Ring Cleavage of Benzofurans and Tetrahydrobenzofurans by *m*-Chloroperbenzoic Acid Epoxidation

Waldemar Adam*, Michael Ahrweiler, and Markus Sauter

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

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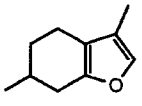
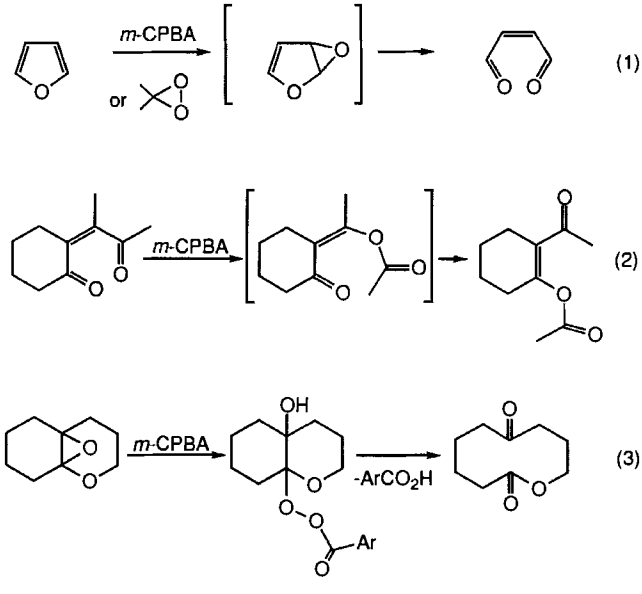
The oxidation of the benzofurans **1a–f** (tetrahydrobenzofurans **1g, h**) with excess *m*-CPBA is reported. The in situ generated, highly reactive benzofuran epoxides **2a–f** and their quinone methides **3a–f** (*cis*-ene diones **3g, h**) afford the labile tautomeric peroxy esters **5** and **5′** by nucleophilic addition of the peroxy acid. On elimination of *m*-chlorobenzoic acid, the peroxy esters **5/5′** of the benzofuran derivatives **1a–f** rearrange thermally to the keto esters **6** by C–C cleavage or to the spiro epoxides **7** by C–O cleavage. The latter undergo thermal isomerization to the 1,3-benzodioxoles **8** and Diels-Alder cycloaddition to the corresponding dimers **9**. Independently, the keto esters **6** and the 1,3-dioxoles **8** were synthesized by thermolysis of the dioxetanes **11**. The tautomeric *m*-CPBA adducts **5/5′** of the persistent ene diones **3g, h**, derived from the tetrahydrobenzofuran derivatives **1g, h**, rearrange as well to the spiro epoxides **7g, h**. In contrast to the benzofuran derivatives **6a–f**, the keto enol ester **6h** suffers Baeyer-Villiger rearrangement with another molecule of *m*-CPBA to form the ene diester **10h**.

Benzofurans and their tetrahydro derivatives constitute an important group of heterocyclic arenes. Menthofuran, for instance, a naturally occuring compound, is of interest as a cytotoxic terpene in mint oil and as a proximate genotoxic mammalian metabolite of the monoterpene (*R*)-(+)-pulegone[1]. In the oxidative metabolism of such cytotoxic natural furans, the corresponding epoxides have been proposed quite generally to be the active agents in the mutagenicity by alkylation[2]. For example, the benzofuran epoxides appear to be the ultimate mutagens in the high mutagenicity exhibited by the corresponding dioxetanes[3] for the *Salmonella typhimurium* strain TA100[4].



menthofuran

On the other hand, experimental evidence for the existence of furan epoxides and their biological activity is still lacking[5]. In this context, the oxidation of furans by *m*-CPBA[6] and dimethyldioxirane[5,7] (DMD) leads to the strongly electrophilic *cis*-ene diones (Eq. 1), the valence isomers of the furan epoxides, which have been shown to be cytotoxic and even mutagenic[8]. In contrast to DMD, the *m*-CPBA oxidation of furans, reported by Jennings[9], is accompanied by side products, which are formed by attack of a second molecule of the peracid on the labile *cis*-ene diones (Eq. 2). This fact was also observed in the *m*-CPBA oxidation of enol ethers (Eq. 3)[10]. The formation of the cyclic keto ester was explained in terms of a nucleophilic attack of the peracid on the epoxide of the enol ether to generate an β-hydroxy perester, which by Criegee-Hock rearrangement[11] gave the C=C cleavage product.



The *m*-CPBA oxidation of benzofurans has been investigated by Royer[12] and Winternitz[13]. The isolation of the epoxide derived from the oxidation of 6-hydroxy-3-(*p*-methoxyphenyl)-2-methylbenzofuran by *m*-CPBA was claimed, after subsequent etherification with methyl iodide[12]. However, we have rigorously established that in such DMD oxidations the quinone methide, formed by valence isomerization of the corresponding epoxide, constitutes the

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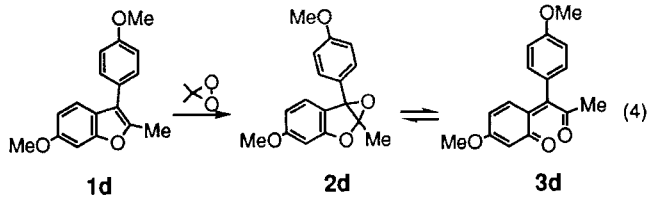
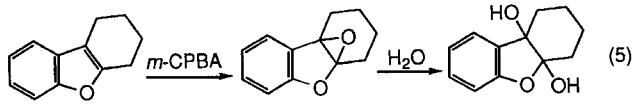
only oxygen transfer product (Eq. 4)[14]. Furthermore, the *m*-CPBA oxidation of 4,5,6,7-tetrahydrodibenzofuran was proposed to yield the corresponding epoxide and, in the presence of water, the diol (Eq. 5)[13].





