Photochemical and Thermal Rearrangement of Acyl-Substituted Quinone Methides, Accessible by Dimethyldioxirane Oxidation of Benzofurans and Subsequent Valence Isomerization of the Resulting Epoxides

Waldemar Adam* and Markus Sauter

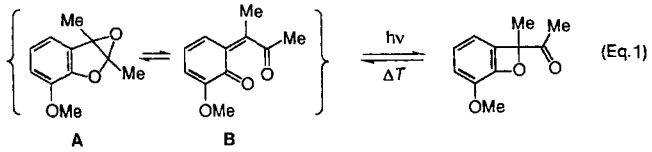
Institut für Organische Chemie der Universität Würzburg,
Am Hubland, D-97074 Würzburg, Germany

Received July 29, 1993

Key Words: Epoxidation / Dioxirane, dimethyl- / Benzofurans, 2-methyl-3-phenyl / Benzofuran epoxides / Quinone methides / (*Z*/*E*) Photoisomerization / Norcaradiene / Benzocycloheptafuran / Thermal rearrangement / Xanthenes, 9-acetyl-

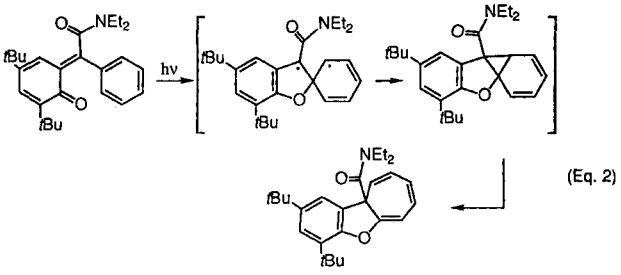
The photoisomerization of quinone methides **3** to benzocycloheptafuran **4** and the thermolysis of the latter to xanthenes **5** are reported. The quinone methides **3** are accessible by dimethyldioxirane oxidation and subsequent valence isomerization of the resulting benzofuran epoxides **2**. On irradiation ($\lambda > 400$ nm), the quinone methides **3** rearrange by cyclization to the corresponding norcaradiene, and ring enlargement affords the benzocycloheptafurans **4**. Thermolysis of the cycloheptatrienes **4** leads to the xanthenes **5**, first by cycloreversion to the norcaradienes, followed by electrocyclization to the chromenes and tautomerization of the latter. The new cycloheptatrienes **4** and xanthenes **5** were fully characterized.

As a part of our work on the oxidation of benzofurans by dimethyldioxirane, we reported[1] on the reversible valence isomerization between the 2,3-dimethylbenzofuran epoxide **A** and its corresponding quinone methide **B**. Unequivocal evidence for the equilibrium reaction **A** ⇌ **B** was obtained by irradiation of a nearly equimolar mixture of the quinone methide **B** and its epoxide **A** to afford the corresponding benzoxetene (Eq. 1)[1f]. When the latter was allowed to stand at −20°C for prolonged times, the same ratio of benzofuran epoxide **A** and its quinone methide **B**, as initially started with, was obtained by cycloreversion of the benzoxetene.

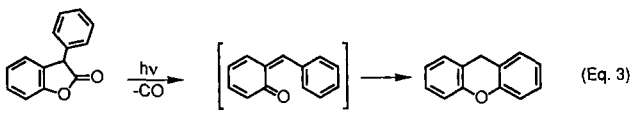


(Eq. 1)

Other examples of quinone methide photochemistry are rare in view of their propensity to dimerize and, consequently, their inherent lack of persistence. Nevertheless, Bos reported on the photoisomerization of a persistent quinone methide, which was stabilized by bulky substituents, to a benzocycloheptafuran (Eq. 2)[2]. As a plausible intermediate, the corresponding 1,3 diradical has been suggested, which after cyclization to the norcaradiene and valence isomerization affords the cycloheptatriene. On the other hand, Padwa investigated the photodecarbonylation of a 2-benzofuranone to the transient quinone methide, which on further photolysis gave the corresponding xanthene (Eq. 3)[3].



