Photoinduced Cyclization of 2-Acetonyl-3-alkoxy-1,4-naphthoquinones: Formation of 2-Alkyl-Substituted 4-Methyl-naphtho[2,3-*d*]-1,3-dioxepin-6,11-diones

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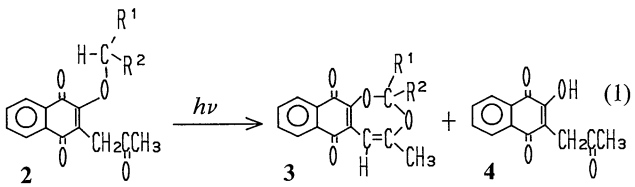
Synopsis. Irradiation of 2-acetonyl-3-alkoxy-1,4-naphthoquinones in benzene gave 2-alkyl-substituted 4-methyl-naphtho[2,3-*d*]-1,3-dioxepin-6,11-dione and 2-acetonyl-3-hydroxy-1,4-naphthoquinone via intramolecular hydrogen-abstraction reaction. Irradiation of quinones in methanol, however, gave the latter product exclusively.

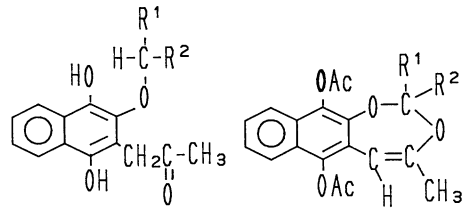
Photochemical reaction of 2-alkoxy-1,4-naphthoquinones usually leads to the formation of quinone dimers[1] and oxetanols[2] in high yields, via intramolecular hydrogen abstraction from the 2′-position of the side chain. This reaction is similar to the Norrish type II photoreaction of aromatic ketones.[3] Recently, we developed the convenient synthesis of 2-acetonyl-3-alkoxy-1,4-naphthoquinones (**2**) by the photochemical reaction of 2-alkoxy-1,4-naphthoquinones (**1**) with 2-methoxy-1-propene.[4] Interestingly, the photochemical reaction of **2** is quite different from those of 2-alkoxy-1,4-naphthoquinones with regard to the mechanistic points.[5] In this paper, the details of the novel photo-induced cyclization of **2** is described.

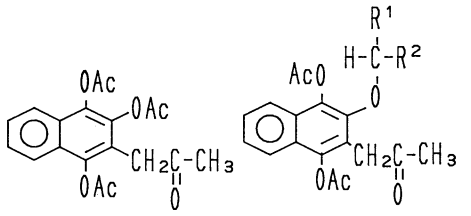
Results and Discussion

When a solution of 2-acetonyl-3-alkoxy-1,4-naphthoquinones (**2**) in benzene (0.0028 mol dm^{-3}) were irradiated with a high-pressure mercury arc lamp (300 W) through Pyrex filter for 15 min, the heterocyclic 1,4-naphthoquinones **3** as a major products, accompanying with 2-acetonyl-3-hydroxy-1,4-naphthoquinone (**4**), were obtained and the results are summarized in Table 1. The structures of **3** were assigned on the basis of their spectroscopic and elemental analyses, and that of **4** was confirmed by comparison with the authentic sample.[6] The yields of the cyclized products **3** increased in the order of **2a**<**2b**<**2c**, reflecting the γ C–H bond strength.[7] In order to confirm the existence of the hydroquinones derived from **2**, **3**, and **4**, the following two experiments were done. After irradiation of **2c** in benzene for 15 min, the reaction mixture was treated with acetic anhydride and pyridine to give a mixture of diacetate **7c**



