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PHOTOCHEMICAL ROUTES TO PROAPORPHINES. A NEW SYNTHESIS OF PRONUCIFERINE.

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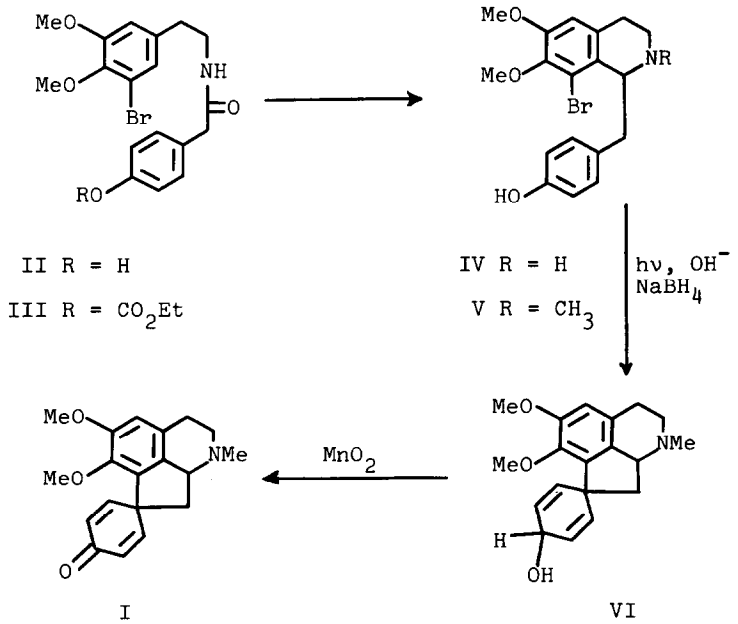
In a previous paper,[1] we described a new synthetic method of spiro-dienone system by photochemical reaction. Now we extend this reaction to the synthesis of pronuciferine (I).[2]

Fusion of 3-bromo-4,5-dimethoxyphenethylamine[3] with methyl p-hydroxyphenylacetate[4] gave the amide (II) which was converted into the ester (III) by condensation with ethyl chloroformate. Bischler-Napieralski reaction of the amide (III) with phosphorous oxychloride and phosphorous pentoxide, followed by reduction with sodium borohydride, gave the tetrahydroisoquinoline (IV). Treat-



ment of the tetrahydroisoquinoline (IV) with 37% formaldehyde solution, followed by reduction with sodium borohydride, gave the N-methyltetrahydroisoquinoline (V) (20% yield from the phenethylamine), M^+ 391, 393, τ ($CDCl_3$) 7.62 (s, 3H, $N\text{-}CH_3$), 6.15 (s, 6H, $2\times OCH_3$), 3.60 (s, 1H, OH), 3.36 (s, 1H, C_5-H), 2.90 and 3.52 (two AB type, J = 9, 4H, p-hydroxyphenyl). Irradiation of the isoquinoline (V) in aqueous sodium hydroxide in the presence of sodium borohydride with a 100 w high-pressure mercury lamp for 2 hr. gave the spiro-diene (VI) which was oxidised with manganese dioxide to dl-pronuciferine (I) (20% yield from V) which was identified by comparison with the natural product.[5]

The present paper shows that the other proaporphine alkaloids could be also synthesised via the above photochemical cyclisation reaction.

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