Since the above literature examples on the *m*-CPBA oxidation of benzofurans contradict our experiences with DMD oxidations, which established that benzofuran epoxides constitute the most labile and reactive epoxides known to date[15], we were prompted to reinvestigate the *m*-CPBA oxidation of selected benzofuran derivatives. Herewith, we report on the *m*-CPBA oxidation of the benzofurans **1a–f** and of the tetrahydrobenzofurans **1g**, **h** (Scheme 1).

Results

The product studies are collected in Table 1. For none of the furans **1a–h** the corresponding epoxides **2a–h** could be detected by NMR analysis under the described conditions.

Thus, the reaction of 2,3-dimethylbenzofuran (**1a**) with one equivalent of water-free *m*-CPBA gave after 3 h at room temperature a 76:24 mixture of the alcohols **4a/4'a** in 81% yield and as side-products 5% of 2-(acetoxy)acetophenone (**6a**), 7% of the 1,3-benzodioxole **8a**, and 7% of dimer **9a** (entry 1, Table 1). The structures of **4a/4'a**, **6a**, **8a**, and **9a** were assigned by comparison of their spectral data with those reported[3]. In contrast, with an excess of *m*-CPBA (ca. three equivalents) benzofuran **1a** afforded the dimer **9a** in 74%, the keto ester **6a** in 5%, and the 1,3-benzodioxole **8a** in 21% yield (Scheme 1), as determined by ^{1}H-NMR analysis of the crude product (entry 2).

An NMR experiment on independently prepared epoxide **2a** (by DMD[15] epoxidation) showed that treatment with one equivalent of *m*-CPBA at −50°C in $CDCl_3$ led to a mixture of the adducts **5a** and **5'a**. These were assigned on the basis of their characteristic ^{13}C-NMR shifts at δ = 88.9 (s) and 89.3 (s) for the respective peroxide carbon atoms. After warmup to room temperature, these signals disappeared, and the corresponding rearrangement products **6a** and **7a** were detected.

3-Methyl-2-phenylbenzofuran (**1b**) afforded with *m*-CPBA (2.2 equivalents) the C=C cleavage product **6b** in 34% yield, together with the dimer **9b** of the spiro epoxide **7b** in 66% yield (Scheme 1), as revealed by ^{1}H- and ^{13}C-NMR analysis (entry 3). The structure of **6b** was ascertained by comparison of its characteristic spectral data with those reported; furthermore, the spectral data of dimer **9b** are in good accord with those of dimer **9a**.

Scheme 1

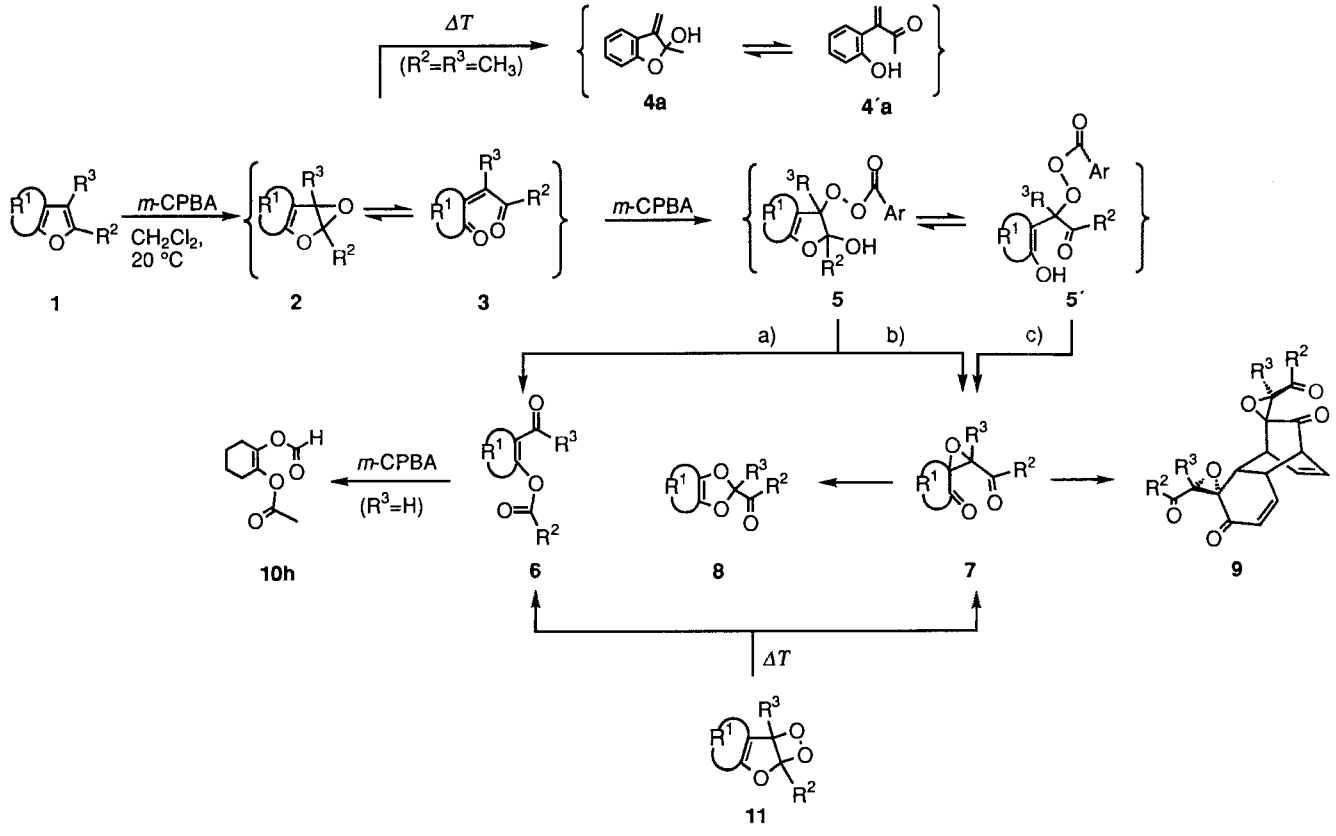
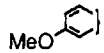
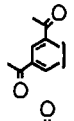