a: R^1=R^2=H, **b**: R^1=H, R^2=CH_3, **c**: R^1=R^2=CH_3





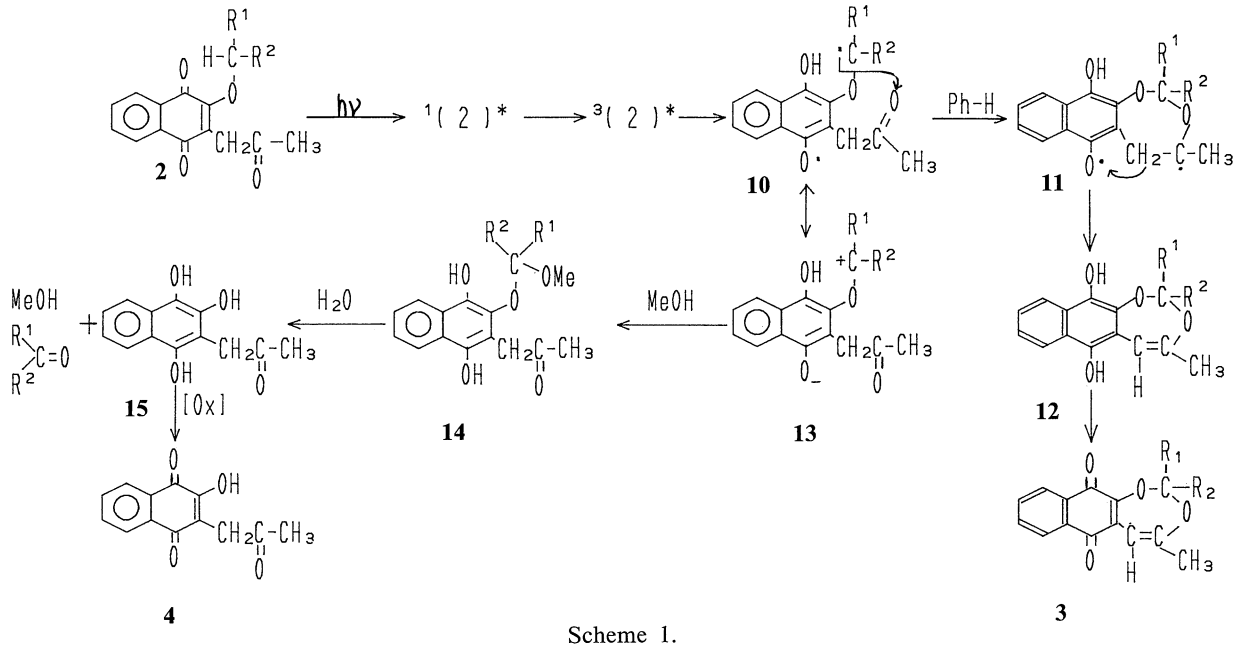
a: R^1=R^2=H, **b**: R^1=H, R^2=CH_3, **c**: R^1=R^2=CH_3

Reduction Products and Reductive Acetylation Products

Table 1. Photochemical Reaction of 2-Acetonyl-3-alkoxy-1,4-naphthoquinone **2**

Quinone R^1	Quinone R^2		Conv.[a] %	Solvent	Isolated yields/%[b] **3**	Isolated yields/%[b] **4**
H	H	**2a**	60	Ph–H	28	16
CH_3	H	**2b**	85	Ph–H	38	16
CH_3	CH_3	**2c**	87	Ph–H	77	11
H	H	**2a**	90	MeOH	—	41
CH_3	H	**2b**	99	MeOH	—	50
CH_3	CH_3	**2c**	81	MeOH	—	70

a) Conversion of **2**. b) Isolated yields were based on the consumed amounts of **2**. Irradiation time, 15 min; [**2**]=2.75×10^{-3} mol dm^{-3}.



Scheme 1.

(37%) and **9c** (20%), and triacetate **8** (5%) at 90% conversion. The structures of these acetates were confirmed by comparison with the authentic samples synthesized by the reductive acetylation of the corresponding quinones (**2c**, **3c**, and **4**).[8] (Experiment 1) These results indicate that hydroquinones derived from **2**, **3**, and **4** are initial photoproducts, but they are oxidized to the corresponding quinones during work-up procedure involving chromatography over silica gel. In addition, after irradiation of **2c** in benzene-d_6 for 5 min (40% conversion), the 400 MHz ^{1}H NMR spectrum of the reaction mixture revealed the peaks assignable to the hydroquinone **5c** at δ=0.97 (d, J=6.11 Hz, 6H), 1.75 (s, 3H), 3.58 (s, 2H), and 3.74 (sept, J=6.41 Hz, 1H) which were in agreement with those of the hydroquinone **5c** obtained by the reduction of **2c** with dithionite, in addition to the peaks due to **3c** and **4**. The peaks due to **5c** disappeared after adding chloranil to the reaction mixture (Experiment 2). This novel photoinduced cyclization of **2** was sensitized by xanthone and quenched by anthracene, indicating that the reaction occurred from the triplet excited state of **2**. From these results, a plausible mechanism for the formation of **3** is given in Scheme 1. Photocylization may begin with intramolecular γ-H-abstraction by the ^{3}(n, π^*) of **2** to give biradical **10**, which intramoleculary attacks the carbonyl oxygen in the oxoalkyl side chain and cyclizes to **11**.

