Base-Induced Chemiluminescence of Acetoxy-Substituted Benzofuran Dioxetanes by an Intramolecular Electron Transfer (CIEEL) Mechanism

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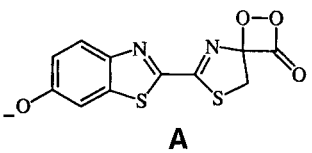
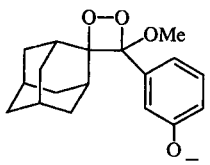
Tetraphenylporphine-sensitized photooxygenation of acetoxy-substituted benzofuran derivatives **2** afforded the corresponding benzofuran dioxetanes **3**. The base-induced decomposition of these dioxetanes was studied and shown to involve an intramolecular CIEEL emission. The CIEEL chemiluminescence quantum yields were measured. The dioxetane **3e**, in which the electron donor is located *meta* to the dioxetane site, exhibits the highest chemiluminescence of all derivatives investigated.

The chemistry of 1,2-dioxetanes has been intensively studied during the last 20 years[1]. It was established that these high-energy molecules generate mainly triplet-excited carbonyl products on thermal decomposition. In contrast, with fluorescent electron donors dioxetanes display *c*hemically *i*nitiated *e*lectron *e*xchange *l*uminescence (CIEEL)[2]. This mechanism was originally discovered by Schuster[3] for diphenoyl peroxide (dibenzo[*d*,*f*][1,2]dioxocin-5,8-dione), in which singlet-excited states play a significant role. An efficient intramolecular example represents the Firefly bioluminescence, in which an α-peroxy lactone (1,2-dioxetanone) **A** intervenes[4]. It is the phenolate moiety which serves as internal electron donor to afford, after electron transfer and decarboxylation, the singlet-excited oxyluciferin as emitter[5].



A



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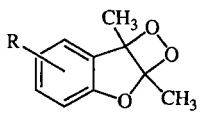

C

As an extension of this phenomenon figures the base- or enzyme-catalyzed release of the phenolate site in the spiroadamantane-dioxetane **B**[6]. The interesting biochemical aspects of such tailor-made dioxetanes have recently been reviewed[7,8], which offer numerous opportunities for clinical applications.

Viewed from this perspective, we have been interested in the mutagenic 2,3-dimethylbenzofuran dioxetanes[9] **C**, which cause DNA damage by alkylation[10] and are readily accessible by photooxygenation of benzofurans. Thus, to develop CIEEL-active dioxetanes of the benzofuran type, which should serve as potential DNA probes, it was of interest to prepare a series of acetoxy-substituted benzofurans, convert them into the corresponding dioxetanes, and trigger CIEEL by base-catalyzed saponification. In this paper we present the results of our investigation and confirm that these dioxetanes are effective for electron transfer chemiluminescence.

Results

Synthesis and Decomposition of Benzofuran Dioxetanes

The hydroxy-substituted benzofurans **1a–c** were prepared according to literature procedures[11]. Derivatives **1d** and **e** were obtained from their corresponding methyl ethers by the reaction with boron tribromide in dichloromethane at 0°C in good yields (49–60%). The required methyl ethers were prepared from 3-methylbenzofuran and 2- or 3-methoxyphenylmercuric chloride by using the Heck arylation[12]. The procedure worked quite well for the *ortho* isomer but poorly for the *meta* isomer. The reported synthesis of 2-(3-methoxyphenyl)-3-methylbenzofuran was found to be more problematic than described[13]. Acetylation of the phenolic derivatives **1a–e** with acetic anhydride in pyridine afforded the desired esters **2a–e** (Scheme 1) in yields of 75–85% after column chromatography.

In the tetraphenylporphine (TPP)-sensitized photooxygenation of the benzofurans **2a–e** in dichloromethane at −25°C the corresponding benzofuran dioxetanes **3a–e** were formed as major (50–66%) and the allylic hydroperoxides **6** as minor (<10%) products (Scheme 1), except in the case of benzofuran **2e**. The latter gave the relatively stable hydroperoxide **6e** in 37% and the dioxetane **3e** in only 20% yield after column chromatography on silica gel at low temperatures (−20 to −30°C). In the photooxygenation of the benzofuran **2d** only 50–60% conversion could

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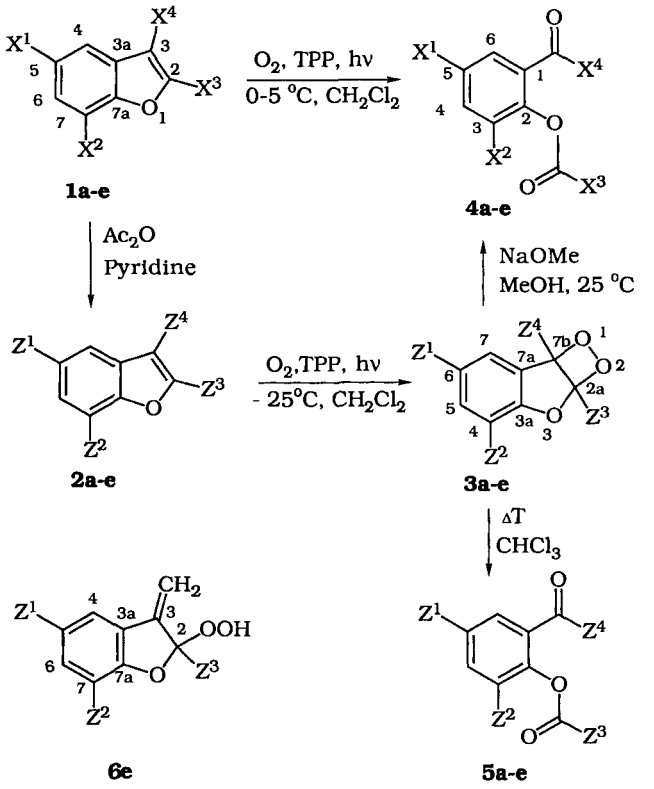
be achieved after 16 h at −25 °C. The structures of the dioxetanes **3a–e** were unequivocally assigned on the basis of their spectral and analytical data and by their chemiluminescence.

