

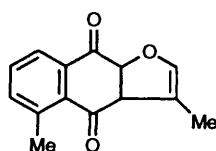
Photoinduced Molecular Transformations. Part 141.¹ New One-step General Synthesis of Benzofuran-4,7-diones by the Regioselective (3 + 2) Photoaddition of 2-Hydroxy-1,4-benzoquinones with Various Alkenes

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A one-step formation of benzofuran-4,7-diones by a (3 + 2) regioselective photoaddition of 2-hydroxy-1,4-benzoquinones with various alkenes is reported.

In previous papers^{1,2a} we have reported on a one-step formation of 2,3-dihydronaphtho[2,3-*b*]furan-4,9-diones and naphtho[2,3-*b*]furan-4,9-diones by the regioselective photoaddition of 2-hydroxy-1,4-naphthoquinones with various alkenes and alkynes. The new (3 + 2) photoaddition was successfully applied to a new synthesis of matorinone.^{2b}



Matorinone

In this paper we report on an extension of this new photoannulation of naphthoquinones to a hydroxybenzoquinone system which has been little used in syntheses.³ Extensive studies have been carried out on the photoaddition of benzoquinones with alkenes, which invariably led to (2 + 2) photoadditions.^{4,5} Our results have demonstrated that the photoaddition of 2-hydroxybenzoquinones with alkenes gives benzofuran-4,7-diones arising from the (3 + 2) photoaddition. The formation of (3 + 2) photoadducts is thus a general photoreaction of the hydroquinone system with alkenes.

The synthesis of benzofuran-4,7-diones, to which natural products such as acamelin belong,⁶ have been reported;⁷ they have also been utilized in syntheses.^{2c,8} The present one-step synthesis of benzofuran-4,7-diones from 2-hydroxybenzoquinones and alkenes, which proceeds only in the presence of photons and a solvent at room temperature, may prove to be useful in the synthesis of this group of molecules.

Results and Discussion

Preparation of Substrates.—Of the three 2-hydroxybenzoquinone derivatives used as substrates for the (3 + 2) photoaddition, 2-hydroxy-5,6-dimethylcyclohexa-2,5-diene-1,4-dione **1**⁹ and 2-hydroxy-5-phenylcyclohexa-2,5-diene-1,4-dione **2**¹⁰ were prepared according to published methods. 1,2,3,4-Tetrahydro-6-hydroxynaphthalene-5,8-dione **4**, an unknown bicyclic quinone, was prepared by demethylation of 1,2,3,4-tetrahydro-5,6,8-trimethoxynaphthalene **3**¹¹ in dichloromethane with boron tribromide at room temperature, followed by oxidation of the resulting trihydroxytetralin with ferric chloride–hydrochloric acid at room temperature (Scheme 1).

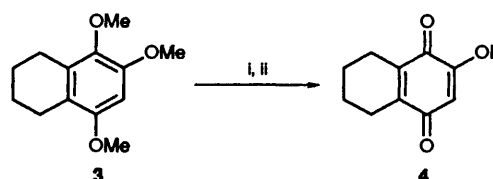
Synthesis of 4,7-Benzofurandiones by the (3 + 2) Photoaddition of 2-Hydroxybenzoquinones.—Irradiation of 2-hydroxy-5,6-dimethylcyclohexa-2,5-diene-1,4-dione **1** and an excess of an alkene (isobutene, 2-methylbut-2-ene, 2,3-dimethylbut-2-ene, α -methylstyrene and 2-methoxypropene) in acetone with a 500-W high-pressure Hg arc through a Pyrex-filter for 4–23 h gave a

Table 1 Results of photoadditions of 2-hydroxybenzoquinones

Quinone	Alkene	Benzofuran-4,7-dione	Yield (%) ^a
1	5a	6a	62
1	5b	6b	51
1	5c	6c	27
1	5d	6d	52
1	5e	6e	41 ^b
2	5a	7a	27
2	5d	7d	32
4	5a	8a	48
4	5d	8d	50

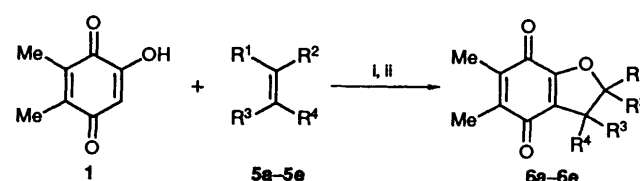
^a Isolated yields after separation by preparative TLC on silica gel.