Intramolecular disproportionation of the biradical **11** produces hydroquinone **12**, which is oxidized by the unreacted **2** or air, to give **3**.

On the other hand, irradiation of **2a**—**c** in methanol gave preferentially **4** (41—70% yield) as shown in Table 1. In the case of the reaction of **2c** the alkoxyl group lost in the course of the photochemical reaction in methanol was detected as acetone by gas chromatography, ^{1}H NMR, and ^{13}C NMR. The yield of acetone increased with increasing irradiation time. From these results, a plausible mechanism for the formation of **4** is given in Scheme 1. The photoinduced C–O bond cleavage may begin with intramolecular γ-H-abstraction as well as the formation of **3**. In methanol the biradical **10** is stabilized by an adjacent heteroatom[9] such as oxygen to produce a zwitterionic intermediate **13**, which reacts with methanol to give the acetal **14**. Hydrolysis of **14** produces ketone (R^1R^2C=O), methanol, and hydroquinone **15**, which is oxidized by the unreacted **2** or air to give **4**.

Experimental

Apparatus. Melting points were measured on Yanagimoto micro-melting points apparatus and are uncorrected. Infrared spectra were taken on a JASCO FT-IR 5000 spectrometer. ^{1}H NMR spectra were recorded on a JEOL GX-400 (400 MHz), a JEOL GX-270 (270 MHz) and a JEOL FX-90Q (90 MHz) spectrometer with use of tetramethylsilane as an internal standard and the chemical shifts are expressed in δ values. UV spectra were taken by using a JASCO Ubest-35 spectrometer. Elemental analyses were performed at the Advanced Instrumentation Center for Chemical Analysis, Ehime University. Mass spectra were recorded on a Hitachi M-2000 spectrometer. GC analyses were performed on a Hitachi Model 163, using a 3 mm i.d., ×2 m stainless steel column packed with 10% SE-30 on celite 545 AW. Preparative separations were performed by column chromatography over silica gel (Wakogel C-200). UV irradiations were carried out in a Pyrex vessel (Fuji glass) under a nitrogen atmosphere with a Fuji glass 300W high-pressure mercury arc lamp.

Materials. 2-Acetonyl-3-alkoxy-1,4-naphthoquinones **2** were prepared by the photochemical reaction of 2-alkoxy-1,4-naphthoquinones with 2-methoxy-1-propene in benzene.[4]

General Procedure for the Photochemical Reaction of 2-Acetonyl-3-alkoxy-1,4-naphthoquinones 2. A degassed solution of 2-acetonyl-3-alkoxy-1,4-naphthoquinones **2** (0.5 mmol) in 180 cm^3 of benzene or methanol in a Pyrex vessel, using a 300 W high-pressure mercury lamp from inside. The progress of the reaction was followed by thin-layer chromatography (TLC), NMR, or GC. After removal of solvent, the residual oil was separated by chromatography on

silica gel with dichloromethane-hexane as an eluant. Final purification was usually accomplished by preparative TLC and recrystallization.