Scheme 1. Synthesis of benzofuran dioxetanes **3** and their cleavage products



	X^1	X^2	X^3	X^4
1a, 4a	OH	H	Me	Me
1b, 4b	H	OH	Me	Me
1c, 4c	H	H	Me	4′-C_6H_4OH
1d, 4d	H	H	2′-C_6H_4OH	Me
1e, 4e	H	H	3′-C_6H_4OH	Me
	Z^1	Z^2	Z^3	Z^4
2a, 3a, 5a	OAc	H	Me	Me
2b, 3b, 5b	H	OAc	Me	Me
2c, 3c, 5c	H	H	Me	4′-C_6H_4OAc
2d, 3d, 5d	H	H	2′-C_6H_4OAc	Me
2e, 3e, 5e, 6e	H	H	3′-C_6H_4OAc	Me

The thermal decomposition of the benzofuran dioxetanes **3a–e** gave the expected carbonyl compounds **5a–e** (Scheme 1), all literature-known except derivative **5e**. The decomposition products were isolated and identified on the basis of their spectral and analytical data.

The thermal stability of the dioxetanes **3** depends on their substitution pattern at the dioxetane ring. For example, it was observed that the 2a,7b-dimethyl derivatives **3a, b** are more stable then the 7b-aryl one **3c**. Furthermore, the 2a-aryl derivatives **3d, e** show a significant difference in their thermal stability in regard to regioisomers. Thus, the *ortho* isomer **3d** was considerable more reluctant towards thermal decomposition than the *meta* isomer **3e**.

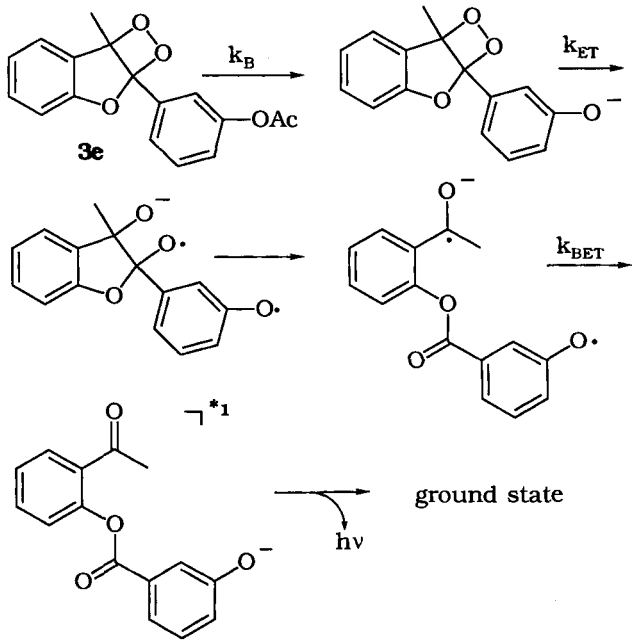
Synthesis of the Base-Induced Decomposition Products of the Benzofuran Dioxetanes

The hydroxy-substituted products **4a–e** were formed in the decomposition of the acetoxy-substituted benzofuran dioxetanes **3a–e** under basic conditions; their phenolate ions are considered to be the light-emitting species in the supposed CIEEL mechanism. Since it was too cumbersome to isolate these decomposition products directly from the base-catalyzed decomposition mixture (subsequent saponification of the newly generated ester functionality at the 2-position), the derivatives **4a–e** were prepared by TPP-sensitized photooxygenation of the hydroxy-substituted benzofurans **1a–e** in dichloromethane at 0–5 °C. At these elevated temperatures the corresponding dioxetanes do not survive and decompose to give the cleavage products **4a–e**. These compounds are new and had to be fully characterized. Before recording the optical spectra (UV/fluorescence), **4a, b** were purified by preparative HPLC and **4c–e** by repeated recrystallization.

Chemiluminescence Measurements of the Benzofuran Dioxetanes 3a–e

The base-induced decomposition of the acetoxy-substituted dioxetanes **3a–e** was performed by treatment with NaOMe in methanol to set free the corresponding phenolate ion, the species responsible for the CIEEL decomposition (Scheme 2)[6]. The results of the base-induced chemiluminescence of **3a–e** are displayed in Table 1. The observed intensity-time profiles were evaluated according to first-or-

Scheme 2. CIEEL mechanism for the base-induced decomposition of benzofuran dioxetanes



der kinetics and the chemiluminescence yields (Φ^{CIEEL}) determined as described in the literature procedure. The Hastings-Weber[14] scintillation "cocktail" was used as light standard. With the 2a-aryl derivative **3e**, that bears the electron donor in the *meta* position, the highest chemiluminescence yield of all cases investigated here was detected.

Table 1. CIEEL data for the benzofuran dioxetanes **3a–e** in methanol at 25°C

Dioxetane[a]	k [min^{-1}][b]	$\Phi^{CIEEL} \cdot 10^7$ [Einstein/mol]
3a	0.67	0.49
3b	0.37	1.12
3c	0.50	0.15
3d	0.59	1.50
3e[c]	0.19	42.0

[a] [Diox] = 0.001 M. – [b] 3 Equivalents of NaOMe in MeOH were added in all cases, error 10%. – [c] [Diox] = 0.0001 M.

Although the chemiluminescence curves fit first-order kinetics, it must be noted that the decomposition rate depended on the amount of base used. At a higher base concentration a faster decomposition with a greater emission of light took place, but the experimental chemiluminescence yields remained the same within ca. 20% error.