Table 1. *m*-CPBA oxidation of benzofurans **1a–f** and of tetrahydrobenzofurans **1g, h**

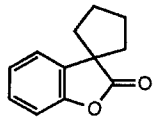
Entry		R^1	R^2	R^3	*m*-CPBA (equiv.)	Time [h]	Product Distribution[a] 4	4′	5	6	7	8	9	10	yield[b](%)
1	**1a**		Me	Me	1.0	3	62	19	-	5	-	7	7	-	83
2	**1a**	"	Me	Me	2.7	5	-	-	-	5	-	21	74	-	79
3	**1b**	"	Ph	Me	2.2	2	-	-	-	34	-	-	66	-	93
4	**1c**	"	Me	Ph	1.0	3	-	-	-	33	-	67	-	-	67
5	**1c**	"	Me	Ph	2.3	3	-	-	-	69	-	31	-	-	73
6	**1d**		Me	*p*-An[c]	2.2	1	-	-	-	-	-	100	-	-	48
7	**1e**		CH_2CH_2	CH_2 CH_2	2.4	6	-	-	-	-	-	-	100	-	93
8	**1f**		Me	Me	2.5	7	-	-	100[d]	-	-	-	-	-	54
9	**1g**		Me	Me	2.3	1	-	-	-	-	100	-	-	-	90
10	**1h**		Me	H	2.1	0.5	-	-	-	62	22[e]	-	-	16	61

[a] Product distribution normalized to 100%; conversion >95%; values determined by ^{1}H-NMR analysis directly on the crude product mixture (±5% error of stated values). – [b] Isolated yield. – [c] *p*-An = *para*-anisyl. – [d] On prolonged storage at room temperature, **5f/5′f** rearranged to **6f**. – [e] Suffered decomposition on workup.

For benzofuran **1c** (entry 4), the *m*-CPBA oxidation (one equivalent) yielded the corresponding cleavage product **6c** and the 1,3-benzodioxole **8c** in a ratio of 33:67 (67% yield, referred to consumed *m*-CPBA). However, the use of an excess (2.3 equivalents) of *m*-CPBA under the identical conditions afforded a **6c**:**8c** ratio of 69:31 (entry 5). Authentic samples of the cleavage product **6c** and 1,3-benzodioxole **8c** were prepared by thermolysis of dioxetane **11c**.

Benzofuran **1d**, for which Royer has reported[12] the epoxide **2d**, afforded under the nearly identical conditions the 1,3-benzodioxole **8d** (entry 6). Neither epoxide **2d** nor its valence-isomeric quinone methide **3d** could be detected by NMR analysis.

Unusual was the chemical fate of the benzofuran **1e** towards an excess (2.4 equivalent) of *m*-CPBA, since after workup exclusively the dimeric spiro epoxide **9e** was isolated (entry 7). To ascetain that the corresponding C=C cleavage product **6e** was not formed, the latter was prepared by thermolysis of the dioxetane **11e**. Moreover, the epoxide **2e** reported by Winternitz[13] could not be detected. Even on DMD oxidation of benzofuran **1e** at –20°C the corresponding epoxide **2e** could not be detected. Rather, the spiro-2-benzofuranone **12e** was isolated and characterized.



12e

In the oxidation of the electron-poor benzofuran **1f** (entry 8) with *m*-CPBA (2.50 equivalents), the peresters **5f/5′f** (82:18) were detected, as revealed by the characteristic ^{13}C-NMR signals of the peroxidic carbons at δ = 81.8 (s), 88.5 (s), and 89.3 (s). On prolonged exposure to room temperature **5f** rearranged to **6f**.

