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A NEW PREPARATION OF AN OCHOTENSIN-TYPE ISOQUINOLINE BY PHOTOLYSIS

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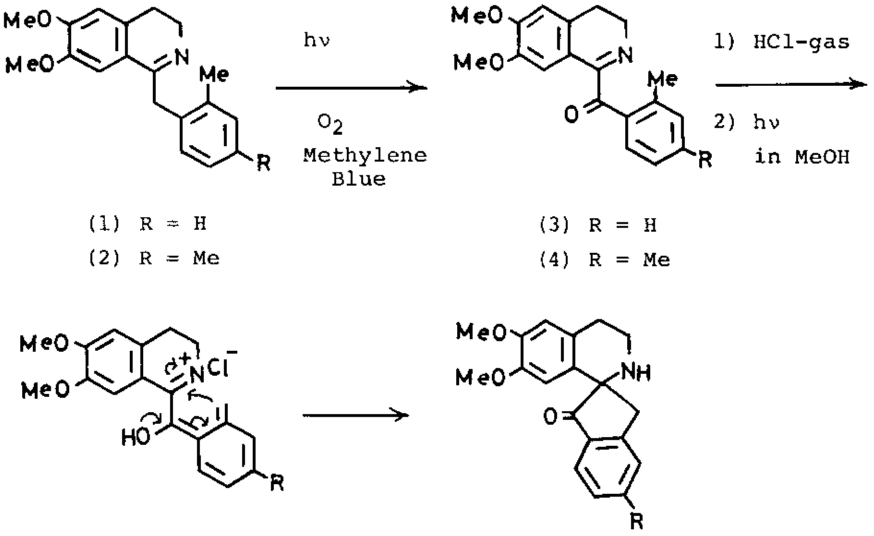
Abstract —— The photolysis of 1-benzoyl-3,4-dihydroisoquinoline hydrochlorides (3) and (4) gave spirobenzylisoquinolines (5) and (6).

It has been demonstrated that photolytic rearrangement[1] of 13-ketotetrahydroprotoberberine metho salts and thermal base catalyzed rearrangements[2] of 13-methyldihydroprotoberberine metho salts gave spirobenzylisoquinolines via an o-quinodimethide intermediate. Also, kametani and co-workers[3] have reported the synthesis of spirobenzylisoquinoline via an o-quinodimethane intermediate by thermal rearrangement of a benzocyclobutenyl precursor. These reports prompted us to investigate the photochemistry of an o-toluyl-keto-imine[4]. We thought that the photoenolization of the o-toluyl-keto-iminium salt (3) might produce the o-quinodimethane. Intramolecular nucleophilic addition of the methylene group to the iminium double bond would then yield the spiroketone (5)[1]. Kessar and co-workers have already reported the preparation of the protoberberine compound by the photolyticenolization of an o-toluyl-keto-imine.[5] However, they have not isolated the spirobenzylisoquinoline compound. In this paper we describe a photolytic preparation of spirobenzylisoquinoline compounds which are structurally related to the alkaloid ochotensine[6], starting from the 1-benzoyl-3,4-dihydroisoquinoline compounds.