To determine the singlet-excitation efficiencies (Φ^S) of **3b–e** in their base-catalysed decomposition, the fluorescence quantum yields (Φ^{Fl}) of the emitting phenolate ions of the esters **4b–e** are essential[15]. Unfortunately, these are not known and efforts were made to measure them. In the case of the dioxetanes **3b, c** no fluorescence could be detected from the phenolate ions of the base-induced decomposition products **4b, c**. The fluorescence quantum yields of the phenolate ions of the esters **4d, e**, which are formed in the base-catalysed decomposition of the dioxetanes **3d, e**, could not be determined because subsequent hydrolysis and/or methanolysis of the esters **4d, e** took place under basic conditions. Experiments to generate the anion with weaker bases such as pyrrolidine in dichloromethane showed, that the phenolate ions of the esters **4d, e** are too weakly fluorescent for quantitative measurements with our instrumentation. Only in the case of dioxetane **3a** did we succeed to determine the fluorescence quantum yield of the phenolate ion derived from the base-induced decomposition product **4a** in methanol at pH 10–11, namely $\Phi^{Fl} = 0.040 \pm 0.004$. With this fluorescence quantum yield a singlet-excitation efficiency of $\Phi^S = 1.2 \pm 0.2 \cdot 10^{-6}$ was estimated.

Discussion

The results presented herein demonstrate that the decomposition of the acetyl-protected hydroxy-substituted benzofuran dioxetanes **3a–e**, prepared by photooxygenation of the corresponding benzofurans **2a–e** at low temperatures, can rapidly be induced by saponification by base. This base-promoted decomposition results in appreciable chemiluminescence, which is considerably higher than the light emission derived from the direct thermal decomposition of these dioxetanes. This speaks for an intramolecular electron transfer (CIEEL) mechanism[2], which yields a high proportion of singlet-excited carbonyl species and hence fluorescence.

The proposed mechanism (Scheme 2) involves first the formation of a phenolate ion by saponification, which subsequently acts as intramolecular electron donor. After single-electron transfer (SET), breakage of the O–O bond with formation of a ketyl radical, and electron back-transfer (BET) the electronically excited ester phenolate ion is generated, which deactivates with fluorescence.

The fact, however, that the chemiluminescence emission did not obey strict first-order kinetics for this CIEEL reaction, suggests a more complicated process. Indeed, a product study showed that from the reaction of the dioxetanes **3a, b** with NaOMe, besides the expected cleavage products **4a, b**, substantial amounts of unidentified higher-molecular-weight material were obtained. On the other hand, in the case of the dioxetanes **3c–e**, however, the base-promoted reactions were cleaner and in addition to the expected cleavage products **4c–e** also their saponified esters were detected by ^{1}H- and ^{13}C-NMR spectroscopy. Actually, the saponification of the esters **4** was unavoidable under the experimental conditions, even when only one equivalent of base was used. In the latter case, the consumption of the dioxetane was incomplete, so that for the representative experiments in Table 1 an excess (3 equiv.) of base was employed.

The observation that the time profile of the emission decay and the absolute light intensity itself depended on the concentration of base used, additionally bear out the complexity of the CIEEL system, the acetylated hydroxy-substituted benzofuran dioxetanes **3** studied herein. Presumably the rate of deacetylation (k_B in Scheme 2) to generate the phenolate ion and the rate of electron transfer (k_{ET} in Scheme 2) from the phenolate site to the dioxetane moiety are within the same order of magnitude, which necessarily implies complex kinetics. Moreover, while the base-induced decomposition of the *meta* acetoxy-substituted dioxetane **3e** resulted in a long and intense glow-like chemiluminescence, the corresponding *ortho* isomer **3d** and the dioxetanes **3a–c** exhibited flash-like chemiluminescence. This behavior was previously described for base-induced CIEEL, but appears not yet fully understood[6,7,16]. It is significant in this context to emphasize that the dioxetane **3e** with the glow-like emission on alkaline saponification is also the most efficient CIEEL-active system investigated here.

The CIEEL experiments with NaOH in water or with nBu$_4$NOH in CH_2Cl_2 gave higher light intensities than in MeOH, but in view of the very fast decomposition, these conditions were of no particular advantage and were not further investigated. Furthermore, problems were encountered in the determination of the fluorescence quantum yields (Φ^{Fl}) of the phenolate ions derived from the esters **4a–e**, because, except for derivative **4a**, the observed fluorescence was too weak under the conditions employed for quantification with our instrumentation. Thus, for the phenolate ion derived from ester **4a** a fluorescence quantum yield $\Phi^{Fl} = 0.040 \pm 0.004$ was determined, from which together

with the experimental CIEEL quantum yield $\Phi^{CIEEL} = 4.9 \cdot 10^{-8}$ Einstein/mol a singlet efficiency $\Phi^{S} = 1.2 \pm 0.2 \cdot 10^{-6}$ Einstein/mol was estimated for **4a**. These benzofuran dioxetanes **3** are, indeed, rather inefficient base-promoted CIEEL systems, but not worse than the reported acetoxy-substituted spiroadamantane-type dioxetanes[7]. This is especially borne out, if the CIEEL quantum yields Φ^{CIEEL} of the corresponding *meta*-substituted dioxetanes are compared; the *meta* derivative **3e** is the most efficient system investigated herein.

In summary, we report in this paper on the successful synthesis of the first CIEEL-active benzofuran dioxetanes **3**. The ability of these dioxetanes to undergo base-triggered decomposition with appreciable chemiluminescence is demonstrated. It was shown that in the chemically initiated electron transfer (CIEEL) mechanism operates under alkaline saponification of these dioxetanes with the highest CIEEL quantum yields Φ^{CIEEL} observed for the *meta* acetoxy-substituted dioxetane **3e**.

We thank the *Deutsche Forschungsgemeinschaft* (SFB 172 "Molekulare Mechanismen kanzerogener Primärveränderungen"), the *Wilhelm-Sander-Stiftung*, and the *Fonds der Chemischen Industrie* for generous financial support.

