

THE PHOTOCHEMISTRY OF EPOXYQUINONES III; PHOTOISOMERIZATION OF 2-ACYL-3-METHYL-2, 3-EPOXY-2,3-DIHYDRO-1,4-NAPHTHOQUINONES

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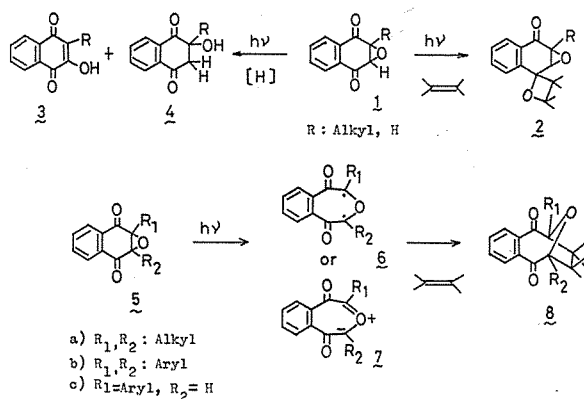
(Received July 5, 1978)

ABSTRACT

The photochemical reactions of 2-acyl-3-methyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinones have been examined. On the irradiation of 2-acetyl-3-methyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone, photoisomerization readily occurs to give 3-(1-acetylacetylidene)phthalide. In the photochemical reaction of 2-propionyl-3-methyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone, similar photoisomerization occurs to yield two stereoisomeric phthalides. The reasonable mechanism involving initial α -cleavage (Norrish Type-I cleavage) and subsequent free radical rearrangement is proposed.

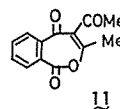
The Photochemistry of oxiranes,¹ α , β -epoxy ketones,² and β , γ -epoxy ketones³ has been well studied. However, little attention has been paid to the photochemistry of epoxyquinones which are characterized as "epoxydiones" until quite recently. In our recent papers, we showed that the photochemical behaviors of epoxynaphthoquinones was highly dependent upon the substitution pattern at C-2 and C-3 of epoxyquinones.^{4,5} In the photochemical reaction of 2-alkyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinones **1** with olefins such as norbornene, oxetane formation is the predominant reaction. In the photochemical reactions of these epoxyquinones **1** in the presence of hydrogen donors, the C-O bond cleavage of the oxirane ring occurs to

Scheme I

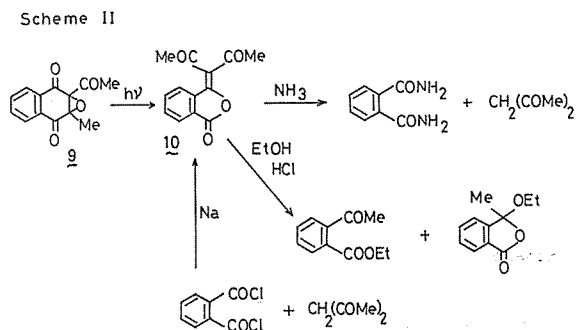


give the alcoholic products **3** and **4**.⁴ On the other hand, in the photochemical reactions of 2,3-dialkyl, 2,3-diaryl, and aryl conjugated epoxy-naphthoquinones **5** with olefins, the primary photochemical reaction is the cleavage of the internal C-2: C-3 bond and formation of reactive diradicals **6** or carbonyl ylides **7**, trapped by olefins to give the adducts **8** of 1,3-dipolar cycloaddition type (Scheme I).⁵

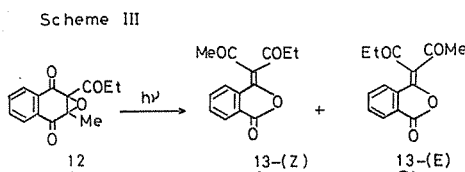
In addition to these reactions, we found another type of reaction in the photolysis of 2-acyl-3-methyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinones. Upon the irradiation of the solution of 2-acetyl-3-methyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone (**9**) in acetonitril or benzene, photorearrangement readily occurs to give 3-(1-acetylacetylidenephthalide) (**10**) (yield: 45% in acetonitril, 31% in benzene). In the previous paper, we erroneously assigned seven-membered lactone structure **11** for this product.⁶ However, reexamination of structure analysis showed that it should be corrected to the phthalide structure **10**.



Structure assignment of **10** rests on the following physical and chemical evidences. The IR spectrum of **10** showed three characteristic bands at 1795 (five-membered lactone C=O), 1705 (COMe), 1650 (C=C) cm^{-1} , and NMR spectrum showed two singlets at δ 2.49 and 2.70 due to two methyl groups. Mass spectrum and elemental analysis were also compatible with structure **11**. Chemical evidences of structure **10** are outlined below. When the absolute ethanol solution of the photoproduct **10** was saturated with dry ammonia, it transformed to phthalamide and acetylacetone, and treatment of **10** with dry hydrogen chloride gave *o*-acetylbenzoic acid ethyl ester and 3-methyl-3-ethoxyphthalide (Scheme II). Furthermore, this structure was confirmed by its independent synthesis; condensation of phthaloyl chloride and acetylacetone in ether with sodium.⁷

