in a quartz vessel under nitrogen for six hours with a 2537 Å light source. The methanol was then removed by evaporation, the residue was dissolved in 5% aqueous sodium hydroxide and this solution was washed with ether to remove any non-phenolics. The aqueous solution was then made ammoniacal with ammonium chloride and was extracted with chloroform. Drying (K_2CO_3) of the chloroform extract and solvent removal gave 133 mg (92% yield) of crude (±) -1-hydroxy-2, 9, 10-trimethoxyaporphine (2). The nmr spectrum of this crude material was identical with that of an authentic sample of synthetic 2.[5] Preparative tlc on two 1 mm x 8" x 8" neutral alumina (E. Merck, Type E) plates eluted with ether: chloroform: methanol (7:2:1) gave 75 mg of pure 2 (R_f = 0.8) in 52% yield. The mp, R_f, nmr, ir, and mass spectrum of this material were identical with those of an authentic sample of synthetic (±)-1-hydroxy-2, 9, 10-trimethoxyaporphine.[5] The bromophenol 1 was prepared from the known dihydrobenzylisoquinoline 3[6] by N-methylation, reduction, and debenzylation.[7]

The synthesis described here offers several advantages over other known photochemical aporphine syntheses[8] in that the photocyclization (a) does not require a nitrogen protecting group, (b) proceeds directly to an aporphine, (c) proceeds from a readily accessible 1-benzyltetrahydroisoquinoline precursor, and (d) produces aporphine 2 in good yield relative to other aporphine syntheses. Studies in progress with additional 1-(2-bromobenzyl)-7-hydroxytetrahydroisoquinolines indicate that the method described here is of general utility in aporphine synthesis.

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