Experimental

IR: Perkin Elmer 1420. – UV: Hitachi U-3200. – Fluorescence spectra: Perkin Elmer LS 50. – ^{1}H and ^{13}C NMR: Bruker AC 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz) or Bruker AC 250 (^{1}H: 250 MHz, ^{13}C: 63 MHz), tetramethylsilane or deuteriochloroform as internal standards. – Elemental analyses: Microanalytical Division of the Institute of Inorganic Chemistry, University of Würzburg or of the University of Gießen. – Melting points: Reichert Thermovar apparatus. – Silica gel (63–200 mesh; Woelm) was used for column chromatography. – TLC analyses: silica gel foils Polygram SIL G/UV_{254} (40 × 80), Macherey & Nagel.

Starting Materials: The hydroxy-substituted benzofuran derivatives **1a–c** were prepared as described[11]. Derivatives **1d** and **1e** were obtained by demethylation of the corresponding methyl ethers with BBr_3 analogous to the literature procedure[17]. The required methyl ethers were synthesized by Heck-arylation of 3-methylbenzofuran with 2-methoxyphenylmercuric chloride or 3-methoxyphenylmercuric chloride analogous to the reported procedure[12]. The physical and spectral data of these compounds were consistent with those reported[13,18,19].

2-(3-Hydroxyphenyl)-3-methylbenzofuran (**1e**) was obtained as a yellow oil in 66% yield after column chromatography by eluting with petroleum ether (30–70°C)/ether (1:1). – IR (film): $\tilde{\nu}$ = 3640–3100 cm^{-1} (OH), 3050, 2910, 1860, 1610, 1580 (C=C), 1455, 1230, 1190, 1110, 1080, 900, 745. – ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.46 (s, 3H, CH_3), 5.20 (br. s, 1H, OH), 6.83 (m, 1H, arom. H), 7.20–7.55 (m, 7H, arom. H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 9.42 (q, CH_3), 110.9 (d), 111.6 (d), 113.3 (d), 114.9 (d), 119.3 (2 d), 122.3 (d), 124.4 (d), 129.8 (d), 131.0 (s), 132.8 (s), 150.1 (s, C-2), 153.6 (s, C-7a), 155.6 (s, C–OH).

$C_{15}H_{12}O_2$ (224.3) Calcd. C 80.34 H 5.39
Found C 80.73 H 5.49

The acetoxy-substituted benzofuran derivatives **2a–e** were prepared from the corresponding hydroxy compounds **1a–e** by acetylation with acetic anhydride in pyridine according to the literature procedure[19]. Derivatives **2a**, **b**, and **d** are known and their physical and spectral data are consistent with those reported[20,21].

3-(4-Acetoxyphenyl)-2-methylbenzofuran (**2c**) was obtained in 75% yield as colorless needles after column chromatography by eluting with petroleum ether (30–70°C)/ether (1:1); m.p. 59–61°C. – IR (KBr): $\tilde{\nu}$ = 3060 cm^{-1}, 2910, 1740 (C=O), 1500 (C=C), 1445, 1370, 1245, 1210, 1190, 1160, 960, 915, 750. – ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.35 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 7.18–7.26 (m, 4H, arom. H), 7.44–7.59 (m, 4H, arom. H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 12.8 (q, CH_3), 21.2 (q, CH_3), 110.8 (2 d), 116.1 (d), 119.2 (d), 121.9 (d), 122.7 (d), 123.0 (d), 123.6 (d), 128.6 (s), 129.9 (2 d), 130.5 (s), 149.5 (s, C-2), 151.4 (s, *C*–OAc), 154.0 (s, C-7a), 169.6 (s, C=O).

$C_{17}H_{14}O_3$ (266.3) Calcd. C 76.67 H 5.30
Found C 76.51 H 5.36

2-(3-Acetoxyphenyl)-3-methylbenzofuran (**2e**) was obtained in 82% yield as colorless needles after column chromatography by eluting with petroleum ether (30–70°C)/ether (1:1); m.p. 44–45°C. – IR (KBr): $\tilde{\nu}$ = 3080 cm^{-1}, 2970, 2930, 2880, 1770 (C=O), 1620, 1585 (C=C), 1460, 1375, 1210, 1180, 1165, 940, 700. – ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.25 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 7.00 (m, 1H, arom. H), 7.14–7.26 (m, 2H, arom. H), 7.35–7.50 (m, 4H, arom. H), 7.60 (m, 1H, arom. H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 9.41 (q, CH_3), 21.1 (q, CH_3), 110.9 (d), 112.0 (s), 119.3 (d), 119.6 (d), 120.9 (d), 122.4 (d), 123.9 (d), 124.6 (d), 129.5 (d), 130.9 (s), 132.8 (s), 149.5 (s, C-2), 150.8 (s, *C*–OAc), 153.7 (s, C-7a), 169.3 (s, C=O).

$C_{17}H_{14}O_3$ (266.3) Calcd. C 76.67 H 5.30
Found C 77.02 H 5.50

Preparation of the Benzofuran Dioxetanes **3** *by Photooxygenation of the Benzofuran Derivatives* **2**. – *General Procedure:* Into a 100-ml test tube, equipped with a gas inlet and outlet, was placed a solution of the corresponding benzofuran **2** (0.40–2.50 mmol) and 2–10 mg of tetraphenylporphine (TPP) in metal-free (distilled from EDTA) dichloromethane. The solution was cooled to the appropiate temperature (–20 to –35°C) by means of a methanol bath with the help of a MGW Lauda Cryomat. A gentle stream of dry oxygen gas was bubbled through the solution while irradiating with two 150-W sodium lamps (Philips G/98/2 SON 150-W). The reaction progress was monitored by TLC. After complete consumption of the starting material the solution was concentrated in a rotary evaporator at 0°C/15 Torr and the residue chromatographed on silica gel (63–200 mesh) at –25°C.