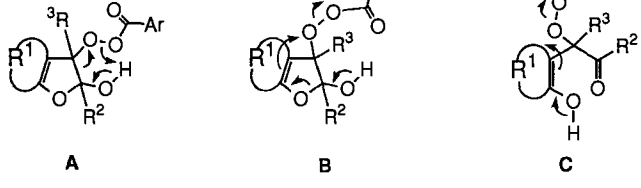
The *m*-CPBA (2.3 equivalents) oxidation of tetrahydrobenzofuran (entry 9) **1g** afforded at room temperature for 1 h the spiroepoxide **7g**[5] nearly quantitatively; not even traces of the C=C cleavage product **6g** were detected by NMR spectroscopy. That the keto enol ester **6g** was not formed or was lost during the workup was established by repeating the reaction in $CDCl_3$ at 0°C and by ^{1}H-NMR monitoring. The only detectable compounds were the *cis*-ene dione **3g** as the first oxidation product and the spiro epoxide **7g** as the double-oxidation product. Interestingly, the *m*-CPBA adduct **5g** was not observed. In contrast to the thermolysis of the corresponding dioxetane[5], the C=C cleavage product **6g** was not formed.

The tetrahydrobenzofuran **1h** (entry 10) gave on reaction with an excess of dry (!) *m*-CPBA (2.5 equivalents) in $CDCl_3$ the keto enol ester **6h**, the spiro epoxide **7h**, and the oxidation product **10h** (Baeyer-Villiger rearrangement of the C=C cleavage product **6h**) in a ratio of 62:16:22 (NMR analysis on the crude oxidation mixture). On workup, during extraction with an aqueous solution of $NaHCO_3$ or NaOH, the spiro epoxide **7h** suffered decomposition. Moreover, by using wet *m*-CPBA (15–20% water), **7h** was not detected.

Discussion

Benzofuran epoxides **2** are to date the most reactive epoxides known towards the addition of nucleophiles, e.g. without acid assistance they add methanol at −78°C[15d], a reactivity not exhibited even by arene oxides[17]. Therefore, it is not surprising that we could not observe the epoxides **2a–f** in the *m*-CPBA oxidation of the benzofurans **1a–f**. The reason is that the in situ formed epoxides **2** are attacked by another molecule of *m*-CPBA to yield the α-hydroxy peroxy esters **5** and **5′** (Scheme 1). However, when the *m*-CPBA concentration is low or the epoxide **2** too reactive, as it is the case for derivative **2a** (Table 1, entry 1), the epoxide **2a** rearranges to the alcohol **4a** and its ring-opened tautomer **4′a**[3] (Scheme 1). The β-hydroxy peroxy esters **5/5′**, due to their peroxidic nature, are also very labile compounds and only the 4,6-diacetyl derivative **5f** (Table 1, entry 8) could be isolated. The peroxy esters **5**, derived from the benzofurans **1a–e**, could only be detected by NMR spectroscopy at −40°C.

Two decomposition modes are available to the peroxy esters **5/5′**: in the transition state **A**, C–C cleavage in the ring-closed tautomer **5** with elimination of *m*-chlorobenzoic acid leads to the keto esters **6** (Table 1, entries 1–6, 8). Alternatively, the ring-closed tautomer **5** suffers also C–O cleavage via the transition state **B** to afford on elimination of *m*-chlorobenzoic acid the corresponding spiro epoxides **7** (Table 1, entries 1–7). These spiro epoxides **7** may also result from the ring-opened tautomers **5′** according to transition state **C**. The transition states **B** and **C** constitute backside nucleophilic attack of the aromatic π system on the peroxide bond. In this context it is relevant to mention that on thermolysis the benzofuran dioxetanes **11** (Scheme 1) afforded the expected keto esters **6** and the spiro epoxides **7**, unusual rearrangement products for which precedents have been reported[3].



The resulting spiro epoxides **7** undergo highly stereoselective dimerization[3] by a Diels-Alder reaction (Scheme 1) to the corresponding dimers **9** (Table 1, entries 1–3, 7). Alternatively, the spiro epoxides **7** rearrange thermally (Scheme 1) to the 1,3-benzodioxoles **8** (Table 1, entries 1, 2, 4–6).

The tetrahydro derivatives **1g, h** behave very similarly towards *m*-CPBA as the benzo systems **1a–f**. Thus, the observed valence-isomeric ene diones **3g, h** (Table 1, entries 9, 10) yield either the keto enol ester **6h** (Table 1, entry 10) on C–C bond cleavage or the spiro epoxides **7g, h** (Table 1, entries 9, 10) on C–O bond scission (Scheme 1). In contrast to the benzo keto ester **6a**, which is resistant towards further oxidation by *m*-CPBA, the keto enol ester **6h** gives on Baeyer-Villiger rearrangement by *m*-CPBA (Table 1, entry 10) the ene diester **10h** (Scheme 1).

In summary, we have shown that *m*-CPBA oxidation of the benzofurans **1** affords the highly reactive epoxides **2** as intermediates, which are nucleophilically trapped by additional *m*-CPBA to afford the peroxy esters **5/5′**. The latter cleave to the keto esters **6** and spiro epoxides **7** as the final oxidation products, which are also formed in the thermal decomposition products of the corresponding 1,2-dioxetanes (Scheme 1). Our results do not substantiate the claim[12,13] that benzofuran epoxides can be prepared under these conditions. Such labile epoxides **2** and their valence-isomeric quinone methides **3** can be spectrally detected[14,15] in the low-temperature epoxidation of the benzofurans **1** by dimethyldioxirane. Furthermore, the formation of the spiro epoxides **7g, h** by *m*-CPBA reaction of the ene diones **3g, h** is the more likely oxidation pathway than the Baeyer-Villiger rearrangement postulated by Jennings[9] for the *m*-CPBA oxidation of the ene diones **3** derived from the tetrahydrobenzofuran derivatives.