(Eq. 2)



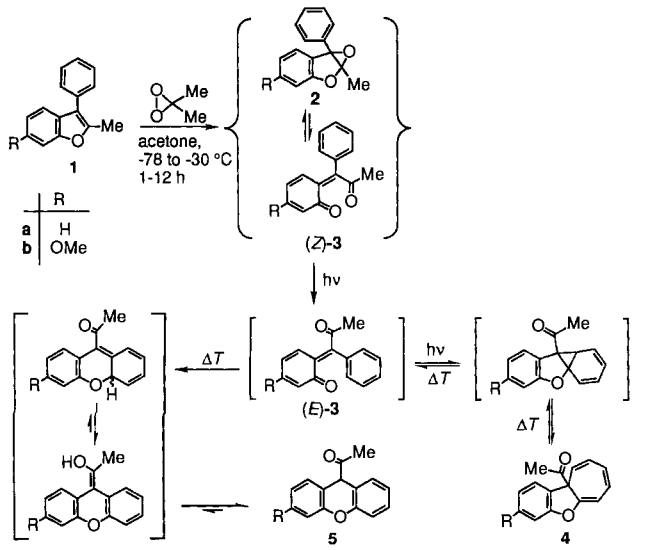
(Eq. 3)

In this paper we report on the photochemical behavior of the 3-phenyl-substituted quinone methides **3a,b** (Scheme 1). Epoxidation of 3-phenylbenzofurans **1a,b** by dimethyldioxirane afforded the epoxide **2a** and the quinone methide **3b** as confirmed by NMR spectroscopy[1e]. In view of the reversible valence isomerization **2a** ⇌ **3a**, the concentration of **3a** is high enough in the sample of **2a** for effective photolysis. Indeed, **3a** in the colored solution of **2a** shows an absorption with a $\lambda_{max} = 411$ nm and a strong tailing up to 575 nm, while **3b** starts absorbing at 570 nm with no absorption maximum below this wavelength.

Irradiation of **2a** and **3b** in acetone at −30°C and $\lambda > 400$ nm afforded essentially quantitatively (^{1}H NMR) the benzocycloheptafurans **4a,b**. In contrast to the 2,3-dimethylbenzofuran derivatives of Eq. 1[1f], no benzoxetenes were detected. The acid- and base-sensitive products were isolated in good yields by column chromatography on silica gel or alumina and fully characterized by IR, ^{1}H- and ^{13}C-NMR spectra, and elemental analysis.

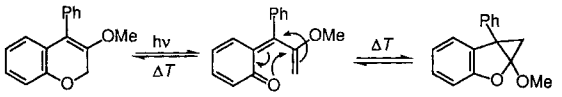
We propose that the mechanism for the formation of the cycloheptatrienes **4a,b** is analogous to that reported for the

Scheme 1



photoisomerization of the quinone methide shown in Eq. 2[2]. First, valence isomerization of the benzofuran epoxides **2a,b** leads to the quinone methides (*Z*)-**3a,b**, which on photoisomerization afford the (*E*)-**3a,b** diastereomers (Scheme 1). Subsequent photolysis of the quinone methides (*E*)-**3a,b** generates the transient norcaradiene and thermal valence isomerization finally the cycloheptatrienes **4a,b**.

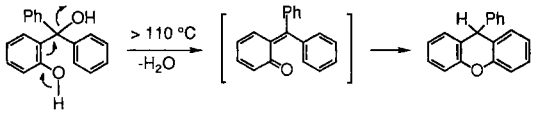
Alternatively, the formation of the norcaradiene in Scheme 1 can be rationalized in terms of a concerted process analogous to the photoisomerization of 3-phenyl-2*H*-chromene to an *ortho*-quinone allide (Eq. 4) reported by Padwa[4]. This quinone allide does not undergo [4 + 2] photocycloaddition, but rather rearranges to a benzocyclopropafuran. In contrast to the norcaradiene (Eq. 2, Scheme 1), the benzocyclopropafuran (Eq. 4) is detectable and even isolable.



(Eq. 4)

On heating in a sealed tube, the cycloheptatrienes **4a,b** isomerized to the corresponding xanthenes **5a,b** (Scheme 1). A rigorous structural assignment of the xanthenes **5a,b** was achieved by independent synthesis (see Experimental) of the derivative **5a**, whose spectral data are identical with those obtained from the thermolysis product of cycloheptatriene **4a**. Thermal repopulation of the norcaradienes and cycloreversion to the quinone methides (*E*)-**3a,b**, analogous to the retrocyclization of the benzocyclopropafuran (Eq. 4), constitute plausible transformations (Scheme 1). At elevated temperatures, the in situ regenerated quinone methides **3a,b** undergo electrocyclization to the intermediary chromenes. Sequential keto-enol tautomerization gives finally the corresponding xanthenes **5a,b**.