6-Acetoxy-2a,7b-dihydro-2a,7b-dimethyl-1,2-dioxeto[3,4-b]benzofuran (**3a**) was previously described[9].

4-Acetoxy-2a,7b-dihydro-2a,7b-dimethyl-1,2-dioxeto[3,4-b]benzofuran (**3b**): Photooxygenation of 450 mg (2.20 mmol) of **2b** in 50 ml of dichloromethane at –35°C for 2 h gave 300 mg (58%) of **3b** as a yellow oil after column chromatography of the crude product by eluting with petroleum ether (30–50°C)/ether (2:1). On standing at –20°C for 6 h pale yellow needles were obtained, m.p. 60–61°C. – IR (CCl_4): $\tilde{\nu}$ = 2940 cm^{-1}, 1780 (C=O), 1480, 1370, 1260, 1220, 1200, 1020. – ^{1}H NMR ($CDCl_3$, –20°C, 200 MHz): δ = 1.90 (s, 6H, 2 CH_3), 2.30 (s, 3H, CH_3), 7.05–7.25 (m, 3H, arom. H). – ^{13}C NMR ($CDCl_3$, –20°C, 50 MHz): δ = 17.4 (q, CH_3), 17.9 (q, CH_3), 20.9 (q, CH_3), 94.7 (s, C-7b), 112.5 (s), 119.3 (s, C-2a), 121.3 (d), 123.2 (d), 125.4 (d), 130.5 (s, C-3a), 134.7 (s, *C*–OAc), 168.9 (s, C=O).

$C_{12}H_{12}O_5$ (236.2) Calcd. C 61.02 H 5.12
Found C 61.12 H 5.44

7b-(4-Acetoxyphenyl)-2a,7b-dihydro-2a-methyl-1,2-dioxeto[3,4-b]benzofuran (**3c**): Photooxygenation of 300 mg (1.13 mmol) of **2c** in 50 ml of dichloromethane (10 ml of acetone was added for so-

lubilization) at −25°C for 2 h gave 230 mg (68%) of **3c** as a yellow oil after column chromatography of the crude product by eluting with dichloromethane. On standing for 3 d at −20°C yellow needles were obtained, m.p. 55−56°C. − IR (CCl_4): $\tilde{\nu}$ = 3020 cm^{-1}, 1795 (C=O), 1540, 1500 (C=C), 1400, 1290, 1220, 1185, 1110, 1010. − ^1H NMR ($CDCl_3$, −30°C, 200 MHz): δ = 1.52 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 7.08−7.21 (m, 5H, arom. H), 7.40−7.52 (m, 3H, arom. H). − ^{13}C NMR ($CDCl_3$, −30°C, 50 MHz): δ = 18.9 (q, CH_3), 21.3 (q, CH_3), 97.6 (s, C-7b), 111.7 (d), 119.3 (s, C-2a), 122.0 (2 d), 123.0 (d), 126.0 (d), 127.4 (s), 128.7 (2 d), 131.0 (s), 132.4 (d), 151.0 (s, *C*−OAc), 161.4 (s, C-3a), 169.7 (s, C=O).

$C_{17}H_{14}O_5$ (298.3) Calcd. C 68.45 H 4.73
Found C 68.52 H 4.66

2a-(2-Acetoxyphenyl)-2a,7b-dihydro-7b-methyl-1,2-dioxeto[3,4-b]benzofuran (**3d**): Photooxygenation of 160 mg (0.600 mmol) of **2d** in 50 ml of dichloromethane at −20°C for 16 h (62% conversion) gave 65.0 mg (58%) of **3d** as a brown-yellow solid after column chromatography of the crude product by eluting with petroleum ether (30−50°C)/ether (2:1). Recrystallization from petroleum ether (30−50°C)/dichloromethane (10:1) afforded yellow needles, m.p. 87−90°C. − IR (CCl_4): $\tilde{\nu}$ = 2960 cm^{-1}, 2930, 2870, 1775 (C=O), 1605 (C=C), 1465, 1365, 1280, 1225, 1185, 1105, 1000, 910. − ^1H NMR ($CDCl_3$, −25°C, 200 MHz): δ = 1.54 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 7.08−7.20 (m, 3H, arom. H), 7.35−7.60 (m, 4H, arom. H), 7.90 (dd, *J* = 7.5/1.8 Hz, 1H, arom. H). − ^{13}C NMR ($CDCl_3$, −25°C, 50 MHz): δ = 17.7 (q, CH_3), 20.1 (q, CH_3), 96.5 (s, C-7b), 111.5 (d), 117.1 (s, C-2a), 122.0 (s), 123.5 (d), 123.8 (d), 124.8 (d), 126.2 (d), 128.0 (s), 128.5 (d), 131.5 (d), 132.1 (d), 147.3 (s, *C*−OAc), 160.6 (s, C-3a), 168.8 (s, C=O).

$C_{17}H_{14}O_5$ (298.3) Calcd. C 68.45 H 4.73
Found C 68.43 H 4.56

2a-(3-Acetoxyphenyl)-2a,7b-dihydro-7b-methyl-1,2-dioxeto[3,4-b]benzofuran (**3e**): Photooxygenation of 110 mg (0.431 mmol) of **2e** in 20 ml of dichloromethane at −25°C for 16 h (90% conversion) gave after column chromatography of the crude product by eluting with petroleum ether (30−50°C)/ether (2:1) 25.0 mg (20%) of **3e** as a yellow oil and 45.0 mg (37%) of **6e**, which was fully characterized. − **3e**: IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 2950, 2920, 1760 (C=O), 1610 (C=C), 1595, 1460, 1440, 1365, 1280, 1260, 1195, 1115, 1010, 930. − ^1H NMR ($CDCl_3$, −20°C, 200 MHz): δ = 1.58 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 7.10−7.75 (m, 8H, arom. H). − ^{13}C NMR ($CDCl_3$, −20°C, 50 MHz): δ = 18.4 (q, CH_3), 21.3 (q, CH_3), 96.7 (s, C-7b), 112.0 (d), 120.7 (d), 123.0 (d), 123.5 (s, C-2a), 123.9 (d), 124.1 (d), 124.8 (d), 127.9 (s), 130.0 (d), 132.1 (d), 133.7 (s), 150.5 (s, *C*−OAc), 160.5 (s, C-3a), 169.8 (s, C=O).