Physical Properties of Photoproducts. 4-Methylnaphtho-[2,3-*d*]-1,3-dioxepin-6,11-dione (3a): Mp 197—198°C; ^{1}H NMR (270 MHz, $CDCl_3$) δ=2.13 (3H, s), 5.51 (2H, s), 6.00 (1H, s), 7.53—7.76 (2H, m), 7.83—8.13 (2H, m); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ=22.38 (q), 93.78 (t), 95.14 (d), 124.23 (s), 126.29 (d), 126.72 (d), 131.11 (s), 131.59 (s), 133.71 (d), 155.70 (s), 165.18 (s), 178.18 (s, C=O), 183.76 (s, C=O); IR (KBr) 1660, 1650, 1625, 1595, 1260 cm^{-1}; MS (20 eV), *m/z* 242 (M^+); UV (λ_{max}, nm (log ε), CH_2Cl_2) 248 (4.30), 280 (4.27), 337 (3.54), 442 (3.30); Found: C, 69.40; H, 4.10%. Calcd for $C_{14}H_{10}O_4$: C, 69.42; H, 4.16%.

2,4-Dimethylnaphtho[2,3-*d*]-1,3-dioxepin-6,11-dione (3b): Mp 188—190°C; ^{1}H NMR (270 MHz, $CDCl_3$), δ=1.79 (3H, d, *J*=7.1 Hz), 2.09 (3H, s), 5.29 (1H, q, *J*=7.1 Hz), 5.94 (1H, s), 7.67—7.70 (2H, m), 8.07—8.10 (2H, m); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ=20.81 (q), 22.60 (q), 94.81 (d), 101.15 (d), 124.66 (s), 126.34 (d), 126.66 (d), 131.76 (s), 133.71 (d), 154.55 (s), 163.45 (s), 170.63 (s, C=O), 183.93 (s, C=O); IR (KBr) 1676, 1659, 1638, 1597, 1576 cm^{-1}; MS (20 eV), *m/z* 256 (M^+); UV (λ_{max}, nm (log ε), CH_2Cl_2) 278 (4.31), 452 (3.50); Found: C, 70.42; H, 4.70%. Calcd for $C_{15}H_{12}O_4$: C, 70.31; H, 4.72%.

2,2-Dimethylnaphtho[2,3-*d*]-1,3-dioxepin-6,11-dione (3c): Mp 90—91°C; ^{1}H NMR (270 MHz, $CDCl_3$), δ=1.64 (6H, s), 2.11 (3H, s), 6.04 (1H, s), 7.55—7.75 (2H, m), 7.95—8.15 (2H, m); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ=23.68 (q), 25.74 (q), 95.51 (d), 104.56 (s), 126.23 (d), 126.61 (d), 131.76 (s), 133.49 (d), 133.60 (d), 150.66 (s), 160.31 (s), 179.16 (s, C=O), 183.98 (s, C=O); IR (KBr) 1650, 1620, 1590, and 1260 cm^{-1}; MS (20 eV), *m/z* 270 (M^+); UV (λ_{max}, nm (log ε), CH_2Cl_2) 273 (4.44), 446 (3.62); Found: C, 71.15; H, 5.18%. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22%.

Reductive Acetylation of the Quinones. Quinones (0.1 mmol), an excess amount of zinc powder (200 mg), and sodium acetate (30 mg) were added to acetic anhydride (3 cm^3). Then, the mixture was refluxed for 30 min. After the yellow color due to the quinone disappeared completely, the reaction mixture was hydrolyzed and neutralized with sodium carbonate. The acetate was extracted with dichloromethane from the reaction mixture and purified further by p-TLC.

Physical Properties of the Diacetate. 6,11-Diacetoxy-4-methylnaphtho[2,3-*d*]-1,3-dioxepin (7a): Mp 169—170°C; ^{1}H NMR (270 MHz, $CDCl_3$) δ=2.05 (3H, s), 2.43 (3H, s), 2.46 (3H, s), 5.43 (2H, s), 7.25—7.50 (2H, m), 7.55—7.85 (2H, m); IR (KBr) 1760, 1655, 1603, 1185, 1082 cm^{-1}; MS (20 eV), *m/z* 328 (M^+).

6,11-Diacetoxy-2,4-dimethylnaphtho[2,3-*d*]-1,3-dioxepin (7b): Mp 158—160°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.63 (3H, d, *J*=5.1 Hz), 2.05 (3H, s), 2.43 (3H, s), 2.49 (3H, s), 5.38 (1H, q, *J*=5.1 Hz), 5.49 (1H, s), 7.28—7.50 (2H, m), 7.55—7.90 (2H, m); IR (KBr) 1756, 1647, 1605, 1183, 1087 cm^{-1}; MS (20 eV), *m/z* 342 (M^+).