In support of this mechanism we cite the thermolysis of (*o*-hydroxyphenyl)-diphenylcarbinol, in which the quinone methide is formed by dehydration, and subsequent tautomerization leads to the expected 9-phenylxanthene (Eq. 5)[5]. Another example constitutes photodecarbonylation of the 3-phenyl-2-benzofuranone on irradiation at $\lambda = 245$ nm to the quinone methide, followed by electrocyclization and tautomerization to the corresponding xanthene (Eq. 3)[3].



(Eq. 5)

In conclusion, we have shown that the photolysis ($\lambda > 400$ nm) of the quinone methides (*Z*)-**3a,b** gives, after (*Z,E*) isomerization, the benzocycloheptafurans **4a,b**. Furthermore, thermolysis of the benzocycloheptafurans **4a,b** afford quantitatively the xanthenes **5a,b**. In the photochemical transformation (*E*)-**3**→**4** and the thermal process **4**→(*E*)-**3**→**5** the corresponding norcaradienes figure as key intermediates due to reversible valence isomerizations.

We thank the *Deutsche Forschungsgemeinschaft* (SFB 172 „Molekulare Mechanismen kanzerogener Primärveränderungen") and the *Fonds der Chemischen Industrie* for generous funding.

Experimental

Melting points: Reichert Thermovar hot stage apparatus. – IR: Perkin-Elmer 1420. – ^{1}H and ^{13}C NMR: Bruker AC 200 (200 MHz) or WM 400 (400 MHz); chemical shifts refer to $CDCl_3$. – Dimethyldioxirane[6] (as acetone solution) was prepared as previously described, for which the required potassium monoperoxy sulfate, the triple salt $2\,KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, was used as received. The 2-methyl-3-phenylbenzofurans **1a,b** were prepared in moderate overall yields according to ref.[7] and ref.[8], by first forming the 3-(aroyloxy)propiophenones followed by cyclization with concentrated sulfuric acid.

Epoxidation of 2-Methyl-3-phenylbenzofurans **1a,b** *by Dimethyldioxirane. – General Procedure:* A cooled (–78 °C) solution of dimethyldioxirane (1.2–1.4 equiv.) in acetone (ca. 0.01 M), dried over molecular sieves (3 Å) at –20 °C, was rapidly added to a cooled (–78 °C), and stirred solution of the 2-methyl-3-phenylbenzofurans **1a,b** (0.84–1.00 mmol) in absolute CH_2Cl_2 (2 ml) unter N_2. Stirring was continued until complete consumption (monitored by TLC) of the benzofurans **1**, while the reaction temperature was allowed to increase to –20 °C. The solvent was evaporated (–20 °C/0.01 Torr, 1–2 h) to yield quantitatively the epoxide **2a** and quinone methide **3b** in high purity (^{1}H NMR).

2,3-Dihydro-2,3-epoxy-4-methoxy-2-methyl-3-phenylbenzofuran (**2a**) was obtained quantitatively from 164 mg (0.79 mmol) benzofuran **1a** and 11 ml (0.92 mmol) dimethyldioxirane (0.084 M) according the above procedure at –78 to –10 °C for 7 h. – ^{1}H NMR (200 MHz, $CDCl_3$, –20 °C): δ = 1.73 (s, 3H), 7.01–7.09 (m, 2H), 7.34–7.55 (m, 7H). – ^{13}C NMR (50 MHz, $CDCl_3$, –20 °C): δ = 13.7 (q), 70.6 (s), 96.4 (s), 112.0 (d), 121.9 (d), 125.8 (d), 127.5 (d), 129.2 (d), 129.3 (d), 129.9 (s), 130.7 (d), 131.8 (s), 161.3 (s).