$C_{17}H_{14}O_5$ (298.3) Calcd. C 68.45 H 4.73
Found C 68.28 H 4.83

2-(3-Acetoxyphenyl)-2,3-dihydro-2-(hydroperoxy)-3-methylenebenzofuran (**6e**): Colorless powder, m.p. 84−85°C. − IR (KBr): $\tilde{\nu}$ = 3420−3120 cm^{-1} (OOH), 3070, 1735 (C=O), 1610, 1585 (C=C), 1460, 1230, 1005, 945, 900, 755, 695. − ^1H NMR ($CDCl_3$, 200 MHz, −20°C): δ = 2.30 (s, 3H, CH_3), 5.31 (s, 1H, $=CH_2$), 5.83 (s, 1H, $=CH_2$), 6.99−7.06 (m, 3H, arom. H), 7.27−7.31 (m, 2H, arom. H), 7.41−7.48 (m, 3H, arom. H), 9.25 (s, 1H, OOH). − ^{13}C NMR ($CDCl_3$, 50 MHz, −20°C): δ = 21.4 (q, CH_3), 110.3 (t, CH_2), 110.5 (d), 113.9 (s), 119.3 (d), 121.4 (d), 122.0 (d), 122.5 (d), 123.4 (d), 123.7 (s), 129.7 (d), 130.9 (d), 138.5 (s), 142.9 (s), 150.3 (s), 159.2 (s, C-7a), 170.1 (s, O−C=O).

$C_{17}H_{14}O_5$ (298.3) Calcd. C 68.45 H 4.73
Found C 68.25 H 4.90

Preparation of the Base-Induced Cleavage Products **4a−e** *by Photooxygenation of the Corresponding Benzofurans* **1**. − *General Procedure:* Into a 100-ml test tube, equipped with a gas inlet and outlet, was placed a solution of the corresponding benzofuran **1** (0.12−3.10 mmol) and 2−10 mg of tetraphenylporphine (TPP) dichloromethane. The solution was cooled to the appropriate temp. (−5 to +5°C) by means of a methanol bath with the help of a MGW Lauda Cryomat. A gentle stream of dry oxygen gas was bubbled through the solution while irradiating with two 150-W sodium lamps (Philips G/98/2 SON 150-W). The reaction progress was monitored by TLC. After complete consumption of the starting material, the solution was concentrated in a rotary evaporator at room temp. and 15 Torr and the residue chromatographed on silica gel (63−200 mesh).

2-Acetoxy-5-hydroxyacetophenone (**4a**): Photooxygenation of 500 mg (3.10 mmol) of **1a** in 50 ml of dichloromethane at −5°C for 2 h gave 90 mg (15%) of **4a** after column chromatography of the crude product by eluting with petroleum ether (30−70°C)/ether (1:1). The impure product was purified by means of preparative HPLC to afford 60.0 mg (10%) of **4a** as colorless needles, m.p. 105−106°C. − IR (CCl_4): $\tilde{\nu}$ = 3500−3100 cm^{-1} (OH), 2940, 1760 (C=O), 1660 (C=O), 1575 (C=C), 1490, 1375, 1295, 1215, 1185, 1010, 965, 905, 880, 835, 795. − UV (MeOH): λ_{max} (lg ε) = 219 nm (4.21), 244 (3.67), 301 (3.44). − ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.32 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 6.50 (s, 1H, OH), 6.85−6.95 (m, 2H, arom. H), 7.12 (dd, $J_{6,4}$ = 2.4, $J_{6,3}$ = 0.4 Hz, 1H, 6-H). − ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 21.2 (q, CH_3), 29.2 (q, CH_3), 116.9 (d), 120.6 (d), 124.7 (d), 130.6 (s), 142.0 (s, C-2), 153.9 (s, C-5), 171.1 (s, O−C=O), 198.0 (C=O).

$C_{10}H_{10}O_4$ (194.2) Calcd. C 61.86 H 5.19
Found C 61.61 H 5.17

2-Acetoxy-3-hydroxyacetophenone (**4b**): Photooxygenation of 300 mg (1.85 mmol) of **1b** in 50 ml of dichloromethane at −5°C for 2 h gave 137 mg (38%) of **4b** after column chromatography of the crude product by eluting with petroleum ether (30−70°C)/ether (2:1). The impure product was recrystallized from dichloromethane/petroleum ether (30−50°C) (9:1) and purified by preparative HPLC to afford 50.0 mg (13%) of **4b** as colorless needles, m.p. 53−55°C. − IR (CCl_4): $\tilde{\nu}$ = 3040 cm^{-1}, 1785 (C=O), 1655 (C=O), 1450, 1375, 1330, 1260, 1210, 1185, 1090, 1020, 990, 935, 840. − UV (MeOH): λ_{max} (lg ε) = 212 nm (4.24), 255 (3.91), 331 (3.43). − ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.35 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 6.90 (dd, $J_{5,4}$ = 8.0, $J_{5,6}$ = 8.1 Hz, 1H, 5-H), 7.26 (dd, $J_{4,5}$ = 8.0, $J_{4,6}$ = 1.6 Hz, 1H, 4-H), 7.65 (dd, $J_{6,5}$ = 8.1, $J_{6,4}$ = 1.6 Hz, 1H, 6-H), 12.4 (s, 1H, OH). − ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 20.4 (q, CH_3), 26.7 (q, CH_3), 118.2 (d), 120.9 (s), 128.0 (d), 129.1 (d), 139.5 (s, C-2), 154.3 (s, C-3), 168.7 (s, O−C=O), 204.4 (s, C-7).