^b Oxidized with Ag₂O before the separation by TLC.



Scheme 1 Reagents and conditions: i, BBr₃–CH₂Cl₂; ii, FeCl₃–HCl–MeOH

corresponding single (3 + 2) photoadduct, respectively, in 27–62% yields, as outlined in Scheme 2 and Table 1. These

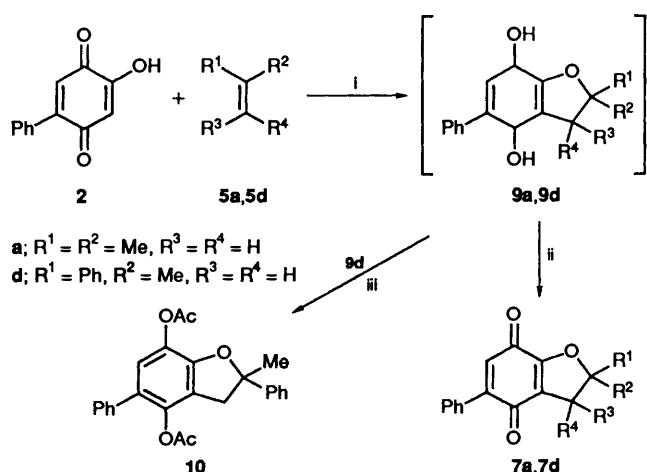


a: R¹ = R² = Me, R³ = R⁴ = H, **b:** R¹ = R² = R³ = Me, R⁴ = H,
c: R¹ = R² = R³ = R⁴ = Me, **d:** R¹ = Ph, R² = Me, R³ = R⁴ = H,
e: R¹ = OMe, R² = Me, R³ = R⁴ = H

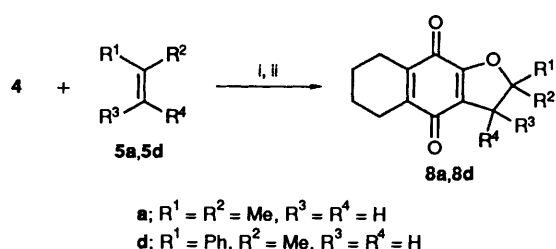
Scheme 2 Reagents and conditions: i, hv–acetone; ii, SiO₂ or Ag₂O.

photoadditions were completely regioselective, as in the case of those of 2-hydroxynaphthoquinones² and 2-hydroxyanthra-*cen*edione.¹² Similar photoannulation of 2-hydroxy-5-phenylcyclohexa-2,5-diene-1,4-dione **2**¹⁰ with an excess of isobutene or α -methylstyrene under the conditions mentioned above gave 2,3-dihydro-2,2-dimethyl-5-phenylbenzofuran-4,7-dione **7a** or 2,3-dihydro-2-methyl-2,5-diphenylbenzofuran-4,7-dione **7d** in 27 and 32% yields, respectively (Scheme 3). The photoaddition was again completely regioselective.

Finally, the regioselective (3 + 2) photoaddition of 1,2,3,4-tetrahydro-6-hydroxynaphthalene-5,8-dione with isobutene or



Scheme 3 Reagents and conditions: i, $h\nu$ -acetone; ii, O_2 - SiO_2 or Ag_2O ; iii, $AcCl$ -pyridine



Scheme 4 Reagents and conditions: i, $h\nu$ -acetone; ii, SiO_2 or Ag_2O

α -methylstyrene under the conditions mentioned above gave 2,3,5,6,7,8-hexahydro-2,2-dimethylnaphtho[2,3-*b*]furan-4,9-dione **8a** or 2,3,5,6,7,8, hexahydro-2-methyl-2-phenylnaphtho[2,3-*b*]furan-4,9-dione **8d** in 48 and 50% yields (Scheme 4).