6-(1-Acetyl-1-phenyl)methylene-3-methoxy-2,4-cyclohexadienone (**3b**) was obtained quantitatively from 130 mg (0.55 mmol) benzofuran **1b** and 9 ml (0.71 mmol) dimethyldioxirane (0.079 M) according the above procedure at –78 to –20 °C for 1 h. – ^{1}H NMR (400 MHz, CD_2Cl_2, –20 °C): δ = 2.20 (s, 3H), 3.75 (s, 3H), 5.70 (d, J = 1.6 Hz, 1H), 6.19 (dd, J_1 = 10.1 Hz, J_2 = 1.6 Hz, 1H), 6.78 (d, J = 10.1 Hz, 1H), 7.35–7.50 (m, 5H). – ^{13}C NMR (100 MHz,

CD_2Cl_2, −20°C): δ = 28.0 (q), 56.1 (q), 101.2 (d), 122.6 (d), 127.3 (s), 128.6 (d), 129.2 (d), 130.1 (s), 131.4 (d), 131.8 (d), 160.0 (s), 170.5 (s), 185.1 (s), 203.9 (s).

Irradiation (λ > 360 nm) of Epoxide **2a** *and Quinone Methide* **3b**. — *General Procedure:* The epoxide **2a** (ca. 0.5 mmol) or the quinone methide **3b**, which were prepared as described above, were irradiated by sodium lamps (2 × 250 W) in ca. 10 ml of acetone at −10°C under N_2 until the conversion was complete (12−18 h, monitored by TLC). After solvent distillation, the residue was purified by column chromatography on neutral alumina and Et_2O as eluent.

Benzocycloheptafuran **4a** was obtained in 72% yield (127 mg) as a pale yellow oil according to the above procedure. — IR (CCl_4): $\tilde{\nu}$ = 3000 cm^{-1}, 2905, 1705, 1640, 1590, 1460, 1450, 1340, 1270, 1230, 1160, 1145, 900, 695. — ^1H NMR (200 MHz, $CDCl_3$): δ = 1.93 (s, 3H), 5.42 (d, *J* = 9.3 Hz, 1H), 6.35−6.49 (m, 4H), 7.07−7.16 (m, 2H), 7.27−7.42 (m, 2H). — ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.9 (q), 64.9 (s), 101.2 (d), 110.6 (d), 120.3 (d), 123.1 (d), 123.6 (d), 125.8 (d), 126.2 (d), 127.1 (d), 128.6 (s), 130.0 (d), 152.4 (s), 157.3 (s), 202.0 (s). — $C_{15}H_{12}O_2$ (224.3): calcd. C 80.34, H 5.39; found C 80.56, H 5.30.

Benzocycloheptafuran **4b** was obtained in 56% yield (83 mg) as a pale yellow oil according to the above procedure. — IR (CCl_4): $\tilde{\nu}$ = 3065 cm^{-1}, 3000, 2865, 1750, 1685, 1640, 1620, 1520, 1460, 1350, 1160, 1120, 1040, 925. — ^1H NMR (200 MHz, $CDCl_3$): δ = 1.90 (s, 3H), 3.81 (s, 3H), 5.41 (d, *J* = 10.4 Hz, 1H), 6.28−6.55 (m, 4H), 6.62−6.68 (m, 2H), 7.28 (d, *J* = 9.0 Hz, 1H). — ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.9 (q), 55.7 (q), 64.9 (s), 101.2 (d), 110.6 (d), 120.3 (d), 123.1 (d), 123.6 (d), 125.8 (d), 126.2 (d), 127.1 (d), 128.6 (s), 130.0 (d), 152.4 (s), 157.3 (s), 202.0 (s). — $C_{16}H_{14}O_3$ (254.3): calcd. C 75.57, H 5.55; found C 75.08, H 5.70.

Thermolysis of the Benzocycloheptafurans **4a,b**. — *General Procedure:* The benzocycloheptafurans **4a,b** were heated at reflux in $CDCl_3$ in a sealed NMR tube at ca. 100°C until complete conversion (monitored by ^1H NMR). The products were purified by column chromatography on silica gel with Et_2O/pentane (1:4) as eluent.

9-Acetylxanthene (**5a**) was obtained in 94% yield (119 mg) as colorless needles, mp 62−63°C (Et_2O), as described above. — IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 3020, 1690, 1465, 1440, 1290, 1240, 1175, 1110, 890. — ^1H NMR (200 MHz, $CDCl_3$): δ = 1.93 (s, 3H), 4.89 (s, 1H), 7.03−7.36 (m, 8H). — ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.7 (q), 54.3 (d), 117.2 (d), 118.3 (s), 123.6 (d), 128.9 (d), 129.4 (d), 150.8 (s), 205.7 (s). — $C_{15}H_{12}O_2$ (224.3): calcd. C 80.34, H 5.39; found C 80.40, H 5.55.

