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ONE-POT REGIOSELECTIVE SYNTHESIS OF NAPHTHO[2,1-g]QUINOLINE-7,12-DIONE DERIVATIVES

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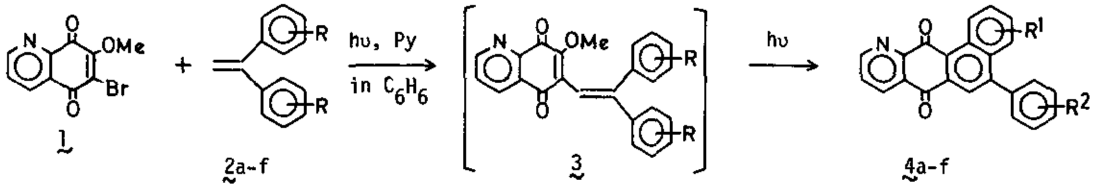
Abstract —— Substituted naphtho[2,1-g]quinoline-7,12-diones were synthesized regioselectively by one-pot photochemical reaction of 6-bromo-7-methoxy-5,8-quinolinedione with 1,1-diarylethylene.

Polycyclic aromatic compounds containing hetero-atom as well as their quinone derivatives are recently of much attention because of their expected biochemical and physicochemical properties.[1] However, quinone derivatives of naphthoquinoline containing a nitrogen atom in the D-ring of benz[a]anthracene skeleton have never been investigated so far. In the previous report, synthesis of naphtho[1,2-g]quinoline-7,12-dione derivatives, starting from 7-bromo-6-methoxy-5,8-quinolinedione and 1,1-diarylethylene was described.[2] Extending further this methodology, here we wish to report a photochemically induced facile regioselective synthesis of naphtho[2,1-g]quinoline-7,12-diones from 6-bromo-7-methoxy-5,8-quinolinedione and 1,1-diarylethylene. 6-Bromo-7-methoxy-5,8-quinolinedione (1) as starting quinone was prepared by bromination[3] of 7-methoxy-5,8-quinolinedione[4].

Typically a benzene solution (400 ml) of 6-bromo-7-methoxy-5,8-quinolinedione 1 (1 mmol) and 1,1-diphenylethylene 2a (2 mmol) was irradiated with a high pressure Hg arc lamp (300 W) in the presence of pyridine (1 mmol) at room temper-



Scheme I

ature for 0.7 h. Purification of the reaction mixture by column chromatography on silica gel[5] followed by recrystallization gave exclusively 5-phenylnaphtho[2,1-g]quinoline-7,12-dione (4a) as yellow needles. Another possible regio-isomer, 5-phenylnaphtho[1,2-g]quinoline-7,12-dione (5), was not detected in the reaction mixture. Similarly, other 1,1-diarylethylene (2b-f) gave successfully the corresponding naphtho[2,1-g]quinoline-7,12-dione derivatives (4b-f) in a regioselective manner in the photochemical reaction with 6-bromo-7-methoxy-5,8-quinolinedione (1) (see Scheme I and Table 1). The spectral data of 4 (Table 2) are all compatible with 5-arylnaphtho[2,1-g]quinoline-7,12-dione derivatives. The structure of 4a, especially the location of nitrogen atom was further confirmed by comparing their ^{1}H-NMR chemical shift changes of the ring protons induced by addition of Eu(fod)$_3$ (Fig. 1). If 4a has a structure of naphtho[2,1-g]quinoline-7,12-dione derivatives, the coordination of europium ion (as depicted