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Experimental

Melting points: Reichert Thermovar hot-stage apparatus. – IR: Perkin Elmer 1420. – ^1H and ^{13}C NMR: Bruker AC 200 (200 MHz), AC 250 (250 MHz), WM 400 (400 MHz), chemical shifts refer to $CDCl_3$. – MS: Varian 8200 Finnigan MAT. – Elemental analyses: Analytical Division of the Institute of Inorganic Chemistry (University of Würzburg). – All solvents were purified by following standard literature methods. The oxidations were carried out with dry *m*-CPBA, unless otherwise stated. Dimethyldioxirane (as acetone solution) was prepared according to the published procedure[16]. The dimethyldioxirane solutions were stored over molecular sieves at −20°C.

Caution: Although we have not experienced any problems in handling the peroxidic oxidants used in this work, all safety precautions must be observed and practiced!

General Procedure for the m-CPBA Oxidations of the Furans **1a–h**: Following the Jennings'[9] procedure, to a stirred solution of furan **1** in 5 to 10 ml of CH_2Cl_2 at room temp. was added over a period of 1 to 2 min a solution of *m*-CPBA in CH_2Cl_2. A flocculent precipitate of *m*-chlorobenzoic acid formed within a few min. Stirring was continued for 0.5 to 7 h. The reaction mixture was washed with an aqueous $NaHCO_3$ solution (5 × 20 ml) and dried with $MgSO_4$. After removal of the solvent and NMR analysis of the crude product mixture, the oxidation products were isolated and purified by chromatography (silica gel) or bulb-to-bulb distillation; the details are described in the individual experiments.

2-Acetylphenyl Acetate (**6a**), *2-Acetyl-2-methyl-1,3-benzodioxole* (**8a**), *and Dispiro Compound* **9a**

a) By following the above procedure, 150 mg (1.03 mmol) of benzofuran **1a** was treated with 176 mg (1.03 mmol) of *m*-CPBA (1.0 equiv.) for 3 h. The crude product was purified by column chromatography (25 g silica gel; ether/pentane, 1:1) to afford 130 mg of **4a** and **4′a**, 5.0 mg of **6a**, 9.0 mg of **8a**, and 7.0 mg of **9a** in a total yield of 83%.

b) As above, 200 mg (1.37 mmol) of **1a** was treated with 638 mg (3.70 mmol) of *m*-CPBA (2.7 equiv.) for 5 h. The crude product

was purified by column chromatography (25 g silica gel; ether/pentane, 1:1) to afford 8.0 mg of **6a**, 43.0 mg of **8a**, and 141 mg of **9a** in a total yield of 79%. – The physical and spectral data of the oxidation products **4a/4'a**, **6a**, **8a**, and **9a** were identical to those reported[3a].

Dispiro Compound **9b**: According to the above procedure, 208 mg (1.00 mmol) of benzofuran **1b** was treated with 380 mg (2.20 mmol) of *m*-CPBA (2.2 equiv.) for 2 h. The crude product was purified by column chromatography (25 g silica gel; ether/pentane, 1:1) to afford 70.0 mg of the known **6b**[18] and 153 mg of **9b** as colorless needles from pentane, m.p. 244–245°C in a total yield of 93%. – **9b**: IR (KBr): $\tilde{\nu}$ = 3060 cm^{-1}, 2930, 1725, 1720, 1680, 1670, 1615, 1590, 1440, 1310, 1280, 1250, 1240, 1210, 1155, 1140, 1050, 965, 820, 760, 710, 690. – ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.78 (s, 3H), 1.79 (s, 3H), 3.10 (m, 2H), 3.58 (m, 2H), 6.03 (m, 2H), 6.58–6.77 (m, 2H), 7.40–7.63 (m, 6H), 8.02 (m, 4H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 16.9 (q), 17.0 (q), 34.8 (d), 39.2 (d), 39.4 (d), 52.9 (d), 66.0 (s), 66.6 (s), 72.4 (s), 73.2 (s), 128.6 (2 d), 128.7 (2 d), 128.8 (2 d), 129.1 (2 d), 130.1 (d), 132.3 (d), 132.8 (d), 133.5 (s), 133.7 (d), 133.8 (s), 134.0 (d), 145.8 (d), 191.2 (s), 195.5 (s), 195.6 (s), 201.3 (s). – $C_{30}H_{24}O_6$ (480.4): calcd. C 74.99, H 5.03; found C 75.23, H 4.95.