The initial products in the present (3 + 2) photoaddition of 2-hydroxybenzoquinones with alkenes are the hydroquinones. The residue obtained by evaporating an irradiated acetone

solution of 2-hydroxy-5-phenylcyclohexa-2,5-diene-1,4-dione **2** and α -methylstyrene was dissolved in diethyl ether and the solution was immediately treated with acetyl chloride and pyridine under an argon atmosphere at room temperature to give 4,7-dihydroxy-2,3-dihydro-2-methyl-2,5-diphenylbenzofuran **9** in 36% yield as virtually a single product (Scheme 5).

The mechanism of this (3 + 2) photoaddition of 2-hydroxybenzoquinone with alkenes should be parallel to the (3 + 2) photoaddition of 2-hydroxynaphthoquinones with alkenes previously reported by us.^{1,2a}

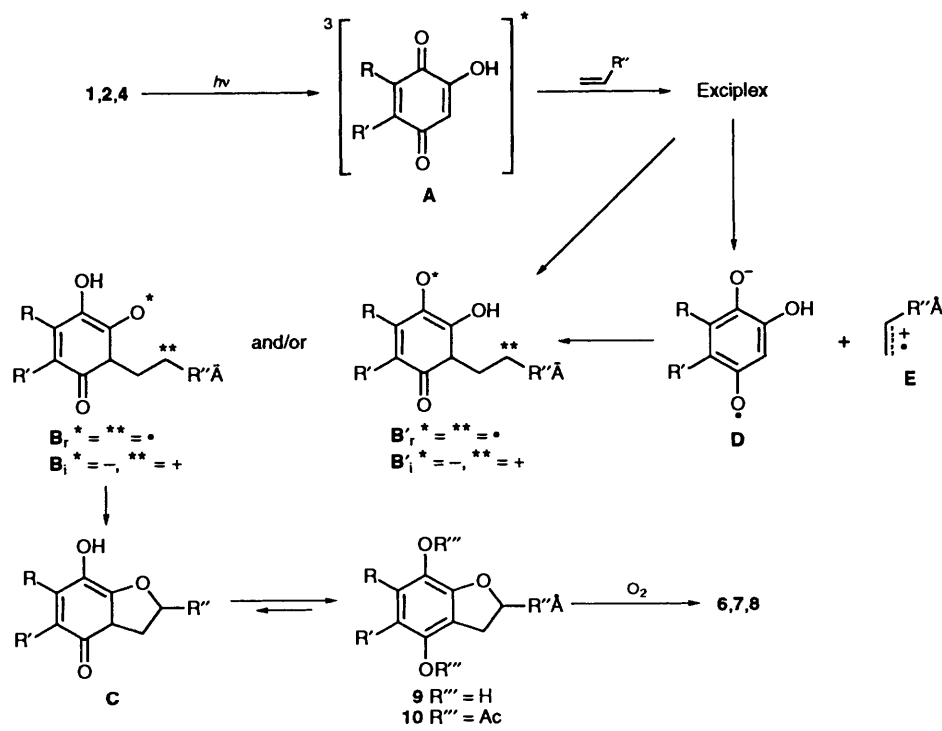
A probable gross reaction path from the benzoquinones **1**, **2** and **4** to the benzofuranquinones **6**, **7** and **8** is outlined in Scheme 5. The irradiation of benzoquinone derivatives **1**, **2** or **4** in acetone generates triplet excited benzoquinones. These form, respectively, an exciplex with each alkene, which collapses to give a polar biradical B_r , B'_r or anionic intermediate B_i , B'_i generated by electron transfer. Electron transfer would be considered to be especially facile in a biradical B_r , B'_r by virtue of the strong electron-accepting character of the quinones.¹³ The mechanism for formation of the biradical B_r , B'_r would be similar to the first stage in the (2 + 2) photoaddition of enones.¹⁴ As suggested in our previous paper, an alternative mechanism for the formation of the anionic intermediates B_i , B'_i would be possible; these ionic intermediates can be formed through a pair of radical ions **D** and **E** formed from the exciplex.^{15,16}

The regioselectivity found in this photoaddition clearly indicates the involvement of a more stabilized biradical, or ionic intermediate such as B_r , B'_r and B_i , B'_i . An intramolecular cyclization of the intermediates affords a hydroquinone **C** which is oxidized by air during the work-up to give the observed furanoquinones **6**, **7** and **8**.