Table 1. Yields and Physical Properties of Naphtho[2,1-g]quinoline-7,12-diones

Starting Materials		Irradiation	Products			
Quinone	Ethylene	Time (h)		Yields %		mp(°C)
1	2a; R=H	0.7	4a; $R^1=R^2=H$	13	yellow needles	241-242
1	2b; p-OMe	5	4b; R^1=2-OMe, R^2=p-OMe	22	orange crystals	268-269
1	2c; m-OMe	4	4c; 3-OMe, m-OMe	10	brown needles	220-221
1	2d; o-OMe	2	4d; 4-OMe, o-OMe	7	red crystals	231-232
1	2e; p-Me	1	4e; 2-Me, p-Me	17	yellow needles	>300
1	2f; m-Me	1	4f; 3-Me, m-Me	10	yellow needles	276-277

Table 2. Spectral Data of Naphtho[2,1-g]quinoline-7,12-diones

	4a	4b	4c
NMR($CDCl_3$); δ ppm	9.76(1H,d,J=8Hz) 9.08(1H,dd,J=5,1.5Hz) 8.54(1H,dd,J=7.5,1.5Hz) 8.28(1H,s) 7.98(1H,dd,J=8,1.5Hz) 7.4-7.9(3H,m) 7.50(5H,s)	9.32(1H,d,J=2.5Hz) 9.02(1H,dd,J=4.5,2Hz) 8.48(1H,dd,J=8,2Hz) 8.08(1H,s) 7.87(1H,d,J=9.5Hz) 7.63(1H,dd,J=8,4.5Hz) 7.40(2H,d,J=8.5Hz) 7.05(2H,d,J=8.5Hz) 7.1-7.3(1H,m) 4.03(3H,s) 3.89(3H,s)	9.56(1H,d,J=9Hz) 8.96(1H,dd,J=4.5, 2Hz) 8.40(1H,dd,J=7.5, 2Hz) 8.12(1H,s) 6.8-7.6(7H,m) 3.83(3H,s) 3.73(3H,s)
IR(KBr); cm^{-1}	1670(C=0)	1670(C=0)	1665(C=0)
UV max($CHCl_3$); nm (logε)	245 (4.15) 310 (4.16) 372 (3.12) 426 (3.32)	248 (4.71) 324 (4.43) 390 (3.80) 477 (3.89)	243 (4.61) 322 (4.59) 400 (3.81) 440 (3.65)
Mass(m/e);	335 (M^+)	395 (M^+)	395 (M^+)

in Scheme II) would result in the much larger shift of H^1 than that of H^6. On the contrary, if 4a is assumed to be another possible isomer (5); 5-phenylnaphtho[1,2-g]quinoline-7,12-dione, the chemical shift change of H^6 is expected to be much larger than that of H^1. Actually, the S value of proton-H^1 induced by addition of $Eu(fod)_3$ is larger than that of proton-H^6 as illustrated in Fig. 1. Consequently, 4a was unequivocally assigned to 5-phenylnaphtho[2,1-g]quinoline-7,12-dione.

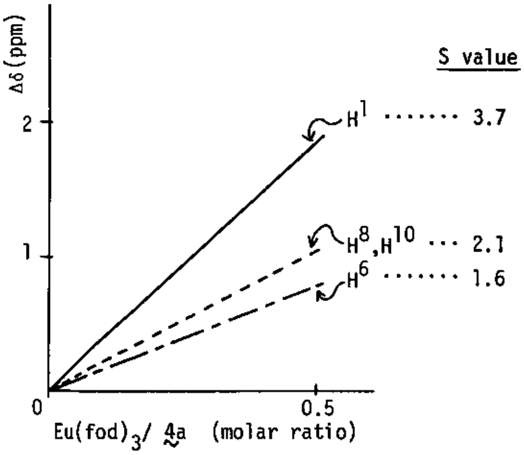


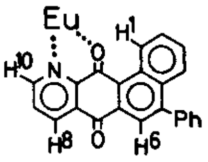
Fig. 1

Although the intermediate 3 was not isolated in this work,[6] the regioselective condensation[7] to naphtho[2,1-g]quinoline-7,12-dione 4 would be understood in terms of the two-step reaction mechanism as shown in Scheme I.