Irradiation of the 1-benzyl-3,4-dihydroisoquinolines (1)[7] and (2)[8] in chloroform containing methylene blue (ca. 10^{-4} M) as a sensitizer under an oxygen atmosphere with a 40 watt tungsten filament lamp gave the 1-benzoyl-3,4-dihydroisoquinoline (3) and (4) in 60% isolated yield, respectively.[10] 3,4-Dihydro-6,7-dimethoxy-1-(2'-methylbenzoyl)isoquinoline (3): IR(nujol)cm^{-1} 1600 and 1670; ^1H NMR(60MHz, ppm, $CDCl_3$) 2.63(3H, s, CH_3), 2.77(2H, t, J=8Hz, C_4-H_2), 3.87(3H, s, OCH_3), 3.98(3H, s, OCH_3), 3.70-4.30(2H, m, C_4-H_2), 6.75(1H, s, C_5-H), 7.10(1H, s, C_8-H), 7.20-7.75 (4H, m, Ar-H); Mass($^m/_e$) 309(M^+); 3,4-Dihydro-6,7-dimethoxy-1-(2',4'-dimethylbenzoyl)isoquinoline (4): IR(nujol)cm^{-1} 1660; ^1H NMR(60MHz, ppm, $CDCl_3$) 2.34 (3H, s, C_4'-CH_3), 2.56(3H, s, C_2'-CH_3), 2.77(2H, t, J=8Hz, C_4-H_2), 3.82(3H, s, OCH_3), 3.88(2H, t, J=8Hz, C_3-H_2), 3.96(3H, s, OCH_3), 6.76(1H, s, C_5-H), 7.04 (1H, s, C_8-H), 7.06(1H, d, J=8Hz, C_5'-H), 7.11(1H, s, C_3'-H), 7.56(1H, d, J=8Hz, C_6'-H); Mass($^m/_e$) 323(M^+).[11] Next, the photochemistry of the 1-benzoyl-3,4-dihydroisoquinolines (3) and (4) was examined. The photolysis of the hydrochlorides (3) and (4) in methanol with a 200 watt high pressure mercury lamp 25hr gave the spirobenzylisoquinolines (5) and (6) in 11% and 16.3% isolated yield, respectively.[12] The n.m.r. spectra of (5) and (6) show the double doublet pattern at δ 3.48 and 3.45, respectively, which is typical for spirobenzylisoquinolines. 1', 2,2'3,3',4'-Hexadehydro-6',7'-dimethoxyspiro(inden-2,1'-isoquinolin)-1-one (5): IR(nujol)cm^{-1} 1600 and 1700; ^1H NMR(200MHz, ppm, $CDCl_3$) 2.50-3.20(4H, m, C_3' and C_4'-H_2), 3.48(2H, dd, J=18Hz and 22Hz, C_3-H_2), 3.58(3H, s, OCH_3), 6.10(1H, s, C_8'-H), 6.62(1H, s, C_5'-H), 7.40-7.90(4H, m, ArH); Mass($^m/_e$) 309(M^+); UV(MeOH)nm 235 and 285; 1',2,2',3,3'4'-Hexadehydro-6',7'-dimethoxy-5-methylspiro(inden-2,1'-isoquinolin)-1-one (6): IR(nujol)cm^{-1} 1600 and 1700; ^1H NMR(200MHz, ppm, $CDCl_3$) 2.48(3H, s, CH_3) 2.68-3.20(4H, m, C_3' and C_4'-H_2), 3.45(2H, dd, J=22Hz and 18Hz, C_3-H_2), 3.60(3H, s, OCH_3), 3.86(3H, s, OCH_3) 6.14(1H, s, C_8'-H), 6.64(1H, s, C_5'-H), 7.24-7.36(2H, m, ArH), 7.78(1H, d, J=8Hz, C_7-H); Mass($^m/_e$) 323(M^+); UV(MeOH)nm 254 and 285.[11]

The structures of (5) and (6) were established by comparison with the spectral data of analogous spirobenzylisoquinoline compounds[1,13]. To our knowledge, this is the first synthesis of spirobenzylisoquinoline from keto-imine-compounds.[14] The applications of this novel method to the synthesis of ochotensine-type alkaloids and the photolysis of indole compounds containing the o-tolulyl-imine system are now in progress.



(1) R = H
(2) R = Me

(3) R = H
(4) R = Me

(5) R = H
(6) R = Me

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11. Satisfactory elemental analyses were obtained on new compounds.

12. Starting materials (3) and (4) were recovered in 67% and 52% yield, respectively.

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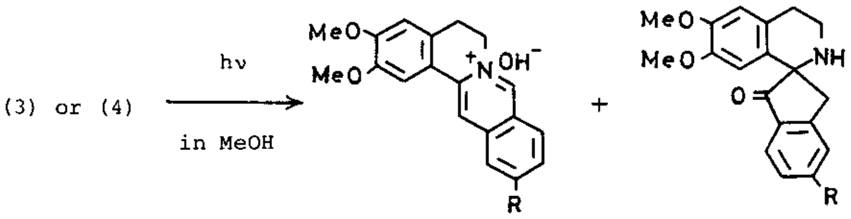
14. The photolysis of free base (3) and (4) in methanol with 200 watt high pressure lamp for 24hr gave the berberinium hydroxides[5] (7) and (8) in 14.3% and 22% yield with (5) (6%) and (6) (15.6%), respectively. Starting materials (3) and (4) were recovered in 44% and 39% yield, respectively.



(7) R = H
(8) R = Me

(5) R = H
(6) R = Me

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