2-Acetoxybenzophenone (**6c**) *and 2-Acetyl-2-phenyl-1,3-benzodioxole* (**8c**)

a) Following the above procedure 150 mg (0.721 mmol) of benzofuran **1c** was treated with 125 mg (0.721 mmol) of *m*-CPBA (1.0 equiv.) for 5 h. The crude product was purified by column chromatography (20 g silica gel; ether/pentane, 1:3) to afford 14.0 mg of **6c** and 44.0 mg of **8c**, both as colorless oils, in a total yield of 67%, calculated on the basis of consumed *m*-CPBA.

b) As above, 150 mg (0.721 mmol) of **1c** was treated with 286 mg (1.73 mmol) of *m*-CPBA (2.3 equiv.) for 5 h. The crude product was purified by column chromatography (20 g silica gel; ether/pentane, 1:3) to afford 95.0 mg of **6c** and 35.0 mg of **8c**, both as colorless oils, in a total yield of 73%. – **6c**: IR (CCl_4): $\tilde{\nu}$ = 3040 cm^{-1}, 1790, 1755, 1750, 1645, 1580, 1465, 1430, 1355, 1280, 1255, 1180, 1090, 930, 900. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.95 (s, 3H), 7.23–7.82 (m, 9H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.4 (q), 123.2 (d), 125.6 (d), 128.3 (d), 129.7 (d), 130.5 (d), 131.4 (s), 132.2 (d), 133.0 (d), 137.5 (s), 148.6 (s), 169.1 (s), 194.8 (s). – $C_{15}H_{12}O_3$ (240.3): calcd. C 74.99, H 5.03; found C 74.88, H 4.68. – **8c**: IR (CCl_4): $\tilde{\nu}$ = 3040 cm^{-1}, 1720, 1615, 1470, 1435, 1350, 1225, 1060, 690. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 6.84–6.97 (m, 5H), 7.41–7.46 (m, 2H), 7.65–7.70 (m, 2H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 24.6 (q), 109.1 (d), 113.3 (s), 122.2 (d), 125.7 (d), 128.7 (s), 130.0 (d), 134.7 (s), 146.3 (s), 200.9 (s). – $C_{15}H_{12}O_3$ (240.3): calcd. C 74.99, H 5.03; found C 74.62, H 4.82.

2-Acetyl-5-methoxy-2-(4-methoxyphenyl)-1,3-benzodioxole (**8d**): According to the above procedure, 50.0 mg (0.187 mmol) of benzofuran **1d** was treated with 71.0 mg (0.410 mmol) of *m*-CPBA (2.2 equiv.) for 1 h. The crude product was purified by column chromatography (10 g silica gel; ether/pentane, 1:2) to afford 27.0 mg (48%) of the 1,3-dioxole **8d** as a colorless oil. – IR (CCl_4): $\tilde{\nu}$ = 2980 cm^{-1}, 2965, 2815, 1720, 1580, 1480, 1250, 1195, 1175, 1145, 835. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.28 (s, 3H), 3.72 (s, 3H), 3.81 (s, 3H), 6.34 (dd, J_1 = 8.6, J_2 = 2.6 Hz, 1H), 6.56 (d, J = 2.6 Hz, 1H), 6.84 (d, J = 8.6 Hz, 1H), 6.93 (dd, J_1 = 6.8, J_2 = 2.1 Hz, 2H), 7.53 (dd, J_1 = 6.8, J_2 = 2.1 Hz, 2H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 24.4 (q), 55.3 (q), 55.9 (q), 97.6 (d), 105.4 (d), 108.4 (d), 114.1 (2 d), 114.2 (s), 114.3 (d), 126.6 (s), 127.2 (2 d), 134.3 (s), 140.5 (s), 147.1 (s), 155.5 (s), 160.9 (s), 201.4 (s). – $C_{17}H_{16}O_5$ (300.3): calcd. C 67.98, H 5.37; found C 67.72, H 5.62.

Tetraspiro Compound **9e**: According to the above procedure, 172 mg (1.00 mmol) of benzofuran **1e** was treated with 403 mg (2.40 mmol) of *m*-CPBA (2.4 equiv.) for 6 h. The crude product was purified by column chromatography (20 g silica gel; ether/pentane, 1:2) to afford 190 mg (93%) of **9e** as a colorless powder, m.p. 194–195°C from dichloromethane/pentane. – IR (KBr): $\tilde{\nu}$ = 3060 cm^{-1}, 2930, 1725, 1720, 1680, 1670, 1615, 1590, 1440, 1310, 1280, 1250, 1240, 1210, 1155, 1140, 1050, 965, 820, 760, 710, 690. – ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.50–1.80 (m, 5H), 1.80–2.13 (m, 9H), 2.56 (m, 2H), 2.97 (m, 1H), 3.10 (m, 1H), 3.58 (m, 2H), 6.20 (m, 2H), 6.58–6.65 (m, 2H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 24.1 (t), 24.4 (t), 27.0 (t), 27.2 (t), 31.3 (t), 32.5 (t), 34.5 (d), 38.9 (t), 39.2 (t), 42.6 (d), 42.7 (d), 53.0 (d), 65.9 (s), 68.0 (s), 74.1 (s), 74.9 (s), 130.0 (d), 132.3 (d), 133.7 (d), 144.6 (d), 190.3 (s), 200.7 (s), 201.8 (s), 202.6 (s). – $C_{24}H_{24}O_6$ (408.4): calcd. C 70.57, H 5.91; found C 70.42, H 5.99.