$C_{10}H_{10}O_4$ (194.2) Calcd. C 61.86 H 5.19
Found C 62.00 H 5.21

2-Acetoxy-4'-hydroxybenzophenone (**4c**): Photooxygenation of 25.0 mg (0.111 mmol) of **1c** in 10 ml of dichloromethane (1 ml of acetone added for solubilization) at 5°C for 1 h gave 15.0 mg (60%) of **4c** after column chromatography of the crude product by eluting with petroleum ether (30−70°C)/ether (1:2) and recrystallization from petroleum ether (30−50°C)/ether (10:1) as colorless needles, m.p. 125−126°C. − IR (KBr): $\tilde{\nu}$ = 3350 cm^{-1} (OH), 3050, 2920, 1740 (C=O), 1645 (C=O), 1600 (C=C), 1570, 1510, 1370, 1310, 1285, 1220, 1190, 1150, 1100, 940, 910, 850, 755. − UV (MeOH): λ_{max} (lg ε) = 224 nm (3.98), 294 (4.11). − ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.96 (s, 3H, CH_3), 6.18 (br. s, 1H, OH), 6.76 (AA'BB' pattern, *J* = 8.8 Hz, 2H, arom. H), 7.08−7.29 (m, 2H, arom. H), 7.39−7.50 (m, 2H, arom. H), 7.65 (AA'BB' pattern, *J* = 8.7 Hz, 2H, arom. H). − ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 20.6 (q, CH_3), 115.3 (2 d), 123.1 (d), 125.7 (d), 130.0 (d), 130.1 (s), 131.8 (d), 132.0

(s), 132.7 (2 d), 148.4 (s, C-2), 160.5 (s, C-4'), 169.5 (s, O–C=O), 193.6 (s, C=O).

$C_{15}H_{12}O_4$ (256.2) Calcd. C 70.31 H 4.72
Found C 69.99 H 4.61

2-(2-Hydroxybenzoyloxy)acetophenone (**4d**): Photooxygenation of 400 mg (1.78 mmol) of **1d** in 25 ml of dichloromethane at 5°C for 5 h gave 112 mg (24%) of **4d** after column chromatography of the crude product by eluting with petroleum ether (30–70°C)/ether (1:1) as a pale yellow oil, which solidified after 6 h at −20°C, m.p. 58–60°C. – IR (KBr): $\tilde{\nu}$ = 3150 cm^{-1} (OH), 3060, 3000, 1685 (2 C=O), 1620, 1600, 1585 (C=C), 1480, 1290, 1250, 1200, 1150, 1070, 755. – UV (MeOH): λ_{max} (lg ε) = 239 nm (4.16), 308 (3.69). – ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.54 (s, 3H, CH_3), 6.93–7.07 (m, 2H, arom. H), 7.22 (dd overlapped by $CDCl_3$ signal, $J_{3,4}$ = 7.7, $J_{3,5}$ = 1.3 Hz, 1H, 3-H), 7.39 (dt, J_1 = J_2 = 7.6, J_3 = 1.1 Hz, 1H, arom. H), 7.49–7.64 (m, 2H, arom. H), 7.87 (dd, $J_{6',5'}$ = 7.8, $J_{6',4'}$ = 1.7 Hz, 1H, 6'-H), 8.07 (dd, $J_{6,5}$ = 8.0, $J_{6,4}$ = 1.7 Hz, 1H, 6-H), 10.3 (s, 1H, OH). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 29.4 (q, CH_3), 111.7 (s), 117.8 (d), 119.6 (d), 123.8 (d), 126.5 (d), 130.4 (2 d), 130.9 (s), 133.4 (d), 136.5 (d), 148.4 (s, C-2), 162.0 (s, C-2'), 168.7 (s, O–C=O), 197.0 (s, C=O).

$C_{15}H_{12}O_4$ (256.2) Calcd. C 70.31 H 4.72
Found C 69.94 H 4.65

2-(3-Hydroxybenzoyloxy)acetophenone (**4e**): Photooxygenation of 30.0 mg (0.134 mmol) of **1e** in 20 ml of dichloromethane at 0°C for 15 h gave 12.0 mg (35%) of **4e** after column chromatography of the crude product by eluting with petroleum ether (30–70°C)/ether (1:1) and recrystallization from dichloromethane/petroleum ether (30–70°C) (2:1) as colorless needles, m.p. 105–106°C. – IR (KBr): $\tilde{\nu}$ = 3500–3100 cm^{-1} (OH), 3060, 2995, 1730 (C=O), 1670 (C=O), 1605, 1590, 1480, 1360, 1290, 1190, 1080, 995, 925, 760, 740. – UV (MeOH): λ_{max} (lg ε) = 238 nm (4.37), 306 (3.74). – ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.49 (s, 3H, CH_3), 5.95 (br. s, 1H, OH), 7.05 (ddd, J_1 = 8.1, J_2 = 2.6, J_3 = 0.8 Hz, 1H, arom. H), 7.16 (dd, J_1 = 8.1, J_2 = 1.0 Hz, 1H, arom. H), 7.25–7.35 (m, 2H, arom. H), 7.52 (dt, J_1 = 7.9, J_2 = 1.5 Hz, 1H, arom. H), 7.58 (dd, $J_{2',4'}$ = $J_{2',6'}$ = 2.0 Hz, 1H, 2'-H), 7.68 (ddd, J_1 = 7.8, J_2 = J_3 = 0.4 Hz, 1H, arom. H), 7.79 (dd, $J_{6,5}$ = 7.7, $J_{6,4}$ = 1.6 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 29.7 (q, CH_3), 116.8 (d), 121.1 (d), 122.6 (d), 123.9 (d), 126.2 (d), 129.9 (d), 130.3 (d), 130.5 (s), 131.0 (s), 133.6 (d), 149.3 (s, C-2), 156.0 (s, C-3'), 165.1 (s, O–C=O), 198.2 (C=O).