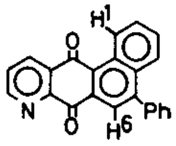
Thus, the photochemical reaction of 6-bromo-7-methoxy-5,8-quinolinedione 1 with 1,1-diarylethylene 2 provides us a facile regioselective one-pot synthetic route to naphtho[2,1-g]quinoline-7,12-dione derivatives 4 as a new member of quinonoid compounds containing nitrogen atom.

Table 2. (Continued)

4d	4e	4f
9.29(1H,dd,J=8.5,1Hz) 9.03(1H,dd,J=4.5,2Hz) 8.48(1H,dd,J=8,2Hz) 8.07(1H,s) 6.8-7.8(7H,m) 3.61(3H,s) 3.46(3H,s)	9.51(1H,s) 9.06(1H,dd,J=4.5,1.5Hz) 8.53(1H,dd,J=7.5,1.5Hz) 8.19(1H,s) 7.88(1H,d,J=9Hz) 7.67(1H,dd,J=7.5,4.5Hz) 7.1-7.6(5H,m) 2.64(3H,s) 2.50(3H,s)	9.58(1H,d,J=8.5Hz) 9.00(1H,dd,J=4,1.5Hz) 8.48(1H,dd,J=7.5,1.5Hz) 8.18(1H,s) 7.2-7.8(7H,m) 2.48(6H,s)
1670(C=O)	1660(C=O)	1665(C=O)
245 (4.45) 271 (4.24) 324 (4.32) 360 (3.57) 479 (3.44)	243 (4.44) 253 (4.39) 316 (4.41) 374 (3.45) 444 (3.62)	244 (4.42) 252 (4.38) 315 (4.51) 384 (3.62) 427 (3.62)
395 (M^+)	363 (M^+)	363 (M^+)



Scheme II



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REFERENCES AND NOTES

1)K.Dietz, H.J.Keller, D.Nöthe, and D.Wehe, *J.Am.Chem.Soc.*,**104**,7581(1982).
J.Koutecky and R.Zahradnik, *Coll.Czech.Chem.Comm.*,**28**,2089(1963).
M.Das and R.Bhattacharya, *J.Chim.Phys.*, **57**.947(1960).
M.J.Shear and J.Leiter, *J.Natl.Cancer Inst.*,**2**,241(1941).

2)K.Maruyama, S.Tai, and T.Otsuki, *Chem.Lett.*,1565(1981).

3)Treatment of 7-methoxy-5,8-quinolinedione[4] with molecular bromine and sodium acetate in acetic acid gave 6-bromo-7-methoxy-5,8-quinolinedione (**1**) as yellow crystals, mp; 157-158°C(dec), yield 67%, Mass; m/e=266(M^+),268(M^+), IR(KBr): 1680, 1660, 1250cm^{-1}, NMR($CDCl_3$); δ 9.00ppm (1H,dd,J=4.5,1.5Hz), 8.44(1H,dd,J=8,1.5Hz), 7.66(1H,dd,J=8,4.5Hz), 4.37(3H,s), UV max($CHCl_3$); 260nm (logε=3.97), 277 (3.87), 383 (2.98).

4)Y.T.Pratt and N.L.Drake, *J.Am.Chem.Soc.*,**79**,5024(1957).

5)Thick slurry matters produced in this photochemical reaction can be removed by this operation.

6)The intermediate **3**, though not isolated in this work, was detected at the earlier stage of the reaction by TLC analysis of the reacting mixture. Isolation of the intermediate such as **3** was described elsewhere (see ref. 7b). Upon further irradiation the intermediate **3** is found to cyclize to give quantitatively the corresponding naphtho[2,1-g]quinoline-7,12-dione derivatives.

7)a)K.Maruyama, T.Otsuki, and K.Mitsui, *J.Org.Chem.*,**45**,1424(1980).
b)K.Maruyama, M.Tojo, H.Iwamoto, and T.Otsuki, *Chem.Lett.*,827(1980).

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