Experimental

For descriptions of the instruments and the general procedure of photolysis, see ref. 17.

6-Hydroxy-1,2,3,4-tetrahydronaphthalene-5,8-dione 4.—To a stirred solution of **3**¹¹ (279 mg, 1.26 mmol) in dichloromethane



Scheme 5

(15 cm³) at -50 °C was added dropwise boron tribromide (4.8 g, 19.2 mmol) under argon; the mixture was allowed to warm to room temperature. After being stirred for 30 min, the mixture was cooled to 0 °C, diluted with diethyl ether and poured into water. The aqueous layer was saturated with sodium chloride and extracted with diethyl ether. The combined diethyl ether extracts were washed with brine, dried (Na₂SO₄) and worked up to give the crude trihydroxytetralin, which was stirred with 1 cm³ of concentrated hydrochloric acid, and then 1 cm³ of 1 mol dm⁻³ ferric chloride-hydrochloric acid for 3 h at room temperature. The mixture was extracted with diethyl ether. The ethereal solution was washed with brine, dried (MgSO₄) and worked up to give the oily crude quinone **4** (186 mg, 83%), which was used in the photoreaction without further purification; $\nu_{\max}/\text{cm}^{-1}$ (neat) 3600–2400, 1659 and 1619; δ_{H} (90 MHz) 1.55–1.85 (4 H, m, 2- and 3-H), 2.3–2.6 (4 H, m, 1- and 4-H) and 5.95 (1 H, s, 7-H); m/z 178 (M⁺, 100) (Found: M⁺, 178.0615. C₁₀H₁₀O₃ requires M, 178.0630).

2,3-Dihydro-2,2,5,6-tetramethylbenzofuran-4,7-dione 6a.—A solution of **1** (100 mg, 0.66 mmol) and isobutene (1.12 g, 20 mmol) in acetone (20 cm³) was irradiated through a Pyrex filter with a 500-W high-pressure Hg arc in an atmosphere of nitrogen for 7 h at room temperature. After the precipitated materials had been filtered off, the filtrate was evaporated and the residue was subjected to PLC (1 : 3 ethyl acetate-hexane) on silica gel to give **6a** (84 mg, 62%); m.p. 118–120 °C (from diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1667, 1645, 1630 and 1599; δ_{H} (90 MHz) 1.52 (3 H, s, 2-Me), 2.00 (6 H, s, 5- and 6-Me) and 2.84 (2 H, s, 3-H); m/z 206 (M⁺, 56) and 178 [(M - CO)⁺, 100] (Found: C, 69.7; H, 6.9. C₁₂H₁₄O₃ requires C, 69.88; H, 6.84%).

2,3-Dihydro-2,2,3,5,6-pentamethylbenzofuran-4,7-dione 6b.—The irradiation of a solution of **1** (74 mg, 0.54 mmol) and 2-methylbut-2-ene (338 mg, 5.4 mmol) in acetone (15 cm³) for 4 h and separation of the product by PLC on silica gel were carried out in a similar way to that described above to give **6b** (61 mg, 51%); m.p. 61–62 °C (from hexane); $\nu_{\max}/\text{cm}^{-1}$ 1670, 1650, 1639 and 1605; δ_{H} (90 MHz) 1.21 (3 H, d, *J* 7.03, 3-Me), 1.42 and 1.44 (6 H, 2s, 2-Me), 2.00 (6 H, s, 5- and 6-H) and 3.10 (3 H, q, *J* 7.03, 3-H); m/z 220 (M⁺, 100) (Found: C, 70.8; H, 7.2. C₁₃H₁₆O₃ requires C, 70.89; H, 7.32%).

