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A METHOD OF SYNTHESIZING 8-OXOPROTOBERBERINE DERIVATIVES INVOLVING A NOVEL PHOTOARYLATION OF 3-CHLORO-1-ISOQUINOLONES

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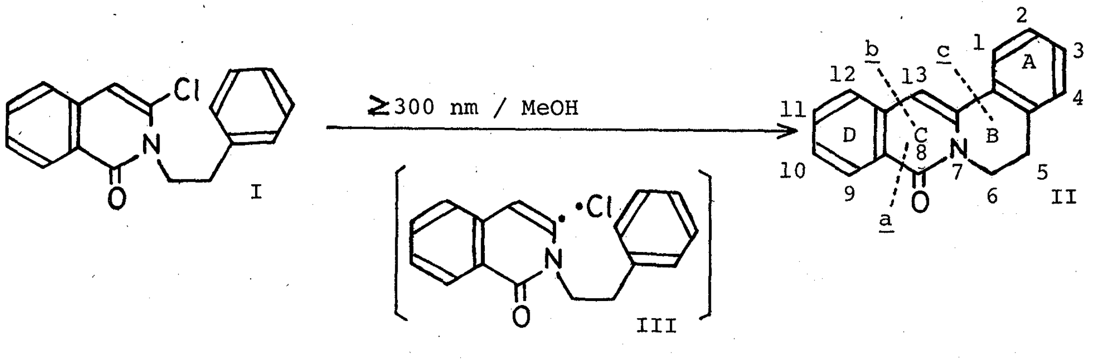
The novel photochemical annulation of isoquinoline derivatives to form the 8-oxoprotoberberine derivatives is described. The key step of the reaction is an intramolecular photochemical arylation of 3-chloro-2-phenethyl-1-isoquinolone. The same arylation also proceeds intermolecularly, when 3-chloro-1-isoquinolones are irradiated in benzene.

KEYWORDS——photochemical synthesis; photochemical arylation; 5,6-dihydro-8-oxo-8H-dibenzo[a,g]quinolizine; 3-chloro-2-phenethyl-1-isoquinolone; 3-phenyl-1-isoquinolones

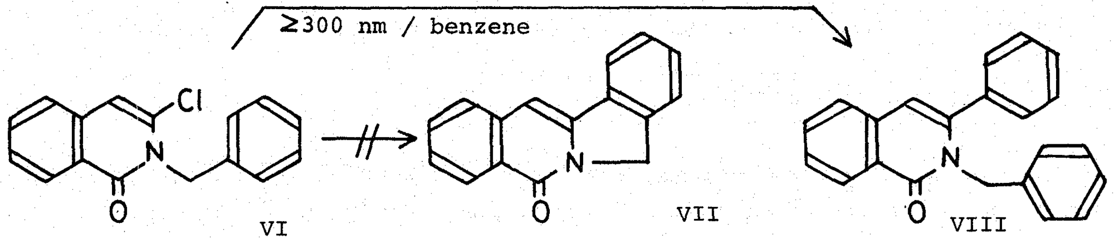
The 5,6-dihydro-8-oxo-8H-dibenzo[a,g]quinolizine skeleton (II) is the fundamental structural unit of protoberberine alkaloids.[1] So far, two photochemical synthetic routes to II from suitably functionalized 1,2-disubstituted isoquinolines involving the construction of ring C as a key step have been reported. In the first route, the key step is the intramolecular photoarylation of carbamates to form bond a.[2] In the second route, the key step is the photocyclization of unsaturated enamides to form bond b.[3,4] Here, we report another new route for II based on the photochemical formation of bond c, thus constructing ring B.



Irradiation[5] of a 0.003 M methanolic solution of 3-chloro-2-phenethyl-1-isoquinolone[6,7] (I) at room temperature afforded the 8-oxoprotoberberine (II) in 56% yield. The melting point (mp 90-91°C) and spectral data [ν_{max} cm^{-1}: 1643, 1620, 1595, and 762; λ_{max} nm (log ε): 211 (4.61), 233 (4.41), 321.5 (4.28), 343 (4.18), and 358.5 (4.00); δ: 2.96 (t, J=6.2 Hz, 2H), 4.32 (t, J=6.2 Hz, 2H), 6.89 (s, 1H), 7.05-7.85 (m, 7H), and 8.32 (bd, J=7.2 Hz, 1H)] were identical with those reported by Yang *et al.*[2]

The 8-oxoprotoberberine (II) may be derived from an intramolecular photoarylation of I through bond c formation, *via* a solvent-caged biradical (III) formed by homolytic fission of the C-Cl bond. In support of this idea, irradiation of 3-chloro-2-methyl-1-isoquinolone$^{6)}$ (IV) in benzene resulted in the formation of 2-methyl-3-phenyl-1-isoquinolone (V: mp 54.5-55°C) in 79% yield, though a much longer irradiation period was necessary for the reaction than for that of I. The structure of V was supported by spectral data [ν_{max} cm^{-1}: 1647, 1620, 1595, and 770; λ_{max} nm (log ε): 207.5 (4.64), 226 (4.38), 292 (4.12), 329 (3.87); δ: 3.36 (s, 1H), 6.35 (s, 1H), 7.2-7.6 (m, 8H), and 8.2-8.45 (m, 1H)] and finally identified by comparison with an authentic sample prepared from 3-phenyl-1-isoquinolone.$^{8)}$ Though photochemical arylation using aryl iodides is common,$^{9)}$ the similar reaction using aryl chlorides is rare.$^{10)}$ This fact indicates an inherent photochemical instability of the C-Cl bond in the 3-chloro-1-isoquinolone system.

An efficiency of the intramolecular arylation over the intermolecular one in I is clearly demonstrated by an exclusive formation of II when I was irradiated in benzene. On the contrary, 2-benzyl-3-chloro-1-isoquinolone (VI) did not afford the cyclization product (VII) in any condition, but gave the 3-phenyl derivative [VIII: mp 103.5-105.5°C; δ: 5.18 (s, 2H), 6.34 (s, 1H), 6.7-7.7 (m, 13H), 8.40 (bd, J=8 Hz, 1H)] by irradiation in benzene. The difference between I and VI implies that some geometrical requirement is needed to accomplish such arylation between the attacking benzene ring and accepting carbon radical in the solvent-caged biradical, which otherwise reverts to the original 3-chloro-1-isoquinolones. The scope and mechanism of these reactions as well as their application to the synthesis of berberine alkaloids are being investigated.



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