Tetrahedron Letters No.26, pp. 2937-2940, 1966. Pergamon Press Ltd.
Printed in Great Britain.

A PHOTOCHEMICAL APORPHINE SYNTHESIS

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(Received 12 April 1966)

Aporphine alkaloids have been synthesized previously only by the Pschorr cyclization of 1-(o-aminobenzyl)tetrahydroisoquinolines.[1] We now wish to report a fundamentally new aporphine synthesis in which a structurally simpler aporphine precursor is used, and in which the key synthetic step is a special application of the stilbene-phenanthrene photocyclization.[2] The method is illustrated here by a new synthesis of dl-nuciferine (V).

The reaction of 1-benzyl-6,7-dimethoxy-3,4-dihydroisoquinoline (I)[3] with ethyl chloroformate gave, in 67% yield (calculated on unrecovered starting material), 1-benzylidene-2-carbethoxy-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (II), m.p. 132-134°, λ_{max} 227 mμ (ϵ = 23,000) and 328 (25,000).[4] Compound II was assigned the trans configuration of the aromatic substituents about the double bond, since its NMR spectrum revealed considerable shielding of the methyl of the carbethoxy group (triplet at δ 0.78) by the benzylidene phenyl.

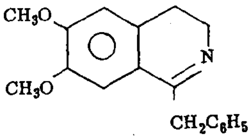
Ultraviolet irradiation of II in ethanol solution in the presence of iodine (0.6 equivalents) gave, in 15% yield, N-carbethoxy-6a,7-dehydronornuciferine (III), m.p. 128-130°, λ_{max} 256 mμ (ϵ = 39,000), 263 (44,000), 311 (11,500), 323 (11,500), 356 (1,800), and 375 (1,900). The NMR spectrum of III, which was fully consistent with the assigned structure, showed as points of special interest a normal carbethoxy methyl (triplet at δ 1.31) and the expected low field proton at C-11 (δ 9.58) of the aporphine system.

Lithium aluminum hydride reduction of III in ether solution afforded, in 70% yield, 6a,7-dehydronuciferine (IV), m.p. 126-130°, λ_{max} 253 mμ (ε 93,000), 264 (96,000), 293 (18,000), and 327 (31,000). The NMR of IV showed, as features of major significance, the low field C-11 proton at δ 9.48, and a 3-proton singlet at δ 3.02 attributable to the N-methyl group. Compound IV was identical (IR, UV, m.p. and R_f) with material obtained by the oxidation of synthetic nuciferine[5] with potassium permanganate in acetone.[6]

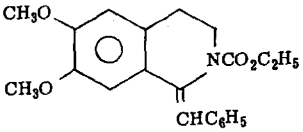
Catalytic reduction (PtO_2 catalyst) of IV in acetic acid solution afforded, in 70% yield, dl-nuciferine (V), identical in all respects (IR, UV, m.p. and R_f) with authentic nuciferine.[5]

Work is in progress to extend this new aporphine synthesis to more complex examples, and to improve the overall yield of the process.[7]

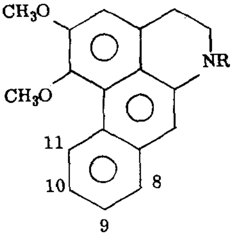
Acknowledgement. We thank the National Science Foundation for grant GP-4931 and a Predoctoral Fellowship (to S. C. H.) in partial support of this work.



I

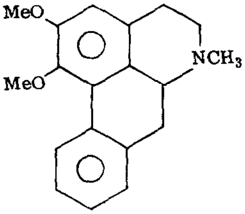


II



III, R = $CO_2C_2H_5$

IV, R = CH_3



V

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7. For an independent report of the results similar to ours, see the accompanying communication of N. C. Yang, et al.