Synthesis of 9-Acetylxanthene (**5a**): To a stirred solution of xanthene (500 mg, 2.74 mmol) in Et_2O (10 ml) under N_2 at 0°C was added slowly *n*BuLi (1.90 ml, 2.75 mmol; 1.42 M in hexane). After 2 h at 0°C, the reaction mixture was cooled to −20°C, and acetaldehyde (128 mg, 2.90 mmol) was added. The mixture was allowed to reach room temperature during 15 h and subsequently poured into an aqueous NH_4Cl solution (50 ml) and extracted with Et_2O (3 × 20 ml). After drying of the combined extracts with $MgSO_4$ and evaporation of the solvent, the crude product was oxidized without further purification by Jones reagent (CrO_3/H_2SO_4) in Et_2O at 20°C for 10 h. Usual workup and chromatography (silica gel, Et_2O/pentane) afforded 360 mg (59%) of 9-acetylxanthene (**5a**), mp 62−63°C. The spectral data were identical with those obtained from the thermolysis product of the cycloheptatriene **4a**.

9-Acetyl-3-methoxyxanthene (**5b**) was obtained in 96% yield (80 mg) as colorless needles, mp 54−55°C (Et_2O), as described above. — IR (CCl_4): $\tilde{\nu}$ = 2970 cm^{-1}, 2940, 1730, 1645, 1520, 1500, 1450, 1250, 1165, 1100. — ^1H NMR (200 MHz, $CDCl_3$): δ = 1.90 (s, 3H), 3.83 (s, 3H), 4.82 (s, 1H), 6.65−6.71 (m, 2H), 7.02−7.17 (m, 5H). — ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.5 (q), 53.6 (d), 55.5 (q), 102.0 (d), 110.3 (s), 110.4 (d), 117.1 (d), 118.4 (s), 123.6 (d), 128.9 (d), 129.3 (d), 129.5 (d), 150.7 (s), 151.6 (s), 160.5 (s), 206.1 (s). — $C_{16}H_{14}O_3$ (254.3): calcd. C 75.57, H 5.55; found C 75.25, H 5.76.

[1] [1a] W. Adam, J. Bialas, L. Hadjiarapoglou, M. Sauter, *Chem. Ber.* **1992**, *125*, 231−234. — [1b] W. Adam, H. Hadjiarapoglou, T. Mosandl, C. Saha-Möller, D. Wild, *J. Am. Chem. Soc.* **1991**, *113*, 8005−8011. — [1c] W. Adam, M. Sauter, *Liebigs Ann. Chem.* **1992**, 1095−1096. — [1d] W. Adam, L. Hadjiarapoglou, T. Mosandl, C. R. Saha-Möller, D. Wild, *Angew. Chem.* **1991**, *103*, 187−189; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 200−202. — [1e] W. Adam, L. Hadjiarapoglou, K. Peters, M. Sauter, *Angew. Chem.* **1993**, *105*, 769−770, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 735−736. — [1f] W. Adam, L. Hadjiarapoglou, K. Peters, M. Sauter, *J. Am. Chem. Soc.*, in press.

[2] W. Verboom, H. J. T. Bos, *Tetrahedron Lett.* **1978**, 1229−1230.

[3] A. Padwa, G. A. Lee, *J. Am. Chem. Soc.* **1973**, *95*, 6147−6149.

[4] A. Padwa, A. Au, G. A. Lee, W. Owens, *J. Am. Chem. Soc.* **1976**, *98*, 3555−3564.

[5] M. Gomberg, D. Nishida, *J. Am. Chem. Soc.* **1923**, *45*, 190−222.

[6] W. Adam, J. Bialas, L. Hadjiarapoglou, *Chem. Ber.* **1991**, *124*, 2377.

[7] G. Cardillo, R. Cricchio, L. Merlini, *Tetrahedron* **1971**, *27*, 1875−1883.

[8] R. Royer, C. Hudry, *Bull. Soc. Chim. Fr.* **1961**, 939−943.

[248/93]