2,3-Dihydro-2,2,3,3,5,6-hexamethylbenzofuran-4,7-dione 6c.—The irradiation of **1** (25 mg, 0.16 mmol) and 2,3-dimethylbut-2-ene (135 mg, 1.6 mmol) in acetone (5 cm³) for 5.5 h gave **6c** (10 mg, 27%); an oil; *R*_f 0.52 (1 : 3 ethyl acetate-hexane); $\nu_{\max}/\text{cm}^{-1}$ (neat) 1672, 1648 and 1606; δ_{H} (90 MHz) 1.26 (6 H, s, 3-Me₂), 1.38 (6 H, s, 2 Me₂) and 1.99 (6-H, s, 5- and 6-Me); m/z 234 (M⁺, 78) and 219 [(M - Me)⁺, 100] (Found: M⁺, 234.1256. C₁₄H₁₈O₃ requires M, 234.1243).

2,3-Dihydro-2,5,6-trimethyl-2-phenylbenzofuran-4,7-dione 6d.—The irradiation of **1** (110 mg, 0.72 mmol) and α -methylstyrene (260 mg, 2.2 mmol) in acetone (40 cm³) for 23 h gave **6d** (99 mg, 52%); m.p. 91–92 °C (diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1674, 1652, 1640 and 1607; δ_{H} (90 MHz) 1.80 (3 H, s, 2-Me), 2.02 (6 H, s, 5 and 6-Me), 3.15 (1 H, d, *J* 17.28, 3-H), 3.36 (1 H, d, *J* 17.28, 3-H) and 7.25–7.45 (5 H, m, ArH); m/z 268 (M⁺, 4.2), 240 [(M - CO)⁺, 34] and 118 [(CH₂CMePh)⁺, 100%]. (Found: C, 75.95; H, 6.1. C₁₇H₁₆O₃ requires C, 76.10; H, 6.01%).

2,3-Dihydro-2-methoxy-2,5,6-trimethylbenzofuran-4,7-dione 6e.—The irradiation of **1** (100 mg, 0.66 mmol) and 2-methoxypropene (476 mg, 6.6 mmol) in acetone (20 cm³) for 4.5 h in a similar manner to that described above, followed by evaporation of the solvent, gave a residue, which was dissolved

in diethyl ether. Silver(I) oxide (100 mg, 0.43 mmol) and sodium sulfate (100 mg, 0.70 mmol) were added to the solution at room temperature under argon, and the solution was set aside overnight. After filtration of the reaction mixture, the filtrate was concentrated and the residue was subjected to chromatography on silica gel to afford **6e** (60 mg, 41%); an oil; *R*_f 0.38 (ethyl acetate-hexane 1 : 3); $\nu_{\max}/\text{cm}^{-1}$ (neat) 1673, 1651, 1640 and 1605; δ_{H} 90 MHz, 1.70 (3 H, s, 2-Me), 2.01 (6 H, s, 5- and 6-Me), 2.87 (1 H, d, *J* 17.80, 3-H), 3.13 (1 H, d, *J* 17.80, 3-H), 3.37 (3 H, s, OMe); m/z 222 (M⁺, 6.0), 194 [(M - CO)⁺, 55], 179 [(M - CO - Me)⁺, 65] and 43 (100) (Found: M⁺, 222.0918. C₁₂H₁₄O₄ requires M, 222.0892).

2,3-Dihydro-2,2-dimethyl-5-phenylbenzofuran-4,7-dione 7a.—The irradiation of **2** (100 mg, 0.50 mmol) and isobutene (560 mg, 10 mmol) in acetone (30 cm³) for 4.5 h gave **7d** (34 mg, 27%); m.p. 143–144 °C (from diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1669, 1647, 1640, 1588 and 1573; δ_{H} (90 MHz) 1.57 (6 H, s, 2-Me), 2.95 (2 H, s, 3-H), 6.63 (1 H, s, 6-H) and 7.44 (5 H, s, ArH); m/z 254 (M⁺, 100%) (Found: C, 75.6; H, 5.5. C₁₆H₁₄O₃ requires C, 75.57; H, 5.55%).

