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A Photolysis of N-[3-(2-Hydroxy-3-methoxyphenyl)propyl]-6-bromobenzamides. One-step Synthesis of 5,6-Dihydro-4H,8H-pyrido[3,2,1-de]phenanthridin-8-ones

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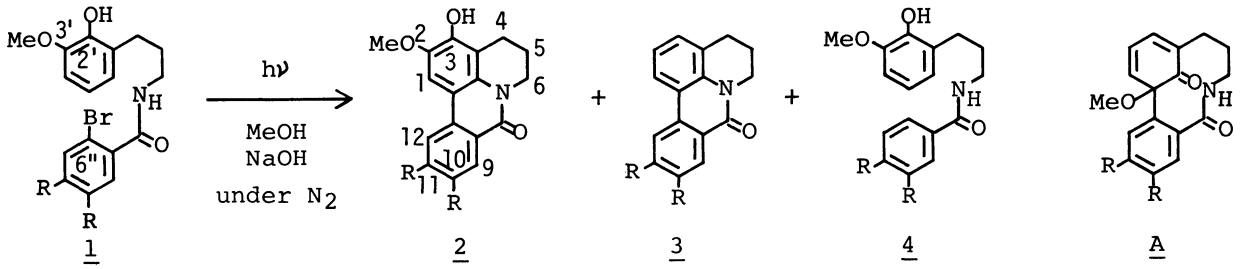
A photolysis of phenolic bromoarylalkanamides in methanol containing sodium hydroxide gave two kinds of 5,6-dihydro-4H,8H-pyrido[3,2,1-de]phenanthridin-8-ones accompanied with debrominated amides.

In connection of our studies[1] exploring the utility of photochemical reaction for synthesis of biologically active heterocyclic compounds, we found that N-[3-(2-hydroxy-3-methoxyphenyl)propyl]-6-bromobenzamides (1) gave pyrido[3,2,1-de]phenanthridin-8-ones (2 and 3) in moderate yields. The present paper describes a novel synthesis of the title compounds.

In a typical example, an ice-cooled, stirred 0.22% methanolic solution (90 ml) of 1a[2] (mp 119-120 °C) in the presence of sodium hydroxide (40 equiv.) was irradiated with 200 W high pressure mercury lamp[3] using a quarz filter under nitrogen stream for 2 h. Usual work-up followed by separation of the reaction mixture on preparative thin layer chromatography (TLC) (Kieselgel $60F_{254}$, Merck ; developing solvent ; $CHCl_3$: MeOH : AcOEt = 50 : 1 : 2) gave 2a[2,4] (22.6%) and 3a[4,5] (6.4%), together with a debrominated amide (4a)[2] (21.1%) (mp 124-125 °C).

Structures of 2a and 3a were determined to be 5,6-dihydro-3-hydroxy-2,10,11-trimethoxy- and 5,6-dihydro-10,11-dimethoxy-4H,8H-pyrido[3,2,1-de]phenanthridin-8-ones on the basis of the ^{1}H-NMR spectral and elemental analyses or high-resolution mass spectrum. Formation of the latter (3a) would be explicable by addition-elimination of an intermediate A formed by a photochemical coupling[1a] of 3'- and 6"-positions in 1a.



1 2 3 4 A

a : R=OMe, b : R+R=OCH_2O, c : R=H

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Similarly, photolysis of 1b[2,6](mp 131-133 °C) or 1c[2,7](mp 106-108 °C) gave 2b[2,4](9.6%), 3b[4,5](7.4%), and 4b(32.9% : mp 113-115 °C) or 2c[2,4](21.3%) and 3c[2,4] (3.0%), respectively. In the case of 1c, however, no debrominated amide (4c) was obtained.