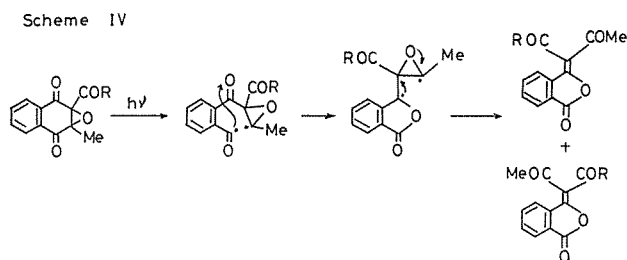


Similar photorearrangement was observed in the photolysis of 2-propionyl-3-methyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone (**12**) (Scheme III). However, in this case, equal amounts of two stereoisomers **13**-(Z) and **13**-(E) were formed in 26% yield. Although the Z and E isomer mixture could not be resolved, even on a

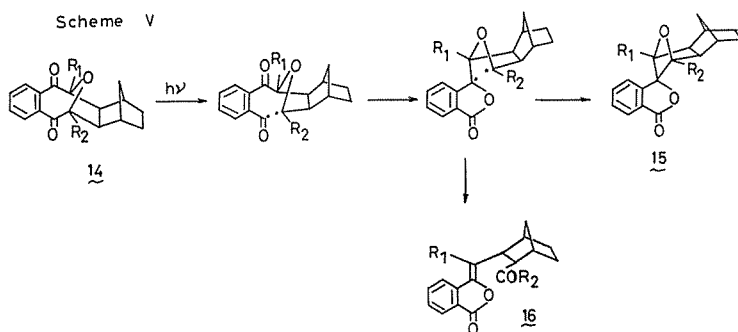


thin layer chromatography, unequivocal structure assignment was possible by NMR analysis. The methyl proton of the acetyl group of the Z isomer (appearing at δ 2.71) is deshielded relative to that of the E isomer (appearing at δ 2.44) by the effect of the proximal aromatic ring proton.⁸

The reasonable mechanism for this photoisomerization is shown in Scheme IV. This mechanism involves initial α -cleavage (Norrish Type-I), followed by free radical rearrangement. If there is no substituent on C-3, i.e. in the photolysis of 2-acetyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone, no photoisomerization of this type is observed and this epoxyquinone is rather stable under the irradiation conditions. Since α -methyl groups to carbonyl chromophores accelerate Norrish Type-I cleavage,⁹ the mechanism shown in Scheme IV is reasonable. Furthermore, in the previous



paper, we proposed analogous mechanism for the photoisomerization of the adducts **14** derived from the photochemical reaction of epoxyquinones **5-a** and **5-b** with norbornene.⁵ This photoisomerization proceeds via the initial α -cleavage and subsequent free radical rearrangement to afford spirophthalides **15** and alkylidene-phthalides **16** (Scheme V).



The efficiency of the photorearrangement process described above is shown to be dependent upon the substitution pattern at C-2 and C-3 of epoxyquinones by the following facts. On the irradiation of 2-alkyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinones **1** in the absence of olefins or hydrogen donors, these epoxyquinones are rather stable and little chemical change occurs. However, 2, 3-diphenyl-2, 3-epoxy-dihydro-1, 4-naphthoquinone has been shown to undergo similar photorearrangement very slowly to give two stereoisomeric phthalides by Kato et al.,¹⁰ while cycloaddition reactions of 1, 3-dipolar type readily occur in the presence of reactive olefins such as norbornene and N-phenylmaleimide. In contrast with the photolysis of 2, 3-diphenyl derivatives, the irradiation of 2, 3-dimethyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphtho-

quinone readily gives the dimeric products whose structural analyses are now under investigation.

Thus, the photochemistry of epoxynaphthoquinones is complex and many problems remain unresolved. Therefore, further systematic studies will be required.

Experimental Section

Melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were performed by the Microanalytical Laboratory of Kyoto University, Kyoto, Japan. IR spectra were recorded with a JASCO IR-G spectrophotometer, and NMR spectra were taken with a JEOL PS-100 spectrometer with tetramethylsilane as an internal standard and the chemical shifts expressed in δ values. UV spectra were recorded with a Shimadzu UV-200 spectrophotometer. Mass spectra were taken with a Hitachi M-52 mass spectrometer. Preparative TLC was carried out on Merk Kieselgel PF₂₅₄. UV irradiation was carried out in a Pyrex vessel at room temperature, using an Eikosha 300-W high-pressure mercury lamp.