Spiro[benzofuran-3(2H),1'-cyclopentan]-2-one (**12e**): To a cold (–78°C) solution of 100 mg (0.581 mmol) of benzofuran **1e** in 2 ml of anhydrous CH_2Cl_2 were rapidly added while stirring under N_2 13.0 ml (0.720 mmol) of a cold (–78°C) solution of dimethyldioxirane in acetone (0.054 M). The stirring was continued for 3 h until complete consumption of **1e** (monitored by TLC), while the reaction temperature was allowed to rise to –20°C. The solvent was evaporated (–20°C/0.01 Torr, 1–2 h) and the crude product spectrally examined at –20°C, which confirmed the presence of **12e**. After column chromatography (5 g of silica gel, ether), **12e** (73.0 mg, 67%) was obtained as a colorless oil. – IR (CCl_4): $\tilde{\nu}$ = 2955 cm^{-1}, 2860, 1800, 1610, 1470, 1455, 1230, 1190, 1115, 1045, 1035, 970, 875. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.95–2.39 (m, 8H), 7.07–7.28 (m, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.4 (2 t), 39.7 (2 t), 52.0 (s), 110.4 (d), 122.6 (d), 124.4 (d), 128.2 (d), 134.3 (s), 152.4 (s), 181.8 (s). – $C_{12}H_{12}O_2$ (188.3): calcd. C 76.57, H 6.43; found C 76.32, H 6.55.

4,6-Diacetyl-3-(3-chlorobenzoyldioxy)-2,3-dihydro-2,3-dimethylbenzofuran-2-ol (**5f**): According to the above procedure, 100 mg (0.435 mmol) of benzofuran **1f** was treated with 187 mg (1.09 mmol) of *m*-CPBA (2.5 equiv.) for 7 h. The crude product was purified by column chromatography (5 g of alumina; ether/pentane, 1:2) to afford 62.0 mg (54%) of an 82:18 tautomeric mixture of **5f** (d.r. 78:22) and **5'f** as a colorless powder, m.p. ca. 65°C (dec.). – ^1H NMR (200 MHz, $CDCl_3$): major diastereomer of **5f**: δ = 1.77 (s, 3H), 1.85 (s, 3H), 2.54 (s, 3H), 2.61 (s, 3H), 7.33–7.51 (m, 5H), 7.91–7.99 (m, 2H). – Minor diastereomer of **5f** and its tautomer **5'f**: δ = 1.42 (s, 3H), 1.71 (s, 3H), 1.90 (s, 3H), 2.12 (s, 3H), 2.44 (s, 3H), 2.54 (s, 3H), 2.58 (s, 3H), 2.65 (s, 3H), 7.33–7.51 (m, 10H), 7.91–7.99 (m, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$): major diastereomer of **5f**: δ = 20.8 (q), 23.1 (q), 26.7 (q), 28.5 (q), 88.5 (s), 111.4 (s), 115.5 (d), 122.7 (d), 127.2 (d), 128.2 (d), 129.7 (d), 130.1 (d), 131.0 (s), 131.2 (s), 133.6 (d), 138.6 (s), 156.4 (s), 166.4 (s), 166.8 (s), 196.7 (s), 198.8 (s). – Minor diastereomer of **5f** and its tautomer **5'f**: δ = 15.2 (q), 18.9 (q), 23.1 (q), 26.2 (q), 26.4 (q), 27.0 (q), 29.7 (q), 30.4 (q), 81.8 (s), 89.3 (s), 110.7 (d), 111.9 (s), 113.6 (d), 120.8 (d), 124.4 (d), 126.4 (d), 126.8 (d), 127.5 (d), 128.5 (d), 129.3 (d), 131.8 (s), 132.0 (s), 132.1 (s), 132.4 (s), 132.6 (d), 132.9 (s), 133.5 (d), 133.7 (d), 138.8 (s), 139.1 (s), 157.5 (s), 158.9 (s), 167.3 (s), 169.4 (s), 194.1 (s), 196.0 (s), 199.3 (s), 199.9 (s); four singlets are superposed. – Iodometry gave 92% peroxide content.

2,3,5-Triacetylphenyl Acetate (**6f**): A solution of 50.0 mg (0.120 mmol) of the 82:18 tautomeric mixture of **5f** and **5'f** in 1 ml of $CDCl_3$ was stored at room temp. for 7 d until negative peroxide test (KI, HOAc). After column chromatography (3 g of silica gel, ethyl ether/dichloromethane, 1:1) was obtained ester **6f** (21 mg,

68%) as a pale yellow oil. – IR (CCl_4): $\tilde{\nu}$ = 2980 cm^{-1}, 2900, 1750, 1670, 1585, 1445, 1405, 1350, 1295, 1230, 1220, 1185, 1010, 960. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.30 (s, 3H), 2.47 (s, 3H), 2.64 (s, 3H), 2.66 (s, 3H), 7.89 (d, *J* = 1.4 Hz, 1H), 8.31 (d, *J* = 1.4 Hz, 1H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.7 (q), 26.7 (q), 27.1 (q), 30.9 (q), 126.4 (d), 127.6 (d), 136.5 (s), 138.0 (s), 139.7 (s), 147.2 (s), 168.6 (s), 195.4 (s), 197.0 (s), 201.2 (s). – $C_{14}H_{14}O_5$ (262.3): calcd. C 64.10, H 5.38; found C 63.83, H 5.25.