$C_{15}H_{12}O_4$ (256.2) Calcd. C 70.31 H 4.72
Found C 70.54 H 4.79

Preparation of the Thermal Decomposition Products **5a–e** *of the Benzofuran Dioxetanes* **3**. – *General Procedure:* The dioxetanes **3** (0.020–0.500 mmol) were heated in dichloromethane or chloroform for several hours, until all of the starting material was consumed (monitored by TLC, negative peroxide test). The solution was then evaporated in a rotary evaporator at room temp./15 Torr and the crude product crystallized or chromatographed on silica gel (63–200 mesh). **5a** and **5b** were not isolated from the thermal dioxetane decomposition but prepared independently by acetylation of the corresponding hydroxy compounds **4a** and **4b** with acetic anhydride in pyridine analogous to the literature procedure[19]. Their ^{1}H-NMR data matched those of the thermal dioxetane decomposition products. The compounds **5a–d** are known and their melting points and spectral data matched those reported.

2,5-Diacetoxyacetophenone (**5a**) was obtained in 61% yield from **4a** and recrystallized from ether/petroleum ether (50–70°C) (3:1) to afford colorless needles, m.p. 67–68°C (Lit.[22] 68°C). – IR (KBr): $\tilde{\nu}$ = 1765 cm^{-1} (O–C=O), 1695 (C=O).

2,3-Diacetoxyacetophenone (**5b**) was obtained in 25% yield from **4b** and recrystallized from ether/petroleum ether (50–70°C) (1:1) to afford colorless needles, m.p. 108–109°C (Lit.[23] 109°C). – IR (KBr): $\tilde{\nu}$ = 1730 cm^{-1} (O–C=O), 1685 (C=O).

2,4'-Diacetoxybenzophenone (**5c**) was obtained in 60% yield from dioxetane **3c** after recrystallization from petroleum ether (50–60°C)/dichloromethane (10:1) as pale yellow needles, m.p. 87–88°C (Lit.[24] 88°C). – IR (KBr): $\tilde{\nu}$ = 1762 cm^{-1} (O–C=O), 1752 (O–C=O), 1667 (C=O).

2-(2-Acetoxybenzoyloxy)acetophenone (**5d**) was obtained in 63% yield from dioxetane **3d** after column chromatography by eluting with petroleum ether (50–60°C)/ether (1:1) as a pale yellow oil, which was crystallized from ethanol to afford colorless needles, m.p. 92–93°C (Lit.[25] 93°C). – IR (KBr): $\tilde{\nu}$ = 1765 cm^{-1} (O–C=O), 1750 (O–C=O), 1680 (C=O). – UV (MeOH): λ_{max} (lg ε) = 233 nm (4.54), 281 (3.75).

2-(3-Acetoxybenzoyloxy)acetophenone (**5e**): A solution of 10 mg (0.034 mmol) of dioxetane **3e** in 8 ml of chloroform was refluxed for 6 h and the solvent evaporated. The residue was recrystallized from petroleum ether (30–70°C)/dichloromethane (1:1) to afford 6.00 mg (60%) of **5e** as colorless needles, m.p. 64–65°C. – IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1}, 2860, 1770 (O–C=O), 1730 (O–C=O), 1680 (C=O), 1600 (C=C), 1450, 1370, 1290, 1280, 1200, 1190, 1070, 940, 780. – UV (MeOH): λ_{max} (lg ε) = 233 nm (4.62), 282 (3.84). – ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.27 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 7.15 (d, J = 8.1 Hz, 1H, arom. H), 7.28–7.36 (m, 2H, arom. H), 7.43–7.58 (m, 2H, arom. H), 7.80 (dd, J_1 = 8.1, J_2 = 1.1 Hz, 1H, aromat. H), 7.85 (dd, $J_{2',4'}$ = $J_{2',6'}$ = 2.0 Hz, 1H, 2'-H), 8.02 (d, $J_{6,5}$ = 8.0 Hz, 1H, 6-H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 21.1 (q, CH_3), 29.7 (q, CH_3), 123.5 (d), 123.9 (d), 126.3 (d), 127.2 (d), 127.7 (d), 129.8 (d), 130.3 (d), 130.8 (s), 131.1 (s), 133.5 (d), 149.2 (s, C-2), 150.8 (s, *C*–OAc), 164.3 (s, O–C=O), 169.2 (s, O–C=O), 197.4 (s, C=O).

$C_{17}H_{14}O_5$ (298.3) Calcd. C 68.45 H 4.73
Found C 68.56 H 4.72

CIEEL Measurements of the Benzofuran Dioxetanes **4**. – *General Procedure:* All measurements were performed on a Mitchell-Hastings photometer. From a 0.001 M stock solution of the dioxetane in methanol or dichloromethane was transferred 3 ml into a scintillation tube and the latter placed into the photometer, which was thermostated with the help of a MGW Lauda Cryomat at 25 or 37°C. After 5–7 min an appropriate amount of base (0.1 M NaOMe or 0.1 M tetra-*n*-butylammonium hydroxide in methanol) was added by means of a syringe through the rubber septum under rigorous exclusion of light, with the photomultiplier open for immediate measurement. The light emission was recorded with a Servogor Z10 recorder and the intensity-time traces processed according to first-order kinetics. The light intensity was calibrated by means of the scintillation "cocktail" of Hastings and Weber[14] as a light standard. The CIEEL results are summarized in Table 1.

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