Preparation of Epoxyquinones 9 and 12

2-Acetyl-3-methyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone (**9**) and 2-propionyl-3-methyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone (**12**) were prepared by the method of Read and Ruitz.¹¹ 2-Acetyl-3-methyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone (**9**): mp 94–95°C; IR (KBr) 1723 (acetyl C=O), 1685 (Ph C=O), 1266, 902 and 850 (epoxide ring) cm⁻¹; NMR (CDCl₃) δ 1.61 (s, 3H, CH₃), 2.42 (s, 3H, acetyl CH₃), and 7.7–8.1 (4H, m, aromatic-H); UV (CHCl₃) λ_{\max} 268, 306 nm (ϵ 6300, 2300). 2-Propionyl-3-methyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone (**12**): mp 102–103°C; IR (KBr) 1720 (propionyl C=O), 1686 (Ph C=O), 855 (epoxide ring) cm⁻¹; NMR (CDCl₃) δ 1.19 (t, 3H, CH₃), 1.59 (s, 3H, CH₃), 2.70 (q, 2H, CH₂), and 7.6–8.1 (m, 4H, aromatic-H); UV (CHCl₃) λ_{\max} 262, 307 nm (ϵ 5900, 2000). Anal. Calcd for C₁₄H₁₂O₃: C, 66.84; H, 4.95. Found: C, 68.68; H, 5.05.

Irradiation of 2-Acetyl-3-methyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone (9)

A solution of epoxyquinone **9** (200 mg) in acetonitrile or benzene (60 ml) was irradiated for 8 h with a 300-W high-pressure mercury lamp. Evaporation of the solvent gave an oily residue which crystallized on the addition of methanol. Recrystallization of the crude solids from hexane-benzene gave the pure solids of 3-(1-acetylacetylidene)phthalide (**10**) (yield 45% in acetonitrile, 31% in benzene); colorless needles, mp 133–134°C; IR (KBr) 1795, 1705 (C=O), and 1650 (C=C) cm⁻¹; NMR (CDCl₃) δ 2.49 (s, 3H, CH₃), 2.70 (s, 3H, CH₃), and 7.5–8.0 (m, 4H, aromatic-H); UV (CHCl₃) λ_{\max} 283 and 314 nm (ϵ 16000 and 13000); mass spectrum m/e 230 (M⁺), 188, 173. Anal. Calcd for C₁₃H₁₀O₄: C, 67.82; H, 4.38. Found: C, 67.72; H, 4.23.

Chemical Reactions of 10 with Ammonia and Hydrogen Chloride in Ethanol

A solution of **10** (100 mg) in absolute ethanol (20 ml) was saturated with dry ammonia and allowed to stand for 3 days. The solution was concentrated to 10 ml, and deposited crystals were collected. Recrystallization of the crude crystals from ethanol gave phthalamide (53 mg, 74%). Acetylacetone could be detected out of the

reaction mixture by GPC analysis.

A solution of **10** (100 mg) in absolute ethanol (20 ml) was saturated with dry hydrogen chloride and allowed to stand for 3 days. The solution was poured into ice-water (100 ml) and extracted with ether. The dried extract was evaporated and the resultant residue was chromatographed on a silica gel. The elution with chloroform gave the mixture of *o*-acetylbenzoic acid ethyl ester and 3-methyl-3-ethoxyphthalide in 70% combined yield (ester:phthalide=32:38, determined by NMR). These products were confirmed by their unequivocal syntheses. The 2:3 mixture of ester and phthalide (bp 157.5–160°C/20 mmHg) were obtained by the preparation of the method of Yale.¹²

The photoproduct **10** was also synthesized by another route. Condensation of phthaloyl chloride and acetylacetone in ether with sodium gave the phthalide **10**.⁷

Irradiation of 2-Propionyl-3-methyl-2, 3-epoxy-2, 3-dihydro-1, 4-naphthoquinone (12)

A solution of **12** (300 mg) in acetonitrile (60 ml) was irradiated for 10 h. After the evaporation of the solvent, the resulting residue was separated on a thin layer chromatography. The mixture of two stereoisomeric phthalides **13**-(Z) and **13**-(E) was obtained in 26% (78 mg) combined yield. NMR analysis indicated the mixture of equal amounts of two isomers, but the two isomers could not be resolved, even on a thin layer chromatography. 3-(1-Propionylacetylidene)phthalide (**13**-(Z) and **13**-(E)); colorless needles, from *n*-hexane, mp 94–96°C; IR (KBr) 1805, 1780 (five-membered lactone C=O), 1710, 1698 (propionyl, acetyl C=O), 1650 (C=C) cm⁻¹; NMR (CDCl₃) δ: **13**-(Z), 1.11 (t, 3H, CH₃), 2.71 (s, 3H, CH₃), 2.80 (q, 2H, CH₂), and 7.7–8.2 (m, 4H, aromatic-H); **13**-(E), 1.13 (t, 3H, CH₃), 2.44 (s, 3H, CH₃), 3.11 (q, 2H, CH₂), and 7.7–8.2 (aromatic-H). Anal. Calcd for C₁₄H₁₂O₄: C, 68.84; H, 4.95. Found: C, 68.79; H, 4.81.

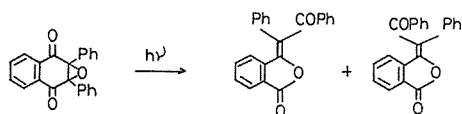
ACKNOWLEDGMENT

In this investigation the author is particularly indebted to Professor K. Maruyama for his discussions, encouragements and invaluable suggestions.

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