6,11-Diacetoxy-2,2,4-trimethylnaphtho[2,3-*d*]-1,3-dioxepin (7c): Mp 205—206°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.58 (6H, s), 2.03 (3H, s), 2.48 (3H, s), 5.50 (1H, s), 7.24—7.51 (2H, m), 7.53—7.80 (2H, m); IR (KBr) 1760, 1655, 1603, 1185, 1086 cm^{-1}; MS (20 eV), *m/z* 356 (M^+).

2-Acetonyl-1,4-diacetoxy-3-methoxynaphthalene (9a): Mp 118—120°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.97 (3H, s), 2.43 (3H, s), 2.47 (3H, s), 3.75 (2H, s), 3.88 (3H, s), 7.30—7.57 (2H, m), 7.60—7.90 (2H, m); IR (KBr) 1760, 1715, 1603, 1210, 1178 cm^{-1}; MS (20 eV), *m/z* 328 (M^+).

2-Acetonyl-1,4-diacetoxy-3-ethoxynaphthalene (9b): Mp 98—100°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.37 (3H, t, *J*=7.0 Hz), 2.11 (3H, s), 2.43 (3H, s), 2.45 (3H, s), 3.74 (2H, s), 4.08 (2H, q, *J*=7.0 Hz), 7.30—7.58 (2H, m), 7.60—7.88 (2H, m); IR (KBr) 1763, 1718, 1606, 1206, 1181 cm^{-1}; MS (20 eV), *m/z* 344 (M^+).

2-Acetonyl-1,4-diacetoxy-3-isopropoxynaphthalene (9c): Oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.28 (6H, d, *J*=6.1 Hz), 2.06 (3H, s), 2.40 (3H, s), 2.42 (3H, s), 3.74 (2H, s), 4.44 (1H, sept, *J*=6.1 Hz), 7.30—7.55 (2H, m), 7.57—7.82 (2H, m); IR (KBr) 1774, 1709, 1603, 1178 cm^{-1}; MS (20 eV), *m/z* 358 (M^+).

2-Acetonyl-1,3,4-triacetoxynaphthalene (8): Mp 165—167°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ=2.06 (3H, s), 2.34 (3H, s), 2.44 (3H, s), 2.47 (3H, s), 3.60 (2H, s), 7.30—7.90 (4H, m); IR (KBr) 1779, 1726, 1606, 1178 cm^{-1}; MS (20 eV), *m/z* 358 (M^+).

Reduction of 2-Acetonyl-3-isopropoxy-1,4-naphthoquinone 2c: A degassed solution of **2c** (0.1 mmol) in ether (5 cm^3) was added to a degassed solution of sodium hydrosulfite (0.23 mmol) in water (4 cm^3) and stirred vigorously under a nitrogen. The solution became pale yellow in 30 min. The reaction mixture was poured into a separatory funnel. After removing the aqueous layer, the etheral solution was washed with saturated brine and dried over anhydrous sodium sulfate. The filtrate was evaporated under reduced pressure to give the hydroquinone **5c** with a small amount of **2c** which was produced by the oxidation of **5c** in the usual work up. From ^{1}H NMR spectrum of the reaction mixture in benzene-d_6, the presence of **2c** was confirmed by direct comparison with ^{1}H NMR spectrum of an anthentic sample in benzene-d_6 and the structure of **5c** was determined by the follow ^{1}H NMR spectral deta: Isopropoxy substituent at δ=0.97 (d, *J*=6.1 Hz, 6H, $-OCH(\underline{CH_3})_2$), and 3.74 (sept, *J*=6.4 Hz, 1H, $-O\underline{CH}(CH_3)_2$) and acetonyl substituent at δ=1.75 (s, 3H, $-CH_2COCH_3$), and 3.58 (s, 2H, $-CH_2CO\underline{CH_3}$), and aromatic hydrogen at δ=7.18—7.38 (m, 2H), and 8.25—8.45 (m, 2H).

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