Although pyrido[3,2,1-de]phenanthridin-8-ones are synthesized by Pschorr reaction[8] or photolysis[5] of N-(amino- or bromoaroyl)-1,2,3,4-tetrahydroquinolines, there is no precedent for their one-step formation. Therefore, the present reaction seems to serve as a novel method for synthesis of pyrido[3,2,1-de]phenanthridin-8-one derivatives.

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References

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2) All new compounds described in this paper gave satisfactory elemental and mass spectral analyses.

3) Ishii Shoten UV-HT lamp was used.

4) 2a : mp 225-227 °C(AcOEt). ^{1}H-NMR($CDCl_3$)δ: 1.94-2.24(2H, m, 5-H_2), 2.95(2H, t, J=6.3 Hz, 4-H_2), 4.02, 4.04, 4.09(9H, each s, 3xOCH_3), 4.20-4.28(2H, m, 6-H_2), 7.34, 7.35(2H, each s, 2xArH), 7.89(1H, s, 9-H). 3a : mp 226-228 °C(AcOEt)(lit.[5] mp 241-243 °C). ^{1}H-NMR($CDCl_3$)δ: 2.00-2.32(2H, m, 5-H_2), 3.02(2H, t, J=6 Hz, 4-H_2), 4.04, 4.09(6H, each s, 2xOCH_3), 4.22-4.40(2H, m, 6-H_2), 7.08-7.28(2H, m, 2-, 3-H), 7.58, 7.92(2H, each s, 12-, 9-H), 7.90-8.05(1H, m, 1-H). 2b : mp 233-236 °C (dec.)(AcOEt). ^{1}H-NMR($CDCl_3$)δ: 1.92-2.24(2H, m, 5-H_2), 2.94(2H, t, J=5.7 Hz, 4-H_2), 4.01(3H, s, OCH_3), 4.18-4.36(2H, m, 6-H_2), 6.08(2H, s, OCH_2O), 7.30, 7.41 (2H, each s, 2xArH), 7.85(1H, s, 9-H). 3b : mp 172-173 °C(AcOEt)(lit.[5] mp 178-180 °C). ^{1}H-NMR($CDCl_3$)δ: 1.96-2.28(2H, m, 5-H_2), 3.00(2H, t, J=6 Hz, 4-H_2), 4.18-4.40(2H, m, 6-H_2), 6.10(2H, s, OCH_2O), 7.06-7.27(2H, m, 2-, 3-H), 7.59, 7.88(2H, each s, 12-, 9-H), 7.82-7.98(1H, m, 1-H). 2c : mp 213-215 °C(dec.)(AcOEt). ^{1}H-NMR ($CDCl_3$)δ: 1.92-2.24(2H, m, 5-H_2), 2.98(2H, t, J=6 Hz, 4-H_2), 4.03(3H, s, OCH_3), 4.16-4.28(2H, m, 6-H_2), 7.38-7.78(2H, m, 10-, 11-H), 7.52(1H, s, 1-H), 8.07, 8.50(2H, dd, J=8.6, 1.4 Hz, 12-, 9-H). 3c : mp 180-182 °C(AcOEt). ^{1}H-NMR($CDCl_3$)δ: 1.98-2.30(2H, m, 5-H_2), 3.02(2H, t, J=6 Hz, 4-H_2), 4.31(2H, m, 6-H_2), 7.08-7.36 (2H, m, 2-, 10-H), 7.40-7.84(2H, m, 3-, 11-H), 8.02-8.32(2H, m, 1-, 12-H), 8.51 (1H, dd, J=8.6, 1.7 Hz, 9-H).

5) R. K.-Y. Zee-Cheng, S.-J. Yan, and C. C. Cheng, J. Med. Chem., 21, 199(1978).

6) Development on preparative TLC($CHCl_3$:MeOH:AcOEt=100:1:2) was performed twice.

7) 0.19% MeOH solution(210 ml) was used. Separation was done by SiO_2 column chromatography($CHCl_3$:hexane=5:1) and preparative TLC($CHCl_3$:MeOH:AcOEt=100:1:3).

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