2,3-Dihydro-2-methyl-2,5-diphenylbenzofuran-4,7-dione 7d.—The irradiation of **2** (100 mg, 0.50 mmol) and α -methylstyrene (178 mg, 1.5 mmol) in acetone (30 cm³) for 16 h followed by separation by PLC on silica gel gave **7d** (50 mg, 32%); m.p. 85–87 °C (from diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1673, 1644, 1586 and 1571; δ_{H} (90 MHz) 1.86 (3 H, s, 2-Me), 3.24 (1 H, d, *J* 18.18, 3-H), 3.44 (1 H, d, *J* 18.18, 3-H), 6.67 (1 H, s, 6-H) and 7.25–7.45 (10 H, m, ArH); m/z 316 (M⁺, 36) and 118 [(CH₂CMePh)⁺, 100] (Found: C, 79.6; H, 5.2. C₂₁H₁₆O₃ requires C, 79.73; H, 5.10%).

2,3-Dihydro-4,7-dihydroxy-2-methyl-2,5-diphenylbenzofuran 9.—After irradiation, the solvent was evaporated. The residue was dissolved in diethyl ether (5 cm³) and to this solution were added pyridine (158 mg, 2 mmol) and acetyl chloride (118 mg, 1.5 mmol). The resulting mixture was stirred at room temperature for 2.5 days under argon and then diluted with diethyl ether. It was then washed with aqueous sodium hydrogen carbonate and brine, dried (K₂CO₃) and evaporated. Separation of the resulting residue by PLC on silica gel gave **9** (72 mg, 36%); m.p. 108–109 °C (from diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1767 and 1629; δ_{H} (90 MHz) 1.82 (3 H, s, 2-Me), 2.05 (3 H, s, COMe), 2.35 (3 H, s, COMe), 3.34 (2 H, s, 3-H), 6.97 (1 H, s, 6-H) and 7.25–7.5 (10 H, m); m/z 402 (M⁺, 20) and 318 [(M - 2(CH₂CO))⁺, 100] (Found: C, 74.7; H, 5.8. C₂₅H₂₂O₅ requires C, 74.61; H, 5.51%).

2,3,5,6,7,8-Hexahydro-2,2-dimethylnaphtho[2,3-*b*]furan-4,9-dione 8a.—The irradiation of **4** (41 mg, 0.23 mmol) and isobutene (392 mg, 7 mmol) in acetone (15 cm³) for 2 h gave **8d** (26 mg, 48%); m.p. 196–197 °C (from diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1668, 1648, 1635 and 1605; δ_{H} (90 MHz) 1.45–1.75 and 1.52 (combined 10 H m and s, 6-, 7-H and 2-Me₂), 2.35–2.5 (4 H, m, 5- and 8-H), 2.83 (2 H, s, 3-H); m/z 232 (M⁺, 60) and 204 [(M - CO)⁺, 100] (Found: C, 72.15; H, 6.9. C₁₄H₁₆O₃ requires C, 72.39; H, 6.94%).

2,3,5,6,7,8-Hexahydro-2-methyl-2-phenylnaphtho[2,3-*b*]furan-4,9-dione 8d.—The photolysis of **4** (55 mg, 0.31 mmol) and α -methylstyrene (106 mg, 0.9 mmol) in acetone (20 cm³) for 2.5 h gave **8d** (46 mg, 50%); m.p. 129–131 °C (diethyl ether-hexane); $\nu_{\max}/\text{cm}^{-1}$ 1667, 1650, 1635 and 1603; δ_{H} (90 MHz) 1.55–1.90 and 1.80 (combined 7 H, m and s, 6-, 8-H and 2-Me), 2.35–2.55 (4 H, m, 5- and 8-H), 3.15 (1 H, d, *J* 17.55, 3-H), 3.36 (1 H, d, *J* 17.55, 3-H) and 7.25–7.5 (5 H, m); m/z 294 (M⁺, 7.7),

266 [(M - CO)⁺, 49] and 118 [(CH₂CMePh)⁺, 100] (Found: C, 77.7; H, 6.1. C₁₉H₁₈O₃ requires C, 77.53; H, 6.16%).

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