2-Acetyl-2,6,6-trimethyl-1-oxaspiro[2.5]octane-4,8-dione (**7g**): According to the above procedure, 150 mg (0.781 mmol) of benzofuran **1g** was treated with 309 mg (1.80 mmol) of *m*-CPBA (2.3 equiv.) for 1 h. The crude product was purified by bulb-to-bulb distillation to afford 103 mg (59%) of **7g** as colorless needles from ether, m.p. 51–53°C. – IR (KBr): $\tilde{\nu}$ = 2940 cm^{-1}, 2900, 1730, 1700, 1410, 1355, 1210, 1120, 1070. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.99 (s, 3H), 1.23 (s, 3H), 1.42 (s, 3H), 2.30 (s, 3H), 2.62–2.81 (m, 4H). – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 13.1 (q), 26.7 (q), 27.4 (q), 30.0 (q), 31.0 (s), 54.6 (t), 54.8 (t), 72.8 (s), 73.7 (s), 199.3 (s), 200.3 (s), 205.0 (s). – $C_{12}H_{16}O_4$ (224.3): calcd. C 64.26, H 7.19; found C 64.39, H 7.11.

2-Acetyl-1-oxaspiro[2.5]octan-4-one (**7h**): According to the above procedure, 150 mg (1.10 mmol) of benzofuran **1h** was treated with 400 mg (2.32 mmol) of *m*-CPBA (2.1 equiv.) for 0.5 h in $CDCl_3$ to afford a 62:22:16 mixture of **6h**, **7h**, and **10h**. During the attempt to separate the product mixture, the spiro epoxide **7h** decomposed. A 77:23 mixture of **6h**[9] and **10h**[9] (114 mg) was isolated by bulb-to-bulb distillation in 61% yield. – ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.49–1.54 (m, 4H), 1.67–1.71 (m, 2H), 2.13 (s, 3H), 2.32–2.35 (m, 2H), 3.40 (s, 1H). – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 23.8 (t), 25.4 (t), 27.6 (q), 34.8 (t), 42.4 (t), 66.2 (d), 67.0 (s), 203.9 (s), 204.0 (s). – Due to the labile nature of **7h**, it was not possible to obtain a satisfactory elemental analysis.

2a,7b-Dihydro-2a-methyl-7b-phenyl-1,2-dioxeto[3,4-b]benzofuran (**11c**): Into a 20-ml test tube, equipped with gas inlet and outlet tubes, was placed a solution of benzofuran **1c** (208 mg, 1.00 mmol) and 5 mg of tetraphenylporphine in 5 ml of metal-free dichloromethane. The solution was cooled to −20°C by means of an ethanol bath, cooled by a MGW Lauda Cryomat. A gentle stream of dry O_2 gas was allowed to pass through the reaction mixture 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 (0°C/18 Torr) and the residue chromatographed on 15 g silica gel (60–239 mesh) at −30°C to yield dioxetane **11c** (187 mg, 78%) as a pale yellow oil. – IR (CCl_4): $\tilde{\nu}$ = 3020 cm^{-1}, 3110, 3000, 1640, 1495, 1410, 1345, 1295, 1170, 1120, 1000, 860. – ^1H NMR (400 MHz, $CDCl_3$): δ = 1.64 (s, 3H), 7.19–7.56 (m, 9H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.7 (q), 97.8 (s), 111.4 (d), 119.2 (s), 122.8 (d), 125.8 (d), 127.0 (d), 127.6 (d), 128.5 (d), 129.3 (d), 132.1 (d), 133.2 (s), 161.3 (s). – $C_{15}H_{12}O_3$ (240.3): calcd. C 74.99, H 5.03; found C 74.72, H 4.90.

3,4,5,6-Tetrahydro-1-benzoxonine-2,7-dione (**6e**) *and 2a,7b-Butano-1,2-dioxeto[3,4-b]benzofuran* (**11e**): According to the above procedure, 100 mg (0.876 mmol) of benzofuran **1e** was photooxygenated in 10 ml dichloromethane for 1.5 h at −20°C. The solvent was removed by distillation (20°C/0.1 Torr) and the residue chromatographed (15 g silica gel, ether/pentane, 1:2) to give 92.0 mg (87%) of the cleavage product **6e** as colorless plates, m.p. 58–60°C. – IR (CCl_4): $\tilde{\nu}$ = 3060 cm^{-1}, 2940, 2860, 1765, 1685, 1600, 1450, 1270, 1190, 1120, 1100, 1020. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.03 (m, 4H), 2.64 (t, *J* = 6.0 Hz, 2H), 2.81 (t, *J* = 6.1 Hz, 2H), 7.20–7.34 (m, 2H), 7.53–7.68 (m, 2H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.7 (t), 25.0 (t), 33.7 (t), 41.6 (t), 123.3 (d), 126.5 (d), 128.7 (d), 132.6 (d), 134.0 (s), 149.5 (s), 172.1 (s), 203.7 (s). – $C_{12}H_{12}O_3$ (204.3): calcd. C 70.57, H 5.91; found C 70.34, H 5.80.

On repetition of the above experiment in $CDCl_3$ at −50°C the dioxetane **11e** was detected by NMR spectroscopy: ^1H NMR (200 MHz, $CDCl_3$, −40°C): δ = 1.45–1.63 (m, 4H), 1.80–2.14 (m, 4H), 6.98 (m, 2H), 7.40 (m, 2H). – ^{13}C-NMR (50 MHz, $CDCl_3$, −40°C): δ = 19.2 (t), 19.4 (t), 29.9 (t), 31.2 (t), 92.5 (s), 111.5 (d), 119.7 (s), 122.5 (d), 123.9 (d), 134.4 (d), 141.6 (s), 160.8 (s). – In view of its thermal lability, it was not possible to obtain a satisfactory elemental analysis of **11e**.

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